Turk J Chem
31 (2007) , 141 – 147.

Synthesis of Nitrogen-Containing Heterocycles from the Reaction of Amidrazones with α-Haloesters

Hany M. DALLOUL[1*], **Peter H. BOYLE**[2]
[1] *Chemistry Department, Faculty of Science, Al-Aqsa University of Gaza, Gaza Strip, PALESTINE*
e-mail: hanydallool@yahoo.com
[2] *Chemistry Department, Trinity College, Dublin 2, IRELAND*

Received 04.07.2006

The reaction of amidrazones **1** with α-haloesters **2** formed 1,3,5-substituted 4,5-dihydro-1,2,4-triazin-6-ones (**4a-z**) rather than 1,2,4-triazin-5-one derivatives (**5a-z**). The microanalysis and spectral data of the synthesized compounds are in full agreement with their molecular structure.

Key Words: Amidrazones, α-haloesters**,** 4,5-dihydro-1,2,4-triazin-6-one.

Introduction

Our search of the literature revealed that some dihydro-1,2,4-triazin-6-one derivatives are reported to possess antibacterial, antimicrobial, fungicide, insecticide, pesticide, and crop protection agents, as well as blood platelet aggregation-inhibition activates.[1−10] Furthermore, researchers have also reported that some 1,2,4-triazin-6-one derivatives constitute an important class of compounds possessing antitumoral activity against leukemia/lymphoma, ovarian cancer, small and large lung cancer cells, and breast cancer.[6,11−13] As part of our program aimed at developing new biologically active compounds, this work reports the synthesis of some new 1,2,4-triazin-6-one derivatives from the reaction between different amidrazones and α-haloesters, which remains, however, unexplored in the literature.

Experimental

Melting points were determined on a Stuart electrothermal apparatus and are uncorrected. The IR spectra were obtained using a Satellite 3000 mid-IR spectrophotometer in potassium bromide (KBr) pellets. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker spectrometer (300 MHz) at room temperature in $CDCl_3$, if not noted otherwise, using TMS as an internal reference. All chemical shifts (δ) were reported in ppm from TMS. Elemental analysis was performed at Cairo University, Egypt, and the results agreed with the calculated values within experimental errors. The amidrazones **1** were prepared according to the literature.[14−16] The α-haloesters **2** were purchased from Avocado Research Chemicals, UK, and were used without further purification.

*Corresponding author

General procedure for the synthesis of compounds (4a-z)

To a stirred solution of amidrazones **1** (5 mmol) and α-haloesters **2** (5.5 mmol) in tetrahydrofuran (THF) (50 mL) was added triethylamine (6 mmol) dropwise at room temperature. After the addition was completed, the reaction mixture was refluxed for 2-4 h, cooled, and the solvent was then removed under reduced pressure. The residual solid was washed several times with water to remove the triethylamine salt. The resulting crude product was collected and recrystallized from aqueous ethanol to afford the desired triazinones. The following compounds were synthesized using this method:

3-Acetyl-1-(chlorophenyl)-4,5-dihydro-1,2,4-triazin-6-one (4a): Yield: 66%; mp: 200-202 °C (Lit[17] 204-205); IR (ν/cm^{-1}): 3330 (N-H), 1710 (C=O), 1675 (lactam C=O); $C_{11}H_{10}ClN_3O_2$ (Mw 251.67).

3-Acetyl-1-(chlorophenyl)-5-methyl-4,5-dihydro-1,2,4-triazin-6-one (4b): Yield: 69%; mp: 140-142 °C (Lit[17] 142-143); IR (ν/cm^{-1}): 3325 (N-H), 1705 (C=O), 1673 (lactam C=O); $C_{12}H_{12}ClN_3O_2$ (Mw 265.70).

3-Acetyl-1-(chlorophenyl)-5-isopropyl-4,5-dihydro-1,2,4-triazin-6-one (4c): Yield: 60%; mp: 138-140 °C (Lit[17] 141-142); IR (ν/cm^{-1}): 3325 (N-H), 1715 (C=O), 1672 (lactam C=O); $C_{14}H_{16}ClN_3O_2$ (Mw 293.76).

3-Acetyl-5-benzyl-1-(chlorophenyl)-4,5-dihydro-1,2,4-triazin-6-one (4d): Yield: 72%; mp: 131-133 °C (Lit[17] 132-133); IR (ν/cm^{-1}): 3330 (N-H), 1720 (C=O), 1675 (C=O); $C_{18}H_{16}ClN_3O_2$ (Mw 341.80).

3-Benzoyl-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one (4e): Yield: 74%; mp: 146-148 °C; Analysis (% Calculated/found) for $C_{16}H_{13}N_3O_2$ (Mw 279.30) C: 68.81/69.10, H: 4.69/4.80, N: 15.04/14.80; IR (ν/cm^{-1}): 3350 (N-H), 1690 (lactam C=O), 1650 (C=O); ^{1}H-NMR (δ/ppm): 8.15-7.10 (10H, m, Ar-H), 6.12 (1H, s, N-H), 4.24 (2H, s, CH_2); ^{13}C NMR (δ/ppm): 185.5 (C=O), 159.1 (lactam C=O), 139.1 (C=N), 142.1-116.0 (C=C, Ar), 44.0 (CH_2).

3-Benzoyl-5-methyl-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one (4f): Yield: 75%; mp: 166-168 °C; Analysis (% Calculated/found) for $C_{17}H_{15}N_3O_2$ (Mw 293.33) C: 69.61/69.50, H: 5.15/5.30, N: 14.33/14.20; IR (ν/cm^{-1}): 3355 (N-H), 1692 (lactam C=O), 1655 (C=O); ^{1}H-NMR (δ/ppm): 8.17-7.15 (10H, m, Ar-H), 6.14 (1H, s, N-H), 4.33 (1H, q, CH, J =6.7 Hz), 1.57 (3H, d, CH_3,J =6.7 Hz); ^{13}C-NMR (δ/ppm): 185.7 (C=O), 162.5 (lactam C=O), 139.2 (C=N), 142.5-115.8 (C=C, Ar), 49.5 (CH), 19.8 (CH_3).

3-Benzoyl-1-(chlorophenyl)-5-methyl-4,5-dihydro-1,2,4-triazin-6-one (4g): Yield: 77%; mp: 141-143 °C (Lit[18] 144-146); Analysis (% Calculated/found) for $C_{17}H_{14}ClN_3O_2$ (Mw 327.77) C: 62.30/62.00, H: 4.31/4.10, N: 12.82/13.00; IR (ν/cm^{-1}): 3360 (N-H), 1690 (lactam C=O), 1653 (C=O); ^{1}H-NMR (δ/ppm): 8.20-7.20 (9H, m, Ar-H), 6.15 (1H, s, NH), 4.32 (1H, q, CH,J =6.7 Hz), 1.56 (3H, d, CH_3,J =6.7 Hz); ^{13}C NMR (δ/ppm): 185.70 (C=O), 162.60 (lactam C=O), 139.30 (C=N), 142.60-125.60 (C=C, Ar), 49.70 (CH), 19.50 (CH_3).

3-Benzoyl-1-(chlorophenyl)-5-isopropyl-4,5-dihydro-1,2,4-triazin-6-one (4h): Yield: 66%; mp: 133-135 °C; Analysis (% Calculated/found) for $C_{19}H_{18}ClN_3O_2$ (Mw 355.83) C: 64.14/64.30, H: 5.10/4.90, N: 11.81/12.00; IR (ν/cm^{-1}): 3355 (N-H), 1695 (lactam C=O), 1650 (C=O);^{1}H-NMR (δ/ppm): 8.25-7.24 (9H, m, Ar-H), 6.15 (1H, s, NH), 4.28 (1H, d, CH,J =6 Hz), 2.45-2.37 (1H, m, CH), 1.07 (d, 6H, 2CH_3,J =6.8 Hz);^{13}C NMR (DMSO-d_6) (δ/ppm): 185.6 (C=O), 161.8 (lactam C=O), 139.2 (C=N),

142.5-125.3 (C=C, Ar), 53.2 (CH), 33.3 (CH), 18.3, 17.7 ($2CH_3$).

3-Benzoyl-5-benzyl-1-(chlorophenyl)-4,5-dihydro-1,2,4-triazin-6-one (4i): Yield 71%; mp: 176-178 °C; Analysis (% Calculated/found) for $C_{23}H_{18}ClN_3O_2$ (Mw 403.87) C: 68.40/68.20, H: 4.49/4.60, N: 10.40/10.20; IR (ν/cm^{-1}): 3365 (N-H), 1685 (lactam C=O), 1660 (C=O); ^{1}H-NMR (δ/ppm): 8.30-7.25 (14H, m, Ar-H), 6.20 (1H, s, NH), 4.4 (1H, t, CH,J =6 Hz), 3.17 (2H, d, CH_2,J =8 Hz); ^{13}C-NMR (δ/ppm): 185.0 (C=O), 160.7 (lactam C=O), 139.1 (C=N), 142.3-125.0 (C=C, Ar), 55.2 (CH), 40.2 (CH_2).

3-(2-Naphthoyl)-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one (4j): Yield: 78%; mp: 221-223 °C; Analysis (% Calculated/found) for $C_{20}H_{15}N_3O_2$ (Mw 329.36) C: 72.94/73.20, H: 4.59/4.40, N: 12.76/12.90; IR (ν/cm^{-1}): 3380 (N-H), 1670 (lactam C=O), 1640 (C=O); ^{1}H-NMR (δ/ppm): 8.95-7.05 (12H, m, Ar-H), 6.20 (1H, s, NH), 4.26 (2H, s, CH_2); ^{13}C-NMR (δ/ppm): 185.1 (C=O), 159.0 (lactam C=O), 139.1 (C=N), 142.8-115.3 (C=C, Ar), 43.8 (CH_2).

5-Methyl-3-(2-naphthoyl)-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one (4k): Yield: 67%; mp: 200-202 °C; Analysis (% Calculated/found) for $C_{21}H_{17}N_3O_2$ (Mw 343.39) C: 73.45/73.20, H: 4.99/5.20, N: 12.24/14.10; IR (ν/cm^{-1}): 3370 (N-H), 1685 (lactam C=O), 1645 (C=O); ^{1}H-NMR (δ/ppm): 8.93-7.02 (12H, m, Ar-H), 6.22 (1H, s, NH), 4.35 (1H, q, CH,J =6.7 Hz), 1.57 (3H, d, CH_3,J =6.7 Hz); ^{13}C-NMR (δ/ppm): 185.2 (C=O), 162.4 (lactam C=O), 139.3 (C=N), 142.7-115.5 (C=C, Ar), 50.8 (CH), 20.1 (CH_3).

5-Isopropyl-3-(2-naphthoyl)-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one (4l): Yield: 69%; mp: 177-179 °C; Analysis (% Calculated/found) for $C_{23}H_{21}N_3O_2$ (Mw 371.44) C: 74.37/74.50, H: 5.70/5.60, N: 11.31/11.50; IR (ν/cm^{-1}): 3367 (N-H), 1682 (lactam C=O), 1640 (C=O); ^{1}H-NMR (δ/ppm): 8.95-7.05 (12H, m, Ar-H), 6.20 (1H, s, NH), 4.30 (1H, d, CH,J =6 Hz), 2.46-2.36 (1H, m, CH), 1.04 (6H, d, $2CH_3$,J =6.8 Hz); ^{13}C-NMR (DMSO-d_6) (δ/ppm): 185.0 (C=O), 161.8 (lactam C=O), 139.3 (C=N), 142.8-115.8 (C=C, Ar), 53.0 (CH), 32.7 (CH), 17.8, 16.8 ($2CH_3$).

5-Benzyl-3-(2-naphthoyl)-1-phenyl-4,5-dihydro-1,2,4-triazin-6-one (4m): Yield: 70%; mp: 156-158 °C; Analysis (% Calculated/found) for $C_{27}H_{21}N_3O_2$ (Mw 419.49) C: 77.31/77.50, H: 5.05/4.90, N: 10.02/10.20; IR (ν/cm^{-1}): 3372 (N-H), 1680 (lactam C=O), 1642 (C=O); ^{1}H-NMR (δ/ppm): 8.98-7.10 (17H, m, Ar-H), 6.30 (1H, s, NH), 4.50 (1H, t, CH,J =6 Hz), 3.20 (2H, d, CH_2,J =8 Hz); ^{13}C-NMR (δ/ppm): 185.0 (C=O), 161.2 (lactam C=O), 139.2 (C=N), 142.3-114.9 (C=C, Ar), 54.1 (CH_2).

5-Methyl-1-(4-chlorophenyl)-3-(2-naphthoyl)-4,5-dihydro-1,2,4-triazin-6-one (4n): Yield: 74%; mp: 183-185 °C (Lit[18] 186-188) ; Analysis (% Calculated/found) for $C_{21}H_{16}ClN_3O_2$ (Mw 377.83) C: 66.76/66.60, H: 4.27/4.40, N: 11.12/11.30; IR (ν/cm^{-1}): 3350 (N-H), 1685 (lactam C=O), 1643 (C=O); ^{1}H-NMR (δ/ppm): 8.94-7.24 (11H, m, Ar-H), 6.22 (1H, s, NH), 4.35 (1H, q, CH,J =6.7 Hz), 1.59 (3H, d, CH_3,J =6.7 Hz); ^{13}C-NMR (δ/ppm): 185.3 (C=O), 162.6 (lactam C=O), 139.4 (C=N), 142.9-125.5 (C=C, Ar), 49.7 (CH), 19.5 (CH_3).

1-(4-Methylphenyl)-3-(2-naphthoyl)-4,5-dihydro-1,2,4-triazin-6-one (4o): Yield: 78%; mp: 143-145 °C; Analysis (% Calculated/found) for $C_{21}H_{17}N_3O_2$ (Mw 343.39) C: 73.45/73.30, H: 4.99/5.20, N: 12.24/12.40; IR (ν/cm^{-1}): 3360 (N-H), 1682 (lactam C=O), 1640 (C=O); ^{1}H-NMR (δ/ppm): 8.92-7.15 (11H, m, Ar-H), 6.21 (1H, s, NH), 4.26 (2H, s, CH_2), 2.27 (3H, s, CH_3); ^{13}C-NMR (δ/ppm): 185.2 (C=O), 159.1 (lactam C=O), 139.2 (C=N), 142.8-125.2 (C=C, Ar), 44.0 (CH_2), 21.7 (CH_3).

5-Methyl-1-(4-methylphenyl)-3-(2-naphthoyl)-4,5-dihydro-1,2,4-triazin-6-one (4p): Yield:

71%; mp: 176-178 °C; Analysis (% Calculated/found) for $C_{22}H_{19}N_3O_2$ (Mw 357.42) C: 73.93/74.10, H: 5.36/5.20, N: 11.76/11.90; IR (ν/cm^{-1}): 3367 (N-H), 1680 (lactam C=O), 1638 (C=O); ^{1}H-NMR (δ/ppm): 8.93-7.18 (11H, m, Ar-H), 6.23 (1H, s, NH), 4.33 (1H, q, CH,J =6.7 Hz), 2.26 (3H, s, CH_3), 1.55 (3H, d, CH_3,J =6.7 Hz); ^{13}C-NMR (δ/ppm): 185.1 (C=O), 162.2 (lactam C=O), 139.4 (C=N), 142.6-125.7 (C=C, Ar), 49.8 (CH), 21.2 (CH_3), 19.9 (CH_3).

5-Isopropyl-1-(4-methylphenyl)-3-(2-naphthoyl)-4,5-dihydro-1,2,4-triazin-6-one (4q): Yield: 66%; mp: 198-200 °C; Analysis (% Calculated/found) for $C_{24}H_{23}N_3O_2$ (Mw 385.47) C: 74.78/75.00, H: 6.01/5.90, N: 10.90/10.70; IR (ν/cm^{-1}): 3362 (N-H), 1680 (lactam C=O), 1650 (C=O); ^{1}H-NMR (δ/ppm): 8.90-7.12 (11H, m, Ar-H), 6.22 (1H, s, NH), 4.31 (1H, d, CH,J =6 Hz), 2.44-2.33 (1H, m, CH), 2.26 (3H, s, CH_3,J =6.8 Hz), 1.02 (6H, d, $2CH_3$); ^{13}C-NMR (DMSO-d_6) (δ/ppm): 184.9 (C=O), 161.7 (lactam C=O), 139.0 (C=N), 142.9-125.8 (C=C, Ar), 52.8 (CH), 33.0 (CH), 21.7 (CH_3), 18.7, 16.8 ($2CH_3$).

5-Benzyl-1-(4-methylphenyl)-3-(2-naphthoyl)-4,5-dihydro-1,2,4-triazin-6-one (4r): Yield: 72%; mp: 188-190 °C; Analysis (% Calculated/found) for $C_{28}H_{23}N_3O_2$ (Mw 433.51) C: 77.58/77.40, H: 5.35/5.50, N: 9.69/9.50; IR (ν/cm^{-1}): 3370 (N-H), 1681 (lactam C=O), 1640 (C=O); ^{1}H-NMR (δ/ppm): 8.93-7.14 (16H, m, Ar-H), 6.28 (1H, s, NH), 4.52 (1H, t, CH,J =6 Hz), 3.19 (2H, d, CH_2,J =8 Hz), 2.26 (3H, s, CH_3); ^{13}C-NMR (DMSO-d_6) (δ/ppm): 184.9 (C=O), 161.8 (lactam C=O), 139.2 (C=N), 142.5-125.1 (C=C, Ar), 54.0 (CH), 36.6 (CH_2), 21.3 (CH_3).

1-(4-Chlorophenyl)-3-(2-furoyl)-4,5-dihydro-1,2,4-triazin-6-one (4s): Yield 76%; mp: 163-165 °C; Analysis (% Calculated/found) for $C_{14}H_{10}ClN_3O_3$ (Mw 303.71) C: 55.37/55.50, H: 3.32/3.50, N: 13.84/14.00; IR (ν/cm^{-1}): 3355 (N-H), 1675 (lactam C=O), 1660 (C=O); ^{1}H-NMR (δ/ppm): 8.20-7.20 (7H, m, Ar-H), 6.22 (1H, s, NH), 4.24 (2H, s, CH_2); ^{13}C-NMR (δ/ppm): 173.4 (C=O), 160.6 (lactam C=O), 140.1 (C=N), 141.6-125.6 (arom. C), 44.6 (CH_2).

1-(4-Chlorophenyl)-3-(2-furoyl)-5-methyl-4,5-dihydro-1,2,4-triazin-6-one (4t): Yield: 77%; mp: 139-141 °C; Analysis (% Calculated/found) for $C_{15}H_{12}ClN_3O_3$ (Mw 317.73) C: 56.70/56.90, H: 3.81/4.00, N: 13.22/13.40; IR (ν/cm^{-1}): 3350 (N-H), 1675 (lactam C=O), 1655 (C=O); ^{1}H-NMR (δ/ppm): 8.19-7.16 (7H, m, Ar-H), 6.24 (1H, s, NH), 4.30 (1H, q, CH,J =6.7 Hz), 1.59 (3H, d, CH_3,J =6.7 Hz); ^{13}C-NMR (δ/ppm): 173.7 (C=O), 160.8 (lactam C=O), 140.7 (C=N), 141.3-125.3 (C=C, Ar), 49.6 (CH), 19.6 (CH_3).

1-(4-Chlorophenyl)-3-(2-furoyl)-5-isopropyl-4,5-dihydro-1,2,4-triazin-6-one (4u): Yield: 69%; mp: 182-183 °C; Analysis (% Calculated/found) for $C_{17}H_{16}ClN_3O_3$ (Mw 345.79) C: 59.05/58.90, H: 4.66/4.80, N: 12.15/12.30; IR (ν/cm^{-1}): 3352 (N-H), 1670 (lactam C=O), 1657 (C=O); ^{1}H-NMR (δ/ppm): 8.23-7.17 (7H, m, Ar-H), 6.26 (1H, s, NH), 4.28 (1H, d, CH,J =6 Hz), 2.46-2.38 (1H, m, CH), 1.01 (6H, d, $2CH_3$,J =6.8 Hz); ^{13}C-NMR (δ/ppm): 173.6 (C=O), 160.6 (lactam C=O), 140.2 (C=N), 141.5-125.1 (C=C, Ar), 52.5 (CH), 32.9 (CH), 18.3, 16.7 ($2CH_3$).

5-Benzyl-1-(4-chlorophenyl)-3-(2-furoyl)-4,5-dihydro-1,2,4-triazin-6-one (4v): Yield: 74%; mp: 193-195 °C; Analysis (% Calculated/found) for $C_{21}H_{16}ClN_3O_3$ (Mw 393.83) C: 64.05/63.90, H: 4.10/4.30, N: 10.67/10.50; IR (ν/cm^{-1}): 3350 (N-H), 1676 (lactam C=O), 1660 (C=O); ^{1}H-NMR (δ/ppm): 8.20-7.18 (12H, m, Ar-H), 6.32 (1H, s, NH), 4.41 (1H, t, CH,J =6 Hz), 3.20 (2H, d, CH_2,J =8 Hz); ^{13}C-NMR (δ/ppm): 173.2 (C=O), 160.5 (lactam C=O), 140.5 (C=N), 142.2-125.5 (C=C, Ar), 55.2 (CH), 39.0 (CH_2).

1-(4-Chlorophenyl)-3-(2-thenoyl)-4,5-dihydro-1,2,4-triazin-6-one (4w): Yield: 76%; mp: 203-205 °C; Analysis (% Calculated/found) for $C_{14}H_{10}ClN_3O_2S$ (Mw 319.77) C: 52.59/52.70, H: 3.15/3.30, N: 13.14/13.00; IR (ν/cm^{-1}): 3360 (N-H), 1675 (lactam C=O), 1655 (C=O); ^{1}H-NMR (δ/ppm): 8.28-7.16 (7H, m, Ar-H), 6.20 (1H, s, NH), 4.26 (2H, s, CH_2); ^{13}C-NMR (δ/ppm): 174.3 (C=O), 160.7 (lactam C=O), 140.0 (C=N), 142.1-125.3 (C=C, Ar), 44.2 (CH_2).

1-(4-Chlorophenyl)-5-methyl-3-(2-thenoyl)-4,5-dihydro-1,2,4-triazin-6-one (4x): Yield: 75%; mp: 171-173 °C; Analysis (% Calculated/found) for $C_{15}H_{12}ClN_3O_2S$ (Mw 333.80) C: 53.97/54.10, H: 3.62/3.90, N: 12.59/12.40; IR (ν/cm^{-1}): 3352 (N-H), 1670 (lactam C=O), 1650 (C=O); ^{1}H-NMR (δ/ppm): 8.30-7.17 (7H, m, Ar-H), 6.24 (1H, s, NH), 4.34 (1H, q, CH,J =6.7 Hz), 1.57 (3H, d, CH_3,J =6.7 Hz); ^{13}C-NMR (δ/ppm): 174.2 (C=O), 161.6 (lactam C=O), 140.6 (C=N), 142.1-125.1 (C=C, Ar), 50.2 (CH), 20.1 (CH_3).

1-(4-Chlorophenyl)-5-isopropyl-3-(2-thenoyl)-4,5-dihydro-1,2,4-triazin-6-one (4y): Yield: 66%; mp: 179-181 °C; Analysis (% Calculated/found) for $C_{17}H_{16}ClN_3O_2S$ (Mw 361.85) C: 56.43/56.60, H: 4.46/4.30, N: 11.61/11.80; IR (ν/cm^{-1}): 3355 (N-H), 1675 (lactam C=O), 1660 (C=O); ^{1}H-NMR (δ/ppm): 8.26-7.16 (7H, m, Ar-H), 6.22 (1H, s, NH), 4.29 (1H, d, CH,J =6 Hz), 2.46-2.37 (1H, m, CH), 1.01 (6H, d, 2CH_3,J =6.8 Hz); ^{13}C-NMR (DMSO-d_6) (δ/ppm): 174.3 (C=O), 161.4 (lactam C=O), 140.3 (C=N), 142.0-125.2 (C=C, Ar), 52.7 (CH), 33.2 (CH), 19.0, 17.8 (CH_3).

5-Benzyl-1-(4-chlorophenyl)-3-(2-thenoyl)-4,5-dihydro-1,2,4-triazin-6-one (4z): Yield: 72%; mp: 167-169 °C; Analysis (% Calculated/found) for $C_{21}H_{16}ClN_3O_2S$ (Mw 409.90) C: 61.54/61.80, H: 3.93/4.10, N: 10.25/10.40; IR (ν/cm^{-1}): 3353 (N-H), 1680 (lactam C=O), 1657 (C=O); ^{1}H-NMR (δ/ppm): 8.30-7.18 (12H, m, Ar-H), 6.28 (1H, s, N-H), 4.45 (1H, t, CH,J =6 Hz), 3.22 (2H, d, CH_2,J =8 Hz); ^{13}C-NMR (DMSO-d_6) (δ/ppm): 174.1 (C=O), 161.2 (lactam C=O), 140.2 (C=N), 142.2-125.3 (C=C, Ar), 55.0 (CH), 39.6 (CH_2).

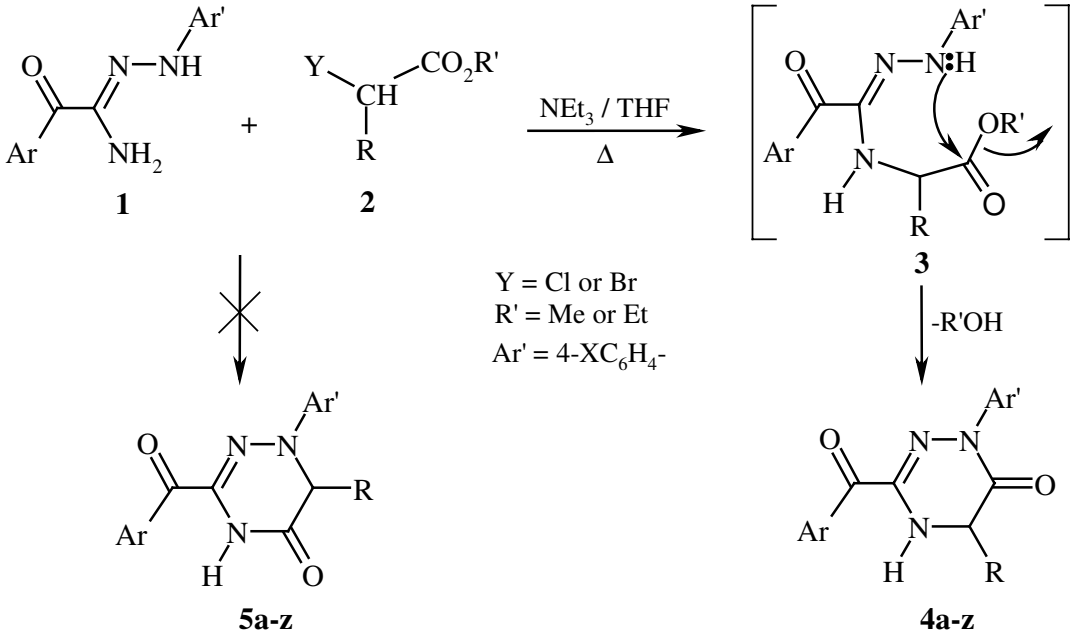
Results and Discussion

The amidrazones **1** were synthesized from the hydrazonoyl halides as previously reported.[14–16] The treatment of amidrazones **1** with α-haloesters **2** in the presence of triethylamine as a base under reflux afforded 1,3,5-substituted 4,5-dihydro-1,2,4-triazin-6-ones (**4a-z**) (Scheme) in good yields (experimental part).

The formation of the compounds (**4a-z**) is assumed to involve the formation of intermediate **3**, which cannot be isolated or observed by TLC, which ultimately undergoes intramolecular cyclization through the elimination of R'OH to yield the 4,5-dihydro-1,2,4-triazin-6-one derivatives (**4a-z**) (Scheme). The 1,2,4-triazin-5-one derivatives (**5a-z**), which may form by losing an alcohol molecule and then cyclizing through the dehydrohalogenation process, were not obtained. The purity of the synthesized compounds was checked by TLC in different solvents.

Spectral data analysis

The structures of the products (**4a-z**) were elucidated on the basis of analytical and spectral data; no further investigations concerning their optical purity and activity were performed.



Entry	Ar	R	X
a	Me	H	Cl
b	Me	Me	Cl
c	Me	$CHMe_2$	Cl
d	Me	CH_2Ph	Cl
e	Ph	H	H
f	Ph	Me	H
g	Ph	Me	Cl
h	Ph	$CHMe_2$	Cl
i	Ph	CH_2Ph	Cl
j	2-Naphthyl	H	H
k	2-Naphthyl	Me	H
l	2-Naphthyl	$CHMe_2$	H
m	2-Naphthyl	CH_2Ph	H

Entry	Ar	R	X
n	2-Naphthyl	Me	Cl
o	2-Naphthyl	H	Me
p	2-Naphthyl	Me	Me
q	2-Naphthyl	$CHMe_2$	Me
r	2-Naphthyl	CH_2Ph	Me
s	2-Furyl	H	Cl
t	2-Furyl	Me	Cl
u	2-Furyl	$CHMe_2$	Cl
v	2-Furyl	CH_2Ph	Cl
w	2-Thienyl	H	Cl
x	2-Thienyl	Me	Cl
y	2-Thienyl	$CHMe_2$	Cl
z	2-Thienyl	CH_2Ph	Cl

Scheme. Synthetic pathway for the preparation of the compounds (4a-z).

The IR spectra of the compounds (**4a-z**) exhibit a characteristic absorption band of NH at the 3380-3350 cm^{-1} region and a lactam C=O band at the 1690-1670 cm^{-1} region. Other absorptions were observed at 1660-1640 cm^{-1} (Ar-C=O) and 1610-1590 cm^{-1} (C=N) (experimental part). The ^{1}H-NMR spectra of the compounds (**4a-z**) showed a characteristic signal at 6.4-6.1 ppm for the NH protons of the 1,2,4-triazinone ring.

The ^{13}C-NMR spectra display the characteristic signals of the suggested structures. The signal of the carbonyl of the ring (lactam) resonates at about 163-159 ppm and the signal at about 140-139 ppm is attributed to C=N of the 1,2,4-triazinone ring. This assignment is in good agreement with literature data for azomethine carbons in 6-membered heterocycles.[15–17]

The ^{1}H- and ^{13}C-NMR spectral data of the synthesized compounds are presented in the experimental part.

In conclusion, the reaction of amidrazones **1** with α-haloesters **2** leads to the formation of 4,5-dihydro-1,2,4-triazin-6-ones (**4a-r**).

References

1. R.M. Abdel-Rahman, **Pak. J. Sci. Ind. Res. 30,** 490 (1987).
2. K.C. Joshi, A. Dandia and S. Khanna, **Indian J. Chem. 26**, 496 (1992).
3. K.C. Joshi, R. Jain, A. Dandia and K. Sharma, **Indian J. Chem. 28**, 698 (1989).
4. R.M. Abdel-Rahman, **Pharmazine 56**, 275 (2001).
5. R.M. Abdel-Rahman and M.S. Abdel-Malik, **Pak. J. Sci. Ind. Res. 33**, 142 (1990).
6. R.M. Abdel-Rahman, **Pharmaco 46**, 379 (1991).
7. J. Wiley and H.U.S. Richard, **U. S.** 358590; **Chem. Abstr. 98**, 1072143 v (1983).
8. B. Boehner, (Ciba-Geigy A.G.) **Eur. Pat.** (1986); **Chem. Abstr. 105**, 6522 e (1986).
9. M.Z. Badr, M.M. Aly, Z.H. Khalil and A.A. Attalla, **Indian J. Chem., Sect. B, 21**, 115 (1982).
10. G. Pitet, F. Court and Fr. Demande, **FR** 2500830; **Chem. Abstr. 98**, 72140 s (1983).
11. Z. El-Gendy and R.M. Abdel-Rahman, **Indian J. Heterocyclic Chem.** 4, 293 (1995).
12. Z. El-Gendy, J.M. Morsy, H.A. Allimony, W.R. Abdel-Monem and R. M. Abdel- Rahman, **Pharmazine 56**, 376 (2001).
13. R.M. Abdel-Rahman, M. Seada, M. Fawzy and M. El-Baz, **Pharmazine 49**, 729 (1994).
14. A.S. Shawali, H.M. Hassaneen, A.A. Fahmi and N.M. Abu-Nada, **Phosphorous, Sulfur and Silicon 53**, 259 (1990).
15. A.S. Ferwanah, A.M. Awadallah, E.A. El-Sawi and H.M. Dalloul, **Synth. Commun. 33**, 1245-1253 (2003).
16. H.M. Dalloul and P.H. Boyle, **Heterocycl. Commun. 9**, 507 (2003).
17. M.M. El-Abadelah, A.Q. Hussein and B.A. Thaher, **Heterocycles, 32**, 1879 (1991).
18. A.M. Awadallah, A.S. Ferwanah, E.A. El-Sawi and H.M. Dalloul, **Heterocycl. Commun. 8,** 369 (2002).