Supporting Information

β -(Methoxy-(substituted phenyl)-methyl)- γ -butyrolactones: A short synthesis from cinnamyl acetate

Buddh Singh,^{a*} Shiromani Sharma,^b Subhash C. Taneja ^a Ravi Shankar,^a

Payare L. Sangwan,^a

^a*Bio-Organic Chemistry Division, CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu Tawi 180001, India*

^b*Dev Nagari College, Chaudhary Charan Singh University, Meerut 250001, India*

[#]IIIM manuscript no. IIIM/1844/2015

*Corresponding author. Tel.: +91- 9419373404, E-mail address: bsingh@iiim.ac.in

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1. General Information

Commercial manganese (III) acetate $[\text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O}]$ was purchased from Aldrich chemical. Column chromatography was carried out with silica gel (60-120 mesh) eluting with ethyl acetate and petroleum ether. ^1H NMR spectra and ^{13}C NMR spectra were recorded at 200 and 500 MHz (Bruker) with CDCl_3 as solvent. The diastereomeric ratio *syn* and *anti* of β -(methoxy-(4-substituted phenyl)-methyl)- γ -butyrolactone was established by HPLC. IR spectra were recorded on a Shimadzu IR-450 FT-IR spectrophotometer.

Two set of reactions were carried out for free radical reaction using $\text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O}$, however both the experiments gave almost similar results.

In Method A, the reaction of cinnamyl acetates was carried out with manganese (III) acetate $\text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O}$ purchased from M/s Sigma Aldrich Chemicals, and in Method B, *in situ* generation of $\text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O}$ by refluxing potassium permanganate in glacial acetic acid.

2. General procedure for the formation of intermediate lactone 2 and its acid 3 using manganese (III) acetate

A mixture of 3-phenyl-2-propen-1-ol-acetate (1 mmol) and commercial manganese (III) acetate $\text{Mn}(\text{OAc})_3 \cdot 2\text{H}_2\text{O}$ (2.5 mmol) in 100ml glacial acetic acid : acetic anhydride (80:20) was refluxed until the dark brown colour of manganic acetate disappeared. The reaction mixture was concentrated under reduced pressure, diluted with water (20 mL) and extracted with ethyl acetate (3×30 mL). The combined organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated, and crude residue was purified by column chromatography to obtain the pure product lactone **2**, and corresponding carboxylic acid **3** in combined yield of 80%.

3. General procedure for the formation of intermediate lactones by insitu generated manganese (III) acetate

KMnO₄, 140 mmol (22.1g) was slowly added to boiling glacial acetic acid (500 mL). The mixture was refluxed for 5-6 hours, and then the solution was concentrated to half its volume. Acetic anhydride (50 mL) and 3-phenyl-2-propen-1-ol-acetate (20 mmol, 3.5g) added to the reaction mixture and refluxed till the brown colour disappeared. The reaction mixture was concentrated under reduced pressure, diluted with water (20 mL) and extracted with ethyl acetate (3× 30 mL). The combined organic layer was washed with water and dried over anhydrous sodium sulfate. The solvent was evaporated, and crude residue was purified by column chromatography to obtain the pure product lactone **2**, and corresponding carboxylic acid **3** in combined yield of 80%.

3. General procedure for the formation of intermediate lactones Dihydro-4-(hydroxy phenyl) methylfuran-2(3*H*)-one (6**) and Dihydro-4-(hydroxy methyl)-5-(phenyl)furan-2(3*H*)-one (**7**):**

Lactones **2** and acid **3** (5.9g, 20 mmol) were refluxed in aqueous alkaline solution for 6 h and cooled. The aqueous layer was extracted with ethyl acetate (3×100 mL) to remove unwanted impurities and then acidified with 10% HCl. The resulting organic products were extracted with ethyl acetate (3×100 mL), washed with water, dried over sodium sulphate and concentrated under thin film rota vapour to furnish 3.4g (87%) light yellow viscous crude products **6** and **7**. The resulting mixture was purified by column chromatography on silica by eluting the column with DCM then 0.1% MeOH: DCM to afford **6** yields 1.02g, 30% and **7** yields: (2.38g, 70%) Both the lactones were also found having ratio of *syn:anti* as 30:70.

4. General procedure for the preparation of β -(methoxy-(substituted phenyl)-methyl)- γ -butyrolactones **8a-c:**

Either the lactone **2** and the acid **3** or lactones **6** and **7**, 6.8g were refluxed in 3% conc.H₂SO₄/dry methanol 250 mL for 32 h. The reaction was monitored by TLC. After the completion of the reaction, the solvent was evaporated on thin film evaporator and the reaction

mixture poured into ice cold water (300 mL), while maintaining pH to 7.0. The contents were extracted with ethyl acetate (3 x 100 mL), the organic layer washed with water (3 x 30 mL), dried on anhydrous sodium sulphate, concentrated and after column chromatography on silica gel using 10% ethyl acetate in petroleum ether as eluent yielded 4.1 gram pure products **8a-e**

5. HPLC graph G-1 for β -(methoxy-(phenyl)-methyl)- γ -butyro lactone (**8a**, **8d** and **8e**)

The diastereomeric ratio of *syn* and *anti* β -(methoxy-(4-substetuted-phenyl)-methyl)- γ -butyro lactone was established by HPLC.

HPLC chromatograms, **Fig-1a** for compound **8a**, *syn* /*anti* ratio was determined 70:30, **Fig-1b** for compound **8d**, 65:35 , **Fig-1c** for compound **8e**, 60:40, respectively , each showing the two peaks

Figure-1. HPLC graph, **Fig-1a** for β -(methoxy-(phenyl)-methyl)- γ -butyro lactone; graph **Fig-1b** for β -(methoxy-(4-chlorophenyl)-methyl)- γ -butyro lactone; graph **Fig-1c** of β -(methoxy-(4-fluorophenyl)-methyl)- γ -butyro lactone, HPLC. Conditions- (R, R)-Whelk-01, chiral column, eluent 2-propanol:hexane (5:95), flow rate: 0.8 mL/min. Retention time =15.6min, 17.47min.

6. Characterization data of all products

Tetrahydro-2-(phenyl)-5-oxofuran-3-yl)-methyl acetate (2):

Yield: 2.78g, 42%, viscous liquid. $^1\text{H NMR}$ (200 MHz, CDCl_3): δ ; 2.03 (3H, s, COCH_3), 2.45-2.66 and 2.77-2.86 (2H, 2xm, CH_2CO), 2.77-2.86 (1H, m, CHCH_2CO), 4.18 (2H, d, $J=6.6\text{Hz}$, $\text{CH}_2\text{-O}$) 5.26 (1H, d, $J=6.3\text{Hz}$, Ar-CHO), 7.28-7.41 (5H, bs, ArH). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δ ; 20.6, 31.2, 43.3, 63.1, 83.2, 125.3, 125.6, 126.4, 128.6, 128.7, 138, 175, 179. **IR** (neat): 1781.3, 1741.3, 1234cm^{-1} **MS** at m/z M^+ = 235, 214.8, 174.1, 146.1, 105.1, 91.0, 77

4-Acetoxy-3-(acetoxymethyl)-4-phenylbutanoic acid (3):

Yield: 3.1g, 45%, light yellow viscous liquid. $^1\text{H NMR}$ (500 MHz, CDCl_3): δ ; 2.03 (3H, s, OCOCH_3), 2.07 (3H, s, OCOCH_3), 2.32-2.34, 2.48-2.53 (2H, m, CH_2COOH), 3.79-3.82 (1H, m, $\text{CHCH}_2\text{OCOCH}_3$), 4.10-4.22 (2H, m, $\text{CH}_2\text{OCOCH}_3$), 5.8-5.84 (1H, m, ArCHO), 7.28-7.35 (5H, m, ArH). $^{13}\text{C NMR}$ (125 MHz, CDCl_3): δ ; 21.09, 21.3, 32.8, 39.9, 63.7, 75.48, 126.9, 127.18, 128.77, 129.0, 129.02, 138, 170.3, 171.1, 178.4. **IR** (neat): 3458.8, 3229.4, 2927.3, 2853.9, 1740.5, 1371.7, 1231.7, 1044.4 cm^{-1} . **MS** at m/z , M^+ = 292.6, 276.8, 250.8, 190.5, 144.8, 116.9.

Dihydro-4-(hydroxy phenyl)methyl)furan-2(3H)-one (6):

Yield: 30% viscous liquid. $^1\text{H NMR}$ (200 MHz, CDCl_3): δ ; 2.21-2.26, and 2.43-2.55 (2H, m, CH_2CO) and 2.64-2.84 (1H, m, CHCH_2CO), 4.0-4.09, 4.21-4.29 & 4.52-4.57 (3H, 3xm, CH_2O and CHOH), 7.29 (5H, s, ArH). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δ ; 30.2, 42.4, 69.0, 74.5, 125.6, 126.0, 126.9, 128.4, 128.7, 141.8, 177.3. **IR** (neat): 3447, 2923, 1771, 1186, 1023, 703 cm^{-1} . **MS** at m/z , $M^+ + \text{Na} = 214.8$, **190.7, 174.7, 146.4**.

Dihydro-4-(hydroxy methyl)-5-(phenyl)furan-2(3H)-one (7):

Yield: 70% light yellow viscous liquid $^1\text{H NMR}$ (200 MHz, CDCl_3): δ ; 2.57-2.77 (3H, m, CH_2CO - and CH_2CHCH_2), 3.76 (2H, d, $J=4.1\text{Hz}$, $\text{CH}_2\text{OCOCH}_2$), 5.39 (1H, d, $J=5.6\text{ Hz}$, ArCHO), 7.36 (5H s, ArH). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δ ; 31.3, 46.1, 61.5, 82.85, 125.3, 125.8, 126.0, 128.6, 128.8, 138, 176.7. **IR** (neat): 3426.3, 2931.4, 1778.4, 1196 cm^{-1} . **MS** at m/z , $M^+ = 193.0$, 175.7, 146.4, 105.0.

NMR data of the final products

β -(Methoxy-(phenyl)-methyl)- γ -butyrolactone (8a):

Yield: 75%, Light yellow viscous liquid. $^1\text{H NMR}$ (200 MHz, CDCl_3): δ ; 2.18-2.31, 2.57-2.69 (2H, 2xm, CH_2CO) 2.76-2.91 (1H, CHCH_2CO), 3.20 (3H, s, OCH_3), 4.01 (1H, d, $J=6.0\text{Hz}$, ArCHOCH_3) 4.38 & 4.01 (2H, 2x, d, 6.9Hz CH_2O -), 7.30-7.43 (5H, m, ArH). $^{13}\text{C NMR}$ (50 MHz, CDCl_3): δ ; 30.9, 31.3, 42.8, 56.8, 69.8, 83.9, 126.8, 126.7, 128.5, 128.8, 139, 177. **IR**

(neat): 3029.7, 2926, 1776, 1632, 1405, 1093 cm^{-1} . **MS** at m/z , M^+ = 206.8, 174.9, 121, 91.
 HR-MS $M+1$ (EI) m/z : 207.1000 [M^+ calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3$: 206.0927].

β -(Methoxy-(4-methoxyphenyl)-methyl)- γ -butyrolactone (8b):

Yield: 18%, Light yellow viscous liquid. **^1H NMR** (400 MHz, CDCl_3): δ ; 2.10-2.36, 2.61-2.66, 2.82-2.84 (3H, 3xm, CH_2CO , CHCH_2CO), 3.18 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 4.36 (1H, d, $J=8\text{Hz}$, ArCHOCH_3) 4.36-4.31 (2H, 2xm CH_2O), 6.91 (2H, d, $J=8.8\text{Hz}$, ArH), 7.19 (2H, d, $J=8.8\text{Hz}$, ArH). **^{13}C NMR** (100 MHz): δ ; 31.3, 42.4, 55.8, 56.6, 69.8, 83.7, 114.2, 114.3, 128.1, 128.4, 130.6, 157.9, 176.1. **IR** (neat): 2935.6, 2836.4, 1777.6, 1610.4, 1512.6, 1247.7, 1175.9, cm^{-1} . **MS** at m/z , $M^+ + \text{Na}$ = 258.9, 204.8, 147.0. HR-MS $M+1$ (EI) m/z : 237.1118 [M^+ calcd for $\text{C}_{13}\text{H}_{16}\text{O}_4$: 236.1049].

β -(Methoxy-(4-chlorophenyl)-methyl)- γ -butyrolactone (8d):

Yield: 45%, Light yellow viscous liquid. **^1H NMR** (200 MHz, CDCl_3): δ ; 2.16-2.43, 2.57-2.65 (2H, 2xm, CH_2CO), 2.74-2.87 (1H, m, CHCH_2CO), 3.2 (3H, s, OCH_3), 4.01-4.07 (1H, d, $J=6.8\text{Hz}$, ArCHOCH_3), 4.07- 4.37 (2H, m, CH_2O), 7.08 (2H, d, $J=7.22\text{Hz}$, ArH), 7.38 (2H, d, $J=8.4\text{Hz}$, ArH). **^{13}C NMR** (50 MHz, CDCl_3): δ ; 31.1, 31.6, 42.7, 57.4, 84, 128.6, 128.6, 129.5, 129.5, 134.7, 137.9, 175. **IR** (neat): 3145, 1779.2, 1407, 1175.4, 1087.6, cm^{-1} , **MS**: (M/Z) M^+ = 243.4, 157.1, 91.0, 78.0. HR-MS (EI) m/z : 240.0549 [M^+ calcd for $\text{C}_{12}\text{H}_{13}\text{ClO}_3$: 240.0476].

β -(Methoxy-(4-fluorophenyl)-methyl)- γ -butyrolactone (8e):

Yield: 65%, Light yellow viscous liquid. **^1H NMR** (200 MHz, CDCl_3): δ ; 2.15-2.43, 2.58- 2.65 (2H, 2xm, CHCH_2CO), 2.74-2.89 (1H, m, CH_2CHCH_2), 3.2 (3H, s, OCH_3), 4.01-4.15 (1H, d, $J=6.8\text{Hz}$, ArCHOCH_3), 4.01-4.38 (2H, 2xm, CH_2O), 7.04-7.13 (2H, m, ArH), 7.2-7.3 (2H, m, ArH). **^{13}C NMR** (50 MHz, CDCl_3): δ ; 30.8, 31.1, 56.7, 69.6, 83, 115.6, 115.8, 128.5, 128.6, 134.4, 161.6, 176.8. **IR** (neat): 2932, 1778, 1604, 1509, 1270, 1222, 1016, cm^{-1} . **MS** at m/z , $\text{M}^+ + \text{Na} = 246.8$, 224.6, 193.1. HR-MS $\text{M}+1$ (EI) m/z : 225.0928 [M^+ calcd for $\text{C}_{12}\text{H}_{13}\text{FO}_3$: 224.0857].

8. Spectral graphs of all synthesised compounds

Qualitative Compound Report

Data File	1.d	Sample Name	1
Sample Type	Sample	Position	Vial 21
Instrument Name	Instrument 1	User Name	
Acq Method	new method.m	Acquired Time	11-11-2014 PM 7:20:56
IRM Calibration Status	Success	DA Method	daily_report.m
Comment			

Sample Group		Info.	
Acquisition SW	6200 series TOF/6500 series		
Version	Q-TOF B.05.01 (B5125)

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
Cpd 41: C12 H14 O3	0.229	206.0927	C12 H14 O3	C12 H14 O3	7.78	C12 H14 O3

Compound Label	m/z	RT	Algorithm	Mass
Cpd 41: C12 H14 O3	207.1	0.229	Find by Molecular Feature	206.0927

MFE MS Spectrum

MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
207.1	1	2028.63	C12 H15 O3	(M+H)+
208.1033	1	463.71	C12 H15 O3	(M+H)+

Predicted Isotope Match Table

Isotope	m/z	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	207.1	207.1016	7.61	100	100	81.39	88.29
2	208.1033	208.105	8.26	22.86	13.27	18.61	11.71

--- End Of Report ---

Qualitative Compound Report

Data File	I.d	Sample Name	1
Sample Type	Sample	Position	Vial 7
Instrument Name	Instrument 1	User Name	
Acq Method	vishal_12-01-13.m	Acquired Time	18-12-2014 PM 1:13:18
IRM Calibration Status	Success	DA Method	daily_report.m
Comment			

Sample Group		Info.
Acquisition SW	6200 series TOF/6500 series	
Version	Q-TOF B.05.01 (B5125)

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
Cpd 10: C13 H16 O4	0.277	236.1049	C13 H16 O4	C13 H16 O4	-0.05	C13 H16 O4

Compound Label	m/z	RT	Algorithm	Mass
Cpd 10: C13 H16 O4	237.1118	0.277	Find by Molecular Feature	236.1049

MFE MS Spectrum

MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
237.1118	1	2510.03	C13 H17 O4	(M+H)+
238.1172	1	516.88	C13 H17 O4	(M+H)+

Predicted Isotope Match Table

Isotope	m/z	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	237.1118	237.1121	1.36	100	100	82.92	87.41
2	238.1172	238.1155	-6.87	20.59	14.41	17.08	12.59

--- End Of Report ---

Qualitative Compound Report

Data File	3.d	Sample Name	3
Sample Type	Sample	Position	Vial 23
Instrument Name	Instrument 1	User Name	
Acq Method	new method.m	Acquired Time	11-11-2014 PM 7:31:35
IRM Calibration Status	Success	DA Method	daily_report.m
Comment

Sample Group	Info.
Acquisition SW	6200 series TOF/6500 series
Version	Q-TOF B.05.01 (85125)

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
Cpd 100: C12 H12 Cl O3	1.854	239.0476	C12 H12 Cl O3	C12 H12 Cl O3	-0.36	C12 H12 Cl O3

Compound Label	m/z	RT	Algorithm	Mass
Cpd 100: C12 H12 Cl O3	240.0549	1.854	Find by Molecular Feature	239.0476

MFE MS Spectrum

MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
240.0549	1	3064.31	C12 H13 Cl O3	(M+H)+

Predicted Isotope Match Table

Isotope	m/z	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	240.0549	240.0548	-0.36	100	100	100	100

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Qualitative Compound Report

Data File	BS-4.d	Sample Name	BS-4
Sample Type	Sample	Position	Vial 2
Instrument Name	Instrument 1	User Name	
Acq Method	vishal_12-01-13.m	Acquired Time	07-02-2015 AM 11:31:02
IRM Calibration Status	Success	DA Method	daily_report.m
Comment

Sample Group	Info.	
Acquisition SW	6200 series TOF/6500 series	
Version	Q-TOF B.05.01 (B5125)	

Compound Table

Compound Label	RT	Mass	Formula	MFG Formula	MFG Diff (ppm)	DB Formula
Cpd 23: C12 H13 F O3	0.276	224.0857	C12 H13 F O3	C12 H13 F O3	-3.56	C12 H13 F O3

Compound Label	m/z	RT	Algorithm	Mass
Cpd 23: C12 H13 F O3	225.0928	0.276	Find by Molecular Feature	224.0857

MFE MS Spectrum

MS Spectrum Peak List

m/z	z	Abund	Formula	Ion
225.0928	1	33905.81	C12 H14 F O3	(M+H)+
226.0967	1	5347.11	C12 H14 F O3	(M+H)+
227.1003	1	1086.42	C12 H14 F O3	(M+H)+
449.1784	1	1567.59	C24 H27 F2 O6	(2M+H)+
450.176	1	360.76	C24 H27 F2 O6	(2M+H)+

Predicted Isotope Match Table

Isotope	m/z	Calc m/z	Diff (ppm)	Abund %	Calc Abund %	Abund Sum %	Calc Abund Sum %
1	225.0928	225.0921	-3.04	100	100	84.05	87.2
2	226.0967	226.0955	-5.26	15.77	13.25	13.26	11.56
3	227.1003	227.0978	-10.81	3.2	1.42	2.69	1.24

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