# Stereoselective Total Synthesis of Crassalactone A, a Natural Cytotoxic Styryl Lactone[1])

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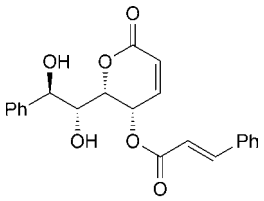
A stereoselective total synthesis of a naturally occurring cytotoxic styryl lactone, crassalactone A (**1**), has been accomplished. The synthesis involves (−)-diisopropyl D-tartrate as the starting material, and the stereoselective additions of *Grignard* reagent and $MeNO_2$ to two chiral aldehyde intermediates as the key steps.

**Introduction.** – *Polyanthia* species are well-known for their valuable constituents with cytotoxic, anti-HIV, antimicrobial, and antimalarial properties [1]. From the cytotoxic AcOEt extract of the leaves and twigs of the plant *Polyanthia crassa*, a styryl lactone, crassalactone A (**1**; *Fig.*), together with several other constituents, have been isolated [2]. The structure of **1** was established on the basis of spectroscopic data, and the absolute configuration by chemical conversions. The cytotoxic effect of **1** was tested, and the compound was found to exhibit broad cytotoxic activity against a panel of mammalian and rat cancer cell lines. Due to fascinating structural features and the impressive bioactivity of **1**, we were interested in its total synthesis. Earlier two syntheses of this compound have been reported [3]. In the first synthesis, (*R*)-mandelic acid was used as the starting material, and $OsO_4$ (which is poisonous and volatile) was employed for *cis*-hydroxylation [3a]. In the second synthesis, 1,5-D-gluconolactone was the starting material, and the overall synthetic time (95 h) was longer [3b]. Herein, we disclose an alternative stereoselective synthesis of **1** without applying $OsO_4$ (used in the first synthesis) and maintaining the synthetic time shorter (59 h) (compared to the second synthesis). We have utilized a different starting material, (−)-diisopropyl D-tartrate, and a different reaction sequence. However, the last step, the lactonization, was analogous to that in the earlier second synthesis [3b].




**1**

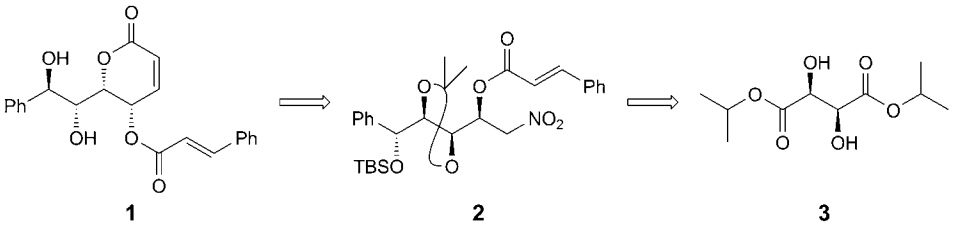
Figure. *Structure of crassalactone A*

[1]) Part 83 of the series, 'Synthetic Studies on Natural Products'.

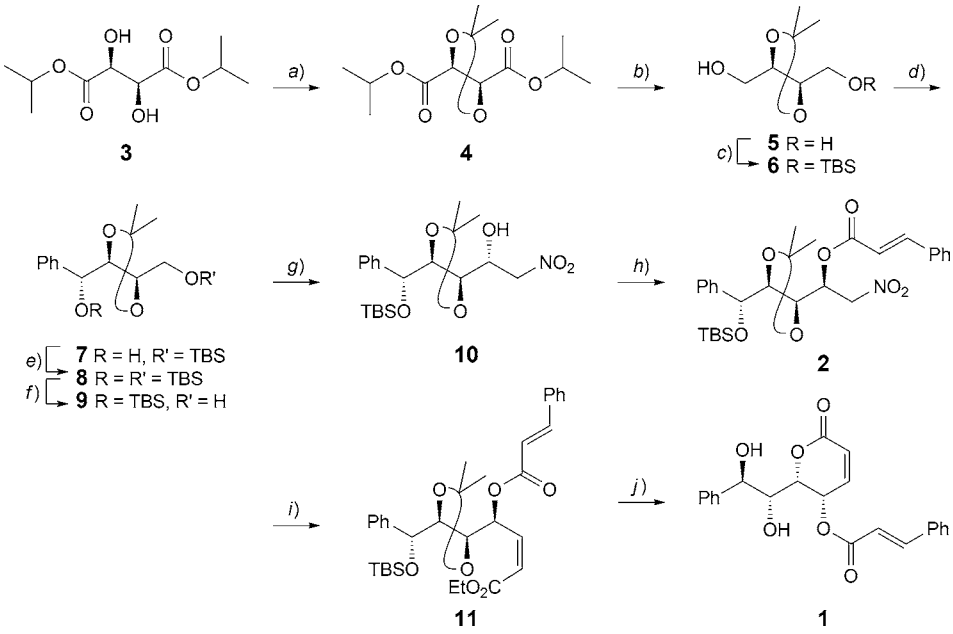
**Results and Discussion.** – In continuation of our works on the stereoselective construction of natural products [4], we have realized that crassalactone A (**1**) can be synthesized from the protected tetrahydroxy compound **2** (*Scheme 1*), which can be derived from the commercially available (−)-diisopropyl D-tartrate (**3**).

Our synthesis (*Scheme 2*) was initiated by protection of two OH groups of **3** by treatment with 2,2-dimethoxypropane (DMP) in toluene in the presence of TsOH to

Scheme 1. *Retrosynthetic Analysis of* **1**




Scheme 2. *Synthesis of* **1**




*a*) 2,2-Dimethoxypropane (DMP), TsOH, toluene, r.t. to reflux, overnight; 92%. *b*) $LiAlH_4$, dry THF, 0° to r.t., 4 h; 88%. *c*) ($^t$Bu)$Me_2SiCl$ (TBSCl), 1*H*-imidazole, $CH_2Cl_2$, 3 h; 93%. *d*) 1) 2-Iodoxybenzoic acid (IBX), DMSO, $CH_2Cl_2$, 0° to r.t., 2 h; 94%. 2) PhMgBr, THF, 6 h; 70%. *e*) TBSCl, 1*H*-imidazole, $CH_2Cl_2$, 4 h; 96%. *f*) Pyridine hydrofluoride (Py · HF), THF, 0°, 2 h; 82%. *g*) 1) IBX, DMSO, $CH_2Cl_2$, 0° to r.t., 2 h; 92%. 2) $MeNO_2$, $K_2CO_3$ (aq.), THF, r.t., overnight; 88%. *h*) Diethyl azodicarboxylate (DEAD), $Ph_3P$, THF, 0° – reflux, 5 h; 79%. *i*) 1) $K_2CO_3$, $KMnO_4$ (aq.), $MgSO_4$, 0°, 1 h. 2) $(F_3CCH_2O)_2P(O)CH_2CO_2Me$, NaH, dry THF, −78°, 1 h; 68% (over two steps). *j*) 3% MeOH/HCl, 0° to r.t., 5 h; 63%.

form the acetonide derivative **4** (*Scheme 2*). The two ester groups of **4** were reduced with $LiAlH_4$ to furnish the diol **5**. One of the OH groups of **5** was protected as the TBS ether **6** by reaction with ($^t$Bu)$Me_2SiCl$ (TBSCl) and 1*H*-imidazole in $CH_2Cl_2$. The free OH group of **6** was oxidized with 2-iodoxybenzoic acid (IBX), and the corresponding aldehyde was treated with PhMgBr to afford compound **7** (dr 95:5). The high selectivity of the reaction was a result of 1,2-chelation control [5]. The major diastereoisomer was separated, and its OH group was protected as the TBS ether to yield compound **8**, which, on treatment with pyridine hydrofluoride (Py · HF), resulted in the selective removal of the TBS group of the primary OH moiety to afford the alcohol **9** [6]. The latter was oxidized with IBX, and the generated aldehyde was reacted with $MeNO_2$ to give the nitro compound **10** (dr 96:4). The conversion was performed in good yield and high *anti*-selectivity, following the reaction conditions reported earlier [7]. The major diastereoisomer was treated with cinnamic acid under *Mitsunobu* esterification conditions [8] to form the ester **2** with inversion of the configuration of the newly generated stereogenic center in **10**. The nitro alkane moiety of **2** was oxidized with alkaline $KMnO_4$ [7] to the corresponding aldehyde, which was utilized for *Wittig* olefination with $(F_3CCH_2O)_2P(O)CH_2COOMe$ to furnish the (*Z*)-olefin **11** [9]. The structure and configuration of **11** were clearly established by its NMR spectra. Finally, the treatment of **11** with 3% MeOH/HCl resulted in the deprotection of both the TBS and acetonide groups, and the simultaneous cyclization, forming a lactone ring, afforded the target molecule **1**. The physical (optical rotation) and spectroscopic ($^1$H- and $^{13}$C-NMR, and MS) properties of **1** were identical to those reported for the naturally occurring crassalactone A [2].

In conclusion, we have developed a simple and straightforward synthesis of crassalactone A (**1**), a natural cytotoxic styryl lactone, by using (−)-diisopropyl D-tartrate as the starting material. The stereoslective additions of a *Grignard* reagent and $MeNO_2$ to two chiral aldehyde intermediates are the key steps involved in the present synthesis.

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## Experimental Part

*General*. The solvents used were all of AR-grade. TLC: *Merck* silica gel *60 $F_{254}$* plates. Column chromatography (CC): silica gel ($SiO_2$, 60–120 mesh; *Qingdao Marine Chemical*, P. R. China). Optical rotations: *JASCO DIP 360* digital polarimeter. NMR Spectra: *Gemini* 500-MHz spectrometer; in $CDCl_3$; $\delta$ in ppm rel. to $Me_4Si$ as internal standard, *J* in Hz. ESI-MS: *VG-Autospec* micromass instrument; in *m*/*z*.

*Bis(1-methylethyl) (4*S*,5*S*)-2,2-Dimethyl-1,3-dioxolane-4,5-dicarboxylate* (**4**). To a soln. of **3** (1.0 g, 4.27 mmol) and 2,2-dimethoxypropane (DMP; 0.627 ml, 5.12 mmol) in toluene (10 ml), TsOH (0.73 g, 4.27 mmol) was added, and the mixture was heated at reflux for overnight. The mixture was cooled and $K_2CO_3$ was added, excess $K_2CO_3$ was removed by filtration. The solvent was removed under reduced pressure to afford crude product. Purification of the latter by CC afforded pure **4** (1.07 g, 92%). White solid. $[\alpha]_D^{22} = +39.6$ ($c = 1.0$, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 5.16–5.10 (*m*, 2 H); 4.70 (*s*, 2 H); 1.50 (*s*, 6 H); 1.31 (*d*, $J = 7.0$, 12 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 169.2; 113.8; 77.3; 69.8; 26.2; 21.9. ESI-MS: 275 ($[M+H]^+$). Anal. calc. for $C_{13}H_{22}O_6$ (274.32): C 56.92, H 8.08; found: C 56.81, H 8.04.

*[(4*R*,5*R*)-2,2-Dimethyl-1,3-dioxolane-4,5-diyl]dimethanol* (**5**). To $LiAlH_4$ (0.416 g, 10.94 mmol) at 0°, dry THF (10 ml) was added slowly, and then a soln. of **4** (1.0 g, 3.64 mmol) in dry THF (5 ml) was added dropwise at 0° under $N_2$. The mixture was stirred at r.t. for 4 h. After completion of the reaction

(TLC), the mixture was cooled to 0°, the reaction was quenched with aq. $Na_2SO_4$ paste, and the mixture was allowed to stir at r.t. Then, it was filtered through a pad of *Celite*, and washed with hot AcOEt (20 ml). The filtrate was washed with brine (2 × 10 ml), dried ($Na_2SO_4$), and evaporated under reduced pressure. The crude product, on purification by CC, afforded pure **5** (0.520 g, 88%). Viscous yellow oil. $[\alpha]_D^{22} = -2.4$ ($c = 1.4$, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 4.04–3.97 (*m*, 2 H); 3.81–3.64 (*m*, 4 H); 1.42 (*s*, 6 H); $^{13}$C-NMR (125 MHz, $CDCl_3$): 109.4; 78.3; 62.2; 27.0. ESI-MS: 163 ($[M+H]^+$). Anal. calc. for $C_7H_{14}O_4$ (162.08): C 51.84, H 8.70; found: C 51.72, H 8.75.

*[(4*R*,5*R*)-5-({[*tert*-Butyl(dimethyl)silyl]oxy}methyl)-2,2-dimethyl-1,3-dioxolan-4-yl]methanol* (**6**). To a soln. of **5** (0.500 g, 3.08 mmol) in 10 ml of dry $CH_2Cl_2$, 1*H*-imidazole (0.209 g, 3.08 mmol) and TBSCl (0.466 g, 3.08 mmol) were added sequentially at 0°. After stirring for 5 min, 4-(dimethylamino)-pyridine (DMAP; cat. amount) was added to the mixture, and stirring was continued for 3 h at r.t. After completion of the reaction (TLC), the mixture was extracted with $CH_2Cl_2$ (2 × 5 ml). The combined org. extracts were washed with brine, dried ($Na_2SO_4$), and concentrated *in vacuo*. The crude product, on purification by CC, afforded pure **6** (0.792 g, 93%). Yellowish oil. $[\alpha]_D^{22} = -15.6$ ($c = 1.5$, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 4.02–3.94 (*m*, 1 H); 3.99–3.85 (*m*, 2 H); 3.78–3.71 (*m*, 2 H); 3.67 (*dd*, *J* = 12.0, 10.0, 1 H); 2.45 (br. *s*, 1 H); 1.42 (*s*, 3 H); 1.40 (*s*, 3 H); 0.89 (*s*, 9 H); 0.09 (*s*, 6 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 109.2; 80.2; 78.1; 63.8; 62.8; 27.0; 26.9; 26.0; 18.4; −5.3. ESI-MS: 277 ($[M+H]^+$). Anal. calc. for $C_{13}H_{28}O_4Si$ (276.45): C 56.48, H 10.21; found: C 56.37, H 10.17.

*(*R*)-[(4*R*,5*R*)-5-({(*tert*-Butyl)(dimethyl)silyl]oxy}methyl)-2,2-dimethyl-1,3-dioxolan-4-yl](phenyl)-methanol* (**7**). To an ice-cold soln. of 2-iodoxybenzoic acid (IBX; 1.52 g, 5.43 mmol) in DMSO (3 ml) was added a soln. of **6** (0.750 g, 2.71 mmol) in dry $CH_2Cl_2$, and the mixture was stirred at r.t. for 2 h. The reaction was quenched with sat. $NaHCO_3$ soln. The mixture was diluted with $CH_2Cl_2$ (5 ml), filtered through a *Celite* pad, and the pad was washed with $CH_2Cl_2$. The combined filtrates were washed with $H_2O$ (10 ml), dried ($Na_2SO_4$), and the residue was concentrated under reduced pressure to afford the aldehyde (0.699 g, 94%), which was used directly after flash chromatography for the next reaction.

The above aldehyde in dry THF (10 ml) was added slowly over 30 min to a stirred soln. of *in situ* prepared PhMgBr (2.89 ml, 2.89 mmol) in THF at 0° under $N_2$ and stirred at the same temp. After completion of the reaction (TLC), the reaction was quenched with aq. $NH_4Cl$, and then the mixture was extracted with $CH_2Cl_2$ (2 × 10 ml). The combined org. extracts were washed with brine, dried ($Na_2SO_4$), and concentrated *in vacuo*. The crude product, on purification by CC, afforded pure **7** (0.597 g, 70%). Viscous gel. $[\alpha]_D^{22} = +1.8$ ($c = 1.5$, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 7.51–7.40 (*m*, 5 H); 4.82 (br. *d*, *J* = 7.0, 1 H); 4.29 (*dd*, *J* = 9.0, 7.0, 1 H); 4.01–3.98 (*m*, 1 H); 3.52 (*dd*, *J* = 12.0, 6.0, 1 H); 3.34 (*dd*, *J* = 12.0, 5.0, 1 H); 3.19 (br. *s*, 1 H); 1.52 (*s*, 6 H); 0.97 (*s*, 9 H); 0.10 (*s*, 3 H); 0.07 (*s*, 3 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 140.0; 128.9; 128.8; 127.0; 109.9; 81.5; 78.1; 74.9; 63.1; 27.4; 27.3; 25.9; 19.2; −5.4. ESI-MS: 353 ($[M+H]^+$). Anal. calc. for $C_{19}H_{32}O_4Si$ (352.55): C 64.73, H 9.15; found: C 64.88, H 9.11.

*(*tert*-Butyl)[(*R*)-[(4*S*,5*R*)-5-({[(*tert*-butyl)(dimethyl)silyl]oxy}methyl)-2,2-dimethyl-1,3-dioxolan-4-yl](phenyl)methoxy]dimethylsilane* (**8**). To a soln. of **7** (0.600 g, 1.69 mmol) in 10 ml of dry $CH_2Cl_2$, 1*H*-imidazole (0.138 g, 2.03 mmol) and TBSCl (0.307 g, 2.03 mmol) were added sequentially at 0°. After stirring for 5 min, DMAP (cat. amount) was added to the mixture, and stirring was continued for 4 h at r.t. After completion of the reaction (TLC), the mixture was extracted with $CH_2Cl_2$ (2 × 10 ml). The combined org. extracts were washed with brine, dried ($Na_2SO_4$), and concentrated *in vacuo*. The crude product, on purification by CC, afforded pure **8** (0.762 g, 96%). Oil. $[\alpha]_D^{22} = +2.2$ ($c = 2.5$, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 7.41–7.31 (*m*, 5 H); 4.88 (*d*, *J* = 7.0, 1 H); 4.12 (*dd*, *J* = 9.0, 7.0, 1 H); 3.88–3.92 (*m*, 1 H); 3.61(*dd*, *J* = 12.0, 5.0, 1 H); 3.40 (*dd*, *J* = 12.0, 6.0, 1 H); 1.45 (*s*, 3 H); 1.31 (*s*, 3 H); 0.96 (*s*, 9 H); 0.95 (*s*, 9 H); 0.11 (*s*, 6 H); 0.08 (*s*, 6 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 140.9; 128.1; 128.0; 127.9; 109.1; 81.0; 78.1; 75.8; 64.0; 27.6; 26.1; 18.2; −4.8. ESI-MS: 467 ($[M+H]^+$). Anal. calc. for $C_{25}H_{46}O_4Si_2$ (466.81): C 64.32, H 9.93; found: C 64.48, H 9.90.

*{(4*R*,5*S*)-5-[(*R*)-{[(*tert*-Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-methanol* (**9**). To a soln. of **8** (0.700 g, 1.49 mmol) in dry THF was added Py · HF (0.008 ml, 0.449 mmol) at 0°, and the mixture was stirred at the same temp. for 2 h. Reaction was monitored frequently, and, after completion, it was quenched with sat. $NaHCO_3$. The mixture was extracted with AcOEt, and combined org. extracts were washed with brine, dried ($Na_2SO_4$), and concentrated *in vacuo*. The crude product, on purification by CC, afforded pure **9** (0.433 g, 82%). Oil. $[\alpha]_D^{22} = -19.2$ ($c = 1.5$, $CHCl_3$). $^1$H-NMR

(500 MHz, $CDCl_3$): 7.42–7.33 (*m*, 5 H); 4.88 (*d*, *J* = 7.0, 1 H); 4.13 (*dd*, *J* = 9.0, 7.0, 1 H); 3.94–3.90 (*m*, 1 H); 3.62 (*dd*, *J* = 12.0, 4.0, 1 H); 3.40 ((*dd*, *J* = 12.0, 6.0, 1 H); 1.47 (*s*, 3 H); 1.30 (*s*, 3 H); 0.94 (*s*, 9 H); 0.08 (*s*, 3 H); 0.05 (*s*, 3 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 140.9; 128.0; 127.9; 127.8; 109.0; 80.9; 78.0; 75.6; 63.8; 27.8; 26.0; 18.2; −4.9. ESI-MS: 353 ($[M+H]^+$). Anal. calc. for $C_{19}H_{32}O_4Si$ (352.55): C 64.73, H 9.15; found: C 64.64, H 9.19.

*(1*R*)-1-{(4*R*,5*S*)-5-[(*R*)-{[(*tert-*Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-2-nitroethanol* (**10**). To an ice-cold soln. of IBX (0.634 g, 2.26 mmol) in DMSO (2 ml), was added a soln. of **9** (0.400 g, 1.13 mmol) in 4 ml of dry $CH_2Cl_2$, and the mixture was stirred at r.t. for 2 h. Then, the reaction was quenched with sat. $NaHCO_3$ soln., and the mixture was diluted with $CH_2Cl_2$ (5 ml), filtered through a *Celite* pad, and the pad was washed with $CH_2Cl_2$. The combined filtrates were washed with $H_2O$ (5 ml), dried ($Na_2SO_4$), and the residue was concentrated under reduced pressure to afford the aldehyde (0.365 g, 92%), which was used directly after flash chromatography for the next reaction.

To a stirred soln. of the above aldehyde and $MeNO_2$ (0.14 ml, 2.70 mmol) in THF (5 ml) was added aq. $K_2CO_3$ (0.193 g, 1.40 mmol) at r.t. The mixture was stirred overnight at r.t. and then treated with $H_2O$. The mixture was extracted with AcOEt, and the combined org. extracts were washed with brine, dried ($Na_2SO_4$), and concentrated *in vacuo*. The crude product, on purification by CC, afforded pure **10** (0.377 g, 88%). Pale-yellow liquid. $[\alpha]_D^{22} = -9.9$ (*c* = 1.0, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 7.40–7.32 (*m*, 5 H); 5.15 (*d*, *J* = 7.0, 1 H); 4.61 (br. *d*, *J* = 12.0, 1 H); 4.48–4.40 (*m*, 2 H); 4.32 (br. *t*, *J* = 6.0, 1 H); 4.10 (*dd*, *J* = 12.0, 6.0, 1 H); 3.55 (*dd*, *J* = 12.0, 10.0, 1 H); 1.40 (*s*, 3 H); 1.29 (*s*, 3 H); 0.92 (*s*, 9 H); 0.11 (*s*, 3 H); 0.04 (*s*, 3 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 138.0; 128.0; 127.9; 127.8; 109.9; 83.8; 78.9; 76.1; 73.9; 70.3; 26.2; 25.9; 18.2; −5.1. ESI-MS: 412 ($[M+H]^+$). Anal. calc. for $C_{20}H_{33}NO_6Si$ (411.57): C 58.37, H 8.08; found: C 58.45, H 8.03.

*(1*S*)-1-{(4*R*,5*S*)-5-[(*R*)-{[(*tert-*Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-2-nitroethyl (2*E*)-3-Phenylprop-2-enoate* (**2**). To a soln. of **10** (0.300 g, 0.728 mmol), cinnamic acid (0.140 g, 0.946 mmol), and $Ph_3P$ (0.381 g, 1.45 mmol) in dry THF (5 ml) was added DEAD (0.20 ml, 1.31 mmol) dropwise during 5 min. The soln. was stirred at 0° for 1 h, and then at reflux for 4 h. After completion (TLC), the reaction was quenched with sat. $NaHCO_3$, and the reaction was extracted with AcOEt (2 × 10 ml). The combined extracts were dried and concentrated *in vacuo*. The crude product, on purification by CC, afforded pure **2** (0.311 g, 79%). Pale-yellow liquid. $[\alpha]_D^{22} = +20.7$ (*c* = 1.5, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 7.40–7.35 (*m*, 10 H); 7.34 (*d*, *J* = 16.0, 1 H); 6.95 (*d*, *J* = 16.0, 1 H); 5.39–5.35 (*m*, 1 H); 4.97 (*d*, *J* = 7.0, 1 H); 4.37–4.31 (*m*, 2 H); 4.01 (*dd*, *J* = 12.0, 8.0, 2 H); 1.28 (*s*, 6 H); 0.92 (*s*, 9 H); 0.10 (*s*, 3 H); 0.01 (*s*, 3 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 163.9; 144.1; 139.0; 128.5; 128.4; 128.3; 127.1; 127.0; 115.9; 110.5; 84.1; 78.2; 74.9; 73.2; 68.8; 29.9; 25.9; 18.2; −5.0. ESI-MS: 542 ($[M+H]^+$). Anal. calc. for $C_{29}H_{39}NO_7Si$ (541.72): C 64.30, H, 7.26; found: C 64.39, H 7.22.

*Ethyl (2*Z*,4*S*)-4-{(4*R*,5*S*)-5-[(*R*)-{[(*tert-*Butyl)(dimethyl)silyl]oxy}(phenyl)methyl]-2,2-dimethyl-1,3-dioxolan-4-yl}-4-{[(2*E*)-3-phenylprop-2-enoyl]oxy}but-2-enoate* (**11**). To the soln. of **2** (0.250 g, 0.461 mmol) in MeOH (3 ml) cooled to 0° was added dropwise a freshly prepared MeOH soln. of $K_2CO_3$ (0.095 g, 0.691 mmol) under inert atmosphere. After stirring for 1 h, a freshly prepared aq. $KMnO_4$ (0.051 g, 0.322 mmol) and $MgSO_4$ (0.041 g, 0.345 mmol) were added dropwise, maintaining the temp. at 0°. The entire mixture was stirred for 1 h at the same temp. and filtered through a pad of silica gel, followed by washing with AcOEt. The combined org. extracts were washed with brine, dried ($Na_2SO_4$), and concentrated *in vacuo*. This residue was used as such for the next step without further purification.

To NaH (0.011 g, 0.422 mmol), 2 ml of dry THF was added at 0°, under $N_2$. After 5 min, bis(2,2,2-trifluoromethyl) [(methoxycarbonyl)methyl]phosphonate (0.161 g, 0.507 mmol) in 2 ml of dry THF was added dropwise at 0°, and the mixture was stirred for 30 min. The mixture was cooled to −78°, and the above aldehyde in dry THF (3 ml) was added dropwise, and the resulting mixture was stirred for 1 h at the same temp. After completion (TLC), the reaction was quenched with sat. $NH_4Cl$ (2 ml), and the product was extracted with AcOEt (2 × 5 ml), dried ($Na_2SO_4$), and evaporated *in vacuo*, and the crude product, on purification by CC, afforded pure **11** (0.182 g, 68%). Yellow liquid. $[\alpha]_D^{22} = +16$ (*c* = 0.9, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 7.75 (*d*, *J* = 16.0, 1 H); 7.54–7.28 (*m*, 10 H); 6.53 (*d*, *J* = 16.0, 1 H); 6.22 (*dd*, *J* = 10.0, 2.0, 1 H); 6.01 (*d*, *J* = 10.0, 1 H); 5.01 (*dd*, *J* = 2.5, 2.0, 1 H); 4.85 (*d*, *J* = 2.5, 1 H); 4.46–4.41 (*m*, 1 H); 4.32–4.21 (*m*, 2 H); 4.18–4.13 (*m*, 1 H); 1.62–1.49 (*m*, 9 H); 1.10 (*s*, 9 H); 0.27 (*s*, 3 H);

0.20 (*s*, 3 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 165.1; 164.2; 149.7; 145.0; 140.1; 134.9; 130.1; 129.0; 128.8; 128.6; 125.2; 121.0; 117.8; 110.1; 75.2; 74.8; 70.2; 65.7; 61.2; 29.8; 25.6; 18.4; 16.6; −4.6; −4.5. ESI-MS: 581 ($[M+H]^+$). Anal. calc. for $C_{33}H_{44}O_7Si$ (580.79): C 68.24, H 7.64; found: C 68.39, H 7.68.

*(2*S*,3*S*)-2-[(1*R*,2*R*)-1,2-Dihydroxy-2-phenylethyl]-6-oxo-3,6-dihydro-2*H*-pyran-3-yl (2*E*)-3-Phenylprop-2-enoate* (**1**). To compound **11** (150 mg, 0.258 mmol) at 0° was added 3% HCl in MeOH (2 ml), and the mixture was stirred at r.t. for 5 h. After completion of the reaction (TLC), the mixture was diluted with AcOEt and washed with $H_2O$ and brine, dried ($Na_2SO_4$), and concentrated *in vacuo* to give crude product. The crude product, on purification by CC, afforded pure *crassalactone A* (**1**; 61 mg, 63%). White solid. $[\alpha]_D^{22} = +320$ ($c = 1.5$, $CHCl_3$). $^1$H-NMR (500 MHz, $CDCl_3$): 7.63 (*d*, $J = 16.0$, 1 H); 7.51–7.28 (*m*, 10 H); 7.01 (*dd*, $J = 10.0$, 6.0, 1 H); 6.35 (*d*, $J = 16.0$, 1 H); 6.20 (*d*, $J = 10.0$, 1 H); 5.28 (*dd*, $J = 6.0$, 2.5, 1 H); 4.90 (*d*, $J = 6.0$, 1 H); 4.75 (*dd*, $J = 6.0$, 2.5, 1 H); 4.25 (*m*, 1 H); 2.00 (br. *s*, 2 H). $^{13}$C-NMR (125 MHz, $CDCl_3$): 165.6; 162.4; 146.5; 140.5; 139.8; 133.5; 130.8; 128.8; 128.6; 128.3; 128.2; 126.4; 123.8; 116.4; 77.5; 73.5; 73.2; 62.6. ESI-MS: 381 ($[M+H]^+$). Anal. calc. for $C_{22}H_{20}O_6$ (380.40): C 69.46, H 5.30; found: C 69.34, H 5.35.

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