

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

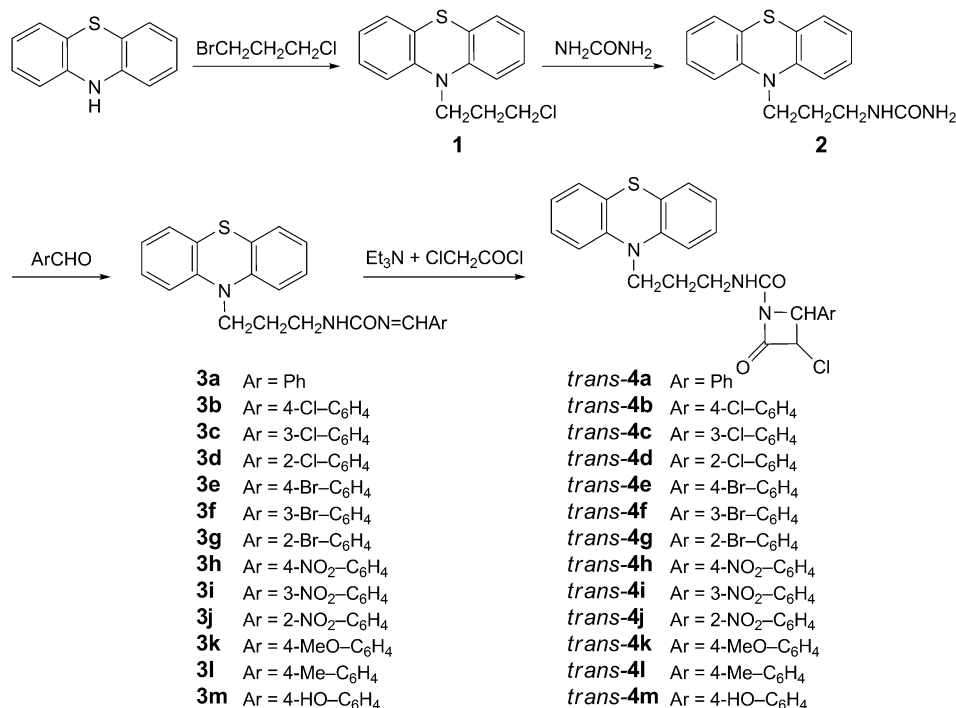
by Ritu Sharma*, Pushkal Samadhiya, S. D. Srivastava, and S. K. Srivastava

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(CH₂)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 ClCH₂COCl in the presence of Et₃N, 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 ¹³C-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(CH₂)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 ClCH₂COCl in the presence of Et₃N, 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 ¹³C-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 ¹³C-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 NH₂ 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 *doublets* 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 ¹³C-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 ¹³C-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 (SiO₂; 230–400 mesh). M.p.: in open

capillaries; uncorrected. Progress of the reaction was monitored by silica gel-*G* coated TLC plates with MeOH/CHCl₃ as the eluent; the spots were visualized by exposing the dry plate to I₂ vapor. IR Spectra: KBr disc; Shimadzu 8201 PC, FT-IR spectrophotometer; in cm⁻¹. ¹H- and ¹³C-NMR spectra: Bruker DRX-300 spectrometer in CDCl₃, 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)-10H-phenothiazine (1). See [10].

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

General Procedure for the Synthesis of 1-(Arylmethylidene)-3-[3-(10H-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 (CHCl₃/MeOH 7:3; 90 ml). The purified product was dried under vacuum and recrystallized from acetone to furnish compound **3**.

1-[3-(10H-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 (CH₂), 3022 (arom. CH), 3363 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.08–2.15 (*m*, CH₂); 3.31–3.37 (*m*, CH₂NH); 4.19 (*t*, *J* = 7.4, CH₂N); 5.78 (*s*, NH); 7.96 (*s*, CH=N); 6.05–8.10 (*m*, 13 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 35.5 (CH₂), 42.6 (CH₂NH); 48.8 (CH₂N); 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 C₂₃H₂₁N₃OS (387.50): C 71.29, H 5.46, N 10.84; found: C 71.24, H 5.38, N 10.81.

1-[3-(4-Chlorophenyl)methylidene]-3-[3-(10H-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 (CH₂), 3031 (arom. CH), 3369 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.18–2.22 (*m*, CH₂); 3.42–3.46 (*m*, CH₂NH); 4.29 (*t*, *J* = 7.4, CH₂N); 5.82 (*s*, NH); 7.98 (*s*, CH=N); 6.80–7.79 (*m*, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 38.6 (CH₂); 44.4 (CH₂NH); 51.8 (CH₂N); 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 C₂₃H₂₀ClN₃OS (421.95): C 65.47, H 4.77, N 9.95; found: C 65.43, H 4.65, N 9.91.

1-[3-(3-Chlorophenyl)methylidene]-3-[3-(10H-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 (CH₂), 3033 (arom. CH), 3372 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.20–2.25 (*m*, CH₂); 3.45–3.49 (*m*, CH₂NH); 4.27 (*t*, *J* = 7.4, CH₂N); 5.88 (*s*, NH); 7.97 (*s*, CH=N); 6.50–7.81 (*m*, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 37.3 (CH₂); 45.8 (CH₂NH); 52.9 (CH₂N); 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 C₂₃H₂₀ClN₃OS (421.95): C 65.47, H 4.77, N 9.95; found: C 65.42, H 4.68, N 9.93.

1-[3-(2-Chlorophenyl)methylidene]-3-[3-(10H-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 (CH₂), 3034 (arom. CH), 3373 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.11–2.15 (*m*, CH₂); 3.42–3.47 (*m*, CH₂NH); 4.30 (*t*, *J* = 7.4, CH₂N); 5.82 (*s*, NH); 7.96 (*s*, CH=N); 6.48–7.86 (*m*, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 39.2 (CH₂); 42.7 (CH₂NH); 51.7 (CH₂N); 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 C₂₃H₂₀ClN₃OS (421.95): C 65.47, H 4.77, N 9.95; found: C 65.45, H 4.69, N 9.90.

1-[3-(4-Bromophenyl)methylidene]-3-[3-(10H-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 (CH₂), 3037 (arom. CH), 3376 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.18–2.22 (*m*, CH₂); 3.41–3.46 (*m*, CH₂NH); 4.31 (*t*, *J* = 7.5, CH₂N); 5.90 (*s*, NH); 8.02 (*s*, CH=N); 6.42–7.76 (*m*, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 38.3 (CH₂); 45.1 (CH₂NH); 51.3 (CH₂N); 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 C₂₃H₂₀BrN₃OS (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-(10H-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 (CH₂), 3035 (arom. CH), 3378 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.20–2.25 (m, CH₂); 3.36–3.43 (m, CH₂NH); 4.37 (t, *J* = 7.6, CH₂N); 5.86 (s, NH); 7.95 (s, CH=N); 6.37–7.81 (m, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 37.5 (CH₂); 44.2 (CH₂NH); 49.4 (CH₂N); 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 C₂₃H₂₀BrN₃OS (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-(10H-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 (CH₂), 3040 (arom. CH), 3381 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.27–2.32 (m, CH₂); 3.43–3.48 (m, CH₂NH); 4.29 (t, *J* = 7.6, CH₂N); 5.91 (s, NH); 7.98 (s, CH=N); 6.43–7.89 (m, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 38.8 (CH₂); 46.3 (CH₂NH); 50.5 (CH₂N); 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 C₂₃H₂₀BrN₃OS (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-(10H-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 (CH₂), 3036 (arom. CH), 3374 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.25–2.28 (m, CH₂); 3.47–3.51 (m, CH₂NH); 4.32 (t, *J* = 7.6, CH₂N); 5.87 (s, NH); 7.93 (s, CH=N); 6.55–7.82 (m, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 39.6 (CH₂); 47.7 (CH₂NH); 52.0 (CH₂N); 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 C₂₃H₂₀N₄O₃S (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-(10H-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 (CH₂), 3031 (arom. CH), 3370 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.14–2.19 (m, CH₂); 3.40–3.44 (m, CH₂NH); 4.25 (t, *J* = 7.6, CH₂N); 5.83 (s, NH); 8.05 (s, CH=N); 6.46–7.91 (m, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 36.9 (CH₂); 47.4 (CH₂NH); 52.6 (CH₂N); 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 C₂₃H₂₀N₄O₃S (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-(10H-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 (CH₂), 3039 (arom. CH), 3379 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.20–2.24 (m, CH₂); 3.50–3.55 (m, CH₂NH); 4.28 (t, *J* = 7.6, CH₂N); 5.92 (s, NH); 8.00 (s, CH=N); 6.51–7.89 (m, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 38.3 (CH₂); 46.9 (CH₂NH); 50.7 (CH₂N); 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 C₂₃H₂₀N₄O₃S (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-(10H-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 (CH₂), 2947 (Me–O), 3024 (arom. CH), 3365 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.11–2.16 (m, CH₂); 3.33–3.38 (m, CH₂NH); 3.51 (s, MeO); 4.22 (t, *J* = 7.6, CH₂N); 5.80 (s, NH); 7.89 (s, CH=N); 6.27–7.62 (m, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 36.2 (CH₂); 43.5 (CH₂NH); 44.4 (CH₂N); 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 C₂₄H₂₃N₃O₂S (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-(10H-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 (CH₂), 2917 (Me); 3019 (arom. CH), 3360 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.03–2.09 (*m*, CH₂); 2.39 (*s*, Me); 3.32–3.39 (*m*, CH₂NH); 4.17 (*t*, *J* = 7.4, CH₂N); 5.74 (*s*, NH); 7.85 (*s*, CH=N); 6.19–7.57 (*m*, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 24.9 (Me); 35.3 (CH₂); 42.5 (CH₂NH); 48.4 (CH₂N); 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 C₂₄H₂₃N₃OS (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-(10H-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 (CH₂), 3027 (arom. CH), 3368 (NH), 3472 (OH). ¹H-NMR (300 MHz, CDCl₃): 2.11–2.16 (*m*, CH₂); 3.40–3.47 (*m*, CH₂NH); 4.09 (*s*, OH); 4.23 (*t*, *J* = 7.65, CH₂N); 5.81 (*s*, NH); 7.92 (*s*, CH=N); 6.32–7.71 (*m*, 12 arom. H). ¹³C-NMR (75 MHz, CDCl₃): 36.7 (CH₂); 43.2 (CH₂NH); 49.5 (CH₂N); 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 C₂₃H₂₁N₃O₂S (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-(10H-phenothiazin-10-yl)propyl]azetidine-1-carboxamides 4. A soln. of **3** (0.007 mol), ClCH₂COCl (0.007 mol), and Et₃N (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/CHCl₃ (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-(10H-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 (CH₂), 2906 (CH(3)), 3025 (arom. CH), 3369 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.10–2.14 (*m*, CH₂); 3.30–3.34 (*m*, CH₂NH); 4.05 (*t*, *J* = 7.4, CH₂N); 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). ¹³C-NMR (75 MHz, CDCl₃): 37.8 (CH₂); 43.9 (CH₂NH); 50.7 (CH₂N); 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 C₂₅H₂₂ClN₃O₂S (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-(10H-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 (CH₂), 2911 (CH(3)), 3032 (arom. CH), 3376 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.20–2.26 (*m*, CH₂); 3.35–3.41 (*m*, CH₂NH); 4.16 (*t*, *J* = 7.6, CH₂N); 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). ¹³C-NMR (75 MHz, CDCl₃): 40.4 (CH₂); 47.7 (CH₂NH); 52.6 (CH₂N); 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 C₂₅H₂₁Cl₂N₃O₂S (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-(10H-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 (CH₂), 2916 (CH(3)), 3036 (arom. CH), 3380 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.21–2.27 (*m*, CH₂); 3.37–3.41 (*m*, CH₂NH); 4.18 (*t*, *J* = 7.5, CH₂N); 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). ¹³C-NMR (75 MHz, CDCl₃): 40.7 (CH₂); 48.5 (CH₂NH); 52.5 (CH₂N); 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 C₂₅H₂₁Cl₂N₃O₂S (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-(10H-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 (CH₂), 2912 (CH–Cl), 3031 (arom. CH), 3382 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.30–2.35 (*m*, CH₂); 3.41–3.45 (*m*, CH₂NH); 4.21 (*t*,

$J = 7.6$, CH_2N); 4.59 (d , $J = 5.1$, $\text{CH}(3)$); 5.30 (d , $J = 5.1$, $\text{CH}(2)$); 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 ($\text{CH}(3)$); 63.6 ($\text{CH}(2)$); 113.1 ($\text{C}(4'')$, $\text{C}(5'')$); 118.9 ($\text{C}(1'')$, $\text{C}(8'')$); 123.1 ($\text{C}(2'')$, $\text{C}(7'')$); 124.6 ($\text{C}(3'')$, $\text{C}(6'')$); 126.5, 127.2 (2 C_o); 128.1, 128.8 (2 C_m); 129.8, 141.6 (2 C_p); 142.5 ($\text{C}(4a'')$, $\text{C}(5a'')$); 148.3 ($\text{C}(1a'')$, $\text{C}(8a'')$); 165.4 ($\text{C}=\text{O}$); 168.6 ($\text{C}=\text{O}$). FAB-MS: 498 (M^+). Anal. calc. for $\text{C}_{25}\text{H}_{21}\text{Cl}_2\text{N}_3\text{O}_2\text{S}$ (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-(10H-phenothiazin-10-yl)propyl]azetidine-1-carboxamide (*trans*-**4e**). Yield: 2.35 g (62%). M.p. 156–158°. IR: 578 ($\text{C}-\text{Br}$), 710 ($\text{C}-\text{S}-\text{C}$), 1343 ($\text{C}-\text{N}$), 1480 ($\text{C}=\text{C}$), 1559 ($\text{N}=\text{N}$), 1679 (CO), 1742 ($\text{C}(4)=\text{O}$), 1444, 2847, 2904 (CH_2), 2945 ($\text{CH}(3)$), 3033 (arom. CH), 3377 (NH). ^1H -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 , $J = 5.2$, $\text{CH}(3)$); 5.21 (d , $J = 5.2$, $\text{CH}(2)$); 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 ($\text{CH}(3)$); 62.3 ($\text{CH}(2)$); 115.8 ($\text{C}(4'')$, $\text{C}(5'')$); 118.5 ($\text{C}(1'')$, $\text{C}(8'')$); 124.2 ($\text{C}(2'')$, $\text{C}(7'')$); 125.4 ($\text{C}(3'')$, $\text{C}(6'')$); 127.6 (2 C_o); 129.6 (2 C_m); 130.1, 139.5 (2 C_p); 140.7 ($\text{C}(4a'')$, $\text{C}(5a'')$); 147.0 ($\text{C}(1a'')$, $\text{C}(8a'')$); 165.8 ($\text{C}=\text{O}$); 169.5 ($\text{C}=\text{O}$). FAB-MS: 543 (M^+). Anal. calc. for $\text{C}_{25}\text{H}_{21}\text{BrClN}_3\text{O}_2\text{S}$ (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-(10H-phenothiazin-10-yl)propyl]azetidine-1-carboxamide (*trans*-**4f**). Yield: 2.43 g (64%). M.p. 157–159°. IR: 572 ($\text{C}-\text{Br}$), 705 ($\text{C}-\text{S}-\text{C}$), 1347 ($\text{C}-\text{NH}$), 1484 ($\text{C}=\text{C}$), 1564 ($\text{N}=\text{N}$), 1677 (CO), 1735 ($\text{C}(4)=\text{O}$), 1448, 2850, 2909 (CH_2), 2938 ($\text{CH}(3)$), 3037 (arom. CH), 3384 (NH). ^1H -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 , $J = 5.2$, $\text{CH}(3)$); 5.27 (d , $J = 5.2$, $\text{CH}(2)$); 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 ($\text{CH}(3)$); 65.7 ($\text{CH}(2)$); 111.4 ($\text{C}(4'')$, $\text{C}(5'')$); 117.6 ($\text{C}(1'')$, $\text{C}(8'')$); 124.7 ($\text{C}(2'')$, $\text{C}(7'')$); 125.8 ($\text{C}(3'')$, $\text{C}(6'')$); 127.9, 128.1 (2 C_o); 129.5, 129.8 (2 C_m); 130.5, 137.7 (2 C_p); 138.6 ($\text{C}(4a'')$, $\text{C}(5a'')$); 148.1 ($\text{C}(1a'')$, $\text{C}(8a'')$); 164.4 ($\text{C}=\text{O}$); 169.1 ($\text{C}=\text{O}$). FAB-MS: 543 (M^+). Anal. calc. for $\text{C}_{25}\text{H}_{21}\text{BrClN}_3\text{O}_2\text{S}$ (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-(10H-phenothiazin-10-yl)propyl]azetidine-1-carboxamide (*trans*-**4g**). Yield: 2.39 g (63%). M.p. 154–156°. IR: 543 ($\text{C}-\text{Br}$), 700 ($\text{C}-\text{S}-\text{C}$), 1353 ($\text{C}-\text{NH}$), 1460 ($\text{C}=\text{C}$), 1568 ($\text{N}=\text{N}$), 1673 (CO), 1746 ($\text{C}(4)=\text{O}$), 1440, 2850, 2911 (CH_2), 2952 ($\text{CH}(3)$), 3016 (arom. CH), 3341 (NH). ^1H -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 , $J = 5.2$, $\text{CH}(3)$); 5.30 (d , $J = 5.2$, $\text{CH}(2)$); 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 ($\text{CH}(3)$); 65.3 ($\text{CH}(2)$); 112.6 ($\text{C}(4'')$, $\text{C}(5'')$); 119.3 ($\text{C}(1'')$, $\text{C}(8'')$); 125.0 ($\text{C}(2'')$, $\text{C}(7'')$); 126.7 ($\text{C}(3'')$, $\text{C}(6'')$); 128.3, 129.4 (2 C_o); 130.3, 130.8 (2 C_m); 131.7, 138.7 (2 C_p); 139.6 ($\text{C}(4a'')$, $\text{C}(5a'')$); 146.3 ($\text{C}(1a'')$, $\text{C}(8a'')$); 164.7 ($\text{C}=\text{O}$); 170.7 ($\text{C}=\text{O}$). FAB-MS: 543 (M^+). Anal. calc. for $\text{C}_{25}\text{H}_{21}\text{BrClN}_3\text{O}_2\text{S}$ (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-(10H-phenothiazin-10-yl)propyl]azetidine-1-carboxamide (*trans*-**4h**). Yield: 2.13 g (60%). M.p. 152–153°. IR: 696 ($\text{C}-\text{S}-\text{C}$), 868 ($\text{C}-\text{NO}$), 1357 ($\text{C}-\text{N}$), 1487 ($\text{C}=\text{C}$), 1540 (NO_2), 1570 ($\text{N}=\text{N}$), 1675 (CO), 1738 ($\text{C}(4)=\text{O}$), 1449, 2854, 2905 (CH_2), 2921 ($\text{CH}-\text{Cl}$), 3038 (arom. CH), 3382 (NH). ^1H -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 , $J = 5.3$, $\text{CH}(2)$); 4.61 (d , $J = 5.3$, $\text{CH}(3)$); 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 ($\text{CH}(3)$); 64.4 ($\text{CH}(2)$); 113.7 ($\text{C}(4'')$, $\text{C}(5'')$); 119.4 ($\text{C}(1'')$, $\text{C}(8'')$); 123.4 ($\text{C}(2'')$, $\text{C}(7'')$); 124.9 ($\text{C}(3)$, $\text{C}(6)$); 126.5 (2 C_o); 128.7 (2 C_m); 129.6, 140.8 (2 C_p); 141.1 ($\text{C}(4a'')$, $\text{C}(5a'')$); 149.7 ($\text{C}(1a'')$, $\text{C}(8a'')$); 163.4 ($\text{C}=\text{O}$); 167.8 ($\text{C}=\text{O}$). FAB-MS: 509 (M^+). Anal. calc. for $\text{C}_{25}\text{H}_{21}\text{ClN}_4\text{O}_4\text{S}$ (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-(10H-phenothiazin-10-yl)propyl]azetidine-1-carboxamide (*trans*-**4i**). Yield: 2.28 g (64%). M.p. 155–157°. IR: 694 ($\text{C}-\text{S}-\text{C}$), 864 ($\text{C}-\text{NO}$), 1358 ($\text{C}-\text{N}$), 1481 ($\text{C}=\text{C}$), 1542 (NO_2), 1566 ($\text{N}=\text{N}$), 1672 (CO), 1743 ($\text{C}(4)=\text{O}$), 1452, 2858, 2912 (CH_2), 2919 ($\text{CH}(3)$), 3042 (arom. CH), 3378 (NH). ^1H -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 , $J = 5.2$, $\text{CH}(3)$); 5.19 (d , $J = 5.2$, $\text{CH}(2)$); 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 ($\text{CH}(3)$); 64.8 ($\text{CH}(2)$); 114.4 ($\text{C}(4'')$, $\text{C}(5'')$); 120.0 ($\text{C}(1'')$, $\text{C}(8'')$); 122.5 ($\text{C}(2'')$, $\text{C}(7'')$); 123.4 ($\text{C}(3'')$,

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 C₂₅H₂₁ClN₄O₄S (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-(10H-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 (NO₂), 1569 (N=N), 1680 (CO), 1745 (C(4)=O), 1447, 2849, 2907 (CH₂), 2924 (CH–Cl), 3035 (arom. CH), 3381 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.26–2.32 (*m*, CH₂); 3.42–3.47 (*m*, CH₂NH); 4.13 (*t*, *J* = 7.5, CH₂N); 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). ¹³C-NMR (75 MHz, CDCl₃): 40.4 (CH₂); 45.8 (CH₂NH); 54.1 (CH₂N); 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 C₂₅H₂₁ClN₄O₄S (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-(10H-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 (CH₂), 2909 (CH(3)), 3028 (arom. CH), 3372 (NH). ¹H-NMR (300 MHz, CDCl₃): 2.14–2.19 (*m*, CH₂); 3.31–3.35 (*m*, CH₂NH); 3.71 (*s*, MeO); 4.07 (*t*, *J* = 7.6, CH₂N); 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). ¹³C-NMR (75 MHz, CDCl₃): 38.2 (CH₂); 44.1 (CH₂NH); 50.9 (CH₂N); 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 C₂₆H₂₄ClN₃O₃S (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-(10H-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 (CH₂), 2905 (CH(3)), 3024 (arom. CH), 3367 (NH); 2927 (Me). ¹H-NMR (300 MHz, CDCl₃): 2.10–2.15 (*m*, CH₂); 2.64 (*s*, Me); 3.25–3.32 (*m*, CH₂NH); 4.03 (*t*, *J* = 7.5, CH₂N); 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). ¹³C-NMR (75 MHz, CDCl₃): 24.7 (Me); 37.5 (CH₂); 43.2 (CH₂NH); 50.1 (CH₂N); 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 C₂₆H₂₄ClN₃O₂S (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-(10H-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 (CH₂), 2910 (CH(3)), 3030 (arom. CH), 3375 (NH); 3467 (OH). ¹H-NMR (300 MHz, CDCl₃): 2.19–2.25 (*m*, CH₂); 3.33–3.39 (*m*, CH₂NH); 4.09 (*t*, *J* = 7.7, CH₂N); 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). ¹³C-NMR (75 MHz, CDCl₃): 38.3 (CH₂); 44.7 (CH₂NH); 50.9 (CH₂N); 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 C₂₅H₂₂ClN₃O₃S (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