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Free radical scavenging and α-glucosidase inhibitory activity of (*E*)-methyl/ethyl-3-(2-hydroxyphenyl)acrylates

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(*E*)-Methyl/ethyl-3-(2-hydroxyphenyl)acrylates **3a-x** have been prepared by the reaction of salicylaldehydes **1a-l** with Wittig reagents such as methyl (triphenylphosphoranylidene)acetate **2a** and ethyl (triphenylphosphoranylidene)acetate **2b** in dry DCM at room temperature. All the synthesized compounds have been evaluated for free-radical scavenging and α-glucosidase inhibitory activities. Compounds **3c** and **3d** display DPPH free radical scavenging activity. All the compounds have shown ABTS free radical scavenging activity except four compounds **3s-t** and **3w-x**. Compounds **3g**, **3p** and **3r** display α-glucosidase inhibitory activity.

Keywords: (*E*)-Methyl/ethyl-3-(2-hydroxyphenyl)acrylates, salicylaldehydes, free radical scavenging, α-glucosidase inhibitory activity

(*E*)-α,β-Unsaturated esters[1] are an important compounds and valuable intermediates for the preparation of various synthetic and natural products[2]. The widely used methods for the preparation of these esters are the Wittig reaction[3] and Horner-Wadsworth-Emmons using alkoxycarbonyl methylene(triphenyl)phosphoranes and trialkyl phosphonoacetates[3-10]. These esters have applications in the food, polymer and perfume industries. Therefore, the commercial scale preparations of these compounds are necessary.

As part of our ongoing research on the preparation of heterocyclic compounds[11,12] and natural products[13,14], recently, we have prepared various novel heterocyclic compounds by the reaction of salicylaldehydes with β-ketoesters[15-18]. The reaction of salicylaldehydes with Wittig reagent provides the (*E*)-α,β-unsaturated esters and its biological properties have not been studied. Therefore, the present manuscript describes the preparation of α,β-unsaturated esters and their evaluation of DPPH, $ABTS^{\cdot+}$ free radical scavenging and α-glucosidase inhibitory activities.

Results and Discussion

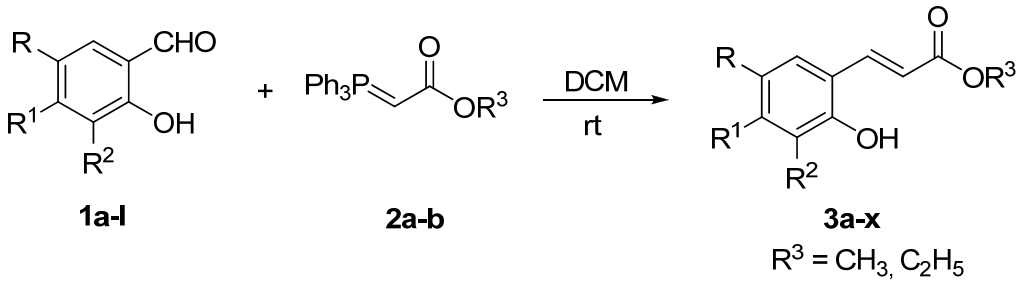
The target (*E*)-methyl/ethyl 3-(2-hydroxyphenyl)acrylate compounds **3a-x** have been prepared by the reaction of salicylaldehydes **1a-l** with Wittig reagents[19] namely methyl (triphenylphosphoranylidene)acetate **2a** and ethyl (triphenylphosphoranylidene)acetate **2b** in dry DCM at RT (Scheme I, Table I). All the compounds are characterized by spectral data.

Biology

The prepared compounds **3a-x** have been evaluated for their biological activities such as DPPH, $ABTS^{\cdot+}$ free radical scavenging and α-glucosidase inhibitory[20] for the first time and the results are described below.

Free radicals scavenging activity

The DPPH and $ABTS^{\cdot+}$ free radical scavenging activity of compounds **3a-x** are presented in Table II along with the standard drugs Ascorbic acid and Trolox (SC_{50} values)[20]. Among the prepared compounds, the methoxy (5^{th} position) substituted compounds **3c** (SC_{50} 6.47 μg/mL) and **3d** (SC_{50} 6.21 μg/mL) have shown the DPPH free radical scavenging activity in comparison with the standard compound Ascorbic acid (SC_{50} 4.08 μg/mL). However, the methoxy compounds **3e-f** positioned at 4^{th} position and remaining compounds **3a-b** and **3g-x** could not display the activity.



Scheme I

Table I — Preparation of (*E*)-methyl/ethyl-3-(2-hydroxyphenyl) acrylates **3a-x**

Entry	Compd	R	R^1	R^2	R^3	Yield [a] (%)
1	**3a**	H	H	H	CH_3	84
2	**3b**	H	H	H	C_2H_5	86
3	**3c**	OCH_3	H	H	CH_3	82
4	**3d**	OCH_3	H	H	C_2H_5	84
5	**3e**	H	OCH_3	H	CH_3	82
6	**3f**	H	OCH_3	H	C_2H_5	82
7	**3g**	CH_3	H	H	CH_3	76
8	**3h**	CH_3	H	H	C_2H_5	80
9	**3i**	F	H	H	CH_3	70
10	**3j**	F	H	H	C_2H_5	72
11	**3k**	Cl	H	H	CH_3	74
12	**3l**	Cl	H	H	C_2H_5	75
13	**3m**	Br	H	H	CH_3	77
14	**3n**	Br	H	H	C_2H_5	79
15	**3o**	Cl	H	Cl	CH_3	74
16	**3p**	Cl	H	Cl	C_2H_5	74
17	**3q**	Br	H	Br	CH_3	68
18	**3r**	Br	H	Br	C_2H_5	70
19	**3s**	NO_2	H	H	CH_3	62
20	**3t**	NO_2	H	H	C_2H_5	65
21	**3u**	NO_2	H	Br	CH_3	56
22	**3v**	NO_2	H	Br	C_2H_5	54
23	**3w**	NO_2	H	NO_2	CH_3	48
24	**3x**	NO_2	H	NO_2	C_2H_5	42

[a] Isolated yields

The $ABTS^{\cdot+}$ free radical scavenging activity of compounds **3a-r** and **3u-v** have shown ranging from SC_{50} 1.24-3.93 μg/mL when compared to standard compound Trolox (SC_{50} 1.16 μg/mL). It is interesting to note that twenty compounds (methyl, methoxy, halo substitution) have shown $ABTS^{\cdot+}$ free radical scavenging activity among the prepared 24 compounds. The nitro substituted compounds **3s-t** and di nitro substituted compounds **3w-x** could not shown $ABTS^{\cdot+}$ free radical scavenging activity.

α-Glucosidase inhibitory activity

α-Glucosidase inhibitory activity of compounds **3a-x** and their IC_{50} values presented in Table II along with the standard drug Acarbose[20]. Three compounds have shown α-glucosidase inhibitory activity in the present series of compounds. The methyl substituted compound **3g** (IC_{50} 4.39 μg/mL) has shown better α-glucosidase inhibitory activity when compared to methoxy **3c-f**, and halo **3i-o**. Interestingly, the dichloro **3p** (IC_{50} 10.79 μg/mL) shown moderate activity and dibromo compound **3r** (IC_{50} 2.31 μg/mL) displayed potent α-glucosidase inhibitory activity (Table II).

Experimental Section

All the chemicals and reagents were purchased from Aldrich (Sigma-Aldrich, USA), AVRA Chemicals Pvt. Ltd (Hyderabad, India) and were used without further purification. Reactions were monitored by thin layer chromatography (TLC) on pre-coated silica gel 60 F_{254} (mesh); spots were visualized under UV light. Melting points were determined on a Stuart melting point apparatus and are uncorrected. IR spectrum was recorded with a Thermo Nicolet Nexus 670 FT spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 300, 400 and 500 MHz spectrometers. Chemical shifts (δ) are quoted in parts per million and are referenced to tetramethylsilane (TMS) as internal standard. ESI-MS were obtained on quarto micro spectrometer.

General experimental procedure for the preparation of compounds, 3a-x

Methyl (triphenylphosphoranylidene)acetate **2a** (1.0 mmol) was added to a stirred solution of salicyl aldehyde **1a** (1.0 mmol) in dry DCM (2 mL) at RT. The reaction mixture was stirred at the same temperature until the starting materials disappeared (TLC). After completion of the reaction, the solvent was removed and the reaction mixture was purified by column chromatography (EtOAc/hexane) to give colourless solid **3a**. Similarly, the compounds **3b-x** have been prepared by the reaction of salicylaldehydes **1a-l** with Wittig reagents such as methyl (triphenylphosphoranylidene)acetate **2a** and

Table II — DPPH, $ABTS^{\cdot+}$, α-glucosidase inhibitory activity profile of compounds **3a-x**

Compd	DPPH % Inhibition 25µg/mL (SC_{50} µg /mL)	$ABTS^{\cdot+}$ % Inhibition 20 µg /mL (SC_{50} µg /mL)	AGI % Inhibition 20 µg/mL (IC_{50} µg /mL)
3a	12.00±0.07	98.19±0.32 (1.25)	25.79±0.62
3b	10.42±0.22	96.71±0.48 (1.34)	35.12±0.61
3c	72.75±0.04 (6.47)	96.37±0.64 (1.36)	ND
3d	73.17±1.23 (6.21)	98.19±0.00 (1.25)	19.72±0.00
3e	40.41±0.86	97.28±0.00 (1.41)	19.01±0.00
3f	42.07±0.07	97.28±0.00 (1.31)	19.01±0.00
3g	26.56±1.49	98.64±0.00 (1.24)	80.19±1.87(4.39)
3h	26.48±0.26	96.37±1.28 (1.36)	32.31±0.87
3i	14.43±0.45	97.51±0.96 (1.37)	34.33±2.49
3j	12.08±0.93	97.96±0.00 (1.29)	29.58±0.75
3k	6.86±0.04	97.28±0.00 (1.31)	38.38±0.50
3l	6.30±0.45	97.51±0.64 (1.37)	40.41±0.12
3m	5.20±0.75	97.51±0.00 (1.37)	42.96±0.00
3n	4.35±0.30	97.51±0.32 (1.37)	34.15±0.25
3o	2.27±1.21	98.19±0.00 (1.25)	57.31±1.62
3p	3.38±0.48	98.41±0.00 (1.38)	64.96±0.00 (10.79)
3q	ND	71.32±1.12 (3.93)	52.90±1.89
3r	3.35±0.37	96.71±0.16 (1.34)	97.36±0.24 (2.31)
3s	ND	5.22±1.28	53.70±0.25
3t	ND	3.29±0.16	ND
3u	8.52±1.72	98.64±0.00 (1.24)	28.61±0.37
3v	8.47±1.198	98.53±0.16 (1.26)	38.91±0.00
3w	ND	6.24 ±0.16	37.68±0.00
3x	ND	2.72±0.00	ND
Ascorbic acid	85.68±0.86 (4.08)	–	–
Trolox	–	98.87±0.00 (1.16)	–
Acarbose	–	–	98.57±0.05 (2.17)

ethyl (triphenylphosphoranylidene)acetate **2b** under our optimized conditions. All the compounds are characterized by spectral data.

Methyl(*E*)-3-(2-hydroxyphynyl)arylate, 3a: Colourless solid. m.p.136-137°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ ^{1}H NMR 8.06 (d, *J* = 16.2 Hz, 1H, CH), 7.47 (dd, *J* = 7.7, 1.2 Hz, 1H, aromatic), 7.27-7.21 (m, 1H, aromatic), 6.92 (t, *J* = 7.5 Hz, 1H, aromatic), 6.86 (dd, *J* = 8.1, 0.7 Hz, 1H, aromatic), 6.72 (s, 1H, OH), 6.65 (d, *J* = 16.2 Hz, 1H, CH), 3.83 (s, 3H, OCH_3); ESI-MS: *m/z* $[M+H]^+$ 179.

Ethyl(*E*)-3-(2-hydroxyphynyl)acrylate, 3b: Colourless solid. m.p.143-144°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 16.1 Hz, 1H, CH), 7.45 (s, 2H, aromatic), 7.22 (t, *J* = 7.2 Hz, 1H, aromatic), 6.89 (d, *J* = 6.9 Hz, 2H, aromatic, OH), 6.67 (d, *J* = 16.1 Hz, 1H, CH), 4.30 (d, *J* = 6.9 Hz, 2H, OCH_2), 1.33 (dd, *J* = 24.8, 18.2 Hz, 3H, $\ominus OCH_3$); ESI-MS: *m/z* $[M+H]^+$ 193.

Methyl(*E*)-3-(2-hydroxy-5-methoxyphenyl)-acrylate, 3c: Colourless solid. m.p.126-130°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 16.2 Hz, 1H, CH), 6.97 (d, *J* = 2.6 Hz, 1H, aromatic), 6.86-6.77 (m, 2H, aromatic), 6.62 (s, 1H, OH), 6.58 (d, *J* = 16.1 Hz, 1H, CH), 3.83 (d, *J* = 5.4 Hz, 3H, OCH_3), 3.77 (s, 3H, OCH_3); ESI-MS: *m/z* $[M+H]^+$ 209.

Ethyl(*E*)-3-(2-hydroxy-5-methoxyphenyl)-acrylate, 3d: Colourless solid. m.p.129-134°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 16.1 Hz, 1H, CH), 6.98 (d, *J* = 2.8 Hz, 1H, aromatic), 6.82 (m, 2H, aromatic), 6.57 (d, *J* = 16.1 Hz, 1H, aromatic), 6.31 (s, 1H, OH), 4.35-4.24 (m, 2H, OCH_2), 3.83-3.73 (m, 3H, OCH_3), 1.40-1.31 (m, 3H, $\ominus OCH_3$); ESI-MS: *m/z* $[M+H]^+$ 223.

Methyl(*E*)-3-(2-hydroxy-4-methoxyphenyl)-acrylate, 3e: Colourless solid. m.p.126-128°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 16.1 Hz, 1H, CH), 7.39 (d, *J* = 8.7 Hz, 1H, aromatic), 7.04 (s, 1H, OH), 6.52 (d, *J* = 16.1 Hz, 1H, CH), 6.49 (dd, *J* = 8.7, 2.4 Hz, 1H, aromatic), 6.41 (d, *J* = 2.4 Hz, 1H, aromatic), 3.83 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3); ESI-MASS: *m/z* $[M+H]^+$ 209.

Ethyl(*E*)-3-(2-hydroxy-4-methoxyphenyl)-acrylate, 3f: Colourless solid. m.p.129-134°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (d, *J* = 16.1 Hz, 1H, CH), 7.39 (d, *J* = 8.7 Hz, 1H, aromatic), 7.32 (s, 1H, OH), 6.54 (d, *J* = 16.1 Hz, 1H, CH), 6.48 (dd, *J* = 8.6, 2.3 Hz, 1H, aromatic), 6.42 (d, *J* = 2.4 Hz, 1H,

aromatic), 4.33-4.24 (m, 2H, OCH_2), 3.79 (s, 3H, OCH_3), 1.39-1.29 (m, 3H, $\ominus CH_3$); ESI-MS: *m/z* $[M+H]^+$ 223.

Methyl(*E*)-3-(2-hydroxy-5-methylphenyl)-acrylate, 3g: Colourless solid. m.p.136-144°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 16.2 Hz, 1H, CH), 7.04 (dd, *J* = 8.2, 1.7 Hz, 1H, aromatic), 6.75 (d, *J* = 8.2 Hz, 1H, aromatic), 6.61 (d, *J* = 16.2 Hz, 1H, CH), 6.38 (s, 1H, OH), 3.88-3.77 (m, 3H, OCH_3), 2.27 (s, 3H, CH_3); ESI-MS: *m/z* $[M+H]^+$ 193.

Ethyl(*E*)-3-(2-hydroxy-5-methylphenyl)-acrylate, 3h: Colourless solid. m.p.132-134°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, *J* = 16.1 Hz, 1H, CH), 7.26 (s, 1H, aromatic), 7.03 (dd, *J* = 8.2, 1.7 Hz, 1H, aromatic), 6.75 (t, *J* = 6.1 Hz, 1H), 6.59 (dd, *J* = 16.1, 5.4 Hz, 1H, CH), 6.24 (s, 1H, OH), 4.32-4.24 (m, 2H, OCH_2), 2.27 (s, 3H, CH_3), 1.34 (t, *J* = 7.1 Hz, 3H, $\ominus CH_3$); ESI-MS: *m/z* $[M+H]^+$ 207.

Methyl(*E*)-3-(5-fluoro-2-hydroxyphenyl)-acrylate, 3i: Colourless solid. m.p.126-128°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.97 (d, *J* = 16.2 Hz, 1H, CH), 7.16 (dd, *J* = 9.1, 3.0 Hz, 1H, aromatic), 6.95 (m, Hz, 1H, aromatic), 6.80 (dd, *J* = 8.9, 4.5 Hz, 1H, aromatic), 6.56 (d, *J* = 16.2 Hz, 1H, CH), 6.22 (d, *J* = 23.5 Hz, 1H, OH), 3.83 (d, *J* = 3.4 Hz, 3H, CH_3). ESI-MS: *m/z* $[M+H]^+$ 197.

Ethyl(*E*)-3-(5-fluoro-2-hydroxyphenyl)acrylate, 3j: Colourless solid. m.p.125-126°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 16.2 Hz, 1H, CH), 7.16 (dd, *J* = 9.2, 3.0 Hz, 1H, aromatic), 6.95 (ddd, *J* = 8.8, 7.8, 3.0 Hz, 1H, aromatic), 6.85-6.78 (m, 1H, aromatic), 6.59-6.54 (d, *J* = 16.2 Hz, 1H, CH), 4.29 (q, *J* = 7.1 Hz, 2H, OCH_2), 1.39-1.32 (m, 3H, $\ominus CH_3$); ESI-MS: *m/z* $[M+H]^+$ 211.

Methyl(*E*)-3-(5-chloro-2-hydroxyphenyl)-acrylate, 3k: Colourless solid. m.p.134-136°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 16.2 Hz, 1H, CH), 7.44 (d, *J* = 2.5 Hz, 1H, aromatic), 7.19 (dd, *J* = 8.6, 2.5 Hz, 1H,aromatic), 6.79 (d, *J* = 8.6 Hz, 1H, aromatic), 6.58 (d, *J* = 16.2 Hz, 1H, CH), 6.30 (s, 1H, OH), 3.83 (s, 3H, OCH_3); ESI-MS: *m/z* $[M+H]^+$ 213.

Ethyl(*E*)-3-(5-chloro-2-hydroxyphenyl)acrylate, 3l: Colour lees solid. m.p.124-126°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, *J* = 16.2 Hz, 1H, CH), 7.72 (s, 1H, OH), 7.42 (d, *J* = 2.5 Hz, 1H, aromatic), 7.17 (dd, *J* = 8.6, 2.5 Hz, 1H, aromatic), 6.83 (d, *J* = 8.6 Hz, 1H, aromatic), 6.64 (d, *J* = 16.2 Hz, 1H, CH), 4.30 (q, *J* = 7.1 Hz, 2H, OCH_2), 1.36 (t, *J* = 7.1 Hz, 3H, $\ominus CH_3$); ESI-MS: *m/z* $[M+H]^+$ 227.

Methyl(*E*)-3-(5-bromo-2-hydroxyphenyl)-acrylate, 3m: Colourless solid. m.p. 135-137°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 16.2 Hz, 1H, CH), 7.58 (d, *J* = 2.3 Hz, 1H, aromatic), 7.32 (dd, *J* = 8.6, 2.4 Hz, 1H, aromatic, aromatic), 6.75 (d, *J* = 8.6 Hz, 1H, aromatic), 6.72 (s, 1H, OH), 6.59 (d, *J* = 16.2 Hz, 1H, CH), 3.83 (s, 3H, OCH_3); ESI-MS: *m/z* $[M+H]^+$ 257.

Ethyl(*E*)-3-(5-bromo-2-hydroxyphenyl)-acrylate, 3n: Colourless solid. m.p.138-140°C. ^{1}H NMR (400 MHz, $CDCl_3$): 7.97 (d, *J* = 16.2 Hz, 1H, CH), 7.57 (d, *J* = 2.4 Hz, 1H, aromatic), 7.51 (s, 1H, OH), 7.36-7.27 (m, 1H, aromatic), 6.78 (d, *J* = 8.6 Hz, 1H, aromatic), 6.63 (d, *J* = 16.2 Hz, 1H, CH), 4.37-4.25 (m, 2H, OCH_2), 1.41-1.30 (m, 3H, $\ominus CH_3$); ESI-MS: *m/z* $[M+H]^+$ 271.

Methyl(*E*)-3-(3,5-dichloro-2-hydroxyphenyl)-acrylate, 3o: Colourless solid. m.p.128-130°C. ^{1}H NMR (400 MHz, $CDCl_3$: δ 7.86 (d, *J* = 16.2 Hz, 1H, CH), 7.37 (dd, *J* = 11.6, 2.4 Hz, 2H, aromatic, CH), 6.57 (d, *J* = 16.2 Hz, 1H, CH), 6.08 (s, 1H, OH), 3.82 (s, 3H, OCH_3); ESI-MS: *m/z* $[M+H]^+$ 247.

Ethyl(*E*)-3-(3,5-dichloro-2-hydroxyphenyl)-acrylate, 3p: Colourless solid. m.p.119-120°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, *J* = 16.2 Hz, 1H, CH), 7.37 (dd, *J* = 18.8, 2.4 Hz, 2H, aromatic, CH), 6.57 (d, *J* = 16.2 Hz, 1H, CH), 6.04 (s, 1H, OH), 4.30-4.25 (m, 2H, OCH_2), 1.37-1.32 (m, 3H, $\ominus CH_3$); ESI-MS: *m/z* $[M+H]^+$ 261.

Methyl(*E*)-3-(3,5-dibromo-2-hydroxyphenyl)-acrylate, 3q: Colourless solid. m.p.122-124°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 16.2 Hz, 1H, CH), 7.61 (d, *J* = 2.3 Hz, 1H, aromatic), 7.55 (d, *J* = 2.3 Hz, 1H, aromatic), 6.56 (d, *J* = 16.1 Hz, 1H, CH), 5.97 (s, 1H, OH), 3.81 (s, 3H, OCH_3). ESI-MS: *m/z* $[M+H]^+$ 335.

Ethyl(*E*)-3-(3,5-dibromo-2-hydroxyphenyl)-acrylate, 3r: Colourless solid. m.p. 125-127°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.84 (d, *J* = 16.2 Hz, 1H, CH), 7.60 (d, *J* = 2.3 Hz, 1H, aromatic), 7.56 (d, *J* = 2.3 Hz, 1H, aromatic), 6.55 (d, *J* = 16.1 Hz, 1H, CH), 6.04 (s, 1H, OH), 4.27 (q, *J* = 7.1 Hz, 2H, OCH_2), 1.34 (dd, *J* = 9.2, 5.0 Hz, 3H, $\ominus CH_3$); ^{13}C NMR (126 MHz, $CDCl_3$): δ 166.75, 150.34, 137.75, 135.05, 130.75, 124.33, 121.33, 112.68, 112.00, 60.73, 14.26; ESI-MS: *m/z* $[M+H]^+$ 249.

Methyl(*E*)-3-(2-hydroxy-5-nitrophenyl)acrylate, 3s: Colourless solid. m.p. 131-133°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, *J* = 2.7 Hz, 1H, aromatic), 8.15 (dd, *J* = 8.9, 2.7 Hz, 1H, aromatic), 7.95 (d, *J* =

16.1 Hz, 1H, CH), 6.94 (d, *J* = 8.9 Hz, 1H, aromatic), 6.70 (d, *J* = 16.2 Hz, 1H, CH), 3.85 (s, 3H, OCH_3); ESI-MS: *m/z* $[M+H]^+$ 224.

Ethyl (*E*)-3-(2-hydroxy-5-nitrophenyl)acrylate, 3t: Colourless solid. m.p.140-143°C. ^{1}H NMR (400 MHz, $CDCl_3$): 8.93 (s, 1H, OH), 8.42 (d, *J* = 2.7 Hz, 1H, aromatic), 8.15 (dd, *J* = 8.9, 2.7 Hz, 1H, aromatic), 8.05 (d, *J* = 16.3 Hz, 1H, CH), 7.00 (d, *J* = 9.0 Hz, 1H, aromatic), 6.81 (d, *J* = 16.3 Hz, 1H, CH), 4.35 (q, *J* = 7.1 Hz, 2H, OCH_2), 1.40 (t, *J* = 7.1 Hz, 3H, CH_3); ESI-MS: *m/z* $[M+H]^+$ 238.

Methyl (*E*)-3-(3-bromo-2-hydroxy-5-nitrophenyl)acrylate, 3u: Colourless solid. m.p.140-142°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, *J* = 23.6 Hz, 1H, aromatic), 8.00 (dd, *J* = 80.4, 69.0 Hz, 1H, aromatic), 6.68 (d, *J* = 16.0 Hz, 1H, CH), 4.43 (d, *J* = 16.0 Hz, 1H, CH), 3.81 (s, 3H, OCH_3); ESI-MS: *m/z* $[M+H]^+$ 302.

Ethyl (*E*)-3-(3-bromo-2-hydroxy-5-nitrophenyl)acrylate, 3v: Colourless solid. m.p.149-151°C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.41 (d, *J* = 18.6 Hz, 2H, aromatic), 7.94 (d, *J* = 16.1 Hz, 1H, CH), 6.68 (d, *J* = 16.1 Hz, 1H, CH), 4.30 (dd, *J* = 13.8, 6.8 Hz, 2H, OCH_2), 1.36 (t, *J* = 6.9 Hz, 3H, CH_3); ESI-MS: *m/z* $[M+H]^+$ 316.

Methyl (*E*)-3-(2-hydroxy-3,5-dinitrophenyl)acrylate, 3w: Colourless solid. m.p.148-150°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.72 (s, 1H, OH), 9.07 (d, *J* = 2.7 Hz, 1H, aromatic), 8.68 (d, *J* = 2.7 Hz, 1H, aromatic), 7.98 (d, *J* = 16.2 Hz, 1H, CH), 6.76 (d, *J* = 16.2 Hz, 1H, CH), 3.86 (s, 3H, OCH_3); ^{13}C NMR (101 MHz, $CDCl_3$): δ 166.22, 157.29, 139.75, 135.03, 133.27, 129.51, 127.64, 124.01, 121.90, 52.20; ESI-MS: *m/z* $[M+H]^+$ 269.

Ethyl (*E*)-3-(2-hydroxy-3,5-dinitrophenyl)acrylate, 3x: Colourless solid. m.p.143-147°C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.72 (s, 1H, OH), 9.07 (d, *J* = 2.7 Hz, 1H, aromatic), 8.68 (d, *J* = 2.7 Hz, 1H, aromatic), 7.97 (d, *J* = 16.2 Hz, 1H, CH), 6.76 (d, *J* = 16.2 Hz, 1H, CH), 4.32 (q, *J* = 7.1 Hz, 2H, OCH_2), 1.37 (t, *J* = 7.1 Hz, 3H, $\ominus CH_3$); ^{13}C NMR (101 MHz, $CDCl_3$): δ 165.76, 157.27, 139.74, 134.72, 133.25, 129.45, 127.74, 124.48, 121.82, 61.16, 14.22; ESI-MS: *m/z* $[M+H]^+$ 283.

DPPH free radical scavenging assay

Assay for the scavenging of stable free radical 1,1-diphenyl-2-picrylhydrazyl (DPPH) was done. Briefly, in a 96-well micro plate, 25 µL of test sample dissolved in DMSO (1 mg/mL), 100 µL of 0.1 M tris-HCl buffer (*p*H 7.4) and 125 µL of 0.5 mM DPPH solution dissolved in absolute ethyl alcohol were added. The reaction mixture was shaken well and incubated in dark for 30 min and read at 517 nm spectrophotometrically (Spectra Max plus 384, Molecular Devices Corporation, Sunnyvale, CA, USA). Percentage of DPPH scavenging was calculated as (1-B/ A) × 100 where A represents absorbance of control without test samples and B represents absorbance in presence of test samples.

$ABTS^{\cdot+}$ free radical scavenging assay

Scavenging of the $ABTS^{\cdot+}$ [2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)] cation was performed as described by Walker and Everette[9]. Briefly, 100 mL stock solution of $ABTS^{\cdot+}$ (0.5 mM) was prepared by addition of 1 mL potassium persulfate (6.89 mM PBS, *p*H 8.0). The mixture was stored in the dark for 16 h. Test compounds were dissolved in DMSO (5mg/mL). Primary screening was done by mixing 10 µL of test compounds in 100 µL of methanol followed by 190 µL of $ABTS^{\cdot+}$ in a 96-well microplate. Absorbance of decolorized $ABTS^{\cdot+}$ was measured at 734 nm after 15 min incubation in the dark on a BioTeksynergy[4] multi-mode microplate reader. For each test sample a separate blank sample (devoid of $ABTS^{\cdot+}$) was used for background subtraction. The percentage of $ABTS^{\cdot+}$ scavenging was calculated applying following formula; % $ABTS^{\cdot+}$ scavenging = [(Absorbance control-Absorbance test)/Absorbance control × 100]. Various serial dilutions of active compounds were prepared and tested for determination of SC_{50} values. Suitable regression analysis was applied for calculation of SC_{50}.

α-Glucosidase inhibitory assay

α-Glucosidase inhibitory activity was determined as per our earlier reported method. Rat intestinal acetone powder in normal saline (100:1; w/v) was sonicated properly and the supernatant was used as a source of crude intestinal α-glucosidase after centrifugation. In brief, 10 µL of test samples (5 mg/mL DMSO solution) were reconstituted in 100 µL of 100 mM-phosphate buffer (*p*H 6.8) in 96-well microplate and incubated with 50 µL of crude intestinal α-glucosidase for 5 min before 50 µL substrate (5 mM, *p*-nitrophenyl-α-D-glucopyranoside prepared in same buffer) was added. Release of *p*-nitrophenol was measured after 15 min incubation at

405 nm spectrophotometrically (SpectraMaxplus384), Molecular Devices Corporation, Sunnyvale, CA, USA) 5 min after incubation with substrate. Individual blanks for test samples were prepared to correct background absorbance where substrate was replaced with 50 µL of buffer. Control sample contained 10 µL DMSO in place of test samples. Percentage of enzyme inhibition was calculated as (1-B/A) × 100 where [A] represents absorbance of control without test samples, and [B] represents absorbance in the presence of test samples.

Conclusions

In conclusion, α,β-unsaturated esters **3a-x** have been prepared by the reaction of salicylaldehydes **1a-e** with Wittig reagents **2a-b** in dry DCM at RT. The compounds were evaluated for their free-radical scavenging and α-glucosidase inhibitory activities. Compounds **3c** and **3d** identified as DPPH free radical scavengers. Twenty compounds **3a-r** and **3u-v** have shown promising $ABTS^{\cdot+}$ free radical scavenging activity. Compound **3r** identified as potent α-glucosidase inhibitor and compounds **3g** and **3p** have shown moderate α-glucosidase inhibitory activity.

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