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Stereoselective Synthesis of the Naturally Occurring Styryllactones (+)-Goniofufurone and (+)-Cardiobutanolide

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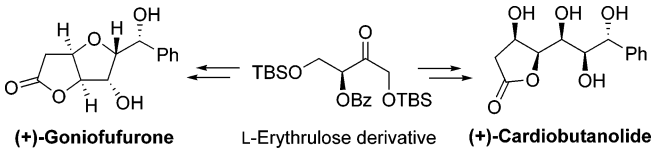

The naturally occurring γ-lactones (+)-goniofufurone **1** and (+)-cardiobutanolide **2**, two pharmacologically active products from *Goniothalamus* species (Annonaceae), have been synthesized in enantiopure form using L-erythrulose as the chiral starting material. Key steps of these syntheses were a stereoselective *anti* boron aldol reaction and an asymmetric allylboration.

Introduction

The plant family Annonaceae, with its about 128 genera and over 2000 species, has for a long time aroused a considerable interest from a pharmacological point of view, most particularly because of its polyketide constituents.[1] One of its most notorious representatives, the Indomalayan genus *Goniothalamus* has given rise to the isolation of a range of compounds endowed with cytotoxic, pesticidal, teratogenic, and other various biological properties.[2] Two of these compounds are (+)-goniofufurone **1** and (+)-cardiobutanolide **2** (Figure 1). The former was isolated in 1990 from *Goniothalamus giganteus* and found to display significant cytotoxic properties.[3,4] Not surprisingly, it has been the object of numerous synthetic efforts,

1 **2**

FIGURE 1. Structures of (+)-goniofufurone **1** and (+)-cardiobutanolide **2**.

not only toward the natural product but also toward several stereoisomers thereof.[5] Cardiobutanolide has very recently been isolated from *Goniothalamus cardiopetalus*.[6] No synthesis has been reported so far for this compound. Within our general interest in the application of aldol reactions to the stereoselective synthesis of bioactive natural compounds,[7] we have now achieved a synthesis of these two natural styryllactones in enantiopure form.

Lactones **1** and **2** contain five contiguous stereocenters and display a clear structural similarity. In fact, **1** may be formally derived from **2** through dehydration between the hydroxyl groups at C-3 and C-6 with cyclic ether formation and configurational retention at both ends. We thus wanted to design a divergent synthesis for both compounds from a common intermediate. Among other methods,[8] a tetrahydrofuran system can be formed through internal 5-*exo*-tet nucleophilic displacement of a suitable leaving group by a hydroxyl function with subsequent configurational inversion. Accordingly, we envisaged the retrosynthetic concept depicted in Scheme

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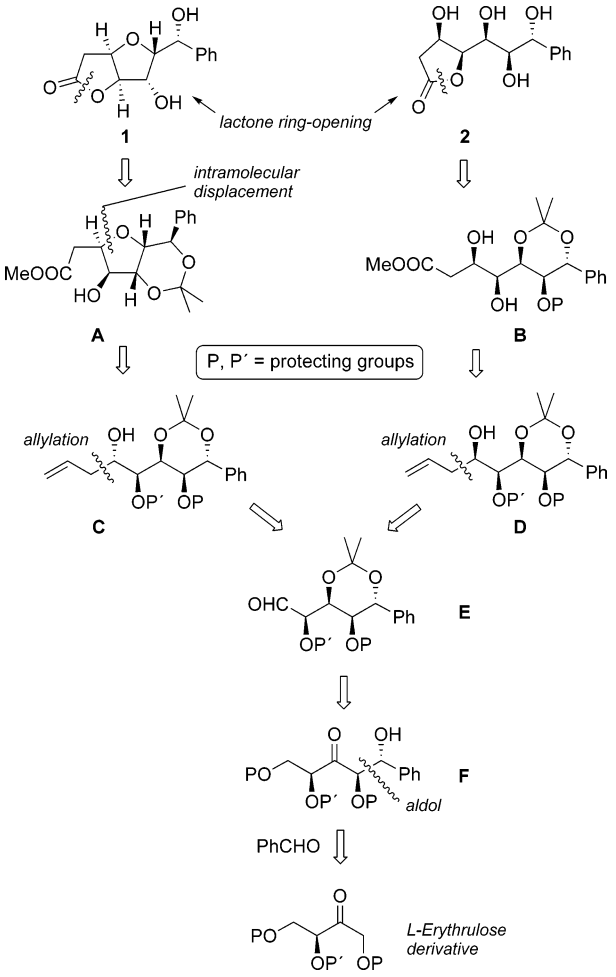
SCHEME 1. Retrosynthetic Plan for Compounds 1 and 2



1. For both compounds, lactone ring-opening and, in the case of **1**, intramolecular displacement would give rise via, respectively, **A** and **B**, to the two epimeric homoallyl alcohols **C** and **D**. These can be prepared from the same precursor aldehyde **E** by means of asymmetric allylation. Compound **E** in turn can be referred to β-hydroxy ketone **F** via standard functional manipulations. The structural features of **F** suggest that it can be obtained by means of an *anti*-aldol addition with a suitably protected L-erythrulose derivative[7d] as the chiral starting material.

Results and Discussion

The synthesis of **1** and **2** is shown in Scheme 2. The common starting material was acetonide **4**, obtained via an *anti* boron aldol reaction of L-erythrulose derivative **3** with benzaldehyde,[7d] followed by functional manipulation.[9] Interchange of protecting groups in compound **4** gave **6**, which was then selectively desilylated with the HF−pyridine complex[10] to primary alcohol **7**. Swern oxidation of the latter gave aldehyde **8**, which was used in crude form in either of the two following allylation steps. The chiral allylborane generated from (−)-DIP−Cl and allymagnesium bromide[11] reacted with **8** to yield homoallyl alcohol **9**. The epimeric alcohol **13** (see below) was not present in the reaction mixture as judged by means of NMR detection. The free hydroxyl group of **9** was then mesylated, and mesylate **10** was treated with TBAF (Scheme 2). This treatment not only caused desilylation but also intramolecular nucleophilic attack of the generated alkoxide anion to the mesylate-bearing carbon, with configurational inversion at the latter and formation of the tetrahydrofuran ring. Compound **11** was then subjected to ozonolytic cleavage of the olefinic double bond in alkaline medium[12] to yield methyl ester **12**. Treatment of the latter with boron trifluoride etherate and dimethyl sulfide[13] caused complete elimination of the two acetal protecting groups and, in addition, in situ lactonization to give (+)-goniofufurone **1**.

Aldehyde **8** was also a key intermediate in the synthesis of cardiobutanolide. Thus, allylation of **8** with (+)-DIP−Cl and allymagnesium bromide[11] exclusively provided homoallyl alcohol **13**. Silylation of the hydroxyl group and oxidative cleavage of the olefinic bond furnished methyl ester **15**. Finally, cleavage of all protecting groups in **15** and subsequent lactonization yielded (+)-cardiobutanolide **2**, with spectral properties identical to those reported in the literature.[6]

Conclusion

We have performed a divergent, stereoselective synthesis of the natural γ-lactones (+)-goniofufurone **1** and (+)-cardiobutanolide **2**. The chiral starting material was the protected L-erythrulose derivative **3**,[7d] which has again been shown to be a useful chiral d^4 synthon that maximizes atom economy.[14] Furthermore, this is the first synthesis of cardiobutanolide reported so far.

Experimental Section

(1*S*)-2-(*tert*-Butyldimethylsilyloxy)-1-[(4*R*,5*R*,6*R*)-5-(*tert*-butyldimethylsilyloxy)-2,2-dimethyl-6-phenyl-[1,3]dioxan-4-yl]ethanol (5). Oil; $[\alpha]_D$ +4 (*c* 1.4, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 4.54 (d, 1H, J = 7.3 Hz), 4.27 (dd, 1H, J = 4.5, 2 Hz), 4.23 (dd, 1H, J = 7.3, 4.5 Hz), 3.95 (m, 1H), 3.75 (dd, 1H, J = 9.4, 8.4 Hz), 3.66 (dd, 1H, J = 9.4, 4.6 Hz), 3.40 (br s, 1H, OH), 1.52 (s, 3H), 1.40 (s, 3H), 0.93 (s, 9H), 0.83 (s, 9H), 0.10 (s, 6H), 0.00 (s, 3H), −0.62 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.3, 101.3, 18.2, 17.8 (C), 128.5 (x 2), 128.4 (x 3), 78.3, 77.0, 71.5, 69.1 (CH), 62.3 (CH_2), 25.9 (x 3), 25.8 (x 4), 24.4, −4.7, −5.5 (x 2), −5.6 (CH_3). IR ν_{max} 3550 (br, OH) cm^{-1}. HR FAB MS *m/z* 519.2942 $(M + Na)^+$; calcd for $C_{26}H_{48}NaO_5Si_2$, 519.2938.

(4*R*,5*R*,6*R*)-5-(*tert*-Butyldimethylsilyloxy)-4-[(1*S*)-2-(*tert*-butyldimethylsilyloxy)-1-(methoxymethoxy)ethyl]-2,2-dimethyl-6-phenyl-[1,3]dioxane (6). Solid, mp 51−52 °C (from hexanes−Et_2O); $[\alpha]_D$ −12.2 (*c* 1.4, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 4.84 (d, 1H, J = 6.5 Hz), 4.78 (d, 1H, J = 6.5 Hz), 4.60 (d, 1H, J = 5.5 Hz), 4.20 (m, 2H), 3.89 (m,

(9) Acetonide **4** corresponds to compound **9b** in ref 7d.

(10) See, for example: Cuzzupe, A. N.; Hutton, C. A.; Lilly, M. J.; Mann, R. K.; McRae, K. J.; Zammit, S. C.; Rizzacasa, M. A. *J. Org. Chem*. **2001**, *66*, 2382−2393.

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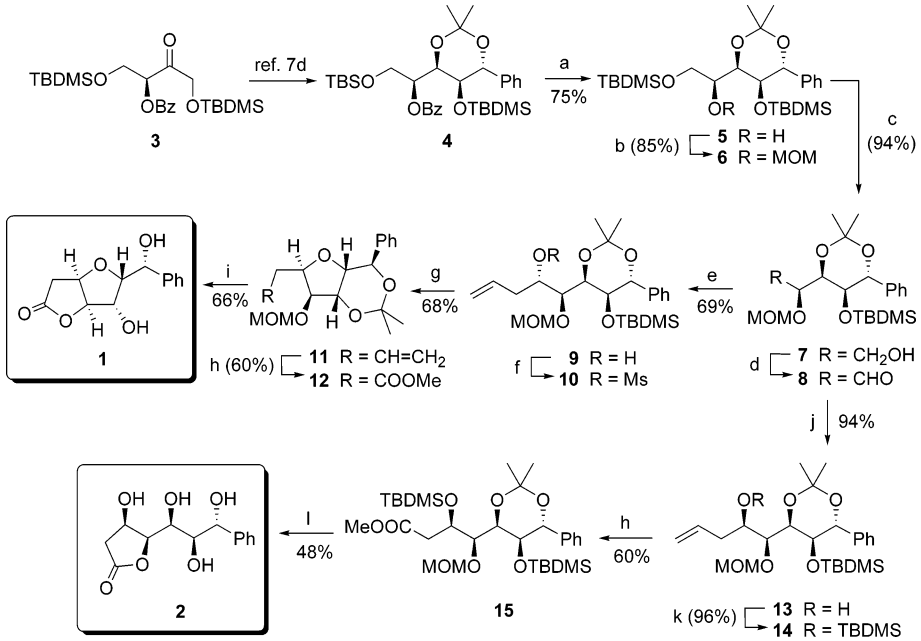
SCHEME 2. Stereoselective Synthesis of Goniofufurone 1 and Cardiobutanolide 2[a]



[a] Reagents and conditions: (a) Excess K_2CO_3, MeOH, rt, 24 h. (b) MOMCl, EtN*i*Pr$_2$, CH_2Cl_2, Δ, 12 h. (c) HF-py, py/THF, rt, 12 h. (d) Swern oxidation, the crude aldehyde **8** is used in the subsequent allylation step (overall yields are given for the two consecutive steps). (e) AllylBIpc$_2$ from (−)-DIP−Cl and allylmagnesium bromide, Et_2O, −90 °C, 1 h. (f) MsCl, Et_3N, DMAP, CH_2Cl_2, rt, 1 h. (g) TBAF, THF, rt, 24 h (overall yield given for the two consecutive steps). (h) O_3, CH_2Cl_2, 2.5 M NaOH/MeOH, −78 °C. (i) $BF_3{\cdot}Et_2O$, SMe_2, −10 °C, 40 min. (j) AllylBIpc$_2$ from (+)-DIP−Cl, Et_2O, −90 °C, 1 h. (k) TBDMSOTf, 2,6-lutidine, rt, CH_2Cl_2, 4 h. (l) (1) $BF_3{\cdot}Et_2O$, SMe_2, −10 °C, 5 min; (2) aq TFA, rt, 24 h; (3) CSA (cat.), toluene, 80 °C, 4 h. Abbreviations and acronyms: DIP−Cl = diisopinocampheylboron chloride; TBAF = tetra-*n*-butylammonium fluoride hydrate; CSA = camphorsulfonic acid.

1H), 3.83 (dd, 1H, J = 10.8, 3 Hz), 3.78 (dd, 1H, J = 10.8, 4.7 Hz), 3.43 (s, 3H), 1.52 (s, 3H), 1.39 (s, 3H), 0.91 (s, 9H), 0.84 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H), −0.14 (s, 3H), −0.32 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.0, 100.9, 18.3, 18.2 (C), 128.5 (x 2), 128.4 (x 2), 128.3, 77.8, 77.0, 74.5, 72.0 (CH), 97.3, 63.4 (CH_2), 55.5, 26.0 (x 3), 25.9 (x 3), 25.8, 24.4, −4.0, −4.8, −5.4, −5.5 (CH_3). HR EIMS *m/z* (% rel intensity) 525.3003 (M^+ − Me, 1), 363 (100), 319 (45), 279 (90); calcd for $C_{28}H_{52}O_6Si_2$ − Me, 525.3067.

(2*S*)-2-[(4*R*,5*R*,6*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,2-dimethyl-6-phenyl-[1,3]dioxan-4-yl]-2-(methoxymethoxy)-ethanol (7). Oil; $[\alpha]_D$ −37.4 (*c* 1.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 4.82 (d, 1H, J = 6.5 Hz), 4.77 (d, 1H, J = 6.5 Hz), 4.56 (d, 1H, J = 6 Hz), 4.22 (dd, 1H, J = 6, 3.5 Hz), 4.14 (dd, 1H, J = 8.3, 3.5 Hz), 3.92 (ddd, 1H, J = Hz), 3.79 (dd, 1H, J = 11.7, 2.5 Hz), 3.65 (dd, 1H, J = 11.7, 5.4 Hz), 3.44 (s, 3H), 2.90 (br s, 1H, OH), 1.52 (s, 3H), 1.38 (s, 3H), 0.84 (s, 9H), −0.15 (s, 3H), −0.36 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.5, 101.1, 18.2 (C), 128.6 (x 2), 128.5 (x 2), 128.4, 78.7, 77.8, 74.4, 72.2 (CH), 97.6, 62.6 (CH_2), 55.8, 26.0 (x 3), 25.6, 24.1, −4.0, −4.8 (CH_3). IR ν_{max} 3470 (br, OH) cm^{-1}. HR EIMS *m/z* (% rel intensity) 411.2231 (M^+ − Me, 8), 231 (100), 177 (25); calcd for $C_{22}H_{38}O_6Si$ − Me, 411.2197.

(1*S*,2*S*)-1-[(4*R*,5*R*,6*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,2-dimethyl-6-phenyl-[1,3]dioxan-4-yl]-1-(methoxymethoxy)-pent-4-en-2-ol (9). Oil; $[\alpha]_D$ −43.2 (*c* 0.7, $CHCl_3$).^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 5.95 (m, 1H), 5.15 (dd, 1H, J = 17.2, 1.8 Hz), 5.11 (dd, 1H, J = 10.2, 1.8 Hz), 4.80 (d, 1H, J = 6.5 Hz), 4.78 (d, 1H, J = 6.5 Hz), 4.60 (d, 1H, J = 5.6 Hz), 4.17 (dd, 1H, J = 5.6, 3.2 Hz), 4.10 (dd, 1H, J = 7.5, 3.2 Hz), 3.93 (m, 2H), 3.44 (s, 3H), 3.10 (d, 1H, J = 7 Hz, OH), 2.35 (t, 2H, J = 6.5 Hz), 1.53 (s, 3H), 1.38 (s, 3H), 0.85 (s, 9H), −0.10 (s, 3H), −0.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6, 101.2, 18.2 (C), 135.6, 128.6 (x 2), 128.5, 128.4 (x 2), 81.9, 78.1, 74.3, 72.7, 70.0 (CH), 117.1, 98.9, 37.4 (CH_2), 56.1, 26.0 (x 3), 25.8, 24.1, −4.0, −4.8 (CH_3). IR ν_{max} 3460 (br, OH) cm^{-1}. HR FAB MS *m/z* 489.2724 (M + Na)$^+$; calcd for $C_{25}H_{42}NaO_6Si$, 489.2649.

(4*R*,4a*R*,6*R*,7*S*,7a*S*)-6-Allyl-7-methoxymethoxy-2,2-dimethyl-4-phenyl-tetrahydrofuro[3,2-*d*][1,3]dioxine (11). Oil; $[\alpha]_D$ +0.7 (*c* 0.75, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, 2H, J = 8 Hz), 7.32 (t, 2H, J = 8 Hz), 7.23 (t, 1H, J = 8 Hz), 5.85 (m, 1H), 5.15 (dd, 1H, J = 17.2, 1.8 Hz), 5.07 (dd, 1H, J = 10.2, 1.8 Hz), 4.76 (d, 1H, J = 6.8 Hz), 4.66 (d, 1H, J = 6.8 Hz), 4.55 (d, 1H, J = 8.5 Hz), 4.42 (d, 1H, J = 5 Hz), 4.33 (dd, 1H, J = 8.5, 5 Hz), 4.25 (dt, 1H, J = 7, 3 Hz), 4.07 (d, 1H, J = 3 Hz), 3.38 (s, 3H), 2.47 (m, 2H), 1.43 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 140.3, 100.8 (C), 134.8, 128.4 (x 2), 127.6, 126.4 (x 2), 82.5, 81.6, 80.1, 75.4, 71.0 (CH), 116.9, 96.3, 32.8 (CH_2), 56.0, 24.8, 24.0 (CH_3). HR EIMS *m/z* (% rel intensity) 319.1511 (M^+ − Me, 1), 363 (100), 319 (45), 279 (90); calcd for $C_{19}H_{26}O_5$ − Me, 319.1545.

Methyl (4*R*,4a*R*,6*R*,7*S*,7a*S*)-2-(7-Methoxymethoxy-2,2-dimethyl-4-phenyltetrahydrofuro[3,2-*d*][1,3]dioxin-6-yl)-acetate (12). Oil; $[\alpha]_D$ −17.3 (*c* 1.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, 2H, J = 8 Hz), 7.34 (t, 2H, J = 8 Hz), 7.27 (t, 1H, J = 8 Hz), 4.75 (d, 1H, J = 6.8 Hz), 4.65 (dt, 1H, J = 7, 3.3 Hz), 4.62 (d, 1H, J = 6.8 Hz), 4.57 (d, 1H, J = 8.5 Hz), 4.44 (d, 1H, J = 5 Hz), 4.33 (dd, 1H, J = 8.5, 5 Hz), 4.23 (d, 1H, J = 3.3 Hz), 3.70 (s, 3H), 3.38 (s, 3H), 2.76 (d, 2H, J = 7 Hz), 1.45 (s, 3H), 1.45 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 140.1, 100.8 (C), 128.4 (x 2), 127.6, 126.4 (x 2), 82.7, 81.7, 76.7, 75.5, 71.0 (CH), 96.3, 33.6 (CH_2), 55.9, 51.7, 24.8, 24.0 (CH_3). IR ν_{max} 1740 (C=O) cm^{-1}. HR FAB MS *m/z* 367.1779 (M + H$^+$); calcd for $C_{19}H_{27}O_7$, 367.1757.

(+)-Goniofufurone (1). Colorless crystals, mp 154−156 °C (from hexanes−EtOAc), lit.[3] mp 152−154 °C); $[\alpha]_D$ +39.5 (*c* 1, $CHCl_3$), lit.[5m] $[\alpha]_D$ +44.9 (*c* 1.12, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45−7.30 (m, 5H), 5.19 (d, 1H, J = 4.8 Hz), 5.10 (dd, 1H, J = 5.7, 4.2 Hz), 4.86 (d, 1H, J = 4.2 Hz), 4.40 (d, 1H, J = 2.7 Hz), 4.10 (dd, 1H, J = 4.8, 2.7 Hz), 2.74 (dd, 1H, J = 18.8, 5.7 Hz), 2.68 (d, 1H, J = 18.8 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.3, 139.1 (C), 128.8 (x 2), 128.4, 126.0 (x 2), 87.5, 83.1, 77.4, 74.6, 73.5 (CH), 36.1 (CH_2). IR ν_{max} 3340 (br, OH), 1755 (C=O) cm^{-1}. EIMS *m/z* (% rel intensity) 251 (M + H$^+$, 1), 233 (M + H$^+$

− H_2O, 11), 126 (60), 107 (100), 79 (64). The spectral features of synthetic **1** were identical to those of the natural compound.[3,5m]

(1*S*,2*R*)-1-[(4*R*,5*R*,6*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,2-dimethyl-6-phenyl-[1,3]dioxan-4-yl]-1-(methoxymethoxy)-pent-4-en-2-ol (13). Colorless solid, mp 71−72 °C (from hexanes−Et_2O); $[\alpha]_D$ −46 (*c* 1.4, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 5.93 (m, 1H), 5.15 (dd, 1H, J = 17.2, 1.5 Hz), 5.12 (dd, 1H, J = 10.2, 1.5 Hz), 4.96 (d, 1H, J = 6.6 Hz), 4.76 (d, 1H, J = 6.6 Hz), 4.58 (d, 1H, J = 5.5 Hz), 4.36−4.30 (m, 2H), 3.80−3.74 (m, 2H), 3.46 (s, 3H), 2.47 (m, 1H), 2.33 (m, 1H), 2.20 (d, 1H, J = 8 Hz, OH), 1.52 (s, 3H), 1.38 (s, 3H), 0.84 (s, 9H), −0.17 (s, 3H), −0.34 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6, 101.0, 18.2 (C), 135.0, 128.6 (x 2), 128.5 (x 2), 128.4, 78.8, 78.0, 76.8, 73.2, 70.0 (CH), 117.7, 98.3, 39.5 (CH_2), 56.4, 26.0 (x 3), 25.7, 24.2, −3.8, −4.7 (CH_3). IR ν_{max} 3460 (br, OH) cm^{-1}. HR EIMS *m/z* (rel intensity) 451.2430 (M^+ − Me, 1), 231 (88), 177 (100), 105 (90); calcd for $C_{25}H_{42}O_6Si$ − Me, 451.2515.

(4*R*,5*R*,6*R*)-5-(*tert*-Butyldimethylsilyloxy)-4-[(1*R*,2*R*)-2-(*tert*-butyldimethylsilyloxy)-1-(methoxymethoxy)pent-4-enyl]-2,2-dimethyl-6-phenyl-[1,3]dioxane (14). Oil; $[\alpha]_D$ −44 (*c* 1.7; $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 5.92 (m, 1H), 5.11 (dd, 1H, J = 17.2, 1.5 Hz), 5.05 (dd, 1H, J = 10.2, 1.5 Hz), 4.95 (d, 1H, J = 6.6 Hz), 4.75 (d, 1H, J = 6.6 Hz), 4.60 (d, 1H, J = 6 Hz), 4.40 (dd, 1H, J = 7, 3.5 Hz), 4.24 (dd, 1H, J = 6, 3.5 Hz), 3.99 (dt, 1H, J = 6.5, 2.9 Hz), 3.75 (dd, 1H, J = 7, 2.9 Hz), 3.46 (s, 3H), 2.56 (m, 1H), 2.43 (m, 1H), 1.52 (s, 3H), 1.40 (s, 3H), 0.95 (s, 9H), 0.84 (s, 9H), 0.16 (s, 3H), 0.13 (s, 3H), −0.12 (s, 3H), −0.42 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.9, 101.0, 18.3, 18.2 (C), 135.6, 128.5 (x 2), 128.4 (x 2), 128.3, 78.0, 77.8, 75.0, 72.9, 72.0 (CH), 117.2, 98.5, 38.8 (CH_2), 56.2, 26.2 (x 6), 25.7, 24.3, −3.1, −3.8, −3.9, −4.0 (CH_3). HR EIMS *m/z* (rel intensity) 565.3446 (M^+ − Me, 12), 403 (16), 231 (100); calcd for $C_{31}H_{56}O_6Si_2$ − Me, 565.3380.

Methyl (3*R*,4*R*)-3-(*tert*-Butyldimethylsilyloxy)-4-[(4*R*,5*R*,6*R*)-5-(*tert*-butyldimethylsilyloxy)-2,2-dimethyl-6-phenyl-[1,3]dioxan-4-yl]-(4-methoxymethoxy)butyrate (15). Oil; $[\alpha]_D$ −26.8 (*c* 2; $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.30 (m, 5H), 4.95 (d, 1H, J = 6.6 Hz), 4.72 (d, 1H, J = 6.6 Hz), 4.59 (d, 1H, J = 6.5 Hz), 4.52 (m, 1H), 4.43 (dd, 1H, J = 5.5, 4 Hz), 4.22 (dd, 1H, J = 6.5, 4 Hz), 3.73 (dd, 1H, J = 5.5, 3.3 Hz), 3.68 (s, 3H), 3.44 (s, 3H), 2.72 (m, 2H), 1.51 (s, 3H), 1.41 (s, 3H), 0.91 (s, 9H), 0.82 (s, 9H), 0.13 (s, 3H), 0.07 (s, 3H), −0.06 (s, 3H), −0.50 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 139.7, 101.1, 18.2 (x 2) (C), 128.6 (x 2), 128.5 (x 2), 128.4, 78.7, 77.6, 75.4, 71.0, 69.9 (CH), 98.4, 39.5 (CH_2), 56.2, 51.4, 26.1 (x 3), 26.0 (x 3), 25.4, 24.6, −4.1, −4.2, −4.3, −4.5 (CH_3). IR ν_{max} 1742 (C=O) cm^{-1}. HR EIMS *m/z* (rel intensity) 597.3313 (M^+ − Me, 1), 555 (M^+ − *t*Bu, 2), 231 (100), 177 (26), 73 (60); calcd for $C_{31}H_{56}O_8Si_2$ − Me, 597.3279.

Cardiobutanolide (2). Colorless crystals, mp 196−198 °C (from acetone), lit.[6] mp 189−190 °C; $[\alpha]_D$ +5.5 (*c* 0.3; MeOH), lit.[6] $[\alpha]_D$ +6.4 (*c* 0.28; MeOH). ^1H NMR (500 MHz, Me_2CO-d_6) δ 7.44 (br d, 1H, J = 7.5 Hz), 7.30 (br t, 7.5 Hz, 1H), 7.23 (br t, 1H, J = 7.5 Hz), 4.80 (dd, 1H, J = 7.3, 5 Hz), 4.70 (d, 1H, J = 5 Hz, OH), 4.62 (br s, 2H), 4.55 (dd, 1H, J = 7.5, 3 Hz), 4.39 (m, 1H), 4.30 (d, 1H, J = 5 Hz, OH), 3.92 (td, 1H, J = 8, 1.5 Hz), 3.80 (d, 1H, J = 8 Hz, OH), 2.82 (m, overlapped by residual water), 2.37 (d, 1H, J = 17 Hz). ^{13}C NMR (125 MHz, Me_2CO-d_6) δ 176.1, 144.2 (C), 128.6, 128.0, 127.8, 86.6, 75.6, 74.2, 70.4, 68.7 (CH), 40.4 (CH_2). IR ν_{max} 3380 (br, OH), 1759 (C=O) cm^{-1}. The spectral features of synthetic **2** were identical to those of the natural compound.[6]

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Supporting Information Available: General information about spectral measurements and experimental procedures and graphical NMR spectra of compounds **1**, **2**, **5**−**7**, **9**, and **11**−**15**. This material is available free of charge via the Internet at http://pubs.acs.org.

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