

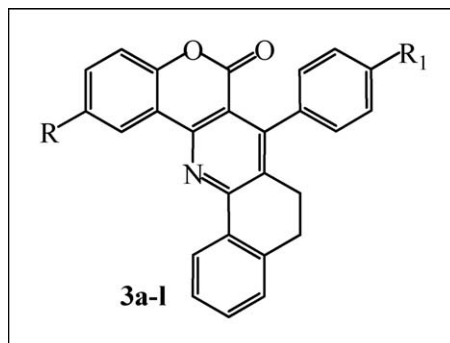
Dinker I. Brahmabhatt,* Niraj H. Patel, Anil K. Patel,
Mehul A. Patel, and Varun G. Patel

Department Of Chemistry, Sardar Patel University, Vallabh Vidyanagar-388 120, Gujarat, India
*E-mail: drdibrahmbhatt@gmail.com

Received March 25, 2010

DOI 10.1002/jhet.648

Published online 12 April 2011 in Wiley Online Library (wileyonlinelibrary.com).



The title compounds, 7-aryl-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-ones **3a-l** have been synthesized by reacting various 4-hydroxy coumarins **1a-c** with 2-arylidene-1-tetralones **2a-d** in the presence of ammonium acetate and acetic acid under Krohnke's reaction condition. The structures of all the synthesized compounds were supported by analytical, IR, ¹H-NMR, and ¹³C-NMR data. All the synthesized compounds **3a-l** have been screened for their antibacterial activities against *Escherichia coli* (Gram -ve bacteria), *Bacillus subtilis* (Gram +ve bacteria), and antifungal activity against *Candida albicans* (Fungi).

J. Heterocyclic Chem., **48**, 840 (2011).

INTRODUCTION

Coumarins are a class of compounds having aromatic δ -lactones system, isolated from variety of plant sources [1]. Coumarin derivatives are reported to have variety of biological activities such as anti-inflammatory [2], antiviral [3], antioxidant [4], antibacterial [5], antifungal [6], anti-HIV [7], and as anticarcinogenic material [8].

Coumarins fused with pyridine nucleus have been reported to possess antiallergic [9], antidiabetic activities [10] and even analgesic properties [11], being characterized by a phenanthrene-like structure as found in tetrahydrocannabinol. In view of such important bioactivity of pyrido fused coumarins, earlier we had synthesized some diarylpyrido[3,2-*c*]coumarins by the reaction of 4-hydroxy coumarins with α,β -unsaturated ketones using Krohnke's reaction [12].

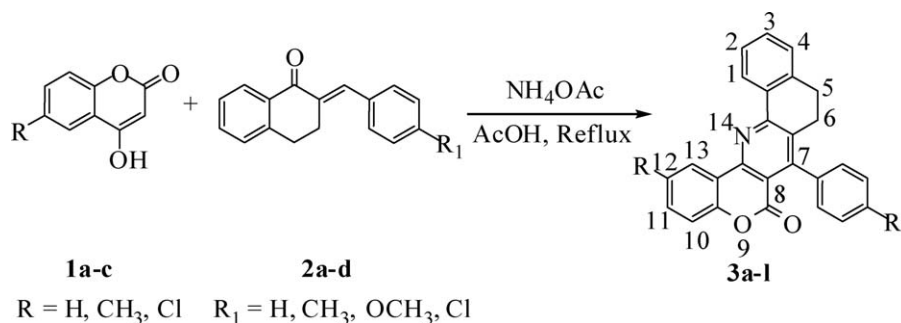
Phenanthrene containing one nitrogen atom is known as azaphenanthrene. During our literature search for azaphenanthrene, we came across some azaphenanthrene derivatives having interesting biological activities. 4-Azaphenanthrene derivatives have been reported to possess wound healing, antibacterial and in vitro antioxidant activity [13]. The 1,3-diamino substituted 4-azaphenanthrene derivative possesses cytotoxic activity

[14], where as 1-chloro-2-azaphenanthrene is found to be a novel activator of cystic fibrosis transmembrane conductance regulator [15]. A 3-(4-methylsulfonylphenyl)-4-azaphenanthren-1-carboxylic acid acts as cyclooxygenase-2 inhibitors [16]. These interesting biological properties of azaphenanthrene derivatives prompted us to incorporate such type of nucleus in coumarin and therefore in this work we have synthesized some 7-aryl-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-ones.

The compounds **3a-l** have been synthesized by reacting various 4-hydroxy coumarins **1a-c** with 2-arylidene-1-tetralones **2a-d** in the presence of ammonium acetate and acetic acid under Krohnke's reaction condition. The synthetic methodology is outline in Scheme 1.

RESULT AND DISCUSSION

The condensation of 4-hydroxy coumarins **1a-c** with 2-arylidene-1-tetralones **2a-d** under Krohnke's reaction condition proceeded smoothly and gave the expected 7-aryl-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-ones **3a-l** in moderate yield (47–60%). A plausible reaction mechanism for the formation of the compounds **3a-l** is depicted in Scheme 2.

Scheme 1. The synthetic scheme for the preparation of compounds **3a-l**.

The structures of all the synthesized compounds **3a-l** were established on the basis of analytical and spectral data.

In IR spectra, compounds **3a-l** showed a very strong band between 1715–1740 cm⁻¹ for the carbonyl (C=O) stretching of δ -lactone ring present in coumarin nucleus. The strong bands for aromatic C=C and C=N stretching vibrations, were observed between 1595–1630 cm⁻¹ and 1495–1520 cm⁻¹, respectively. The aliphatic and aromatic C–H stretching vibrations were observed between 2940–2980 cm⁻¹ and 3040–3065 cm⁻¹, respectively in the form of medium bands.

In the ¹H-NMR spectra of compounds **3a-l**, two triplets were observed between 2.69–2.75 δ and 2.87–2.91 δ each integrating for two protons. These signals are due to protons attached at C₆ and C₅, respectively. In all the compounds the signal for C₁–H appeared either as doublet of doublet or poorly resolved doublet of doublet between 8.63–8.69 δ . The C₁₃–H appeared as a doublet of a doublet between 8.84–8.86 δ in compounds **3a-d**, while it appeared as a doublet or a poorly resolved doublet between 8.60–8.78 δ in compounds **3e-l**. In all the compounds, the other aromatic protons appeared as multiplet between 7.02–7.59 δ . The C₁–H and C₁₃–H signals appear in the downfield region compared with other aromatic protons due to peri effect of the nitrogen atom present in the compound.

The ¹³C-NMR spectra of compounds **3a-l** showed signals at around 25.0 and 28.0 δ , which were due to C₆ and C₅, respectively. This was confirmed by DEPT-135 spectra in which these signals got inverted. The aromatic carbons including carbonyl carbon appeared between 114.0–161.0 δ .

For selected compound **3a**, mass spectrum was recorded. The mass spectrum of compound **3a** showed molecular ion peak at *m/z* 375 along with other fragments peaks. This confirms the structure of compound **3a**.

The results of the antimicrobial screening of the compounds (Table 1) indicate that all the compounds **3a-l** show comparable activity against *E coli* and *B subtilis*. Compared to compounds **3a-h**, the compounds having chlorine substitution in coumarin moiety **3i-l** show better

activity towards *E coli* and *B subtilis* at all concentrations. However though majority of the compounds showed moderate activity against fungi *C albicans*, the compound **3e** showed poor activity and compound **3b** did not show activity at all. Here also the compounds having chlorine substitution in coumarin moiety **3i-l** showed better activity compared with other compounds. The comparison of the antimicrobial activity at different concentrations indicates that the activity decreases with decrease in concentration. All the synthesized compounds show lower activity compared to standard drugs at all the concentrations.

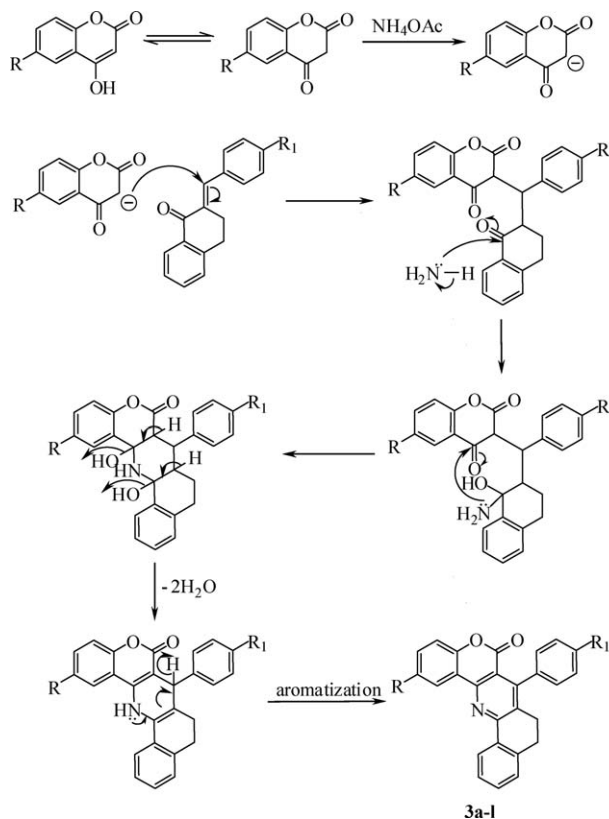
Scheme 2. The plausible mechanism for the formation of the compounds **3a-l**.

Table 1
Antimicrobial activity of compounds **3a-l**.

Compd.	Inhibition zone in mm (1000 ppm concentration)			Inhibition zone in mm (750 ppm concentration)			Inhibition zone in mm (500 ppm concentration)		
	Bacteria		Fungi	Bacteria		Fungi	Bacteria		Fungi
	<i>E coli</i>	<i>B subtilis</i>	<i>C albicans</i>	<i>E coli</i>	<i>B subtilis</i>	<i>C albicans</i>	<i>E coli</i>	<i>B subtilis</i>	<i>C albicans</i>
3a	15	17	15	14	15	13	11	12	11
3b	16	19	–	14	17	–	10	13	–
3c	17	19	12	15	16	12	11	11	08
3d	15	20	16	15	19	15	13	17	12
3e	17	16	6	14	15	5	12	13	5
3f	15	18	13	11	16	11	10	11	10
3g	15	17	10	12	14	9	09	12	07
3h	14	20	12	12	19	11	11	17	07
3i	16	18	14	16	17	13	14	15	11
3j	16	18	17	15	16	15	15	14	12
3k	17	19	18	17	17	15	14	16	10
3l	17	20	14	17	20	12	15	17	11
Ciprofloxacin	18	25	–	18	25	–	18	25	–
Ampicillin	20	27	–	20	27	–	20	27	–
Clotrimazole	–	–	20	–	–	20	–	–	20

EXPERIMENTAL

All the melting points reported are uncorrected. The IR spectra (KBr disc) were recorded on Shimadzu FT-IR 8400-S spectrometer. ¹H-NMR and ¹³C-NMR spectra were recorded on a Bruker Avance 400 spectrophotometer operating at 400 MHz for ¹H-NMR and 100 MHz for ¹³C-NMR. The chemical shift (δ) is reported in ppm using chloroform-d as a solvent and calibrated standard solvent signal. Mass spectrum for compound **3a** was recorded on Shimadzu QP 2010 spectrometer. 4-Hydroxy coumarins **1a-c** and 2-arylidene-1-tetralones **2a-d** were prepared according to literature procedures [17,18].

General procedure for the synthesis of 7-aryl-5,6-dihydro-14-aza[1]benzopyrano [3,4-b]phenanthren-8H-ones (3a-l). In a 100 mL round-bottom flask equipped with a dropping funnel, condenser, guard tube, and magnetic needle, an appropriate 4-hydroxy coumarin (**1a-c**) (0.004 mol) was taken in glacial acetic acid (15 mL). To this, ammonium acetate (0.04 mol) was added with stirring at room temperature. Then a solution of appropriate 2-arylidene-1-tetralone (**2a-d**) (0.004 mol) in acetic acid (15 mL) was added with stirring at room temperature. The reaction mixture was further stirred for 45 min. and then refluxed in an oil bath at 140–150°C for 8 h and cooled to room temperature. The reaction mixture was poured into ice cold water (75 mL) and the gummy mass obtained was extracted with chloroform (3 × 30 mL). The combined chloroform extract was washed with 10% sodium bicarbonate solution (3 × 20 mL) and then with water (3 × 20 mL). It was dried over anhydrous sodium sulfate. The removal of chloroform under vacuum gave a solid product. This was purified by column chromatography using silica gel and chloroform-petroleum ether (60–80) (4:6) as an eluent. Thus 7-aryl-5,6-dihydro-14-aza[1]benzo pyrano[3,4-b]phenanthren-8H-ones (**3a-l**) were obtained as a solid material, which were recrystallized from chloroform-hexane.

7-Phenyl-5,6-dihydro-14-aza[1]benzopyrano[3,4-b]phenanthren-8H-one (3a). White solid; Yield 59%; M.P. 255°C; IR (KBr, cm⁻¹): 3065, 2945, 1734, 1595, 1495, 765, 700 ¹H-NMR

(CDCl₃): δ 2.71 (2H, t, protons at C₆), 2.89 (2H, t, protons at C₅), 7.21–7.59 (11H, m, aromatic protons), 8.69 (1H, dd, $J = 7.2$ and 1.2 Hz, C₁–H), 8.86 (1H, dd, $J = 7.6$ and 1.2 Hz, C₁₃–H); ¹³C-NMR (CDCl₃): 25.40(CH₂), 27.64(CH₂), 113.88(C), 116.70(CH), 119.94(C), 124.31(CH), 125.14(CH), 126.92(CH), 127.19(CH), 127.36(CH), 127.72(CH), 127.89(CH), 128.47(CH), 131.04(CH), 131.62(CH), 131.87(C), 133.85(C), 138.17(C), 139.42(C), 150.62(C), 152.10(C), 152.67(C), 157.27(C), 159.54(C=O). Anal. Calcd. for C₂₆H₁₇NO₂: C, 83.18; H, 4.56; N, 3.73. Found: C, 83.02; H, 4.50; N, 3.70.

7-(4-Methylphenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-b]phenanthren-8H-one (3b). White solid; Yield 55%; M.P. 259–260°C; IR (KBr, cm⁻¹): 3040, 2960, 1715, 1600, 1500, 830; ¹H-NMR (CDCl₃): δ 2.50 (3H, s, CH₃), 2.71 (2H, t, protons at C₆), 2.87 (2H, t, protons at C₅), 7.10–7.58 (10H, m, aromatic protons), 8.67 (1H, dd, $J = 7.2$ and 1.2 Hz, C₁–H), 8.84 (1H, dd, $J = 7.6$ and 1.2 Hz, C₁₃–H); ¹³C-NMR (CDCl₃): 21.51(CH₃), 25.42(CH₂), 27.66(CH₂), 114.03(C), 116.67(CH), 119.98(C), 124.27(CH), 125.14(CH), 126.90(CH), 127.11(CH), 127.33(CH), 127.86(CH), 129.21(CH), 130.97(CH), 131.56(CH), 132.04(C), 133.91(C), 135.12(C), 137.35(C), 139.43(C), 150.58(C), 152.32(C), 152.66(C), 157.15(C), 159.55(C=O). Anal. Calcd. for C₂₇H₁₉NO₂: C, 83.27; H, 4.92; N, 3.60. Found: C, 83.14; H, 4.85; N, 3.55.

7-(4-Methoxyphenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-b]phenanthren-8H-one (3c). White solid; Yield 54%; M.P. 212–214°C; IR (KBr, cm⁻¹): 3055, 2940, 1730, 1605, 1510, 830; ¹H-NMR (CDCl₃): δ 2.73 (2H, t, protons at C₆), 2.88 (2H, t, protons at C₅), 3.92 (3H, s, OCH₃), 7.05–7.58 (10H, m, aromatic protons), 8.67 (1H, poorly resolved dd, C₁–H), 8.84 (1H, dd, $J = 8.0$ and 1.6 Hz, C₁₃–H); ¹³C-NMR (CDCl₃): 25.45(CH₂), 27.69(CH₂), 55.26(OCH₃), 113.92(CH), 114.15(C), 116.66(CH), 119.99(C), 124.28(CH), 125.15(CH), 126.90(CH), 127.34(CH), 127.86(CH), 128.55(CH), 130.14(C), 130.98(CH), 131.57(CH), 132.31(C), 133.93(C), 139.42(C), 150.62(C), 152.05(C), 152.65(C), 157.18(C), 159.10(C), 159.62(C=O). Anal. Calcd. for C₂₇H₁₉NO₃: C, 79.98; H, 4.72; N, 3.45. Found: C, 79.89; H, 4.68; N, 3.42.

7-(4-Chlorophenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3d). White solid; Yield 48%; M.P. 284°C; IR (KBr, cm^{-1}): 3060, 2960, 1735, 1600, 1495, 830; $^1\text{H-NMR}$ (CDCl_3): δ 2.69 (2H, t, protons at C_6), 2.89 (2H, t, protons at C_5), 7.14–7.59 (10H, m, aromatic protons), 8.67 (1H, dd, $J = 6.8$ and 1.6 Hz, $\text{C}_{13}\text{-H}$); $^{13}\text{C-NMR}$ (CDCl_3): 25.42(CH_2), 27.55(CH_2), 113.72(C), 116.72(CH), 119.81(C), 124.43(CH), 125.15(CH), 126.96(CH), 127.43(CH), 127.92(CH), 128.70(CH), 128.82(CH), 131.19(CH), 131.77(CH), 131.80(C), 133.70(C), 133.76(C), 136.53(C), 139.35(C), 150.72(C), 150.79(C), 152.62(C), 157.45(C), 159.59(C=O). Anal. Calcd. for $\text{C}_{26}\text{H}_{16}\text{ClNO}_2$: C, 76.19; H, 3.93; N, 3.42. Found: C, 76.31; H, 3.91; N, 3.39.

12-Methyl-7-phenyl-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3e). Light yellow solid; Yield 52%; M.P. 205°C; IR (KBr, cm^{-1}): 3060, 2960, 1720, 1605, 1500, 710, 750; $^1\text{H-NMR}$ (CDCl_3): δ 2.55 (3H, s, CH_3), 2.70 (2H, t, protons at C_6), 2.88 (2H, t, protons at C_5), 7.21–7.55 (10H, m, aromatic protons), 8.61 (1H, d, $J = 1.2$ Hz, $\text{C}_{13}\text{-H}$), 8.69 (1H, dd, $J = 7.2$ and 0.8 Hz, $\text{C}_1\text{-H}$); $^{13}\text{C-NMR}$ (CDCl_3): 21.16(CH_3), 25.41(CH_2), 27.66(CH_2), 113.89(C), 116.47(CH), 119.50(C), 124.80(CH), 126.91(CH), 127.18(CH), 127.36(CH), 127.67(CH), 127.88(CH), 128.45(CH), 130.99(CH), 131.73(C), 132.61(CH), 133.93(C), 138.26(C), 139.42(C), 150.69(C), 150.79(C), 152.12(C), 157.17(C), 159.70(C=O). Anal. Calcd. for $\text{C}_{27}\text{H}_{19}\text{NO}_2$: 83.27; H, 4.92; N, 3.60. Found: C, 83.36; H, 4.90; N, 3.52.

12-Methyl-7-(4-methylphenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3f). Light yellow solid; Yield 54%; M.P. 220–222°C; IR (KBr, cm^{-1}): 3060, 2960, 1730, 1610, 1510, 825; $^1\text{H-NMR}$ (CDCl_3): δ 2.49 and 2.55 (6H, two singlets, $2 \times \text{CH}_3$), 2.71 (2H, t, protons at C_6), 2.87 (2H, t, protons at C_5), 7.09–7.52 (9H, m, aromatic protons), 8.60 (1H, poorly resolved d, $\text{C}_{13}\text{-H}$), 8.68 (1H, poorly resolved dd, $\text{C}_1\text{-H}$); $^{13}\text{C-NMR}$ (CDCl_3): 21.16(CH_3), 21.50(CH_3), 25.42(CH_2), 27.68(CH_2), 114.04(C), 116.44(CH), 119.54(C), 124.80(CH), 126.90(CH), 127.11(CH), 127.33(CH), 127.85(CH), 129.19(CH), 130.93(CH), 131.89(C), 132.55(CH), 133.87(C), 133.97(C), 135.22(C), 137.28(C), 139.42(C), 150.66(C), 150.78(C), 152.34(C), 157.05(C), 159.70(C=O). Anal. Calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_2$: C, 83.35; H, 5.25; N, 3.47. Found: C, 83.26; H, 5.19; N, 3.49.

12-Methyl-7-(4-methoxyphenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3g). White solid; Yield 60%; M.P. 161–162°C; IR (KBr, cm^{-1}): 3040, 2970, 1735, 1610, 1505, 835; $^1\text{H-NMR}$ (CDCl_3): δ 2.55 (3H, s, CH_3), 2.73 (2H, t, protons at C_6), 2.88 (2H, t, protons at C_5), 3.91 (3H, s, OCH_3), 7.04–7.53 (9H, m, aromatic protons), 8.60 (1H, d, $J = 0.8$ Hz, $\text{C}_{13}\text{-H}$), 8.68 (1H, dd, $J = 7.6$ and 0.8 Hz, $\text{C}_1\text{-H}$); $^{13}\text{C-NMR}$ (CDCl_3): 21.15(CH_3), 25.45(CH_2), 27.71(CH_2), 55.25(OCH_3), 113.89(CH), 114.16(C), 116.43(CH), 119.55(C), 124.81(CH), 126.90(CH), 127.34(CH), 127.84(CH), 128.54(CH), 130.25(C), 130.93(CH), 132.16(C), 132.56(CH), 133.88(C), 133.99(C), 139.41(C), 150.70(C), 150.77(C), 152.07(C), 157.09(C), 159.07(C), 159.77(C=O). Anal. Calcd. for $\text{C}_{28}\text{H}_{21}\text{NO}_3$: C, 80.17; H, 5.05; N, 3.34. Found: C, 80.05; H, 5.01; N, 3.34.

12-Methyl-7-(4-Chlorophenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3h). Light yellow solid; Yield 50%; M.P. 216–217°C; IR (KBr, cm^{-1}): 3045, 2965, 1730, 1630, 1515, 820; $^1\text{H-NMR}$ (CDCl_3): δ 2.56 (3H, s, CH_3), 2.69 (2H, t, protons at C_6), 2.90 (2H, t, protons at C_5),

7.02–7.54 (9H, m, aromatic protons), 8.62 (1H, d, $J = 1.6$ Hz, $\text{C}_{13}\text{-H}$), 8.69 (1H, dd, $J = 7.6$ and 1.2 Hz, $\text{C}_1\text{-H}$); $^{13}\text{C-NMR}$ (CDCl_3): 21.17(CH_3), 25.29(CH_2), 27.63(CH_2), 118.14(CH), 119.03(C), 121.49(C), 124.61(CH), 126.92(CH), 127.37(CH), 127.84(CH), 128.91(CH), 129.74(C), 131.00(CH), 131.28(CH), 133.53(C), 133.85(C), 139.54(C), 149.15(C), 149.39(C), 150.96(C), 157.10(C), 157.34(C), 158.97(C), 161.05(C=O). Anal. Calcd. for $\text{C}_{27}\text{H}_{18}\text{ClNO}_2$: C, 76.50; H, 4.28; N, 3.30. Found: C, 76.38; H, 4.22; N, 3.27.

12-Chloro-7-phenyl-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3i). Yellow solid; Yield 51%; M.P. 184°C; IR (KBr, cm^{-1}): 3055, 2980, 1740, 1605, 1520, 700, 745; $^1\text{H-NMR}$ (CDCl_3): δ 2.73 (2H, t, protons at C_6), 2.91 (2H, t, protons at C_5), 7.22–7.56 (10H, m, aromatic protons), 8.68–8.80 (2H, m, $\text{C}_1\text{-H}$ and $\text{C}_{13}\text{-H}$ merged); $^{13}\text{C-NMR}$ (CDCl_3): 25.50(CH_2), 27.58(CH_2), 113.94(C), 118.28(CH), 121.28(C), 124.71(CH), 126.98(CH), 127.15(CH), 127.52(CH), 127.89(CH), 128.56(CH), 129.90(CH), 131.31(CH), 131.62(CH), 132.59(C), 133.63(C), 137.85(C), 139.38(C), 149.54(C), 150.70(C), 151.07(C), 152.23(C), 157.55(C), 159.02(C=O). Anal. Calcd. for $\text{C}_{26}\text{H}_{16}\text{ClNO}_2$: C, 76.19; H, 3.93; N, 3.44. Found: C, 76.25; H, 3.97; N, 3.44.

12-Chloro-7-(4-methylphenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3j). Light yellow solid; Yield 48%; M.P. 260–262°C; IR (KBr, cm^{-1}): 3040, 2960, 1740, 1600, 1515, 825; $^1\text{H-NMR}$ (CDCl_3): δ 2.49 (3H, singlet, CH_3), 2.72 (2H, t, protons at C_6), 2.88 (2H, t, protons at C_5), 7.08–7.51 (9H, m, aromatic protons), 8.66 (1H, poorly resolved dd, $\text{C}_1\text{-H}$), 8.78 (1H, poorly resolved d, $\text{C}_{13}\text{-H}$); $^{13}\text{C-NMR}$ (CDCl_3): 21.69(CH_3), 25.61(CH_2), 27.70(CH_2), 114.08(C), 118.23(CH), 121.25(C), 124.66(CH), 127.07(CH), 127.45(CH), 127.89(CH), 129.27(CH), 129.86(C), 131.24(CH), 131.53(CH), 132.78(C), 133.65(C), 134.79(C), 137.52(C), 139.47(C), 149.49(C), 151.06(C), 152.47(C), 157.42(C), 159.03(C=O). Anal. Calcd. for $\text{C}_{27}\text{H}_{18}\text{ClNO}_2$: C, 76.50; H, 4.28; N, 3.30. Found: C, 76.38; H, 4.23; N, 3.36.

12-Chloro-7-(4-methoxyphenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3k). Light yellow solid; Yield 55%; M.P. 194–196°C; IR (KBr, cm^{-1}): 3055, 2980, 1725, 1615, 1510, 810; $^1\text{H-NMR}$ (CDCl_3): δ 2.74 (2H, t, protons at C_6), 2.88 (2H, t, protons at C_5), 3.91 (3H, s, OCH_3), 7.04–7.50 (9H, m, aromatic protons), 8.65 (1H, poorly resolved dd, $\text{C}_1\text{-H}$), 8.76 (1H, d, $J = 1.2$ Hz, $\text{C}_{13}\text{-H}$); $^{13}\text{C-NMR}$ (CDCl_3): 25.51(CH_2), 27.60(CH_2), 55.26(OCH_3), 113.97(CH), 114.20(C), 118.19(CH), 121.29(C), 124.68(CH), 127.01(CH), 127.45(CH), 127.89(CH), 128.52(CH), 129.86(C), 131.21(CH), 131.50(CH), 133.03(C), 133.66(C), 139.41(C), 149.51(C), 151.03(C), 152.19(C), 157.44(C), 159.21(C=O). Anal. Calcd. for $\text{C}_{27}\text{H}_{18}\text{ClNO}_3$: C, 73.72; H, 4.12; N, 3.18. Found: C, 73.59; H, 4.18; N, 3.17.

12-Chloro-7-(4-Chlorophenyl)-5,6-dihydro-14-aza[1]benzopyrano[3,4-*b*]phenanthren-8*H*-one (3l). White solid; Yield 47%; M.P. 255–256°C; IR (KBr, cm^{-1}): 3050, 2970, 1730, 1610, 1500, 825; $^1\text{H-NMR}$ (CDCl_3): δ 2.69 (2H, t, protons at C_6), 2.89 (2H, t, protons at C_5), 7.12–7.51 (9H, m, aromatic protons), 8.63 (1H, poorly resolved dd, $\text{C}_1\text{-H}$), 8.73 (1H, poorly resolved d, $\text{C}_{13}\text{-H}$); $^{13}\text{C-NMR}$ (CDCl_3): 25.46(CH_2), 27.45(CH_2), 113.74(C), 118.23(CH), 121.05(C), 124.64(CH), 127.06(CH), 127.53(CH), 127.95(CH), 128.66(CH), 128.87(CH), 130.00(C), 131.42(CH), 131.69(CH), 132.51(C), 133.40(C), 133.90(C), 136.18(C), 139.34(C), 149.54(C),

150.88(C), 150.95(C), 157.67(C), 158.99(C=O). Anal. Calcd. for $C_{26}H_{15}Cl_2NO_2$: C, 70.28; H, 3.40; N, 3.15. Found: C, 70.36; H, 3.45; N, 3.15.

In case of the compounds **3e**, **3h**, **3j**, and **3k**, the number of carbon signals in ^{13}C -NMR spectra are less than expected (in case of compounds **3e**, **3h**, and **3j**, one signal, while in compound **3k**, two signals). This may be due to identical chemical shifts of certain carbons which may appear at same position.

Antimicrobial activities. All the synthesized compounds **3a-l** were screened for their antimicrobial activity using the agar cup diffusion method [19]. Antibacterial activity of the test compounds was evaluated against one gram-positive bacteria, *Bacillus subtilis*, and one gram-negative bacteria, *Escherichia coli*, using Ciprofloxacin and Ampicillin as standard drugs. Antifungal activity was screened against one fungal strain, *Candida albicans*, using Clotrimazole as standard drug. The zone of inhibition was measured in mm and was compared with standard drug. DMF was used as blank. All the compounds were tested at three different concentrations 500, 750, and 1000 $\mu\text{g/mL}$. The results are shown in Table 1.

Acknowledgments. The authors NHP and VGP are thankful to UGC for meritorious research fellowship under RFSMS. The authors are also thankful to the Head, Department of Chemistry, Sardar Patel University, for providing research facilities and Vaibhav Laboratory, Ahmedabad, for recording IR spectra.

REFERENCES AND NOTES

- [1] (a) Geissman, T. A. *The Chemistry of Flavonoid Compounds*; Pergamon Press: Oxford, 1962; (b) Harborne, J. B. *The Flavonoid: The Advances in Research since 1980*; Chapman & Hall: London, 1988; (c) Harborne, J. B. *The Flavonoid: The Advances in Research since 1986*; Chapman & Hall: London, 1994.
- [2] Lin, C. M.; Huang, S. T.; Lee, F. W.; Sawkuo, H.; Lin, M. H. *Bioorg Med Chem* 2006, 14, 4402.
- [3] Massimo, C.; Francesco, E.; Federica, M.; Carla, M. M.; Prieto, G. S.; Carlos, R. J. *Aust J Chem* 2003, 56, 59.
- [4] Tyagi, Y. K.; Kumar, A.; Raj, H. G.; Vohra, P.; Gupta, G.; Kumari, R.; Kumar, P.; Gupta, R. K. *Eur J Med Chem* 2005, 40, 413.
- [5] Modrana, J. N.; Nawrot, E.; Graczyk, J. *Eur J Med Chem* 2006, 41, 1301.
- [6] Sardari, S.; Mori, Y.; Horita, K.; Micetich, R. G.; Nishibe, S.; Dane-shtalab, M. *Bioorg Med Chem* 1999, 7, 1933.
- [7] Huang, L.; Yuon, X.; Yu, D.; Lee, K. H.; Chin, H. C. *Virology* 2005, 332, 623.
- [8] Elinos-Baez, C. M.; Leon, F.; Santos, E. *Cell Biol Int* 2005, 29, 703.
- [9] Ukawa, K.; Ishiguro, T.; Wada, Y.; Nohara, A. *Heterocycles* 1986, 24, 1931.
- [10] Heber, D. *Arch Pharm* 1987, 320, 402.
- [11] Heber, D. *J Heterocycl Chem* 1994, 31, 1353.
- [12] Pandya, S. U.; Pandya, U. R.; Hirani, B. R.; Brahmhatt, D. I. *J Heterocycl Chem* 2006, 43, 795.
- [13] Naik, H. R. P.; Naik, H. S. B.; Naik, T. R. R.; Naika, H. R.; Gouthamchandra, K.; Mahmood, R.; Ahamed, B. M. K. *Eur J Med Chem* 2009, 44, 981.
- [14] Willemann, C.; Grunert, R.; Bednarski, P. J.; Troschutz, R. *Bioorg Med Chem* 2009, 17, 4406.
- [15] Murthy, M.; Pedemonte, N.; Vinish, L. M.; Galiotta, L.; Cuthbert, A. *Eur J Pharmacol* 2005, 516, 118.
- [16] Zarghi, A.; Ghodsi, R.; Azizi, E.; Daraie, B.; Hedayati M.; Dadrass O. G. *Bioorg Med Chem* 2009, 17, 5312.
- [17] Shah, V. R.; Bose, J. L.; Shah R. C. *J Org Chem* 1960, 25, 677.
- [18] Rao, C. J.; Reddy, K. M.; Murthy, A. K. *Indian J Chem* 1981, 20B, 282.
- [19] Copper, K. E.; Kavanagh, F. *Analytical Microbiology*, 2nd ed.; Academic Press: New York, 1972, pp 13.