Supporting Information Available for *Org. Lett.*

First Total Synthesis of Natural 6-Epiplakortolide E

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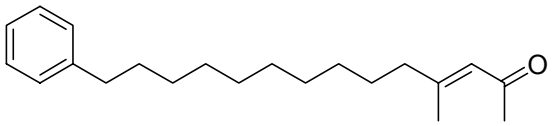


Compd. **3**

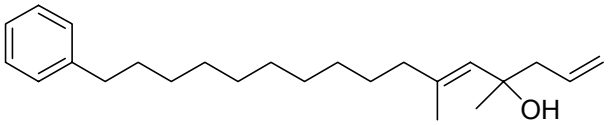
To 10-phenyldecane magnesium bromide, prepared from 1-bromo-10-phenyldecane (2.0 g, 6.7 mmol) and Mg turning (0.2 g, 8.7 mmol) in dry ether (45 ml), was slowly added 4-methoxy pent-3-en-2-one (0.77 g, 6.7 mmol) in dry ether solution at room temperature. After 2 h vigorous stirring, the reaction mixture was quenched with water (5 ml). A saturated solution of NH_4Cl in water was added to dissolve the solid of magnesium salts. Extraction with ether (2×50 ml) and EtOAc (2×50 ml), drying the combined extract with $MgSO_4$, and removing solvent *in vacuo* gave the crude product. The crude product was purified by chromatography on silica gel using 20 % EtOAc in hexane as eluant to obtain the compound **3** (1.4 g, 69 %).

^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.30～7.17(m, 5H), 6.06(s, 1H), 2.60(t, *J*=7.5Hz, 2H), 2.17(s, 3H), 2.07(s, 3H), 1.61(m, 4H), 1.44(m, 2H), 1.30～1.20(m and bs, 12H).

^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 198, 158, 128.8, 128.6, 125.9, 123.8, 41.6, 36.4, 32.2, 31.9, 29.9, 29.8, 29.7, 29.6, 27.9, 25.8, 19.6.

FT-IR (cm^{-1}) : 3022, 2926, 2849, 1678, 1627, 1459, 1368, 1255, 981, 756, 700.

HRMS *m/z* (M+) Calcd for $C_{21}H_{32}O$: 300.2455. Found : 300.2452.



Compd. **4**

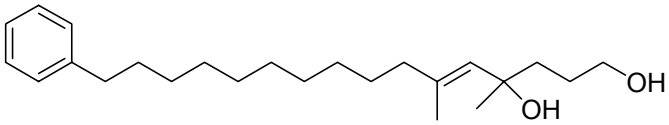
To allymagnesium bromide, prepared from 3-bromopropene (1.4 g, 11.6 mmol) and Mg turning (0.5 g, 20.5 mmol) in dry ether (50 ml), was slowly added compound **3** (1.4 g, 4.7 mmol) in dry ether solution at 0 °C. The mixture was stirred for 1.5h, and quenched with water (5 ml). A saturated solution of NH_4Cl in water was added to dissolve the solid of magnesium salts. Extraction with ether (3×50 ml), drying the combined extract with $MgSO_4$ and removing solvent *in vacuo* gave the crude product. The crude product was purified by chromatography on silica gel using 5 % EtOAc in hexane as eluant to obtain the compound **4** (1.6 g, 60 %).

^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.29～7.13(m, 5H), 5.83(m, 1H), 5.23(d, 1H, *J*=1.1Hz), 5.15(s, 1H), 5.09(dd, *J*=6.6Hz, 2.2Hz, 1.1Hz, 1H), 2.59(t, *J*=7.5Hz, 2H), 2.32(m, 2H), 1.94(t, *J*=7.0Hz, 2H), 1.82(s, 3H), 1.63(m, 2H), 1.40～1.15(m and s, 17H).

^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 143.3, 138.6, 134.6, 130.7, 128.7, 128.6, 125.9, 119.1, 72.7, 48.8, 41.4, 36.4, 31.9, 30.0, 29.9, 29.8, 29.7, 29.6, 29.1, 28.4, 17.3.

FT-IR (cm^{-1}) : 3572, 3460, 3073, 3027, 2930, 2849, 1637, 1500, 1449, 1103, 1006, 914, 746, 711.

HRMS *m/z* (M+) Calcd for for $C_{23}H_{38}O$: 330.2924. Found : 330.2952.



Compd. **5**

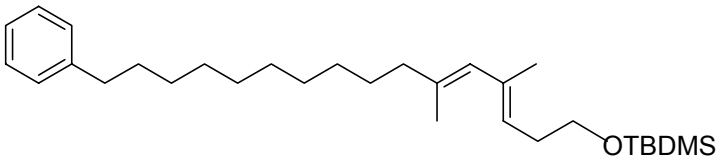
To compound **4** (1.4 g, 4.1 mmol) without solvent at 0 °C under nitrogen was added 9-BBN (0.5M in THF, 2 equiv.). The reaction mixture was warmed to room temperature and stirred for 1.5 h. After the reaction was completed, aq. 3 *N*-NaOH / 30 %-H_2O_2 (vol./vol.=1, 5 ml) was very carefully added during 20 min at room temperature and the mixture was stirred vigorously for 0.5 h. The reaction mixture was diluted with EtOAc (50 ml) and extracted with brine solution (45ml). The aqueous layer was re-extracted with ether (45 ml) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated in *vacuo* to give the crude prodduct. The crude product was purified by chromatography on silica gel using 20 % EtOAc in hexane as eluant to obtain the diol compound **5** (1.33 g, 90 %).

^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.30～7.16(m, 5H), 5.22(bs, 1H), 3.66(t, *J*=5.7Hz, 2H), 2.60(t, *J*=7.5Hz, 2H), 1.94(t, *J*=7.0Hz, 2H), 1.81(s, 3H), 1.66(m, 6H), 1.45～1.20(m and s, 17H).

^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 143.3, 138.3, 131.2, 128.8, 128.6, 125.9, 73.5, 63.8, 41.5, 40.9, 36.4, 31.9,

30.0, 29.9, 29.8, 29.7, 29.6, 28.5, 27.9, 17.3.

FT-IR (cm^{-1}) : 3358, 3033, 2926, 2865, 1668, 1454, 1378, 1062, 1026, 930, 756, 711.



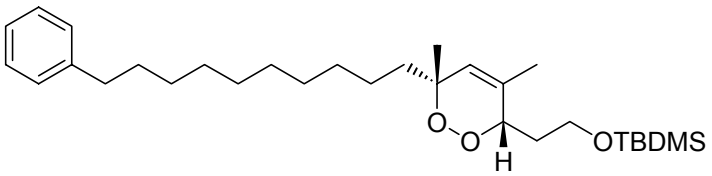
Compd. **6**

To a stirred solution of compound **5** (1.3 g, 3.3 mmol) in DMF (35 ml) at 0 °C was added imidazole (0.36 g, 5.3 mmol) and TBDMS-Cl (0.55 g, 3.6 mmol). The solution was warmed to room temperature and stirred for 4 h. The reaction mixture was added to brine (50 ml) in a separatory funnel and extracted with EtOAc (3×30 ml). The combined organic layers were dried over MgSO4, filtered and concentrated *in vacuo* to give the crude product. The crude product was purified by chromatography on silica gel using 20 % EtOAc in hexane as eluant to obtain the mono TBDMS protected compound **5a** (1.48 g, 98 %). To a solution of **5a** (0.31 g, 0.65 mmol) in benzene, $CaCl_2$ (200 mg) and TsOH (15 mg) was added and stirred vigorously for 2 h., and heated to 50 ^{o}C for 30 min. The reaction mixture was added to brine (15 ml) in a separatory funnel and extracted with EtOAc (3×10 ml). The combined organic layers were dried over MgSO4, filtered and concentrated *in vacuo* to give the crude product. The crude product was purified by chromatography on silica gel using 20 % EtOAc in hexane as eluant to obtain the mono TBDMS protected compound **6** (0.222 g, 80 %).

^{1}H-NMR (250MHz, $CDCl_3$) : δ 7.30～7.13(m, 5H), 5.60(bs, 1H), 5.22(bs, 1H), 3.61(m, 2H), 2.60(t, *J*=7.5Hz, 2H), 2.04(m, 2H), 1.75～1.56(m and s, 10H), 1.50～1.25(m and bs, 14H), 0.96(s, 9H), 0.12(s, 6H).

^{13}C-NMR (63MHz, $CDCl_3$) : δ 143.3, 137.9, 136.4, 135.4, 133.2, 129.4, 128.8, 128.0, 125.9, 125.0, 124.4, 123.4, 63.3, 40.0, 36.4, 33.4, 32.5, 31.9, 30.1, 29.9, 28.4, 26.4, 18.7, 18.1, -4.9.

FT-IR (cm^{-1}) : 3033, 2936, 2859, 2727, 1653, 1627, 1469, 1377, 1261, 1113, 950, 843, 782, 700.



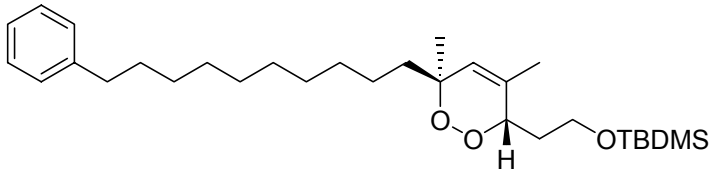
Compd. **7a**

General Method

A solution of compound **6** (71 mg, 0.155 mmol) in methylene chloride and 5% MeOH (10 ml) containing Rose Bengal (0.5 mg) was stirred under oxygen bubbling at 0℃, followed by irradiation with tungsten 500W lamp. When a clean yellow solution was obtaineded after 4 hr., the reaction was completed. The solvent was removed in vacuo, and the resulting crude product was purified by chromatography on silica gel using 5% EtOAc in hexane as eluant to obtain the compounds **7a** (23mg) and **7b** (13 mg).

^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.30～7.14(m, 5H), 5.44(t, *J*=1.4Hz, 1H), 4.24(bd, *J*=9.25Hz, 1H), 3.80(m, 2H), 2.60(t, *J*=7.5Hz, 2H), 1.85(m, 2H), 1.70(s, 3H), 1.59(m, 4H), 1.45(m, 2H), 1.28(s, 3H), 1.25(m, 16H), 0.90(s, 9H), 0.06(s, 6H).

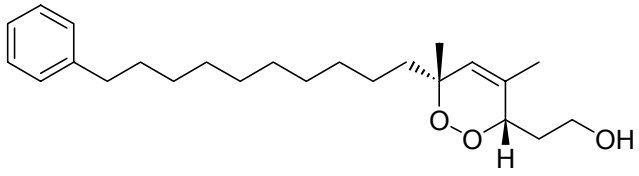
^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 144, 133.7, 128.8, 128.6, 126.7, 125.9, 80.3, 78.2, 64, 59.8, 39.2, 36.4, 35.4, 34.7, 31.9, 30.5, 29.9, 29.8, 29.7, 26.4, 24.4, 24.0, 19.2, 18.7, -4.94.



Compd. **7b**

^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.34～7.20(m, 5H), 5.50(bt, *J*=1.5Hz, 1H), 4.09(bd, *J*=8.4Hz, 1H), 3.61(m, 2H), 2.60(t, *J*=7.5Hz, 2H), 1.72(s, 3H), 1.63～1.56(m, 6H), 1.45～1.25(m and bs, 17H), 0.93(s, 9H), 0.08(s, 6H).

^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 144, 133.5, 128.8, 128.9, 126.7, 125.9, 80.1, 78.2, 64, 59.8, 39.2, 36.4, 35.6, 34.7, 31.9, 30.4, 29.9, 29.8, 29.6, 26.4, 24.4, 24.0, 19.2, 18.6, -4.95.



Compd. **8**

To a stirred solution of compound **7a** (100 mg, 0.21 mmol) in THF / MeOH (1:1, 35 ml) was added 10 % aq. HCl (0.5 ml) at 0 °C. The reaction was stirred for 1 h. at room temperature. Solvent was removed *in vacuo* to give viscous crude product. It was again dissolved in EtOAc (30 ml). EtOAc layer was washed with brine (2×20 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. The crud product

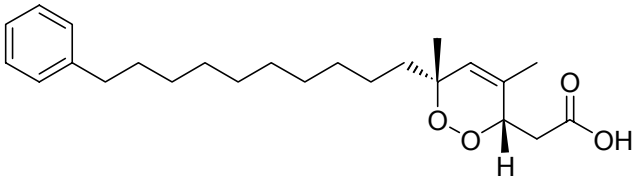
was purified by chromatography on silica gel using 35 % EtOAc in hexane as eluant to obtain the compound **8** (68.4 mg, 87 %).

^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.30～7.14(m, 5H), 5.49(t, *J*=1.3Hz, 1H), 4.28(bd, *J*=8.0Hz, 1H), 3.80(m, 2H), 2.60(t, *J*=7.5Hz, 2H), 1.95(m, 2H), 1.70(s, 3H), 1.60(m, 4H), 1.50(m, 2H), 1.35～1.20(m and s, 17H).

^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 143, 133, 128.8, 128.6, 127.3, 125.9, 80.7, 80, 60.4, 39.1, 36.4, 34.1, 31.9, 31.3, 30.5, 29.9, 29.7, 24.1, 24, 19.2.

FT-IR (cm^{-1}) : 3435, 3033, 2926, 2859, 1739, 1668, 1459, 1373, 1250, 1052, 746, 711.

HRMS *m/z* (M+) Calcd for for $C_{24}H_{38}O_3$: 374.2822. Found : 374.2849.



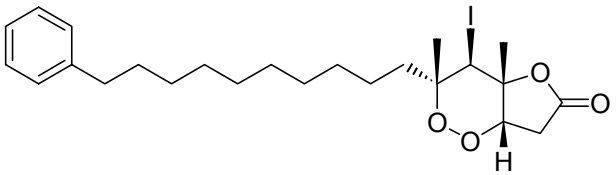
Compd. **9**

To a solution of compound **8** (60 mg, 0.16 mmol) in acetone (12 ml), a solution of 8*N* Jones` reagent (1.5 ml) was slowly added at 0 °C and stirred for 1.5 h at 25 °C. The reaction mixture was diluted with chilled water (15 ml). The solution was extracted with EtOAc (3×25 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. The crud product was purified by chromatography on silica gel using 25 % EtOAc in hexane as eluant to obtain the acid compound **9** (48.5 mg, 78 %).

^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.30～7.14(m, 5H), 5.51(t, *J*=1.35Hz, 1H), 4.54(bd, *J*=9.3Hz, 1H), 2.90(dd, J=16.1Hz, 9.3Hz, 1H), 2.64(dd, J=16.1Hz, 3.1Hz, 1H), 2.60(t, *J*=7.5Hz, 2H), 1.72(s, 3H), 1.60(m, 2H), 1.48(m, 2H), 1.31(s, 3H), 1.30(m, 14H).

^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 175.6, 143.4, 131.8, 128.8, 128.6, 128.2, 125.9, 80.7, 78.6, 63.7, 38.9, 37, 36.4, 31.9, 30.4, 29.9, 29.7, 24.5, 23.9, 19.1.

HRMS *m/z* (M+) Calcd for for $C_{24}H_{36}O_4$: 388.2615. Found : 388.2673.



Compd. **10**

General Method

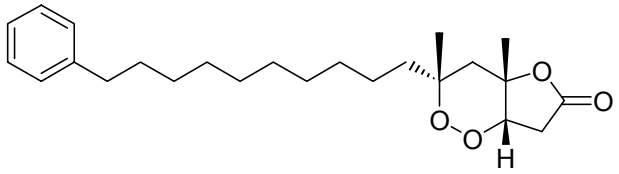
A mixture of 25 mg (0.064 mmol) of compound **9**, 40 mg (0.5 mmol) of $NaHCO_3$ and 5 ml of Distilled-water was placed 50ml flask and stirred until a homogeneous solution was obtained. Chloroform(5 ml) was added, the mixture was cooled in an ice bath , and 150 mg (1.2 mmol) of iodine was added at 0～5 ℃. The reaction mixture was stirred at 25℃ for 2 days. The layers were separated , and the organic phase was washed with 10% $Na_2S_2O_3$ until colorless solution was obtained and then with water (10 ml) and brine (10 ml). The solution was dried over anhydrous $MgSO_4$ and the solvent was removed in vacuo. The crude product was purified by chromatography on silica gel using 20% EtOAc in hexane as eluant to obtain the compound **10** (18mg, 55%).

^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.34～7.14(m, 5H), 4.86(t, *J*=7.8Hz, 1H), 4.32(s, 1H), 2.90(dd, *J*=8.9Hz, 3.5Hz, 2H), 2.60(t, *J*=7.5Hz, 2H), 1.77(s, 3H), 1.61(m, 4H), 1.47(s, 3H), 1.35～1.20(m, 14H).

^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 171.9, 143.3, 128.8, 128.6, 125.9, 84.7, 84.6, 82.8, 41.6, 39.4, 36.4, 32.8, 31.9, 30.1, 30.1, 30.0, 30.0, 29.9, 29.9, 29.1, 23.9, 23.1.

FT-IR (cm^{-1}) : 3026, 2927, 2848, 1789, 1466, 1242, 1137, 1078, 959, 808, 703.

Mass : Low Resolution FAB^{+} = 515$(M+H)^{+}$



Compd. **1a**

To a stirred solution of compound **10** (15 mg, 0.03 mmol) in benzene (15 ml) was added Bu_3SnH (26.2 mg, 0.09 mmol) and AIBN (5 mg, 0.06 mmol) at 25 °C. The solution was refluxed at 80 °C for 1 h. After solvent was removed *in vacuo*, the resultant crude product was purified by chromatography on silica gel using 35 % EtOAc in hexane as eluant to obtain the acid compound **1a** (8.0 mg, 68 %).

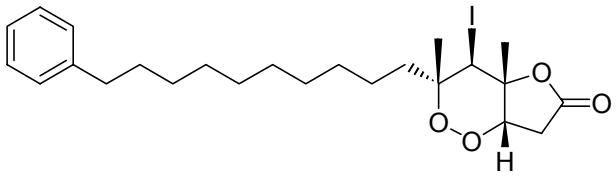
^{1}**H-NMR (250MHz, $CDCl_3$) :** δ 7.36～7.16(m, 5H), 4.48(d, *J*=5.8Hz, 1H), 2.95～2.53(ABq+d, *J*=8.3Hz, 18.5Hz, 5.8Hz, 2H), 2.60(t, *J*=7.5Hz, 2H), 2.30～1.64(ABq, *J*=15.5Hz, 15Hz, 2H), 1.80～1.50(m, 4H), 1.38(s, 3H), 1.30～1.15(m, 14H), 1.20(s, 3H).

^{13}**C-NMR (63MHz, $CDCl_3$) :** δ 174.5, 143, 128.8, 128.6, 125.9, 82.2, 80.9 80.3, 40.6, 36.9, 36.0, 34.1, 31.9, 29.9, 29.6, 29.6, 29.5, 29.4, 26.8, 25.3, 24.8, 23.6.

FT-IR (cm^{-1}) : 3026, 2927, 2855, 1789, 1466, 1387, 1262, 1170, 1078, 953, 703.

HRMS *m/z* (M+) Calcd for for $C_{24}H_{36}O_4$: 388.2615. Found : 388.2644.

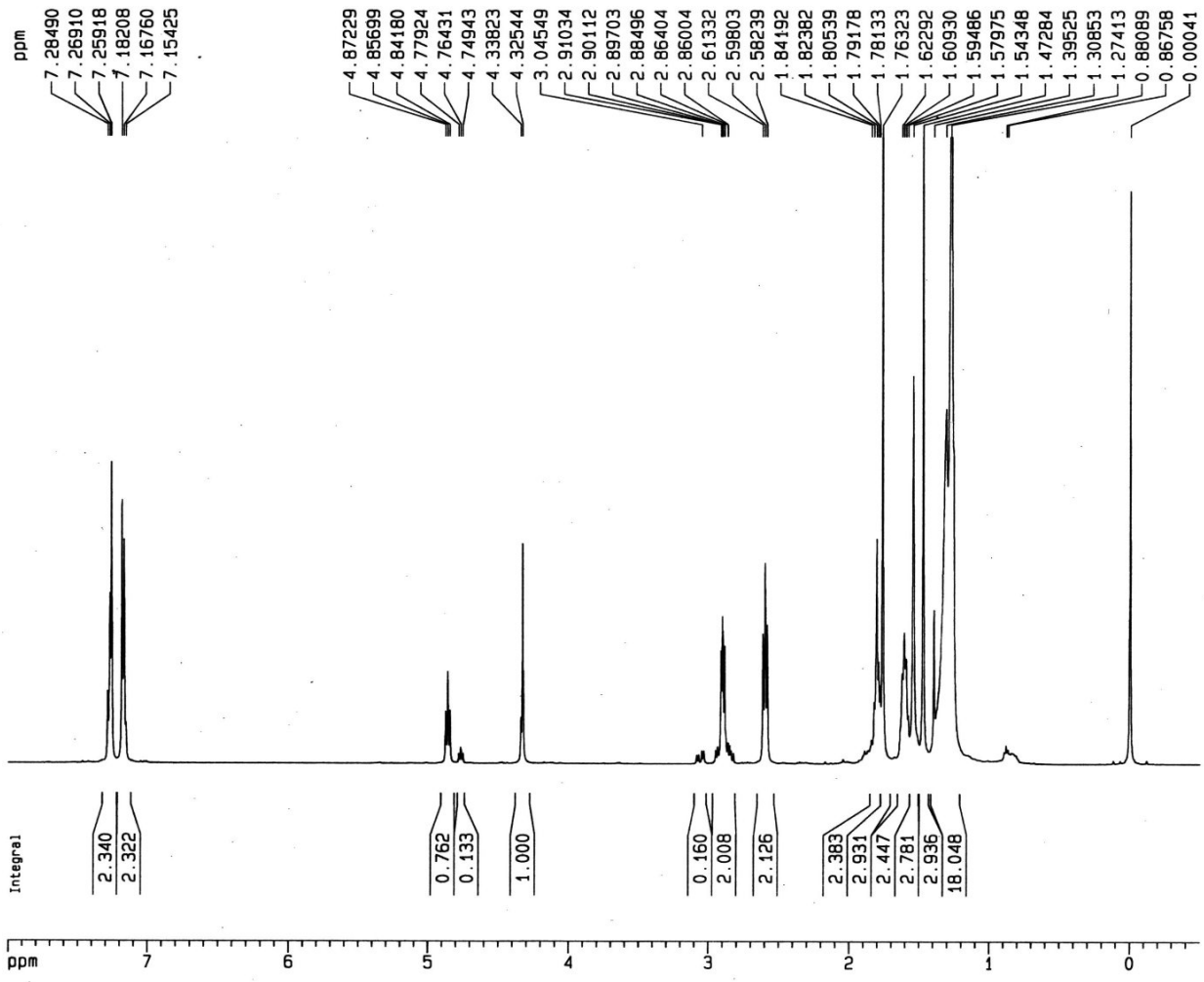
All spectral data of synthetic **1a** are identical to those of natural 6-epiplakortolide E of the literature.[1g]



5β-iodo-6-*epi*-plakortolide E **10**

Fig. S1: 250MHz ^{1}H-NMR spectrum of compound **10** at 300 K.
Fig. S2: 63MHz ^{13}C-NMR spectrum of compound **10** at 300 K.
Fig. S3: 500MHz NOESY spectrum of compound **10** at 300 K.
Fig. S4: 500MHz ROESY spectrum of compound **10** at 300 K.
Fig. S5: 500MHz TOCSY spectrum of compound **10** at 300 K.
Fig. S6: IR spectrum of compound **10** at 300 K.
Fig. S7: MS(FAB) spectrum of compound **10** at 300 K.

S1: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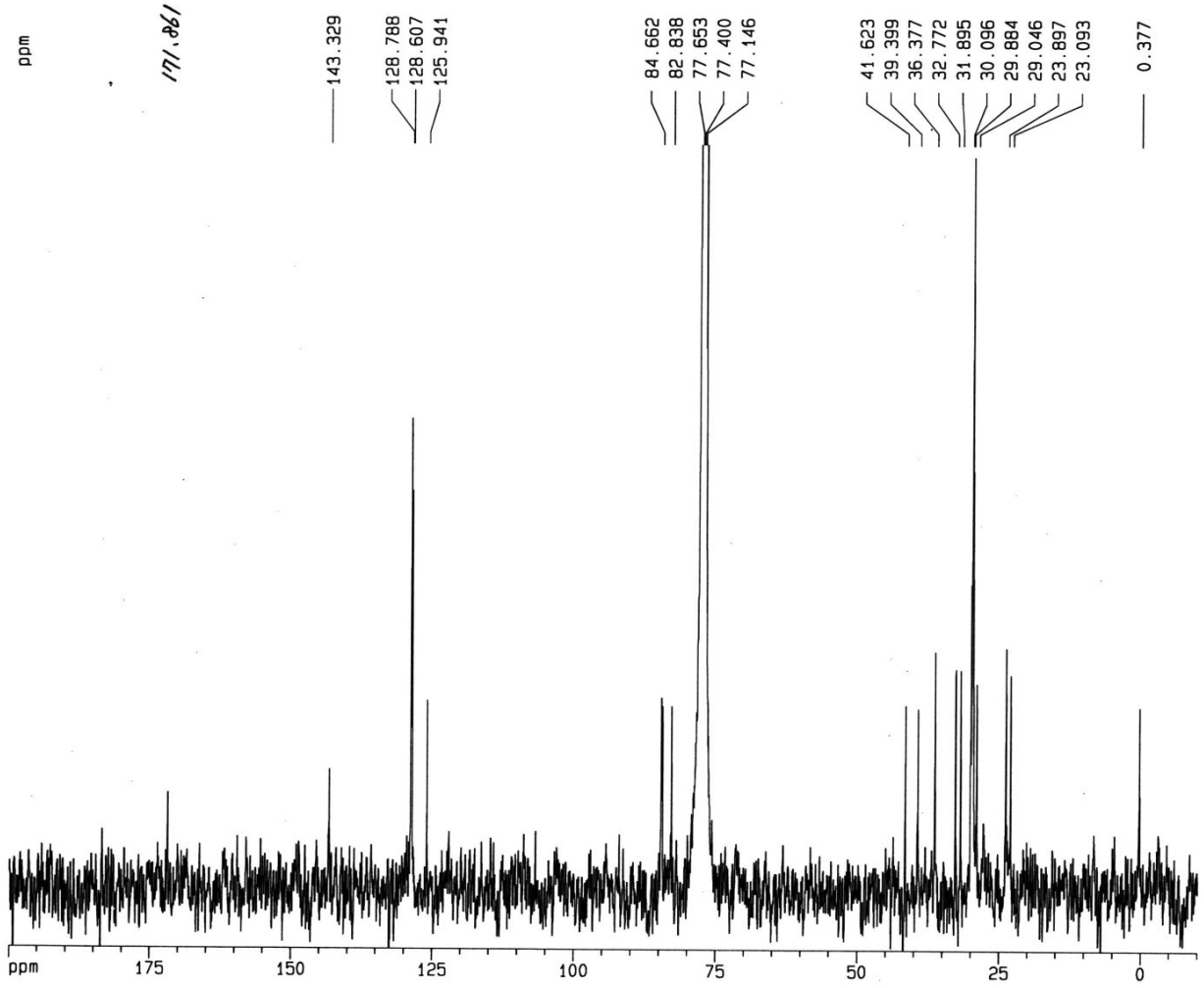
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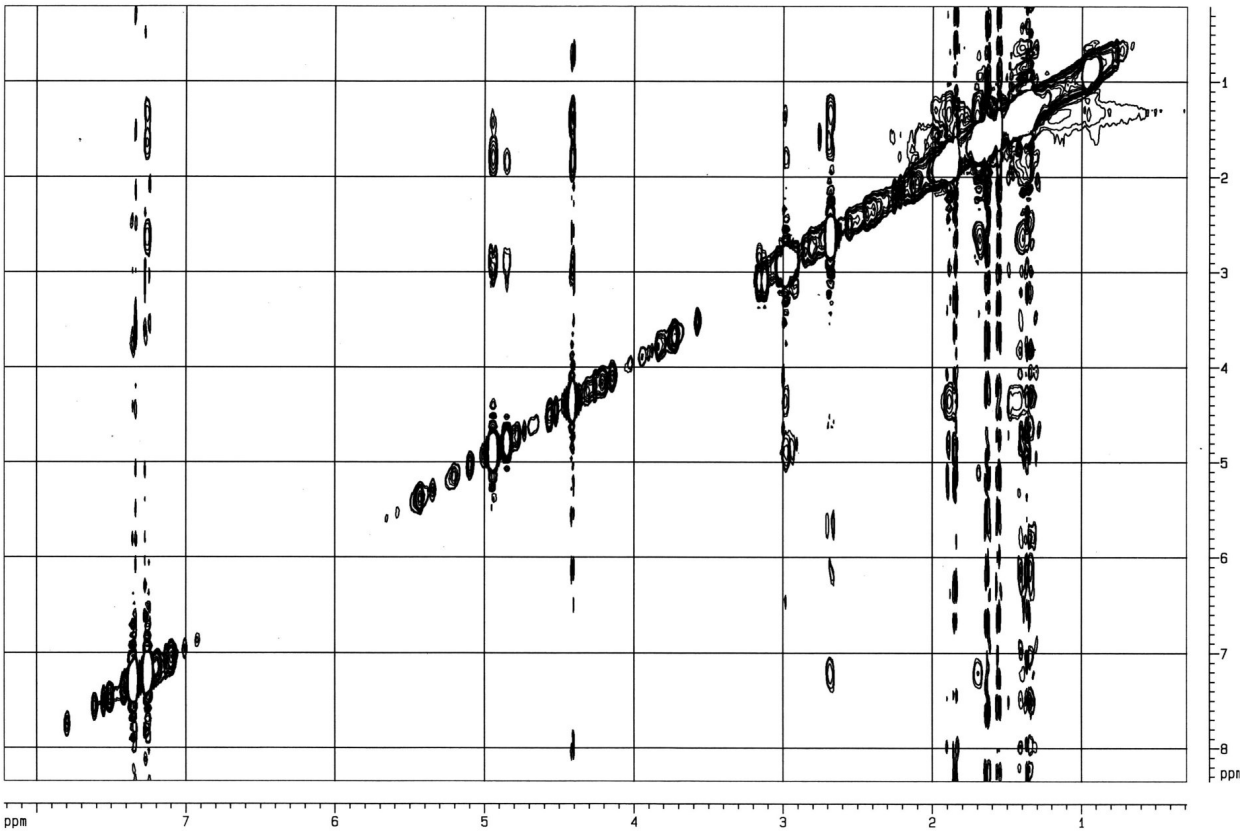

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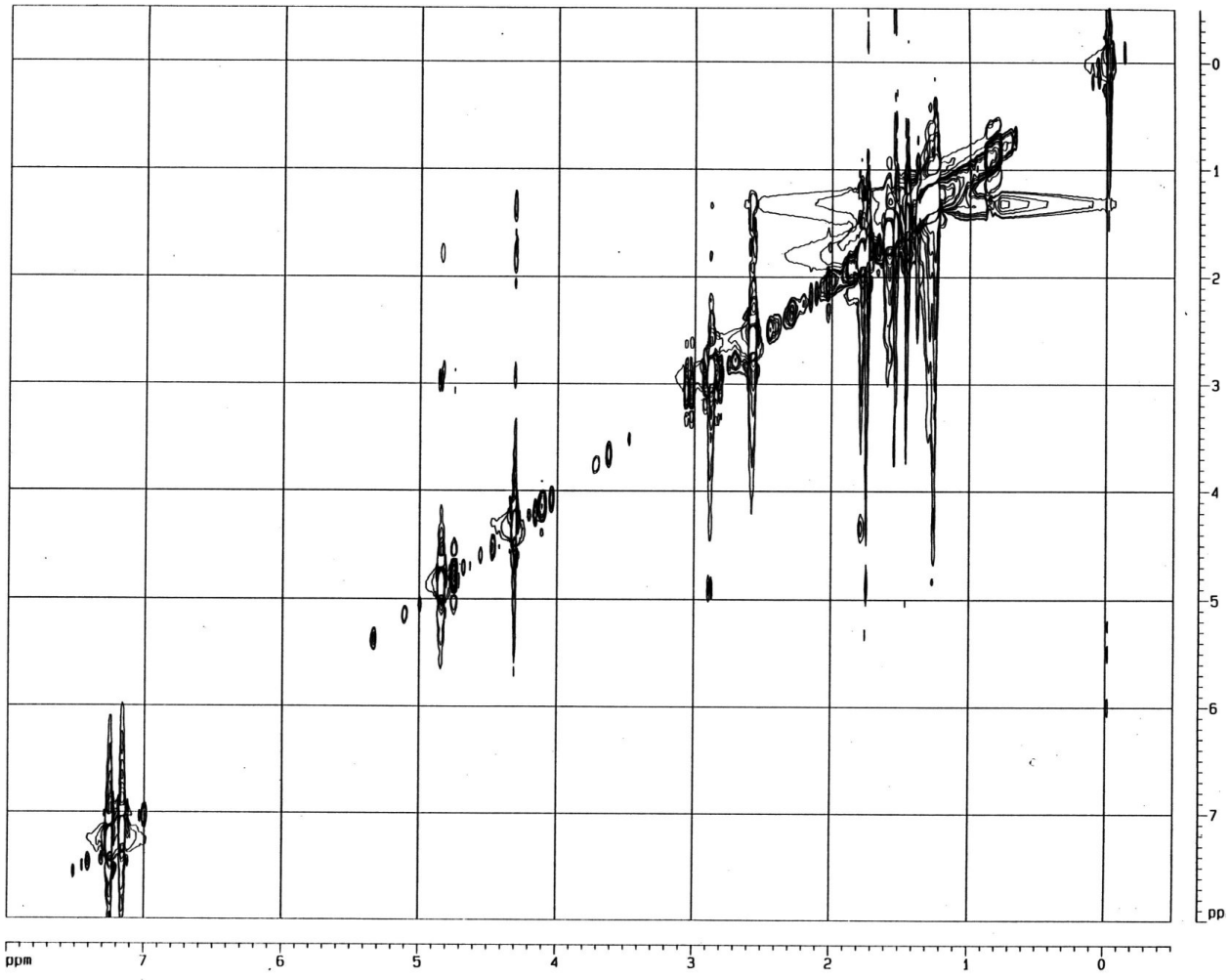

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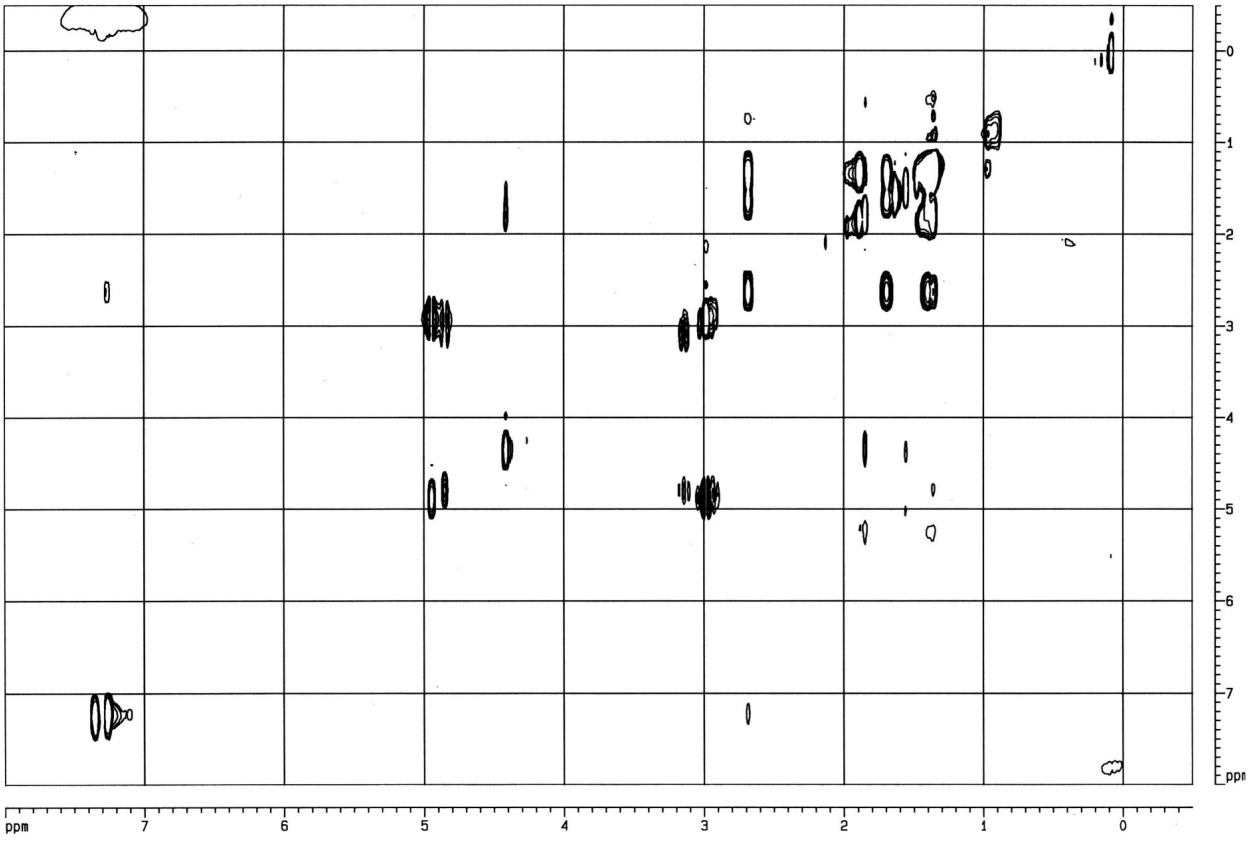

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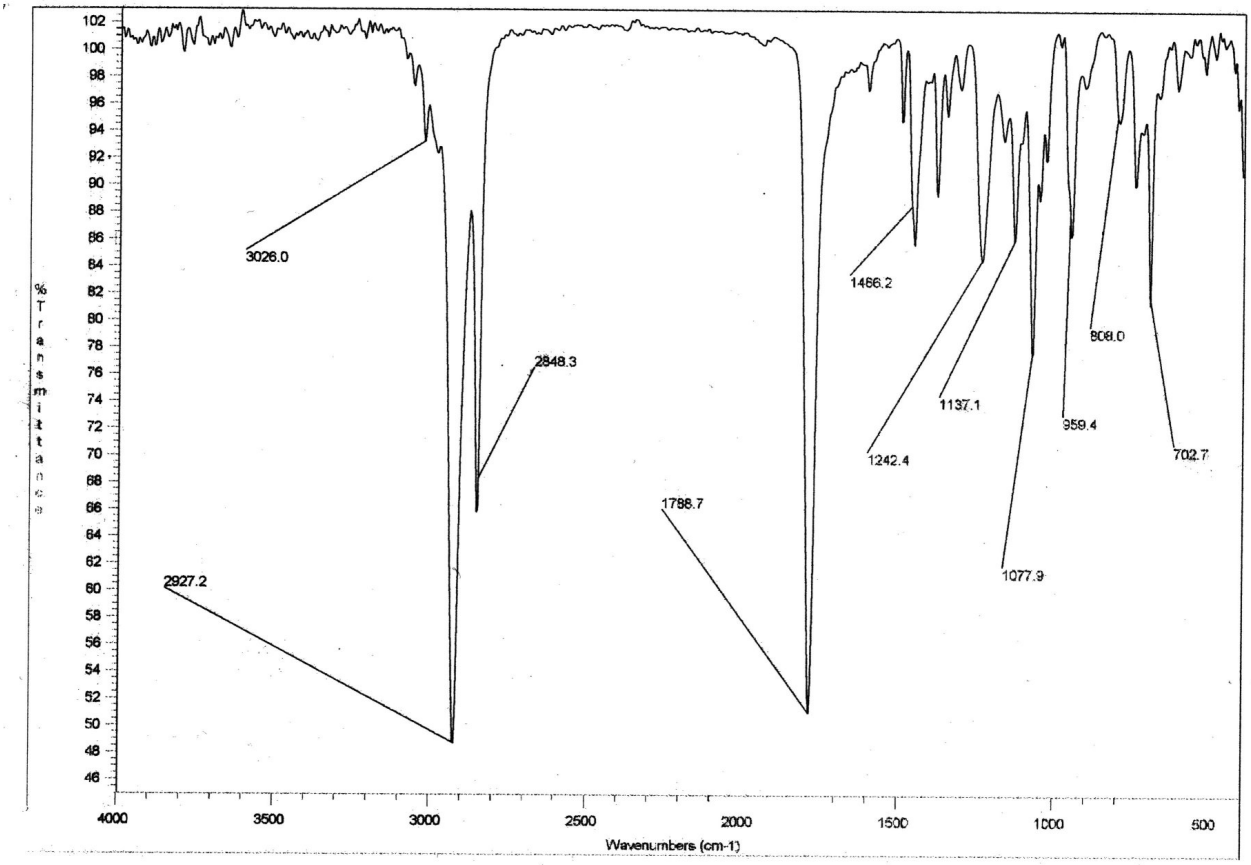
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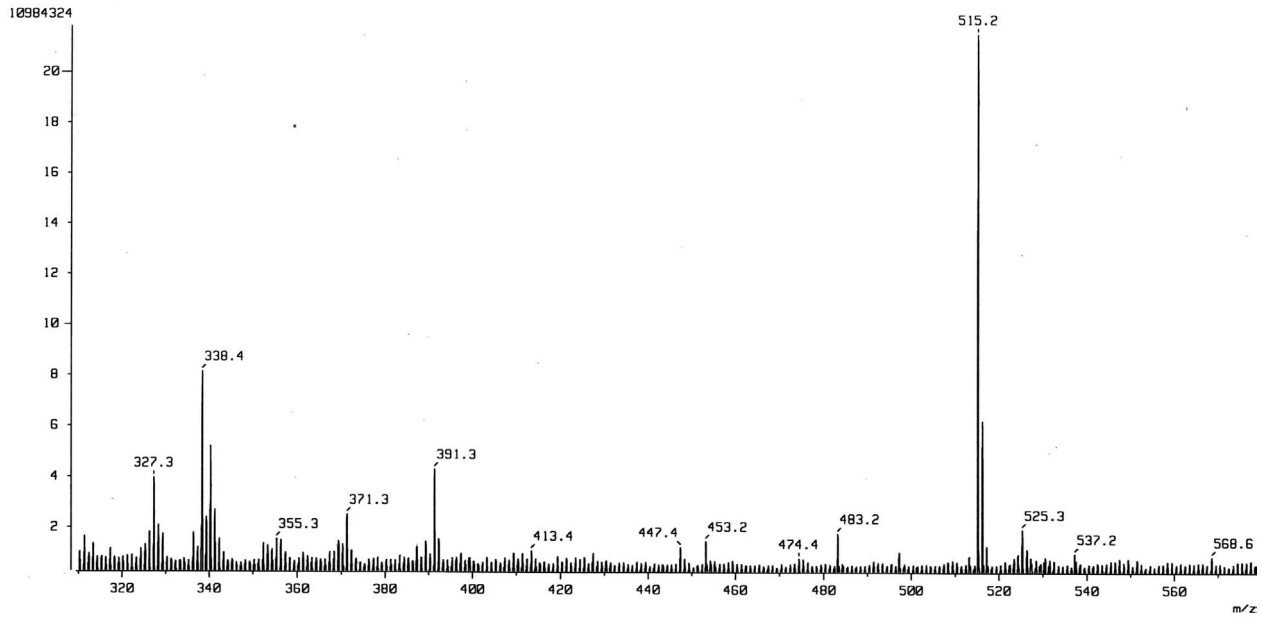
702.7

S7: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12
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327.3
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413.4
447.4
453.2
474.4
483.2
525.3
537.2
568.6
320
340
360
380
400
420
440
460
480
500
520
540
560
m/z