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Cycloaddition between Electron-Deficient π-Systems, Photochemical and Radical-Induced Reactions: A Novel, General, and Stereoselective Route to Polyfunctionalized Bridged Bicyclo[2.2.2]octanes, Bicyclo[3.3.0]octanes, Bicyclo[4.2.0]octanes, and Tricyclo[4.3.1.0^{3,7}]decanes

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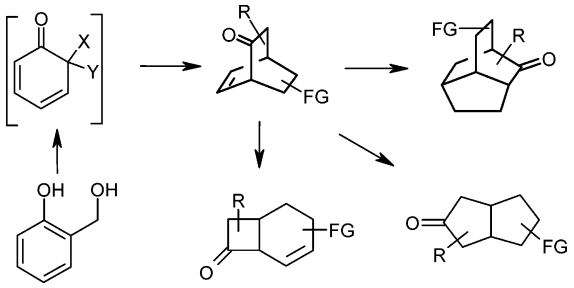

A novel, general, and stereoselective route to functionalized bridged bicyclo[2.2.2]octanes, bicyclo[3.3.0]-octanes, bicyclo[4.2.0]octanes, and tricyclo[4.3.1.0^{3,7}]decanes has been described. Various functionalized and sustituted bicyclo[2.2.2]octanes endowed with a β,γ-enone chromophore were synthesized via cycloaddition of in situ generated cyclohexa-2,4-dienones with electron-deficient 2π partners and manipulation of the resulting adducts. Triplet sensitized irradiation of bridged bicyclooctenones led to synthesis of bicyclo[3.3.0]octanoids, whereas the direct irradiation furnished bicyclo[4.2.0]octanes in stereoselective fashion as a result of modulation of reactivity in excited states. Further, manipulation of the adducts led to appropriately appended and functionalized bicyclo[2.2.2]octanes that upon radical induced cyclization provided an efficient and stereoselective route to the tricyclo[4.3.1.0^{3,7}]decane (isotwistane) framework of pupukeananes.

Introduction

There has been a continuing interest in the chemistry of functionalized bicyclo[3.3.0]octanes of type **1** (Figure 1). This is because of their versatile role as building blocks for the synthesis of both natural and unnatural biologically active compounds such as carbacyclins **2**,[1] alkaloids,[2] and cyclopentanoidal natural products.[3−6] Further, bicyclo[3.3.0]octanoids have also served as precursors for the synthesis of theoretically interesting systems and compounds for various properties.[7,8] Moreover, the isolation of many new natural products that

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(1) (a) Newton, R. F.; Roberts, S. M.; Taylor, R. J. K. *Synthesis* **1984**, 449−478. (b) Schinzer, D. *Carbacyclins*: *Stable* Analogues of Prostacyclins. In *Organic Synthesis High Lights II*; Waldman, H., Ed.; VCH: New York, 1995; p 301. (c) Bund, J.; Gais, H.-J.; Schmitz, E.; Erdelmier, I.; Raabe, G. *Eur. J. Org. Chem.* **1998**, 1319−1335. (d) Okamoto, S.; Subburaj, K.; Sato, F. *J. Am. Chem. Soc.* **2000**, *122*, 11244−11245.

(2) (a) Leonard, J.; Quali, D.; Ratman, S. K. *Tetrahedron Lett.* **1990**, *31*, 739−742. (b) Vidari, G.; Tripolini, M.; Novella, P.; Allegrucci, P.; Garlaschelli, L. *Tetrahedron*: *Assymmetry* **1997**, *8*, 2893−2903.

(3) (a) Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry*; Hafner, K., Rees, C. W., Trost, B. M., Lehn, J.-M., Schleyer, P. v. R., Zahradnik, R., Eds.; Springer-Verlag: Berlin, Germany, 1987; Vol. 26. (b) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997**, *97*, 671−719.

(4) (a) Little, R. D. *Chem. Rev.* **1996**, *96*, 93−114 and references therein. (b) Wender, P. A.; Dore, T. M. CRC *Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Song, P.-S., Eds.; CRC Press: Boca Raton, FL, 1995; pp 280−300. (c) Fu, X.; Cook, J. M. *Aldrichimica Acta* **1992**, *25*, 43−55.

(5) (a) Rawal, V. H.; Reddy, J. *Org. Lett.* **2000**, *2*, 2711−2712. (b) Dvorak, C. A.; Dufour, C.; Iwasa, S.; Rawal, V. H. *J. Org. Chem.* **1998**, *63*, 5302−5303. (c) Dvorak, C. A.; Rawal, V. H. *J. Chem. Soc., Chem. Commun.* **1997**, 2381−2382.

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contain an embellished bicyclo[3.3.0]octane scaffold in their molecular architecture[9,10] has further enhanced the interest in the synthesis of functionalized bicyclo[3.3.0]octanoids.[11,12]

The bicyclo[4.2.0]octane framework of type **3** has also generated significant interest recently.[13−15] This is presumably due to its potential for transformation into other carbocyclic systems.[16] The presence of the bicyclo[4.2.0]octane ring system in endiandric acids of type **4**,[17] many terpenoids,[18] and other recently isolated natural products[15] has further enhanced the interest in this ring system.

The synthesis of the functionalized tricyclo[4.3.1.0^{3,7}]decane ring system **5**, present in the framework of a unique class of natural products known as pupukeananes **6** and **7**,[19] has also generated significant interest recently.[20,21]

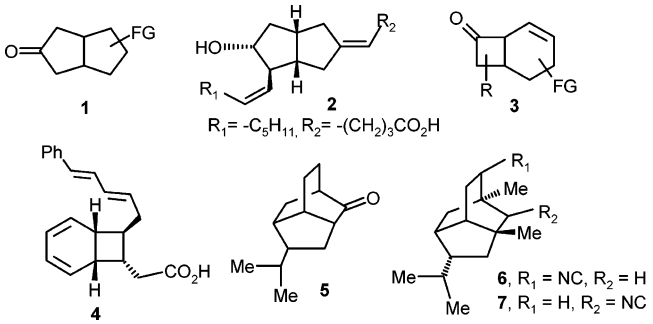


FIGURE 1. Structures of carbacyclin, endiandric acid, pupukeananes, and related molecular frameworks.

While, a number of methods have been developed for the synthesis of bicyclo[3.3.0]octanoids, most methods have limitations regarding the introduction of functionality, and the search for new methods is continuing.[9,10] On the other hand, there are only a few methods for the synthesis of bicyclo[4.2.0]octane ring systems. A majority of the methods employ a π2s+π2s photocycloaddition of olefins[22a−c] and π2s+π2a thermal cycloaddition of keteimines/ketenes to create the four-membered ring.[22d] Similarly, only a few methods are available for the synthesis of the tricyclo[4.3.1.0^{3,7}] decane (isotwistane) framework, the majority of which employ cycloaddition of cyclic dienes with ketene equivalents for the generation of the bridged bicyclo[2.2.2]octane ring system.

In view of the above we thought to devise a general stereoselective methodology that permits introduction of appendages and functional groups on the bicyclo[3.3.0]octanoids, bicyclo[4.2.0]octanoids, and tricyclo[4.3.1.0^{3,7}]decane ring systems. It was contemplated that functionalized carbocyclic systems of type **8**, **9**, and the isotwistane framework **11** may be obtained from a common precursor of type **6**. We thought that a 1,3-acyl shift in **6** would furnish the bicyclo[4.2.0]octanones of type **9** in a single stereoselective step. The bicyclo[3.3.0]-octanes of type **8** were considered to be readily derived from **6** via the tricyclic compound **7** that may be obtained by a 1,2-acyl shift (or oxa-di-π-methane rearrangement) in **6** (Scheme 1). It was further thought that tricyclo[4.3.1.0^{3,7}]decane ring systems of type **11** can also be generated via radical induced cyclization in a suitably designed precursor of type **10**, which

(6) (a) Paquette, L. A.; Doyon, J. *J. Am. Chem. Soc*. **1995**, *117*, 6799−6800. (b) Varma, S. K.; Eleisher, E. B.; Moore, H. W. *J. Org. Chem.* **2000**, *65*, 8564−8573. (c) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059−4071. (d) Enholm, E. J.; Jia, Z. J. *J. Chem. Soc., Chem. Commun.* **1996**, 1567−68.

(7) (a) Ayala, C.; Camps, P.; Duque, M. D.; Font-Bordia, M.; Munoj, M. R.; Solans, X.; Vazquez, S. *J. Org. Chem.* **2003**, *68*, 8715−8718. (b) Cadieux, J. A.; Buller, D. J.; Wilson, P. D. *Org. Lett.* **2003**, *5*, 3983−3988.

(8) (a) Ochiai, H.; Ohtani, T.; Ishida, A.; Kishikawa, K.; Yamamoto, S.; Takeda, H.; Obata, T.; Nakai, H.; Toda, M. *J. Med. Chem.* **2004**, *39*, 555−571. (b) Zhong, Y. W.; Tian, P.; Lin, G. Q. *Tetrahedron*: *Assymmetry* **2004**, *15*, 771−778.

(9) Iliopoulou, D.; Mihopoulos, N.; Vagias, C.; Papazafiri, P.; Roussis, V. *J. Org. Chem.* **2003**, *68*, 7667−7674.

(10) (a) Taglialatela-Scafati, O.; Craig, K. S.; Reberioux, D.; Roberge, M.; Anderson, R. J. *Eur. J. Org. Chem.* **2003**, 3515−3523. (b) Kanazawa, S.; Fusetani, N.; Matsunaga, S. *Tetrahedron Lett.* **1993**, *34*, 1065−1068. (c) Iwasima, M.; Terada, I.; Okamoto, K.; Iguchi, K. *J. Org. Chem.* **2002**, *67*, 2977−2981.

(11) (a) Williams, D. R.; Reeves, J. T. *J. Am. Chem. Soc.* **2004**, *126*, 3434−3435. (b) Bernard, H.; Newton, L. S.; Cabral, S.; Walker, A. J.; Bordner, J. *Org. Lett*. **2004**, *6*, 4343−4345. (c) Subburaj, K.; Okamoto, S.; Sato, F. *J. Org. Chem.* **2002**, *67*, 1024−1026. (d) Ito, H.; Hasegawa, M.; Takenaka, Y.; Kobayashi, T.; Iguchi, K. *J. Am. Chem. Soc*. **2004**, *126*, 4520−4521. (e) Cramer, N.; Laschat, S.; Baro, A.; Schwalbe, H.; Richter, C. *Angew. Chem.* **2005**, *44*, 820−822.

(12) (a) Harmata, M.; Wacharasindhu, S. *Org. Lett.* **2005**, *7*, 2563−65. (b) Wang, J. C.; Krische, M. J. *Angew. Chem., Int. Ed.* **2003**, *43*, 5855−5857. (c) Kitagawa, O.; Yamada, Y.; Sugawara, A.; Taguchi, T. *Org. Lett.* **2002**, *4*, 1011−13. (d) Hodgson, D. M.; Cameron, I. D. *Org. Lett.* **2001**, *3*, 441−444.

(13) (a) Loughlin, W. A.; Rowen, C. C.; Healy, P. C. *J. Org. Chem.* **2004**, *69*, 5690−5698. (b) Inanaga, K.; Takasu, K.; Ihara, M. *J. Am. Chem. Soc.* **2004**, *126*, 1352−1353. (c) Tsutsumi, K.; Nakano, H.; Furutani, A.; Endou, K.; Merpuge, A.; Shintani, T.; Morimoto, T.; Kakiuchi, K. *J. Org. Chem.* **2004**, *69*, 785−789. (d) Kara, Y.; Balci, M. *Tetrahedron* **2003**, *59*, 2063−2066. (e) Mahuteau-Betzer, F.; Ghosez, L. *Tetrahedron*, **2002**, *58*, 6991−7000. (f) Loughlin, W. A.; Rowen, C. C.; Healy, P. C. *J. Chem. Soc., Perkin Trans* 2, **2002**, 296−302. (g) Bolm, C.; Beckman, O.; Palazzi, C. *Can. J. Chem.* **2001**, *79*, 1593−97. (h) Witte, B.; Meyer, L.; Margretha, P. *Helv. Chim. Acta* **2000**, *83*, 554−561.

(14) (a) Shim, P.-J.; Kim, H.-D. *Tetrahedron Lett*. **1998**, *39*, 9517−9520. (b) DeGiacomo, M.; Bettolo, R. M.; Scarpelli, R. *Tetrahedron Lett.* **1997**, *38*, 3469−3470.

(15) (a) Barbarow, J. E.; Miller, A. K.; Trauner, D. *Org. Lett.* **2005**, *7*, 2901−2903. (b) Ready, J. M.; Reisman, S. E.; Hirata, M.; Weiss, M. M.; Tamaki, K.; Ovaska, T. V.; Wood, J. L. *Angew. Chem., Int. Ed.* **2004**, *43*, 1270−1272. (c) Deng, H. B.; Konopelski, J. P. *Org. Lett.* **2001**, *3*, 3001−3004. (d) Jung, M. E.; Slowinski *Tetrahedron Lett.* **2001**, *42*, 6835−38. (e) Lopez-Alvarado, P.; Garcia-granda, S.; Alvarez-Rua, C.; Avendano, C. *Eur. J. Org. Chem.* **2002**, 1702−1707. (f) Cueto, M.; D'Croz, L.; Mate, J. L.; San-martin, A.; Darias, J. *Org. Lett*. **2005**, *7*, 415−418. (g) Jimenez, J. I.; Huber, U.; Moore, R. E.; Patterson, G. M. L. *J. Nat. Prod.* **1999**, *62*, 569−572.

(16) Namyslo, J. C.; Kaufman, D. E. *Chem. Rev.* **2003**, *103*, 1485−1537.

(17) Nicolaou, K. C.; Sorenson, E. J. In *Classics in Total Synthesis*; VCH: Weinheim, Germany, 1996; pp 265−283 and references therein.

(18) (a) Harmata, M.; Bohnert, G. J. *Org. Lett.* **2003**, *5*, 59−61. (b) Ishi, S.; Zhao, S.; Mehta, G.; Knors, C. J.; Helquist, P. *J. Org. Chem.* **2001**, *66*, 3449−3458 and references therein. (c) Fraga, B. M. *Nat. Prod. Rep.* **2003**, *20*, 392−413. (d) Banwell, M. G.; Harfoot, G. J. *Aust. J. Chem.* **2004**, *57*, 895−897. (e) Dhimane, A.-L.; Malacria, M. In *Strategies and Tactics in Organic Synthesis*; Harmata, M., Ed.; Elsevier: New York, 2004; Vol. 5, pp 153−181.

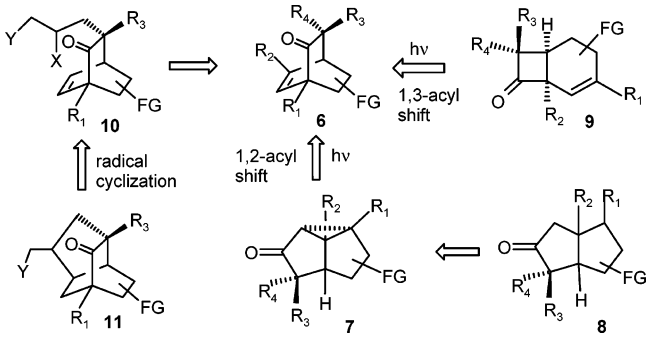
(19) (a) Burreson, B. J.; Scheuer, P. J.; Finer, J.; Clardy, J. *J. Am. Chem. Soc*. **1975**, *97*, 4763−4764. (b) Hagadone, M. R.; Burreson, B. J.; Scheuer, P. J.; Finer, J.; Clardy, J. *Helv. Chim. Acta* **1979**, *62*, 2484−2494.

(20) (a) Takasu, K.; Mizutani, S.; Ihara, M. *J. Org. Chem*. **2002**, *67*, 2881−2884. (b) Srikrishna, A.; Ravi Kumar, P. *Tetrahedron Lett.* **2002**, *43*, 1109−1111. (c) Biju, P. J.; Kalliappan, K.; Laxmisha, M. S.; Subbaarao, G. S. R. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3714−3718. (d) Srikrishna, A.; Reddy, T. J. *J. Chem.. Soc., Perkin Trans. 1* **1998**, 2137−2144. (e) Kalliappan, K.; Subbarao, G. S. R. *J. Chem. Soc., Perkin Trans. 1* **1997**, 3387−3392 and references therein. (f) Chang, N. C.; Chang, C. K. *J. Org. Chem.* **1996**, *61*, 4967−4970.

(21) (a) Heish, S. L.; Chiu, C. T.; Chang, N. C. *J. Org. Chem*. **1989**, *54*, 3820−3823. (b) Piers, E.; Winter, M. *Justus Leibig Ann. Chem*. **1982**, 973−984. (c) Schiesher, G. A.; White A. D. *J. Org. Chem*. **1980**, *45*, 1864−1868. (d) Yamamoto, H.; Sham, H. L. *J. Am. Chem. Soc*. **1979**, *101*, 1609−1611. (e) Corey, E. J.; Behforouz, M.; Ishiguro, M. *J. Am. Chem. Soc*. **1979**, *101*, 1608−1609.

(22) (a) Crimmins, M. T.; Reinhold, T. L. In *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons: New York, 1993; Vol. 44, pp 297−588. (b) Winkler, J. D.; Bowen, C.; Liotta, F. *Chem. Rev.* **1995**, *95*, 2003−2020. (c) Bach, T. *Synthesis* **1998**, 683−703. (d) Snider, B. B. *Chem. Rev.* **1988**, *88*, 793−811.

SCHEME 1



may be easily derived from the bridged bicyclic compound of type **6** containing the appropriate appendage.

We wish to report herein the development of a novel stereoselective methodology for the synthesis of polyfunctionalized bicyclo[2.2.2]octenones of type **6** and their photochemical transformations leading to an efficient route to highly functionalized bicyclo[3.3.0]octanes and bicyclo[4.2.0]octanes from simple precursors. We also report the synthesis and radical induced cyclization in suitably designed bicyclo[2.2.2]octaenones leading to an isotwistane framework of type **11**.[23]

Results and Discussion

Synthesis of Bicyclo[2.2.2]octenones: Cycloaddition between Electron-Deficient π-Partners. While there seems to be no general method for the synthesis of functionalized and substituted bicyclic compounds such as **6**, simple bicyclo[2.2.2]-octenones are prepared by the cycloaddition of cyclic 1,3-dienes with ketene equivalents followed by transformation of adducts.[24] Recently, some new methods have been developed for the synthesis of bicyclo[2.2.2]octenones.[25,26] However, there are limitations with respect to the introduction of functional groups and they often give regio- and stereoisomeric mixtures.

Although cyclohexadienones have been known for long time, their synthetic potential has been realized only recently.[26,27] In principle, the compounds such as **6** should be accessible via the cycloaddition of cyclohexa-2,4-dienones of type **12a**,**b**

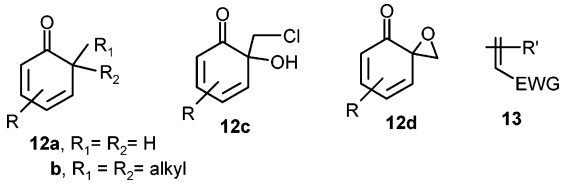
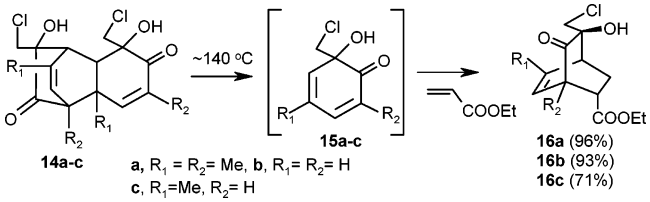


FIGURE 2. Various types of cyclohexa-2,4-dienones and the electron-deficient 2π-system.

SCHEME 2



(Figure 2) with the functionalized 2π-partners. While the parent cyclohexa-2,4-dienones **12a** are not easily obtainable, the preparation of α,α-disubstituted cyclohexadienones such as **12b** via alkylation of phenols[28] and the method developed by Schultz and co-workers[29] appeared to be difficult and unsuitable for our purpose.

Hence, we considered developing an indirect method for the synthesis of bicyclic compounds of type **6** via cycloaddition of cyclohexadienones of type **12c** and or **12d** with electron-deficient 2π-partners such as **13** followed by manipulation of the resulting adducts. However, we were aware that the Diels–Alder reaction, in general, occurs either between electron-rich diene and electron-poor dienophile or electron-poor diene and electron-rich dienophile (inverse electron demand) or neutral dienes and dienophiles.[30] Cycloadditions between electron-deficient partners are observed only rarely.[26a,b]

Thus, the chlorohydroxydimer **14a**, readily prepared from 2-hydroxymethyl-4,6-dimethylphenol following a literature procedure,[31] was heated in the presence of acrolein with a view to generate and intercept the cyclohexadienone **15a**. However, it gave a complex mixture of products. Therefore, generation of **15a** by pyrolysis of **14a** and interception with ethyl acrylate was attempted. Thus, a mixture of the dimer **14a** and ethyl acrylate in *o*-dichlorobenzene was heated in a sealed tube at 140 °C, which gave a crystalline adduct **16a** as the sole product in excellent yield (96%) (Scheme 2). The structure of the adduct **16a** was deduced from its spectral features and further confirmed by X-ray crystal structure.[23]

Similarly, pyrolysis of the dimers **14b**,**c** in the presence of ethyl acrylate gave the adducts **16b** and **16c**, respectively in excellent yields (Scheme 2). The structure of adducts was deduced from their spectral data, COSY analysis, and comparison with the spectral features of **16a**.

(23) A part of the work is described in a preliminary communication. Singh, V.; Pal, S.; Mobin, S. M. *J. Chem. Soc., Chem. Commun.* **2002**, 2050−51.

(24) (a) Evans, D. A.; Scott, W. L.; Truesdale, L. K. *Tetrahedron Lett.* **1972**, *13*, 121−124. (b) Evans, D. A.; Scott, W. L.; Truesdale, L. K. *Tetrahedron Lett.* **1972**, *13*, 137−140. (c) Banwell, M. G.; Dupuche, J. R. *J. Chem. Soc., Chem. Commun.* **1996**, 869−870.

(25) (a) Jung, M. E.; Maderna, A. *Tetrahedron Lett.* **2005**, *46*, 5057−5061. (b) Paquette, L. A.; Guevel, R.; Sakamoto, S.; Kim, I. H.; Crawford, J. *J. Org. Chem.* **2003**, *68*, 6096−6107. (c) Hagiwara, H.; Endou, S.; Fukushima, M.; Hoshi, T.; Suzuki, T. *Org. Lett.* **2004**, *6*, 1115−1118. (d) Ihara, M.; Fukumoto, K. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1010−1022. (e) Jung, M. E.; McCombs, C. A.; Takeda, Y.; Pan, Y.-G. *J. Am. Chem. Soc.* **1981**, *103*, 6677−6685. (f) Ley, S. V.; Mynett, D. M.; Koot, W. J. *Synlett* **1995**, *10*, 1017−1020.

(26) (a) Magdziak, D.; Meek, S. J.; Pettus, T. R. R. *Chem. Rev.* **2004**, *104*, 1383−1429 and references therein. (b) Quideau, S.; Pouysegu, L. *Org. Prep. Proc. Int.* **1999**, *31*, 617−680 and references therein. (c) Liao, C. C.; Peddinti, R. K. *Acc. Chem. Res.* **2002**, *35*, 856−866. (d) Singh, V. *Acc. Chem. Res.* **1999**, *32*, 324−333.

(27) (a) Drutu, I.; Najardson, J. T.; Wood, J. L. *Org. Lett.* **2002**, *4*, 493−496 (b) Wood, J. L.; Graeber, J. K.; Njardarson, J. T. *Tetrahedron* **2003**, *59*, 8855−8858. (c) Quideau, S.; Lebon, M.; Lamidey, A.-M. *Org. Lett.* **2002**, *4*, 3975−3978. (d) Yen, C.-F.; Liao, C. C. *Angew. Chem., Int Ed.* **2002**, *41*, 4090−4093. (e) Sutherland, H. S.; Higgs, K. C.; Taylor, N. J.; Rodrigo, R. *Tetrahedron* **2001**, *57*, 309−317. (f) Bonnarme, V.; Bachmann, C.; Cousson, A.; Mondon, M.; Gesson, J.-P. *Tetrahedron* **1999**, *55*, 433−448.

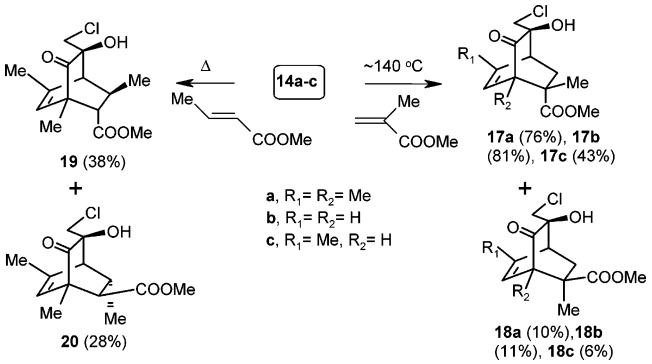
(28) (a) Miller, B. *J. Org. Chem.* **1970**, *35*, 4262−4264. (b) Miller, B. *J. Am. Chem. Soc.* **1965**, *87*, 5115−5120.

(29) Schultz, A. G.; Dittami, J. P.; Lavieri, F. P.; Saloway, C.; Sundararaman, P.; Szymula, M. B. *J. Org. Chem.* **1984**, *49*, 4429−4440.

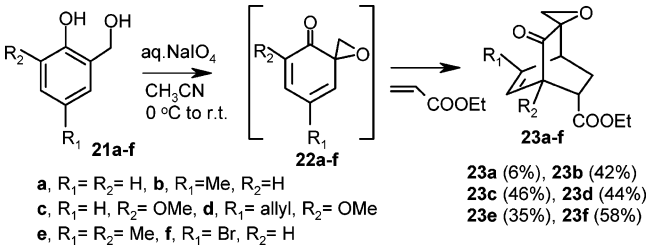
(30) (a) Nicolaou, K. C.; Snyder, S. A. In *Classics in Total Synthesis II*; Wiley-VCH: Wienheim, Germany, 2003; pp 16−30. (b) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668−1698. (c) Flemming, I. *Frontier Orbitals and Organic Chemical Reactions*; John Wiley and Sons: Chichester, UK, 1978. (d) Woodward, R. B.; Hoffman, R. *Conservation of Orbital Symmetry*; Academic Press: New York, 1972.

(31) (a) Adler, E.; Holmberg, K. *Acta Chem. Scand.* **1974**, *28B*, 465−472. (b) Singh, V.; Bedekar, A. V. *Synth. Commun.* **1989**, *19*, 107−117.

SCHEME 3



SCHEME 4

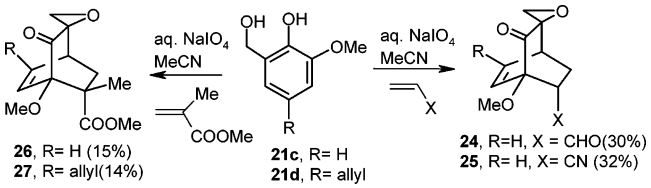


To extend the scope and examine the generality of the aforementioned cycloaddition, in situ generation of cyclohexa-2,4-dienones **15a**−**c** and their interception with other dienophiles such as methyl methacrylate and methyl crotonate was also explored. Thus, heating of the dimer **14a** with methyl methacrylate followed by chromatography of the product mixture afforded the *endo* adduct **17a** along with a minor amount of the *exo* adduct **18a**. Similarly, pyrolysis of **14b**,**c** in the presence of methyl methacrylate furnished *endo* adducts **17b**,**c** and *exo* adducts **18b**,**c** respectively, *endo* being the major products. Remarkably, methyl crotonate also reacted smoothly with the cyclohexa-2,4-dienone **15a**, and gave the adducts **19** and **20** in good yield (Scheme 3). The structures of adducts were deduced from their spectral data. The stereochemical structure **18a** for the *exo* adduct was confirmed through single-crystal X-ray structural determination (see the Supporting Information).

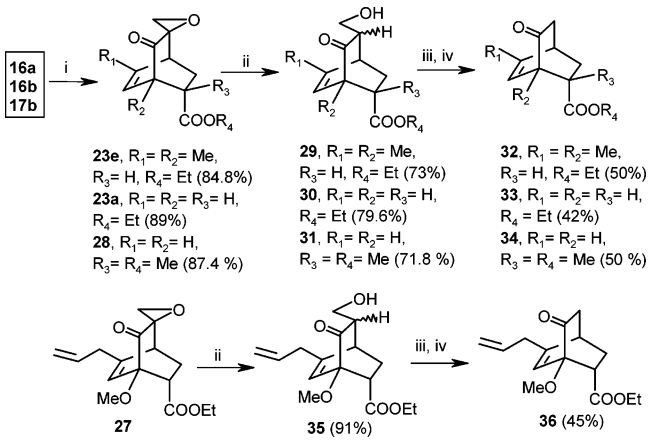
At this juncture, it was thought to explore the interception of spiroepoxycyclohexa-2,4-dienones of type **12d** which are easily generated in situ by the oxidation of *o*-hydroxymethylphenols. Thus, a solution of salicyl alcohol **21a** in acetonitrile containing ethyl acrylate was oxidized with aqueous sodium metaperiodate following a method developed in our laboratory.[26d] However, it gave the adduct **23a** in very low yield (6%) (Scheme 4). Therefore, we considered that the spiroepoxy cyclohexa-2,4-dienones containing electron-donating substituents may undergo a more efficient cycloaddition with acrylates. Indeed, the oxidation of 4-methyl-2-hydroxymethyl phenol **21b** in the presence of ethyl acrylate furnished the *endo* adduct **23b** in good yield (42%) (Scheme 4). Similarly, the oxidation of *o*-hydroxymethyl phenols **21c**−**e** in the presence of ethyl acrylate gave the *endo* adducts **23c**, **23d**, and **23e**, respectively, in reasonably good yields as a result of regio- and stereoselective cycloaddition. It was interesting to note that the cyclohexadienone **22f** derived from 2-hydroxymethyl-6-bromo phenol **21f** also underwent efficient cycloaddition with ethyl acrylate to furnish the adduct **23f** in good yield. The structure of all adducts were clearly suggested from their spectral data and comparison.

Further, the cycloaddition of the in situ generated cyclohexadienone **22c** was also examined with acrolein, acrylonitrile, and methyl methacrylate. Thus, treatment of *o*-vanilyl alcohol **21c** with sodium metaperiodate in the presence of acrolein and acrylonitrile gave the corresponding adducts **24** and **25** respectively in moderate yields (Scheme 5).

SCHEME 5



SCHEME 6[a]



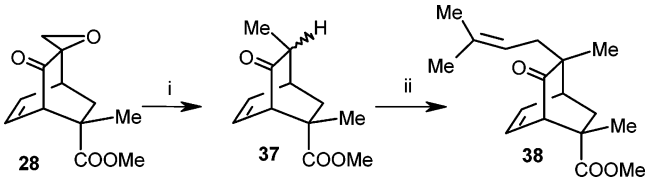
[a] Reagents and conditions: (i) aq KOH, CTAB, $CHCl_3$, rt; (ii) Zn, NH4Cl, aq MeOH, rt; (iii) Jones' oxidation; (iv) aq THF, △.

Transformation of Adducts: Synthesis of Chromophoric Systems. The presence of the chloromethyl and hydroxyl groups in the adducts **16**−**20** and the keto-epoxide in **23**−**27** provided a unique opportunity for further manipulation that led to synthesis of bicyclo[2.2.2]octenones that are not readily accessible otherwise. Thus, treatment of **16a** with aqueous KOH in the presence of CTAB as a phase transfer catalyst gave the ketoepoxide **23e** in excellent yield. This epoxide was found to be identical with that obtained by direct interception of the spiroepoxycyclohexadienone **22e** with ethyl acrylate. Reduction of the ketoepoxide **23e** with zinc−NH_4Cl in aqueous methanol[26d] selectively furnished the β-keto alcohol **29** (as a mixture of syn−anti isomer, ^{1}H NMR). Oxidation of the alcohol **29** followed by decarboxylation gave the ketone **32** (Scheme 6).

Similarly, the adducts **16b**, **17b**, and **27** were also converted into the corresponding epoxides and transformed into the bicyclo[2.2.2]octenones **33**, **34**, and **36**, respectively (Scheme 6). The structure of each of the products was thoroughly established spectroscopically.

(32) (a) Chanon, M.; Baron, R.; Baralotto, C.; Julliard, M.; Hendrickson, J. B. *Synthesis* **1998**, 1559−1583. (b) Corey, E. J.; Cheng, X.-M. *The Logic of Chemical Synthesis*; John-Wiley & Sons: New York, 1989.

SCHEME 7[a]

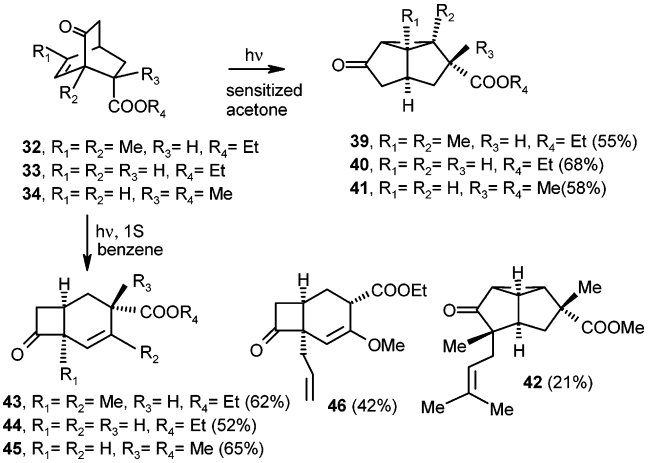


[a] Reagents and conditions: (i) Zn, NH_4Cl, dry dioxane, △, 65.8%; (ii) NaH, THF, $(Me)_2C{=}CHCH_2Br$, 68%.

Further, the ketoepoxide **28** was manipulated in an alternative manner by reduction with zinc−NH_4Cl in dry aprotic medium wherein the oxirane ring is deoxygenated and transformed into a methyl group. Thus, heating the ketoepoxide **28** with zinc−NH_4Cl in dry dioxane selectively gave the ketone **37** (as a mixture of syn−anti isomer, ^{1}H NMR) as a major product. Alkylation of **37** with prenyl bromide in the presence of NaH furnished **38** as a major product in a stereoselective fashion (Scheme 7). This kind of stereoselective alkylation has also been observed earlier.[33]

Studies on the Photochemical Reaction upon Triplet and Singlet Excitation: Stereoselective Synthesis of Bicyclo[3.3.0]-octanes and Bicyclo[4.2.0]octanes. Photochemical reactions of β,γ-unsaturated carbonyl compounds have stimulated interest for a long time,[34,35] which has increased recently due to their synthetic potential.[36−38] Compounds containing a β,γ-enone chromophore in rigid molecular framework undergo two unique photoreactions as a result of interaction between the carbonyl and the alkene groups. In general, it has been observed that sensitized irradiation of constrained β,γ-enones causes a 1,2-acyl shift leading to the formation of cyclopropyl ketone. This photochemical reorganization is commonly known as oxa-di-π-methane rearrangement because of its similarity to the well-known di-π-methane or "Zimmerman rearrangement".[39] The direct irradiation of these enones follows a different course,

SCHEME 8



namely the 1,3-acyl shift,[35a,40] leading to the formation of a cyclobutanone ring, in addition to other competing reactions such as decarbonylation and ketene elimination.[34,35] It may be mentioned that the oxa-di-π-methane reaction of bicyclo[2.2.2]-octenones has been studied earlier.[36,37] In continuation with their seminal studies on photoreaction of β,γ-enones, Demuth and co-workers have also examined the oxa-di-π-methane reaction of several bicyclo[2.2.2]octenones.[37] The synthetic potential of the photoproducts was elegantly demonstrated via their transformation into various natural products.[37c,d]

Keeping the above in mind, we first explored the photoreaction of **32**−**34** and **38** upon triplet excitation. Thus, a solution of the ketone **32** in degassed acetone (both as solvent and sensitizer) was irradiated under nitrogen with a mercury vapor lamp (125 W, APP) during which a clean reaction occurred. Removal of the solvent followed by chromatography furnished the photoproduct **39** (Scheme 8) whose structure was deduced from its spectral features and comparison with its precursor. Similar irradiation of other chromophoric systems **33** and **34** also gave the corresponding oxa-di-π-methane products **40** and **41**, respectively, in good yields. Sensitized irradiation of compound **38** containing an olefinic chain, however, gave the photoproduct **42** in low yield. This inefficiency in the photorearrangement of **38** could be due to the presence of the alkene group present in the aliphatic chain and the partial loss of radiation energy in bond twisting.[35a]

Toward the synthesis of bicyclo[4.2.0]octanes, the photoreaction of chromophoric systems **32**−**34** and **36** was examined upon direct irradiation. Thus, a solution of compound **32** was irradiated in benzene for 1 h. Removal of solvent in vacuo followed by chromatography gave the photoproduct **43** (Scheme 8) in high yield as a result of 1,3-acyl shift along with a small amount of recovered starting material. Similar irradiation of the chromophoric systems **33**, **34**, and **36** also gave the corresponding photoproducts **44**, **45**, and **46** in very good yields (Scheme 8).

Further, the tricyclic keto-esters **39**−**41** were subjected to reductive cleavage of the cyclopropane ring. Though there are various reagents for the cleavage,[41,42] radical-induced reduction was attempted.[42] Thus, treatment of the ketones **40** and **41** with

(33) (a) Stork, G.; Baine, N. H. *Tetrahedron Lett.* **1985**, *26*, 5927−5930. (b) Paquette, L. A.; Ra, C. S.; Silvestri, T. W. *Tetrahedron* **1989**, *45*, 3099−3106.

(34) (a) Houk, K. N. *Chem. Rev.* **1976**, *76*, 1−74. (b) Hixon, S. S.; Mariano, P. S.; Zimmerman, H. E. *Chem. Rev.* **1973**, *73*, 531−551. (c) Givens, R. S.; Oettle, W. F. *J. Chem. Soc., Chem. Commun.* **1969**, 1164−1165.

(35) (a) Schuster, D. I. In *Rearrangement in Ground and Excited States*; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 3, pp 167−279. (b) Engel, P. S.; Schexnayder, M. A. *J. Am. Chem. Soc.* **1975**, *97*, 145−153. (c) Coffin, R. L.; Givens, R. S.; Carlson, R. G. *J. Am. Chem. Soc.* **1974**, *96*, 7554−7556.

(36) (a) Zimmerman, H. E.; Armesto, D. *Chem. Rev.* **1996**, *96*, 3065−3112 and references therein. (b) Padwa, A.; Zhi, L.; Fryxel, Z. E. *J. Org. Chem.* **1991**, *56*, 1077−1083. (c) Paquette. L. A.; Ra, C. S.; Silvestri, T. W. *Tetrahedron* **1989**, *45*, 3099−3106. (d) Yates, P.; Burnell, D. J.; Freer, V. J.; Sawyer, J. F. *Can. J. Chem.* **1987**, *65*, 69−77.

(37) (a) Demuth, M. In *Organic Photochemistry*; Padwa, A., Ed.; Marcell Dekker: New York, 1991; Vol. 11, pp 37−97. (b) Demuth, M.; Hisken, W. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 973−975. (c) Demuth, M.; Schaffner, K. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 820−836 and references therein. (d) Demuth, M.; Raghvan, P. R.; Carter, C.; Nakano, K.; Schaffner, K. *Helv. Chim. Acta* **1980**, *63*, 2434−2439.

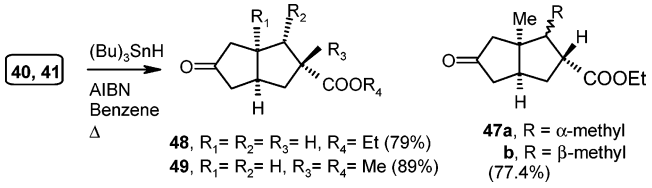
(38) (a) McClure, C. K.; Kiessling, A. J.; Link, J. S. *Org. Lett.* **2003**, *5*, 3811−3813. (b) Armesto, D.; Ortiz, M. J.; Agarrabeitia, A. R. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W., Lenci, F., Eds.; CRC press: Boca Raton, FL, 2004; pp 95.1−95.16. (c) Singh, V. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W., Lenci, F., Eds.; CRC Press: Boca Raton, FL, 2004; pp 78.1−78.34.

(39) (a) Zimmerman, H. E.; Grunewald, G. L. *J. Am. Chem. Soc.* **1966**, *88*, 183−184. (b) Zimmerman, H. E.; Binkley, R. W.; Givens, R. S.; Sherwin, M. A. *J. Am. Chem. Soc.* **1967**, *89*, 3932−3933.

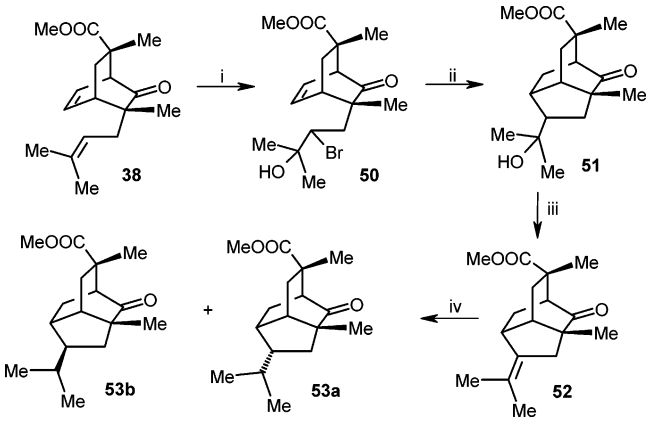
(40) (a) Givens, R. S.; Oettle, W. F.; Coffin, R. L.; Carlson, R. G. *J. Am. Chem. Soc.* **1971**, *93*, 3957−3962. (b) Sato, H.; Furutachi, N.; Nakanishi, K. *J. Am. Chem. Soc.* **1972**, *94*, 2150−2152.

(41) Wong, H. N. C.; Hon, M. Y.; Tse, W. C.; Yib, Y. C.; Taneko, J. C.; Hudlicky, T. *Chem. Rev.* **1989**, *89*, 165−198.

SCHEME 9



SCHEME 10[a]



[a] Reagents and conditions: (i) *N*-bromosuccinimide, aq THF, 60%; (ii) $(Bu)_3SnH$-AlBN, benzene, △, 53%; (iii) *p*-toluenesulphonic acid, benzene, 91%; (iv) H_2, PtO_2, EtOH, 69.5%.

$(Bu)_3SnH-AIBN$ in refluxing benzene furnished the bicyclic keto-esters **48** and **49**, respectively, in excellent yields (Scheme 9) whose structures were clearly revealed from their spectral data and comparison with their precursors. The reaction of **39** under similar condition, however, gave an inseparabe mixture of bicyclo[3.3.0]octanes **47a** (major) and **47b** presumably due to loss of stereochemical integrity during the reduction.

Functionalization of 38 and Radical-Induced Cyclization: Synthesis of the Tricyclo[4.3.1.0^{3,7}]undecanes (Isotwistane) Framework. Radical-induced carbon−carbon bond-forming reactions have proved to be a powerful tool in organic synthesis.[43,44] The bicyclic compound **38** appeared to be a suitable precursor for the synthesis of isotwistane framework present in the pupukeananes via regioselective functionalization of the alkene group present in the prenyl chain and radical-induced cyclization.

Thus, the treatment of **38** with *N*-bromosuccinimide in aqueous THF readily gave the bromohydrin **50** in good yield. Reaction of **50** with $(Bu)_3SnH-AIBN$ in refluxing benzene furnished a mixture of products from which the tricyclic compound **51** was isolated as a major product. Treatment of **51** with *p*-toluenesulfonic acid gave the tricyclic compound **52**, which upon reduction furnished a stereoisomeric mixture of **53a** (major product) and **53b** (minor) having the carbocyclic framework of pupukeananes (Scheme 10).

(42) (a) Enholm, E. J.; Jia, Z. J. *Tetrahedron Lett.* **1995**, *36*, 6819. (b) Enholm, E. J.; Jia, Z. J. *J. Org. Chem.* **1997**, *62*, 174−181.

(43) (a) Giese, B. In *Radicals in Organic Synthesis*: *Formation of Carbon−Carbon Bonds*; Pergamon Press: Oxford, UK, 1986. (b) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237−1286.

(44) (a) Giese, B.; Kopping, B.; Gobel, T.; Dickhaut, J.; Thoma, G.; Kulicke, K. J.; Trach, F. *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons: New York, 1996; Vol. 48, pp 301−856. (b) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, UK, 1991; Vol. 4, pp 778−831.

Conclusion

In summary, we have described cycloaddition of cyclohexa-2,4-dienones with electron-deficient 2π-partners leading to a new, efficient, and stereoselective synthesis of highly functionalized bridged bicyclo[2.2.2]octenones **16**−**20**, **23a**−**f**, and **24**−**27**. Manipulation of these adducts further led to bicyclo[2.2.2]-octenones **28**−**38** of diverse synthetic potential. Photochemical sigmatropic shifts in bicyclooctenones provide a general and stereoselective route to ring-fused bicyclo[3.3.0]octanoids and bicyclo[4.2.0]octanoids from common precursors via modulation of chemical reactivity in the excited state. Further, the bicyclooctenone **38** having a prenyl chain permitted selective functionalization of the alkene group and radical-induced cyclization to the tricyclo[4.3.1.0^{3,7}]decane framework of pupukeananes.

Experimental Section

2-*endo*-Carboethoxy-5-chloromethyl-5-hydroxy-1,8-dimethylbicyclo[2.2.2]oct-7-en-6-one (16a). A mixture of the dimer **14a** (0.5 g, 1.34 mmol) and ethyl acrylate (1.3 mL, excess) in *o*-dichlorobenzene (2 mL) was heated in a sealed tube at 140 °C for 8 h. The reaction mixture was chromotagraphed on silica gel. Elution with petroleum ether−ethyl acetate (95:5) furnished the adduct **16a** as a colorless solid (0.77 g, 96%), which was recrystalized from a petroleum ether−ethyl acetate mixture. Mp 82−84 °C. IR (KBr) ν_{max} 3387, 1719 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.45 (br s, 1H), 4.10 (m, 2H), 3.70 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.45 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.07 (br m, 1H), 2.77−2.73 (m, 2H), 2.50 (m, 1H), 1.98 (d, J = 1.5 Hz, 3H), 1.69 (ddd, J_1 = 13 Hz, J_2 = 6 Hz, J_3 = 2.8 Hz, 1H), 1.25 (t partly overlapped with s, J = 7.12 Hz, 3H), 1.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.8, 173.1, 144.9, 123.5, 73.1, 60.7, 50.3, 49.9, 45.1, 44.2, 26.2, 20.7, 15.3, 14.1 (14 carbons). HRMS (ESI) (*m*/*z*) found 309.0874 (M^+ + Na), calcd for $C_{14}H_{19}ClO_4Na$ 309.0864. Anal. Calcd for $C_{14}H_{19}ClO_4$: C, 58.63, H, 6.6. Found: C, 59.07, H, 6.76.

2-*endo*-Carboethoxy-5-chloromethyl-5-hydroxybicyclo[2.2.2]-oct-7-en-6-one (16b). Heating the dimer **14b** (1.0 g, 3.15 mmol) and ethyl acrylate (3.5 mL) as described above followed by chromatography [petroleum ether−ethyl acetate (94:6)] furnished the adduct **16b** as a thick colorless liquid (1.53 g, 93%). IR (film) ν_{max} 3387, 1736, 1709 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.54 (superimposed dd, J = 6.1 Hz, 1H), 6.20 (superimposed dd, J = 6.1 Hz, 1H), 4.12 (q, J = 7 Hz, 2H), 3.64 (part of an AB system merged with m, J_{AB} = 12 Hz, 1H), 3.62 (m merged with AB system, 1H), 3.51 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.28−3.24 (br m, 1H), 3.10−3.06 (m, 1H), 2.66 (br s, 1H), 2.54−2.47 (m, 1H), 1.80 (m of d, J = 12 Hz, 1H), 1.25 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.0, 172.1, 136.3, 127.2, 73.1, 61.0, 50.3, 49.5, 40.2, 39.6, 23.2, 14.3. HRMS (ESI) (*m*/*z*) found 281.0558 (M^+ + Na), calcd for $C_{12}H_{15}ClO_4Na$ 281.0557.

2-*endo*-Carboethoxy-5-chloromethyl-5-hydroxy-8-methylbicyclo[2.2.2]oct-7-en-6-one (16c). The reaction of ethyl acrylate (3.5 mL, excess) and chlorohydroxy dimer **14c** (1 g, 2.89 mmol) as described above and chromatography of product [petroleum ether−ethyl acetate (94:6)] furnished the adduct **16c** as a colorless solid (1.13 g, 71%). Mp 71−73 °C. IR (KBr) ν_{max} 3482, 1739, cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.74−5.72 (br m, 1H), 4.09 (q, J = 7.2 Hz, 2H), 3.63 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.48 (dd, J_1 = 6.6 Hz, J_2 = 2.4 Hz, 1H), 3.42 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.06−2.09 (m, 2H), 2.74 (s, 1H), 2.40 (ddd, J_1 = 15 Hz, J_2 = 9.5 Hz, J_3 = 3 Hz, 1H), 1.91 (d, J = 1.52 Hz, 3H), 1.77 (ddd, J_1 = 15 Hz, J_2 = 5.4 Hz, J_3 = 3 Hz, 1H), 1.21 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.7, 172.6, 146.4,

118.5, 73.1, 61.1, 49.7, 49.2, 44.4, 40.6, 22.5, 20.9, 14.1. HRMS (ESI) (*m*/*z*) found 295.0708 (M^+ + Na), calcd for $C_{13}H_{17}ClO_4Na$ 295.0713. Anal. Calcd for $C_{13}H_{17}ClO_4$: C, 57.24, H, 6.23. Found: C, 57.82, H, 6.55.

2-Methyl-2-*endo*-carbomethoxy-5-chloromethyl-5-hydroxy-1,8-dimethylbicyclo[2.2.2]oct-7-en-6-one (17a) and 2-Methyl-2-*exo*-carbomethoxy-5-chloromethyl-5-hydroxy-1,8-dimethylbicyclo-[2.2.2]oct-7-en-6-one (18a). The reaction of dimer **14a** (1.0 g, 2.68 mmol) and methyl methacrylate (3.5 mL) as described earlier followed by chromatography [petroleum ether−ethyl acetate (94:6)] furnished the *endo* adduct **17a** as a colorless solid (1.17 g, 76%). Elution with petroleum ether−ethyl acetate (93:7) gave the *exo* adduct **18a** as a colorless solid (0.16 g, 10%).

Data for *endo* adduct 17a: Mp 107−108 °C. IR (KBr) ν_{max} 3429, 1717 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.42 (br m, 1H), 3.66 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.46 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.61 (s, 3H), 2.94 (br m, 1H), 2.75 (s, 1H), 2.18 (d of part of an AB system, J_{AB} = 13.5 Hz, J = 3.3 Hz, 1H), 2.06 (d of part of an AB system, J_{AB} = 13.5 Hz, J = 2.7 Hz, 1H), 1.89 (d, J = 1.5 Hz, 1H), 1.20 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.8, 175.4, 144.3, 126.0, 73.4, 54.9, 51.9, 50.7, 49.5, 44.1, 33.8, 21.5, 20.6, 13.4. HRMS (ESI) (*m*/*z*) found 309.0875 (M^+ + Na), calcd for $C_{14}H_{19}ClO_4$ 309.0870. Anal. Calcd for $C_{14}H_{19}ClO_4$: C, 58.63, H, 6.63. Found: C, 58.90, H, 7.03.

Data for *exo* adduct 18a: Mp 115−117 °C. IR (KBr) ν_{max} 3497, 1727 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.33 (d, J = 1.5 Hz 1H), 4.95 (d, J = 1.2 Hz, 1H), 3.88 (part of an AB system, J_{AB} = 11.7 Hz, 1H), 3.33 (part of an AB system, J_{AB} = 11.7 Hz, 1H), 3.70 (s, 3H), 3.08 (br m, 1H), 2.59 (d of part of an AB system, J_{AB} = 14.4 Hz, J = 2.7 Hz, 1H), 1.93 (d, J = 1.8 Hz, 3H), 1.37 (d of part of an AB system, J_{AB} = 14.4 Hz, J = 2.7 Hz, 1H), 1.14 (s, 3H), 1.07 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.1, 179.7, 146.4, 124.4, 72.6, 56.0, 53.0, 52.0, 50.3, 44.5, 34.9, 21.3, 20.6, 13.3. HRMS (ESI) (*m*/*z*) found 287.1054 (M^+), calcd for $C_{14}H_{20}ClO_4$ 287.1050. Anal. Calcd for $C_{14}H_{19}ClO_4$: C, 58.63, H, 6.63. Found: C, 58.28, H, 6.55.

2-Methyl-2-*endo*-carbomethoxy-5-chloromethyl-5-hydroxybicyclo[2.2.2]oct-7-en-6-one (17b) and 2-Methyl-2-*exo*-carbomethoxy-5-chloromethyl-5-hydroxybicyclo[2.2.2]oct-7-en-6-one (18b). A mixture of methyl methacrylate (3 mL) and chlorohydroxy dimer **14b** (1 g, 3.15 mmol) was heated for 8 h as described earlier after which the reaction mixture was chromatographed. Elution with petroleum ether−ethyl acetate (94:6) gave *endo* adduct **17b** (1.34 g, 81%) as a colorless solid. Continued elution with petroleum ether−ethyl acetate (93:7) afforded *exo* adduct **18b** (0.193 g, 11%) as a colorless solid.

Data for *endo* adduct 17b: Mp 61−63 °C. IR (KBr) ν_{max} 3445, 1719 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.44 (superimposed dd, J = 7.2 Hz, 1H), 6.21 (superimposed dd, J = 7.2 Hz, 1H), 3.64 (s, 3H), 3.61 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.50 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.41 (dd, J_1 = 6 Hz, J_2 = 1.2 Hz, 1H), 3.13 (m, 1H), 2.74 (s, 1H), 2.28 (d of part of an AB system, J_{AB} = 12.8 Hz, J = 3.3 Hz, 1H), 2.06 (d of part of an AB system, J_{AB} = 13.8 Hz, J = 2.4 Hz, 1H), 1.31 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.3, 176.0, 135.8, 129.2, 73.6, 55.8, 52.4, 51.0, 47.8, 39.5, 30.3, 25.3. Anal. Calcd for $C_{12}H_{15}ClO_4$: C, 55.70, H, 5.80. Found: C, 55.85, H, 5.67.

Data for *exo* adduct 18b: Mp 102−104 °C. IR (KBr) ν_{max} 3370, 1739 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.55 (superimposed dd, J = 7.5 Hz, 1H), 6.16 (superimposed dd, J = 7.5 Hz, 1H), 4.19 (br s, 1H), 3.80 (part of an AB system, J_{AB} = 11.7 Hz, 1H), 3.71 (s, 3H), 3.38 (part of an AB system, J_{AB} = 11.7 Hz, 1H), 3.30 (br m, 1H), 3.21 (d, J = 6.3 Hz, 1H), 2.70 (dd, J_1 = 13.8 Hz, J_2 = 2.4 Hz, 1H), 1.30 (dd, J_1 = 13.8 Hz, J_2 = 2.4 Hz, 1H), 1.20 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.3, 178.7, 137.0, 126.9, 72.3, 57.1, 53.2, 50.8, 47.9, 40.3, 32.1, 24.3. Anal. Calcd for $C_{12}H_{15}ClO_4$: C, 55.70, H, 5.80. Found: C, 55.53 H, 5.66.

2-Methyl-2-*endo*-carbomethoxy-5-chloromethyl-5-hydroxy-8-methylbicyclo[2.2.2]oct-7-en-6-one (17c) and 2-Methyl-2-*exo*-carbomethoxy-5-chloromethyl-5-hydroxy-8-methylbicyclo[2.2.2]-oct-7-en-6-one (18c). The dimer **14c** (1.0 g, 2.89 mmol) and methyl methacrylate (3 mL) in *o*-dichlorobenzene (2 mL) was heated at 140 °C in a sealed tube for 8 h after which more methyl methacrylate (0.5 mL) was added and the reaction mixture was again heated at 155 °C for 5 h. Column chromotagrophy of the reaction mixture (94:6 petroleum ether−ethyl acetate) first gave the *endo* adduct **17c** (0.687 g, 43%) as a colorless solid. Further elution with petroleum ether−ethyl acetate (93:7) gave *exo* adduct **18c** (0.106 g, 6%) as a colorless solid.

Data for *endo* adduct 17c: Mp 114−116 °C. IR (KBr) ν_{max} 3428, 1725 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 5.77 (d, J = 6.3 Hz 1H), 3.67 (s, 3H), 3.63 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.44 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.27 (d, J = 5.7 Hz, 1H), 2.96 (s, 1H), 2.70 (s, 1H), 2.28 (d of part of an AB system, J_{AB} = 13.5 Hz, J = 3.3 Hz, 1H), 2.03 (d of part of an AB system, J_{AB} = 13.5 Hz, J = 2.4 Hz, 1H), 1.93 (br s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 207.9, 175.7, 146.1, 120.8, 73.3, 55.7, 52.3, 50.1, 48.1, 44.5, 29.9, 25.3, 21.0. HRMS (ESI) (*m*/*z*) found 273.0898 (M^+ + H), calcd for $C_{13}H_{18}ClO_4$ 273.0894. Anal. Calcd for $C_{13}H_{17}ClO_4$: C, 57.24, H, 6.23. Found: C, 57.10, H, 6.43.

Data for *exo* adduct 18c: Mp 142−144 °C. IR (KBr) ν_{max} 3419, 1733 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 5.75 (d, J = 5.4 Hz 1H), 4.00 (s, 1H), 3.78 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.74 (s, 3H), 3.29 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.10 (s, 1H), 3.05 (d, J = 6.6 Hz, 1H), 2.71 (d, J = 13.8 Hz, 1H), 1.98 (s, 3H), 1.23 (d, J = 13.8 Hz, 1H), 1.20 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 205.6, 178.5, 147.1, 118.9, 72.2, 57.2, 53.1, 49.8, 48.3, 45.5, 32.0, 24.6, 20.9. HRMS (ESI) (*m*/*z*) found 295.0719 (M^+ + Na), calcd for $C_{13}H_{17}ClO_4Na$ 295.0713. Anal. Calcd for $C_{13}H_{17}ClO_4$: C, 57.24, H, 6.23. Found: C, 56.99, H 5.85.

2-*endo*-Carbomethoxy-5-chloromethyl-5-hydroxy-1,3,8-trimethylbicyclo [2.2.2]oct-7-en-6-one (19) and 2-*exo*-Carbomethoxy-5-chloromethyl-5-hydroxy-1,3,8-trimethylbicyclo[2.2.2]oct-7-en-6-one (20). Reaction of the chlorohydroxy dimer **14a** (0.2 g, 0.54 mmol) and methyl crotonate (1.5 mL, excess) in *o*-dichlorobenzene as described earlier followed by chromatography [petroleum ether−ethyl acetate (94:6)] afforded *endo* adduct **19** (0.122 g, 38%) as a colorless solid. Continued elution with petroleum ether−ethyl acetate (93:7) gave *exo* adduct **20** (0.089 g, 28%) as a colorless solid.

Data for *endo* adduct 19: Mp 124−126 °C. IR (KBr) ν_{max} 3439, 1712 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.61 (s, 1H), 3.74 (s, 3H), 3.65 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.55 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.38 (t, J = 2 Hz, 1H), 3.02 (dd, J_1 = 6 Hz, J = 2 Hz, 1H), 2.60 (s, 1H), 2.20−2.16 (br m, 1H), 1.97 (d, J = 2 Hz, 3H), 1.20 (s, 3H), 1.06 (d, J = 7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.2, 174.7, 143.2, 128.2, 73.8, 52.8, 52.1, 50.1, 47.0, 46.3, 43.3, 21.7, 16.8, 15.5. Anal. Calcd for $C_{14}H_{19}ClO_4$: C, 58.63, H, 6.63. Found: C, 58.81, H, 6.65.

Data for *exo* adduct 20: Mp 111−114 °C. IR (KBr) ν_{max} 3449, 1736, 1715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.44 (s, 1H), 4.39 (s, 1H), 3.87 (part of an AB system, J_{AB} = 12 Hz, 1H), 3.72 (s, 3H), 3.33 (part of an AB system, J_{AB} = 12 Hz, 1H), 2.99 (s, 1H), 2.72−2.68 (br m, 1H), 2.14 (d, J = 6 Hz, 1H), 1.96 (s, 3H), 1.14 (s, 3H), 1.08 (d, J = 7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.9, 177.1, 146.0, 124.0, 73.3, 57.5, 52.8, 51.5, 51.4, 50.4, 33.3, 22.8, 21.4, 16.4. Anal. Calcd for $C_{14}H_{19}ClO_4$: C, 58.63, H, 6.63. Found: C, 58.89, H, 6.68.

2-*endo*-Carboethoxy-5-spiroepoxybicyclo[2.2.2]oct-7-en-6-one (23a). To a stirred solution of salicyl alcohol **21a** (3 g, 24.19 mmol) and ethyl acrylate (6 mL, excess) in acetonitrile (70 mL) at 0 °C was added a solution of sodium metaperiodate [7.76 g, 36.27 mmol, in water (50 mL)] dropwise over a period of 2 h. The reaction mixture was further stirred overnight at ambient temperature then

saturated with sodium chloride, the organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combine organic layer was washed with brine and dried over anhydrous sodium sulfate. Removal of solvent gave a residue that was chromatographed on silica gel. Elution with petroleum ether−ethyl acetate (94:6) afforded the adduct **23a** (0.19 g, 6%) as a colorless solid. Mp 75−77 °C. IR (KBr) ν_{max} 1733 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.56 (superimposed dd, J = 7.2 Hz, 1H), 6.20 (superimposed dd, J = 7.2 Hz, 1H), 4.12 (q, J = 7.2 Hz, 2H), 3.72−3.69 (m, 1H), 3.12 (part of an AB system, J_{AB} = 6 Hz, 1H), 3.11−3.05 (complex m, 1H), 2.84 (part of an AB system, J_{AB} = 6 Hz, 1H), 2.62−2.59 (m, 1H), 2.32 (ddd, J_1 = 12.8 Hz, J_2 = 9 Hz, J_3 = 2.4 Hz, 1H), 2.05 (ddd, J_1 = 12.8 Hz, J_2 = 5.1 Hz, J_3 = 2.7 Hz, 1H), 1.23 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.1, 172.3, 135.5, 127.2, 61.3, 57.5, 53.2, 50.1, 40.0, 38.1, 25.2, 14.1. HRMS (ESI) (*m*/*z*) found 223.0977 (M^+ + H), calcd for $C_{12}H_{15}O_4$ 223.0970. Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.86, H, 6.30. Found: C, 64.91, H, 6.08.

2-*endo*-Carboethoxy-8-methyl-5-spiroepoxybicyclo [2.2.2]oct-7-en-6-one (23b). Oxidation of a solution of 4-methyl-2-hydroxymethylphenol **21b** (3.0 g, 21.73 mmol) and ethyl acrylate (6 mL) in acetonitrile (70 mL) with sodium metaperiodate [(6.97 g, 32.58 mmol in water (50 mL)] as described earlier followed by workup and chromatography [elution with petroleum ether−ethyl acetate (95:5)] gave the desired adduct **23b** (2.15 g, 42%) as a colorless liquid. IR (film) ν_{max} 1735 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (m of d, J = 6.3 Hz, 1H), 4.15 (q, J = 7 Hz, 2H), 3.64 (dd, J_1 = 6.3 Hz, J_2 = 2.5 Hz, 1H), 3.15 (part of an AB system, J_{AB} = 6 Hz, 1H), 3.08 (ddd, J_1 = 10 Hz, J_2 = 5 Hz, J_3 = 2.2 Hz, 1H), 2.91 (part of an AB system, J_{AB} = 6 Hz, 1H), 2.39 (dd, J_1 = 5 Hz, J_2 = 2 Hz, 1H), 2.30−2.25 (m, 1H), 1.90 (s, 3H), 1.26 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.3, 172.5, 145.7, 119.0, 61.2, 57.4, 52.4, 50.1, 43.5, 40.6, 24.7, 20.6, 14.1. HRMS (ESI) (*m*/*z*) found 237.1116 (M^+ + H), calcd for $C_{13}H_{17}O_4$ 237.1127.

1-Methoxy-2-*endo*-carboethoxy-5-spiroepoxybicyclo[2.2.2]oct-7-en-6-one (23c). A solution of *o*-vanilyl alcohol **21c** (1 g, 6.49 mmol) and ethyl acrylate (4 mL, excess) in acetonitrile (40 mL) was oxidized with sodium metaperiodate [2.08 g, 9.72 mmol in water (20 mL)] as described earlier. Workup and chromatography of the product on silica gel [petroleum ether−ethyl acetate (94:6)] afforded the adduct **23c** (0.75 g, 46%) as a colorless solid. Mp 67−69 °C. IR (KBr) ν_{max} 1741 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.52 (superimposed dd, J = 7.8 Hz, 1H), 6.27 (d, J = 7.8 Hz, 1H), 4.14 (m, 2H), 3.58 (s, 3H), 3.24 (dd, J_1 = 9.9 Hz, J_2 = 5.7 Hz, 1H), 3.15 (part of an AB system, J_{AB} = 6.3 Hz, 1H), 2.81 (part of an AB system, J_{AB} = 6.3 Hz, 1H), 2.56 (m, 1H), 2.44 (superimposed dd, J = 12.5 Hz, 1H), 1.90 (d with structure, J = 12.5 Hz, 1H), 1.27 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.2, 171.8, 132.0, 129.6, 85.8, 60.8, 57.1, 53.9, 52.8, 42.7, 37.8, 28.8, 14.3. HRMS (ESI) (*m*/*z*) found 253.1066 (M^+ + H), calcd for $C_{13}H_{17}O_5$ 253.1076.

1-Methoxy-2-*endo*-carboethoxy-5-spiroepoxy-8-allylbicyclo-[2.2.2]oct-7-en-6-one (23d). A solution of 4-allyl-2-hydroxymethyl-6-methoxyphenol **21d** (1.0 g, 5.15 mmol) and ethyl acrylate (6 mL, excess) in acetonitrile (40 mL) was oxidized with sodium metaperiodate [1.65 g, 7.71 mmol in water (20 mL)]. Workup as described earlier followed by chromatography of the crude product (petroleum ether−ethyl acetate (96:4) gave the adduct **23d** (0.656 g, 44%) as a low-melting solid. IR (film) ν_{max} 1738 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.93 (br s, 1H), 5.71−5.84 (complex m, 1H), 5.19−5.13 (m, 2H), 4.22−4.10 (m, 2H), 3.60 (s, 3H), 3.25−3.20 (m, 1H), 3.17 (part of an AB system, J_{AB} = 6 Hz, 1H), 3.00 (d, J = 6.6 Hz, 1H), 2.87 (part of an AB system, J_{AB} = 6 Hz, 1H), 2.45−2.36 (br m, 2H), 1.19−1.85 (br m, 1H), 1.26 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.6, 172.0, 143.8, 133.8, 121.9, 118.2, 85.9, 60.8, 57.2, 53.9, 52.3, 43.4, 41.4, 39.2, 28.4, 14.2. HRMS (ESI) (*m*/*z*) found 293.1379 (M^+ + H), calcd for $C_{16}H_{21}O_5$ 293.1389.

1,8-Dimethyl-2-*endo*-carboethoxy-5-spiroepoxybicyclo[2.2.2]-oct-7-en-6-one (23e). Oxidation of 2-hydroxymethyl-4,6-dimethylphenol **21e** (3.0 g, 19.74 mmol) with sodium metaperiodate [6.33 g, 29.58 mmol in water (50 mL)] in the presence of ethyl acrylate (15 mL) as described above followed by workup and chromatography of the crude product [petroleum ether−ethyl acetate (94:6)] gave the adduct **23e** (1.75 g, 35%) as a colorless solid. Mp 83−85 °C. IR (KBr) ν_{max} 1731 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 5.46 (s, 1H), 4.13−4.10 (m, 2H), 3.11 (part of an AB system, J_{AB} = 6.3 Hz, 1H), 2.82 (part of an AB system, J_{AB} = 6.3 Hz, 1H), 2.77−2.72 (m, 1H), 2.40−2.33 (merged m, 2H), 1.95 (s, 3H), 1.86 (dd, J_1 = 11.4 Hz, J_2 = 4.8 Hz, 1H), 1.29−1.25 (t merged with s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 203.2, 172.7, 143.5, 124.6, 60.5, 56.9, 52.1, 51.2, 44.9, 43.5, 28.4, 20.6, 15.7, 14.4. HRMS (ESI) (*m*/*z*) found 273.1116 (M^+ + Na), calcd for $C_{14}H_{18}O_4Na$ 273.1103.

2-*endo*-Carboethoxy-5-spiroepoxy-8-bromobicyclo[2.2.2]oct-7-en-6-one (23f). Oxidation of 6-bromo-2-hydroxymethylphenol **21f** (1 g, 4.93 mmol) with sodium metaperiodate [1.58 g, 7.39 mmol in water (20 mL)] in the presence of ethyl acrylate (7 mL) as described above followed by workup and chromatography [petroleum ether−ethyl acetate (94:6)] gave the adduct **23f** (0.864 g, 58%) as a colorless solid. Mp 47−48 °C. IR (film) ν_{max} 1739, 1723 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 6.37 (d, J = 6.9 Hz, 1H), 4.17(q, J = 6.9 Hz, 2H), 3.71 (d, J = 6.6 Hz, 1H), 3.17 (part of an AB system, J_{AB} = 6.3 Hz, 1H), 3.12−3.07 (m, 1H), 3.00 (part of an AB system, J_{AB} = 6.3 Hz, 1H), 2.72 (br m, 1H), 2.43−2.25 (br m, 2H), 1.28 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 200.7, 171.3, 126.5, 124.3, 61.4, 57.0, 52.36, 52.33, 49.0, 40.1, 26.1, 14.3. HRMS (ESI) (*m*/*z*) found 301.0079 (M^+), calcd for $C_{12}H_{13}O_4Br$ 301.0075. Anal. Calcd for $C_{12}H_{13}O_4Br$: C, 47.84, H, 4.31. Found: C, 47.51, H, 4.21.

1-Methoxy-2-*endo*-formyl-5-spiroepoxybicyclo[2.2.2]oct-7-en-6-one (24). Oxidation of a solution of *o*-vanilyl alcohol **21c** (0.5 g, 3.24 mmol) and acrolein (4 mL, excess) in acetonitrile (30 mL) with aqueous sodium metaperiodate (1.04 g, 4.86 mmol) as described earlier followed by workup and chromatography of the crude product [elution with petroleum ether−ethyl acetate (94:6)] gave compound **24** as a colorless solid (0.203 g, 30%). Mp 93−95 °C. IR (KBr) ν_{max} 1724, 1743 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.76 (s, 1H), 6.59 (superimposed dd, J = 8 Hz, 1H), 6.34 (d, J = 7.7 Hz, 1H), 3.65 (s, 3H), 3.19 (part of an AB system merged with m, J_{AB} = 7 Hz, 1H), 3.16−3.14 (m, 1H), 2.91 (part of an AB system, J_{AB} = 7 Hz, 1H), 2.66 (d, J = 5 Hz, 1H), 2.28−2.17 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.3, 200.0, 134.5, 128.3, 86.2, 57.8, 54.4, 53.5, 50.4, 37.7, 23.8. HRMS (ESI) (*m*/*z*) found 209.0814 (M^+ + H), calcd for $C_{11}H_{13}O_4$ 209.0814. Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.46, H, 5.76. Found: C, 62.93, H, 5.45.

1-Methoxy-2-*endo*-cyano-5-spiroepoxybicyclo[2.2.2]oct-7-en-6-one (25). Oxidation of *o*-vanilyl alcohol **21c** (0.5 g, 3.24 mmol) and acrylonitrile (4 mL, excess) in acetonitrile (30 mL) with sodium metaperiodate [1.04 g, 4.86 mmol in water (30 mL)] followed by workup and chromatography [petroleum ether−ethyl acetate (70:30)] gave the adduct **25** (0.22 g, 32%) as a colorless solid. Mp 169−171 °C. IR (KBr) ν_{max} 1747, 2245 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.72 (dd, J_1 = 8.8 Hz, J_2 = 6.8 Hz, 1H), 6.50 (m of d, J = 8.8 Hz, 1H), 3.66 (s, 3H), 3.35 (ddd, J_1 = 9.6 Hz, J_2 = 4.2 Hz, J_3 = 1 Hz, 3H), 3.22 (part of an AB system, J_{AB} = 6 Hz, 1H), 2.94 (part of an AB system, J_{AB} = 6 Hz, 1H), 2.72−2.58 (complex m, 2H), 2.06 (dt, J_1 = 15 Hz, J_2 = 3 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 201.4, 134.6, 129.8, 119.0, 84.3, 57.4, 54.3, 53.6, 37.2, 31.4, 28.6. HRMS (ESI) (*m*/*z*) found 206.0817 (M^+ + H), calcd for $C_{11}H_{12}NO_3$ 206.0817. Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.39, H, 5.36, N, 6.82. Found: C, 64.06, H, 5.04, N, 6.83.

1-Methoxy-2-*endo*-carbomethoxy-2-methyl-5-spiroepoxybicyclo-[2.2.2]oct-7-en-6-one (26). A solution of *o*-vanilyl alcohol **21c** (1.0 g, 6.49 mmol) and methyl methacrylate (8 mL, excess) in acetonitrile (40 mL) was oxidized with an aqueous solution of sodium metaperiodate (2.08 g, 9.72 mmol). Workup as described

earlier and chromatography [petroleum ether−ethyl acetate (93:7)] of the crude product on silica gel gave the adduct **26** (0.25 g, 15%) as a colorless solid. Mp 91−93 °C. IR (film) ν_{max} 1743, 1727 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.59−6.51 (br m, 2H), 3.68 (s, 3H), 3.56 (s, 3H), 3.25 (part of an AB system, J_{AB} = 6 Hz, 1H), 2.89 (part of an AB system, J_{AB} = 6 Hz, 1H), 2.58 (m, 1H), 2.25 (d of a part of an AB system, J_{AB} = 12 Hz, J = 3 Hz, 1H), 2.02 (d of a part of an AB system, J_{AB} = 12 Hz, J = 3 Hz, 1H), 1.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 174.5, 132.3, 128.8, 89.3, 56.8, 54.8, 53.2, 52.2, 49.3, 38.2, 37.5, 21.0. HRMS (ESI) (*m*/*z*) found 253.1072 (M^+ + H), calcd for $C_{13}H_{17}O_5$ 253.1076. Anal. Calcd for $C_{13}H_{16}O_5$: C, 61.90, H, 6.34. Found: C, 61.60, H, 6.16.

1-Methoxy-2-*endo*-carbomethoxy-2-methyl-5-spiroepoxy-8-allylbicyclo[2.2.2]oct-7-en-6-one (27). Oxidation of 4-allyl-2-hydroxymethyl-6-methoxyphenol **21d** (5 g, 25.77 mmol) and methyl methacrylate (15 mL, excess) in acetonitrile (140 mL) with sodium metaperiodate [8.25 g, 38.57 mmol in water (70 mL)] followed by workup and chromatography [petroleum ether−ethyl acetate (93:7)] furnished the adduct **27** (1.12 g, 14%) as a colorless solid. Mp. 98−100 °C. IR (film) ν_{max} 1743, 1723 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.11 (br s, 1H), 5.84−5.70 (br m, 1H), 5.19−5.13 (m, 2H), 3.68 (s, 3H), 3.54 (s, 1H), 3.23 (part of an AB system, J_{AB} = 7 Hz, 1H), 3.00 (m of d, J = 7.5 Hz, 2H), 2.87 (part of an AB system, J_{AB} = 7 Hz, 1H), 2.37 (m, 1H), 2.21 (d of part of an AB system, J_{AB} = 12 Hz, J = 3 Hz, 1H), 1.95 (d of part of an AB system, J_{AB} = 12 Hz, J = 3 Hz, 1H), 1.31 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 202.5, 174.6, 144.2, 133.7, 120.9, 118.1, 89.5, 56.8, 54.8, 52.6, 52.2, 49.9, 41.1, 39.2, 37.8, 20.9. HRMS (ESI) (*m*/*z*) found 293.1397 (M^+ + H), calcd for $C_{16}H_{21}O_5$ 293.1389.

Transformation of Adduct 16b into 23a. To a solution of the adduct **16b** (3 g, 11.60 mmol) in chloroform (250 mL) containing cetyltrimethylammonium bromide (CTAB) (0.300 g) was added aqueous KOH [1.29 g, 32.25 mmol in water (50 mL)]. The reaction mixture was stirred at room temperature (∼30 °C) for 4 h, after which the organic phase was separated and the aqueous layer was extracted with chloroform. The combined organic extract was washed with brine then dried over anhydrous sodium sulfate. Removal of solvent and chromatography of the residue on silica gel [petroleum ether−ethyl acetate (93:7)] gave the keto-epoxide **23a** (2.30 g, 89%) as a colorless solid, which was identical in all respects with the compound obtained previously.

Transformation of Adduct 16a into 23e. To a solution of the adduct **16a** (5 g, 17.45 mmol) in chloroform (400 mL) containing cetyltrimethylammonium bromide (CTAB) (0.300 g) was added aqueous KOH (2.170 g, 54.25 mmol in 80 mL of H_2O) and the reaction mixture was stirred at room temperature for 5 h. Workup as described above followed by chromatography of the residue [petroleum ether−ethyl acetate, (93:7)] gave the epoxy ketone **23e** (3.70 g, 84.86%) as a solid, mp 83−85 °C, which was identical with the compound obtained previously.

2-Methyl-2-*endo*-carbomethoxy-5-spiroepoxybicyclo[2.2.2]-oct-7-en-6-one (28). To a solution of the adduct **17b** (4 g, 15.47 mmol) in chloroform (327 mL) containing cetyltrimethylammonium bromide (CTAB) (0.230 g) was added aqueous KOH [1.73 g, 43 mmol]. The reaction mixture was stirred at room temperature for 6 h. The usual workup and chromatography [petroleum ether−ethyl acetate (94:6)] gave the epoxy ketone **28** (3 g, 87.4%) as a colorless solid. Mp. 67−69 °C. IR (KBr) ν_{max} 1733 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$ + CCl_4) δ 6.52 (superimposed dd, J = 6 Hz, 1H), 6.26 (superimposed dd, J = 6 Hz, 1H), 3.69 (s, 3H), 3.52 (d, J = 3 Hz, 1H), 3.16 (d, J = 6 Hz, 1H), 2.82 (d, J = 6 Hz, 1H), 2.53−2.48 (m, 2H), 1.93−1.89 (m, 1H), 1.31 (d, J = 6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$ + CCl_4) δ 203.5, 175.5, 135.1, 129.4, 57.2, 56.1, 53.0, 52.4, 46.7, 38.0, 33.9, 25.8. HRMS (ESI) (*m*/*z*) found 223.0979 (M^+ + H), calcd for $C_{12}H_{15}O_4$ 223.0970.

1,8-Dimethyl-2-*endo*-carboethoxybicyclo[2.2.2]oct-7-en-6-one (32). To a solution of the epoxy ketone **23e** (4.2 g, 16.8 mmol) in MeOH−H_2O (6:1, 140 mL) was added activated zinc (32 g, excess) and NH_4Cl (4.0 g, 74.76 mmol). The reaction mixture was stirred at ambient temperature (∼30 °C) for 15 h. It was then filtered through a Celite bed and washed with ethyl acetate. The filtrate was concentrated in vacuo, and the residue was diluted with water and extracted with ethyl acetate. The combined extract was washed with brine and dried over anhydrous sodium sulfate. Removal of solvent followed by chromatography [petroleum ether−ethyl acetate (86:14)] gave the keto-alcohol **29** as a colorless liquid [(syn:anti mixture, 3.1 g, 73%), ^{1}H NMR], which was subjected to oxidation and decarboxylation as described below.

A solution of the β-keto-alcohol **29** (2.7 g, 17.77 mmol) in acetone (120 mL) was oxidized with freshly prepared Jones' reagent. After completion of the reaction (TLC), acetone was removed in vacuo and water was added to the residue and extracted with ethyl acetate. The extract was combined and dried and the solvent was removed under vacuum to give the crude acid, which was dissolved in THF−H_2O mixture (1:1, 120 mL) and refluxed for 16 h. The reaction mixture was saturated with sodium chloride, extracted with ether, and dried. Removal of solvent and chromatography of the product [petroleum ether−ethyl acetate (94:6)] gave compound **32** as a colorless liquid (1.70 g, 50% 2 steps). IR (film) ν_{max} 1725 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.37 (s, 1H), 4.17−4.07 (m, 2H), 2.78−2.74 (m, 1H), 2.63 (dd, J_1 = 10 Hz, J_2 = 6 Hz, 1H), 2.12−2.01 (m, 3H), 1.89 (d, J = 2 Hz, 3H), 1.85−1.76 (m, 1H), 1.25 (t, J = 7 Hz, 3H), 1.21 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.3, 173.5, 146.1, 122.6, 60.4, 50.8, 44.3, 38.6, 37.1, 31.6, 19.9, 15.5, 14.1. HRMS (ESI) (*m*/*z*) found 223.1342 (M^+ + H), calcd for $C_{13}H_{19}O_3$ 223.1334.

2-*endo*-Carboethoxybicyclo[2.2.2]oct-7-en-6-one (33). Reduction of **23a** (2 g, 9.00 mmol) with zinc (16.0 g) and NH_4Cl (2.0 g, 37.3 mmol) in MeOH−H_2O (6:1, 70 mL) for 12 h as described previously followed by workup and chromatography [petroleum ether−ethyl acetate (82:18)] gave the β-keto-alcohol **30** as a liquid [(syn:anti mixture, 1.60 g, 79.6%), ^{1}H NMR]. This compound was subjected to oxidation and decarboxylation as described below.

The β-keto-alcohol **30** (1 g, 4.46 mmol) in acetone (30 mL) at ∼5 °C was oxidized with Jones' reagent as described earlier and the resulting carboxylic acid was dissolved in a THF−H_2O mixture (1:1, 60 mL) and refluxed for 12 h. Workup and chromatography [elution with petroleum ether−ethyl acetate (90:10)] gave compound **33** as a colorless liquid (0.360 g, 42%, both steps). IR (film) ν_{max} 1727 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.55 (superimposed dd, J_1 = J_2 = 8 Hz, 1H), 6.13 (superimposed dd, J_1 = J_2 = 8 Hz, 1H), 3.55 (d, J = 6 Hz, 1H), 3.10−3.03 (m, 1H), 2.99−2.93 (m, 1H), 2.06 (d, J = 2.5 Hz, 2H), 2.00−1.93 (m, 2H), 1.24 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.4, 172.8, 137.7, 125.9, 60.8, 50.7, 39.3, 39.0, 31.9, 28.7, 14.0. HRMS (ESI) (*m*/*z*) found 217.0843 (M^+ + Na), calcd for $C_{11}H_{14}O_3Na$ 217.0841.

2-Methyl-2-*endo*-carbomethoxybicyclo[2.2.2]oct-7-en-6-one (34). Reduction of epoxy ketone **28** (2 g, 9.00 mmol) with zinc (16 g) and NH_4Cl in methanol−water (6:1, 70 mL) for about 8 h followed by workup and chromatography gave the β-keto-alcohol **31** as a syn/anti mixture [(1.45 g, 71.85%), ^{1}H NMR]. The β-keto-alcohol **31** thus obtained (4 g, 17.77 mmol) was oxidized with Jones' reagent and the resulting carboxylic acid was decarboxylated as described above to give compound **34** as a colorless liquid (1.70 g, 50% after 2 steps). IR (film) ν_{max} 1731 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48 (superimposed dd, J_1 = 7.5 Hz, 1H), 6.17 (superimposed dd, J_1 = 7.5 Hz, 1H), 3.67 (s, 3H), 3.39 (d with structure, J = 5.4 Hz, 1H), 3.03−2.90 (m, 1H), 2.51−2.45 (m, 1H), 2.14−1.99 (m, 2H), 1.52 (dd, J_1 = 13 Hz, J_2 = 2.3 Hz, 1H), 1.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.7, 176.1, 137.3, 128.1, 56.8, 52.2, 46.2, 39.8, 37.2, 32.0, 27.0. HRMS (ESI) (*m*/*z*) found 195.1015 (M^+ + H), calcd for $C_{11}H_{15}O_3$ 195.1021.

1-Methoxy-8-allyl-2-*endo*-carboethoxybicyclo[2.2.2]oct-7-en-6-one (36). Treatment of adduct **27** (1 g, 3.42 mmol) with zinc (8 g, excess) and NH_4Cl (1.0 g, 18.69 mmol) for 8 h as described previously followed by workup and chromatography [petroleum ether−ethyl acetate (84:16)] gave the β-keto-alcohol **35** as a liquid

(syn:anti mixture, 0.8920 g, 91%; IR (film) ν_{max} 3454, 1730 cm^{-1}; ^{1}H NMR). The β-keto-alcohol **35** (1 g, 3.40 mmol) thus obtained was oxidized with Jones' reagent and the resulting carboxylic acid was refluxed in THF−H_2O mixture (1:1, 40 mL) for 10 h. Workup as described earlier and chromatography [petroleum ether−ethyl acetate (96:4)] gave compound **36** as a colorless liquid (0.41 g, 45% after 2 steps). IR (film) ν_{max} 1734, 1720 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88−5.73 (m, 2H), 5.19−5.08 (m, 2H), 4.20−4.08 (m, 2H), 3.58 (s, 3H), 3.07 (dd, J_1 = 10 Hz, J_2 = 6 Hz, J_3 = 1.2 Hz, 1H), 2.97 (dd, J_1 = 6 Hz, J_2 = 1.5 Hz, 2H), 2.17−2.07 (m, 3H), 1.85−1.76 (m, 1H), 1.25 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.8, 172.6, 146.6, 133.9, 119.5, 117.6, 86.0, 60.8, 54.1, 43.3, 39.4, 39.0, 35.3, 32.0, 14.1. Mass (*m*/*z*) found 264 (M^+), calcd for $C_{15}H_{20}O_4$ 264.

2,5-Dimethyl-5-prenyl-2-*endo*-carbomethoxybicyclo[2.2.2]oct-7-en-6-one (38). To a suspension of activated zinc (24 g, excess) and ammonium chloride (3 g, excess) in dry dioxane (90 mL) was added the keto-epoxide **28** (3 g, 13.51 mmol) and the reaction mixture was refluxed for 18 h. The reaction mixture was filtered through a Celite bed and washed with ethyl acetate. The filtrate was evaporated under reduced pressure; the residue was diluted with water and extracted with ethyl acetate. The combined organic layer was washed with brine and dried. Removal of solvent followed by chromatography of the residue on silica gel [petroleum ether−ethyl acetate (97:3)] gave compound **37** [(syn:anti mixture, 1.85 g, 65.8%; IR (film) ν_{max} 1722 cm^{-1}; ^{1}H NMR]. This was subjected to alkylation as described below.

Sodium hydride [1.15 g (60% w/w), 47.91 mmol] was taken in a two-necked flask fitted with a nitrogen inlet. It was washed with dry petroleum ether (3 × 5 mL), and dry THF (10 mL) was added. A solution of compound **37** (1 g, 4.8 mmol) in dry THF (15 mL) was added to the reaction mixture and refluxed for 1 h and prenyl bromide (2 mL, excess) was added. The reaction mixture was further refluxed for 6 h after which it was cooled (0 °C) and quenched by addition of ammonium chloride solution. It was diluted with ether, the organic layer was separated, and the aqueous layer was extracted with ether. The combined extract was dried and solvent was removed under vacuum and residue was chromatographed. Elution with petroleum ether−ethyl acetate (96:4) gave compound **38** (0.9 g, 68%) as a colorless solid. Mp 81−83 °C. IR (KBr) ν_{max} 1724 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.37 (superimposed dd, J = 7 Hz, 1H), 6.07 (superimposed dd, J = 7 Hz, 1H), 5.03 (t with structure, J = 8 Hz, 1H), 3.59 (s, 3H), 3.26 (d, J = 6 Hz, 1H), 2.61−2.59 (m, 1H), 2.26 (dd, J_1 = 14 Hz, J_2 = 3.5 Hz, 1H), 2.05−1.92 (m, 2H), 1.80−1.67 (m, 1H), 1.65 (s, 3H), 1.50 (s, 3H), 1.21 (s, 3H), 1.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.0, 176.5, 137.6, 134.7, 127.2, 118.6, 57.1, 52.3, 47.6, 47.3, 40.5, 37.8, 31.8, 26.0, 25.6, 19.7, 18.0. HRMS (ESI) (*m*/*z*) found 277.1817 (M^+ + H), calcd for $C_{17}H_{25}O_3$ 277.1804.

5,6-Dimethyl-7-carboethoxytricyclo[3.3.0.0^{4,6}]octan-3-one (39). A solution of compound **32** (0.1 g, 0.420 mmol) in dry acetone (100 mL) was irradiated with a mercury vapor lamp (125 W, Applied Photophysics) in a Pyrex immersion well under nitrogen for about 1 h. Removal of solvent followed by chromatography [petroleum ether−ethyl acetate (94:6)] gave some unreacted starting material (0.10 g). Further elution with petroleum ether−ethyl acetate (90:10) furnished compound **39** as a colorless liquid (0.055 g, 55%). IR (film) ν_{max} 1731 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.26−4.08 (m, 2H), 2.91 (dd, J_1 = 11 Hz, J_2 = 6 Hz, 1H), 2.72−2.44 (br. m, 3H), 1.73 (d, J = 17 Hz, 1H), 1.63−1.58 (m, 2H), 1.41 (s, 3H), 1.28 (t, J = 7 Hz, 3H), 1.12 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.3, 173.2, 60.7, 50.9, 49.4, 48.5, 47.0, 44.2, 43.3, 41.3, 15.9, 14.2, 13.9. HRMS (ESI) (*m*/*z*) found 223.1341 (M^+ + H), calcd for $C_{13}H_{19}O_3$ 223.1334.

7-Carboethoxytricyclo[3.3.0.0^{4,6}]octan-3-one (40). Irradiation of **33** (0.1 g, 0.515 mmol) in degassed acetone (100 mL) for 1.5 h as described above and removal of solvent followed by chromatography [petroleum ether−ethyl acetate (90:10)] gave some unreacted starting material (0.012 g, 12%). Further elution with petroleum ether−ethyl acetate (88:12) afforded the photoproduct **40** (0.068 g, 68%) as a colorless liquid. IR (film) ν_{max} 1724 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.17 (q, J = 7 Hz, 2H), 3.06−2.97 (m, 1H), 2.89−2.79 (m, 1H), 2.55 (dd, J_1 = 18 Hz, J_2 = 8 Hz, 1H), 2.37−2.25 (m, 2H), 2.06−2.01 (m, 1H), 1.96−1.88 (m, 1H), 1.79 (d, J = 18 Hz, 1H), 1.27 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.4, 174.1, 60.9, 46.9, 45.5, 43.1, 37.7, 37.6, 36.0, 32.8, 14.2. HRMS (ESI) (*m*/*z*) found 195.1027 (M^+ + H), calcd for $C_{11}H_{15}O_3$ 195.1021.

7-Methyl-7-carbomethoxytricyclo[3.3.0.0^{4,6}]octan-3-one (41). Irradiation of ketone **34** (0.1 g, 0.512 mmol) as described earlier followed by removal of solvent and chromatography [petroleum ether−ethyl acetate (93:7)] furnished the product **41** (0.058 g, 58%) as a colorless liquid. IR (film) ν_{max} 1731, 1715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (s, 3H), 3.05−2.99 (m, 1H), 2.92 (q, J = 6 Hz, 1H), 2.78−2.72 (m, 1H), 2.53−2.47 (m, 1H), 2.05 (d with structure, J_1 = 10 Hz, 1H), 1.53 (d, J = 13 Hz, 1H), 1.36 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.3, 177.5, 52.3, 51.4, 50.4, 49.1, 41.6, 38.6, 38.5, 37.6, 24.0. HRMS (ESI) (*m*/*z*) found 195.1026 (M^+ + H), calcd for $C_{11}H_{15}O_3$ 195.1021.

2,7-Dimethyl-2-prenyl-7-carbomethoxytricyclo[3.3.0.0^{4,6}]octan-3-one (42). Ketone **38** (0.1 g, 0.362 mmol) was irradiated in acetone (100 mL) for 4 h. Solvent was removed and the residue was chromatographed. Elution with petroleum ether−ethyl acetate (96:4) gave unreacted starting material (0.035 g, 35%). Further elution with the same solvent afforded the photoproduct **42** (0.021 g, 21%) as a colorless liquid. IR (film) ν_{max} 1722 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.14−5.09 (m, 1H), 3.72 (s, 3H), 2.79 (dd, J_1 = 11 Hz, J_2 = 5 Hz, 1H), 2.63 (dd, J_1 = 8 Hz, J_2 = 5 Hz, 1H), 2.50−2.20 (m, 2H), 2.04 (dd, J_1 = 14 Hz, J_2 = 6.6 Hz, 1H), 1.94 (dd, J_1 = 9.7 Hz, J_2 = 5 Hz, 1H), 1.71−1.67 (merged m, total 4H), 1.61 (d, J = 1.5 Hz, 3H), 1.61−1.56 (m, 1H), 1.25 (s, 3H), 0.93 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.7, 177.8, 135.3, 118.5, 57.4, 52.3, 51.5, 48.2, 43.0, 41.8, 39.0, 36.5, 34.6, 26.0, 22.8, 17.9, 16.6. HRMS (ESI) (*m*/*z*) found 277.1812 (M^+ + H), calcd for $C_{17}H_{25}O_3$ 277.1804.

1,7-Dimethyl-6-carboethoxybicyclo[4.2.0]oct-7-en-2-one (43). A solution of **32** (0.2 g, 0.84 mmol) in benzene (100 mL) was irradiated with a mercury vapor lamp (125 W, Applied Photophysics) in a Pyrex immersion well for 1 h. Benzene was removed and the residue was chromatographed on silica gel. Elution with petroleum ether−ethyl acetate (96:4) afforded the 1,3-acyl shift product **43** (0.124 g, 62%) as a colorless liquid. IR (film) ν_{max} 1775, 1728 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.31 (s, 1H), 4.24−4.14 (m, 2H), 3.11−3.00 (m, 2H), 2.73 (dd, J_1 = 17 Hz, J_2 = 6 Hz, 1H), 2.48−2.38 (m, 1H), 2.13−2.02 (m, 1H), 1.95−1.86 (m, 1H), 1.77 (s, 3H), 1.28 (d, J = 8 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.7, 173.7, 133.3, 123.2, 63.4, 60.8, 46.8, 42.8, 28.7, 26.9, 22.1, 20.7, 14.2. HRMS (ESI) (*m*/*z*) found 223.1327 (M^+ + H), calcd for $C_{13}H_{18}O_3$ 223.1334.

6-Carboethoxybicyclo[4.2.0]oct-7-en-2-one (44). A solution of compound **33** (0.1 g, 0.515 mmol) in dry benzene (100 mL) was irradiated for 1.45 h. Removal of solvent followed by the chromatography of the residue [petroleum ether−ethyl acetate (95:5)] gave the 1,3-acyl shift product **44** (0.052 g, 52%) as a liquid. IR (film) ν_{max} 1779, 1730 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.12 (m of d, J = 7.7 Hz, 1H), 5.83−5.79 (m, 1H), 4.22−4.12 (m, 2H), 3.86−3.75 (m, 1H), 3.20−3.06 (m, 2H), 2.90−2.68 (m, 2H), 2.04−1.96 (m, 1H), 1.92−1.86 (m, 1H), 1.28 (t, J = 7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 173.5, 127.4, 121.9, 60.9, 58.7, 49.2, 37.4, 25.6, 20.8, 14.1. HRMS (ESI) (*m*/*z*) found 195.1014 (M^++ H), calcd for $C_{11}H_{15}O_3$ 195.1021.

6-Methyl-6-carbomethoxybicyclo[4.2.0]oct-7-en-2-one (45). A solution of **34** (0.1 g, 0.512 mmol) in benzene (100 mL) was irradiated for 1 h. Benzene was removed in vacuo and the photolyzate was chromatographed [petroleum ether−ethyl acetate (96:4)] to give the 1,3-acyl shift product **45** (0.065 g, 65%) as a colorless liquid. IR (film) ν_{max} 1779, 1729 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (br s, 2H), 3.77−3.73 (m, 1H), 3.30 (ddd, J_1

= 17 Hz, J_2 = 8.7 Hz, J_3 = 1.8 Hz, 1H), 2.89−2.75 (m, 1H), 2.62−2.47 (m, 2H), 1.31 (s, 3H), 1.10 (dd, J_1 = 13.5 Hz, J_2 = 12.06 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 206.7, 175.7, 133.3, 121.7, 58.7, 52.0, 51.4, 42.8, 38.8, 26.8, 20.8. HRMS (ESI) (*m*/*z*) found 195.1016 (M^+ + H), calcd for $C_{11}H_{15}O_3$ 195.1021.

1-Allyl-7-methoxy-6-carboethoxybicyclo[4.2.0]oct-7-en-2-one (46). Irradiation of a solution of ketone **36** (0.1 g, 3.78 mmol) in benzene under nitrogen for 1 h followed by removal of the solvent and chromatography [petroleum−ether/ethyl acetate 97:3] of the residue furnished the product **46** (0.042 g, 42%). IR (film) ν_{max} 1775, 1737 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.82−5.68 (m, 1H), 5.11−5.06 (m, 2H), 4.46 (s, 1H), 4.16 (q, J = 7 Hz, 2H), 3.43 (s, 3H), 3.16−3.11 (m, 1H), 2.98 (dd, J_1 = 17 Hz, J_2 = 9 Hz, 1H), 2.69 (dd, J_1 = 17 Hz, J_2 = 7 Hz, 1H), 2.46−2.37 (m, 3H), 2.18−2.03 (m, 1H), 1.98−1.91 (m, 1H), 1.28 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.7, 171.8, 154.8, 133.3, 118.3, 93.7, 65.7, 60.7, 54.6, 46.3, 41.8, 39.8, 27.7, 26.6, 14.3. Mass (*m*/*z*) found 264 (M^+), calcd for $C_{15}H_{20}O_4$ 264.

5,6-Dimethyl-7-carboethoxybicyclo[3.3.0]octan-3-one (47a,b). To a solution of compound **39** (0.140 g, 0.630 mmol) and tributytinhydride (0.6 mL, 2.06 mmol) in dry benzene was added AIBN (0.010 g, 0.060 mmol) and the reaction mixture was refluxed for 14 h under nitrogen atmosphere. The solvent was removed in vacuo and the residue was chromatographed. Elution with petroleum ether−ethyl acetate (94:6) furnished a diastereoisomeric mixture of compound **47a**,**b** (0.110 g, 77.4%) as a colorless liquid. IR (film) ν_{max} 1735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.20−4.11 (m, 2H), 2.40−2.30 (complex m, 4H), 2.25−2.05 (m, 3H), 1.90−1.70 (set of br s, 1H), 1.62−1.50 (m, 1H), 1.27 (t, J = 7 Hz, 3H), 1.14 and 1.12 (s, total 3H), 1.00 and 0.99 (d, J = 6.6 Hz, total 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 218.8, 175.6, 60.4, 51.0, 49.8, 48.4, 45.6, 45.0, 44.3, 35.1, 25.2, 14.2, 13.8 (signals due to major isomer). HRMS (ESI) (*m*/*z*) found 225.1494 (M^+ + H), calcd for $C_{13}H_{21}O_3$ 225.1491.

7-Carboethoxybicyclo[3.3.0]octan-3-one (48). A solution of keto-ester **40** (0.2 g, 1.03 mmol) in dry benzene (70 mL) containing AIBN (0.015 g, 0.09 mmol) and tributyltin hydride (0.8 mL, 2.74 mmol) was refluxed for 10 h under an atmosphere of nitrogen. Removal of solvent followed by chromatography [petroleum ether−ethyl acetate (92:8)] furnished compound **48** (0.160 mg, 79.2%) as a colorless liquid. IR (film) ν_{max} 1738, 1732 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (q, J = 7 Hz, 2H), 3.03−2.82 (m, 3H), 2.57−2.45 (m, 2H), 2.29−2.18 (m, 2H), 2.03 (dd, J_1 = 18 Hz, J_2 = 4.3 Hz, 2H), 1.81−1.70 (m, 2H), 1.26 (t, J = 7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 219.9, 175.6, 60.5, 44.4, 43.2, 39.2, 36.7, 14.2. HRMS (ESI) (*m*/*z*) found 197.1170 (M^+ + H), calcd for $C_{11}H_{17}O_3$ 197.1178.

7-Methyl-7-carbomethoxybicyclo[3.3.0]octan-3-one (49). Reduction of compound **41** (0.2 g, 1.025 mmol) with tri-*n*-butyltin hydride (0.7 mL, 2.4 mmol) and AIBN (0.020 g, 0.12 mmol) for 14 h in dry benzene (70 mL) followed by chromatography [petroleum ether−ethyl acetate (93:7)] furnished compound **49** (0.180 g, 89%) as a colorless liquid. IR (film) 1731 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.73 (s, 3H), 2.85−2.75 (m, 2H), 2.63 (dd, J_1 = 14 Hz, J_2 = 6 Hz, 2H), 2.56−2.47 (m, 2H), 2.05 (dd, J_1 = 19 Hz, J_2 = 4.5 Hz, 2H), 1.34 (s, 3H), 1.28 (dd, J_1 = 13 Hz, J_2 = 8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 219.8, 178.0, 51.9, 51.7, 45.3, 44.52, 39.0, 25.3. HRMS (ESI) (*m*/*z*) found 197.1177 (M^+ + H), calcd for $C_{11}H_{17}O_3$ 197.1178.

2,5-Dimethyl-2-carbomethoxy-5-(2-bromo-3-hydroxy-3-methylbutyl)bicyclo[2.2.2]oct-7-en-6-one (50). To a stirred solution of compound **38** (1.0 g, 3.62 mmol) in THF (20 mL) and water (5 mL) was slowly added NBS (1.2 g, 6.74 mmol) over a period of 1 h at −10 °C. After further stirring for 24 h at ambient temperature, water was added and the reaction mixture was extracted with CH_2Cl_2. The combined organic layer was washed with brine and dried over anhydrous sodium sulfate. Removal of solvent followed by chromatography [petroleum ether−ethyl acetate (96:4)] first gave the starting material (0.2 g, 20%). Further elution with petroleum ether−ethyl acetate (90:10) furnished compound **50** (0.8 g, 59.7%) as a colorless solid. Mp 121−124 °C. IR (KBr) ν_{max} 1733, 1708 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.58 (superimposed dd, J = 7 Hz, 1H), 6.13 (superimposed dd, J = 7 Hz, 1H), 4.21 (dd, J_1 = 8.5 Hz, J_2 = 1.5 Hz, 1H), 3.67 (s, 1H), 3.34 (d, J = 14 Hz, 1H), 3.16−3.12 (m, 1H), 2.41 (dd, J_1 = 14.4 Hz, J_2 = 3.5 Hz, 1H), 2.17−2.13 (m, 2H), 1.98 (dd, J_1 = 16 Hz, J_2 = 8 Hz, 1H), 1.82 (dd, J_1 = 14 Hz, J_2 = 2 Hz, 1H), 1.31 (s, 3H), 1.29 (s, 3H), 1.25 (s, 3H), 1.19 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 215.8, 176.5, 138.9, 126.6, 70.0, 63.5, 57.0, 52.5, 47.7, 46.5, 44.0, 41.1, 31.9, 25.9, 25.8, 25.7, 19.8. HRMS (ESI) (*m*/*z*) found 395.0820 (M^+ + Na), calcd for $C_{17}H_{25}O_4$ BrNa 395.0834.

3,9-Dimethyl-5-(2-hydroxyprop-2-yl)-9-carbomethoxytricyclo-[4.3.1.0^{3,7}]decan-2-one (51). To a solution of tributyltin hydride (1.2 g, 4.12 mmol) and AIBN (0.030 g, 0.18 mmol) in dry benzene (200 mL) was added bromohydrin **50** (0.6 g, 1.61 mmol) under nitrogen atmosphere. The reaction mixture was refluxed for 6 h after which it was chromatographed on silica gel. Elution with petroleum ether−ethyl acetate (85:15) furnished compound **51** (0.250 g, 53%) as a solid, which was recrystallized from a petroleum ether−ethyl acetate mixture. Mp 109−111 °C. IR (KBr) ν_{max} 3471, 1728, 1701 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.71 (s, 3H), 2.66 (dd, J_1 = 15 Hz, J_2 = 2.5 Hz, 1H), 2.55 (d, J = 4.4 Hz, 1H), 2.28 (dd, J_1 = 9 Hz, J_2 = 5 Hz, 1H), 2.01−1.84 (m, 3H), 1.57 (dd, J_1 = 15 Hz, J_2 = 3.5 Hz, 1H), 1.50−1.36 (m, 3H), 1.25 (dd, J_1 = 14 Hz, J_2 = 5 Hz, 1H), 1.19 (s, 3H), 1.18 (s, 3H), 1.17 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 220.6, 177.1, 72.7, 57.8, 54.2, 52.5, 50.2, 45.4, 43.9, 40.4, 36.8, 31.9, 28.5, 27.21 27.20 27.1, 19.1. HRMS (ESI) (*m*/*z*) found 295.1906 (M^+ + H), calcd for $C_{17}H_{27}O_4$ 295.1909.

3,9-Dimethyl-5-isopropylidine-9-carbomethoxytricyclo[4.3.1.0^{3,7}]-decan-2-one (52). A solution of keto-alcohol **51** (0.035 g, 0.119 mmol) and PTSA (catalytic) in dry benzene (4 mL) was refluxed for 4 h, after which it was cooled, washed with saturated $NaHCO_3$ and brine, and then dried. Removal of solvent followed by chromatography of the residue [petroleum ether−ethyl acetate (95:5)] gave the tricyclic olefin **52** (0.030 g, 91%) as a colorless solid. Mp 99−100 °C. IR (KBr) ν_{max} 1717 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.71 (s, 3H), 2.85 (dd, J_1 = 9.5 Hz, J_2 = 5 Hz, 1H), 2.70 (dd, J_1 = 15 Hz, J_2 = 2.5 Hz, 1H), 2.50 (d, J = 3.6 Hz, 1H), 2.38 (d, J = 16 Hz, 1H), 2.08 (d with stucture, J = 16 Hz, 1H), 1.94−1.80 (m, 2H), 1.63−1.57 (m merged with s, total 4H), 1.51 (s, 3H), 1.30 (dd, J_1 = 14 Hz, J_2 = 5 Hz, 1H), 1.21 (s, 3H), 1.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 220.6, 177.1, 136.9, 122.6, 53.4, 52.6, 50.2, 45.4, 44.6, 43.2, 38.3, 28.7, 27.5, 27.4, 20.79, 20.77, 19.00. HRMS (ESI) (*m*/*z*) found 277.1797 (M^+ + H), calcd for $C_{17}H_{24}O_3$ 277.1804.

3,9-Dimethyl-5-isopropyl-9-carbomethoxytricyclo[4.3.1.0^{3,7}]-decan-2-one (53a,b). To the activated platinum oxide (0.025 g) was added a solution of tricyclic olefin **52** (0.05 g, 0.181 mmol) in ethanol (6 mL). The reaction mixture was stirred for 24 h under hydrogen atmosphere at room temperature. Evaporation of solvent and chromatography of the residue on silica gel [petroleum ether−ethyl acetate (95:5)] furnished an inseparable mixture of **53a**,**b** (0.035 g, 69.5%) as a solid. Mp 45−47 °C. IR ν_{max} 1726, 1716 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.72 (s, 3H), 2.74 (dd, J_1 = 14 Hz, J_2 = 2.8 Hz, 1H), 2.42−2.8 (m, 1H), 2.26−2.00 (m, 1H), 1.90−1.80 (merged m, 2H), 1.62−1.20 (merged m, 6H), 1.14 (s, 6H), 0.82 (d, J = ∼6 Hz, 3H), 0.81 (d, J = ∼6 Hz, 3H) (signals due to major isomer). ^{13}C NMR (100 MHz, $CDCl_3$) δ 220.6, 176.9, 54.1, 53.4, 52.5, 49.6, 46.3, 45.5, 42.6, 36.4, 33.0, 29.4, 27.6, 27.3, 21.7, 20.5, 19.0 (signals for major isomer). HRMS (ESI) (*m*/*z*) found 279.1956 (M^+ + H), calcd for $C_{17}H_{27}O_3$ 279.1960.

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Supporting Information Available: ^{13}C NMR spectra of compounds **16**−**29**, **31**−**36**, and **38**−**53**, ^{1}H NMR spectra of compounds **30** and **36**, ORTEP diagrams of compounds **16a** and **18a**, crystal data for **18a**, and CIF data for compound **18a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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