Synthesis and antibacterial screening of some 3-(3-arylacryloyl) anthracen-10(9H)-ones

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Abstract
Some 3-(3-arylacryloyl)anthracen-10(9H)-one derivatives have been synthesized in two steps. In first step, anthracen-10-one (1) underwent Friedel Craft acetylation with acetyl chloride using anhydrous dichloromethane as a solvent and anhydrous powdered aluminum chloride as catalyst. 3-acetylanthracen-10(9H)-one (2) so formed was then dissolved in absolute ethanol and reacted with substituted benzaldehydes in a base catalyzed reaction to form the target compounds (3a-g). Reactions were monitored by thin layer chromatography using different solvent systems. Synthesized compounds were characterized using FTIR, H-1\(^{1}\)-NMR and mass spectroscopic techniques. The compounds were screened for their antibacterial activity against two gram positive and two gram negative bacterial strains taking ciprofloxacin as a standard drug. Some of the compounds showed significant antibacterial activity.

Keywords: anthracene, anthrone, antibacterial activity, chalcone, Friedel Craft acetylation

1. Introduction
Anthracene, one of the most important classes of organic and medicinal chemistry, has been considered to be pharmacologically very important nucleus, owing to the potent and broad spectrum activities of the several anthracene analogs like anthraquinone, anthranol, anthrone, dithranol or anthralin. Anthracene moiety is an important member of pharmaceutical, synthetic and biochemical industries. Anthracene is present as anthranol, anthralin, anthraquinone, anthrone in a large number of therapeutic agents, naturally occurring pigments, vitamins, enzymes and in some synthetic dyes. Anthracene nucleus is present as pharmacophore in a variety of medicinal agents like Doxorubicin, Daunorubicin, Mitoxantrone, Anetantrone\(^{1}\), Epirubicin\(^{2}\), Sapaturmecin, Fluraminycin, Dynemycin, and pharmacognostic agents like Heterophyllin, Rauadin, Postaline, Danacanthol, Soranjodiol\(^{3}\), Alizarin, Emodin, Rhein and Adriamycin\(^{4}\).

Compounds having anthracene as basic moiety are widely distributed in nature exhibiting some interesting biological activities, such as antimicrobial\(^{5}\), antifungal\(^{6}\), hypotensive\(^{7}\), analgesic\(^{8}\), antimalarial\(^{9}\), antitumor\(^{10}\), antileukemic and mutagenic\(^{11,12}\), antipsoriatic\(^{13}\), antiviral\(^{14}\), MAO-A and MAO-B inhibitory\(^{15}\), antiplasmodial\(^{16}\) activities. The anthraquinone derivatives occupy a very important place among the different classes of anticancer agents. The amino and hydroxyl derivatives of anthracene are considered to be pharmacologically useful.

2. Material and Methods
Melting points were determined by decibel melting point apparatus and were uncorrected. All reactions were monitored by thin layer chromatography (TLC) using silica gel G (Spectrochem Pvt. Ltd., Mumbai). The plates were developed by exposing to iodine chamber. Infrared spectra were recorded by FTIR ATR Thermo Scientific NICOLET Is10 spectrophotometer using KBr disks. Proton nuclear magnetic resonance spectra (\(^{1}\)H-NMR) were recorded on Bruker Avance II 400 NMR Spectrophotometer using CDCl\(_3\) as solvent. Mass spectra of the compounds were carried out on API-4000 Quadrupole Mass Spectrometer using electro spray ionization (ESI) technique in positive ion mode. Elemental analyses were carried out on Carlo Erba1106 CHN Analyzer. Chemical shifts are expressed as \(\delta\) values (ppm).

2.1 Experimental
2.1.1 Synthesis of 3-acetylanthracen-10(9H)-one (2):
A solution of anhydrous acetyl chloride (0.01 mol) dissolved in anhydrous dichloromethane (5 ml) was added drop by drop with continues stirring to a clear solution of anthracen-10(9H)-one (1) (0.01 mol) dissolved in anhydrous dichloromethane (10 ml). Anthracen-10(9H)-one (1) (0.01 mol) dissolved in anhydrous dichloromethane (10 ml) was added to the reaction mixture and stirred at 0°C by keeping an ice bath over a magnetic stirrer. The ice bath was removed after the complete addition of anthracen-10(9H)-one and solution was stirred for 8-10 hrs. at room temperature. To this solution, was added dilute HCI and stirred well. Organic layer was separated and dichloromethane was evaporated resulting 3-acetylanthracen-10(9H)-one (2) in a good yield\(^{16}\).

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2.1.2 Synthesis of 3-(3-arylacryloyl) anthracen-10(9H)-ones (3a-g):

To the solution of sodium hydroxide in water and ethanol, was added 3-acetylanthracen-10(9H)-one (2) and kept over a magnetic stirrer for 20 min and stirred. While stirring, substituted benzaldehydes (0.01 mol) were slowly added to the flask and stirred for another 5-6 hrs. After the completion of reaction, stirrer was removed and mixture was kept whole night in a refrigerator. Next day, the solution was poured in to crushed ice and pH was adjusted to neutral. Crude 3-(3-arylacryloyl)anthracen-10(9H)-ones (3a-g) were thus precipitated out, filtered, washed and recrystallised with ethanol.

General scheme for the synthesis of 3-(3-arylacryloyl)anthracen-10(9H)-ones:

2.2 Analytical characterization

**Anthracen-10(9H)-one (1):** IR (KBBr, cm⁻¹): 3058.82 (C-H stretching, aromatic), 1714.54 (C=O stretching, aromatic), 1598.54 (C=C, alkene), 932.30 (C-H, bending, alkene); ¹H NMR (CDCl₃): δ (ppm) 8.37-7.25 (m, 8H, Ar-H), 4.36 (s, 2H, CH₂); MS, m/z (%): 194 [M+H⁺] (100%); Anal.: Calcd for C₁₅H₁₂O: C, 85.16; H, 4.97; O, 9.86. Found: C, 85.11; H, 4.98; O, 9.83.

**3-acetylanthracen-10(9H)-one (2):** IR (KBBr, cm⁻¹): 3042.01 (C-H stretching, aromatic), 1712.39 (C=O stretching, aromatic), 1602.79 (C=C, alkene), 932.06 (C-H, bending, alkene); ¹H NMR (CDCl₃): δ (ppm) 8.68 (m, 7H, Ar-H), 4.36 (s, 2H, CH₂), 2.74 (s, 3H, CH₃); MS, m/z (%): 236 [M⁺H⁺] (100%); Anal.: Calcd for C₁₅H₁₄O: C, 81.34; H, 5.12; O, 13.54. Found: 81.30; H, 5.07; O, 13.51.

**3-(3-phenylacryloyl)anthracen-10(9H)-one (3a):** IR (KBBr, cm⁻¹): 3063.49 (C-H stretching, aromatic), 1717.17 (C=O stretching, aromatic), 1595.51 (C=C, alkene), 933.91 (C-H, bending, alkene); ¹H NMR (CDCl₃): δ (ppm) 8.26-7.20 (m, 12H, Ar-H), 7.10 (d, 1H, =CH-CO-Ar), 7.08 (d, 1H, =CH-Ar), 3.82 (s, 2H, CH₂); MS, m/z (%): 324 [M⁺H⁺] (100%); Anal.: Calcd for C₁₅H₁₂O₂: C, 85.16; H, 4.97; O, 9.86. Found: C, 85.11; H, 4.98; O, 9.83.

**3-(3-(4-chlorophenylacryloyl)anthracen-10(9H)-one (3b):** IR (KBBr, cm⁻¹): 2002.80 (C-H stretching, aromatic), 1717.11 (C=O stretching, aromatic), 1575.48 (C=C, alkene), 897.78 (C-H, bending, alkene), 850.83 (C-Cl, stretching, aromatic); ¹H NMR (CDCl₃): δ (ppm) 8.26-7.23 (m, 11H, Ar-H), 7.18 (d, 1H, =CH-CO-Ar), 7.17 (d, 1H, =CH-Ar), 3.82 (s, 2H, CH₂); MS, m/z (%): 358 [M⁺H⁺] (100%); Anal.: Calcd for C₁₅H₁₂ClO: C, 76.99; H, 4.21; Cl, 9.88; O, 8.92. Found: C, 76.94; H, 4.18; Cl, 9.90; O, 8.90.

**3-(3-(3-chloroacyl)anthracen-10(9H)-one (3c):** IR (KBBr, cm⁻¹): 3064.42 (C-H stretching, aromatic), 1715.51 (C=O stretching, aromatic), 1616.78 (C=C, alkene), 934.60 (C-H, bending, alkene), 809.00 (C-Cl, stretching, aromatic); ¹H NMR (CDCl₃): δ (ppm) 8.89-7.19 (m, 11H, Ar-H), 7.17 (d, 1H, =CH-CO-Ar), 7.14 (d, 1H, =CH-Ar), 4.28 (s, 2H, CH₂); MS, m/z (%): 358 [M⁺H⁺] (100%); Anal.: Calcd for C₁₅H₁₂ClO: C, 76.99; H, 4.21; Cl, 9.88; O, 8.92. Found: C, 76.95; H, 4.16; Cl, 9.91; O, 8.89.

**3-(3-(2-chloroacyl)anthracen-10(9H)-one (3d):** IR (KBBr, cm⁻¹): 3029.31 (C-H stretching, aromatic), 1712.35 (C=O stretching, aromatic), 1603.64 (C=C, alkene), 929.48 (C-H, bending, alkene), 813.89 (C-Cl, stretching, aromatic); ¹H NMR (CDCl₃): δ (ppm) 8.99-7.22 (m, 11H, Ar-H), 7.17 (d, 1H, =CH-CO-Ar), 7.14 (d, 1H, =CH-Ar), 4.34 (s, 2H, CH₂); MS, m/z (%): 358 [M⁺H⁺] (100%); Anal.: Calcd for C₁₅H₁₂ClO: C, 76.99; H, 4.21; Cl, 9.88; O, 8.92. Found: C, 76.92; H, 4.16; Cl, 9.84; O, 8.87.

**3-(3-(4-hydroxyphenacyl)anthracen-10(9H)-one (3e):** IR (KBBr, cm⁻¹): 3315.62 (C=O, stretching, aromatic), 3042.83 (C=O, stretching, aromatic), 1714.68 (C=O stretching, aromatic), 1661.53 (C=C, alkene), 933.91 (C-H, bending, alkene); ¹H NMR (CDCl₃): δ (ppm) 8.89-7.17 (m, 11H, Ar-H), 7.15 (d, 1H, =CH-CO-Ar), 7.13 (d, 1H, =CH-Ar), 5.68 (s, 1H, Ar-OH), 4.19 (s, 2H, CH₂); MS, m/z (%): 340 [M⁺H⁺] (100%); Anal.: Calcd for C₁₅H₁₂O₂: C, 81.16; H, 4.74; O, 14.10. Found: C, 81.11; H, 4.70; O, 14.08.

**3-(3-(3-hydroxyphenacyl)anthracen-10(9H)-one (3f):** IR (KBBr, cm⁻¹): 3335.96 (C=O, stretching, aromatic), 3070.02 (C=O stretching, aromatic), 1709.58 (C=O stretching, aromatic), 1591.97 (C=C, alkene), 967.98 (C-H, bending, alkene); ¹H NMR (CDCl₃): δ (ppm) 8.97-7.17 (m, 11H, Ar-H), 7.15 (d, 1H, =CH-CO-Ar), 7.13 (d, 1H, =CH-Ar), 5.52 (s, 1H, Ar-OH), 3.98 (s, 2H, CH₂); MS, m/z (%): 340 [M⁺H⁺] (100%); Anal.: Calcd for C₁₅H₁₂O₂: C, 81.16; H, 4.74; O, 14.10. Found: C, 81.13; H, 4.71; O, 14.12.

**3-(3-(2-hydroxyphenacyl)anthracen-10(9H)-one (3g):** IR (KBBr, cm⁻¹): 3384.01 (C=O, stretching, aromatic), 3058.82 (C=O, stretching, aromatic), 1715.52 (C=O stretching, aromatic), 1598.16 (C=C, alkene), 933.27 (C-H, bending, alkene); ¹H NMR (CDCl₃): δ (ppm) 8.81-7.19 (m, 11H, Ar-H), 7.15 (d, 1H, =CH-CO-Ar), 7.15 (d, 1H, =CH-Ar), 5.64 (s, 1H, Ar-OH), 4.17 (s, 2H, CH₂); MS, m/z (%): 340 [M⁺H⁺] (100%); Anal.: Calcd for C₁₅H₁₂O₂: C, 81.16; H, 4.74; O, 14.10. Found: C, 81.14; H, 4.72; O, 14.07.
3. Results and Discussion

3.1 Antibacterial Screening:
Synthesized 3-(3-arylacryloyl) anthracen-10(9H)-ones (3a-g) were tested in vitro for their antibacterial profile using Tube Dilution Method against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa*. MIC values calculated for all the synthesized compounds using ciprofloxacin as the standard are listed in the Table 2. The tested solutions were serially diluted to give concentrations of 5, 2.5, 1.25, 0.625, 0.312, 0.156, 0.078 µg/mL respectively which were later converted to µM concentrations.

### Table 2: Antibacterial activity of 3-(3-arylacryloyl) anthracen-10(9H)-ones

<table>
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<tr>
<th>Sr. No.</th>
<th>Compound</th>
<th>Minimum Inhibitory concentration (µM)</th>
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<tr>
<td></td>
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<td>B. subtilis</td>
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<tr>
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<tr>
<td>7</td>
<td>3g</td>
<td>1.50</td>
</tr>
<tr>
<td>8</td>
<td>Ciprofloxacin</td>
<td>0.90</td>
</tr>
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</table>

4. Conclusion
Among the newly synthesized derivatives, 3-(3-phenylacryloyl)anthracen-10(9H)-one (3a) and 3-(3-(2-chlorophenyl)acryloyl)anthracen-10(9H)-one (3d) were found to be most active against gram positive bacteria while 3-(3-(4-hydroxyphenyl)acryloyl)anthracen-10(9H)-one (3e), 3-(3-(2-hydroxyphenyl)acryloyl)anthracen-10(9H)-one (3g) were found to be most active against gram negative bacteria. One of the derivative 3-(3-(4-chlorophenyl)acryloyl)anthracen-10(9H)-one (3b) was found to inhibit the growth of both gram positive and gram negative bacteria. Further studies are required to generate more information about structure activity relationship of these derivatives.

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References