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Synthesis of Aryl Tetralone Derivatives by Chalcone Route

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Abstract

The tetralone analogues of podophyllotoxin were synthesized by the chalcone route. This route attracts the attention because of its simple operating conditions and easy availability of the chemicals. Initially, chalcones were prepared in high yields by Claisen-Schmidt reaction of acetophenones derivatives with 3,4,5-trimethylthoxybenzaldehyde. The cyclopropyl ketones were prepared in good yields by Simmon-Smith reaction of chalcones with diiodomethane with Zn-Cu couple in presence of ether. Tetralones were prepared in good yields by the intramolecular cyclization reaction of cyclopropyl ketones in the presence of *p*-toluene sulphonic acid and acetic anhydride. The structures of the synthesized compounds were confirmed by IR, ^{1}H NMR and Mass spectral technique. The title compounds were screened for their antimitotic and antimicrobial activities.

Keywords: Acetophenones; Chalcones; Cyclopropylketones; Tetralones; Antimitotic activity; Antimicrobial activity

Introduction

Podophyllotoxin (Figure 1) is a potent antimitotic agent [1,2]. Podophyllin is a resinous extract of medicinal plants *Podophyllum emodi* and *Podophyllum peltatum* belonging to the family Berbideraceae in which the podophyllotoxin is one of the main constituent [3]. The toxicity of podophyllotoxin liberates as diarrhea, nausea, vomiting. Hence modifications in podophyllotoxin structure are required to reduce its toxicity and to enhance its biological activity [4]. The biologically active and less cytotoxic new tetralone intermediates of podophyllotoxin have been synthesized. The modification of podophyllotoxin structure might enhance the biological activity with favorable solubility and reduced toxicity [5,6]. Some synthesized analogues of podophyllotoxin showed better antibacterial activity. The structures of the synthesized new tetralone compounds were confirmed by IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectral data. They will be screened for biological activities.

It was planned to synthesize analogues of podophyllotoxin by modifying lactone ring-A with some linked to ring **A** is replaced by dimethoxy, methoxy, methyl, H [7-10]. Chalcones **3a-d** were prepared by Claisen-Schmidt reaction of acetophenone **1a-d** with 3, 4, 5-trimethoxybenzaldehyde separately in the presence of potassium hydroxide in water-ethanol mixture. Cyclopropyl ketones **4a-d** was prepared in good yields by the reaction of chalcones **2a-d** with diiodomethane in presence of Zn-Cu couple. The tetralones **5a-d** was prepared by cyclization of cyclopropyl ketones **4a-d** in presence of *p*-toluene sulphonic acid and acetic anhydride in dichloromethane. The structures of **5a-d** were based on IR, ^{1}H- NMR, ^{13}C NMR, mass spectra and elemental analysis data.

Experimental

Materials and methods

All the reagents and chemicals were purchased from Merck chemicals used without further purification. Melting points were taken in open capillary tubes and are uncorrected. TLC is performed with E. Merck precoated silica gel plates (60F-254) with iodine as a spot developing agent. Acme, India silica gel, 60–120 mesh is used for column chromatography. IR spectra in KBr were recorded on Perkin-Elmer model 683 spectrometers. ^{1}H NMR (400 MHz) and 13C NMR (100 MHz) spectra were recorded $CDCl_3$ solvent containing tetra methyl silane (TMS) as internal references were recorded on Bruker spectrometer; Elemental analyses were performed on a Perkin-Elmer 2400. Mass spectra were obtained by Water-Q-TOF ultima spectrometer. Micro analytical data were obtained by elemental-Vario EL-III (Scheme 1).

Synthesisof4-(3,4,5-trimethoxyphenyl)-3,4-dihydronaphthalen-1(2H)-one derivative (5a-d)

General procedure for the synthesis of chalcones: A mixture of acetophenone 14 (a-d) 0.01 mole and 3,4,5-trimethoxybenzaldehyde 0.01 mole were stirred at room temperature in ehanolic solution of potassium hydroxide for 2-3 hours. The formed yellowish crystals were filtered off washed with distilled water, dried and recrystallised from ethanol to give product as yellow crystals.

(E)-1-(3, 4-dimethoxyphenyl)-3-(3, 4, 5-trimethoxyphenyl) prop-2-en-1-one 3a: Color: light yellow solid. Yield: 80.10%. Mp: 98–100 °C. IR: 3162–2953 (Ar-CH), 1675 (C=O), 1549 (C=C); ^{1}H NMR: 8.01 (1 H, d, J = 8.2, β-CH), 7.67–7.12 (4 H, m, Ar-H), 6.70(2 H, s, Ar-CH), 7.51 (1 H, d, J = 8.2, α-CH), 3.82 (15 H, s, OCH_3); ^{13}C NMR: 196.7, 155.5, 153.2, 150.3, 145.3, 130.3, 126.4, 123.2, 122.3, 112.7, 107.5, 60.8, 56.1; MS, *m/z*: 358.14 (*M*+). $C_{20}H_{22}O_6$: C, 67.03; H, 6.19 O, 26.79. Found: C, 67.05; H, 6.18; O, 26.78%.

(E)-1-(4-methoxyphenyl)-3-(3, 4, 5-trimethoxyphenyl) prop-2-en-1-one 3b: Color: light yellow solid. Yield: 80.10%. Mp: 98–100 °C. IR: 3162–2953 (Ar-CH), 1675 (C=O), 1549 (C=C); ^{1}H NMR: 8.11–7.12 (6 H, m, Ar-H), 8.01 (1 H, d, J = 8.2, β-CH), 6.77(2 H, s, Ar-CH), 7.61 (1 H, d, J = 8.2, α-CH), 3.82 (12 H, s, OCH_3); ^{13}C NMR: 189.7, 166.5, 153.2, 145.3, 138.5, 130.9, 130.8, 130.3, 126.4, 121.3, 114.7, 103.5, 60.8, 56.1, 55.6; MS, *m/z*: 328.14 (*M*+). $C_{19}H_{20}O_5$: C, 69.50; H, 6.14 O, 24.37. Found: C, 69.58; H, 6.16; O, 24.38%.

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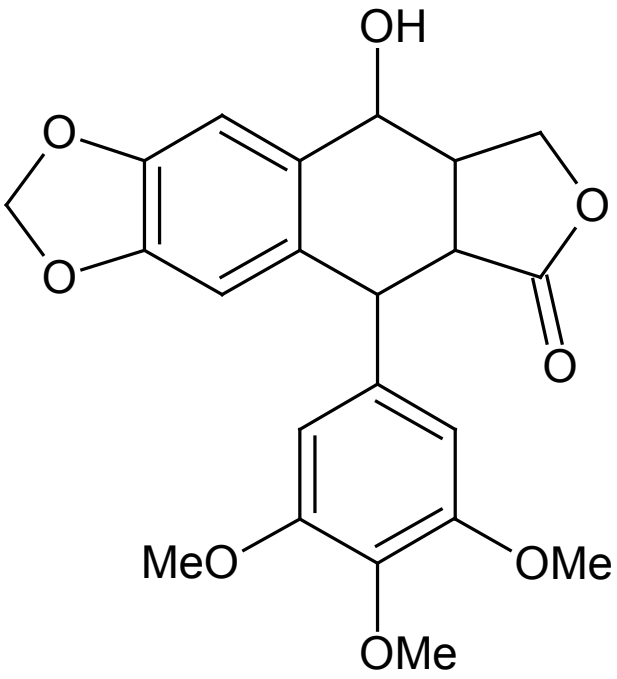
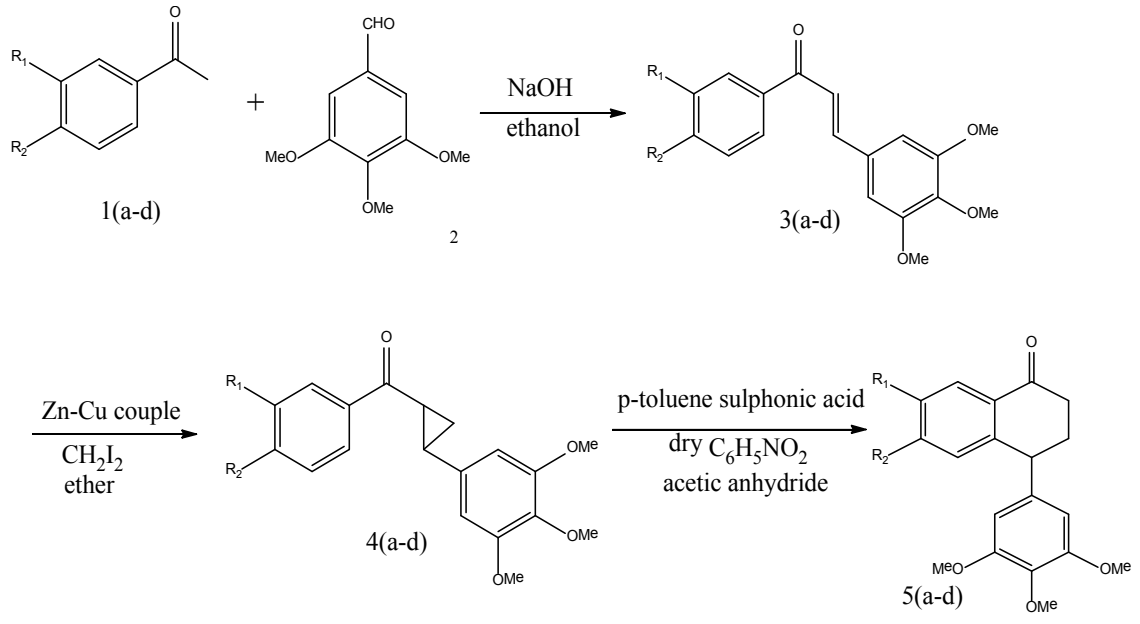


Figure 1: The structure of podophyllotoxin.



Where	R_1	R_2
a	OCH_3	OCH_3
b	H	OCH_3
c	H	CH_3
d	H	H

Scheme 1: Protocol for the synthesis of tetralones (**5a–d**).

(E)-1-(4-methylphenyl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one 3c: Color: light yellow solid. Yield: 79.25%. Mp: 111–113 °C. IR: 3158–2968 (Ar-CH), 1683 (C=O), 1558 (C=C); ^{1}H NMR: 8.07 (1 H, d, *J* = 7.5, β-CH), 7.95–7.42 (6 H, m, Ar-H),6.78(2H, s, Ar-CH), 7.59 (1 H, d, *J* = 7.3, α-CH), 3.89(9H, s, OCH_3), 2.32 (3 H, s, CH_3); ^{13}C NMR: 189.9, 153.4, 145.3, 144.2, 138.5,134.9, 130.8, 129.8, 129.6, 126.4, 103.8, 60.8,56.9, 21.6; MS, *m*/*z*: 312.15 (*M*+). $C_{19}H_{20}O_4$: C, 73.07; H, 6.48 O, 20.49. Found: C, 73.08; H, 6.49; O, 20.48%.

(E)-1-(4-phenyl)-3-(3, 4, 5-trimethoxyphenyl) prop-2-en-1-one 3d: Color: light yellow solid. Yield: 85.90%. Mp: 95–97 °C. IR: 3150–2972 (Ar-CH), 1677 (C=O), 1543 (C=C); ^{1}H NMR: 8.05 (d, 1H, *J* = 7.8, β-CH), 7.89–7.68 (9 H, m, Ar-H), 7.59 (1 H, d, *J* = 7.8, α-CH),6.78(2 H, s, Ar-CH), 3.92 (9H, s, OCH_3); ^{13}C NMR: 189.6, 153.0, 145.1, 138.5, 137.9,134.6,129.3, 126.8, 121.5,103.8, 60.7,56.3; MS, *m*/*z*: 298.10 (*M*+). Anal. calcd. For $C_{18}H_{18}O_4$: C, 72.47; H, 6.08 O, 21.45. Found: C, 72.44; H, 6.09; O, 21.44%.

General procedure for the synthesis of cyclopropyl ketones 4 (a-d): Freshly prepared zinc cupper couple 0.5 mole was taken in conical flask which was fitted with a condenser, dropping funnel and magnetic stirrer. 50 ml of ether was added to the Zn-Cu couple followed by a few milliliters of the dihalomethane. The reaction was started immediately which was indicated by bubbles rising from the couple while the stirred suspension was kept at gentle reflux for two minutes. A mixture of chalcone 0.25 mole and the remaining dihalomethane 0.35 mole was added drop wise for 2 hours. The reaction mixture was refluxed for 20-30 hours. After completion of the reaction, the ether solution was decanted slowly from the unchanged couple into a separating funnel containing a mixture of ice and 1n HCl. The ethereal solution was separated, washed with a second portion of ice-HCl mixture, followed by water and finally dried over potassium carbonate.

(3, 4-dimethoxyphenyl)(2-(3, 4, 5-trimethoxyphenyl) cyclopropyl) methanone 4a: Color: dark brown semi-solid. Yield: 76.90%. IR: 3183–2975 (Ar-CH), 1689 (C=O), 1269 (C–C); ^{1}H NMR: 7.42–7.07 (4 H, m, Ar-H), 6.67(2H, s, Ar-CH), 3.82 (15 H, s, OCH_3), 2.10–2.03 (2 H, m, cyclopro-CH), 0.79 (2 H, d, *J* = 6.3, cyclopro-CH_2); ^{13}C NMR: 192.4,154.2, 152.3, 149.7, 137.6, 130.0, 122.1, 111.7, 110.2, 102.4, 60.8, 56.5, 27.4, 25.9, 14.6; MS, *m*/*z*: 372.13 (*M*+). Anal. Calcd. For $C_{20}H_{22}O_4$: C, 67.73; H, 6.59 O, 25.78 Found: C, 67.71; H, 6.58 O, 25.79%.

(4-methoxyphenyl)(2-(3, 4, 5-trimethoxyphenyl) cyclopropyl) methanone 4b: Color: dark brown semi-solid. Yield: 76.90%. IR: 3183–2975 (Ar-CH), 1689 (C=O), 1269 (C–C); ^{1}H NMR: 7.86–7.01 (4 H, m, Ar-H), 6.67(2H, s, Ar-CH), 3.89 (12H, s, OCH_3), 2.10–2.03 (2 H, m, cyclopro-CH), 0.54 (2 H, d, *J* = 6.3, cyclopro-CH_2); ^{13}C NMR: 192.4, 165.1, 152.3, 137.6, 135.6, 129.8, 129.0, 114.2, 102.4, 60.8, 56.1, 55.5, 27.1, 25.8, 14.7; MS, *m*/*z*: 342.13 (*M*+). Anal. Calcd. For $C_{20}H_{22}O_5$: C, 70.16; H, 6.49 O, 23.36 Found: C, 70.15; H, 6.45 O, 23.39%.

(4-methylphenyl)(2-(3, 4, 5-trimethoxyphenyl) cyclopropyl) methanone 4c: Color: dark brown semisolid. Yield: 69.65%. IR: 3186–2974 (Ar-CH), 1688 (C=O), 1270 (C–C); ^{1}H NMR: 7.37–6.75 (5 H, m, Ar-H), 6.62(2H, s, Ar-CH), 3.58 (9 H, s, OCH3), 2.34 (3 H, s, CH_3), 2.18–2.02 (2 H, m, cyclopro-CH), 0.81 (2 H, d, *J* = 6.6, cyclopro-CH_2); ^{13}C NMR: 192.4, 153.1, 142.8, 137.1, 135.3, 133.7, 128.9, 128.7, 102.1. 60.9. 56.1, 27.6, 25.4, 21.3, 14.5; MS, *m*/*z*: 326.10 (*M*+). Anal. Calcd. $C_{20}H_{22}O_4$: C, 73.60; H, 6.79 O, 19.61 Found: C, 73.61; H, 6.75 O, 19.69%.

4-phenyl-(2-(3, 4, 5-trimethoxyphenyl) cyclopropyl) methanone 4d: Color: dark brown semisolid. Yield: 71.40%. IR: 3183–2972 (Ar-CH), 1685 (C=O), 1273 (C–C); ^{1}H NMR: 7.97–7.52 (6 H, m, Ar-H), 6.62(2H, s, Ar-CH), 3.78 (9 H, s, OCH_3), 2.16–2.01 (2 H, m, cyclopro-CH),0.54 (2 H, d, *J* = 6.8, cyclopro-CH_2); ^{13}C NMR: 192.9, 152.7, 137.6, 136.7, 135.6, 133.2, 128.8, 128.6, 104.1, 60.9, 56.5, 27.1, 25.8, 14.6, 14.5; MS, *m*/*z*: 312.12 (*M*+). Anal. Calcd. For $C_{20}H_{22}O_4$: C, 73.06; H, 6.49 O, 20.49 Found: C, 73.01; H, 6.50 O, 20.48%.

General procedure for the synthesis of tetralones 5 (a-d)

6, 7-dimethoxy-4-(3, 4, 5-trimethoxyphenyl)-3, 4-dihydronaphthalen-1(2H)-one 5a: Color: dark brown gummy solid. Yield: 75.18%. IR: 3128–2939 (Ar-CH), 1697 (C=O); ^{1}H NMR: 7.58–7.05 (4 H, m, Ar-H), 6.52(2 H, s, Ar-H), 4.04 (1 H, t, *J* = 4.7, CH), 3.83 (15 H, s, OCH_3), 2.66–2.25 (4 H, t, *J* = 6.4, CH_2),; ^{13}C NMR: 198.0, 165.9, 141.7, 140.1, 130.5, 129.5, 128.5, 126.5, 111.9, 104.7, 55.7, 45.6, 37.4, 31.4, 14.5; MS, *m*/*z*: 372.15 (*M*+). Anal. Calcd. For $C_{21}H_{24}O_6$: C, 67.73; H, 6.50 O, 25.78 Found: C, 67.76; H, 6.51 O, 25.79%.

6-methoxy-4-(3, 4, 5-trimethoxyphenyl)-3, 4-dihydronaphthalen-1(2H)-one 5b: Color: dark brown gummy solid. Yield: 75.18%. IR: 3128–2939 (Ar-CH), 1697 (C=O); ^{1}H NMR: 8.28–6.85 (5 H, m, Ar-H), 6.52(2 H, s, Ar-H), 4.04 (1 H, t, *J* = 4.7, CH), 3.80(12H, s, OCH_3), 2.66–1.95 (4 H, t, *J* = 6.4, CH_2); ^{13}C NMR: 198.0, 165.9,153.6, 141.5, 137.5,136.7, 130.5, 126.5, 111.9, 106.7, 60.9, 56.1, 55.8, 45.9, 37.4, 31.4; MS, *m*/*z*: 342.15 (*M*+). Anal. Calcd. For $C_{20}H_{22}O_5$: C, 70.16; H, 6.49 O, 23.36 Found: C, 70.17; H, 6.45 O, 23.39%.

6-methyl-4-(3, 4, 5-trimethoxyphenyl)-3, 4-dihydronaphthalen-1(2H)-one 5c: Color: dark brown gummy solid. Yield: 71.94%. IR: 3125–2938 (Ar-CH), 1695 (C=O); ^{1}H NMR: 7.80–7.13 (5 H, m, Ar-H), 6.52(2 H, s, Ar-H), 4.06 (1 H, t, *J* = 4.8, CH), 3.80(9H, s, OCH_3), 2.65–2.28 (4 H, t, *J* = 6.5, CH_2), 2.34 (3 H, s, CH_3); ^{13}C NMR: 198.1, 153.4, 143.3, 140.4, 137.3, 136.7,131.4, 128.0,126.4, 125.2,106.7, 60.9, 56.3, 45.9, 37.5, 31.6, 21.6; MS, *m*/*z*: 326.14 (*M*+). Anal. Calcd. For $C_{20}H_{22}O_4$: C, 73.60; H, 6.79 O, 19.61 Found: C, 73.61; H, 6.75 O, 19.69%.

4-(3, 4, 5-trimethoxyphenyl)-3, 4-dihydronaphthalen-1(2H)-one 5d: Color: dark brown gummy solid. Yield: 78.81%. IR: 3128–2935 (Ar-CH), 1691 (C=O); ^{1}H NMR: 7.83–7.33 (6 H, m, Ar-H), 6.52(2 H, s, Ar-H), 4.02 (1 H, t, *J* = 4.6, CH), 3.83(9H, s, OCH_3), 2.64–2.26 (4 H, t, *J* = 6.3, CH_2). ^{13}C NMR: 198.0, 153.4, 140.6, 140.5, 137.3, 136.7, 133.6, 128.1, 126.1, 106.1, 60.8, 56.5, 45.6, 37.6, 31.4, 14.9; MS, *m*/*z*: 312.07 (*M*+). Anal. Calcd. For $C_{19}H_{20}O_4$: C, 73.06; H, 6.45 O, 20.49. Found: C, 73.07; H, 6.43, O, 20.50%.

Biological assays

Antimicrobial activity: Antibacterial activity of the synthesized compounds was determined against Gram-positive bacteria (*Bacilus subtilius, Streptococcus*) and Gram-negative bacteria (*Escherichia coli*, *Proteus*) in DMF by disc diffusion method on nutrient agar medium. The sterile medium (nutrient agar medium, 15 ml) in each petriplate was uniformly smeared with cultures of Gram-positive and Gram-negative bacteria. Sterile discs of 10 mm diameter (Hi-Media) was placed in the petriplates, to which different concentrations of drug (20 µg, 40, 80, 100 µg/disc) of the different synthesized compounds were added. Gentamycin was used as positive control for comparison. For each treatment, three replicates were maintained. The plates were incubated at 37 °C for 24 h and the zone of inhibition was determined.

Antioxidant assays

DPPH radical scavenging assay: DPPH radical reacts with an Anti-oxidant compound that can donate hydrogen and get reduced. DPPH, when acted upon by an Anti-oxidant, is converted into diphenyl picryl hydrazine. This can be identified by the conversion of purple to light yellow.

DPPH radical scavenging activity was done by the method of Shone et al. Briefly, 1 ml of DPPH solution (0.1 Mm, in 95% ethanol) was mixed with different concentration of compounds, shaken and incubated for 20 min at room temperature and absorbance was read at 517 nm against a blank. The radical scavenging activity was measured as the decrease in the absorbance of DPPH and calculated using the following equation:

Scavenging effect (%)=A control (540 nm)-A sample (540 nm)/A control (540 nm) × 100

Nitric oxide radical scavenging assay: Nitric oxide was generated from sodium nitroprusside and measured by the Griess reaction. Sodium nitroprusside, in aqueous solution at physiological pH, spontaneously generates nitric-oxide, which in turn reacts with oxygen to produce nitric ions that can be estimated by the Griess reagent spectrophotometrically at 540 nm.

Scavengers of nitric oxide compete with oxygen leading to reduced production of nitric oxide. Sodium nitroprusside (5 mM) in phosphate buffer saline was mixed with the compounds and incubated at 25°C for 120 minutes. The samples from the above were reacted with Griess reagent. The absorbance of the chromophore form during the diazotization of nitrate with sulphonyl amide and subsequent coupling with naphthyl ethylene diamine was read at 540 nm and refer to the absorbance standard solutions of BHT, treated in the same way with Griess reagent. The radical scavenging activity was measured using the equation described below

Scavenging effect (%)=A control (540 nm)-A sample (540 nm)/A control (540 nm) × 100

Anti-inflammatory activity

Inhibition of phospholipaseA2: The PLA2 obtained from viper venom were assayed by indirect hemolytic activity using the method of Boman and Kaletta Initially packed human erythrocyte, egg yolk and phosphate-buffered saline (1:1:8, v/v) were mixed. One ml of thus obtained suspension was incubated with the enzyme (10 µg), which was pre incubated with compounds of different concentrations for 10 min at 37°C. The reaction was stopped by adding 9 ml phosphate-buffered saline; the reaction mixture was centrifuged at 4°C for 10 min at 1500 rpm. The amount of haemoglobin released in the supernatant due to hemolysis was measured at 540 nm. The enzyme substrate mixture was used as positive control. Values are presented as the mean of three independent determinations.

Results and Discussion

Chemistry

The new tetralone analogues of podophyllotoxin were synthesized by chalcone route Scheme 1. Chalcones (3a-d) was prepared in high yields by Claisen-Schmidt reaction of acetophenone (1a-d) with 3,4,5-trimethoxybenzaldehyde in the presence of potassium hydroxide in water-ethanol mixture. The structures of the chalcones were confirmed by IR and ^{1}H NMR spectra. IR spectra of compounds (2a-d) showed the C=C stretching frequency in the range 1601-1591 cm^{-1} and ^{1}H NMR showed the absence of aldehyde proton at 9.83 ppm. The cyclopropyl ketones (4a-d) were prepared in good yields by the Simmons-smith reaction of chalcones (2a-d) with diiodomethane in the presence of Zn-Cu couple in ether. Carbanion attacks nucleophilically the β-carbon atom of the chalcone which acts as Michael receptors to form an enolate ion, which undergoes nucleophilic attack on the methylene carbon atom to form the desired cyclopropyl ketones. The structures of compounds (4a-d) were confirmed by IR spectra. The IR spectra showed the C=O stretching band in the range 1664-1653 cm^{-1} and 1H NMR showed the cyclopropane CH and CH_2 peak at the range 2.21-2.00 and 0.83-0.78 ppm respectively.

Tetralones (5a-d) were prepared in good yields by the cyclization reaction of cyclopropyl ketones (4a-d) in the presence of *p*-toluene sulphonic acid and acetic anhydride in dry dichloromethane. The cyclopropyl ketones undergoes electrophilic ring opening in the presence of Lewis acid to give benzyl carbocationic intermediate which attacked by aryl ring π-electrons resulting in the formation of a six membered ring with a pendant carbocation. This readily gives up proton to form tetralones. Acetic anhydride facilitates the formation of tetralones. In its IR spectra appeared absorption bands in the range 2923-2853 cm^{-1} and 1683-1675 cm^{-1} corresponds respectively to C-H and C=O stretching frequencies and ^{1}H NMR of the ring B protons appears in the range 2.65-2.18 ppm. They are key intermediates for the synthesis of the novel nitrogen containing analogues of podophyllotoxin.

Anti-microbial activities

Compounds (5a, 5b, 5c, and 5d) were tested *in vitro* for their antimicrobial activity against 2 Gram-positive, 2 Gram-negative bacteria and a yeast type fungi *C. albican* strains. Commercial antibiotics such as Gentamycin and Flucanozole were used as reference drugs. The results were compared with reference drugs and depicted in the above table. The table reveals that 5a, 5b, 5d is potent compound of all the compounds which were under study with the MIC values ranging from 1.2 µg to 7 µg. Compounds 5c was not acting on Gram-positive bacteria such as *B. subtilis*. Compared to the reference compounds the activity of the tetralone derivatives is significant (Table 1).

Antioxidant activities

DPPH radical scavenging assay: All the compounds of tetralin derivatives showed significant scavenging activity of the DPPH radicals compared to the reference compound BHT. Compounds 5a and 5c showed potent DPPH scavenging activity with an IC_{50} value of 16.89 µg/mL, 17.24 µg/mL 18.12 µg/mL, 18.15 µg/mL, 18.75 µg/mL. Compound 5b showed less DPPH scavenging activity (Table 2 and Figure 2).

Nitric oxide radical scavenging assay: All the tetralone derivatives showed the scavenging of nitric oxide radicals, scavenging is not significant compared to the reference compound BHT 6.4 µg/mL (Table 3 and Figure 3).

Indirect hemolytic assay: The tetralin derivatives 2a and 4a showed the maximum inhibition with a IC_{50} value of 14.37 µg/mL, 13.78 µg/mL and the other compounds showed moderate inhibition. A1 did not inhibit the enzyme (Table 4 and Figure 4).

Conclusion

The tetralone intermediates (5a-d) were prepared in good yield

Compounds	Minimum inbitory concentration (µg)				
	S. aureus	*B. subtilis*	*E. coli*	*Proteus*	*C. albicans*
5a	3	7	4	3	1.4
5b	1.3	3.5	2.4	3	1.3
5c	3.5	-	3.5	4	55
5d	1.2	3.3	2.3	2	1.2
Gentamycin	0.5	0.72	1	1.3	-
Flucanozole	-	-	-	-	0.75

Table 1: *In vitro* Anti-Microbial activities of synthesized compounds.

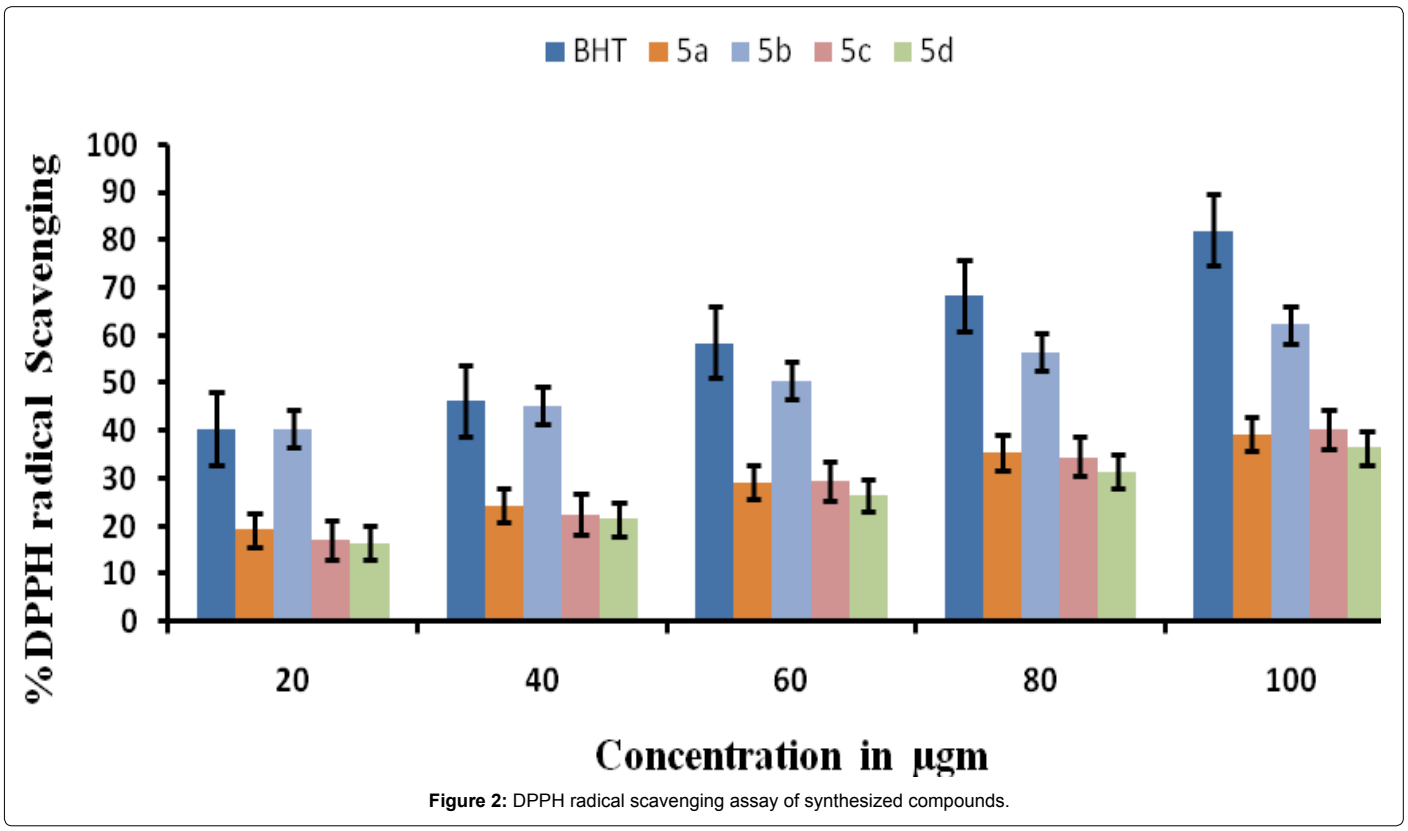


Figure 2: DPPH radical scavenging assay of synthesized compounds.

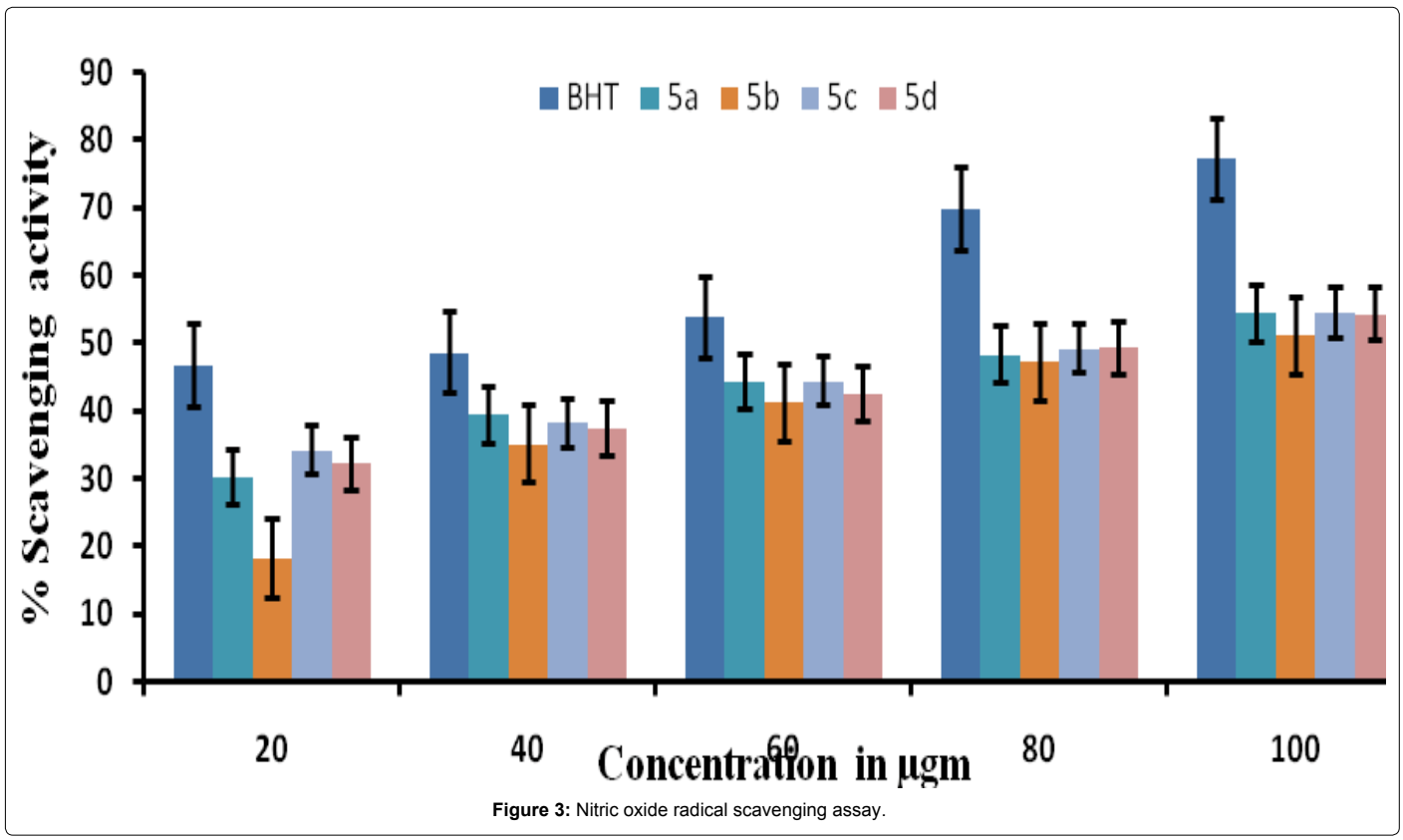


Figure 3: Nitric oxide radical scavenging assay.

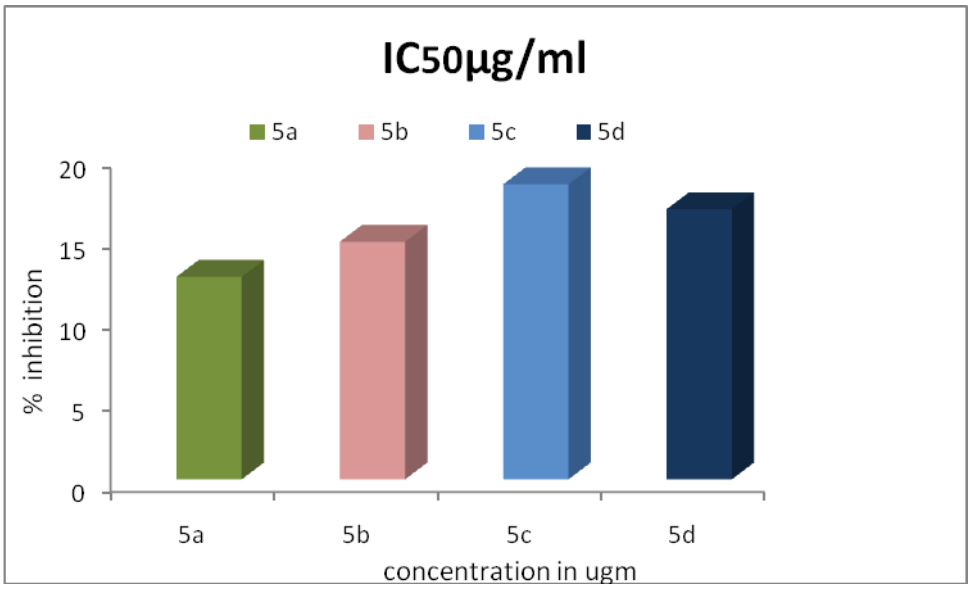


Figure 4: PLA_2 Inhibition of tetralone derivatives.

Compounds	IC_{50} µg/ml
5a	17.24
5b	35.62
5c	15.25
5d	25.83
BHT	37.4

Table 2: *In vitro* DPPH radical scavenging assay of synthesized compounds.

Compounds	IC_{50} (µg/ml)
5a	30.62
5b	35
5c	30.62
5d	36
5e	31.25
BHT	6.4

Table 3: *In vitro* nitric oxide radical scavenging assay of synthesized compounds.

Compounds	IC_{50} µg/ml
5a	12.53
5b	14.70
5c	18.25
5d	16.71

Table 4: PLA_2 Inhibition of tetralone derivatives.

which are very essential for the synthesis and they showed good anti-microbial, anti-oxidant and anti-inflammatory activities.

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