Synthesis of Some New 2-Oxo-*N*-[(10*H*-phenothiazin-10-yl)alkyl] Derivatives of Azetidine-1-carboxamides

by **Ritu Sharma***, **Pushkal Samadhiya**, **S. D. Srivastava**, and **S. K. Srivastava**

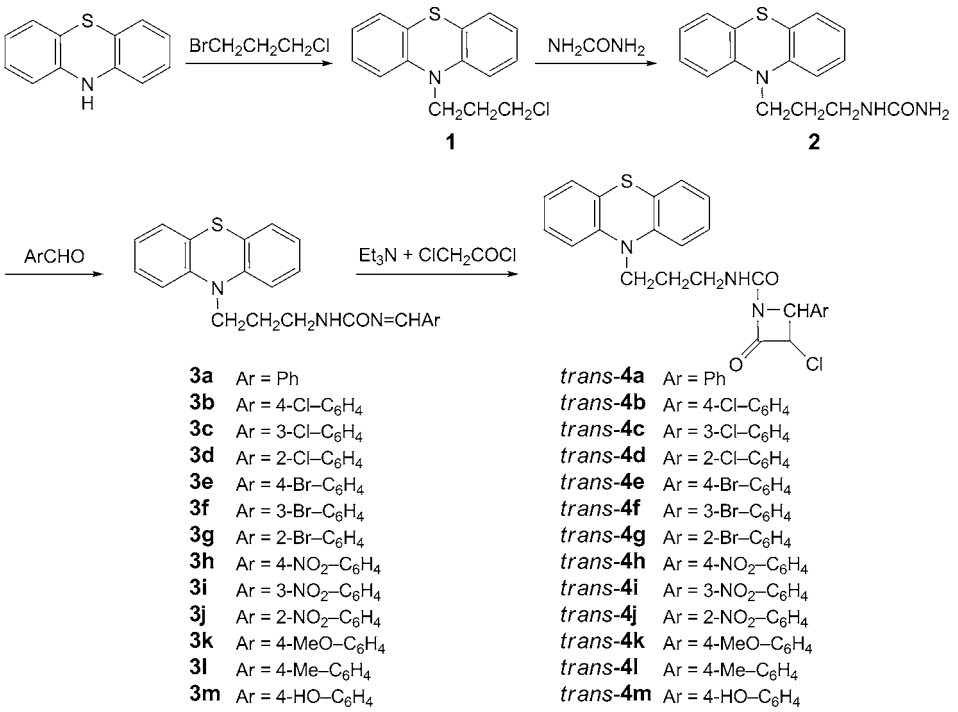
Synthetic Organic Chemistry Laboratory, Department of Chemistry, Dr. H. S. Gour University (A Central University); Sagar-470003, India
(phone: +91-9907656136; e-mail: ritusharmaic@rediffmail.com)

The synthesis of a new series of 4-aryl-3-chloro-2-oxo-*N*-[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamides, **4a**–**4m**, is described. Phenothiazine on reaction with $Cl(CH_2)_3Br$ at room temperature gave 10-(3-chloropropyl)-10*H*-phenothiazine (**1**), and the latter reacted with urea to yield 1-[3-(10*H*-phenothiazin-10-yl)propyl]urea (**2**). Further reaction of **2** with several substituted aromatic aldehydes led to *N*-(arylmethylidene)-*N*′-[3-(phenothiazin-10-yl)propyl]ureas **3a**–**3m**, which, on treatment with $ClCH_2COCl$ in the presence of Et_3N, furnished the desired racemic *trans*-2-oxoazetidin-1-carboxamide derivatives **4a**–**4m**. The structures of all new compounds were confirmed by IR, and ^1H- and ^{13}C-NMR spectroscopy, FAB mass spectrometry, and chemical methods.

Introduction. – The 2-oxoazetidine skeleton has been recognized as a useful building block in synthesis of biologically important compounds [1][2]. This is mainly due to the strain energy associated with the four-membered azetidine ring, which makes it susceptible for nucleophilic ring cleavage. This factor is also responsible for their application of azetidines as synthones for various stereoselective syntheses of biologically active heterocyclic compounds [3]. Recently, several reports have highlighted different methodologies for the stereoselective syntheses of β-lactams [4–6]. 10*H*-Phenothiazine is also of pharmaceutical importance because of different biological activities, *viz*. antibacterial [7], antitubercular [8], and anti-inflammatory properties [9]. Chemically, phenothiazine has two active sites, C(2) and N(10). Here, we report on substitution at N(10) of phenothiazine and the combination with the 2-oxoazetidine ring in a single molecule.

Results and Discussion. – The title compounds were synthesized in four steps as depicted in the *Scheme*. 10*H*-Phenothiazine, on reaction with $Cl(CH_2)_3Br$ at room temperature, gave 10-(3-chloropropyl)-10*H*-phenothiazine (**1**) [10], which was reacted with urea at room temperature to yield 1-[3-(10*H*-phenothiazin-10-yl)propyl]urea (**2**) [11]. Compound **2**, on further reaction with several substituted aromatic aldehydes, afforded 1-(arylmethylidene)-3-[3-(10*H*-phenothiazin-10-yl)propyl]ureas **3a**–**3m** [12]. The latter, on treatment with $ClCH_2COCl$ in the presence of Et_3N, furnished the final products, racemic *trans*-4-aryl-3-chloro-2-oxo-*N*-[3-(10*H*-phenothiazin-10-yl)propyl]-azetidine-1-carboxamides **4a**–**4m** [13]. The structures of all the newly synthesized compounds were confirmed by IR, ^1H- and ^{13}C-NMR spectroscopy, FAB-mass spectrometry, and chemical methods.

Scheme. *Synthesis of Compounds* **3a – 3m** *and* **4a – 4m**



The characteristic IR absorption for *Schiff* bases **3a – 3m** appeared in the range of 1539 – 1560 cm^{-1}, and, in the ^1H- and ^{13}C-NMR spectra, the CH=N signals appeared in the range of 7.85 – 8.05 and 152.1 – 157.6 ppm, respectively. In the ^1H-NMR spectrum, the broad signal of NH_2 in **2** has disappeared. In the IR spectra of **4a – 4m**, the C=O group of the β-lactam ring showed a characteristic absorption in the range of 1725 – 1746 cm^{-1}, and ^1H-NMR spectra exhibited two *doublet*s for CHN and CHCl in the range of 5.09 – 5.23 and 4.40 – 4.61 ppm, respectively. The coupling constant $J(3,4)$ of 5.00 – 5.25 Hz in the ^1H-NMR spectra of **4a – 4m**, clearly indicated the formation of the *trans*-diastereoisomer of azetidine [14 – 17]. In the ^{13}C-NMR spectra of **4a – 4m**, three characteristic signals appeared for CHN, CHCl, and CO in the ranges of 60.2 – 65.7, 51.6 – 56.7, and 165.7 – 170.7 ppm, respectively. The IR absorption, as well as the ^1H- and ^{13}C-NMR signals corresponding to the N=CH moieties have disappeared.

Conclusions. – In the present study, the successful synthesis of compound **3a – 3m** and **4a – 4m** was developed. These compounds serve as synthones for further transformations towards potentially bioactive derivatives.

Experimental Part

General. Reagent-grade chemicals were purchased from commercial sources and further purified before use. Column chromatography (CC): *Merck* silica gel *60* (SiO_2; 230 – 400 mesh). M.p.: in open

capillaries; uncorrected. Progress of the reaction was monitored by silica gel-*G* coated TLC plates with MeOH/$CHCl_3$ as the eluent; the spots were visualized by exposing the dry plate to I_2 vapor. IR Spectra: KBr disc; *Shimadzu 8201 PC*, FT-IR spectrophotometer; in cm^{-1}. ^{1}H- and ^{13}C-NMR spectra: *Bruker DRX-300* spectrometer in $CDCl_3$, at 300 and 75 MHz, resp.; TMS as an internal standard; chemical shifts in δ [ppm]. FAB-MS: *Jeol SX-102* mass spectrometer. Elemental analyses: *Carlo Erba-1108* analyzer. The anal. data of all the compounds were satisfactory.

*Synthesis of 10-(3-Chloropropyl)-10*H*-phenothiazine* (**1**). See [10].

*Synthesis of 1-[3-(10*H*-Phenothiazin-10-yl)propyl]urea* (**2**). See [11].

*General Procedure for the Synthesis of 1-(Arylmethylidene)-3-[3-(10*H*-phenothiazin-10-yl)propyl]-ureas* **3**. A soln. of **2** (0.026 mol) and aromatic aldehyde (0.026 mol) in EtOH (100 ml) in the presence of 2–4 drops of AcOH was first magnetically stirred for *ca.* 2.0 h at r.t., followed by heating to reflux on a steam bath for *ca.* 3.3 h. The reaction was monitored by TLC. The product was filtered, cooled, and purified by CC ($CHCl_3$/MeOH 7:3; 90 ml). The purified product was dried under vacuum and recrystallized from acetone to furnish compound **3**.

*1-[3-(10*H*-Phenothiazin-10-yl)propyl]-3-(phenylmethylidene)urea* (**3a**). Yield: 6.29 g (64%). M.p. 153–155°. IR: 684 (C–S–C), 1332 (N–C), 1464 (C=C), 1541 (N=CH), 1664 (CO), 1430, 2836, 2894 (CH_2), 3022 (arom. CH), 3363 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.08–2.15 (*m*, CH_2); 3.31–3.37 (*m*, C*H*$_2$NH); 4.19 (*t*, *J* = 7.4, CH_2N); 5.78 (*s*, NH); 7.96 (*s*, CH=N); 6.05–8.10 (*m*, 13 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 35.5 (CH_2), 42.6 (CH_2NH); 48.8 (CH_2N); 109.1 (C(4), C(5)); 116.7 (C(1), C(8)); 120.8 (C(2), C(7)); 121.6 (C(3), C(6)); 123.6 (2 C_o)); 125.5 (2 C_m); 126.8 (C_p); 135.6 (C_{ipso}); 136.9 (C(4a), C(5a)); 144.7 (C(1a), C(8a)); 152.6 (CH=N); 160.4 (C=O). FAB-MS: 387 (M^+). Anal. calc. for $C_{23}H_{21}N_3OS$ (387.50): C 71.29, H 5.46, N 10.84; found: C 71.24, H 5.38, N 10.81.

*1-[(4-Chlorophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3b**). Yield: 7.24 g (66%). M.p. 161–162°. IR: 684 (C–S–C), 740 (C–Cl), 1303 (N–C), 1472 (C=C), 1548 (N=CH), 1648 (CO), 1448, 2869, 2913 (CH_2), 3031 (arom. CH), 3369 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.18–2.22 (*m*, CH_2); 3.42–3.46 (*m*, C*H*$_2$NH); 4.29 (*t*, *J* = 7.4, CH_2N); 5.82 (*s*, NH); 7.98 (*s*, CH=N); 6.80–7.79 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 38.6 (CH_2); 44.4 (CH_2NH); 51.8 (CH_2N); 110.7 (C(4), C(5)); 120.4 (C(1), C(8)); 124.5 (C(2), C(7)); 125.4 (C(3), C(6)); 127.6 (2 C_o); 126.5 (2 C_m); 128.8, 137.3 (2 C_p); 138.4 (C(4a), C(5a)); 148.3 (C(1a), C(8a)); 153.2 (CH=N); 165.8 (C=O). FAB-MS: 421 (M^+). Anal. calc. for $C_{23}H_{20}ClN_3OS$ (421.95): C 65.47, H 4.77, N 9.95; found: C 65.43, H 4.65, N 9.91.

*1-[(3-Chlorophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3c**). Yield: 7.0 g (64%). M.p. 165–166°. IR: 693 (C–S–C), 744 (C–Cl), 1344 (N–C), 1476 (C=C), 1551 (N=CH), 1676 (CO), 1440, 2845, 2902 (CH_2), 3033 (arom. CH), 3372 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.20–2.25 (*m*, CH_2); 3.45–3.49 (*m*, C*H*$_2$NH); 4.27 (*t*, *J* = 7.4, CH_2N); 5.88 (*s*, NH); 7.97 (*s*, CH=N); 6.50–7.81 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 37.3 (CH_2); 45.8 (CH_2NH); 52.9 (CH_2N); 111.6 (C(4), C(5)); 120.3 (C(1), C(8)); 124.5 (C(2), C(7)); 125.6 (C(3), C(6)); 126.3, 126.8 (2 C_o); 127.4, 127.9 (2 C_m); 128.5, 137.2 (2 C_p); 138.1 (C(4a), C(5a)); 146.5 (C(1a), C(8a)); 157.5 (CH=N); 163.6 (C=O). FAB-MS: 421 (M^+). Anal. calc. for $C_{23}H_{20}ClN_3OS$ (421.95): C 65.47, H 4.77, N 9.95; found: C 65.42, H 4.68, N 9.93.

*1-[(2-Chlorophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3d**). Yield: 7.46 g (68%). M.p. 168–169°. IR: 692 (C–S–C), 753 (C–Cl), 1338 (N–C), 1474 (C=C), 1553 (N=CH), 1674 (CO), 1439, 2848, 2906 (CH_2), 3034 (arom. CH), 3373 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.11–2.15 (*m*, CH_2); 3.42–3.47 (*m*, C*H*$_2$NH); 4.30 (*t*, *J* = 7.4, CH_2N); 5.82 (*s*, NH); 7.96 (*s*, CH=N); 6.48–7.86 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 39.2 (CH_2); 42.7 (CH_2NH); 51.7 (CH_2N); 111.3 (C(4), C(5)); 119.4 (C(1), C(8)); 123.4 (C(2), C(7)); 124.1 (C(3), C(6)); 126.5, 127.4 (2 C_o); 128.1, 128.8 (2 C_m); 129.5, 136.1 (2 C_p); 137.7 (C(4a), C(5a)); 149.9 (C(1a), C(8a)); 157.6 (CH=N); 162.7 (C=O). FAB-MS: 421 (M^+). Anal. calc. for $C_{23}H_{20}ClN_3OS$ (421.95): C 65.47, H 4.77, N 9.95; found: C 65.45, H 4.69, N 9.90.

*1-[(4-Bromophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3e**). Yield: 7.87 g (65%). M.p. 165–166°. IR: 636 (C–Br), 697 (C–S–C), 1342 (N–C), 1472 (C=C), 1549 (N=CH), 1672 (CO), 1441, 2850, 2907 (CH_2), 3037 (arom. CH), 3376 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.18–2.22 (*m*, CH_2); 3.41–3.46 (*m*, C*H*$_2$NH); 4.31 (*t*, *J* = 7.5, CH_2N); 5.90 (*s*, NH); 8.02 (*s*, CH=N); 6.42–7.76 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 38.3 (CH_2); 45.1 (CH_2NH); 51.3 (CH_2N); 112.5 (C(4), C(5)); 117.8 (C(1), C(8)); 122.7 (C(2), C(7)); 123.8 (C(3), C(6)); 124.4 (2 C_o); 127.3 (2 C_m); 128.8, 140.8

(2 C_p); 141.2 (C(4a), C(5a)); 147.4 (C(1a), C(8a)); 154.7 (CH=N); 162.3 (C=O). FAB-MS: 466 (M^+). Anal. calc. for $C_{23}H_{20}BrN_3OS$ (466.40): C 59.23, H 4.32, N 9.00; found: C 59.15, H 4.23, N 8.94.

*1-[(3-Bromophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3f**). Yield: 7.51 g (62%). M.p. 163–164°. IR: 643 (C–Br), 691 (C–S–C), 1346 (N–C), 1479 (C=C), 1552 (N=CH), 1677 (CO), 1445, 2852, 2910 (CH_2), 3035 (arom. CH), 3378 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.20–2.25 (*m*, CH_2); 3.36–3.43 (*m*, CH_2NH); 4.37 (*t*, *J* = 7.6, CH_2N); 5.86 (*s*, NH); 7.95 (*s*, CH=N); 6.37–7.81 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 37.5 (CH_2); 44.2 (CH_2NH); 49.4 (CH_2N); 112.2 (C(4), C(5)); 117.5 (C(1), C(8)); 122.6 (C(2), C(7)); 123.4 (C(3), C(6)); 125.3, 126.4 (2 C_o); 128.5, 128.9 (2 C_m); 129.6, 140.5 (2 C_p); 141.8 (C(4a), C(5a)); 145.3 (C(1a), C(8a)); 156.9 (CH=N); 164.2 (C=O). FAB-MS: 466 (M^+). Anal. calc. for $C_{23}H_{20}BrN_3OS$ (466.40): C 59.23, H 4.32, N 9.00; found: C 59.18, H 4.28, N 8.97.

*1-[(2-Bromophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3g**). Yield: 8.0 g (66%). M.p. 164–166°. IR: 638 (C–Br), 699 (C–S–C), 1339 (N–C), 1473 (C=C), 1554 (N=CH), 1675 (CO), 1438, 2846, 2904 (CH_2), 3040 (arom. CH), 3381 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.27–2.32 (*m*, CH_2); 3.43–3.48 (*m*, CH_2NH); 4.29 (*t*, *J* = 7.6, CH_2N); 5.91 (*s*, NH); 7.98 (*s*, CH=N); 6.43–7.89 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 38.8 (CH_2); 46.3 (CH_2NH); 50.5 (CH_2N); 112.6 (C(4), C(5)); 119.2 (C(1), C(8)); 123.5 (C(2), C(7)); 124.3 (C(3), C(6)); 125.9, 127.4 (2 C_o); 127.6, 128.1 (2 C_m); 128.4, 139.0 (2 C_p); 140.6 (C(4a), C(5a)); 148.6 (C(1a), C(8a)); 155.8 (CH=N); 161.6 (C=O). FAB-MS: 466 (M^+). Anal. calc. for $C_{23}H_{20}BrN_3OS$ (466.40): C 59.23, H 4.32, N 9.00; found: C 59.19, H 4.29, N 8.96.

*1-[(4-Nitrophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3h**). Yield: 7.19 g (64%). M.p. 160–162°. IR: 696 (C–S–C), 1337 (C–N), 1478 (C=C), 1530 (N=O), 1556 (N=CH), 1680 (CO), 1444, 2851, 2909 (CH_2), 3036 (arom. CH), 3374 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.25–2.28 (*m*, CH_2); 3.47–3.51 (*m*, CH_2NH); 4.32 (*t*, *J* = 7.6, CH_2N); 5.87 (*s*, NH); 7.93 (*s*, CH=N); 6.55–7.82 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 39.6 (CH_2); 47.7 (CH_2NH); 52.0 (CH_2N); 113.7 (C(4), C(5)); 118.3 (C(1), C(8)); 124.0 (C(2), C(7)); 125.3 (C(3), C(6)); 126.6 (2 C_o); 128.7 (2 C_m); 129.3, 139.9 (2 C_p); 140.5 (C(4a), C(5a)); 149.2 (C(1a), C(8a)); 155.3 (CH=N); 165.4 (C=O). FAB-MS: 432 (M^+). Anal. calc. for $C_{23}H_{20}N_4O_3S$ (432.50): C 63.87, H 4.66, N 12.95; found: C 63.74, H 4.61, N 12.91.

*1-[(3-Nitrophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3i**). Yield: 7.53 g (67%). M.p. 161–163°. IR: 694 (C–S–C), 1334 (C–N), 1475 (C=C), 1528 (N=O), 1551 (N=CH), 1678 (CO), 1437, 2854, 2905 (CH_2), 3031 (arom. CH), 3370 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.14–2.19 (*m*, CH_2); 3.40–3.44 (*m*, CH_2NH); 4.25 (*t*, *J* = 7.6, CH_2N); 5.83 (*s*, NH); 8.05 (*s*, CH=N); 6.46–7.91 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 36.9 (CH_2); 47.4 (CH_2NH); 52.6 (CH_2N); 113.1 (C(4), C(5)); 119.6 (C(1), C(8)); 125.7 (C(2), C(7)); 126.1 (C(3), C(6)); 127.2, 128.4 (2 C_o); 129.0, 129.4 (2 C_m); 130.7, 138.4 (2 C_p); 139.2 (C(4a), C(5a)); 149.6 (C(1a), C(8a)); 154.5 (CH=N); 164.4 (C=O). FAB-MS: 432 (M^+). Anal. calc. for $C_{23}H_{29}N_4O_3S$ (432.50): C 63.87, H 4.66, N 12.95; found: C 63.78, H 4.63, N 12.92.

*1-[(2-Nitrophenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3j**). Yield: 7.30 g (65%). M.p. 159–160°. IR: 698 (C–S–C), 1341 (C–NH), 1473 (C=C), 1533 (N=O), 1560 (N=CH), 1671 (CO), 1446, 2849, 2912 (CH_2), 3039 (arom. CH), 3379 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.20–2.24 (*m*, CH_2); 3.50–3.55 (*m*, CH_2NH); 4.28 (*t*, *J* = 7.6, CH_2N); 5.92 (*s*, NH); 8.00 (*s*, CH=N); 6.51–7.89 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 38.3 (CH_2); 46.9 (CH_2NH); 50.7 (CH_2N); 111.8 (C(4), C(5)); 118.2 (C(1), C(8)); 125.5 (C(2), C(7)); 126.4 (C(3), C(6)); 127.5, 128.2 (2 C_o); 129.6, 130.1 (2 C_m); 130.4, 138.7 (2 C_p); 139.3 (C(4a), C(5a)); 147.0 (C(1a), C(8a)); 156.6 (CH=N); 163.7 (C=O). FAB-MS: 432 (M^+). Anal. calc. for $C_{23}H_{29}N_4O_3S$ (432.50): C 63.87, H 4.66, N 12.95; found: C 63.77, H 4.60, N 12.90.

*1-[(4-Methoxyphenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3k**). Yield: 6.73 g (62%). M.p. 152–154°. IR: 702 (C–S–C), 1336 (N–C), 1467 (C=C), 1543 (N=CH), 1667 (CO), 1433, 2839, 2895 (CH_2), 2947 (Me–O), 3024 (arom. CH), 3365 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.11–2.16 (*m*, CH_2); 3.33–3.38 (*m*, CH_2NH); 3.51 (*s*, MeO); 4.22 (*t*, *J* = 7.6, CH_2N); 5.80 (*s*, NH); 7.89 (*s*, CH=N); 6.27–7.62 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 36.2 (CH_2); 43.5 (CH_2NH); 44.4 (CH_2N); 63.7 (MeO); 109.8 (C(4), C(5)); 116.0 (C(1), C(8)); 121.7 (C(2), C(7)); 122.4 (C(3), C(6)); 124.8 (2 C_o); 126.0 (2 C_m); 127.7, 136.6 (2 C_p); 137.0 (C(4a), C(5a)); 144.6 (C(1a), C(8a)); 152.8 (CH=N); 160.2 (C=O). FAB-MS: 417 (M^+). Anal. calc. for $C_{24}H_{23}N_3O_2S$ (417.53): C 69.04, H 5.55, N 10.06; found: C 68.92, H 5.48, N 10.02.

*1-[(4-Methylphenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3l**). Yield: 6.0 g (58%). M.p. 144–146°. IR: 699 (C–S–C), 1326 (N–C), 1460 (C=C), 1539 (N=CH), 1661 (CO), 1428,

2833, 2891 (CH_2), 2917 (Me); 3019 (arom. CH), 3360 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.03–2.09 (*m*, CH_2); 2.39 (*s*, Me); 3.32–3.39 (*m*, CH_2NH); 4.17 (*t*, *J* = 7.4, CH_2N); 5.74 (*s*, NH); 7.85 (*s*, CH=N); 6.19–7.57 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 24.9 (Me); 35.3 (CH_2); 42.5 (CH_2NH); 48.4 (CH_2N); 109.0 (C(4), C(5)); 115.3 (C(1), C(8)); 120.4 (C(2), C(7)); 121.2 (C(3), C(6)); 123.4 (2 C_o); 125.2 (2 C_m); 126.3, 135.4 (2 C_p); 136.3 (C(4a), C(5a)); 144.5 (C(1a), C(8a)); 152.1 (CH=N); 160.0 (C=O). FAB-MS: 401 (M^+). Anal. calc. for $C_{24}H_{23}N_3OS$ (401.53): C 71.79, H 5.77, N 10.46; found: C 71.75, H 5.73, N 10.44.

*1-[(4-Hydroxyphenyl)methylidene]-3-[3-(10*H*-phenothiazin-10-yl)propyl]urea* (**3m**). Yield: 6.81 g (65%). M.p. 162–164°. IR: 702 (C–S–C), 1337 (N–C), 1468 (C=C), 1546 (N=CH), 1670 (CO), 1435, 2841, 2898 (CH_2), 3027 (arom. CH), 3368 (NH), 3472 (OH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.11–2.16 (*m*, CH_2); 3.40–3.47 (*m*, CH_2NH); 4.09 (*s*, OH); 4.23 (*t*, *J* = 7.65, CH_2N); 5.81 (*s*, NH); 7.92 (*s*, CH=N); 6.32–7.71 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 36.7 (CH_2); 43.2 (CH_2NH); 49.5 (CH_2N); 110.2 (C(4), C(5)); 116.4 (C(1), C(8)); 121.6 (C(2), C(7)); 122.2 (C(3), C(6)); 124.6 (2 C_o); 126.1 (2 C_m); 127.4, 136.5 (2 C_p); 137.2 (C(4a), C(5a)); 144.7 (C(1a), C(8a)); 153.1 (CH=N); 161.5 (C=O). FAB-MS: 403 (M^+). Anal. calc. for $C_{23}H_{21}N_3O_2S$ (403.50): C 68.46, H 5.24, N 10.41; found: C 68.41, H 5.22, N 10.35.

*General Procedure for the Synthesis of 4-Aryl-3-chloro-2-oxo-*N*-[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamides* **4**. A soln. of **3** (0.007 mol), $ClCH_2COCl$ (0.007 mol), and Et_3N (0.007 mol) in MeOH (50 ml) was first magnetically stirred for *ca.* 2.0 h at r.t., followed by heating to reflux on a steam bath for *ca.* 4.0 h. The completion of the reaction was monitored by TLC. The product was filtered and purified by CC using MeOH/$CHCl_3$ (7:3 *v*/*v*) as eluent (70 ml). The purified product was dried under vacuum and recrystallized from EtOH to furnish compound **4**.

trans-*3-Chloro-2-oxo-*N*-[3-(10*H*-phenothiazin-10-yl)propyl]-4-phenylazetidine-1-carboxamide* (*trans*-**4a**). Yield: 1.94 g (60%). M.p. 148–149°. IR: 692 (C–S–C), 1331 (C–N), 1472 (C=C), 1664 (CO), 1730 (C(2)=O), 1434, 2841, 2900 (CH_2), 2906 (CH(3)), 3025 (arom. CH), 3369 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.10–2.14 (*m*, CH_2); 3.30–3.34 (*m*, CH_2NH); 4.05 (*t*, *J* = 7.4, CH_2N); 4.44 (*d*, *J* = 5.00, CH(3)); 5.12 (*d*, *J* = 5.00, CH(4)); 5.72 (*s*, NH); 6.40–7.74 (*m*, 13 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 37.8 (CH_2); 43.9 (CH_2NH); 50.7 (CH_2N); 52.1 (CH(3)); 60.7 (CH(4)); 110.6 (C(4″), C(5″)); 116.9 (C(1″), C(8″)); 121.4 (C(2″), C(7″)); 122.7 (C(3″), C(6)); 124.4 (2 C_o); 126.6 (2 C_m); 127.6 (C_p); 136.7 (C_{ipso}); 137.7 (C(4a″), C(5a″)); 145.3 (C(1a″), C(8a″)); 161.6 (C=O); 165.7 (C=O). FAB-MS: 464 (M^+). Anal. calc. for $C_{25}H_{22}ClN_3O_2S$ (463.99): C 64.71, H 4.77, N 9.05; found: C 64.62, H 4.72, N 9.01.

trans-*3-Chloro-2-(4-chlorophenyl)-4-oxo-*N*-[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4b**). Yield: 2.16 g (62%). M.p. 160–161°. IR: 695 (C–S–C), 765 (C–Cl), 1342 (C–N), 1479 (C=C), 1558 (N=N), 1670 (CO), 1737 (C(4)=O), 1439, 2846, 2905 (CH_2), 2911 (CH(3)), 3032 (arom. CH), 3376 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.20–2.26 (*m*, CH_2); 3.35–3.41 (*m*, CH_2NH); 4.16 (*t*, *J* = 7.6, CH_2N); 4.53 (*d*, *J* = 5.1, CH(3)); 5.25 (*d*, *J* = 5.1, CH(2)); 5.81 (*s*, NH); 6.82–7.99 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 40.4 (CH_2); 47.7 (CH_2NH); 52.6 (CH_2N); 54.4 (CH(3)); 61.9 (CH(2)); 114.5 (C(4″), C(5)); 121.4 (C(1″), C(8″)); 125.2 (C(2″), C(7″)); 126.9 (C(3″), C(6″)); 128.9 (2 C_o); 130.3 (2 C_m); 131.1, 139.8 (2 C_p); 140.6 (C(4a″), C(5a″)); 146.4 (C(1a″), C(8a″)); 162.7 (C=O); 166.7 (C=O). FAB-MS: 498 (M^+). Anal. calc. for $C_{25}H_{21}Cl_2N_3O_2S$ (498.43): C 60.24, H 4.24, N 8.43; found: C 60.16, H 4.19, N 8.36.

trans-*3-Chloro-2-(3-chlorophenyl)-4-oxo-*N*-[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4c**). Yield: 2.26 g (65%). M.p. 158–159°. IR: 701 (C–S–C), 776 (C–Cl), 1345 (C–N), 1483 (C=C), 1561 (N=N), 1673 (CO), 1740 (C(4)=O), 1443, 2851, 2910 (CH_2), 2916 (CH(3)), 3036 (arom. CH), 3380 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.21–2.27 (*m*, CH_2); 3.37–3.41 (*m*, CH_2NH); 4.18 (*t*, *J* = 7.5, CH_2N); 4.55 (*d*, *J* = 5.1, CH(3)); 5.21 (*d*, *J* = 5.1, CH(2)); 5.87 (*s*, NH); 6.77–7.90 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 40.7 (CH_2); 48.5 (CH_2NH); 52.5 (CH_2N); 55.8 (CH(3)); 63.2 (CH(2)); 115.5 (C(4″), C(5″)); 121.7 (C(1″), C(8″)); 125.4 (C(2″), C(7″)); 127.7 (C(3″), C(6″)); 128.4, 129.2 (2 C_o); 130.2, 130.7 (2 C_m); 131.4, 141.5 (2 C_p); 142.4 (C(4a″), C(5a″)); 149.5 (C(1a″), C(8a″)); 163.5 (C=O); 167.9 (C=O). FAB-MS: 498 (M^+). Anal. calc. for $C_{25}H_{21}Cl_2N_3O_2S$ (498.43): C 60.24, H 4.24, N 8.43; found: C 60.18, H 4.22, N 8.38.

trans-*3-Chloro-2-(2-chlorophenyl)-4-oxo-*N*-[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4d**). Yield: 2.09 g (60%). M.p. 160–162°. IR: 706 (C–S–C), 773 (C–Cl), 1338 (C–N), 1482 (C=C), 1562 (N=N), 1669 (CO), 1741 (C(4)=O), 1440, 2853, 2906 (CH_2), 2912 (CH–Cl), 3031 (arom. CH), 3382 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.30–2.35 (*m*, CH_2); 3.41–3.45 (*m*, CH_2NH); 4.21 (*t*,

J = 7.6, CH_2N); 4.59 (d, J = 5.1, CH(3)); 5.30 (d, J = 5.1, CH(2)); 5.84 (s, NH); 6.79–7.85 (m, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 38.8 (CH_2); 47.6 (CH_2NH); 51.2 (CH_2N); 56.3 (CH(3)); 63.6 (CH(2)); 113.1 (C(4″), C(5″)); 118.9 (C(1″), C(8″)); 123.1 (C(2″), C(7″)); 124.6 (C(3″), C(6″)); 126.5, 127.2 (2 C_o); 128.1, 128.8 (2 C_m); 129.8, 141.6 (2 C_p); 142.5 (C(4a″), C(5a″)); 148.3 (C(1a″), C(8a″)); 165.4 (C=O); 168.6 (C=O). FAB-MS: 498 (M^+). Anal. calc. for $C_{25}H_{21}Cl_2N_3O_2S$ (498.43): C 60.24, H 4.24, N 8.43; found: C 60.15, H 4.18, N 8.40.

trans-*2-(4-Bromophenyl)-3-chloro-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4e**). Yield: 2.35 g (62%). M.p. 156–158°. IR: 578 (C–Br), 710 (C–S–C), 1343 (C–N), 1480 (C=C), 1559 (N=N), 1679 (CO), 1742 (C(4)=O), 1444, 2847, 2904 (CH_2), 2945 (CH(3)), 3033 (arom. CH), 3377 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.07–2.11 (m, CH_2); 3.40–3.44 (m, CH_2NH); 4.23 (t, J = 7.6, CH_2N); 4.59 (d, J = 5.2, CH(3)); 5.21 (d, J = 5.2, CH(2)); 5.86 (s, NH); 6.80–8.05 (m, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 41.3 (CH_2); 46.4 (CH_2NH); 53.1 (CH_2N); 53.7 (CH(3)); 62.3 (CH(2)); 115.8 (C(4″), C(5″)); 118.5 (C(1″), C(8″)); 124.2 (C(2″), C(7″)); 125.4 (C(3″), C(6″)); 127.6 (2 C_o); 129.6 (2 C_m); 130.1, 139.5 (2 C_p); 140.7 (C(4a″), C(5a″)); 147.0 (C(1a″), C(8a″)); 165.8 (C=O); 169.5 (C=O). FAB-MS: 543 (M^+). Anal. calc. for $C_{25}H_{21}BrClN_3O_2S$ (542.88): C 55.31, H 3.89, N 7.74; found: C 55.26, H 3.83, N 7.68.

trans-*2-(3-Bromophenyl)-3-chloro-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4f**). Yield: 2.43 g (64%). M.p. 157–159°. IR: 572 (C–Br), 705 (C–S–C), 1347 (C–NH), 1484 (C=C), 1564 (N=N), 1677 (CO), 1735 (C(4)=O), 1448, 2850, 2909 (CH_2), 2938 (CH(3)), 3037 (arom. CH), 3384 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.20–2.27 (m, CH_2); 3.41–3.48 (m, CH_2NH); 4.22 (t, J = 7.7, CH_2N); 4.54 (d, J = 5.2, CH(3)); 5.27 (d, J = 5.2, CH(2)); 5.83 (s, NH); 6.41–7.83 (m, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 39.2 (CH_2); 44.5 (CH_2NH); 51.7 (CH_2N); 55.6 (CH(3)); 65.7 (CH(2)); 111.4 (C(4″), C(5″)); 117.6 (C(1″), C(8″)); 124.7 (C(2″), C(7″)); 125.8 (C(3″), C(6)); 127.9, 128.1 (2 C_o); 129.5, 129.8 (2 C_m); 130.5, 137.7 (2 C_p); 138.6 (C(4a″), C(5a″)); 148.1 (C(1a″), C(8a″)); 164.4 (C=O); 169.1 (C=O). FAB-MS: 543 (M^+). Anal. calc. for $C_{25}H_{21}BrClN_3O_2S$ (542.88): C 55.31, H 3.89, N 7.74; found: C 55.22, H 3.87, N 7.65.

trans-*2-(2-Bromophenyl)-3-chloro-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4g**). Yield: 2.39 g (63%). M.p. 154–156°. IR: 543 (C–Br), 700 (C–S–C), 1353 (C–NH), 1460 (C=C), 1568 (N=N), 1673 (CO), 1746 (C(4)=O), 1440, 2850, 2911 (CH_2), 2952 (CH(3)), 3016 (arom. CH), 3341 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.22–2.29 (m, CH_2); 3.45–3.51 (m, CH_2NH); 4.14 (t, J = 7.6, CH_2N); 4.56 (d, J = 5.2, CH(3)); 5.30 (d, J = 5.2, CH(2)); 5.92 (s, NH); 6.37–7.82 (m, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 39.1 (CH_2); 48.6 (CH_2NH); 53.5 (CH_2N); 56.7 (CH(3)); 65.3 (CH(2)); 112.6 (C(4″), C(5″)); 119.3 (C(1″), C(8″)); 125.0 (C(2″), C(7″)); 126.7 (C(3″), C(6″)); 128.3, 129.4 (2 C_o); 130.3, 130.8 (2 C_m); 131.7, 138.7 (2 C_p); 139.6 (C(4a″), C(5a″)); 146.3 (C(1a″), C(8a″)); 164.7 (C=O); 170.7 (C=O). FAB-MS: 543 (M^+). Anal. calc. for $C_{25}H_{21}BrClN_3O_2S$ (542.88): C 55.31, H 3.89, N 7.74; found: C 55.24, H 3.85, N 7.69.

trans-*3-Chloro-2-(4-nitrophenyl)-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4h**). Yield: 2.13 g (60%). M.p. 152–153°. IR: 696 (C–S–C), 868 (C–NO), 1357 (C–N), 1487 (C=C), 1540 (NO_2), 1570 (N=N), 1675 (CO), 1738 (C(4)=O), 1449, 2854, 2905 (CH_2), 2921 (CH–Cl), 3038 (arom. CH), 3382 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.20–2.25 (m, CH_2); 3.31–3.37 (m, CH_2NH); 4.24 (t, J = 7.7, CH_2N); 5.31 (d, J = 5.3, CH(2)); 4.61 (d, J = 5.3, CH(3)); 5.82 (s, NH); 6.49–7.76 (m, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 41.8 (CH_2); 46.7 (CH_2NH); 55.5 (CH_2N); 55.9 (CH(3)); 64.4 (CH(2)); 113.7 (C(4″), C(5″)); 119.4 (C(1″), C(8″)); 123.4 (C(2″), C(7″)); 124.9 (C(3), C(6)); 126.5 (2 C_o); 128.7 (2 C_m); 129.6, 140.8 (2 C_p); 141.1 (C(4a″), C(5a″)); 149.7 (C(1a″), C(8a″)); 163.4 (C=O); 167.8 (C=O). FAB-MS: 509 (M^+). Anal. calc. for $C_{25}H_{21}ClN_4O_4S$ (508.98): C 58.99, H 4.15, N 11.00; found: C 58.91, H 4.08, N 10.92.

trans-*3-Chloro-2-(3-nitrophenyl)-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4i**). Yield: 2.28 g (64%). M.p. 155–157°. IR: 694 (C–S–C), 864 (C–NO), 1358 (C–N), 1481 (C=C), 1542 (NO_2), 1566 (N=N), 1672 (CO), 1743 (C(4)=O), 1452, 2858, 2912 (CH_2), 2919 (CH(3)), 3042 (arom. CH), 3378 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.23–2.29 (m, CH_2); 3.36–3.42 (m, CH_2NH); 4.12 (t, J = 7.6, CH_2N); 4.57 (d, J = 5.2, CH(3)); 5.19 (d, J = 5.2, CH(2)); 5.89 (s, NH); 6.36–7.71 (m, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 41.9 (CH_2); 47.4 (CH_2NH); 53.3 (CH_2N); 56.5 (CH(3)); 64.8 (C(2)); 114.4 (C(4″), C(5″)); 120.0 (C(1″), C(8″)); 122.5 (C(2″), C(7″)); 123.4 (C(3″),

C(6″)); 125.1, 126.2 (2 C_o); 127.3, 127.9 (2 C_m); 128.4, 140.5 (2 C_p); 141.7 (C(4a″), C(5a″)); 147.8 (C(1a″), C(8a″)); 163.6 (C=O); 168.5 (C=O). FAB-MS: 509 (M^+). Anal. calc. for $C_{25}H_{21}ClN_4O_4S$ (508.98): C 58.99, H 4.15, N 11.00; found: C 58.94, H 4.10, N 10.95.

trans-*3-Chloro-2-(2-nitrophenyl)-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4j**). Yield: 2.17 g (61%). M.p. 159–160°. IR: 690 (C–S–C), 869 (C–NO), 1355 (C–N), 1485 (C=C), 1542 (NO_2), 1569 (N=N), 1680 (CO), 1745 (C(4)=O), 1447, 2849, 2907 (CH_2), 2924 (CH–Cl), 3035 (arom. CH), 3381 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.26–2.32 (*m*, CH_2); 3.42–3.47 (*m*, CH_2NH); 4.13 (*t*, *J* = 7.5, CH_2N); 4.58 (*d*, *J* = 5.3, CH(3)); 5.23 (*d*, *J* = 5.3, CH(2)); 5.85 (*s*, NH); 6.42–7.80 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 40.4 (CH_2); 45.8 (CH_2NH); 54.1 (CH_2N); 54.7 (CH(3)); 62.3 (C(2)); 113.3 (C(4″), C(5″)); 120.6 (C(1″), C(8″)); 123.1 (C(2″), C(7″)); 124.2 (C(3″), C(6″)); 126.0, 127.4 (2 C_o); 128.7, 129.1 (2 C_m); 129.6, 138.5 (2 C_p); 139.3 (C(4a″), C(5a″)); 147.6 (C(1a″), C(8a″)); 162.5 (C=O); 170.7 (C=O). FAB-MS: 509 (M^+). Anal. calc. for $C_{25}H_{21}ClN_4O_4S$ (508.98): C 58.99, H 4.15, N 11.00; found: C 58.89, H 4.12, N 10.96.

trans-*3-Chloro-2-(4-methoxyphenyl)-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4k**). Yield: 2.17 g (63%). M.p. 156–157°. IR: 696 (C–S–C), 1165 (C–O); 1329 (N–C), 1475 (C=C), 1555 (N=N), 1666 (CO), 1731 (C(4)=O), 1437, 2843, 2901 (CH_2), 2909 (CH(3)), 3028 (arom. CH), 3372 (NH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.14–2.19 (*m*, CH_2); 3.31–3.35 (*m*, CH_2NH); 3.71 (*s*, MeO); 4.07 (*t*, *J* = 7.6, CH_2N); 4.48 (*d*, *J* = 5.1, CH(3)); 5.16 (*d*, *J* = 5.1, CH(2)); 5.77 (*s*, NH); 6.37–7.75 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 38.2 (CH_2); 44.1 (CH_2NH); 50.9 (CH_2N); 52.6 (CH(3)); 61.1 (C(2)); 110.8 (C(4″), C(5″)); 116.7 (C(1″), C(8″)); 121.9 (C(2″), C(7″)); 123.0 (C(3″), C(6″)); 124.6 (2 C_o); 126.9 (2 C_m); 128.1, 136.8 (2 C_p); 138.2 (C(4a″), C(5a″)); 145.5 (C(1a″), C(8a″)); 161.9 (C=O); 166.0 (C=O). FAB-MS: 494 (M^+). Anal. calc. for $C_{26}H_{24}ClN_3O_3S$ (494.01): C 63.21, H 4.89, N 8.50; found: C 63.15, H 4.84, N 8.46.

trans-*3-Chloro-2-(4-methylphenyl)-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4l**). Yield: 1.84 g (55%). M.p. 149–151°. IR: 697 (C–S–C), 1327 (C–N), 1469 (C=C), 1551 (N=N), 1663 (CO), 1725 (C(4)=O), 1432, 2836, 2898 (CH_2), 2905 (CH(3)), 3024 (arom. CH), 3367 (NH); 2927 (Me). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.10–2.15 (*m*, CH_2); 2.64 (*s*, Me); 3.25–3.32 (*m*, CH_2NH); 4.03 (*t*, *J* = 7.5, CH_2N); 4.40 (*d*, *J* = 5.0, CH(3)); 5.09 (*d*, *J* = 5.0, CH(2)); 5.68 (*s*, NH); 6.48–7.93 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 24.7 (Me); 37.5 (CH_2); 43.2 (CH_2NH); 50.1 (CH_2N); 51.6 (CH(3)); 60.2 (C(2)); 110.2 (C(4″), C(5″)); 116.7 (C(1″), C(8″)); 121.1 (C(2″), C(7″)); 122.3 (C(3″), C(6″)); 124.6 (2 C_o); 126.1 (2 C_m); 127.2, 136.1 (2 C_p); 137.2 (C(4a″), C(5a″)); 145.1 (C(1a″), C(8a″)); 161.3 (C=O); 165.6 (C=O). FAB-MS: 478 (M^+). Anal. calc. for $C_{26}H_{24}ClN_3O_2S$ (478.01): C 65.32, H 5.06, N 8.79; found: C 65.29, H 5.05, N 8.78.

trans-*3-Chloro-2-(4-hydroxyphenyl)-4-oxo*-N-*[3-(10*H*-phenothiazin-10-yl)propyl]azetidine-1-carboxamide* (*trans*-**4m**). Yield: 2.21 g (66%). M.p. 154–155°. IR: 699 (C–S–C), 1336 (C–NH), 1478 (C=C), 1556 (N=N), 1669 (CO), 1734 (C(4)=O), 1438, 2845, 2903 (CH_2), 2910 (CH(3)), 3030 (arom. CH), 3375 (NH); 3467 (OH). ^{1}H-NMR (300 MHz, $CDCl_3$): 2.19–2.25 (*m*, CH_2); 3.33–3.39 (*m*, CH_2NH); 4.09 (*t*, *J* = 7.7, CH_2N); 4.17 (*s*, OH); 4.50 (*d*, *J* = 5.2, CH(3)); 5.17 (*d*, *J* = 5.2, CH(2)); 5.79 (*s*, NH); 6.33–7.81 (*m*, 12 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 38.3 (CH_2); 44.7 (CH_2NH); 50.9 (CH_2N); 52.7 (CH(3)); 61.6 (C(2)); 111.3 (C(4″), C(5″)); 117.2 (C(1″), C(8″)); 122.6 (C(2″), C(7″)); 123.8 (C(3″), C(6″)); 125.5 (2 C_o); 127.7 (2 C_m); 128.4 , 137.0 (2 C_p); 138.8 (C(4a″), C(5a″)); 145.6 (C(1a″), C(8a″)); 161.9 (C=O); 166.0 (C=O). FAB-MS: 480 (M^+). Anal. calc. for $C_{25}H_{22}ClN_3O_3S$ (479.99): C 62.52, H 4.61, N 8.75; found: C 62.47, H 4.57, N 8.71.

The authors are grateful to *SAIF, Central Drugs Research Institute*, Lucknow, India, for providing spectral and analytical data of the compounds. We are also thankful to the head of the Department of Chemistry, Dr. *H. S. Gour*, University, Sagar, India, for enabling us to carry out this work.

REFERENCES

[1] D. K. Shukla, S. D. Srivastava, *Indian J. Chem., Sect. B* **2008**, *47*, 463.
[2] A. Nema, S. K. Srivastava, *J. Indian Chem. Soc.* **2007**, *84*, 1037.
[3] D. Bandyopadhyay, G. Rivera, I. Salinas, H. Aguilar, B. K. Banik, *Molecules* **2010**, *15*, 1082.

[4] J. W. Skiles, D. McNeil, *Tetrahedron Lett.* **1990**, *3*, 7277.
[5] G. Wu, W. Tormos, *J. Org. Chem.* **1997**, *62*, 6412.
[6] H.-Y. Kang, A. N. Pae, H. Y. Koh, M. H. Chang, *Bull. Korean Chem. Soc.* **1991**, *12*, 75.
[7] S. D. Srivastava, P. Kohli, *Proc. Natl. Acad. Sci. India* **2007**, *77*, 199.
[8] A. R. Trivedi, A. B. Siddiqui, V. H. Shah, *Arkivoc* **2008**, *(ii)*, 210.
[9] A. Rajasekaran, P. P. Tripathi, *Acta Pharm. Turc.* **2003**, *45*, 235.
[10] G. P. Sarmiento, R. G. Vitale, J. Afeltra, G. Y. Moltrasio, A. G. Moglioni, *Eur. J. Med. Chem.* **2010**, *46*, 101.
[11] G. Cerbai, G. F. Di Paco, *Boll. Chim. Farm.* **1963**, *102*, 709.
[12] K. G. Desai, K. R. Desai, *Indian J. Chem., Sect. B* **2005**, *44*, 2093.
[13] N. Siddiqui, A. Rana, S. A. Khan, S. E. Haque, M. S. Alam, W. Ahsan, M. F. Arshada, *Acta Chim. Slov.* **2009**, *56*, 462.
[14] A. K. Sharma, S. N. Mazumdar, M. P. Mahajan, *J. Org. Chem.* **1996**, *61*, 5506.
[15] A. Arrieta, F. P. Cossío, B. Lecea, *J. Org. Chem.* **1999**, *64*, 1831.
[16] R. Singh, J. M. Nuss, *Tetrahedron Lett.* **1999**, *40*, 1249.
[17] J. Anaya, S. D. Gero, M. Grande, J. I. M. Hernando, N. M. Laso, *Bioorg. Med. Chem.* **1999**, *7*, 837.

Received September 14, 2011