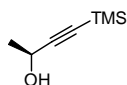


**Selective Synthesis of Epolactaene Featuring Efficient Construction of Methyl
(Z)-2-Iodo-2-butenolate and (2R,3S,4S)-2-Trimethylsilyl-2,3-epoxy-4-methyl- γ -
butyrolactone**

Ze Tan and Ei-ichi Negishi

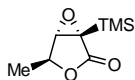
Supplemental Information

General Procedures. All reactions were run under a dry Ar atmosphere. Reactions were monitored by GC analysis of reaction aliquots. GC analysis was performed on an HP6890 Gas Chromatograph using an HP-5 capillary column (30 m x 0.32 mm, 0.5 μ M film) packed with SE-30 on Chromosorb W. Column chromatography was carried out on 230-400 mesh silica gel. ^1H and ^{13}C NMR spectra were recorded on a Varian-Inova-300 spectrometer. THF was distilled from sodium/benzophenone. ZnBr_2 was flame-dried under vacuum. The starting materials were purchased from commercial sources and used as received. Optical rotations were measured on an Autopol III polarimeter.



(S)-4-Trimethylsilyl-3-butyn-2-ol.^a To a mixture of (S)-3-butyn-2-ol (3.91 mL, 50 mmol) in THF (250 mL) at -78 °C was added dropwise *n*-butyllithium (2.5 M in hexanes, 40 mL, 100 mmol). After stirring for 1 h at -78 °C, TMSCl (15.8 mL, 125 mmol) was added via syringe. The reaction mixture was slowly warmed to room temperature and stirred overnight. The reaction mixture was concentrated via vacua to around 50 mL, then 50 mL of 3 N HCl was added. The mixture was stirred for 1 h and extracted with ether. The combined organic layers were washed with NaHCO_3 , brine,

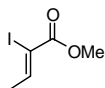
dried over MgSO_4 , filtered and concentrated. Vacuum distillation gave 7.1 g of the desired product in 85% yield: b.p. 75°C (15 mmHg),



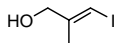
(2R,3S,4S)-2-Trimethylsilyl-2,3-epoxy-4-methyl- γ -butyrolactone (4).^b To a mixture of *i*-BuMgCl (2.0 M in Ether, 50 mL, 100 mmol) in ether (50 mL) was added Cp_2TiCl_2 (0.5 g, 2.0 mmol) at 0°C . The mixture was stirred for 15 min and (*S*)-4-trimethylsilyl-3-butyne-2-ol (5.68 g, 40 mmol) was added slowly. The reaction mixture was warmed up to room temperature and stirred overnight. Then CO_2 was vigorously bubbled through the reaction mixture until the whole reaction mixture turned into a gel. 3 N HCl (40 mL) was added carefully and the mixture was stirred at room temperature for 2 h. The mixture was extracted with ether and the ether layers were combined. The combined ether layers were washed with NaHCO_3 , brine, dried over MgSO_4 , filtered and concentrated. Vacuum distillation gave 5.03 g of the desired product in 71% yield:

To a mixture of the lactone obtained above (1.31 g, 7.7 mmol) in pyridine (30 mL) at 0°C was added NaOCl (10-13%, 16.2 mL, 23 mmol). After 12 h at 0°C , aqueous NaHCO_3 (1 M, 12 mL) was added and the resultant solution was extracted with ether. The organic layers were washed several times with 6 N HCl until all the pyridine was neutralized (checking with pH-paper). It was washed with NaHCO_3 , brine, dried over MgSO_4 , filtered and concentrated. Flash column chromatography on silica gel (90:10 hexanes:ethyl acetate) gave 730 mg the desired product as a low-melting solid in 51% yield: $[\alpha]_D^{23} -52^\circ$ (c 1.1 CHCl_3); ^1H NMR (CDCl_3 , 300 MHz) δ 0.22 (s, 9 H), 1.35 (d, $J = 6.7$ Hz, 3 H), 3.75 (s, 1 H), 4.69 (q, $J = 6.7$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ -3.61

(3C), 18.32, 51.99, 63.68, 75.43, 173.68. ppm; IR 2962, 2904, 1767, 1450, 1383, 1333, 1254 cm^{-1} ; HRMS for $\text{C}_8\text{H}_{14}\text{O}_3\text{Si}$ (M^+) calcd. 186.0712, found 186.0713.

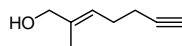


Methyl (Z)-2-Iodo-2-buten-1-olate (3). To a mixture of CuI (19 g, 100 mmol) in 150 mL of ether, TMEDA (20 mL) under Ar at $-45\text{ }^{\circ}\text{C}$ was added 62.5 mL of Methyllithium (1.6 M in ether). After 3.5 h at $-45\text{ }^{\circ}\text{C}$, the mixture was cooled to $-78\text{ }^{\circ}\text{C}$ and methyl propiolate (8.4 g, 100 mmol) was added slowly. The mixture was stirred and kept at $-78\text{ }^{\circ}\text{C}$ for 12 h until a solution of I_2 (30.5 g, 120 mmol) in THF was added via canula. After 3 h, the reaction mixture was quenched with saturated NH_4Cl . The reaction mixture was extracted with ether and the combined organic layers were washed with $\text{Na}_2\text{S}_2\text{O}_3$, brine, dried over MgSO_4 , filtered and concentrated. The residue was purified through column chromatography (silica gel, 2% EA/Hexanes) to give 14 g of the desired product in 62% yield as a colorless liquid. The compound is stable in freezer for several months, however, decomposition slowly took place: ^1H NMR (CDCl_3 , 300 MHz) δ 1.95 (d, $J = 6.7\text{ Hz}$, 3 H), 3.82 (s, 3 H), 7.32 (q, $J = 6.7\text{ Hz}$, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 22.90, 53.40, 95.92, 148.75, 163.28 ppm.



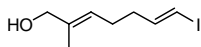
(E)-3-Iodo-2-methyl-2-propen-1-ol (5).^d To a mixture of Me_3Al (25 mL, 250 mmol) and Cp_2ZrCl_2 (29.2 g, 100 mmol) in CH_2Cl_2 (100 mL) at $0\text{ }^{\circ}\text{C}$ was added dropwise a solution of propargyl alcohol (5.68 g, 100 mmol) in CH_2Cl_2 (20 mL). After stirring for 14 h at rt, the reaction mixture was treated with a solution of I_2 (30.5 g, 120 mmol) in THF (50 mL) at $-78\text{ }^{\circ}\text{C}$, warmed to $23\text{ }^{\circ}\text{C}$, and quenched with 3 N HCl. The mixture was extracted with ether, washed with NaHCO_3 , $\text{Na}_2\text{S}_2\text{O}_3$, brine, dried over MgSO_4 , filtered

and concentrated. The residue was distilled under vacuum to afford 11 g of the desired product (55%): b.p. 82-85 °C (2.5 mmHg); ^1H NMR (CDCl_3 , 300 MHz) δ 1.83 (s, 3 H), 2.15 (bs, 1 H), 4.10 (s, 2 H), 6.26 (s, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 21.30, 67.00, 77.28, 147.10 ppm.



(E)-2-Methyl-hepta-2-en-6-yn-1-ol. In a flame-dried round-bottom flask was placed Mg turnings (0.72 g, 30 mmol) in THF (10 mL). The Mg turnings were activated with an I_2 crystal and dibromoethane (0.1 mL). To this mixture was added a solution of 4-bromo-1-trimethylsilyl-1-butyne (3.05 g, 15 mmol) and anhydrous ZnBr_2 (3.35 g, 15 mmol) in THF (40 mL). After the addition was completed, the reaction mixture was placed in an oil bath and heated at 55 °C for 6 h until GLC analysis indicated the complete consumption of the homopropargyl bromide. In another reaction flask was placed 3-iodo-2-methyl-1-propenol (1.98 g, 10 mmol) in THF (10 mL). It was treated with 1 equivalent of EtZnBr generated *in situ* from EtMgBr (10 mL, 10 mmol, 1 M in THF) and anhydrous ZnBr_2 . After the mixture was stirred for 30 min at room temperature, Pd(dppf)Cl_2 (400 mg, 0.55 mmol) and anhydrous DMF (20 mL) was added followed by the homopropargylzinc bromide generated above. The reaction mixture was stirred overnight and quenched with saturated NH_4Cl . After extracting the mixture with ether, the combined organic layers were dried over MgSO_4 , filtered and concentrated. The crude product was treated with K_2CO_3 in MeOH until GC analysis showed the complete disappearance of crude product. The reaction mixture was diluted with saturated NH_4Cl and extracted with ether. The combined organic layers were dried over MgSO_4 , filtered and concentrated. Flash column chromatography on silica gel (90:10

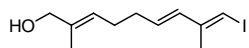
hexanes:ethyl acetate) gave 0.92 g of the desired product in 74% over two steps: ^1H NMR (CDCl_3 , 300 MHz) δ 1.59 (s, 3 H), 1.91 (t, J = 2.4 Hz, 1 H), 2.1-2.3 (m, 4 H), 2.45 (bs, 1 H), 4.0 (s, 2 H), 5.42 (t, J = 6.9 Hz, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 13.77, 18.62, 26.71, 68.46, 68.50, 84.22, 123.67, 136.46 ppm; LRMS (CI) for $\text{C}_8\text{H}_{12}\text{O}$ (M^+) calcd. 124, found 125 ($\text{M}^+ + \text{H}$).



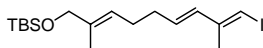
(*E,E*)-7-Iodo-2-methy-2,6-heptadien-1-ol. In a flame-dried flask under Ar was placed the alcohol obtained above (268 mg, 2.0 mmol) in THF (2 mL). DIBAL-H (0.36 mL, 2 mmol) was added via syringe slowly at 0 °C and the mixture was warmed to room temperature and stirred for 1 h. In another flame-dried flask covered with aluminum foil under Ar was placed Cp_2ZrCl_2 (700 mg, 2.4 mmol) in THF (3 mL). To this mixture was added dropwise DIBAL-H (0.43 mL, 2.4 mmol) at 0 °C. After 30 min, the pretreated alcohol mixture was transferred via canula into the second reaction flask and the resultant mixture was stirred at room temperature for 2 h until all the solid dissolved. Then, it was treated with a solution of I_2 (762 mg, 3.0 mmol) in THF (5 mL) at -78 °C. After stirring at 0 °C for 1 h, the reaction mixture was diluted with ether and quenched with saturated NH_4Cl . The reaction mixture was extracted with ether and the combined organic layers were washed sequentially with $\text{Na}_2\text{S}_2\text{O}_3$, brine, dried over MgSO_4 , filtered and concentrated. Flash column chromatography on silica gel (90:10 hexanes:ethyl acetate) gave 370 mg of the desired product in 73% yield.

2-Methyl-2,6-nonadien-8-yn-1-ol. To a mixture of ZnBr_2 (2.25 g, 10 mmol) in THF (20 mL) was added dropwise ethynylmagnesium bromide (20 mL, 10 mmol, 0.5 M in THF) via syringe. After 30 min, (*E,E*)-7-Iodo-2-methy-2,6-heptadien-1-ol (2.0 g, 8.0

mmol), which was pretreated with one equivalent of EtZnBr (10 mmol), DMF (10 mL) and Pd(PPh₃)₄ (200 mg) were added sequentially. The reaction mixture was stirred for 5 h at room temperature and quenched with saturated NH₄Cl. After extracting the mixture with ether, the organic layers were washed with brine, dried over MgSO₄, filtered and concentrated. Flash column chromatography on silica gel (90:10 hexanes:ethyl acetate) afforded 1.0 g of the desired product in 84% yield: ¹H NMR (CDCl₃, 300 MHz) δ 1.66 (s, 3 H), 2.1-2.25 (m, 4 H), 2.79 (d, *J* = 2.1 Hz, 1 H), 4.0 (s, 2 H), 5.35-5.55 (m, 2 H), 6.2-6.35 (m, 1 H); ¹³C NMR (CDCl₃, 75 MHz) δ 13.74, 26.65, 32.83, 68.72, 75.91, 82.42, 109.03, 124.51, 135.83, 145.96 ppm.

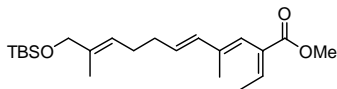


(*E,E,E*)-2,8-Dimethyl-9-iodo-2,6,8-nonatrien-1-ol. To a mixture of Cp₂ZrCl₂ (584 mg, 2.0 mmol), Me₃Al (0.6 mL, 6 mmol) in CH₂Cl₂ (8 mL) was added at 0 °C the conjugated enyne obtained above (320 mg, 2.0 mmol). The mixture was warmed to room temperature and stirred overnight. The reaction mixture was cooled down to -78 °C and treated with a solution of I₂ (762 mg, 3.0 mmol) in THF (5 mL). The reaction vessel was placed in an ice-water bath and stirred for 1 h. The reaction was quenched with 3 N HCl and extracted with ether. The ether layers were combined and washed successively with Na₂S₂O₃, brine, dried over MgSO₄, filtered and concentrated. Flash column chromatography on silica gel (90:10 hexanes:ethyl acetate) gave 408 mg of the desired product in 70% yield: ¹H NMR (CDCl₃, 300 MHz) δ 1.39 (bs, 1 H), 1.67 (s, 3 H), 1.94 (s, 3 H), 2.1-2.2 (m, 4 H), 4.0 (s, 2 H), 5.4 (bs, 1 H), 5.76 (dt, *J* = 6.4, 15.6 Hz, 1 H), 6.16 (d, *J* = 15.6 Hz, 1 H), 6.20 (s, 1 H); ¹³C NMR (CDCl₃, 75 MHz) δ 13.74, 20.17, 27.29, 32.60, 68.82, 81.40, 125.05, 130.75, 131.52, 135.46, 145.12 ppm.



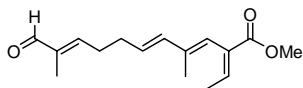
(*E,E,E*)-9-*tert*-Butyldimethylsiloxy-1-iodo-2,8-dimethyl-1,3,7-nonatriene (2).

To a mixture of the alcohol obtained above (292 mg, 1.0 mmol) in DMF (3 mL) were added imidazole (102 mg, 1.5 mmol) and TBSCl (180 mg, 1.2 mmol). The reaction mixture was stirred for 3 h, diluted with ether, and quenched with saturated NH_4Cl . After extracting the mixture with ether, the combined organic layers were washed with water, brine, dried over MgSO_4 , filtered and concentrated. Flash column chromatography on silica gel (hexanes) gave 365 mg of the desired product in 90% yield; ^1H NMR (CDCl_3 , 300 MHz) δ 0.03 (s, 6 H), 0.89 (s, 9 H), 1.57 (s, 3 H), 1.91 (s, 3 H), 2.1-2.2 (m, 4 H), 3.99 (s, 2 H), 5.3-5.45 (m, 1 H), 5.7-5.8 (m, 1 H), 6.13 (d, $J = 15.9$ Hz, 1 H), 6.16 (s, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ -5.27 (2C), 13.49, 18.41, 20.14, 25.94 (3C), 27.18, 32.70, 68.43, 81.19, 123.34, 131.01, 131.41, 135.04, 145.16 ppm.



Methyl (2*E*,3*E*,5*E*,9*E*)-2-Ethylidene-4,10-dimethyl-11-*tert*-butyldimethylsiloxy-3,5,9-undecatrienoate (10). To a mixture of the vinyl iodide obtained above (406 mg, 1.0 mmol) in THF (3 mL) at -78°C under Ar was added dropwise *t*-BuLi (1.7 M in pentane, 1.2 mL, 2.1 mmol). The mixture was stirred at -78°C for 1 h, then a solution of anhydrous ZnBr_2 (225 mg, 1.0 mmol) in THF (1 mL) was added via canula. The mixture was warmed to room temperature and stirred for 30 min. The volatiles were removed via vacuum and anhydrous DMF (4 mL) was added. In another flask were placed $\text{Pd}_2(\text{dba})_3$ (23 mg, 0.025 mmol), TFP (23 mg, 0.1 mmol) in anhydrous DMF (2 mL). The mixture was stirred for 10 min until it turned clear. To this green solution were added methyl (*Z*)-2-iodo-2-butenate (249 mg, 1.1 mmol) followed

by the organozinc reagent generated above. The reaction was stirred for 3 h and quenched with saturated NH_4Cl . After extracting the mixture with ether, the organic layers were washed with brine, dried over MgSO_4 , filtered and concentrated. Flash column chromatography on silica gel (95:5 hexanes:ethyl acetate) gave 282 mg of the desired product in 74% yield: ^1H NMR (CDCl_3 , 300 MHz) δ 0.05 (s, 6 H), 0.94 (s, 9 H), 1.65 (s, 3 H), 1.66 (s, 3 H), 1.75 (dd, $J = 1.2, 7.1$ Hz, 3 H), 2.1-2.3 (m, 4 H), 3.76 (s, 3 H), 4.05 (bs, 2 H), 5.4-5.5 (m, 1 H), 5.78 (dt, $J = 6.7, 15.6$ Hz, 1 H), 5.97 (s, 1 H), 6.25 (d, $J = 15.6$ Hz, 1 H), 6.96 (q, $J = 7.1$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ -5.29 (2C), 13.46, 14.34, 15.77, 18.39, 25.93 (3C), 27.46, 32.82, 51.77, 68.49, 122.08, 123.69, 130.16, 130.66, 134.17, 134.82, 139.04, 139.40, 167.95 ppm; HRMS for $\text{C}_{22}\text{H}_{38}\text{O}_3\text{Si}$ (M^+) calcd. 378.2590, found 378.2588.

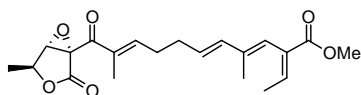


Methyl (2E,3E,5E,9E)-2-Ethylidene-4,10-dimethyl-11-oxo-3,5,9-

undecatrienoate (9).^b To a solution of the compound obtained above (512 mg, 1.2 mmol) in THF (5 mL) was added TBAF (1 M in THF, 1.5 mL, 1.5 mmol) and AcOH (1.5 mmol). The reaction mixture was stirred at room temperature for 20 h and quenched with saturated NH_4Cl . After extracting the mixture with ether, the organic layers were washed with brine, dried over MgSO_4 , filtered and concentrated. Flash column chromatography on silica gel (95:5 hexanes:ethyl acetate) gave 310 mg of the desired product in 87% yield.

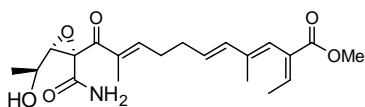
To a solution of the compound obtained above (255 mg, 0.96 mmol) in hexanes (5 mL) was added activated MnO_2 (1.26 g 14.5 mmol). The mixture was vigorously stirred until TLC analysis showed the complete disappearance of the starting material. The

mixture was filtered and concentrated. Flash column chromatography on silica gel (95:5 hexanes:ethyl acetate) gave 210 mg of the desired product in 83% yield: ^1H NMR (CDCl_3 , 300 MHz) δ 1.64 (d, $J = 1.2$ Hz, 3 H), 1.72 (dd, $J = 1.2, 7.0$ Hz, 3 H), 1.76 (s, 3 H), 2.3-2.45 (m, 2 H), 2.45-2.6 (m, 2 H), 3.73 (m, 3 H), 5.72 (dt, $J = 6.5, 15.8$ Hz, 1 H), 5.98 (s, 1 H), 6.26 (d, $J = 15.8$ Hz, 1 H), 6.54 (dt, $J = 1.1, 7.7$ Hz, 1 H), 6.95 (q, $J = 7.0$ Hz, 1 H), 9.42 (s, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 8.89, 14.03, 15.46, 28.49, 31.18, 51.43, 122.68, 127.98, 130.14, 134.86 (2C), 137.27, 153.19, 167.31, 194.71 ppm; IR 2983, 2849, 2850, 1716, 1687, 1641, 1435 cm^{-1} ; HRMS for $\text{C}_{16}\text{H}_{22}\text{O}_3$ (M^+) calcd. 262.1569, found 262.1568.



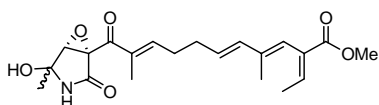
(1R,4S,5R)-4-methyl-1-[(2E,6E,8E,10E)-2,8-dimethyl-10-methoxycarbonyl-1-oxododeca-2,6,10-trienyl]-3,6-dioxabicyclo[3.1.0]hexan-2-one (11):^b To a solution of **9** (132 mg, 0.5 mmol), TBAF (0.08 mmol, 15 mol%, pretreated with dry MS4A (1g/mmol)) and activated MS4A (0.5 g) in THF/hexane (1:1, 1 mL) at room temperature was added a solution of **4** (186 mg, 1.0 mmol) in THF (1.5 mL) slowly using a syringe pump in 12 h. After 36 h, the reaction mixture was diluted with EtOAc, filtered through a celite pad and concentrated. The crude product was treated with 3% HF in 3 mL of CH_3CN for 30 min. After the mixture was quenched with NaHCO_3 , extracted with EtOAc, The combined organic layers were dried over MgSO_4 , filtered and concentrated. The residue was purified via column chromatography (silica gel, 20-30% EtOAc:hexanes) and the reaction was repeated by using the recovered **9**. The combined amount of the desired aldol adduct isolated is 81 mg.

To a solution of DMSO (101 μ L, 0.65 mmol) in CH_2Cl_2 (1 mL) was added TFAA (93 μ L, 0.13 mmol) at -78°C . After 30 min, a solution of the compound obtained above in CH_2Cl_2 (1 mL) was added via canula. After 3 h at -78°C , Et_3N (0.31 mL, 2.2 mmol) was added and the mixture was warmed to rt and stirred for 1 h. The reaction mixture was quenched with water and extracted with CH_2Cl_2 . the combined organic layers were washed with brine, dried over MgSO_4 , filtered and concentrated. The residue was purified via column chromatography (silica gel, 2:1 ethyl acetate:hexane) to give **11** (72 mg, 39% overall) as a pale yellow oil: $[\alpha]_{\text{D}}^{23} -2.4^\circ$ (c 1.2 CHCl_3); ^1H NMR (CDCl_3 , 300 MHz) δ 1.50 (d, $J = 7.0$ Hz, 3 H), 1.62 (d, $J = 1.2$ Hz, 3 H), 1.73 (dd, $J = 1.2, 7.0$ Hz, 3 H), 1.87 (s, 3 H), 2.3-2.4 (m, 2 H), 2.45-2.55 (m, 2 H), 3.73 (s, 3 H), 4.09 (s, 1 H), 4.71 (q, $J = 7.0$ Hz, 1 H), 5.72 (dt, $J = 6.5$ Hz, 15.8 Hz, 1 H), 5.97 (s, 1 H), 6.26 (d, $J = 15.8$, 1 H), 6.88 (t, $J = 5.8$ Hz, 1 H), 6.94 (q, $J = 7.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 11.14, 14.28, 15.77, 17.77, 29.22, 31.30, 51.76, 60.24, 64.03, 75.48, 123.04, 127.98, 130.34, 135.42, 135.98, 137.55, 139.69, 149.37, 167.73, 168.27, 188.20 ppm; IR 2852, 1782, 1713, 1680, 1637, 1435 cm^{-1} ; HRMS for $\text{C}_{21}\text{H}_{26}\text{O}_6$ (M^+) calcd. 374.1729, found 374.1732.



Methyl (3E,5E,9E,12R,13R,14S)-12-carbamoyl-12,13-epoxy-2-[(E)-ethylidene]-4,10-dimethyl-14-hydroxy-11-oxopentadeca-3,5,9-trienoate. To a solution of compound **11** obtained above (38 mg, 0.1 mmol) in 0.5 mL of methanol at 0°C was added NH_3 (2 mL, 8 M in methanol). After 30 min, the volatile was removed via vacua and the residue was purified through column chromatography (silica gel, 60:40,

ethyl acetate:hexanes) to give 34 mg of the desired product in 87% yield: $[\alpha]_D^{23} -55^\circ$ (c 0.6 CHCl_3); ^1H NMR (CDCl_3 , 300 MHz) δ 1.37 (d, $J = 6.5$ Hz, 3 H), 1.62 (s, 3 H), 1.73 (d, $J = 7.0$ Hz, 3 H), 1.80 (s, 3 H), 2.3-2.5 (m, 4 H), 3.18 (d, $J = 7.6$ Hz, 1 H), 3.67 (bs, 1 H), 3.73 (bs, 4 H), 5.72 (dt, $J = 6.5, 15.8$ Hz, 1 H), 5.95 (s, 1 H), 6.24 (d, $J = 15.8$ Hz, 1 H), 6.62 (bs, 2 H), 6.95 (q, $J = 7.0$ Hz, 1 H), 7.09 (t, $J = 7.0$ Hz, 1 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 11.20, 14.23, 15.77, 20.24, 28.94, 31.30, 51.87, 65.04, 65.40, 65.99, 122.76, 128.32, 130.28, 134.92, 135.37, 138.06, 139.86, 149.74, 167.59, 167.87, 192.92 ppm; IR 3460, 3344, 2978, 2951, 2929, 2854, 1689, 1635, 1599 cm^{-1} ; HRMS for $\text{C}_{21}\text{H}_{29}\text{NO}_6$ (M^+) calcd. 391.1995, found 391.1997.



(+)-Epolactaene (1):^{b,c} To 110 mg (0.25 mmol) of Dess-Martin reagent in 2 mL of CH_2Cl_2 was added 0.5 mL of pyridine. After 0.5 h, 27 mg (0.07 mmol) of the compound obtained above in CH_2Cl_2 (0.5 mL) was added and the reaction was stirred until TLC showed the consumption of the starting material (2 h). After diluting the mixture with ether, a saturated solution of $\text{Na}_2\text{S}_2\text{O}_3$ was added and the mixture was stirred for 0.5 h. The layers were separated, and the aqueous phase was extracted with EtOAc. The combined organic phases were dried over MgSO_4 , concentrated, and purified by column chromatography (30:70, hexanes:EtOAc) to give 19 mg (70%) of the desired aldehyde: dr = 1.8/1; $[\alpha]_D^{23} +36.3^\circ$ (c 0.38 MeOH) lit.¹ $[\alpha]_D^{22} +32^\circ$ (c 0.1 MeOH); ^1H NMR (CD_3OD , 300 MHz) δ 1.60 (s, 2 H), [minor isomer 1.64 (s, 1 H)], 1.69 (s, 3 H), 1.80 (d, $J = 7.0$ Hz, 3 H), 1.91 (s, 3 H), 2.35-2.5 (m, 2 H), 2.5-2.7 (m, 2 H), 3.79 (s, 2 H), [minor isomer 3.80 (s, 1 H)], 4.06 (s, 0.66 H), [minor isomer 4.14 (s, 0.33 H)], 4.92 (s, 1

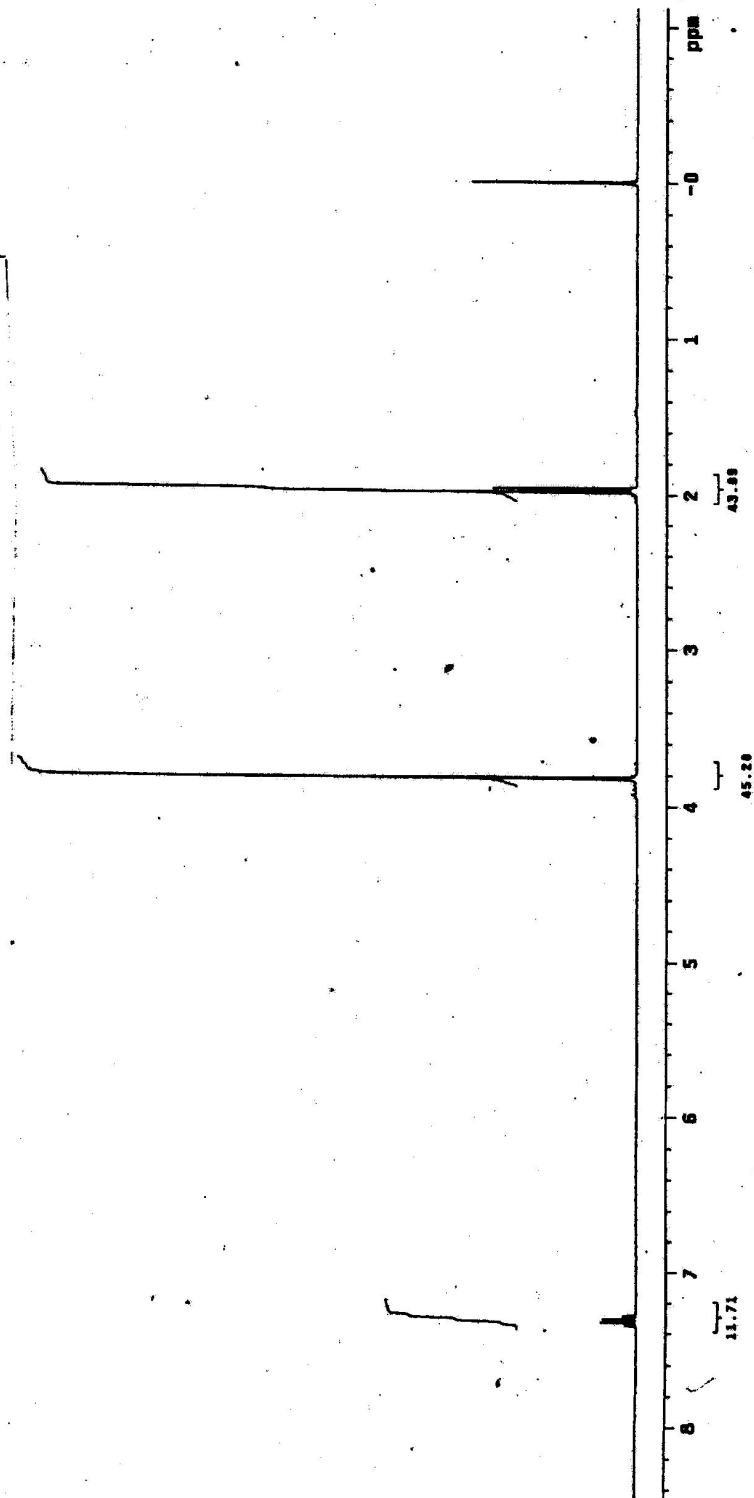
H), 5.86 (dt, $J = 6.4, 15.8$ Hz, 1 H), 6.03 (s, 1 H), 6.36 (d, $J = 15.8$ Hz, 0.66 H), [minor isomer 6.33 (d, $J = 15.8$ Hz, 0.33 H)], 6.9-7.1 (m, 1 H), 7.10 (dt, $J = 1.1, 7.0$ Hz, 0.66 H), [minor isomer 6.80 (t, $J = 6.7$ Hz, 0.33 H) ppm; ^{13}C NMR (CD_3OD , 75 MHz) δ 11.29, 14.75, 16.15, 22.38, 25.64, 29.82, 30.30, 31.06, 32.70, 52.53, 64.10, 64.86, 65.34, 66.21, 84.20, 84.87, 123.81, 124.18, 129.85, 131.90, 132.01, 136.73, 136.84, 137.40, 139.53, 139.76, 140.99, 141.16, 149.22, 150.20, 169.57, 169.68, 170.38, 172.32, 191.86, 192.22 ppm; IR 3440, 3315, 2950, 2925, 1720, 1682, 1633 cm^{-1} ; HRMS for $\text{C}_{21}\text{H}_{27}\text{NO}_6$ (M^+) calcd. 389.1838, found 389.1844.

Reference

- (a) Sato, F.; Ishikawa, H.; Watanabe, H.; Miyake, T.; Sato, M. *J. Chem. Soc., Chem. Commun.* **1981**, 718.
- (b) Kuramochi, K.; Nagata, S.; Itaya, H.; Takao, K.; Kobayashi, S. *Tetrahedron Lett.* **1999**, 40, 7367. (b) Kuramochi, K.; Nagata, S.; Itaya, H.; Takao, K.; Kobayashi, S. *Tetrahedron Lett.* **1999**, 40, 7371.
- (c) Kuramochi, K.; Nagata, H.; Matsubara, Y.; Sunoki, T.; Uchiro, H.; Takao, K.; Kobayashi, S. *Tetrahedron* **2003**, 59, 9743.
- (c) (a) Hayashi, Y. ; Narasaka, K. *Chem. Lett.* **1998**, 313. (b) Hayashi, Y.; Kanayama, J.; Yamaguchi, J.; Shoji, M. *J. Org. Chem.* **2002**, 67, 9443.
- (d) Liu, F.; Negishi, E. *J. Org. Chem.*, **1997**, 62, 8591.

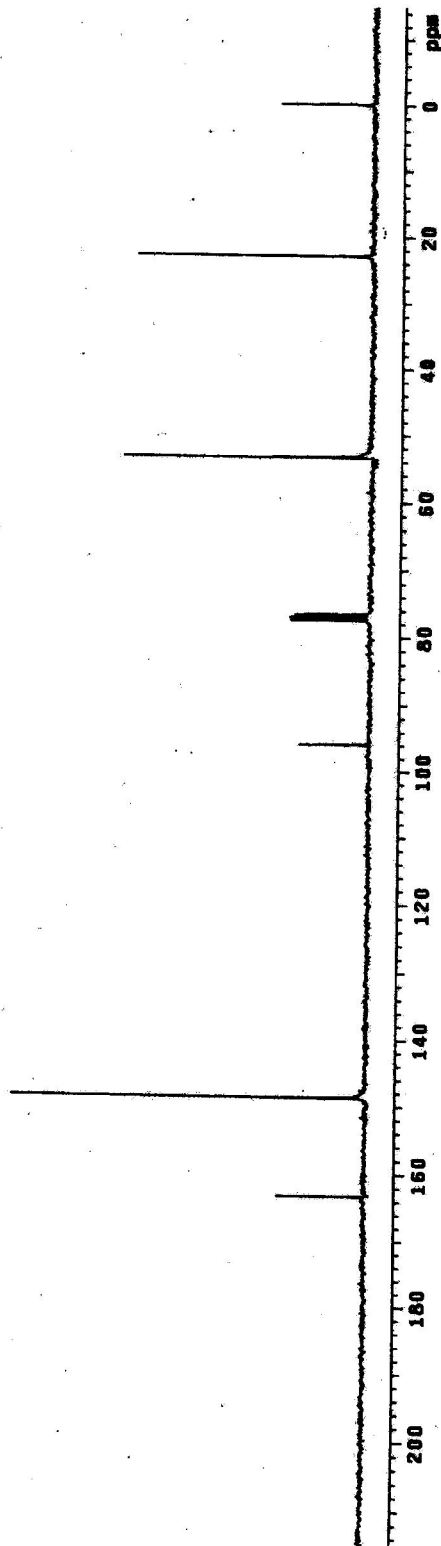
Selective Synthesis of Epolactaene Featuring Efficient.... Ze Tan and Ei-ichi Negishi*

INDEX	FREQUENCY PPM	HEIGHT
1	2265.169	7.352
2	2100.719	7.320
3	2131.685	7.387
4	2183.241	7.286
5	1140.519	2.822
6	593.219	1.944
7	500.198	1.991
8	0.000	8.000

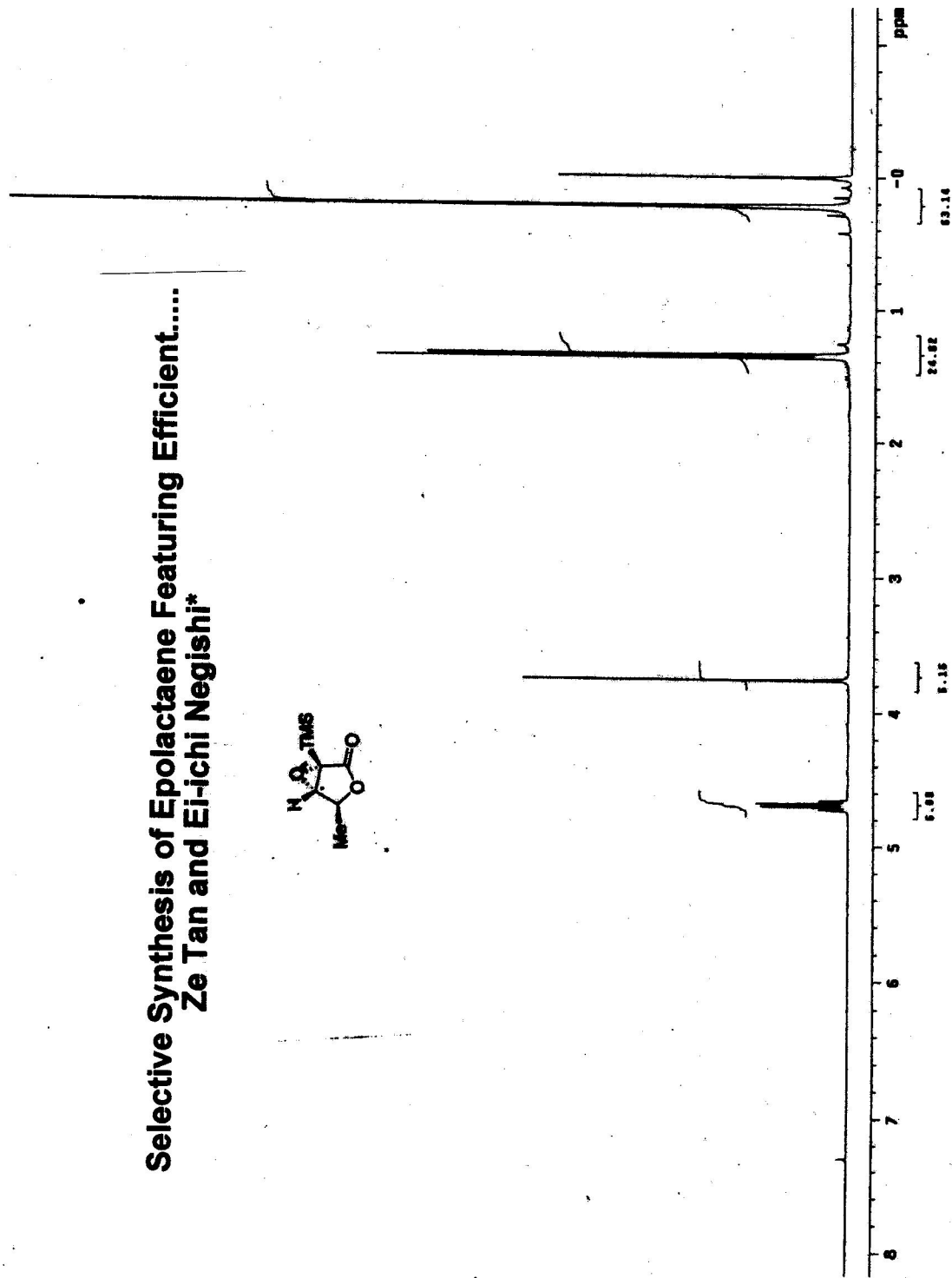
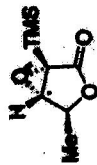


INDEX	FREQUENCY	PPM	HEIGHT
1	12386.142	103.157	14.4
2	11213.544	149.871	59.1
3	7282.769	95.993	11.4
4	5839.435	77.421	13.9
5	5897.724	77.989	13.1
6	5775.982	76.379	12.4
7	4322.723	93.324	49.5
8	1723.188	57.848	39.4
9	-8.879	-9.118	15.3

Selective Synthesis of Epolactaene Featuring Efficient..... Ze Tan and Ei-ichi Negishi*

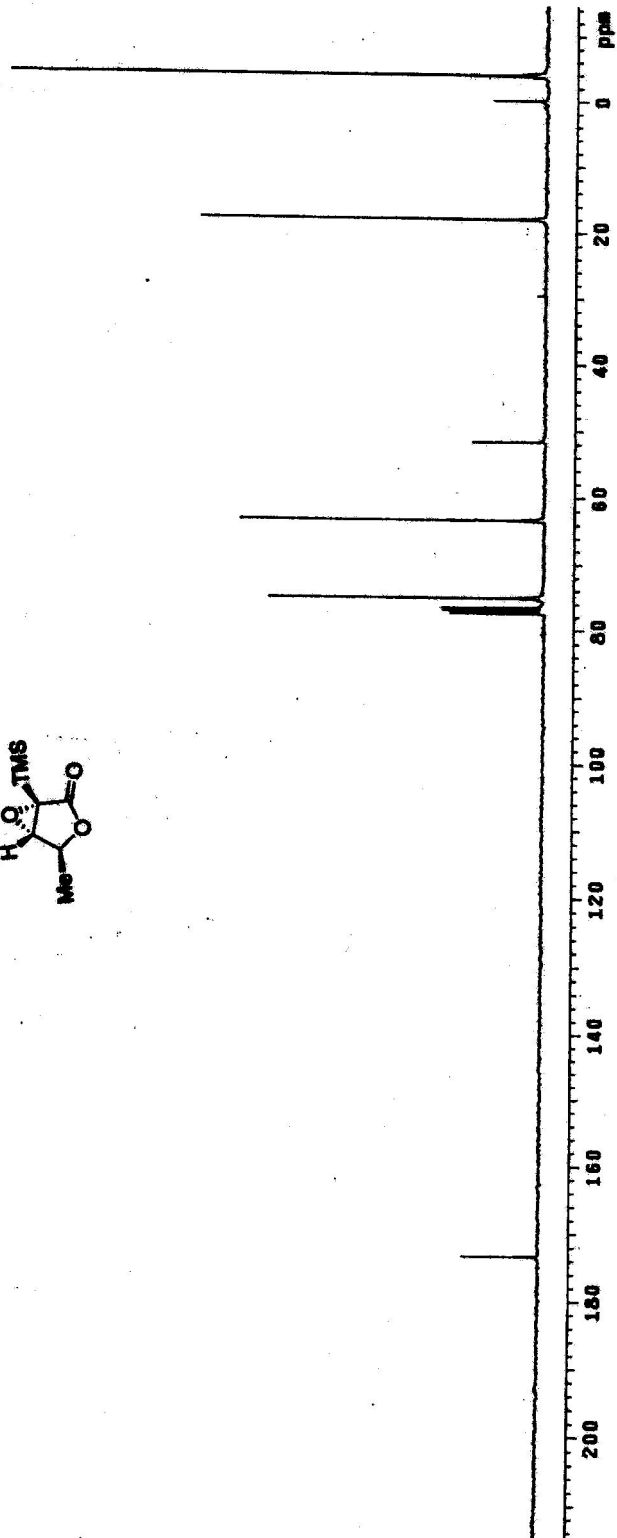
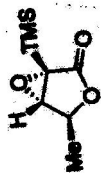


Selective Synthesis of Epolactaene Featuring Efficient.... Ze Tan and Ei-ichi Negishi*



INDEX	FREQUENCY	PPM	HEIGHT
1	13076.489	179.376	12.6
2	6039.485	77.421	15.3
3	6007.713	77.000	16.5
4	3775.942	76.579	16.7
5	5665.855	75.119	44.9
6	4776.521	63.326	49.6
7	3603.589	61.822	11.3
8	1364.751	17.982	56.6
9	-8.878	-8.118	6.3
10	-298.868	-3.564	48.5

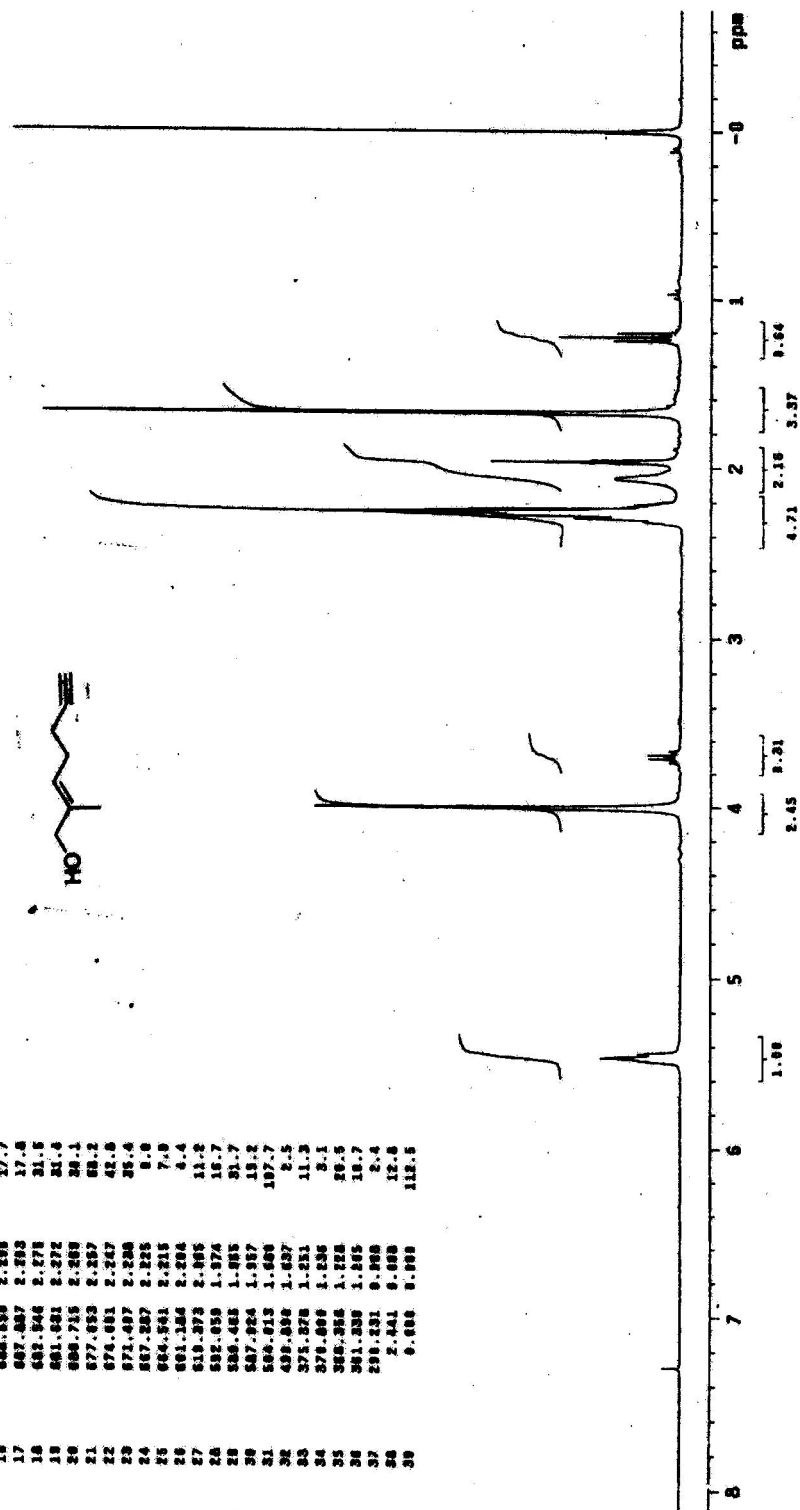
Selective Synthesis of Epolactaene Featuring Efficient..... Ze Tan and Ei-ichi Negishi*



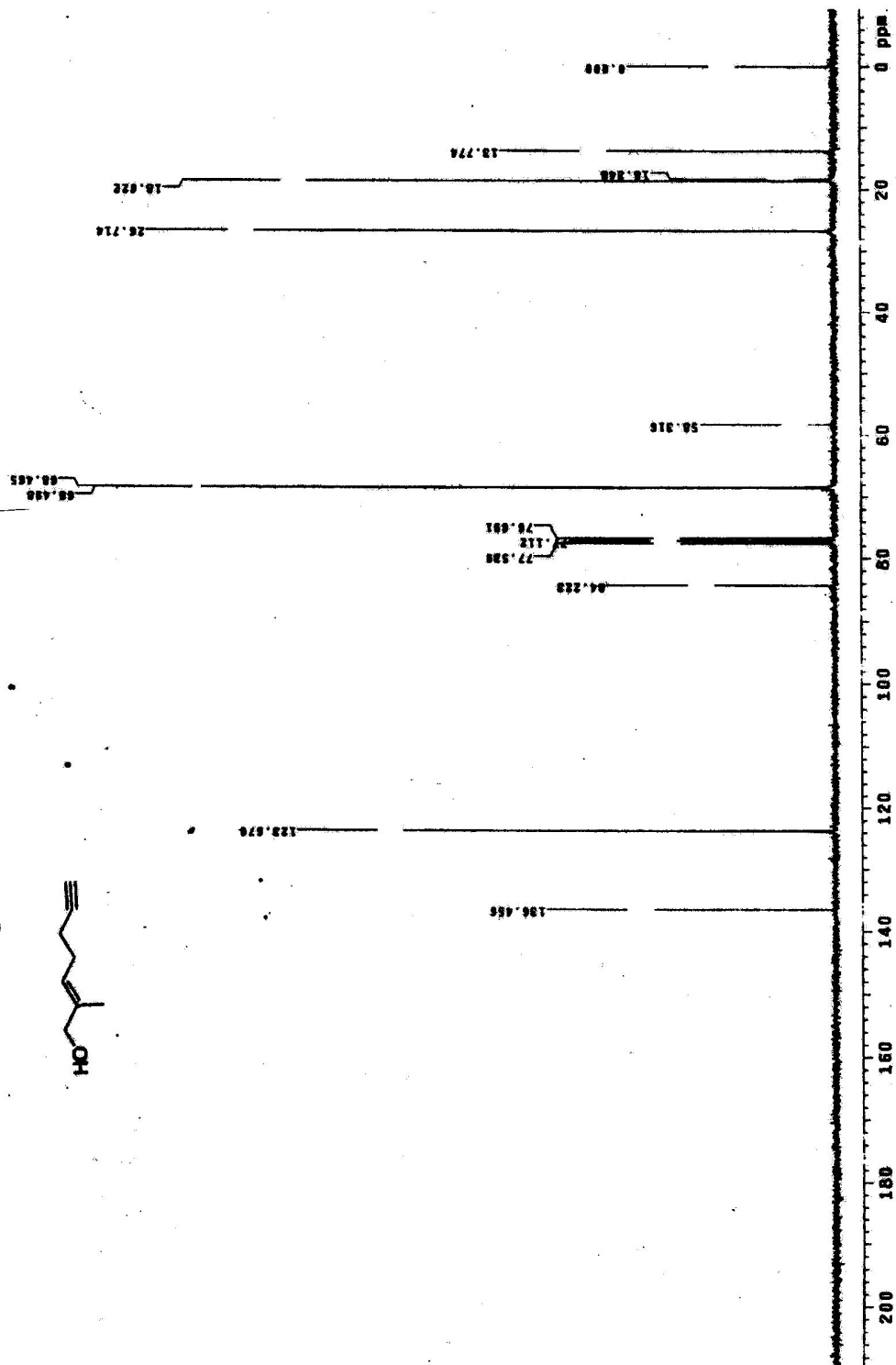
INDEX	FREQUENCY PPM	HEIGHT	INDEX	FREQUENCY PPM	HEIGHT
1	2240.825	7.284	40	-2.698	-0.918
2	1647.308	5.492	41	-3.357	-0.911
3	1646.168	5.483			
4	1644.798	5.483			
5	1643.117	5.478			
6	1641.743	5.478			
7	1640.322	5.469			
8	1639.149	5.465			
9	1637.928	5.460			
10	1634.724	5.448			
11	1633.593	5.440			
12	1291.914	6.085			
13	1112.786	3.718			
14	1105.846	3.686			
15	893.529	8.312			
16	884.820	2.298			
17	887.887	2.293			
18	683.846	2.278			
19	681.841	2.272			
20	686.716	2.269			
21	877.633	2.257			
22	674.681	2.247			
23	871.497	2.230			
24	867.287	2.225			
25	664.541	2.215			
26	661.164	2.204			
27	819.278	2.205			
28	832.650	1.976			
29	809.483	1.955			
30	847.924	1.937			
31	604.813	1.640			
32	498.894	1.627			
33	375.878	1.251			
34	378.009	1.236			
35	368.356	1.128			
36	361.238	1.105			
37	299.231	0.968			
38	2.441	0.606			
39	0.608	0.908			



Selective Synthesis of Epolactaene Featuring Efficient.... Ze Tan and Ei-ichi Negishi*

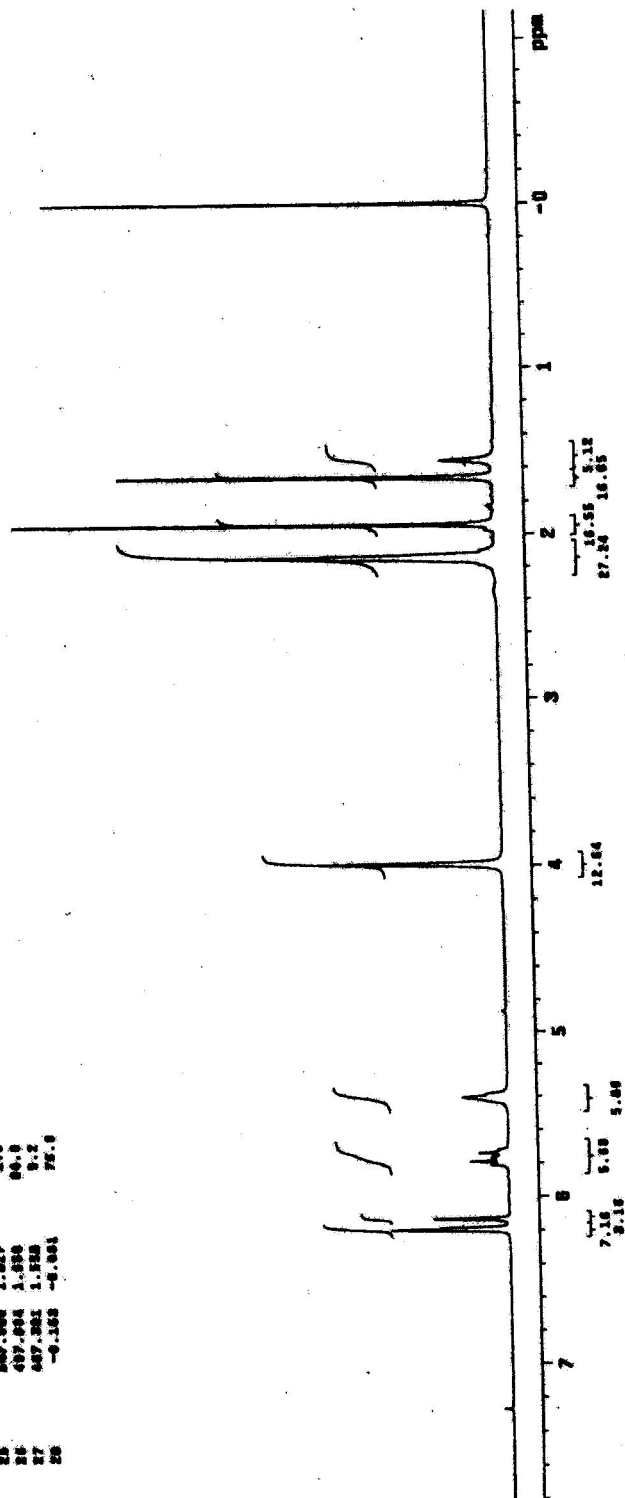


**Selective Synthesis of Epolactone Featuring Efficient.....
Ze Tan and Ei-ichi Negishi***



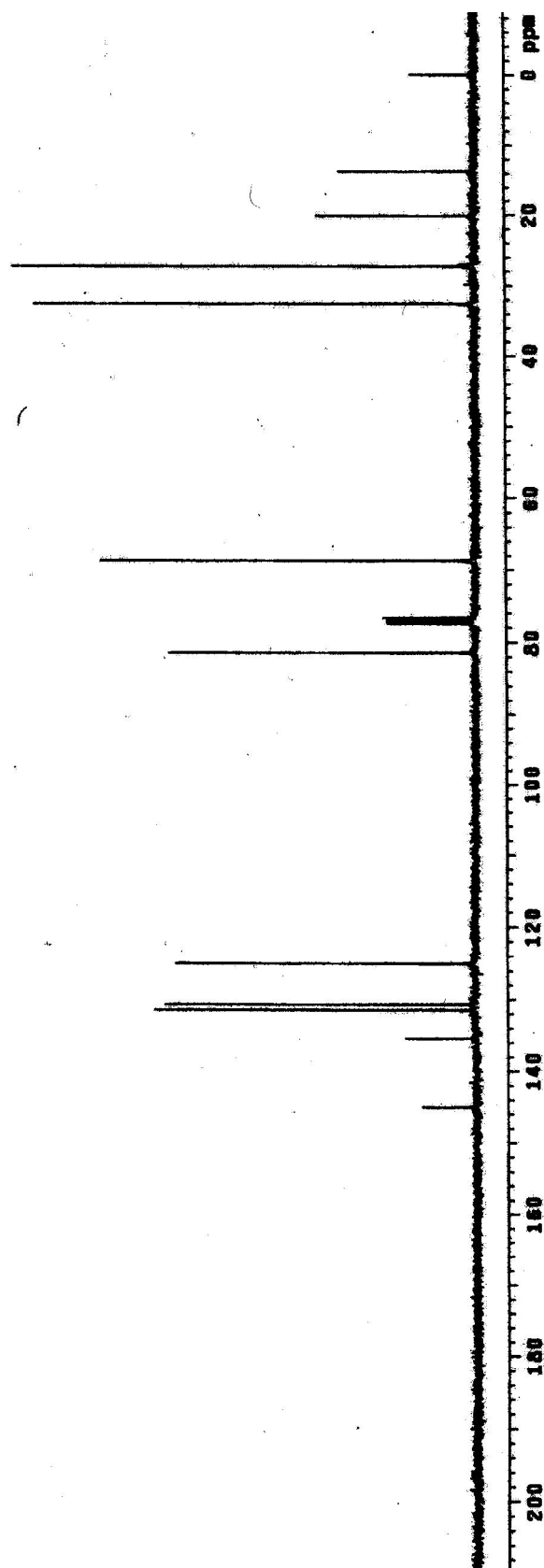
INDEX	FREQUENCY	PPM	HEIGHT
1	51.04	201	7.428
2	1093	248	8.138
3	1093	248	8.138
4	1093	248	8.138
5	1743	326	5.015
6	1743	326	5.015
7	1743	326	5.015
8	1743	326	5.015
9	1743	326	5.015
10	1743	326	5.015
11	1743	326	5.015
12	1743	326	5.015
13	1743	326	5.015
14	1743	326	5.015
15	1743	326	5.015
16	1743	326	5.015
17	1743	326	5.015
18	1743	326	5.015
19	1743	326	5.015
20	1743	326	5.015
21	1743	326	5.015
22	1743	326	5.015
23	1743	326	5.015
24	1743	326	5.015
25	1743	326	5.015
26	1743	326	5.015
27	1743	326	5.015
28	1743	326	5.015

Selective Synthesis of Epolactaene Featuring Efficient..... Ze Tan and Ei-ichi Negishi*

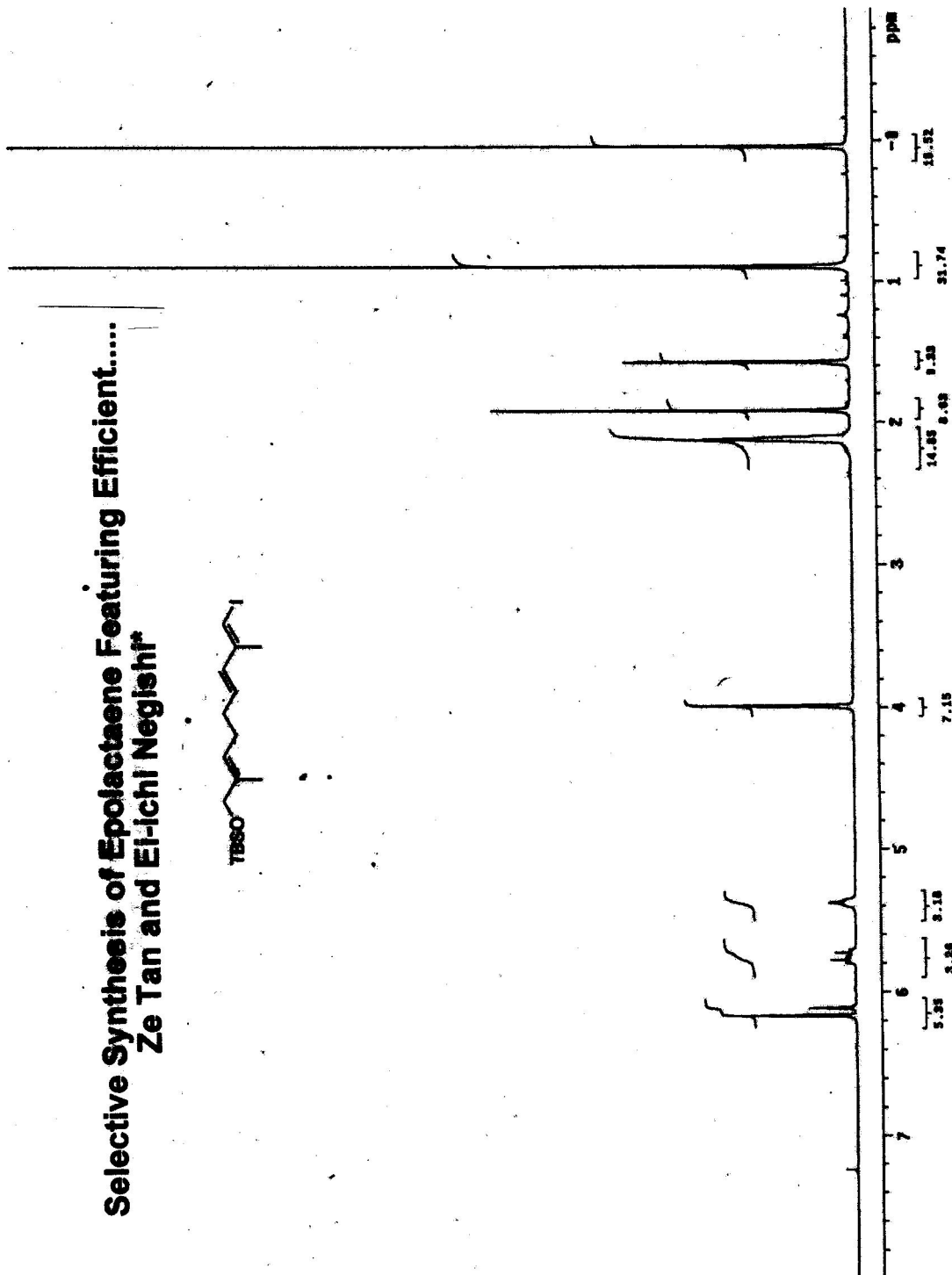


Selective Synthesis of Epoxideane Featuring Efficient.....

Ze Tan and Ei-ichi Negishi*



Selective Synthesis of Epolactaene Featuring Efficient..... Ze Tan and Ei-ichi Negishi*

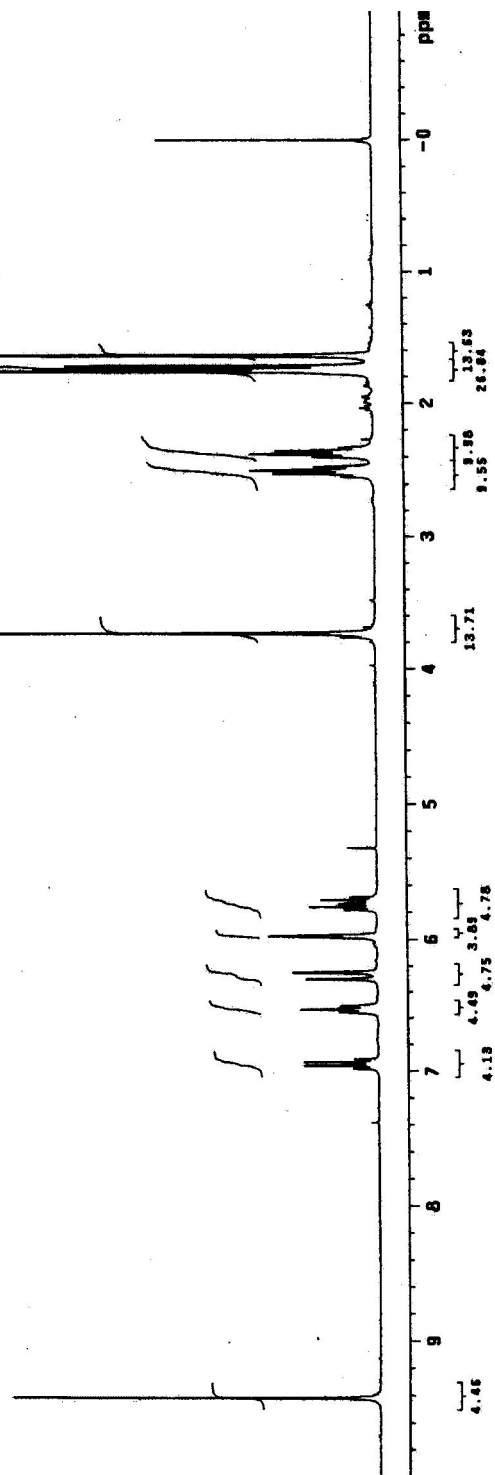
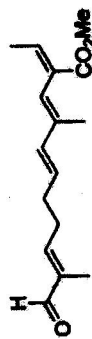


CC1=CC=C(C=C1)C=CC=CC=C1

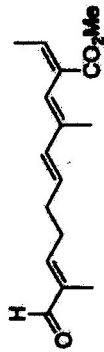
CC(C)=CC/C=C/C/C=C/C(C)=C/C=C/C(=C)C(C)C(=O)OC

COC(=O)C=C(C)C/C=C\C/C=C\CC(C)=CCTBS

**Selective Synthesis of Epolactone Featuring Efficient.....
Ze Tan and Ei-ichi Negishi***

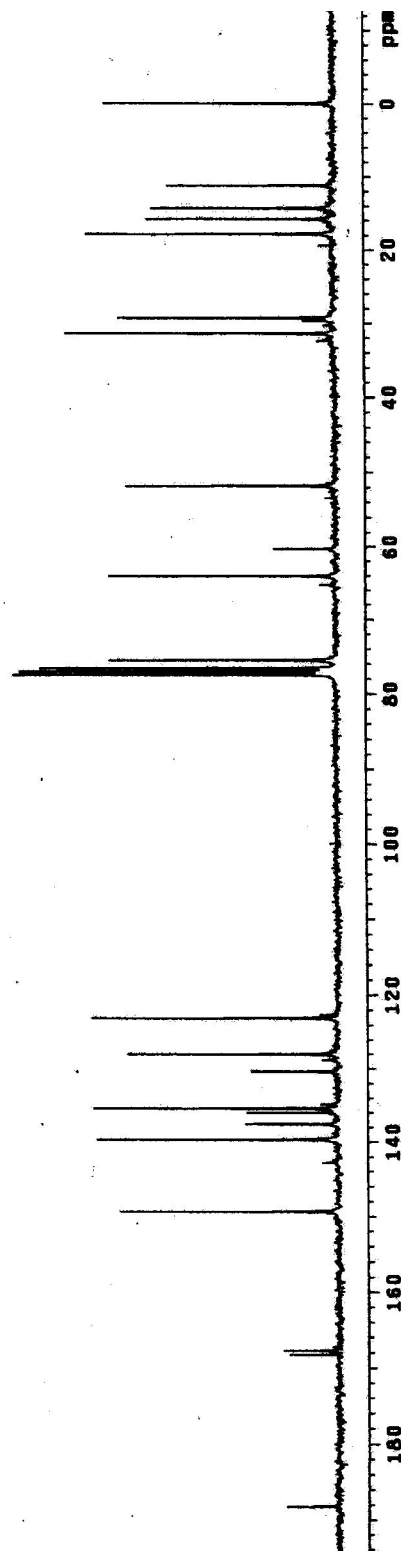
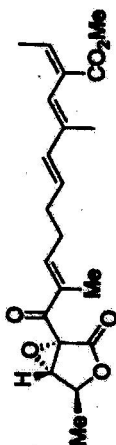


Selective Synthesis of Epolactaone Featuring Efficient....

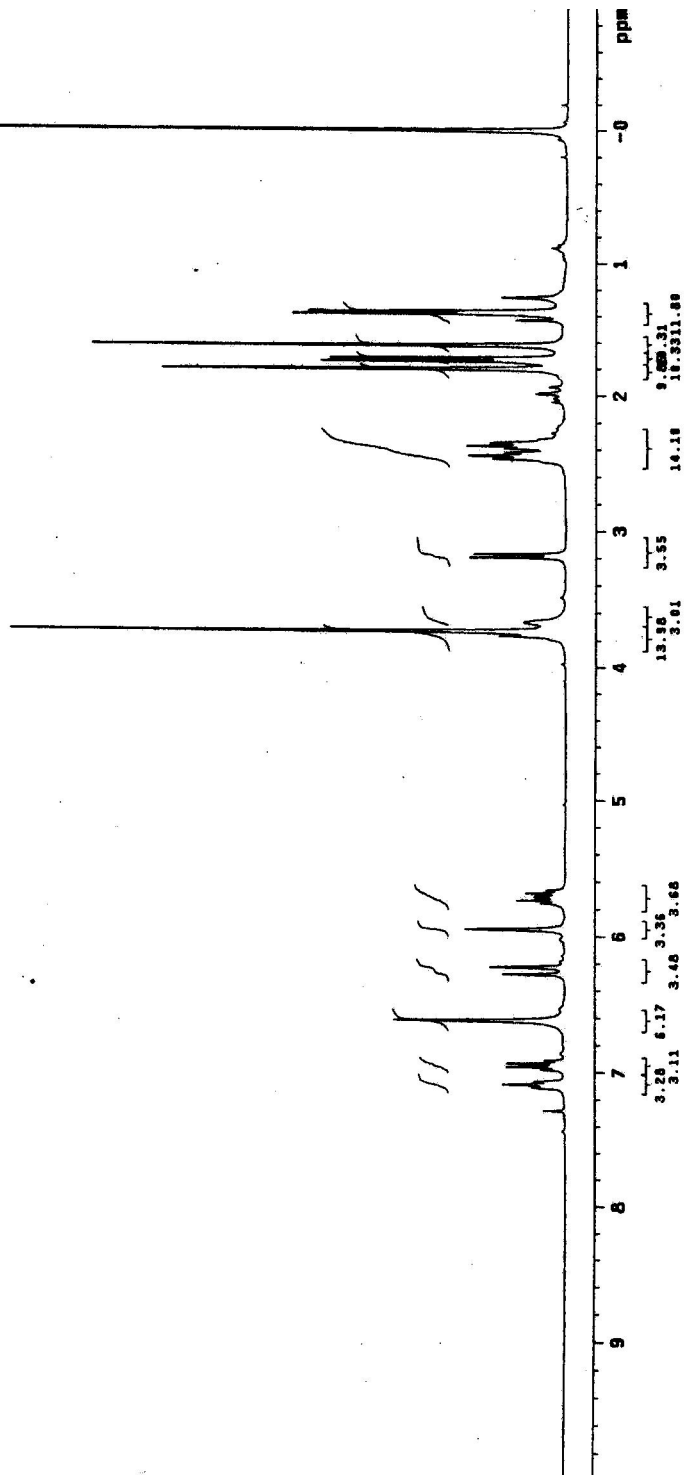
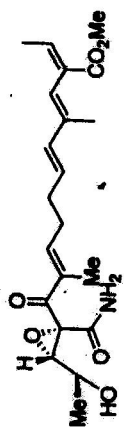


INDEX	FREQUENCY	PPM	HEIGHT
1	14194.898	100.199	8.4
2	12891.515	100.267	8.0
3	12851.204	107.793	8.4
4	11266.428	148.373	35.4
5	10825.893	139.600	39.0
6	10875.898	137.554	15.1
7	10856.491	135.082	16.8
8	10714.112	135.421	39.6
9	8830.856	130.340	14.8
10	8252.391	127.061	34.1
11	9208.582	123.040	38.9
12	5838.485	77.421	52.5
13	5067.723	77.000	51.4
14	5776.802	75.578	49.1
15	5093.382	75.484	38.7
16	4825.467	84.030	36.7
17	4543.613	89.540	19.0
18	3884.147	51.762	32.9
19	2369.534	31.498	43.7
20	2269.844	29.218	35.1
21	1939.929	17.795	40.2
22	1180.501	15.772	30.4
23	1077.267	14.284	28.6
24	849.213	11.140	28.9
25	-5.702	-0.000	37.2

Selective Synthesis of Epolactaene Featuring Efficient..... Ze Tan and Ei-ichi Negishi*

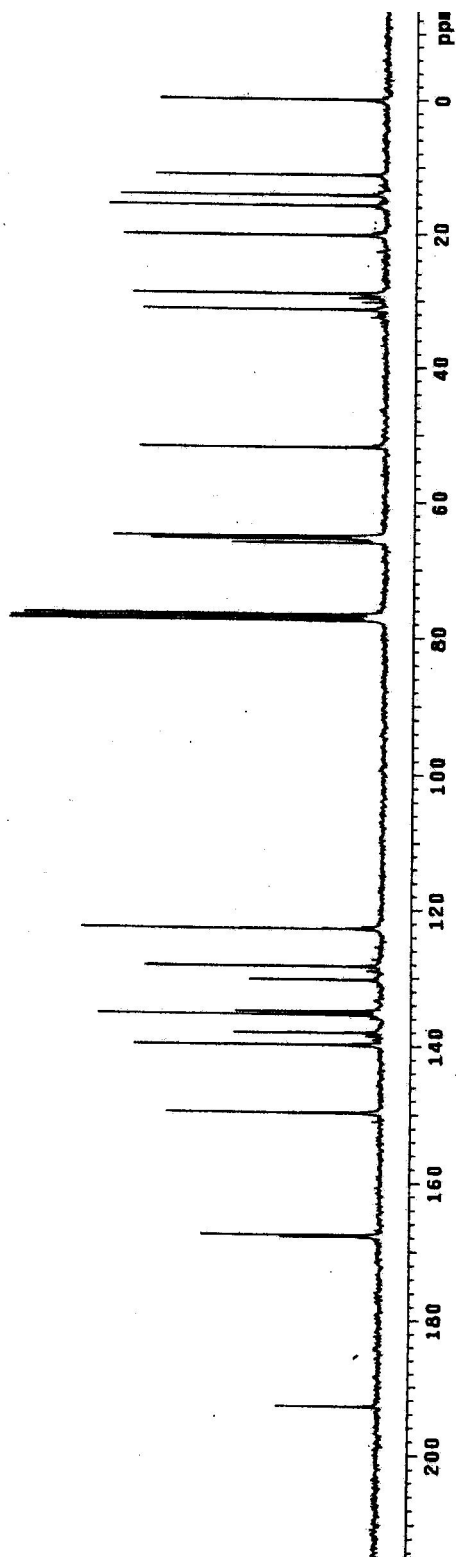
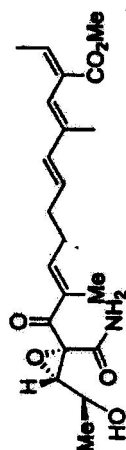


Selective Synthesis of Epolactaene Featuring Efficient..... Ze Tan and Ei-ichi Negishi*

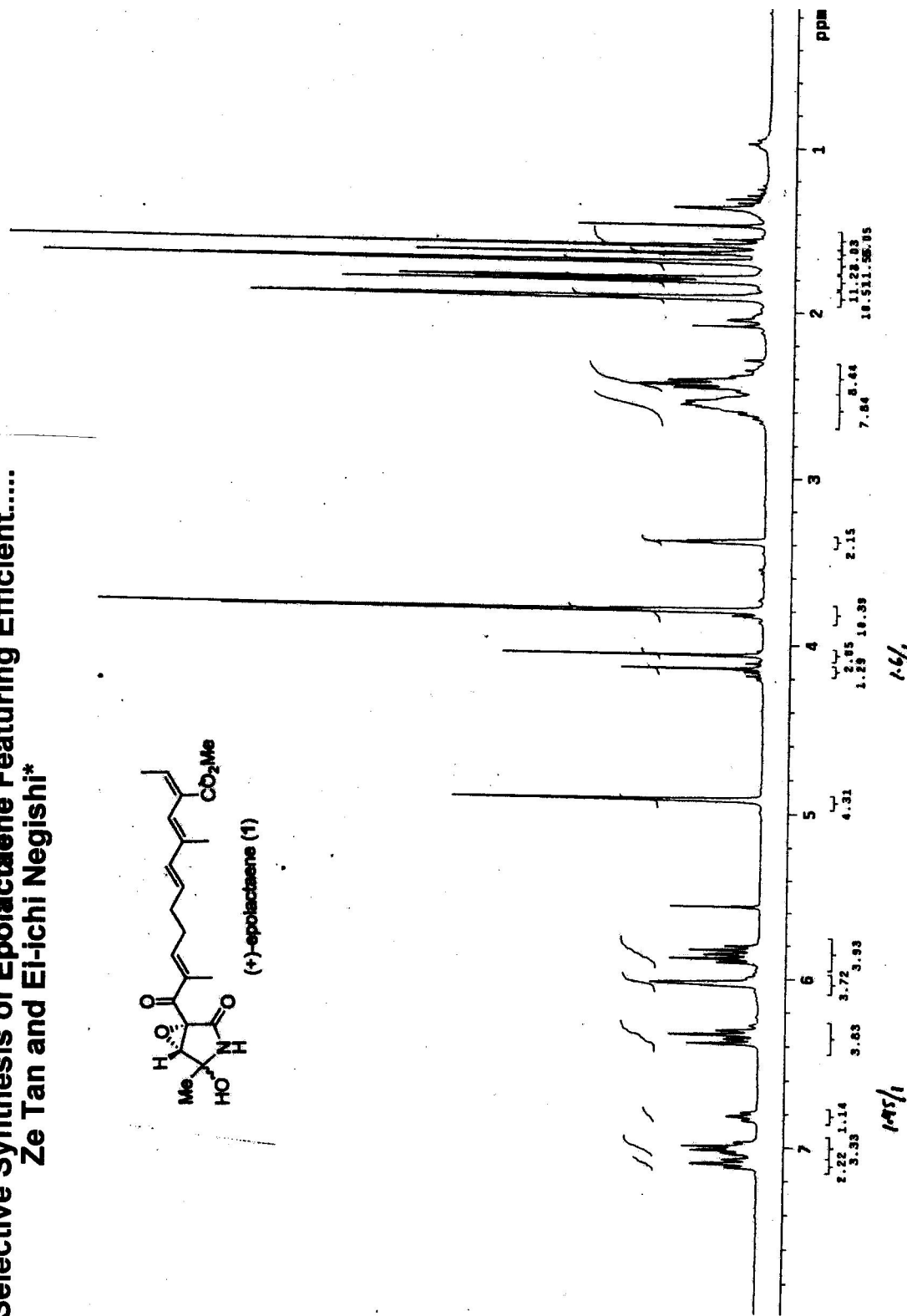
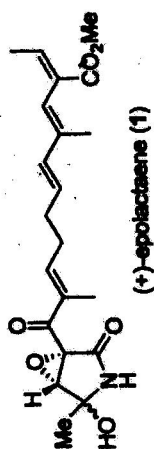


INDEX	FREQUENCY	PPM	HEIGHT
1	14558.628	152.815	16.4
2	12661.871	137.874	15.9
3	12646.898	137.593	28.6
4	11254.886	149.738	34.3
5	10548.687	139.856	39.5
6	10413.151	138.868	23.6
7	10289.877	135.385	45.5
8	10175.898	134.815	23.4
9	9826.621	139.283	21.1
10	9876.488	139.318	37.9
11	9259.148	152.769	48.2
12	5839.485	77.421	88.3
13	5807.723	77.099	89.2
14	5775.862	76.578	57.8
15	4977.888	85.885	24.4
16	4938.221	85.496	37.4
17	4985.895	85.941	43.5
18	3912.816	51.874	39.3
19	2360.534	31.296	38.9
20	2182.888	28.830	40.5
21	1526.283	20.236	42.2
22	1288.591	15.772	44.5
23	1073.132	14.228	42.6
24	844.468	11.198	36.9
25	-4.845	-8.862	86.3

Selective Synthesis of Epolactaene Featuring Efficient..... Ze Tan and Ei-ichi Negishi*



Selective Synthesis of Epolactaene Featuring Efficient.....
Ze Tan and Ei-ichi Negishi*



Selective Synthesis of Epolactaene Featuring Efficient..... Ze Tan and Ei-ichi Negishi*

