JOC*Note*

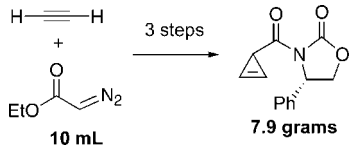
Synthesis of Stable Derivatives of Cycloprop-2-ene Carboxylic Acid

Ni Yan, Xiaozhong Liu, Mahesh K. Pallerla, and Joseph M. Fox*

Brown Laboratories, Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716

jmfox@udel.edu

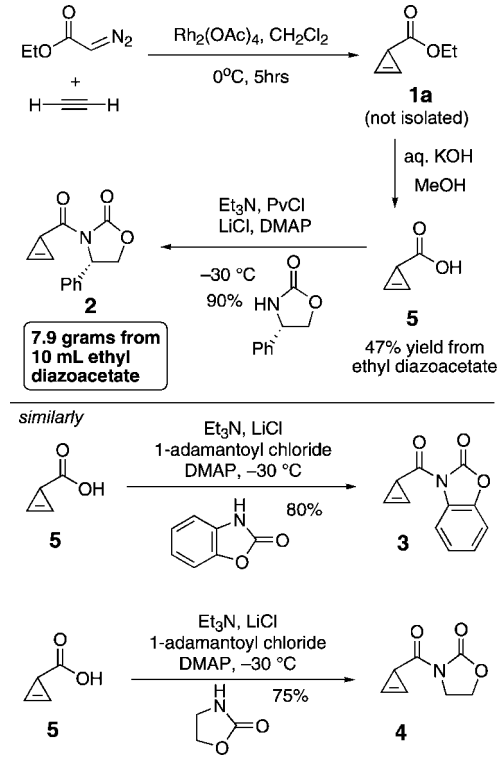
Received January 8, 2008



Large-scale syntheses of 3-(cycloprop-2-en-1-oyl)oxazolidinones from acetylene and ethyl diazoacetate are described. Unlike other cyclopropenes that bear a single substitutent at C-3, these compounds are stable to long-term storage. Although the cyclopropene derivatives are unusually stable, they are reactive toward cyclic and acyclic dienes in stereoselective Diels−Alder reactions.

The Rh-catalyzed reaction of α-diazo esters with alkynes is an exceptionally useful and operationally simple method for the preparation of cycloprop-2-ene carboxylates[1]—substances that are useful building blocks for a number of strain-assisted transformations.[2] In theory, the Rh-catalyzed reaction of acetylene with ethyl diazoacetate should provide a particularly inexpensive route to ethyl cycloprop-2-ene carboxylate (**1a**).[3] Compound **1a** and derivatives might serve as useful tools for diastereoselective synthesis. However, the usefulness of cyclopropenes with a single substituent at their sp^3 centers has been limited by their instability. Thus, 3-methylcyclopropene is extremely unstable, whereas 3,3-dimethylcyclopropene is quite stable at room temperature.[4] Although cycloprop-2-ene carboxylates (**1**) are more stable than 3-alkylcyclopropenes, their long-term storage is also not practical.[3a] Herein, we describe scalable syntheses of 3-(cycloprop-2-en-1-oyl)oxazolidinone derivatives **2**−**4**: crystalline derivatives of cycloprop-2-ene carboxylic acid that are stable over long periods (Figure 1). Although derivatives **2**−**4** are unusually stable, they are reactive dienophiles that undergo Diels−Alder reactions with high stereoselectivity.

SCHEME 1. Synthesis of 3-(Cycloprop-2-en-1-oyl)oxazolidinones



Several preparations of cycloprop-2-ene carboxylates have been described in the literature.[3] In an important study, Baldwin and Villerica compared several routes to cycloprop-2-ene-1-carboxylates and described a scalable, Rh-catalyzed procedure for the preparation of methyl cycloprop-2-ene carboxylate (**1b**).[3a] Despite the considerable merits of the procedure, there were two limitations that detracted from the preparative utility: the need to prepare methyl diazoacetate (which has been reported to "detonate with extreme violence"[5]) and the modest thermal stability of cyclopropenes of structure **1**. Methyl cycloprop-2-ene-1-carboxylate (**1b**) is stable in the refrigerator for several days.[3a] However, our own experience with **1a** suggests that storage over longer periods is not practical. Furthermore, because

(1) (a) Baird, M. S. In *Carbocyclic Three-Membered Ring Compounds*, 4th ed.; de Meijere, A., Ed.; Georg Thieme Verlag: Stuttgart, 1996; Vol. E17d, pp 2695−2744. (b) Petiniot, N.; Anciaux, A. J.; Noels, A. F.; Hubert, A. J.; Teyssié, P. *Tetrahedron Lett.* **1978**, *19*, 1239. (c) Liao, L.-a.; Zhang, F.; Yan, N.; Golen, J. A.; Fox, J. M. *Tetrahedron* **2004**, *60*, 1803. and references therein.

(2) Selected reviews to the reaction chemistry of cyclopropenes: (a) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117. (b) Rubin, M.; Rubina, M.; Gevorgyan, V. *Synthesis* **2006**, 1221. (c) Halton, B.; Banwell, M. G. In *The Chemistry of the Cyclopropyl Group*; Patai, S., Rappoport, Z., Eds.; Wiley: Chichester, 1987; pp 1224−1339. (d) Baird, M. S. *Top. Curr. Chem.* **1988**, *144*, 137. (e) Nakamura, M.; Isobe, H.; Nakamura, E. *Chem. Rev.* **2003**, *103*, 1295. (f) Fox, J. M.; Yan, N. *Curr. Org. Chem.* **2004**, *9*, 719. (g) Marek, I.; Simaan, S.; Masarwa, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 7364. (h) Chuprakov, S.; Malyshev, D. A.; Trofimov, A.; Gevorgyan, V. *J. Am. Chem. Soc.* **2007**, *129*, 14868. and references therein.

(3) For preparations of alkyl cycloprop-2-ene carboxylates: (a) Baldwin, J. E.; Villarica, K. A. *J. Org. Chem.* **1995**, *60*, 186. (b) Shapiro, E. A.; Kalinin, A. V.; Nefedov, O. M. *Org. Prep. Proc. Int.* **1992**, *24*, 517. (c) Doering, W. V. E.; Laber, G.; Vonderwahl, R.; Chamberlain, N. F.; Williams, R. B. *J. Am. Chem. Soc.* **1956**, *78*, 5448. (d) Myhre, P. C.; Maxey, C. T.; Bebout, D. C.; Swedberg, S. H.; Petersen, B. L. *J. Org. Chem.* **1990**, *55*, 3417. (e) Sachs, R. K.; Kass, S. R. *J. Am. Chem. Soc.* **1994**, *116*, 783. (f) Kimura, K.; Horie, S.; Minato, I.; Odaira, Y. *Chem. Lett.* **1973**, 1209.

(4) Closs, G. L.; Closs, L. E.; Böll, W. A. *J. Am. Chem. Soc.* **1963**, *85*, 3796.

(5) Searle, N. E. In *Organic Syntheses*; Wiley & Sons; New York, 1963; Collect. Vol. IV, pp 424−426.

10.1021/jo800042w CCC: $40.75 © 2008 American Chemical Society
Published on Web 05/02/2008

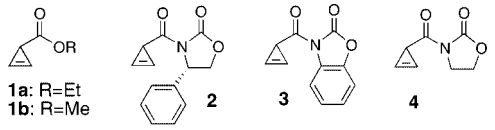


FIGURE 1. Derivatives of cycloprop-2-ene carboxylic acid.

of its volatility, it is difficult to completely isolate **1a** free from solvent (CH_2Cl_2).

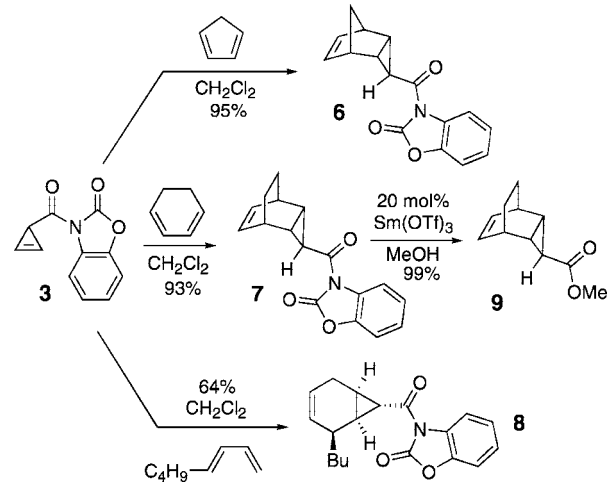
In earlier studies from our group on the resolution and kinetic resolution of cyclopropenes,[1c,6] we noted that the *N*-acyloxazolidinones of cycloprop-2-ene carboxylic acids were stable solids with long shelf-lives. We anticipated that cyclopropenes **2**−**4** would also be stable, and accordingly we set out to develop the synthesis and reaction chemistry of these derivatives.

Cyclopropenes **2**−**4** can be prepared from acetylene and ethyl diazoacetate as shown in Scheme 1. The preparation of ethyl cycloprop-2-ene carboxylate (**1a**) mirrored Baldwin's synthesis of **1b**,[3a] with the exception that **1a** was not purified. Instead, the solution of crude **1a** was filtered through a bed of silica gel and directly combined with KOH/MeOH to give acid **5** in 47% yield (based on ethyl diazoacetate). Carboxylic acid **5** is a hydroscopic white solid[7] that can be isolated in pure form. The stability of **5** is comparable to that of **1b**: it is stable over short periods but decomposes within 1 week when stored at freezer temperatures (−20 °C). In one instance, **5** decomposed exothermically and with the evolution of gas (presumably CO_2). Accordingly, it is recommended that **5** be handled in solution and not as a neat material.

The reaction of (*S*)-4-phenyloxazolidinone with the anhydride from pivaloyl chloride and **5** gave acyloxazolidinone **2** in 90% yield.[8] Importantly, 7.9 g of **2** can be prepared from 10 mL of ethyl diazoacetate. Compounds **3** and **4** can be prepared in analogous fashion (Scheme 1). For the preparations of **3** and **4**, 1-adamantoyl chloride was used in place of pivaloyl chloride because the former is a crystalline solid that is more conveniently handled in small-scale preparations.[9]

The crystalline derivatives **2**−**4** can be handled at rt without special precaution and are stable over much longer periods than **1** or **5**. The stability was quantified for **2**: a sample was measured to be >92% pure (^{1}H NMR) after storage in a freezer (−20 °C) for 2 years. In solution, compound **2** decomposes only slowly when heated. Thus, a sample of **2** in DMSO-d_6 was heated to 80 °C and monitored by ^{1}H NMR spectroscopy, and after 1, 3, and 12 h, the compound was measured to be 89%, 83%, and 50% pure, respectively. In the DSC of **2** there is a large broad endothermic transition (210 J/g) at 118−119 °C that corresponds to the melting point. There is also a small, sharp exothermic transition (48 J/g) at 269 °C that may correspond to decomposition. Because the heat flow associated with the exotherm is small, these data suggest that **2** would not require any unusual safety precautions. Although the stabilities of **3** and **4** were not quantified, these derivatives are also stable for months when stored in the freezer.

SCHEME 2. Stereoselective Diels−Alder Reactions of 3



The well-defined faces of 3-substituted cyclopropenes make them excellent candidates for diastereoselective synthesis. To illustrate the synthetic utility of 3-(cycloprop-2-en-1-oyl)oxazolidinones, the Diels−Alder[10] reactions in Scheme 2 were carried out. Thus, **3** reacts with cyclopentadiene and 1,3-cyclohexadiene to give **6** and **7** in 95% and 93% yields, respectively. Similarly, compound **3** reacts with (*E*)-1,3-octadiene to give **8** in 64% yield. The cyclopropene controls the endo selectivity[11] of the cycloadditions to provide the Diels−Alder adducts as single diastereomers. The stereochemical assignments for the structures of **6**−**8** were based on X-ray analysis of **6** and **7**, NOE analysis of **8**, and correlation with literature precedents.[10] Methanolysis of **7** under $Sm(OTf)_3$-catalyzed conditions[12] proceeded uneventfully to give **9** in 99% yield.

In summary, scalable syntheses of 3-(cycloprop-2-en-1-oyl)oxazolidinones (**2**−**4**) from acetylene and ethyl diazoacetate have been described. Unlike other cyclopropenes that bear only a single substituent at C-3, these derivatives are stable to long-term storage. Although these cyclopropenes are stable, they participate smoothly in diastereoselective Diels−Alder reactions. We anticipate that these readily accessible cyclopropene derivatives will find broad utility in stereoselective synthesis.

Experimental Section

Cycloprop-2-ene carboxylic Acid (5). A flame-dried 1 L round bottomed flask containing $Rh_2(OAc)_4$ (120 mg, 0.271 mmol) in 800

(6) Liao, L.-a.; Zhang, F.; Dmitrenko, O.; Bach, R. D.; Fox, J. M. *J. Am. Chem. Soc.* **2004**, *126*, 4490.

(7) For a prior synthesis of cycloprop-2-ene carboxylic acid, see: (a) Nefedov, O. M.; Dolgij, I. E.; Okonnischnikova, G. P.; Schwedova, I. B. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 929. For syntheses of 2-silyl derivatives of cycloprop-2-ene carboxylic acid, see also: (b) Maier, G.; Hoppe, M.; Reisenauer, H. P.; Krüger, C. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 437. (c) Kohn, D. W.; Chen, P. *J. Am. Chem. Soc.* **1993**, *115*, 2844.

(8) Ho, G.-J.; Mathre, D. J. *J. Org. Chem.* **1995**, *60*, 2271. (b) Ager, D. J.; Allen, D. R.; Schaad, D. R. *Synthesis* **1996**, 1283.

(9) Compound **3** was also prepared in similar yield with the modification that pivaloyl chloride was used in place of 1-adamantoyl chloride.

(10) For reviews on Diels−Alder reactions of cyclopropenes, see ref 2b–d. For Diels−Alder reactions of cycloprop-2-ene carboxylates, see ref 3b and: (a) Paulini, K.; Reissig, H. U. *J. Prakt. Chem. Chem. Z.* **1995**, *337*, 55. (b) Tomilov, Y. V.; Shapiro, E. A.; Protopopova, M. N.; Ioffe, A. I.; Dolgii, I. E.; Nefedov, O. M. *Bull. Acad. Sci. USSR., Div. Chem. Sci.* **1985**, *34*, 576. (c) Shapiro, E. A.; Lun'kova, G. V.; Nefedov, A. O.; Dolgii, I. E.; Nefedov, O. M. *Bull. Acad. Sci. USSR., Div. Chem. Sci.* **1981**, *30*, 2097. (d) Lind, H.; Deutschman, A. J., Jr. *J. Org. Chem.* **1967**, *32*, 326. (e) Lou, Y.; Horikawa, M.; Kloster, R. A.; Hawryluk, N. A.; Corey, E. J. *J. Am. Chem. Soc.* **2004**, *126*, 8916. For other, recent examples of Diels−Alder reactions of cyclopropenes, see: (f) Orugunty, R. S.; Wright, D. L.; Battiste, M. A.; Helmich, R. J.; Abboud, K. *J. Org. Chem.* **2004**, *69*, 406. (g) Al Dulayymi, J. R.; Baird, M. S.; Hussain, H. H.; Alhourani, B. J.; Alhabashna, A. Y.; Coles, S. J.; Hursthouse, M. B. *Tetrahedron Lett.* **2000**, *41*, 4205.

(11) For recent theoretical studies on the endo selectivity of cyclopropene Diels−Alder reactions, see: (a) Xidos, J. D.; Gosse, T. L.; Burke, E. D.; Poirer, R. A.; Burnell, D. J. *J. Am. Chem. Soc.* **2001**, *123*, 5482. (b) Imade, M.; Hirao, H.; Omoto, K.; Fujimoto, H. *J. Org. Chem.* **1999**, *64*, 6697. (c) Sodupe, M.; Rios, R.; Branchadell, V.; Nicholas, T.; Oliva, A.; Dannenberg, J. J. *J. Am. Chem. Soc.* **1997**, *119*, 4232.

(12) Ortiz, A.; Quintero, L.; Hernández, H.; Maldonado, S.; Mendoza, G.; Bernéz, S. *Tetrahedron Lett.* **2003**, *44*, 1129.

mL of CH_2Cl_2 was cooled by a bath of ice−water. The flask was swept with N_2. The N_2 was then turned off, and the solution was sparged for 30 min with acetylene gas [acetone was removed from the acetylene by first it passing through two cold traps (−60 to −65 °C)]. Ethyl diazoacetate (Aldrich, contains 15% CH_2Cl_2, 10 mL, 9.2 g, 81 mmol) was added over the course of 5 h via syringe pump at 0 °C. The color of the mixture was dark green while ethyl diazoacetate was added. In some runs, the reaction color turned yellow or light red during the last hour of the addition, but this did not affect the yield significantly. After the addition of ethyl diazoacetate was complete, the acetylene was turned off, and the mixture was sparged with N_2 for about 20 min followed by filtration through a short silica gel plug to remove the $Rh_2(OAc)_4$. Without removal of solvent, the light yellow filtrate was transferred to a 2 L round bottomed flask. The flask was cooled by an ice bath, and methanol (800 mL) was added. After the mixture had cooled, 200 mL of aqueous KOH (1.8 M) was added dropwise, and the homogeneous yellow mixture was allowed to stir overnight under N_2 atmosphere. The progress of the reaction was monitored periodically by TLC analysis to ensure that the hydrolysis was complete. The mixture was then concentrated on the rotary evaporator (at rt) to remove the organic solvents. To the resulting aqueous solution was added methyl *tert*-butyl ether (300 mL), and the mixture was cooled by an ice bath. Aqueous HCl solution (3 M) was added dropwise until the aqueous phase was rendered acidic (pH ∼3), and solid NaCl was added until the aqueous layer was saturated. The aqueous layer was extracted twice with 300 mL portions of methyl *tert*-butyl ether. The combined organics were dried over $MgSO_4$, filtered, and concentrated until the total volume was ∼50 mL. The residue was subjected to rapid flash chromatography on a short silica gel column (3 in. high × 3 in. diameter) using MTBE as the eluent. Solvent removal gave 3.2 g (38 mmol, 47%) of compound **5** as a white solid, mp 40−41 °C (the previously reported[7a] mp was much higher: 147−148 °C). In some cases, **5** was obtained as an oil that was spectroscopically pure.

NOTE: In one case, pure **5** decomposed exothermically and with the release of gas (presumably CO_2). To avoid this decomposition, it is recommended that **5** should not be evaporated to dryness after the final chromatography. Rather, it is advised that solvent be removed until the concentration of **5** in MTBE is an ∼30% solution by weight (i.e., ∼9 g total weight). The yield of **5** can be estimated by analyzing the ^{1}H NMR spectrum of the MTBE solution. We have handled solutions of **5** many times without event. MTBE solutions of **5** can be used directly for the preparations of **2**−**4**.

Spectral properties of pure **5**: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.43 (br s, 1H), 6.92 (s, 2H), 2.21 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 182.5 (C), 103.0 (CH), 16.5 (CH); IR (neat, cm^{-1}) 2973 (br), 1694, 1659, 1650, 1416, 1323, 1280, 1238, 1093, 978, 897, 697; HRMS-CI (M^+) *m*/*z* calcd for $C_4H_4O_2$ 84.0211, found 84.0207.

4(*S*)-3-(Cycloprop-2-en-1-oyl)-4-phenyloxazolidinone (2). A flame-dried 1 L round bottomed flask containing a solution of **5**[13] (3.2 g, 38 mmol) in 800 mL of THF was chilled by a cold bath that was maintained between −25 and −30 °C (dry ice/30% ethanol in ethylene glycol). The mixture was allowed to stir under nitrogen atmosphere. Distilled triethylamine (14.1 g, 19.4 mL, 139 mmol) and pivaloyl chloride (7.0 g, 7.1 mL, 58 mmol) were added sequentially, and stirring at −25 to −30 °C was continued for 2 h, during which time a large volume of a white solid ($Et_3N\cdot HCl$) precipitated. LiCl (7.0 g, 170 mmol) was added, and after 10 min, (*S*)-4-phenyloxazolidinone (11.2 g, 69 mmol) and 4-dimethylaminopyridine (500 mg, 4.10 mmol) were added. The reaction mixture was allowed to stir for 20 h, during which time the dry ice in the bath dissipated and the mixture gradually warmed to rt. The mixture was then filtered on a Buchner funnel to remove precipitated $Et_3N\cdot HCl$, and the precipitate was rinsed with additional THF. The solvents were removed under reduced pressure at rt, and the residue was immediately partitioned between 300 mL of CH_2Cl_2 and 100 mL water. The aqueous layer was extracted twice with 100 mL portions of CH_2Cl_2, and the combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed on a column of silica gel (8 in. high × 1.5 in. diameter). The initial eluent was 3:1 methylene chloride/hexane, followed by elution with 10:10:1 CH_2Cl_2/hexane/ethyl acetate. The yield of **2** was 7.90 g (34.3 mmol, 90%). Compound **2** is a white solid: mp 118−119 °C; $[\alpha]_D$ +140.0 (*c* 1.00, THF); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38−7.31 (m, 5H), 6.79 (dd, J = 0.6, 1.3 Hz, 1H), 6.74 (dd, J = 0.6, 1.4 Hz, 1H), 5.43 (dd, J = 3.9, 8.7 Hz, 1H), 4.71 (app t, J = 8.8 Hz, 1H), 4.30 (dd, J = 3.9, 8.9 Hz, 1H), 3.52 (app t, J = 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 175.9 (C), 154.2 (C), 139.1 (C), 129.1 (CH), 128.6 (CH), 126.1 (CH), 101.9 (CH), 101.7 (CH), 70.2 (CH_2), 58.0 (CH), 17.1 (CH); IR (neat, cm^{-1}): 1758, 1698, 1660, 1364, 1323, 1240, 1205, 1181, 1083, 1066, 1036, 985, 762, 734, 701, 644, 623; HRMS-CI (M + H) *m*/*z* calcd for $C_{13}H_{12}NO_3$ 230.0844, found 230.0806.

3-(Cycloprop-2-en-1-oyl)-3*H*-benzooxazol-2-one (3). A flame-dried 100 mL round bottomed flask containing **5**[13] (84 mg, 1.0 mmol) and 20 mL of THF was chilled by a cold bath at −25 to −30 °C (dry ice/30% ethanol in ethylene glycol). The mixture was allowed to stir under nitrogen atmosphere. Distilled triethylamine (0.36 g, 0.50 mL, 3.5 mmol) and 1-adamantoyl chloride[9] (238 mg, 1.2 mmol) were added sequentially, and stirring at −25 to −30 °C was continued for 1 h. LiCl (0.21 g, 5.0 mmol) was added. After 5 min, 2-benzoxazolinone (203 mg, 1.50 mmol), and 4-dimethylaminopyridine (13 mg, 0.10 mmol) were added. The reaction mixture was allowed to stir overnight, during which time the dry ice in the bath dissipated, and the mixture had gradually warmed to rt. The solvents were removed at rt under reduced pressure, and the residue was immediately partitioned between 20 mL of CH_2Cl_2 and 20 mL of water. The aqueous layer was extracted twice with 20 mL portions of CH_2Cl_2, and the combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed on silica gel. The eluent was 1:3:6 CH_2Cl_2/ethyl acetate/hexane. The yield of **3** was 161 mg (0.80 mmol, 80%). Compound **3** is a white solid: mp 82−83 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.01−7.99 (m, 1H), 7.24−7.19 (m, 3H), 6.92 (d, J = 0.6 Hz, 1H), 3.63 (t, J = 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 175.7 (C), 151.8 (C), 142.2 (C), 128.1 (C), 125.1 (CH), 124.7 (CH), 115.9 (CH), 109.7 (CH), 101.6 (CH), 17.9 (CH); IR (neat, cm^{-1}) 1787, 1704, 1669, 1477, 1467, 1248, 1138, 754, 698, 605; HRMS-CI (M + H) *m*/*z* calcd for $C_{11}H_8NO_3$ 202.0504, found 202.0497.

Synthesis of 3-(Cycloprop-2-en-1-oyl)oxazolidinone (4). A flame-dried 100 mL round-bottomed flask containing **5**[13] (84 mg, 1.0 mmol) and 20 mL of THF was chilled by a cold bath at −25 to −30 °C (dry ice/30% ethanol in ethylene glycol). The mixture was allowed to stir under nitrogen atmosphere. Distilled triethylamine (0.36 g, 0.50 mL, 3.5 mmol), 1-adamantoyl chloride[9] (238 mg, 1.2 mmol) were added sequentially, and stirring at −25 to −30 °C was continued for 1 h. LiCl (0.21 g, 5.0 mmol) was added. A solution of oxazolidinone (131 mg, 1.50 mmol) in THF (2.0 mL) was prepared in the glovebox, and after 5 min, the oxazolidinone solution and 4-dimethylaminopyridine (13 mg, 0.10 mmol) were sequentially added. The reaction mixture was allowed to stir overnight, during which time the dry ice in the bath dissipated and the mixture gradually warmed to rt. The solvents were removed at rt under reduced pressure, and the residue was immediately partitioned between 20 mL of CH_2Cl_2 and 20 mL water. The aqueous layer was extracted twice with 20 mL portions of CH_2Cl_2, and the combined organics were dried (Na_2SO_4), filtered, and concentrated. The residue was chromatographed on silica gel. The eluent was 1:3:6 CH_2Cl_2/ethyl acetate/hexane. The yield of **4** was 115 mg (0.752 mmol, 75%). Compound **4** is a semisolid: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.82 (d, J = 1.3 Hz, 2H), 4.30 (t, J = 8.2 Hz, 2H), 4.03 (t, J = 8.1 Hz, 2H), 3.51 (t, J = 1.3 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 176.5 (CH), 154.0 (CH), 101.8 (CH), 62.3 (CH_2), 43.0 (CH_2), 16.6 (CH); IR (neat, cm^{-1}) 1742, 1700,

(13) For the preparations of **2**−**4**, similar yields were obtained when **5** was added as neat material or as a ∼30% wt solution in MTBE.

1651, 1364, 1323; HRMS-CI (M + H) *m*/*z* calcd for $C_7H_8NO_3$ 154.0504, found 154.0505.

General Procedure for Diels−Alder Reactions. A 3 dram vial containing a stirbar was sequentially charged with the indicated amounts of CH_2Cl_2, diene, and **3**. The reaction mixture was allowed to stir at rt for the indicated time. The mixture was then concentrated under reduced pressure, and the crude residue was purified on a column of silica gel (2% ethyl acetate in hexanes was the eluent).

3-(Tricyclo[3.2.1.0^{2,4}]oct-6-ene-3-carbonyl)-3*H*-benzooxazol-2-one (6). The general procedure was followed using CH_2Cl_2 (2 mL), cyclopentadiene (330 mg, 4.99 mmol), and **3** (100 mg, 0.498 mmol). The mixture was allowed to stir for 5 min. Obtained were 126 mg (0.471 mmol, 95%) of **6** as a colorless solid. The purity was measured to be greater than 95% by ^{1}H NMR: mp 129−131 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.98−7.96 (m, 1H), 7.23−7.18 (m, 3H), 5.99 (m, 2H), 3.06 (m, 2H), 3.02 (app t, J = 2.4 Hz, 1H), 2.33 (m, 2H), 1.97 (td, J = 1.6, 7.2 Hz, 1H), 1.74 (d, J = 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2 (C), 151.6 (C), 142.0 (C), 132.2 (CH), 128.0 (C), 125.0 (CH), 124.6 (CH), 115.9 (CH), 109.6 (CH), 64.4 (CH_2), 43.4 (CH), 32.0 (CH), 26.3 (CH); IR (neat, cm^{-1}) 1781, 1699, 1477, 1380, 1316, 1278, 1135, 1046, 761, 733, 698; HRMS-CI(NH_3) *m*/*z* [M + H] calcd for $C_{16}H_{14}NO_3$ 268.0974, found 268.0964.

3-(Tricyclo[3.2.2.0^{2,4}]non-6-ene-3-carbonyl)-3*H*-benzooxazol-2-one (7). The general procedure was followed using CH_2Cl_2 (0.3 mL), cyclohexadiene (400 mg, 4.99 mmol), and **3** (100 mg, 0.498 mmol). The mixture was allowed to stir for 5 h. Obtained was 130 mg (0.462 mmol, 93%) of **7** as a colorless solid. The purity was measured to be greater than 95% by ^{1}H NMR: mp 129−131 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.97−7.96 (m, 1H), 7.22−7.18 (m, 3H), 5.98 (m, 1H), 2.96 (m, 2H), 2.81 (t, J = 2.8 Hz, 1H), 1.93 (m, 2H), 1.62 (dd, J = 1.2, 6.8 Hz, 2H), 1.28 (dd, J = 1.2, 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.8 (C), 151.7 (C), 141.9 (C), 129.9 (CH), 128.1 (C), 124.9 (CH), 124.6 (CH), 115.9 (CH), 109.6 (CH), 30.4 (CH), 25.3 (CH), 24.4 (CH_2), 18.8 (CH); IR (neat, cm^{-1}) 1791, 1711, 1481, 1319, 1278, 1137, 1027, 748, 710; HRMS-CI(NH_3) *m*/*z* [M + H] calcd for $C_{17}H_{16}NO_3$ 282.1130, found 282.1134.

3-[*rel*-(1*R*,2*R*,6*R*,7*R*)-2-Butylbicyclo[4.1.0]hept-3-ene-7-carbonyl]-3*H*-benzooxazol-2-one (8). The general procedure was followed using CH_2Cl_2 (0.2 mL), (*E*)-1,3-octadiene (54 mg, 0.49 mmol), and **3** (11 mg, 0.055 mmol) and the mixture allowed to stir for 12 h. Obtained was 11 mg (0.35 mmol, 64%) of **8** as a colorless solid. A minor impurity that could not be removed by chromatography was detected at 1.9 ppm in the ^{1}H NMR spectrum: mp 95−97 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96−7.94 (m, 1H), 7.18−7.13 (m, 3H), 5.41 (m, 1H), 5.34 (m, 1H), 3.21 (m, 1H), 2.39−2.36 (m, 3H), 2.07 (m, 2H), 1.37−1.23 (m, 7H), 0.79 (t, J = 7.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.4 (C), 151.8 (C), 141.9 (C), 128.3 (CH), 128.2 (C), 125.0 (CH), 124.6 (CH), 122.3 (CH), 116.0 (CH), 109.7 (CH), 35.2 (CH_2), 31.9 (CH), 31.8 (CH), 29.1 (CH_2), 26.1 (CH), 23.2 (CH_2), 22.7 (CH_2), 20.9 (CH), 14.0 (CH_3); IR (neat, cm^{-1}) 1792, 1699, 1479, 1315, 1251, 1141, 1040, 751, 699; HRMS-CI(NH_3) *m*/*z* [M + H] calcd for $C_{19}H_{22}NO_3$ 312.1600, found 312.1590.

Acknowledgment. This work was supported by NIH Grant No. GM068640-01. We thank Glenn P. A. Yap for determination of the X-ray structures. We thank Andrew DeAngelis and Vinod Tarwade for experimental assistance, Guotao Luo for obtaining DSC data, and Daniel Hill and John McCauley for assistance in DSC interpretation.

Supporting Information Available: Copies of ^{1}H NMR and ^{13}C NMR spectra are provided for new compounds. Characterization details and a procedure for the preparation of **9** are provided. NOE and 2-D NMR data are provided for **8**. DSC data for **2** and CIF files for **2**, **6**, and **7** are provided. This material is available free of charge via the Internet at http://pubs.acs.org.

JO800042W