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SYNTHESIS OF POLYCYCLIC OXA-COUMARINS, POTENTIAL ANTITUMOUR AGENTS AND A SHORT AND CONVENIENT SYNTHESIS OF NAPHTHOPYRANOQUINOLINES FROM NAPHTHOPYRAN CHLOROALDEHYDES.

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Key words : Oxa-coumarins, antitumour agent, enaminoimine hydrochloride, oxa-azaarene, naphthopyranoquinolines.

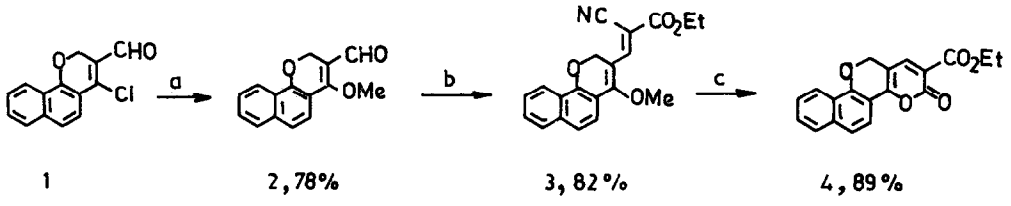
Abstract : A three step high yielding synthesis of some novel oxa-coumarins (**4**, **8** and **9**) from chloroaldehyde derivatives (**1**&**5**) have been described. The chloroaldehydes have also been used for two step synthesis of some novel naphthopyranoquinolines (**12**, **15**) via regioselective thermal cyclisation of enaminoimine hydrochloride derivative (**11**, **14**).

Chemoprotection against cancer has been the subject matter of much recent research. Some chemical compounds containing electrophilic centres that can function as Michael reaction acceptors, can raise the level of enzymes[1] protective against electrophilic chemical carcinogens. Coumarin analogs are found to inhibit induction of polyaromatic hydrocarbon induced tumarogenesis in rodents[2,3]. Recently it has been shown that coumarin derivatives structurally related to benzo[a]pyrene (BP) and 7,12-dimethylbenzanthracene (DMBA) are more efficient in blocking tumour induction[4,5]. Thus several coumarin derivatives attached to polycyclic arenes are needed to establish structure activity relationships in this class of compounds. Systematic investigation of structural modification of molecules of this type[6] in relation to anticarcinogenic activity have not been reported.

In this report, we like to present the synthesis of some polycyclic coumarin analogs of potent carcinogenic oxa-arenes starting from the chloroaldehyde **1** or **5**[7]. The chloroaldehyde (**1** or **5**) was converted to the methoxy derivative **2** or **6** in about 73-78% yield by refluxing with sodium methoxide in methanol. The methoxyaldehyde (**2** or **6**) on condensation with cyanoacetic ester in presence of 30% aqueous ethanolic KOH produced the nitrile derivative **3** or **7** as yellow to

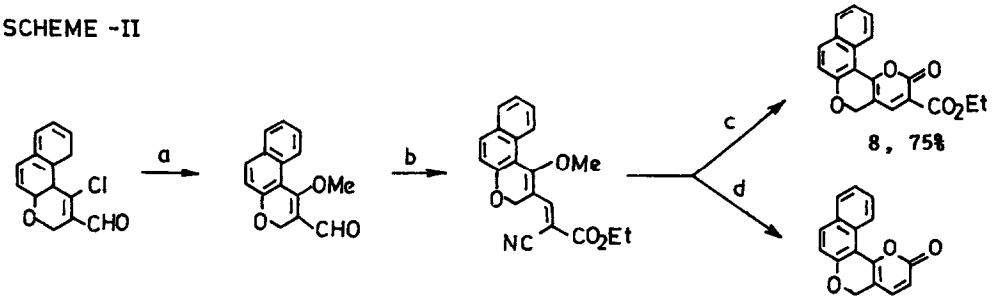
deep red solid. Conversion of the nitriles to the oxa-coumarin derivatives were achieved in excellent yields by heating the nitrile derivatives with pyridine hydrochloride under nitrogen atmosphere. The nitrile **7** on heating with pyridine hydrochloride (neat) produced the ester derivative **8** as the major product containing little amount ($\sim$5-6%) of the decarboxylated product **9**. However, when the reaction was carried out by heating with pyridine hydrochloride in refluxing quinoline the decarrboxylated product **9** was obtained in about 72% yield and no ester derivative was found in the mixture. The nitrile **3** under analogous condition produced no decarboxylated analog but the ester derivative **4** as the only product. All the three oxa-coumarins (**4,8** or **9**) show intense greenish yellow fluorescence in solution.

SCHEME-I



1 2,78% 3, 82% 4, 89%

SCHEME -II

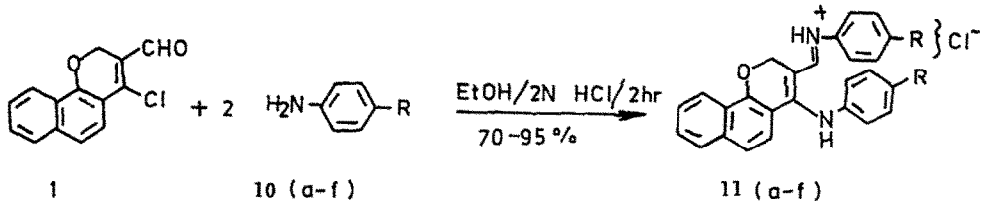


5 6,73% 7, 61% 8, 75% 9, 72%

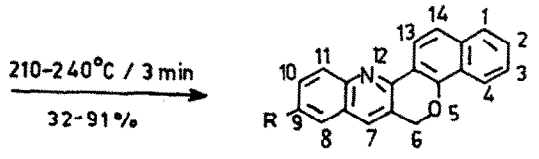
a. $NaOCH_3$/MeOH/reflux, 2h. b. $CH_2(CN)CO_2Et$/Ethanolic KOH/reflux, 20 min.
c. $C_5H_5N.HCl$/reflux, 15 min. d. $C_5H_5N.HCl$/quinoline/reflux, 15 min.

Though the coumarin moiety fused with polyaromatic hydrocarbon (PAH) have been reported to act as antitumour agent, aza isomer of PAH i.e. polycyclic azaarenes have been found to be carcinogenic in nature.

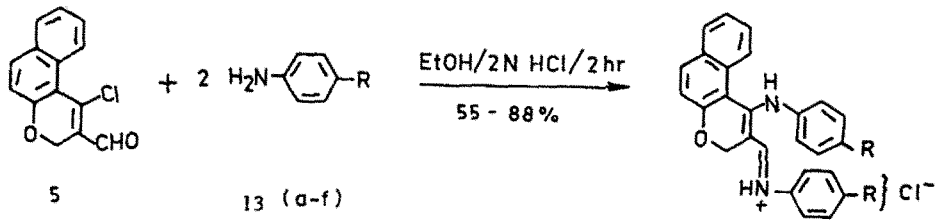
SCHEME -III



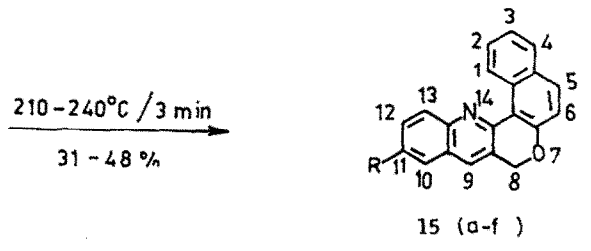
1 10 (a-f) 11 (a-f)



12 (a-f)



5 13 (a-f) 14 (a-f)



15 (a-f)

a, R = H
b, R = CH_3
c, R = OCH_3
d, R = Cl
e, R = NO_2
f, R = CO_2Et

Benzopyranoquinolines[8-12] are reported to be potent carcinogens[2,3] however, until now there is no report on the synthesis or biological evaluation of corresponding naphthopyranoquinolines.

In connection with our studies[13] on the syntheses of polycyclic azaarenes bearing potential functional groups at the terminal ring to convert them to trans dihydrodiols, we were interested in the thermal cyclisation of enaminoimine hydrochlorides derived from naphthopyran chloroaldehydes.

Here, we present a short and convenient synthesis of some naphthopyranoquinolinnes having bay region and Fjord region in the molecules, through the thermal cyclisation of suitable enaminoimine hydrochlorides **11** and **14.**

The chloroaldehydes **1** or **5**[7] when treated with 2.5 equivalents of aniline or substituted aniline in ethanol in presence of 2N hydrochloric acid at room temperature afforded the enaminoimine hydrochlorides **11** or **14** as orange yellow to red solid in 55-95% yield. The enaminoimine hydrochloride on brief heating at a temperature slightly above their melting points underwent ring closure with elimination of one equivalent of arylamine hydrochloride to afford the corresponding naphthopyranoquinolines **12** or **15** in moderate to excellent yield.

In ^{1}H-nmr of the compound **12(a-f)** i.e. 6-H naphtho[2',1':5,6]pyrano[4,3-b]quinolines, the $-O\underline{CH}_2$ and H^7 proton appeared as sharp singlets at 5.52-5.56 δ and 7.79-7.89 δ respectively whereas H^4 was observed as dd at 8.28-8.33 δ. H^{13} showed a very downfield shift to appear at 8.50-8.55 δ as doublet (J~8.5-8.7 Hz). In contrast to this, the angular isomers, i.e. 8-H naphtho[1',2':5,6]pyrano-[4,3-b]quinolines (**15**) showed the expected strong downfield shift at 9.88-10.0 δ (J~8.5 Hz) for the proton H^1 which is situated in the Fjord region of the oxa-azaarene moiety. Here also OCH_2 appear at ~ 5.3 δ as singlet.

We hope that these compounds will also show enhanced carcinogenic activity as compared to the naphthacridine derivatives. The compounds **12(a-f)** posses two bay region whereas the compounds **15(a-f)** have a Fjord region in its structure. Comparison of their mutagenecity/carcinogenecity will be helpful to correlate the bay region-Fjord region effect on mutagenecity in naphthopyranoquinoline system.

EXPERIMENTAL

All melting points are uncorrected and were checked in one side open glass capillary using sulphuric acid bath. ^{1}H-NMR spectra were recorded with Varian (90 MHz), Brucker (250 MHz) and Jeol (100 MHz) machines using TMS as internal standard. Mass spectra were performed on Finnigan 4000 GC/MS machine at 70 eV.

IR spectra were recorded on Perkin-Elmer 800 machine. Elemental analysis have been performed from CDRI, Lucknow (India).

General method for the preparation of 2 or 6 :

To a solution of NaOMe prepared from metallic Na (11 mmol) and anhydrous methanol (100 ml), the chloroaldehyde (**1** or **5**)[7] is added and mixture is refluxed for 2 h. Excess of alcohol is evaporated out and the residue is diluted with water (50 ml) and extracted with ether. the combined organic layer is washed with water, dried (Na_2SO_4) and solvent removed to afford the methoxyaldehyde **2** or **6** in 73-78% yield which is further purified.

2 : Shining yellow solid, mp 107-108°C (ether); yield 78%. IR (KBr) ν_{max} 1610, 1640 cm^{-1}. ^{1}H-NMR δ ($CDCl_3$) 4.1 (s,3H), 5.2 (s,2H), 7.4-7.7 (m,4H), 7.8 (d,1H), J~ 8 Hz), 8.2 (d,1H, J~ 8 Hz), 10.2 (s,1H) ppm. MS, m/z 240 (M^+, 40%) 225 (M $-CH_3$, 45%), 211 (M-CHO, 100%), 196 (55%), 170 (30%), 152 (33%), 139 (30%), 126 (30%), 115 (55%), 114 (75%). (Found C, 74.8; H, 4.75. Calc. for $C_{15}H_{12}O_3$ C, 75.0; H, 5.0%).

6 : Light yellow solid, mp 80-81°C (Column chromatography, neutral Al_2O_3/pet. ether, 40-60°C); Yield 73%. IR (KBr) ν_{max} 1610, 1640 cm^{-1}. ^{1}H-NMR δ ($CDCl_3$) 3.7 (s,3H), 5.0 (s,2H), 7.15 (d,1H, J~9 Hz), 7.4-7.7 (m,2H), 7.8 (dd,1H, J~1.55-2 Hz), 7.85 (d,1H, J~9 Hz), 8.5 (dd,1H, J~1.5-2 Hz), 10.2 (s,1H) ppm. (Found C, 74.75; H, 4.7 Calc. for $C_{15}H_{12}O_3$ C, 75.0; H 5.0%)

General method for the preparation of 3 or 7 :

To a mixture of the methoxy aldehyde **2** or **6** (4.0 mmol) and ethylcyanoacetate (4.5 mmol) in ethanol (20 ml) is added a few drops of 30% aqueous ethanolic KOH and the mixture is refluxed for 15-20 min. The resulting deep red solution is then cooled and poured into ice water. The solid separated is filtered, washed well with water, dried and is recrystallised from suitable solvent.

3 : Deep red solid, mp 140-141°C (ethanol); Yield 82%. IR (KBr) ν_{max} 1615, 1700, 2200 cm^{-1} ^{1}H-NMR δ ($CDCl_3$) 1.4 (t,3H), 3.9 (s,3H), 4.3 (q,2H), 5.6 (s,2H), 7.3-7.6 (m,4H), 7.8 (d,1H, J~ 8.5 Hz), 8.2 (d,1H, J~7.5 Hz), 8.4 (d,1H, J~8.5 Hz) ppm. MS, m/z 335 (M^+,15%), 320 (M-CH_3, 20%), 306 (45%), 248 (26%), 171 (35%), 115 (55%), 114 (100%). (Found C, 71.4; H, 4.8; N, 3.9. Calc. for $C_{20}H_{17}NO_4$ C, 71.64; H, 5.07; N, 4.18%).

7 : Shining yellow solid, mp 166-167°C (ethanol); Yield 61%. IR (KBr) ν_{max} 1610, 1720, 2200 cm^{-1}. ^{1}H-NMR δ ($CDCl_3$) 1.35 (t,3H), 3.65 (s,3H), 4.35 (q,2H), 5.4

(s,2H), 7.2 (d,1H, J~ 9 Hz), 7.3-8.0 (m,4H), 8.4 (d,1H, J~9 Hz), 8.6 (s,1H), ppm, (Found C, 71.5; H, 4.85; N, 3.95, Calc. for $C_{20}H_{17}NO_4$ C, 71.64; H, 5.07; N, 4.18%).

General method for the preparation of 4 and 8

The nitrile derivative **3** or **7** (1.5 mmol) is refluxed with an excess of pyridine hydrochloride (3.0 g) for 10-15 min. After cooling to room temperature it is poured into ice cold dil. hydrochloric acid. The solid separated is filtered and washed well with water and dried. The crude product thus obtained is purified by usual technique.

4 : Yellow solid, mp 213-214°C (ethanol); Yield 89%. IR (KBr) ν_{max} 1626, 1697, 1747 cm^{-1}. ^{1}H-NMR δ ($CDCl_3$) 1.4 (t,3H), 2.4 (q,2H), 5.35 (s,2H), 7.4-7.9 (m,5H), 8.08-8.35 (m,2H) ppm. MS, m/z 322 (M^+, 30%), 221 (25%), 170 (35%), 165 (30%), 115 (30%), 114 (100%). (Found C, 70.6, H, 4.2, Calc. for $C_{19}H_{14}O_5$ C, 70.8; H, 4.35%).

8 : Orange yellow solid, mp 183-184°C (purified by preparative TLC/Neutral Al_2O_3-Benzene-ethylacetate, 9:1); Yield 75%. ^{1}H-NMR δ ($CDCl_3$) : 1.4 (t,3H), 4.4 (q,2H), 5.1 (s,2H), 7.12 (d,1H, J~9 Hz), 7.36-8.04 (m,4H), 8.16 (s,1H), 8.9 (dd,1H, J ~ 1.5 Hz) ppm. (Found C, 70.65; H, 4.25, Calc. for $C_{19}H_{14}O_5$ C, 70.8; H, 4.35%).

6-Oxa-5,6-dihydrophenanthro[4,3-b]pyran-2-one 9

A mixture of the cyanoderivative **7** (200 mg, 0.6 mmol), pyridine hydrochloride (230 mg, 2 mmol) and quinoline (5 ml) is refluxed for 15 min. It is then cooled, and poured in ice cold dil. hydrochloric acid and is extracted with chloroform. Chloroform layer is washed with dil. HCl, water and dried (Na_2SO_4). Removal of solvent gives the crude product which is purified by preparative TLC (silica gel/benzene-ethyl acetate, 9.1) to give **9** as a yellow solid, mp 156-157°C (benzene-pet. ether); yield 107 mg (72%).

IR (KBr) ν_{max}, 1620, 1715 cm^{-1}. ^{1}H-NMR δ ($CDCl_3$) 5.1 (s,2H), 6.25 (d,1H, J ~ 10 Hz), 7.15 (d,1H, J~9 Hz), 7.3 (d,1H, J~10 Hz), 7.4-7.5 (m,1H), 7.6-7.7 (m,1H), 7.8 (d,1H, J~8.5-9 Hz), 7.9 (d,1H, J~9 Hz), 8.95 (d,1H, J~8.5-9 Hz) ppm. MS, m/z 251 (M+1,17%), 250(M^+,100%), 249 (M-1, 48%), 222 (41%), 221 (55%), 171 (32%), 170 (49%), 165 (27%), 142 (30%), 129 (40%), 125 (51%), 116 (42%), 115 (100%). (Found C, 76.65; H, 3.8 Calc. for $C_{16}H_{10}O_3$ C, 76.8; H, 4.0%).

Enaminoimine hydrochlorides 11(a-f) and 14(a-f); General Procedure :

To an ice cooled solution of arylamine (6 mmol) in ethanol (15-20 ml), 2**N**

hydrochloric acid (3 ml) is added. Now to this well stirred solution, the chloroaldehyde 3 or 5 (2.5 mmol) is added in one batch. Stirring is continued for 10 minutes at 5-10°C and then for 2 hours at room temperature. The reaction mixture is then cooled in ice bath and filtered. The orange yellow to red residue is washed with little cold ethanol and dried in air. These are used directly for the next step without further purification.

11a Red solid, m.p. 198-200°C (d), yield 99%, IR(KBr) ν_{max} 1600, 1622, 1640, 3050, 3150 cm^{-1}. **11b** Orange yellow solid, m.p. 185-186°C (d), yield 70%, IR (KBr) ν_{max} 1602, 1625, 1640, 3060, 3142, 3400 cm^{-1}. **11c** Red solid, m.p. 205-206°C (d), yield 92%, IR(KBr) ν_{max} 1602, 1625, 1640, 3060, 3142, 3400 cm^{-1}. **11d** Deep yellow solid, m.p. 203-204°C (d), yield 79%, IR(KBr) ν_{max} 1600, 1622, 1640, 3040, 3160, 3400 cm^{-1}. **11e** Red solid, m.p. 210-212°C (d), yield 83%, IR(KBr) ν_{max} 875, 1332, 1376, 1522, 1572, 1590, 1620, 1640, 3060, 3400 cm^{-1}. **11f** Red solid, m.p. 206-207°C (d), yield 94%, IR(KBr) ν_{max} 1602, 1620, 1640, 1706, 3040, 3400 cm^{-1}. **14a** Red solid, m.p. 195-196°C, yield 55%, IR(KBr) ν_{max} 1602, 1620, 1635, 3040, 3140, 3400 cm^{-1}. **14b** Red solid, m.p. 197-198°C (d), yield 68%, IR(KBr) ν_{max} 1610, 1620, 3040, 3150, 3400 cm^{-1}. **14c** Red solid, m.p. 176-177°C (d), yield 88%, IR(KBr) ν_{max} 1600, 1620, 3040, 3150, 3400 cm^{-1}. **14d** Red solid, m.p. 186-187°C (d), yield 83%, IR(KBr) ν_{max} 1622, 3060, 3160, 3400 cm^{-1}. **14e** Red solid, m.p. 215-216°C (d), yield 69%, IR(KBr) ν_{max} 875, 1298, 1340, 1560, 1575, 1635, 3040, 3400 cm^{-1}. **14f** Red soid, m.p. 186-187°C (d), yield 79%, IR(KBr) ν_{max} 1600, 1620, 1635, 1712, 3050, 3140 cm^{-1}.

Thermolysis of enaminoimine hydrochlorides; General procedure for the synthesis of 6H-naphtho[2',1':5,6]pyrano[4,3-b]quinolines 12(a-f) and 8H-naphtho[1',2':5,6] pyrano[4,3-b]quinolines 15(a-f) :

The anil hydrochloride **3** or **6** (500-700 mg) is heated in a long necked tube at 210-240°C for 3 minutes in a salt bath. The anil derivatives melts and a vigorous reaction sets in with the deposition of arylamine hydrochloride in the cooler part of the tube. After cooling to room temperature, the fused mass is treated with chloroform (75 ml). Chloroform layer is then washed with water, dried (Na_2SO_4) and solvent removed to produce the crude product which is further purified by column chromatography (neutral Al_2O_3/pet.ether or pet.ether-benzene mixture) followed by recrystallisation from suitable solvent.

12a Colourless solid, m.p. 195-196°C [neutral Al_2O_3/pet.ether (60-80°C)], yield 55%, ^{1}H-NMR ($CDCl_3$) δ : 5.56 (s,2H,OCH_2), 7.48-7.85 (m, 7H, H^1-H^3, H^8-H^{10}, H^{14}), 7.89 (s,1H,H^7), 8.14 (d,1H,H^{11}, J = 8.5 Hz), 8.3 (dd,1H,H^4), 8.55 (d,1H,H^{13}, J = 8.5 Hz) ppm. MS, m/e 283 (M^+, 100%) 282 (68%), 254 (25%), 141

(32%), 127 (46%), 126 (21%), 113 (22%). (Found C, 84.65; H, 4.45; N, 4.73 Calc. for $C_{20}H_{13}NO$ C, 84.8; H, 4.59; N, 4.96%). **12b** Colourless solid, m.p. 194-195°C [neutral Al_2O_3/pet.ether (60-80°C), followed by recrystallisation from EtOH], yield 78%, ^{1}H-NMR ($CDCl_3$) δ : 2.55 (s, 3H, CH_3), 5.55 (s, 2H, OCH_2), 7.5-7.63 (m, 5H, H^2, H^3, H^8, H^{10}, H^{14}) 7.8 (s, 1H, H^7), 7.83 (dd, 1H, H^1), 8.05 (d, 1H, H^{11}), 8.3 (dd, 1H, H^4), 8.5 (d, 1H, H^{13}) ppm. MS m/e 297 (M^+, 100%), 296 (85%), 283 (30%), 269 (65%), 268 (50%), 267 (45%), 254 (45%), 240, 148, 142, 136, 128. (Found C, 84.64; H, 4.85; N, 4.4 Calc. for $C_{21}H_{15}NO$ C, 84.84; H, 5.05; N, 4.71%). **12c** Faint yellow solid, m.p. 201-202°C [neutral Al_2O_3/pet.ether (60-80°C) - benzene mixture 9:1, followed by recrystallisation from EtOH], yield 32%, ^{1}H-NMR ($CDCl_3$) δ : 3.9 (s, 3H, OCH_3), 5.55 (s, 2H, OCH_2), 7.05 (d, 1H, H^8, J = 2.8 Hz), 7.25 (dd, 1H, H^{10}), 7.4-7.9 (m, 5H, H^1-H^3, H^7, H^{14}), 8.10 (d, 1H, H^{11}, J = 8.6 Hz), 8.3 (dd, 1H, H^4), 8.55 (d, 1H, H^{13}, J = 8.6 Hz) ppm. (Found C, 80.3 ; H, 4.56; N, 4.27 Calc. for $C_{21}H_{15}NO_2$ C, 80.51; H, 4.79; N, 4.47%). **12d** Light yellow solid, m.p. 222-223°C [neutral Al_2O_3/pet.ether (60-80°C), followed by recrystallization from EtOH], yield 91%, ^{1}H-NMR ($CDCl_3$) δ : 5.52 (s, 2H, OCH_2), 7.4-7.92 (m, 7H, H^1-H^3, H^7, H^8, H^{10}, H^{14}), 8.08 (d, 1H, H^{11}, J = 8.5 Hz), 8.28 (dd, 1H, H^4), 8.52 (d, 1H, H^{13}, J = 8.5 Hz) ppm. (Found C, 75.37; H, 3.63 ; N, 4.24, Calc. for $C_{20}H_{12}NOCl$ C, 75.59; H, 3.78; N, 4.41 %). **12e** Light yellow solid, m.p. 203-204°C [neutral Al_2O_3/pet.ether (60-80°C) - benzene mixture 1:1, followed by recrystallization from EtOH], yield 63%, IR(KBr) ν_{max} 1342, 1530, 1610 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ : 5.54 (s, 2H, OCH_2), 7.35-7.85 (m, 7H, H^1-H^3, H^7, H^8, H^{10}, H^{14}), 8.05 (d, 1H, H^{11}, J = 9.3 Hz), 8.30 (dd, 1H, H^4), 8.5 (d, 1H, H^{13}, J = 8.6 Hz) ppm. (Found C, 72.88; H, 3.44; N, 8.35 Calc. for $C_{20}H_{12}N_2O_3$ C, 73.17; H, 3.66; N, 8.54 %). **12f** Light yellow solid, m.p. 223-224°C [neutral Al_2O_3/pet.ethher (60-80°C) - benzene mixture 9:1, followed by recrystallization from EtOH], yield 37%, IR(KBr) ν_{max} 1622, 1718 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ : 1.45 (t, 3H, CH_3), 4.5 (q, 2H, CH_2), 5.55 (s, 2H, OCH_2), 7.3-8.0 (m, 5H, H^1-H^3, H^7, H^{14}), 8.15-8.4 (m, 3H, H^4, H^{10}, H^{11}), 8.45 (s, br, 1H, H^8), 8.55 (d, 1H, H^{13}, J = 8.5 Hz) ppm. MS, m/e 355 (M^+, 100%), 354, 326, 325, 298, 155, 140, 126. (Found C, 77.45; H, 4.53; N, 3.7 Calc. for $C_{23}H_{17}NO_3$ C, 77.75; H, 4.79; N, 3.94 %). **15a** Light yellow solid, m.p. 144-145°C [neutral Al_2O_3/pet.ether (60-80°C), and recrystallized from EtOH], yield 48%, ^{1}H-NMR ($CDCl_3$) δ : 5.3 (s, 2H, OCH_2), 7.24 (d, 1H, H^6, J = 8.8 Hz), 7.35-8.1 (m, 8H, H^2-H^5, H^9-H^{12}), 8.24 (d, 1H, H^{13}, J = 8.8-9.0 Hz), 10.0 (d, 1H, H^1, J = 8.5-8.7 Hz) ppm. (Found C, 84.6; H, 4.4; N, 4.7 Calc. for $C_{20}H_{13}NO$, C, 84.8; H, 4.59; N, 4.96 %). **15b** Light yellow solid, m.p. 162-163°C [neutral Al_2O_3/pet.ether (60-80°C), and recrystallized from EtOH], yield 42%, ^{1}H-NMR ($CDCl_3$) δ : 2.55 (s, 3H, CH_3), 5.29 (s, 2H, OCH_2), 7.21 (d, 1H, H^6, J = 8.9 Hz), 7.43-7.9 (m, 7H, H^2-H^5, H^9, H^{10}, H^{12}), 8.12 (d,

1H, H^{13}, J = 9.0-9.2 Hz), 9.94 (d, 1H, H^{1}, J = 8.6-8.7 Hz) ppm. (Found C, 84.6; H, 4.74; N, 4.35 Calc. for $C_{21}H_{15}NO$ C, 84.84; H, 5.05; N, 4.71 %). **15c** Light orange yellow solid, m.p. 160-161°(d) [neutral Al_2O_3/pet.ether (60-80°C), recrystallized from EtOH]. Yield 33%, ^{1}H-NMR ($CDCl_3$) δ : 3.96 (s, 3H, OCH_3), 5.3 (s, 2H, OCH_2), 7.1-8.0 (m, 8H, H^2-H^6, H^9, H^{10}, H^{12}), 8.24 (d, 1H, H^{13}, J = 9.0-9.3 Hz), 9.96 (d, 1H, H^1, J = 8.5-8.7 Hz) ppm. (Found C, 80.31; H, 4.5; N, 4.2, Calc. for $C_{21}H_{15}NO_2$, C, 80.51; H, 4.79; N, 4,47 %). **15d** Light orange yellow solid, m.p. 205-206°C(d) [neutral Al_2O_3/pet.ether (60-80°C) + benzene, 9:1 and recrystallized from EtOH], yield 39%, ^{1}H-NMR ($CDCl_3$) δ : 5.3 (s, 2H, OCH_2), 7.2 (d, 1H, H^6, J = 8.8-9.0 Hz), 7.3-8.0 (m, 7H, H^2-H^5, H^9, H^{10}, H^{12}), 8.15 (d, 1H, H^{13}, J = 9.0-9.2 Hz) 9.9 (d, 1H, H^1, J = 8.5-8.6 Hz) ppm. (Found C, 75.3; H, 3.59; N, 4.12. Calc. for $C_{20}H_{12}NOCl$ C, 75.59; H, 3.78; N, 4.41 %). **15e** Brick brown solid, m.p. 210-211°C [neutral Al_2O_3/pet.ether (60-80°C) + benzene, 4:1 and recrystallized from Benzene-pet.ether mixture], yield 31%, IR(KBr) ν_{max} 1340, 1520, 1560, 1610 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ : 5.3 (s, 2H, OCH_2), 7.2-8.36 (m, 7H, H^2-H^6, H^9, H^{13}), 8.48 (dd, 1H,, H^{12}, J = 2.0-2.5 Hz), 8.76 (d, 1H, H^{10}, J = 2.0-2.5 Hz), 9.88 (d, 1H, H^1, J = 8.5-8.6 Hz) ppm. (Found C, 72.79; H, 3.4; N, 8.3 Calc. for $C_{2o}H_{12}N_2O_3$, C, 73.17; H, 3.66; N, 8.54 %). **15f** Yellow solid, m.p. 171-172°C [neutral Al_2O_3/pet.ether (60-80°C) + benzene, 1:4 and recrystallized from EtOH], yield 39%, IR(KBr) ν_{max} 1622, 1712 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ : 1.45 (t, 3H, CH_3), 4.45 (q, 2H, $\underline{CH_2}CH_3$) 5.3 (s,, 2H, OCH_2), 7.20 (d, 1H, H^6, J = 8.9 Hz), 7.45-7.55 (m, 1H, H^3), 7.65-7.75 (m, 1H, H^2), 7.80-7.88 (2 x d, 2H, H^4, H^5), 8.03 (s, 1H, H^9) 8.24 (d, 1H, H^{13}, J = 8.8 Hz), 8.29 (dd, 1H, H^{12} J = 1.6 Hz), 8.55 (d, 1H, H^{10}, J = 1.6 Hz), 9.9 (d, 1H, H^1, J = 8.5-8.6 Hz) ppm. MS, m/e 355 (M^+, 100%), 326 (M-29, 30%), 310 (10%), 298 (12%), 281 (12%), 253 (13%), 178 (15%), 163 (20%), 155 (42%), 141 (45%), 127 (52%), 126 (70%), 113 (28%). (Found C, 77.49; H, 4.6; N, 3.71., Calc. for $C_{23}H_{17}NO_3$, C, 77.75; H, 4.79; N, 3.94 %).

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