Synthetic Studies on Spirovetivane Phytoalexins. III.[1] A Total Synthesis of (±)-Lubiminol[2]

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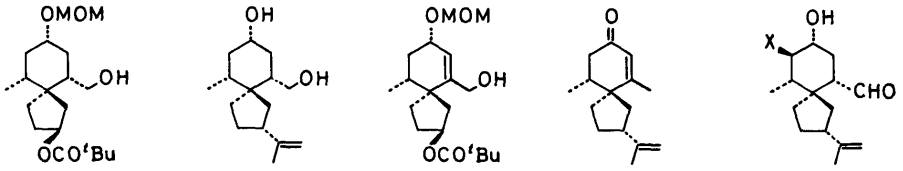
A total synthesis of (±)-lubiminol (2) from the allylic alcohol (3) was achieved through the introduction of a bis(ethoxycarbonyl)methyl group with inversion at C_2 followed by hydrogenation of the C_6–C_7 double bond and transformation of the bis(ethoxycarbonyl)methyl group into isopropenyl. On the other hand, the alcohol (1) was an inefficient starting material for the synthesis.

Keywords spirovetivane sesquiterpene; phytoalexin; lubiminol; total synthesis; *SN*2 reaction; sodio diethyl malonate; bis(ethoxycarbonyl)methyl group; allylic alcohol; hydride reduction; isopropenyl group

In the preliminary paper,[1] we reported the stereoselective synthesis of a potential intermediate, (2*RS*,5*RS*,6*RS*,8*RS*,10*SR*)-6-hydroxymethyl-8-methoxymethoxy-10-methyl-2-pivaloyloxyspiro[4.5]decane (**1**), for highly oxygenated spirovetivane phytoalexins. Herein we wish to describe a total synthesis of (±)-lubiminol (**2**), one of the highly oxygenated phytoalexins, using this potential synthon (**1**) or another key compound (**3**).

Lubiminol (**2**) was isolated from *Solanum* genus infected with *Glomerella cingulata*[3a] or with *Phytophthora infestans*[3b] in 1976—1977. This natural product has two more asymmetric carbon centers than solavetivone (**4**)[4] and has been considered to be a biosynthetic intermediate to other highly oxygenated phytoalexins[5] (*i.e.* lubimin (**5**) and oxylubimin (**6**)). Though solavetivone (**4**) has been synthesized by several groups,[6] little is known concerning successful synthesis of lubimin-type phytoalexins.[7]

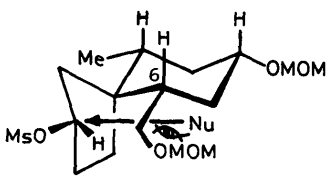
To transform **1** into (±)-lubiminol (**2**), it is necessary to introduce an isopropenyl group with inversion at C_2 in **1**. For this purpose we adapted the *SN*2 reaction with the enolate anion of diethyl malonate by reference to the synthesis of (±)-solavetivone (**4**).[6b] The alcohol (**1**) was transformed into the methoxymethyl (MOM) ether (**7**), which was converted into the alcohol (**8**) by treatment with methyllithium. The mesylate (**9**) was subjected to the reaction with the enolate anion of diethyl malonate to give **10** in only 14% yield from **8** along with a moderate amount of unidentified products. Considering that compound **11** (R^1 = MOM, R^2 = H), the C_6 epimer of **8**, was converted into **12** under the same conditions with ease (67% yield) *via* the mesylate (**11**: R^1 = MOM, R^2 = Ms), the low yield of **10** should be attributable to steric hindrance of the equatorial



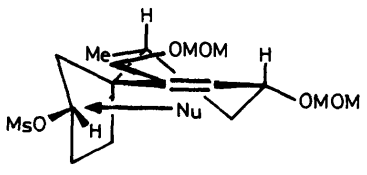
1 2 3 4 5: X=H 6: X=OH

'Bu = *tert*-Bu

Chart 1

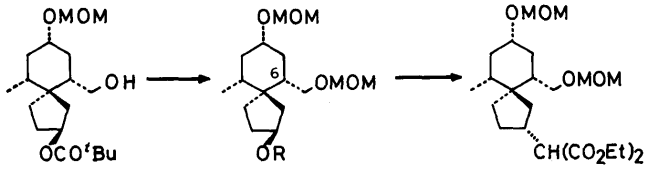


9

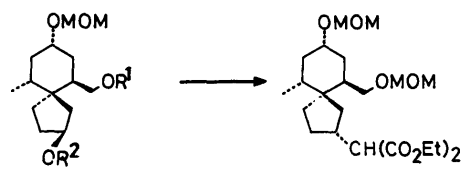


15

Fig. 1

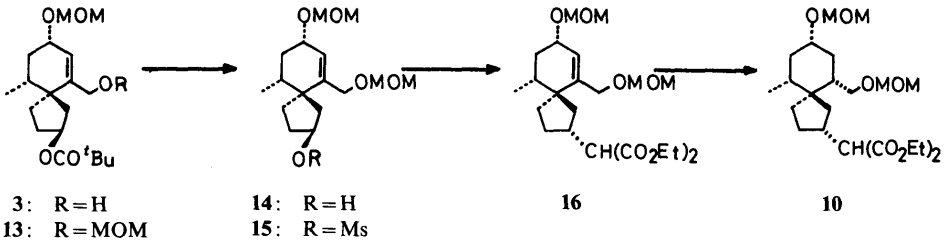


1 7: R=CO'Bu 8: R=H 9: R=Ms 10



11 12

Chart 2



3: R=H
13: R=MOM
14: R=H
15: R=Ms
16
10

Chart 3

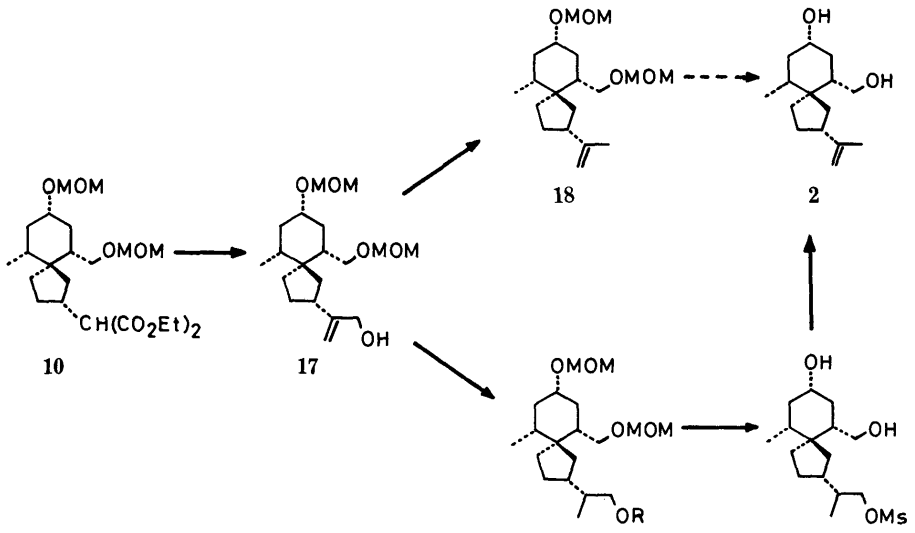


Chart 4

protected hydroxymethyl group at C_6 in **9** (Fig. 1). From this point of view, it is expected that compound **15** having an sp^2 carbon at C_6 would undergo the S_N2 reaction more easily than **9**.

Compound **15** was obtained from the unsaturated alcohol (**3**)[1] *via* **13** and **14** in the same manner as described above. As expected, the reaction of **15** with sodio diethyl malonate proceeded smoothly to afford **16** in 57% yield. Furthermore, hydrogenation of the unsaturated compound (**16**) on Raney Ni (W2) resulted in exclusive formation of a single diastereoisomer (**10**) in 97% yield. This compound was identical with **10** prepared from **1** on the basis of spectral comparisons.

Next, transformation of the bis(ethoxycarbonyl)methyl group into an isopropenyl group was investigated. In the previous synthesis of (±)-solavetivone (**4**),[6b] the same group was converted into an α,β-unsaturated ester in 2 steps,[8] and subsequent reduction of the ester group to a methyl group in 3 additional steps gave the isopropenyl derivative in 32% overall yield. For the present purpose, we planned to synthesize (±)-lubiminol (**2**) from **10** through another route (Chart 4).

After several attempts, we found that reduction with sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al) in dimethoxyethane (DME) afforded mainly the allylic alcohol, with supression of the formation of the saturated alcohol and others. Namely, the sodium salt of **10** was reduced with a large excess of Red-Al in refluxing DME to give **17** in 50% yield. Successive treatment with methanesulfonyl chloride and lithium aluminum hydride furnished (±)-lubiminol bis(methoxymethyl ether) (**18**) in 72% yield. Transformation of **18** into lubiminol (**2**) was tried under various conditions, but unfortunately, was unsuccessful. It is assumed that the double bond of the isopropenyl group is labile under the conditions employed. So, we examined an alternative route which consisted of the final introduction of the C–C double bond after deprotection of methoxymethyl groups. Hydrogenation of **17** on Raney Ni (W2) at room temperature gave the saturated alcohol (**19**), which was converted to the mesylate (**20**) in the usual manner. Hydrolysis of **20** with 3 N hydrochloric acid in tetrahydrofuran (THF) gave the corresponding diol (**21**), which was treated with 1,8-diazabicyclo[5.4.0]undecene (DBU) and sodium iodide in dimethoxyethane to afford the target molecule, (±)-lubiminol (**2**), in 76% yield. This compound and its diacetate were identified with lubiminol and lubiminol diacetate, respectively, by comparison of their spectral data.

Experimental

Melting points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi 260-10 spectrophotometer. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded on a Hitachi R-22 (90 MHz) or JEOL FX-90Q (90 MHz) with tetramethylsilane as an internal standard. The following abbreviations for the signal patterns are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and br=broad. Mass spectra (MS) and high resolution mass spectra (HRMS) were obtained with a JEOL JMS-D300 mass spectrometer. For column chromatography and preparative thin layer chromatography (PLC), Merck Kieselgel 60 (70—

230 mesh) and Merck Kieselgel 60 PF_{254} were used, respectively. Extracts were dried over $MgSO_4$ before evaporation.

(2*RS*,5*RS*,6*RS*,8*RS*,10*SR*)-8-Methoxymethoxy-6-methoxymethoxymethyl-10-methyl-2-pivaloyloxyspiro[4.5]decane (7) *N*,*N*-Diethylaniline (0.35 ml, 2.2 mmol) and MOM-Cl (0.17 ml, 2.2 mmol) were added to a solution of the alcohol (**1**) (507 mg, 1.48 mmol) in CH_2Cl_2 (10 ml) at 0 °C and the resulting solution was stirred for 10 h at room temperature. The mixture was diluted with saturated $NaHCO_3$ solution and extracted with ether. The extract was washed with saturated $NaHCO_3$ solution, H_2O, and brine, and then dried. The solvent was evaporated off under reduced pressure and the residue was chromatographed with benzene–ethyl acetate (4 : 1) to give **7** (526 mg, 92%) as a colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1722. ^{1}H-NMR ($CDCl_3$) δ: 0.97 (3H, d, J=6 Hz, C_{10}-Me), 1.17 (9H, s, *tert*-Bu), 3.0—3.7 (3H, m, C_6-CH_2O and C_8-H), 3.35 (6H, s, OMe × 2), 4.58 and 4.65 (each 2H, s, OCH_2O), 5.00 (1H, m, C_2-H). MS *m*/*z* (%): 386 (M^+, 0.1), 107 (100). HRMS Calcd for $C_{21}H_{38}O_6$: 386.2669. Found: 386.2676.

(2*RS*,5*RS*,6*RS*,8*RS*,10*SR*)-8-Methoxymethoxy-6-methoxymethoxymethyl-10-methylspiro[4.5]decan-2-ol (8) A solution of 1 M methyllithium in ether (3.4 ml, 3.4 mmol) was added to a solution of **7** (525 mg, 1.36 mmol) in dry ether (3 ml) at 0 °C, and stirring was continued for 5 min at the same temperature. After addition of 5% aqueous acetic acid, the resulting mixture was extracted with ether. The extract was washed with saturated $NaHCO_3$ solution, H_2O, and brine, and then dried. Evaporation of the extract under reduced pressure afforded a residue, which was purified by column chromatography with ethyl acetate to give **8** (394 mg, 96%) as a colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 3450. ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, d, J=6 Hz, C_{10}-Me), 3.33 (6H, s, OMe × 2), 3.0—3.7 (3H, m, C_6-CH_2O and C_8-H), 4.15 (1H, m, C_2-H), 4.56 and 4.64 (each 2H, s, OCH_2O). MS *m*/*z* (%): 302 (M^+, 0.2), 93 (100). HRMS Calcd for $C_{16}H_{30}O_5$: 302.2090. Found: 302.2089.

Diethyl (2*RS*,5*SR*,6*SR*,8*SR*,10*RS*)-8-Methoxymethoxy-6-methoxymethoxymethyl-10-methylspiro[4.5]decan-2-ylmalonate (10) a) From **8**: A solution of **8** (62.5 mg, 0.21 mmol) and mesyl chloride (0.03 ml, 0.4 mmol) in pyridine (1.5 ml) was stirred for 4 h to 0 °C. The mixture was quenched with saturated $NaHCO_3$ solution and extracted with ether. The extract was washed with saturated $NaHCO_3$ solution, saturated $CuSO_4$ solution, H_2O, and brine, and then dried. Evaporation of the extract left a crude mesylate (**9**), which was used in the next step without further purification. A solution of the mesylate (**9**) in dry DME (3 ml) was added to a solution of the enolate anion of diethyl malonate, prepared from NaH (60% in mineral oil, 166 mg, 4.1 mmol) and diethyl malonate (0.63 ml, 4.1 mmol) in dry DME (3.5 ml), at room temperature and the mixture was refluxed for 1 h. Saturated NH_4Cl solution was then added under ice-water cooling, and the resulting mixture was extracted with ethyl acetate. The extract was washed with saturated $NaHCO_3$ solution, H_2O, and brine, and then dried. Evaporation of the solvent left a residue, which was purified by PLC with ethyl acetate–petroleum ether (1 : 5) to give the diester (**10**) as a colorless oil (12.6 mg, 14%). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1752, 1735. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, d, J=6 Hz, C_{10}-Me), 1.26 (6H, t, J=7 Hz, $COOCH_2C\underline{H}_3$ × 2), 3.13 (1H, d, J=10 Hz, $C\underline{H}(COOEt)_2$), 3.0—3.8 (3H, m, C_6-CH_2O and C_8-H), 3.35 (6H, s, OMe × 2), 4.15 (4H, q, J=7 Hz, $COOC\underline{H}_2CH_3$ × 2), 4.57 and 4.64 (each 2H, s, OCH_2O). MS (CI) *m*/*z* (%): 445 (M^++1, 5), 383 (100). HRMS Calcd for $C_{22}H_{37}O_7$ (M^+−MeO): 413.2536. Found: 413.2531.

b) From **16**: A solution of **16** (200 mg, 0.452 mmol) and Raney Ni (W2) in EtOH (10 ml) was hydrogenated at atmospheric pressure at room temperature until the starting material had been disappeared. The catalyst was filtered off, and the filtrate was evaporated. The residue was purified by PLC with ethyl acetate–petroleum ether (1 : 5) to obtain **10** as a colorless oil (195 mg, 97%).

Diethyl (2*RS*,5*SR*,6*RS*,8*SR*,10*RS*)-8-Methoxymethoxy-6-methoxymethoxymethyl-10-methylspiro[4.5]decan-2-ylmalonate (12) Compound **11** (R^1=MOM, R^2=H), obtained from **11** (R^1=H, R^2=CO^{t}Bu)[1] by methoxymethylation (91%) and depivaloylation with MeLi (86%), was derived into **12** (a colorless oil) in the same manner as described for the conversion of **8** into **10** in 67% yield. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1752, 1735. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, d, J=6 Hz, C_{10}-Me), 1.23 (6H, t, J=7 Hz), 3.09 (1H, d, J=10 Hz, $CH(COOEt)_2$), 3.32 and 3.35 (each 3H, s, OMe), 3.4—3.9 (3H, m, C_6-CH_2O- and C_8-H), 4.17 (4H, q, J=7 Hz), 4.58 and 4.63 (each 2H, s, OCH_2O). MS *m*/*z* (%): 444 (M^+, 0.1), 161 (100).

(2*RS*,5*RS*,8*RS*,10*SR*)-8-Methoxymethoxy-6-methoxymethoxymethyl-10-methyl-2-pivaloyloxyspiro[4.5]dec-6-ene (13) *N*,*N*-Diethylaniline (0.23 ml, 1.44 mmol) and MOM-Cl (0.11 ml, 1.45 mmol) were added to a stirred solution of the allylic alcohol (**3**) (334 mg, 0.982 mmol) in CH_2Cl_2 (5 ml) at 0 °C, and the mixture was stirred for 20 h at room temperature. After addition of saturated $NaHCO_3$ solution at 0 °C, the mixture was extracted with ether. The extract was washed with saturated $NaHCO_3$ solution, H_2O, and brine, and then dried. After removal of the ether, the residue was purified by column chromatography with benzene–ethyl acetate (4 : 1) to give the MOM ether (**13**) as a colorless oil (329 mg, 87%). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725. ^{1}H-NMR ($CDCl_3$) δ: 1.01 (3H, d, J=6 Hz, C_{10}-Me), 1.16 (9H, s, *tert*-Bu), 3.37 (6H, s, OMe × 2), 3.9—4.3 (3H, m, C_6-CH_2O and C_8-H), 4.60 and 4.65 (each 2H, s, OCH_2O), 5.05 (1H, m, C_2-H), 5.68 (1H, br s, C_7-H). MS *m*/*z* (%): 323 (M^+−61, 28), 176 (100). *Anal.* Calcd for $C_{21}H_{36}O_6$: C, 65.59; H, 9.44. Found: C, 65.76; H, 9.61.

(2*RS*,5*RS*,8*RS*,10*SR*)-8-Methoxymethoxy-6-methoxymethoxymethyl-10-methylspiro[4.5]dec-6-en-2-ol (14) Methyllithium (1 M in ether, 4.2 ml, 4.2 mmol) was added to a solution of the MOM ether (**13**) (328 mg, 0.854 mmol) in dry ether (4 ml) at 0 °C. After being stirred for an additional 5 min at the same temperature, the reaction mixture was treated with 5% aqueous acetic acid and extracted with ether. The extract was washed with saturated $NaHCO_3$ solution, H_2O, and brine, and then dried. The solvent was removed, and the residue was chromatographed with ethyl acetate to give **14** (246 mg, 96%) as a colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620, 3475. ^{1}H-NMR ($CDCl_3$) δ: 1.05 (3H, d, J=6 Hz, C_{10}-Me), 3.35 (6H, s, OMe × 2), 3.8—4.5 (4H, m, C_2-H, C_6-CH_2O, and C_8-H), 4.62 and 4.67 (each 2H, s, OCH_2O), 5.70 (1H, br s, C_7-H). MS *m*/*z* (%): 238 (M^+−62, 89), 135 (100). HRMS Calcd for $C_{14}H_{22}O_3$: 238.1569. Found: 238.1574.

Diethyl (2*RS*,5*SR*,8*SR*,10*RS*)-8-Methoxymethoxy-6-methoxymethoxymethyl-10-methylspiro[4.5]dec-6-en-2-ylmalonate (16) A solution of the alcohol (**14**) (35.1 mg, 0.117 mmol) and mesyl chloride (0.018 ml, 0.23 mmol) in pyridine (1 ml) was stirred for 4 h at 0 °C. The reaction mixture was diluted with saturated $NaHCO_3$ under ice-water cooling and extracted with ether. The extract was washed with saturated $NaHCO_3$ solution, saturated $CuSO_4$ solution, H_2O, and brine, and then dried. The solvent was evaporated off under reduced pressure to obtain a crude mesylate (**15**). This material was used in the next step without further purification. The mesylate (**15**) in dry DME (1.5 ml) was added to a solution of the enolate anion of diethyl malonate, prepared from NaH (60% mineral oil, 23.0 mg, 0.575 mmol) and diethyl malonate (0.087 ml, 0.575 mmol) in dry DME (2 ml), at 0 °C, and the mixture was refluxed for 6.5 h. After addition of saturated NH_4Cl solution under cooling, the resulting mixture was extracted with ethyl acetate. The extract was washed with H_2O and brine, and then dried. The solvent was removed under reduced pressure to afford an oily residue, which was purified by PLC with ether–petroleum ether (1 : 3) to give **16** (29.4 mg, 57%) as a colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750, 1735. ^{1}H-NMR ($CDCl_3$) δ: 0.99 (3H, d, J=6 Hz, C_{10}-Me), 1.24 (6H, t, J=7 Hz, $COOCH_2C\underline{H}_3$ × 2), 3.17 (1H, d, J=10 Hz, $C\underline{H}(COOEt)_2$), 3.34 and 3.36 (each 3H, s, OMe), 3.9—4.4 (3H, m, C_6-CH_2O and C_8-H), 4.17 (4H, q, J=7 Hz, $COOC\underline{H}_2CH_3$ × 2), 4.62 and 4.66 (each 2H, s, OCH_2O), 5.68 (1H, m, C_7-H). MS *m*/*z* (%): 442 (M^+, 0.3), 176 (100). HRMS Calcd for $C_{23}H_{38}O_8$: 442.2564. Found 442.2534.

(2*RS*,5*SR*,6*SR*,8*SR*,10*RS*)-2-(3-Hydroxypropen-2-yl)-8-methoxymethoxy-6-methoxymethoxymethyl-10-methylspiro[4.5]decane (17) A mixture of **10** (97.4 mg, 0.219 mmol), NaH (60% mineral oil, 22.0 mg, 0.55 mmol), and dry DME (5 ml) was refluxed for 30 min. After cooling, a solution of Red-Al (70% toluene solution, 380 mg, 1.32 mmol) in dry DME (1 ml) was added, and the resulting solution was refluxed for a further 30 min. The reaction mixture was diluted with 10% aqueous NaOH under ice-water cooling and extracted with ethyl acetate. The extract was washed with H_2O and brine, dried, and evaporated. Purification of the product was performed by PLC with benzene–ethyl acetate (2 : 1) to afford the allylic alcohol (**17**) (37.5 mg, 50%) as a colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610, 3400, 1650. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (3H, d, J=6 Hz, C_{10}-Me), 3.35 (6H, s, OMe × 2), 3.1—3.9 (3H, m, C_6-CH_2O and C_8-H), 4.07 (2H, br s, C=C$\underline{H}_2$OH), 4.57 and 4.65 (each 2H, s, OCH_2O), 4.87 and 4.99 (each 1H, d, J=1 Hz, C=CH). MS (CI) *m*/*z* (%): 343 (M^++1, 9), 249 (100). HRMS Calcd for $C_{18}H_{30}O_4$ (M^+−MeOH): 310.2141. Found 310.2124.

(±)-Lubiminol Bis(methoxymethyl ether) (18) Methanesulfonyl chloride (0.02 ml, 0.26 mmol) was added to a solution of **17** (37 mg, 0.11 mmol) in dry pyridine (1 ml) at −10 °C, and the resulting solution was stirred for 2 h at the same temperature. After addition of saturated $NaHCO_3$ solution, the mixture was extracted with ether. The organic phase was washed with saturated $NaHCO_3$, saturated $CuSO_4$, H_2O, and brine, and then dried. Evaporation of the solvent gave a residue, which was dissolved in dry ether (2 ml), and an excess of $LiAlH_4$ was added at 0 °C. After being stirred for 10 min, the reaction mixture was treated with saturated potassium sodium tartrate and the precipitate was filtered off. The filtrate was dried and evaporated. The residue was purified by PLC

(ether–petroleum ether = 1 : 3) to give **18** (25.3 mg, 72%) as a colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1640. ^{1}H-NMR ($CDCl_3$) δ: 0.92 (3H, d, J=6 Hz, C_{10}-Me), 1.71 (3H, s, C=C-Me), 3.34 (6H, s, OMe × 2), 3.1—3.9 (3H, m, C_6-C$\underline{H}_2$OH and C_8-H), 4.58 (2H, s, OCH_2O), 4.65 (4H, s, OCH_2O and C=CH_2). MS (CI) m/z: (%): 327 (M^++1, 3.8), 265 (100). HRMS Calcd for $C_{18}H_{32}O_3$ ($M^+ - CH_2O$): 296.2348. Found: 296.2342.

(2*RS*,5*SR*,6*SR*,8*SR*,10*RS*)-2-(2-Hydroxy-1-methylethyl)-8-methoxymethoxy-6-methoxymethoxymethyl-10-methylspiro[4.5]decane (19) A solution of **17** (42.0 mg, 0.123 mmol) in EtOH (5 ml) was hydrogenated on Raney Ni (W2) at atmospheric pressure and room temperature. The catalyst was filtered off, and the filtrate was concentrated. The residue was purified by PLC with benzene–ethyl acetate (1 : 1) to obtain **19** (38.0 mg 91%) as a colorless oil. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610, 3440. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, d, J=6.5 Hz, C_2-CH$\underline{Me}$), 0.97 (3H, d, J=6 Hz, C_{10}-Me), 3.37 (6H, s, OMe × 2), 3.0—3.8 (5H, m, C_6-CH_2O, C_8-H and C$\underline{H}_2$OH), 4.64 and 4.71 (each 2H, s, OCH_2O). MS m/z (%): 313 (M^+ − 31, 0.1), 55 (100). *Anal.* Calcd for $C_{19}H_{36}O_5$: C, 66.24; H, 10.53. Found: C, 66.22; H, 10.32.

(2*RS*,5*SR*,6*SR*,8*SR*,10*RS*)-2-(2-Mesyloxy-1-methylethyl)-8-methoxymethoxy-6-methoxymethoxymethyl-10-methylspiro[4.5]decane (20) A solution of the alcohol (**19**) (35 mg, 0.10 mmol) and mesyl chloride (0.020 ml, 0.26 mmol) in pyridine (1 ml) was stirred for 2 h at 0 °C. After addition of saturated $NaHCO_3$ solution, the resulting mixture was extracted with ether. The ethereal phase was washed with saturated $NaHCO_3$ solution, saturated $CuSO_4$ solution, H_2O, and brine, and then dried. The solvent was evaporated off under reduced pressure, and the residue was purified by PLC with benzene–ethyl acetate (2 : 1) to give **20** (28 mg, 62%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1355, 1330. ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, d, J=7 Hz, C_2-CH-$\underline{Me}$), 1.01 (3H, d, J=6 Hz, C_{10}-Me), 2.98 (3H, s, SO_2Me), 3.33 (6H, s, OMe × 2), 3.0—4.3 (5H, m, C_6-CH_2O, C_8-H and C$\underline{H}_2$OMs), 4.56 and 4.62 (each 2H, s, OCH_2O). MS (CI) m/z (%): 423 (M^++1, 0.5), 329 (100). HRMS Calcd for $C_{18}H_{30}O_5S$ (M^+ − 2MeOH): 358.1814. Found: 358.1842.

(2*RS*,5*SR*,6*SR*,8*SR*,10*RS*)-6-Hydroxymethyl-2-(2-mesyloxy-1-methylethyl)-10-methylspiro[4.5]decan-8-ol (21) A mixture of the MOM ether (**20**) (15 mg, 0.036 mmol), 3 N HCl (1.6 ml), and THF (0.8 ml) was stirred for 40 h at room temperature. The reaction mixture was diluted with CH_2Cl_2, washed with brine, and then dried. The solvent was removed under reduced pressure, and the residue was purified by PLC with ethyl acetate to afford the diol (**21**) (8.0 mg, 70%) as a colorless oil. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590, 3400, 1355, 1330. ^{1}H-NMR ($CDCl_3$) δ: 0.86 (3H, d, J=6 Hz, C_2-CH$\underline{Me}$), 0.99 (3H, d, J=6 Hz, C_{10}-Me), 2.98 (3H, s, SO_2Me), 3.2—4.3 (5H, m, C_6-CH_2O, C_8-H and C$\underline{H}_2$OMs). MS (CI) m/z (%): 335 (M^++1, 5), 221 (100). HRMS Calcd for $C_{16}H_{28}O_4S$ ($M^+ - H_2O$): 316.1706. Found: 316.1705.

(±)-Lubiminol (2) DBU (2 drops) and NaI (large excess) were added to a solution of the diol (**21**) (3.5 mg, 0.010 mmol) in dry DME (2 ml), and the mixture was refluxed for 3 h. The reaction mixture was diluted with CH_2Cl_2 under cooling, and the solution was washed with H_2O and brine, and then dried. Removal of the solvent under reduced pressure gave the residue, which was purified by PLC with ethyl acetate–isopropanol (9 : 1) to give (±)-lubiminol (**2**) (1.9 mg, 76%), colorless needles, mp 114—116 °C (ether–hexane). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3590, 3400, 1640. ^{1}H-NMR ($CDCl_3$) δ: 0.93 (3H, d, J=6.5 Hz, C_{10}-Me), 1.73 (3H, s, C=C-Me), 3.33 (1H, dd, J= 8.6 and 10.4 Hz, C_6-C$\underline{H}$OH), 3.66 (1H, m, C_8-H), 3.94 (1H, dd, J=3.2 and 10.4 Hz, C_6-C$\underline{H}$OH), 4.67 (2H, br s, C=CH_2). MS m/z (%): 238 (M^+, 5), 220 (13), 202 (15), 107 (100). HRMS Calcd for $C_{15}H_{26}O_2$: 238.1933. Found: 238.1951.

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