JOC*Note*

Tandem Diels−Alder Cycloadditions of 2-Pyrone-5-acrylates for the Efficient Synthesis of Novel Tetracyclolactones

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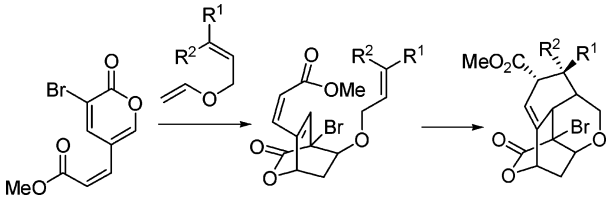
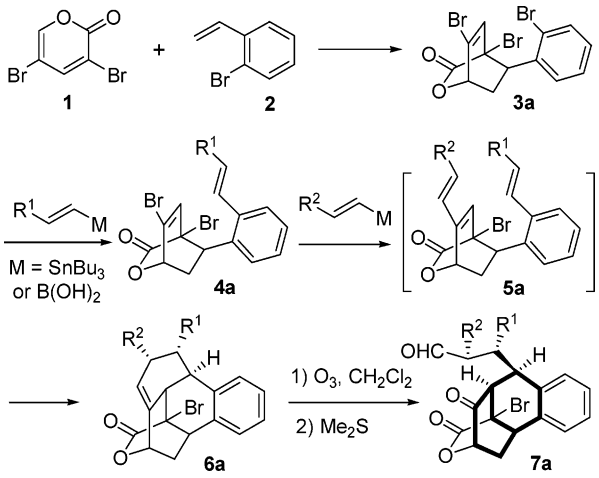
Received May 31, 2006



Readily prepared from the regioselective Pd-catalyzed coupling reactions of 3,5-dibromo-2-pyrone, 3-bromo-2-pyrone-5-carboxylates undergo tandem uninterrupted sequential Diels−Alder cycloaddition reactions with allyl vinyl ethers in a highly regio- and stereoselective fashion to provide a series of novel tetracyclolactones in good yields.

Defined as two sequential cycloaddition reactions following one another, tandem Diels−Alder (D−A) cycloadditions can be exceptionally powerful for the synthesis of intricate polycarbocycles, constructing multiple carbon−carbon bonds in a single chemical operation.[1] A number of tactically different tandem D−A processes have been utilized in the efficient assembly of various biologically and chemically valuable target molecules, including taxans,[2] anhydrolycorinone,[3] (−)-chlorothricolide,[4] (+)-FR182877,[5] delphinium alkaloids,[6] dendralenes,[7] among other polycyclic systems.[8] Winkler has classified the tandem D−A strategies into "interrupted" and "uninterrupted" tandem approaches, where the latter is further categorized into "unsequential" and "sequential" subgroups, depending on the timing of the appearance of diene and/or dienophile groups during the course of the cycloaddition reactions.[1a]

SCHEME 1. Tandem Coupling−IMDA Reaction



As a part of our ongoing research program on 2-pyrones, we have previously reported that **3a**, prepared from the cycloaddition of **1** with *o*-bromostyrene **2**, undergoes tandem coupling/IMDA reactions to furnish novel benzotetracarbocycles **6a** (Scheme 1).[9] In this reaction sequence, **5a** generated from the second coupling reaction with alkenyl tin or boronic acid underwent an IMDA cycloaddition to provide **6a** in the same pot. Subsequent ozonolysis followed by a reductive workup provided **7a** bearing a bicyclo[3.3.1]nonane framework, reminiscent of the carbon skeleton of the hyperforins family of natural products.[10]

We envisaged that the incorporation of a vinyl group at the C5 position of 3,5-dibromo-2-pyrone **1**, prior to the intermolecular cycloaddition with an allyl vinyl ether-type bisdienophile, would allow direct delivery of the similar polycarbocycles in a single operation. Our elaboration is delineated in Scheme 2, where the first cycloaddition unleashes a new 1,3-diene unit in **9**, which would undergo a second cycloaddition reaction to provide highly fused tetracyclic product **10**.

Our study commenced with the regioselective synthesis of methyl 3-bromo-2-pyrone-5-acrylates (*Z*)-**12** and (*E*)-**12** from 3,5-dibromo-2-pyrone. By employing the C5-selective coupling conditions we developed,[11] 3,5-dibromo-2-pyrone was coupled

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(1) (a) Winkler, J. D. *Chem. Rev.* **1996**, *96*, 167. (b) Ho, T.-L. *Tandem Reactions in Organic Synthesis*; Wiley: New York, 1992.
(2) Winkler, J.; Kim, H.; Kim, S. *Tetrahedron Lett.* **1995**, 687.
(3) (a) Wilkie, G. D.; Elliott, G. I.; Blagg, B. S. J.; Wolkenberg, S. E.; Soenen, D. R.; Miller, M. M.; Pollack, S.; Boger, D. L. *J. Am. Chem. Soc.* **2002**, *124*, 11292. (b) Wolkenberg, S. E.; Boger, D. L. *J. Org. Chem.* **2002**, *67*, 7361.
(4) Roush, W. R.; Sciotti, R. J. *J. Am. Chem. Soc.* **1998**, *120*, 7411.
(5) Vosburg, D. A.; Vanderwal, C. D.; Sorensen, E. J. *J. Am. Chem. Soc.* **2002**, *124*, 4552.
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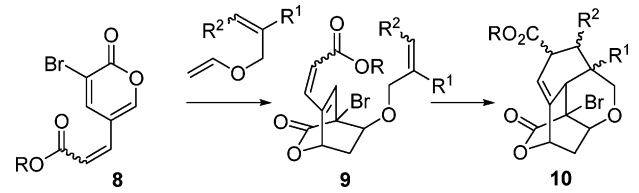
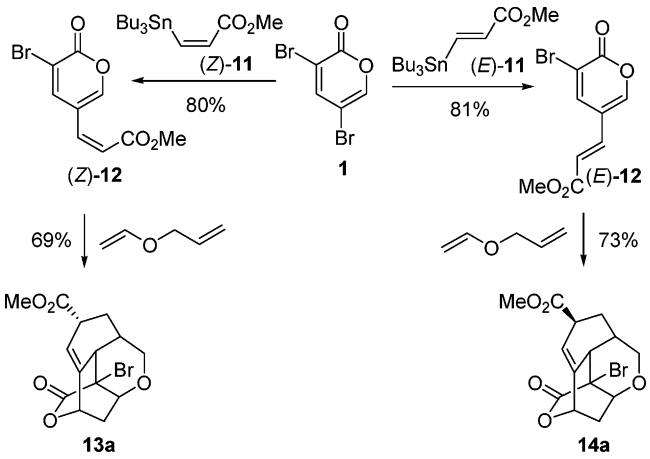
(7) Bräse, S.; Wertal, H.; Frank, D.; Vidoviæ, de Meijere, A. *Eur. J. Org. Chem.* **2005**, 4167.
(8) (a) Imagawa, T.; Kawanisi, M.; Sisido, K. *J. Chem. Soc., Chem. Commun.* **1971**, 1292. (b) Krantz, A.; Lin, C. *J. Am. Chem. Soc.* **1973**, *95*, 5662. (c) Kohnke, F.; Stoddart, J. *Pure Appl. Chem.* **1989**, *61*, 1581. (d) Golobish, T. D.; Burke, J. K.; Kim, A. H.; Chong, S. W.; Probst, E. L.; Carroll, P.; Dailey, W. P. *Tetrahedron* **1998**, *54*, 7013. (e) Sander, M.; Dehmlow, E. V. *Eur. J. Org. Chem.* **2001**, 399. (f) Afarinkia, K.; Bearpark, M. J.; Ndibwami, A. *J. Org. Chem.* **2005**, *70*, 1122.
(9) Pang, S.-J.; Min, S.-H.; Lee, H.; Cho, C.-G. *J. Org. Chem.* **2003**, *68*, 10191.
(10) (a) Ang, C. Y. W.; Hu, L.; Heinze, T. M.; Cui, Y.; Freeman, J. P.; Kozak, K.; Luo, W. *J. Agric. Food Chem.* **2004**, *52*, 6156. (b) Kraus, G. A.; Nguyen, T. H.; Jeon, I. *Tetrahedron Lett.* **2003**, *44*, 659. (c) Usuda, H.; Kanai, M.; Shibasaki, M. *Org. Lett.* **2002**, *4*, 859. (d) Spessard, S. J.; Stoltz, B. M. *Org. Lett.* **2002**, *4*, 1943. (e) Young, D. G. J.; Zeng, D. *J. Org. Chem.* **2002**, *67*, 3134. (f) Grossman, R. B.; Jacobs, H. *Tetrahedron Lett.* **2000**, *41*, 5165. (g) Nicolaou, K. C.; Pfefferkorn, J. A.; Kim, S.; Wei, H. X. *J. Am. Chem. Soc.* **1999**, *121*, 4724.
(11) (a) Ryu, K.-M.; Gupta, A.; Han, J.-W.; Oh, C. H.; Cho, C.-G. *Synlett* **2004**, 2197. (b) Kim, W.-S.; Kim, H.-J.; Cho, C.-G. *J. Am. Chem. Soc.* **2003**, *125*, 14288.

10.1021/jo061119e CCC: $33.50
Published on Web 07/27/2006

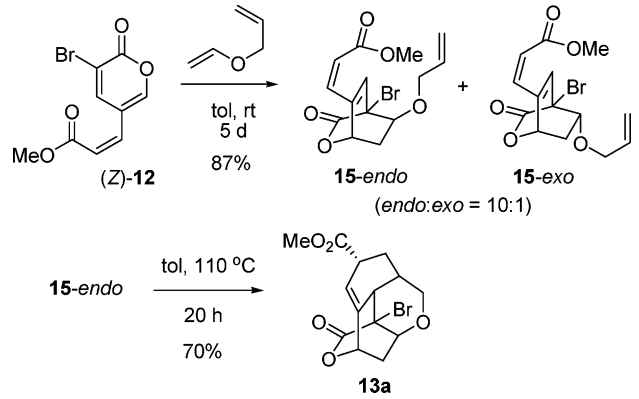
SCHEME 2



SCHEME 3. Regioselective Synthesis of 2-Pyrone-5-acrylates and Tandem Diels−Alder Reactions



SCHEME 4. Stepwise Synthesis of 13a

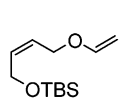
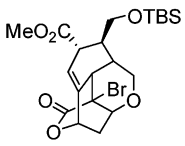
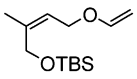
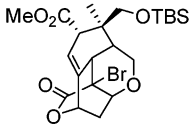
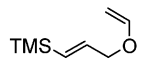
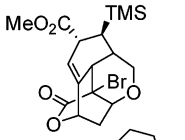
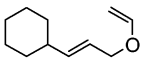
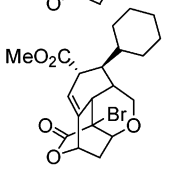
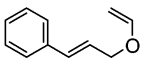
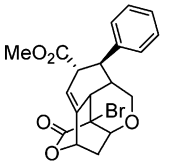
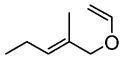
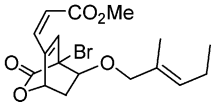


with stannyl acrylate (*Z*)-**11** and (*E*)-**11** regioselectively at the C5 position to provide (*Z*)-**12** and (*E*)-**12**, in 80 and 81% yield, respectively, with no C3 coupling product observed in either case. Subjection of the resultant (*Z*)-**12** and (*E*)-**12** into the tandem cycloaddition conditions by heating with allyl vinyl ether in toluene at 110 °C resulted in the clean formation of **13a** and **14a** in 69 and 73% yield, respectively (Scheme 3). The relative stereochemistry of the products was unambiguously established by ^{1}H NMR spectroscopy and X-ray crystallographic analysis of **13a**.

The initial intermolecular cycloaddition product can be isolated by running the reaction at ambient temperature. After 5 days, the reaction of (*Z*)-**12** with allyl vinyl ether afforded a readily separable 10:1 mixture of *endo*- and *exo*-cycloadducts in 87% combined yield. When heated at 110 °C in toluene, the isolated **15**-*endo* provided **13a** in 70% yield (Scheme 4).

We then exploited the scope of the tandem Diels−Alder cycloadditions of (*Z*)-**12** with various other substituted allyl vinyl ethers.[12] As shown in Table 1, the tandem reactions provided the corresponding tetracycles **13b**−**13f** in good yields, except

TABLE 1. Tandem D−A Reactions of (*Z*)-12

entry	dienophile	time	product	yield
1		20 h		**13b** (64%)
2		20 h		**13c** (65%)
3		20 h		**13d** (57%)
4		120 h		**13e** (20%)
5		20 h		**13f** (67%)
6		120 h		**13g** (60%)

entry 6, where the reaction was arrested at the intermolecular D−A cycloaddition stage. Similar results were obtained when (*E*)-**12** was employed in the tandem process using the same series of substituted allyl vinyl ethers (Table 2).

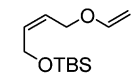
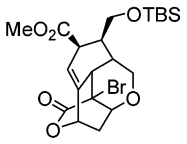
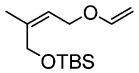
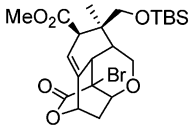
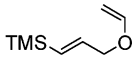
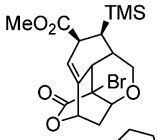
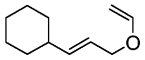
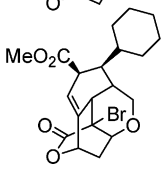
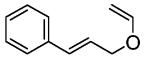
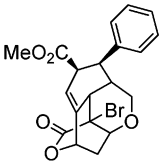
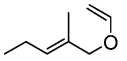
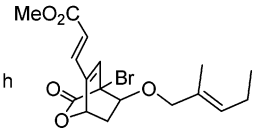
In summary, we have found that 3-bromo-2-pyrone-5-carboxylates (*Z*)-**12** and (*E*)-**12**, readily prepared from the regioselective Pd-catalyzed coupling reactions of 3,5-dibromo-2-pyrone, undergo highly regio- and stereoselective tandem uninterrupted sequential Diels−Alder cycloadditions with various allyl vinyl ethers to provide an array of novel tetracarbocycles in good yields.

Experimental Section

(*Z*)-Methyl-3-(5-bromo-6-oxo-6*H*-pyran-3-yl)acrylate (*Z*)-12. A mixture of 3.0 g (11.82 mmol) of 3,5-dibromo-2-pyrone **1**, 5.7 g (15.36 mmol) of vinyltin (*Z*)-**11**, 0.68 g (5 mol %) of $Pd(PPh_3)_4$, 2.3 g (11.82 mmol) of CuI, and 39 mL of toluene was heated at 60 °C for 3 h. Upon cooling to room temperature, the reaction mixture was treated with saturated aqueous KF, diluted with Et_2O, and filtered through a plug of Celite. The filtrate was dried over $MgSO_4$,

(12) All allyl vinyl ethers not commercially available were prepared according to the literature procedures. (a) For entry 1: Watanabe, W. H.; Conlon, L. E. *J. Am. Chem. Soc*. **1957**, *79*, 2828. (b) For entry 2: Leonard, M. S.; Carroll, P. J.; Joullie, M. M. *J. Org. Chem*. **2004**, *69*, 2526. (c) For entries 3 and 4: Tayama, E.; Saito, A.; Ooi, T.; Maruoka, K. *Tetrahedron* **2002**, *58*, 8307. (d) For entry 5: Maruoka, K.; Banno, H.; Yamamoto, H. *Tetrahedron: Asymmetry* **1991**, *2*, 647. (e) For entry 6: Faulkner, D. J.; Petersen, M. R. *J. Am. Chem. Soc*. **1973**, *95*, 553.

TABLE 2. Tandem D−A Reactions of (*E*)-12

entry	dienophile	time	product	yield
1		20 h		**14b** (64%)
2		20 h		**14c** (69%)
3		20 h		**14d** (66%)
4		120 h		**14e** (76%)
5		20 h		**14f** (66%)
6		120 h		**14g** (62%)

concentrated, and purified by column chromatography (hexane:EtOAc = 10:1) to provide 2.4 g of (*Z*)-**12** in 80% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, J = 2.2 Hz, 1H), 7.98 (dd, J = 2.2, 0.7 Hz, 1H), 6.47 (dd, J = 12.5, 0.7 Hz, 1H), 6.00 (d, J = 12.5 Hz, 1H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9, 157.2, 153.6, 146.0, 134.7, 121.3, 116.3, 111.1, 52.1; FT-IR (CH_2Cl_2) 3084, 2964, 2925, 2858, 1713 cm^{-1}; HRMS (M + 1)$^+$ calcd for $C_9H_8BrO_4$ 258.9606, found 258.9609.

(*E*)-Methyl-3-(5-bromo-6-oxo-6*H*-pyran-3-yl)acrylate (*E*)-12. Prepared with the same procedure as described for (*Z*)-**12**, in 80% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 2.2 Hz, 1H), 7.69 (d, J = 2.2 Hz, 1H), 7.32 (d, J = 16.1 Hz, 1H), 6.21 (d, J = 15.8 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 157.1, 152.0, 140.9, 135.3, 119.3, 116.5, 113.8, 52.2; FT-IR (CH_2Cl_2) 3068, 2960, 1736, 1732 cm^{-1}; HRMS (M + 1)$^+$ calcd for $C_9H_8BrO_4$ 258.9606, found 258.9608.

13a. A solution of 0.1 g (0.39 mmol) of (*Z*)-**12** and 0.1 mL (1.16 mmol, 3 equiv) of allyl vinyl ether in 1.3 mL of toluene was heated at 110 °C in a sealed tube. After 12 h, the reaction mixture was concentrated and chromatographed (hexane:EtOAc = 5:1) to give **13a** in 69% yield: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (dd, J = 6.6, 2.9 Hz, 1H), 5.17 (dd, J = 2.8, 2.4 Hz, 1H), 4.32−4.28 (m, 1H), 3.71 (s, 3H), 3.63 (dd, J = 12.0, 6.0 Hz, 1H), 3.40−3.35 (m, 1H), 3.32−3.28 (m, 1H), 2.98−2.91 (m, 1H), 2.87 (s, 1H), 2.56 (ddd, J = 15.4, 9.5, 2.9 Hz, 1H), 2.32 (ddd, J = 15.0, 6.2, 5.9 Hz, 1H), 2.10 (ddd, J = 15.4, 2.2, 1.5 Hz, 1H), 1.60 (ddd, J = 15.0, 9.2, 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 168.3, 137.3, 119.6, 77.0, 71.9, 64.1, 60.6, 52.8, 40.8, 39.2, 36.5, 30.5, 25.0; FT-IR (CH_2Cl_2) 2950, 2361, 2330, 1729 cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{14}H_{15}BrNaO_5$ 365.0001, found 365.0007.

13b: 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (dd, J = 5.5, 2.9 Hz, 1H), 5.17 (dd, J = 2.6, 2.6 Hz, 1H), 4.29 (d, J = 10.6 Hz, 1H), 3.87 (dd, J = 12.5, 5.5 Hz, 1H), 3.71 (s, 3H), 3.70−3.61 (m, 2H), 3.51 (dd, J = 12.2, 11.7 Hz, 1H), 3.19 (ddd, J = 8.1, 5.9, 2.2 Hz, 1H), 3.01−2.95 (m, 1H), 2.87−2.86 (m, 1H), 2.58−2.51 (m, 2H), 2.06 (ddd, J = 15.4, 2.2, 1.1 Hz, 1H), 0.88 (s, 9H), 0.05 (d, J = 5.5 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 168.2, 136.4, 120.3, 77.0, 72.1, 64.8, 63.7, 59.2, 52.7, 42.8, 42.0, 41.1, 37.2, 34.0, 26.0, 18.3, −5.4, −5.6; FT-IR (CH_2Cl_2) 2953, 2857, 2361, 1738 cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{21}H_{31}BrNaO_6Si$ 509.0971, found 509.0977.

13c: 65% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (dd, J = 4.4, 2.6 Hz, 1H), 5.21 (dd, J = 2.6, 2.6 Hz, 1H), 4.28 (d, J = 9.9 Hz, 1H), 4.00 (dd, J = 12.5, 5.5 Hz, 1H), 3.70 (s, 3H), 3.61 (s, 2H), 3.49 (dd, J = 12.1, 11.7 Hz, 1H), 3.37 (dd, J = 3.7, 3.3 Hz, 1H), 2.98 (s, 1H), 2.64−2.58 (m, 1H), 2.55 (ddd, J = 15.4, 9.9, 2.6 Hz, 1H), 2.02 (d, J = 15.4 Hz, 1H), 0.94 (s, 3H), 0.91 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 168.5, 135.2, 120.0, 77.2, 71.9, 68.9, 65.2, 59.8, 52.2, 46.1, 41.1, 40.1, 38.6, 37.7, 26.1, 20.9, 18.4, −5.3, −5.5; FT-IR (CH_2Cl_2) 2953, 2930, 2857, 2361, 1769, 1734 cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{22}H_{33}BrNaO_6Si$ 523.1127, found 523.1135.

13d: 57% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.96 (dd, J = 2.9, 2.6 Hz, 1H), 5.17 (dd, J = 2.6, 2.2 Hz, 1H), 4.30 (d, J = 9.9 Hz, 1H), 3.73 (s, 3H), 3.43 (dd, J = 12.1, 5.9 Hz, 1H), 3.28 (dd, J = 12.1, 11.7 Hz, 1H), 2.96 (ddd, J = 8.4, 4.4, 2.2 Hz, 1H), 2.83−2.77 (m, 1H), 2.56 (ddd, J = 15.4, 9.5, 2.9 Hz, 1H), 2.50 (s, 1H), 2.13 (ddd, J = 15.0, 2.9, 1.5 Hz, 1H), 0.78 (dd, J = 8.4, 1.5 Hz, 1H), 0.06 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 168.5, 136.1, 122.5, 76.8, 71.8, 64.0, 62.4, 52.7, 41.4, 40.7, 35.2, 30.7, 24.0, −2.6; FT-IR (CH_2Cl_2) 2951, 2866, 1760, 1730 cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{17}H_{23}BrNaO_5Si$ 437.0396, found 437.0397.

13e: 20% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.03 (dd, J = 2.9, 2.6 Hz, 1H), 5.13 (dd, J = 2.9, 2.2 Hz, 1H), 4.30 (ddd, J = 9.5, 1.8, 1.5 Hz, 1H), 3.64 (s, 3H), 3.57 (dd, J = 12.5, 6.2 Hz, 1H), 3.54−3.52 (m, 1H), 3.49 (dd, J = 8.1, 7.0 Hz, 1H), 3.11 (dd, J = 12.3, 12.0 Hz, 1H), 2.78−2.72 (m, 1H), 2.54 (ddd, J = 15.4, 9.5, 2.9 Hz, 1H), 2.13 (ddd, J = 15.4, 1.8, 1.5 Hz, 1H), 2.04 (d, J = 12.5 Hz, 1H), 1.88−1.60 (m, 4H), 1.56−1.38 (m, 1H), 1.35−1.12 (m, 4H), 0.88−0.72 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 168.5, 136.6, 122.0, 76.6, 71.9, 63.5, 61.7, 52.7, 44.2, 43.2, 41.7, 41.6, 34.9, 31.9, 31.4, 28.3, 26.7, 26.6, 26.2; FT-IR (CH_2Cl_2) 3057, 2925, 2853, 1733 cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{20}H_{25}BrNaO_5$ 447.0783, found 447.0785.

13f: 67% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.22 (m, 3H), 7.12−7.10 (m, 2H), 6.10 (dd, J = 5.5, 2.9 Hz, 1H), 5.28 (dd, J = 2.6, 2.6 Hz, 1H), 4.33 (d, J = 9.9 Hz, 1H), 3.84 (dd, J = 11.7, 5.5 Hz, 1H), 3.68 (ddd, J = 13.2, 5.5, 2.2 Hz, 1H), 3.48 (dd, J = 12.1, 11.7 Hz, 1H), 3.26 (s, 3H), 3.24−3.22 (m, 1H), 3.18 (dd, J = 8.1, 1.8 Hz, 1H), 3.01−2.95 (m, 1H), 2.61 (ddd, J = 15.4, 9.5, 2.9 Hz, 1H), 2.13 (ddd, J = 15.4, 2.2, 1.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 168.4, 140.8, 138.1, 128.8, 127.7, 127.4, 119.6, 72.2, 64.1, 61.2, 52.0, 45.9, 42.6, 38.2, 37.4, 36.9; FT-IR (CH_2Cl_2) 2357, 2338, 1752, 1736 cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{20}H_{19}BrNaO_5$ 441.0314, found 441.0318.

13g: 60% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.62 (s, 1H), 6.46 (dd, J = 12.5, 1.1 Hz, 1H), 5.91 (d, J = 12.5 Hz, 1H), 5.83−5.82 (m, 1H), 5.43−5.40 (m, 1H), 4.06−3.96 (m, 3H), 3.76 (s, 3H), 2.64 (ddd, J = 14.3, 8.1, 4.0 Hz, 1H), 2.23 (ddd, J = 14.3, 3.7, 1.8 Hz, 1H), 2.08−2.01 (m, 2H), 1.67 (s, 3H), 0.97 (t, J = 7.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 166.0, 140.1, 139.4, 136.5, 132.4, 130.5, 120.5, 75.7, 75.0, 64.4, 51.8, 36.0, 29.7, 21.0, 14.0, 13.9; FT-IR (CH_2Cl_2) 2960, 2927, 2856, 1773, 1772, 1631 cm^{-1}; HRMS (M + Na$^+$) calcd for $C_{17}H_{21}BrNaO_5$ 407.0470, found 407.0464.

14a: 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.17 (dd, J = 2.9, 2.6 Hz, 1H), 5.21 (dd, J = 2.6, 2.6 Hz, 1H), 4.32 (d, J = 9.9 Hz, 1H), 3.75 (s, 3H), 3.55 (dd, J = 12.5, 6.2 Hz, 1H), 3.26 (dd,

J = 12.1, 12.1 Hz, 1H), 3.11−3.07 (m, 1H), 2.92−2.84 (m, 1H), 2.67−2.65 (m, 1H), 2.57 (ddd, J = 15.4, 9.5, 2.9 Hz, 1H), 2.28 (ddd, J = 17.6, 9.5, 7.7 Hz, 1H), 2.15−2.11 (m, 1H), 1.34 (ddd, J = 14.7, 7.3, 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 168.3, 136.3, 121.1, 76.9, 71.8, 63.7, 61.0, 52.7, 41.5, 38.2, 35.2, 27.8, 25.8; FT-IR (CH_2Cl_2) 2953, 2857, 1731 cm^{-1}; HRMS (M + Na^+) calcd for $C_{14}H_{15}BrNaO_5$ 365.0001, found 365.0003.

14b: 64% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (dd, J = 2.6, 2.2 Hz, 1H), 5.18 (dd, J = 2.6, 2.2 Hz, 1H), 4.29 (d, J = 10.3 Hz, 1H), 3.85 (dd, J = 12.1, 12.1 Hz, 1H), 3.74−3.70 (m, 2H), 3.67 (s, 3H), 3.59 (dd, J = 9.9, 7.7 Hz, 1H), 3.45 (ddd, J = 9.2, 2.6, 2.2 Hz, 1H), 2.91 (ddd, J = 13.2, 9.2, 4.0 Hz, 1H), 2.66 (s, 1H), 2.52 (ddd, J = 15.0, 9.2, 2.9 Hz, 1H), 2.42 (ddd, J = 17.2, 8.1, 4.0 Hz, 1H), 2.11 (ddd, J = 15.4, 2.2, 1.1 Hz, 1H), 0.87 (s, 9H), 0.03 (d, J = 7.3 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 168.4, 136.1, 121.1, 77.0, 72.2, 64.9, 61.5, 59.1, 52.3, 43.1, 41.7, 41.5, 36.5, 30.5, 26.0, 18.3, −5.3, −5.4; FT-IR (CH_2Cl_2) 2932, 2858, 1768, 1735 cm^{-1}; HRMS (M + Na^+) calcd for $C_{21}H_{31}BrNaO_6Si$ 509.0971, found 509.0978.

14c: 69% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.11 (dd, J = 2.6, 2.6 Hz, 1H), 5.20 (dd, J = 2.6, 2.2 Hz, 1H), 4.29 (d, J = 9.9 Hz, 1H), 3.80−3.67 (m, 2H), 3.69 (s, 3H), 3.43 (dd, J = 18.7, 9.9 Hz, 2H), 2.81 (dd, J = 2.6, 2.2 Hz, 1H), 2.74 (s, 1H), 2.57−2.49 (m, 2H), 2.12 (dd, J = 15.4, 1.1 Hz, 1H), 1.24 (s, 3H), 0.87 (s, 9H), 0.01 (d, J = 2.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 168.7, 136.1, 122.3, 77.0, 72.0, 65.6, 64.6, 59.2, 52.2, 49.0, 42.2, 40.5, 39.2, 35.8, 26.1, 26.0, 18.3, −5.5; FT-IR (CH_2Cl_2) 2954, 2857, 1771, 1735 cm^{-1}; HRMS (M + Na^+) calcd for $C_{22}H_{33}BrNaO_6Si$ 523.1127, found 523.1132.

14d: 66%yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.97 (dd, J = 2.9, 2.6 Hz, 1H), 5.19 (dd, J = 2.6, 2.6 Hz, 1H), 4.31 (d, J = 3.9 Hz, 1H), 3.74 (s, 3H), 3.45 (dd, J = 12.1, 5.9 Hz, 1H), 3.29 (dd, J = 12.1, 11.7 Hz, 1H), 2.99−2.95 (m, 1H), 2.84−2.78 (m, 1H), 2.57 (ddd, J = 15.4, 9.5, 2.9 Hz, 1H), 2.51 (s, 1H), 2.14 (dd, J = 15.4, 1.5 Hz, 1H), 0.80 (dd, J = 8.4, 1.1 Hz, 1H), 0.07 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 168.5, 136.1, 122.5, 77.0, 71.8, 64.0, 62.4, 52.7, 41.4, 40.7, 35.2, 30.7, 29.9, −2.6; FT-IR (CH_2Cl_2) 2950, 2866, 1760, 1736 cm^{-1}; HRMS (M + Na^+) calcd for $C_{17}H_{23}BrNaO_5Si$ 437.0396, found 437.0392.

14e: 76% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 (dd, J = 2.9, 2.6 Hz, 1H), 5.18 (dd, J = 2.6, 2.6 Hz, 1H), 4.32 (d, J = 9.9 Hz, 1H), 3.76 (s, 3H), 3.45 (dd, J = 12.1, 5.9 Hz, 1H), 3.25−3.22 (m, 1H), 3.01−2.97 (m, 1H), 2.77−2.73 (m, 1H), 2.60 (s, 1H), 2.55 (ddd, J = 8.8, 5.9, 2.9 Hz, 1H), 2.13 (d, J = 15.0 Hz, 1H), 1.81−1.71 (m, 4H), 1.56−1.38 (m, 2H), 1.35−1.12 (m, 5H), 1.04−0.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 168.5, 136.6, 122.0, 76.6, 71.9, 63.5, 61.7, 52.7, 44.2, 43.2, 41.7, 41.6, 34.9, 31.9, 31.4, 28.3, 26.7, 26.6; FT-IR (CH_2Cl_2) 3057, 2925, 2853, 1733 cm^{-1}; HRMS (M + Na^+) calcd for $C_{20}H_{25}BrNaO_5$ 447.0783, found 447.0789.

14f: 66% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36−7.32 (m, 2H), 7.28 (ddd, J = 6.2, 1.5, 1.1 Hz, 1H), 7.17−7.15 (m, 2H), 6.13 (dd, J = 2.9, 2.9 Hz, 1H), 5.27 (dd, J = 2.6, 2.6 Hz, 1H), 4.34 (d, J = 9.5 Hz, 1H), 3.72 (dd, J = 12.5, 6.2 Hz, 1H), 3.63 (s, 3H), 3.37−3.35 (m, 1H), 3.26 (ddd, J = 8.1, 4.4, 2.6 Hz, 1H), 3.03−2.98 (m, 1H), 2.97−2.91 (m, 1H), 2.63 (dd, J = 8.1, 1.5 Hz, 1H), 2.59 (dd, J = 9.5, 2.9 Hz, 1H), 2.20 (ddd, J = 15.0, 1.8, 1.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 168.3, 143.6, 137.1, 129.3, 127.5, 127.3, 121.5, 76.6, 71.8, 63.1, 61.0, 52.6, 48.1, 44.7, 41.0, 37.6, 35.0; FT-IR (CH_2Cl_2) 2952, 1769, 1737 cm^{-1}; HRMS (M + Na^+) calcd for $C_{20}H_{19}BrNaO_5$ 441.0314, found 441.0329.

14g: 62% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 16.1 Hz, 1H), 6.64 (s, 1H), 6.08 (d, J = 16.1 Hz, 1H), 5.44 (dd, J = 2.2, 1.8 Hz, 1H), 5.42−5.39 (m, 1H), 4.03−3.95 (m, 3H), 3.79 (s, 3H), 2.67 (ddd, J = 13.9, 7.7, 4.0 Hz, 1H), 2.04 (quintet, J = 7.3 Hz, 2H), 1.78 (ddd, J = 13.9, 1.8, 1.5 Hz, 1H), 1.65 (s, 3H), 0.96 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 166.0, 140.1, 139.4, 136.5, 132.4, 130.5, 120.5, 75.7, 75.0, 64.4, 51.8, 36.0, 29.7, 21.0, 14.0, 13.9; FT-IR (CH_2Cl_2) 2962, 2872, 1776, 1719, 1635 cm^{-1}; HRMS (M + Na^+) calcd for $C_{17}H_{21}BrNaO_5$ 407.0470, found 407.0460.

Acknowledgment. This work was supported by a grant of the Korean Science and Technology Foundation (KOSEF, R01-2006-000-11283-0). C.S.-I. thanks the BK21 fellowship.

Supporting Information Available: Spectral data of tandem cycloadducts **13a**−**13g**, **14a**−**14g**, and precursors (*Z*)-**12** and (*E*)-**12**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO061119E