

SYNTHESIS AND ANTIFUNGAL ACTIVITY OF 1-AMINOMETHYL-3-{4-(CHLOROBENZYLOXY) BENZOYLHYDRAZONO}-4, 5/5, 6-DICHLOROINDOLIN-2-ONES

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3-{4-(Chlorobenzoyloxy) benzoylhydrazono}-4,5/5,6-dichloroindolin-2-ones **1a,b-5a,b**, were synthesized by the condensation of 4-(chlorobenzoyloxy) benzoylhydrazines and 4, 5/5, 6-dichloroindolin-2,3-diones. Compounds **1a,b-5a,b** when subjected to Mannich reaction with secondary heterocyclic amines in the presence of formaldehyde, furnished 1-aminomethyl-3-{4-(chlorobenzoyloxy) benzoylhydrazono}-4, 5/5, 6-dichloroindolin-2-ones **6a,b-20a,b**. The structures of the compounds have been established by means of spectral (IR and ¹H NMR) and elemental analysis. The compounds have been screened for their antifungal potential against human pathogenic fungi.

Indolin-2,3-dione¹ and its Schiff and Mannich bases possess a wide variety of biological activities viz; cytotoxic², antimicrobial³, antitubercular⁴, amoebicidal⁵, anti-HIV⁶, CNS⁷, anticonvulsant⁸, antiglycation⁹, antileishmanial¹⁰, analgesic and antiinflammatory¹¹. Number of articles¹²⁻¹⁷ have been published to show chemistry and biological potential of indolin-2,3-dione derivatives. In view of the biological potential of indolin-2,3-dione, it was considered of interest to prepare Schiff and Mannich bases of isomeric dichloroindolin-2,3-diones and to evaluate them for their antifungal potential.

Methyl 4-hydroxybenzoate on reaction with chlorosubstituted benzyl chlorides gave methyl-4-(chlorobenzoyloxy)-benzoates which on hydrazinolysis with hydrazine hydrate gave 4-(chlorobenzoyloxy) benzoylhydrazines¹⁸⁻²¹. Benzoyl hydrazines on condensation with 4, 5/5 6-dichloroindolin-2,3-diones, in equimolar proportion gave 3-{4-(chlorobenzoyloxy) benzoylhydrazono}-4, 5/5, 6-dichloroindolin-2-ones **1a,b-5a,b**. On being subjected to Mannich reaction²² with secondary heterocyclic amines in the presence of formaldehyde, **1a,b-5a,b**, gave 1-aminomethyl-3-{4-(chlorobenzoyloxy) benzoylhydrazono}-4, 5/5, 6-dichloroindolin-2-ones **6a,b-20a,b**. 4,5 and 5,6-dichloroindolin-2,3-diones were synthesized by the

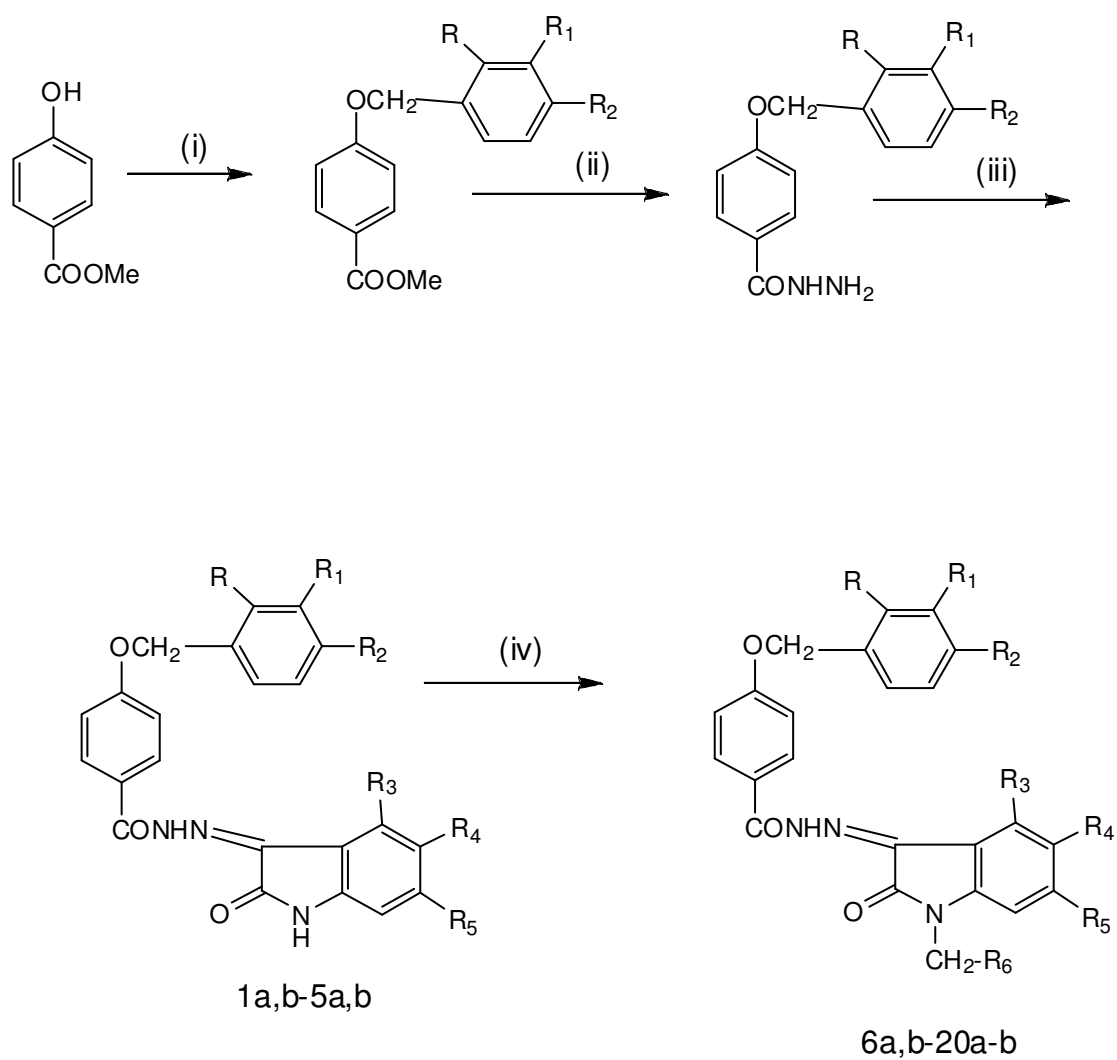
reaction of 3,4-dichloroaniline with chloral hydrate and hydroxylamine hydrochloride to get isonitrosoacetanilide intermediate which on cyclization with concentrated sulfuric acid gave a mixture of 4,5 and 5,6-dichloroindolin-2,3-diones. 4,5 and 5,6-dichloroindolin-2,3-diones were separated by using pH dependent separation method of Varma *et al*²³.

Antifungal activity

Compounds **1a,b- 20a,b** were screened for their antifungal potential against human pathogenic fungi viz. *Candida albicans*, *Cryptococcus neoformans*, *Trichophyton mentagrophytes*, *Aspergillus fumigatus* and *Candida parapsilosis*, using tube dilution method²⁴ at a maximum concentration of 100 µg/ml in DMSO and Minimum Inhibitory Concentration (MIC) values were determined in µg/ml. Fluconazole was taken as standard drug. Antifungal activity data are shown in Table-2.

Experimental

The melting points were determined in open capillary tubes in sulfuric acid bath and are uncorrected. IR spectra were recorded in KBr on a Perkin Elmer RX1 spectrophotometer and ¹H NMR spectra were recorded on a Bruker DRX-300 spectrometer. DMSO-*d*₆/CDCl₃ were taken as solvent.



(i) Chlorobenzyl chlorides, K₂CO₃

(ii) N₂H₄·H₂O

(iii) 4,5/5,6-Dichloroindolin-2,3-diones, EtOH, gl.

AcOH

(iv) Amines, CH₂O, DMF

R, R₁, R₂, R₃, R₄, R₅=H, Cl

R₆= Morpholino, piperidino, pyrrolidino

SCHEME-1

Table-1
Characterization data of the compounds

Compd	R	R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	M.P. (°C)	Yield (%)
1a	H	H	H	Cl	Cl	H	-	>250	70
1b	H	H	H	H	Cl	Cl	-	>250	83
2a	Cl	H	H	Cl	Cl	H	-	>250	67
2b	Cl	H	H	H	Cl	Cl	-	>250	80
3a	H	Cl	H	Cl	Cl	H	-	>250	76
3b	H	Cl	H	H	Cl	Cl	-	>250	76
4a	H	H	Cl	Cl	Cl	H	-	>250	70
4b	H	H	Cl	H	Cl	Cl	-	>250	78
5a	Cl	H	Cl	Cl	Cl	H	-	>250	70
5b	Cl	H	Cl	H	Cl	Cl	-	>250	80
6a	H	H	H	Cl	Cl	H	Morpholino	176-78	77
6b	H	H	H	H	Cl	Cl	Morpholino	170-72	77
7a	H	H	H	Cl	Cl	H	Piperidino	170-72	66
7b	H	H	H	H	Cl	Cl	Piperidino	174-76	74
8a	H	H	H	Cl	Cl	H	Pyrrolidino	194-96	70
8b	H	H	H	H	Cl	Cl	Pyrrolidino	178-80	65
9a	Cl	H	H	Cl	Cl	H	Morpholino	168-70	70
9b	Cl	H	H	H	Cl	Cl	Morpholino	132-34	67
10a	Cl	H	H	Cl	Cl	H	Piperidino	180-82	60
10b	Cl	H	H	H	Cl	Cl	Piperidino	130-32	55
11a	Cl	H	H	Cl	Cl	H	Pyrrolidino	160-62	60
11b	Cl	H	H	H	Cl	Cl	Pyrrolidino	168-70	78
12a	H	Cl	H	Cl	Cl	H	Morpholino	186-88	66
12b	H	Cl	H	H	Cl	Cl	Morpholino	166-68	64
13a	H	Cl	H	Cl	Cl	H	Piperidino	199-200	60

Contd... Table-1

13b	H	Cl	H	H	Cl	Cl	Piperidino	190-92	56
14a	H	Cl	H	Cl	Cl	H	Pyrrolidino	188(d)	50
14b	H	Cl	H	H	Cl	Cl	Pyrrolidino	184-86	56
15a	H	H	Cl	Cl	Cl	H	Morpholino	184-86	50
15b	H	H	Cl	H	Cl	Cl	Morpholino	192-94	67
16a	H	H	Cl	Cl	Cl	H	Piperidino	198(d)	65
16b	H	H	Cl	H	Cl	Cl	Piperidino	202-04	60
17a	H	H	Cl	Cl	Cl	H	Pyrrolidino	188-90	65
17b	H	H	Cl	H	Cl	Cl	Pyrrolidino	198-200	50
18a	Cl	H	Cl	Cl	Cl	H	Morpholino	118-120	68
18b	Cl	H	Cl	H	Cl	Cl	Morpholino	120-122	65
19a	Cl	H	Cl	Cl	Cl	H	Piperidino	188(d)	70
19b	Cl	H	Cl	H	Cl	Cl	Piperidino	198-200	56
20a	Cl	H	Cl	Cl	Cl	H	Pyrrolidino	178(d)	70
20b	Cl	H	Cl	H	Cl	Cl	Pyrrolidino	152-54	60

TMS was taken as internal standard and chemical shifts are expressed in δ ppm. Elemental analysis was performed on Carlo Erba 1108 analyser. Physical data of the synthesized compounds are presented in Table-1.

3-{4-(Chlorobenzoyloxy) benzoylhydrazono}-4,5-dichloroindolin-2-ones 1a-5a

A mixture of 4-(chlorobenzoyloxy) benzoylhydrazines (0.01 mol) and 4,5-dichloroindolin-2,3-diones (0.01 mol) in ethanol (70 ml) containing 3-4 drops of glacial acetic acid was refluxed for 1-2 hr and left overnight at room temperature. The solid product so obtained was filtered, washed with methanol and recrystallised from aq. DMF.

Compounds **1b-5b** were synthesized using same method and gave satisfactory analysis for C,H and N.

1a: IR (KBr) cm^{-1} : 3441, 3187 (NH), 1702, 1669 (C=O), 1606 (C=N), 1252 ($-\text{CH}_2\text{O}$), 765 (C-Cl), ^1H NMR (DMSO- d_6): δ ppm : 5.15 (2H, s, $-\text{CH}_2\text{O}$), 6.95-8.13 (11H, m, ArH), 10.85 (1H, s, CONH), 13.91 (1H, s,

CONH). [Found : C, 59.94, H, 3.37, N, 9.52 $\text{C}_{22}\text{H}_{15}\text{Cl}_2\text{N}_3\text{O}_3$ requires C, 60.02, H, 3.43, N, 9.54%].

2a: IR (KBr): 3422, 3133 (NH), 1705, 1665 (C=O), 1605 (C=N), 1254 ($-\text{CH}_2\text{O}$), 766 (C-Cl). ^1H NMR (DMSO- d_6): 5.25 (2H, s, $-\text{CH}_2\text{O}$), 6.90-8.00 (10H, m, ArH), 10.80 (1H, s, CONH), 13.88 (1H, s, CONH). [Found : C, 55.61, H, 2.90, N, 8.79 $\text{C}_{22}\text{H}_{14}\text{Cl}_3\text{N}_3\text{O}_3$ requires C, 55.66, H, 2.97, N, 8.85%].

3a: IR (KBr): 3446, 3184 (NH), 1709, 1671 (C=O), 1607 (C=N), 1249 ($-\text{CH}_2\text{O}$), 786 (C-Cl). ^1H NMR (DMSO- d_6): 5.17 (2H, s, $-\text{CH}_2\text{O}$), 6.45-8.03 (10H, m, ArH), 10.78 (1H, s, CONH), 13.93 (1H, s, CONH). [Found : C, 55.60, H, 2.93, N, 8.79 $\text{C}_{22}\text{H}_{14}\text{Cl}_3\text{N}_3\text{O}_3$ requires C, 55.66, H, 2.97, N, 8.85%].

4a: IR (KBr) : 3445, 3189 (NH), 1712, 1668 (C=O), 1608 (C=N), 1249 ($-\text{CH}_2\text{O}$), 753 (C-Cl). ^1H NMR (DMSO- d_6): 5.10 (2H, s, $-\text{CH}_2\text{O}$), 6.75-8.23 (10H, m, ArH), 10.78 (1H, s, CONH), 13.87 (1H, s, CONH). [Found : C, 55.60, H, 2.92, N, 8.81 $\text{C}_{22}\text{H}_{14}\text{Cl}_3\text{N}_3\text{O}_3$ requires C, 55.66, H, 2.97, N, 8.85%].

Table-2

Minimum Inhibitory Concentration MIC ($\mu\text{g/ml}$) of compounds against pathogenic fungi by tube dilution method

Compd	<i>Candida albicans</i>	<i>Cryptococcus neoformans</i>	<i>Trichophyton mentagrophytes</i>	<i>Aspergillus fumigatus</i>	<i>Candida parapsilosis</i>
1a	>100	>100	50	50	>100
1b	>100	>100	50	50	>100
2a	>100	>100	50	50	>100
2b	>100	>100	50	50	>100
3a	>100	>100	>100	>100	>100
3b	>100	>100	>100	>100	>100
4a	>100	>100	>100	>100	>100
4b	>100	>100	50	50	>100
5a	>100	>100	>100	>100	>100
5b	>100	>100	>100	>100	>100
6a	>100	6.25	3.12	3.12	>100
6b	>100	3.12	3.12	3.12	>100
7a	>100	25	25	>100	25
7b	>100	>100	>100	>100	>100
8a	>100	6.25	6.25	3.12	>100
8b	>100	6.25	3.12	3.12	>100
9a	>100	6.25	3.12	6.25	>100
9b	>100	12.5	12.5	6.25	>100
10a	>100	6.25	6.25	>100	>100
10b	50	>100	50	>100	50
11a	>100	3.12	6.25	6.25	>100
11b	>100	25	25	25	>100
12a	>100	50	50	25	>100
12b	>100	>100	>100	>100	>100
13a	>100	6.25	6.25	6.25	>100
13b	>100	3.12	6.25	6.25	>100

Contd....Table-2

14a	50	50	3.12	3.12	>100
14b	>100	>100	>100	>100	>100
15a	25	3.12	25	25	>100
15b	50	50	3.12	3.12	>100
16a	>100	25	3.12	3.12	>100
16b	>100	>100	>100	>100	>100
17a	50	50	3.12	3.12	>100
17b	25	3.12	25	25	>100
18a	25	25	3.12	6.25	>100
18b	>100	12.5	25	3.12	>100
19a	25	25	3.12	3.12	>100
19b	>100	>100	>100	>100	>100
20a	12.5	25	3.12	>100	25
20b	>100	25	3.12	3.12	>100
Fluconazole standard drug	0.50	1.0	1.0	2.0	1.0

5a: IR (KBr): 3493, 3179 (NH), 1713, 1670 (C=O), 1608 (C=N), 1253 (-CH₂O-), 755 (C-Cl). ¹H NMR (DMSO-*d*₆): 5.15 (2H, s, -CH₂O-), 6.66-8.03 (9H, m, ArH), 10.67 (1H, s, CONH), 13.85 (1H, s, CONH). [Found : C, 51.85, H, 2.48, N, 8.19 C₂₂H₁₃Cl₄N₃O₃ requires C, 51.90, H, 2.57, N, 8.25%].

**1-Aminomethyl-3-{4-(chlorobenzoyloxy) benzoylhydrazono}-4,5-dichloroindolin-2-ones
6a-20a**

To a suspension of 3-(4-(chlorobenzoyloxy) benzoylhydrazono)-4,5-dichloroindolin-2-ones **1a-5a** (0.005 mol) in DMF, formaldehyde (0.5 ml, 37%) and secondary heterocyclic amines were added with stirring and heated on a water bath for 2 min and left overnight at room temp. The solid product thus obtained was filtered, washed with methanol, dried and recrystallised from chloroform-pet. Ether (60-80°) (1:1).

Compounds **6b-20b** were synthesized using same method and gave satisfactory analysis for C,H and N.

6a : IR (KBr) : cm⁻¹ : 3369 (NH), 2932 (-CH₂-), 1687, 1664 (C=O), 1598 (C=N), 1247 (-CH₂O), 755 (C-Cl). ¹H NMR (CDCl₃): 2.61-2.65 (4H, t, -CH₂-N-CH₂-), 3.70-3.75 (4H, t, -CH₂-O-CH₂-), 4.49 (2H, s, >N-CH₂-N<), 5.15 (2H, s, -CH₂O-), 6.91-8.03 (11H, m, ArH), 13.90 (1H, s, CONH). [Found : C, 60.03, H, 4.40, N, 10.32 C₂₇H₂₄Cl₂N₄O₄ requires C, 60.12, H, 4.48, N, 10.39%].

7a : IR (KBr): 3390 (NH), 2929 (-CH₂-), 1684, 1677 (C=O), 1598 (C=N), 1247 (-CH₂O), 752 (C-Cl). ¹H NMR (CDCl₃): 1.28-1.56 (6H, m, -CH₂CH₂CH₂-), 2.26-2.55 (4H, t, -CH₂-N-CH₂-), 4.48 (2H, s, >N-CH₂-N<), 5.15 (2H, s, -CH₂O-), 6.71-8.03 (11H, m, ArH), 13.96 (1H, s, CONH). [Found : C, 62.50, H, 4.80, N, 10.37 C₂₈H₂₆Cl₂N₄O₃ requires C, 62.57, H, 4.88, N, 10.42%].

8a: IR (KBr): 3387 (NH), 2929 (-CH₂-), 1687, 1675 (C=O), 1607 (C=N), 1239 (-CH₂O), 767 (C-Cl). ¹H NMR (CDCl₃): 1.26-1.59 (4H, m, -CH₂-CH₂-), 2.46-2.69 (4H, t, -CH₂-N-CH₂-), 4.62 (2H, s, >N-CH₂-N<), 5.15 (2H, s, -CH₂O-), 6.97-8.14 (11H, m, ArH), 14.04 (1H, s,

CONH). [Found : C, 61.89, H, 4.51, N, 10.63 $C_{27}H_{24}Cl_2N_4O_3$ requires C, 61.96, H, 4.62, N, 10.70%].

9a: IR (KBr): 3400 (NH), 2932 ($-CH_2-$), 1688, 1661 ($C=O$), 1609 ($C=N$), 1246 ($-CH_2O-$), 767 ($C-Cl$). 1H NMR ($CDCl_3$): 2.50-2.65 (4H, t, $-CH_2-N-CH_2-$), 3.61-3.75 ($-CH_2-O-CH_2-$), 4.49 (2H, s, $>N-CH_2-N<$), 5.25 (2H, s, CH_2O), 6.94-8.13 (10H, m, ArH), 13.88 (1H, s, CONH). [Found : C, 56.46, H, 4.00, N, 9.72 $C_{27}H_{24}Cl_3N_4O_4$ requires C, 56.51, H, 4.04, N, 9.76%].

10a: IR (KBr): 3397 (NH), 2938 ($-CH_2-$), 1684, 1677 ($C=O$), 1600 ($C=N$), 1237 ($-CH_2O-$), 765 ($C-Cl$). 1H NMR ($CDCl_3$): 1.31-1.59 (6H, m, $-CH_2CH_2CH_2-$), 2.22-2.55 (4H, t, $-CH_2-N-CH_2-$), 4.47 (2H, s, $>N-CH_2-N<$), 5.22 (2H, s, $-CH_2O-$), 6.94-8.07 (10H, m, ArH), 13.96 (1H, s, CONH). [Found : C, 56.74, H, 4.35, N, 9.73 $C_{28}H_{25}Cl_3N_4O_3$ requires C, 58.81, H, 4.41, N, 9.80%].

11a: IR (KBr): 3404 (NH), 2926 ($-CH_2-$), 1683, 1665 ($C=O$), 1601 ($C=N$), 1236 ($-CH_2O-$), 761 ($C-Cl$). 1H NMR ($CDCl_3$): 1.37-1.59 (4H, m, $-CH_2CH_2-$), 2.43-2.69 (4H, t, $-CH_2-N-CH_2-$), 4.66 (2H, s, $>N-CH_2-N<$), 5.25 (2H, s, $-CH_2O-$), 6.91-8.05 (10H, m, ArH), 13.97 (1H, s, CONH). [Found : C, 58.03, H, 3.08, N, 9.94 $C_{27}H_{23}Cl_3N_4O_3$ requires C, 58.13, H, 4.14, N, 10.04%].

12a: IR (KBr): 3390 (NH), 2932 ($-CH_2-$), 1690, 1679 ($C=O$), 1598 ($C=N$), 1236 ($-CH_2O-$), 767 ($C-Cl$). 1H NMR ($CDCl_3$): 2.32-2.55 (4H, t, $-CH_2-N-CH_2-$), 3.68-3.75 (4H, t, $-CH_2-O-CH_2-$), 4.48 (2H, s, $>N-CH_2-N<$), 5.11 (2H, s, $-CH_2O-$), 6.91-8.13 (10H, m, ArH), 13.92 (1H, s, CONH). [Found : C, 56.43, H, 3.98, N, 9.70 $C_{27}H_{24}Cl_3N_4O_4$ requires C, 56.51, H, 4.04, N, 9.76%].

13a: IR (KBr): 3395 (NH), 2922 ($-CH_2-$), 1684, 1670 ($C=O$), 1602 ($C=N$), 1247 ($-CH_2O-$), 752 ($C-Cl$). 1H NMR ($CDCl_3$): 1.22-1.56 (6H, m, $-CH_2CH_2CH_2-$), 2.25-2.55 (4H, t, $-CH_2-N-CH_2-$), 4.45 (2H, s, $>N-CH_2-N<$), 5.10 (2H, s, $-CH_2O-$), 6.96-8.03 (10H, m, ArH), 13.90 (1H, s, CONH). [Found : C, 56.77, H, 4.35, N, 9.77 $C_{28}H_{25}Cl_3N_4O_3$ requires C, 58.81, H, 4.41, N, 9.80%].

14a: IR (KBr) : 3406 (NH), 2920 ($-CH_2-$), 1684, 1666 ($C=O$), 1603 ($C=N$), 1236 ($-CH_2O-$), 771 ($C-Cl$). 1H NMR ($CDCl_3$): 1.31-1.59 (4H, m, $-CH_2-CH_2-$), 2.46-2.60 (4H, t, $-CH_2N-CH_2-$), 4.51 (2H, s, $>N-CH_2-N<$), 5.12 (2H, s, $-CH_2O-$), 6.92-8.05 (10H, m, ArH), 14.00 (1H, s, CONH). [Found : C, 58.03, H, 3.10, N, 9.97 $C_{27}H_{23}Cl_3N_4O_3$ requires C, 58.13, H, 4.14, N, 10.04%].

15a: IR (KBr): 3400 (NH), 2926 ($-CH_2-$), 1689, 1660 ($C=O$), 1600 ($C=N$), 1237 ($-CH_2O-$), 765 ($C-Cl$). 1H NMR

($CDCl_3$): 2.54-2.69 (4H, t, $-CH_2-N-CH_2-$), 3.40-3.55 ($-CH_2-O-CH_2-$), 4.66 (2H, s, $>N-CH_2-N<$), 5.11 (2H, s, CH_2O), 6.97-8.03 (10H, m, ArH), 14.00 (1H, s, CONH). [Found : C, 56.48, H, 3.98, N, 9.73 $C_{27}H_{24}Cl_3N_4O_4$ requires C, 56.51, H, 4.04, N, 9.76%].

16a: IR (KBr): 3404 (NH), 2925 ($-CH_2-$), 1689, 1664 ($C=O$), 1500 ($C=N$), 1236 ($-CH_2O-$), 762 ($C-Cl$). 1H NMR ($CDCl_3$): 1.23-1.61 (6H, m, $-CH_2CH_2CH_2-$), 2.39-2.65 (4H, t, $-CH_2-N-CH_2-$), 4.47 (2H, s, $>N-CH_2-N<$), 5.11 (2H, s, $-CH_2O-$), 6.99-8.08 (10H, m, ArH), 13.89 (1H, s, CONH). [Found : C, 56.73, H, 4.34, N, 9.75 $C_{28}H_{25}Cl_3N_4O_3$ requires C, 58.81, H, 4.41, N, 9.80%].

17a: IR (KBr): 3406 (NH), 2928 ($-CH_2-$), 1687, 1672 ($C=O$), 1610 ($C=N$), 1237 ($-CH_2O-$), 762 ($C-Cl$). 1H NMR ($CDCl_3$): 1.24-1.50 (4H, m, $-CH_2CH_2-$), 2.43-2.68 (4H, t, $-CH_2-N-CH_2-$), 4.66 (2H, s, $>N-CH_2-N<$), 5.11 (2H, s, $-CH_2O-$), 6.97-8.03 (10H, m, ArH), 14.00 (1H, s, CONH). [Found : C, 58.03, H, 3.10, N, 9.97 $C_{27}H_{23}Cl_3N_4O_3$ requires C, 58.13, H, 4.14, N, 10.04%].

18a: IR (KBr): 3404 (NH), 2926 ($-CH_2-$), 1692, 1678 ($C=O$), 1597 ($C=N$), 1237 ($-CH_2O-$), 767 ($C-Cl$). 1H NMR ($CDCl_3$): 2.54-2.77 (4H, t, $-CH_2-N-CH_2-$), 3.67-3.77 (4H, t, $-CH_2-O-CH_2-$), 4.41 (2H, s, $>N-CH_2-N<$), 5.20 (2H, s, $-CH_2O-$), 6.97-8.02 (9H, m, ArH), 13.05 (1H, s, CONH). [Found : C, 53.28, H, 3.60, N, 9.18 $C_{27}H_{22}Cl_4N_4O_4$ requires C, 53.31, H, 3.65, N, 9.21%].

19a: IR (KBr): 3409 (NH), 2926 ($-CH_2-$), 1690, 1669 ($C=O$), 1611 ($C=N$), 1237 ($-CH_2O-$), 760 ($C-Cl$). 1H NMR ($CDCl_3$): 1.28-1.57 (6H, m, $-CH_2CH_2CH_2-$), 2.40-2.68 (4H, t, $-CH_2-N-CH_2-$), 4.48 (2H, s, $>N-CH_2-N<$), 5.20 (2H, s, $-CH_2O-$), 6.97-8.04 (9H, m, ArH), 14.06 (1H, s, CONH). [Found : C, 54.39, H, 3.93, N, 9.19 $C_{28}H_{24}Cl_4N_4O_3$ requires C, 55.47, H, 3.99, N, 9.24%].

20a: IR (KBr): 3409 (NH), 2926 ($-CH_2-$), 1685, 1663 ($C=O$), 1602 ($C=N$), 1235 ($-CH_2O-$), 769 ($C-Cl$). 1H NMR ($CDCl_3$): 1.28-1.59 (4H, m, $-CH_2CH_2-$), 2.41-2.67 (4H, t, $-CH_2-N-CH_2-$), 4.50 (2H, s, $>N-CH_2-N<$), 5.22 (2H, s, $-CH_2O-$), 6.99-8.06 (9H, m, ArH), 14.00 (1H, s, CONH). [Found : C, 54.68, H, 3.68, N, 9.40 $C_{27}H_{22}Cl_4N_4O_3$ requires C, 54.75, H, 3.74, N, 9.46%].

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