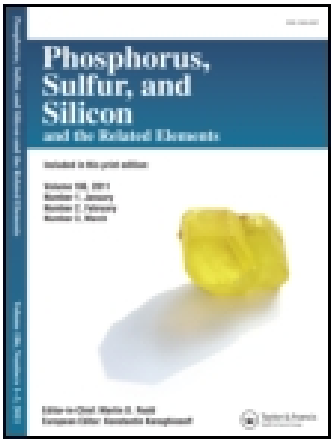

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The Synthesis of Some New Sulfur-Bearing Various Heterocyclic Systems Derived from Asymmetrical N,N′-Disubstituted Thiourea Derivatives

Hosam Saad [a]

[a] Chemistry Department, Faculty of Science , Zagazig University , Zagazig, Egypt

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The Synthesis of Some New Sulfur-Bearing Various Heterocyclic Systems Derived from Asymmetrical *N,N′*-Disubstituted Thiourea Derivatives

Hosam Saad
Chemistry Department, Faculty of Science, Zagazig University, Zagazig, Egypt

The heterocyclization of an asymmetrical N,N′*-disubstituted thiourea (**1a–d**) in ring closure reactions with Br_2/AcOH, ethyl chloroacetate, diethyl oxalate, diethyl malonate, and hydrazine hydrate led to the direct formation of sulfur-bearing various heterocyclic systems (**2–8**) in which the thiaenolization is toward the aryl group. The synthetic work and reactivity investigations have been well supported by standard modern spectroscopic techniques (IR, ^1H NMR, ^{13}C NMR, mass spectrum, and microanalysis).*

Keywords Asymmetrical *N,N′*-disubstituted thiourea; benzo[d]thiazole; thiazolidin-4-one; thioxoimidazol-4,5-dione

INTRODUCTION

One of the major interests of sulfur-bearing asymmetrical disubstituted thioureas is the design, synthesis, and biocidal evaluation of various heterocyclic systems.[1–4] In extension of our work in this area,[5–7] the principal objective of the present work is to propose further analogues of disubstituted thioureas followed by ring closure reactions via treatment with some reagents, which may enhance biocidal effects.

CHEMISTRY

Thioureas and substituted thiourea play an important role in the formation of sulfur-containing and bearing various heterocyclic systems, which have been a broad spectrum as biocidal effects for the treatment of some diseases.[8] Thus, the addition of the nitrogen nucleophile of *p*-toluidine, α-naphthylamine, anthranilic acid, and 4-aminoantipyrine

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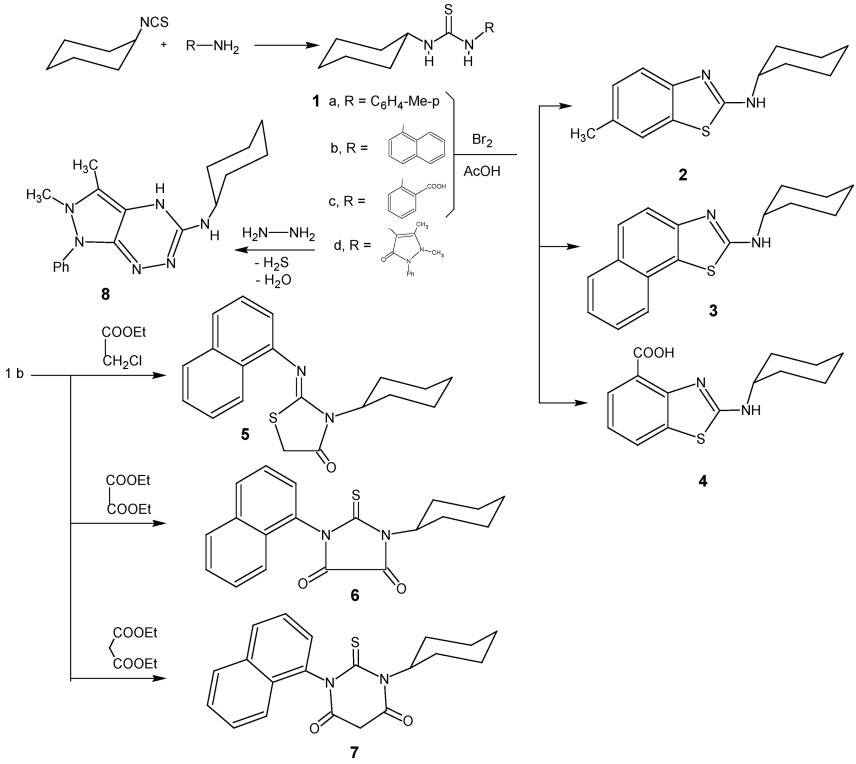
Address correspondence to Hosam Saad, Zagazig University, Chemistry Department, Faculty of Science, Zagazig, Egypt. E-mail: h_saadzag@yahoo.com

to an electrophilic carbon of cyclohexyl isothiocyanate in dry dioxane afforded the starting materials *N*,*N*′-disubstituted thioureas (**1a–d**).

The oxidation of compounds **1a–c** via refluxing with Br_2 in acetic acid produced 2-cyclohexylamino-6-methylbenzo[d]thiazole (**2**), 2-cyclohexylaminonaphtho[2,1-d][1,3]thiazole (**3**), and 2-(cyclohexylamino)-1,3-benzothiazole-4-carboxylic acid (**4**), respectively (Scheme 1).



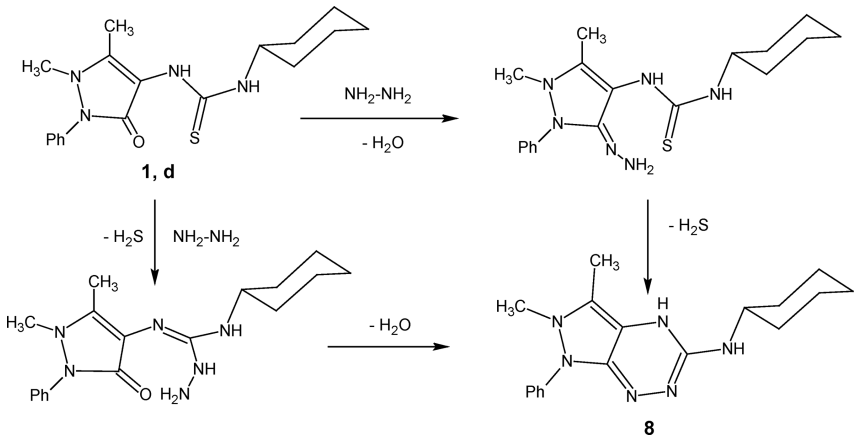
SCHEME 1

On the other hand, ring closure reactions of asymmetrical *N*,*N*′-disubstituted thiourea **1** were deduced from refluxing with oxygen and nitrogen reagents.[1] Thus, warming compound **1b** with ethyl chloroacetate and/or diethyl oxalate in basic media yielded 3-cyclohexyl-2-(1-naphthylimino)-1,3-thiazolidin-4-one (**5**) and 1,3-disubstituted-2-thioxoimidazol-4,5-dione (**6**), respectively.

Thiobarbituric acid derivatives and related compounds have been reported for the treatment of some diseases.[9,10] This encouraged us to synthesize more of their derivatives via refluxing compound **1b** with diethyl

malonate in sodium ethoxide to furnish 1-cyclohexyl-3-(1-naphthyl)-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione (**7**).

Among the full heterocyclization of compound **1d**, on refluxing with hydrazine hydrate (99%) in abs. ethanol resulted in cyclization affording 5-cyclohexylamino-2,3-dimethyl-1-phenyl-2,4-dihydro-1*H*-pyrazolo[4,3-*e*][1,2,4]triazine (**8**) (Scheme 1). The formation of compound **8** may be proceeded via the initial formation of a hydrazono derivative followed by the loss of H_2S, affording the final pyrazolotriazine derivative (Scheme 2).

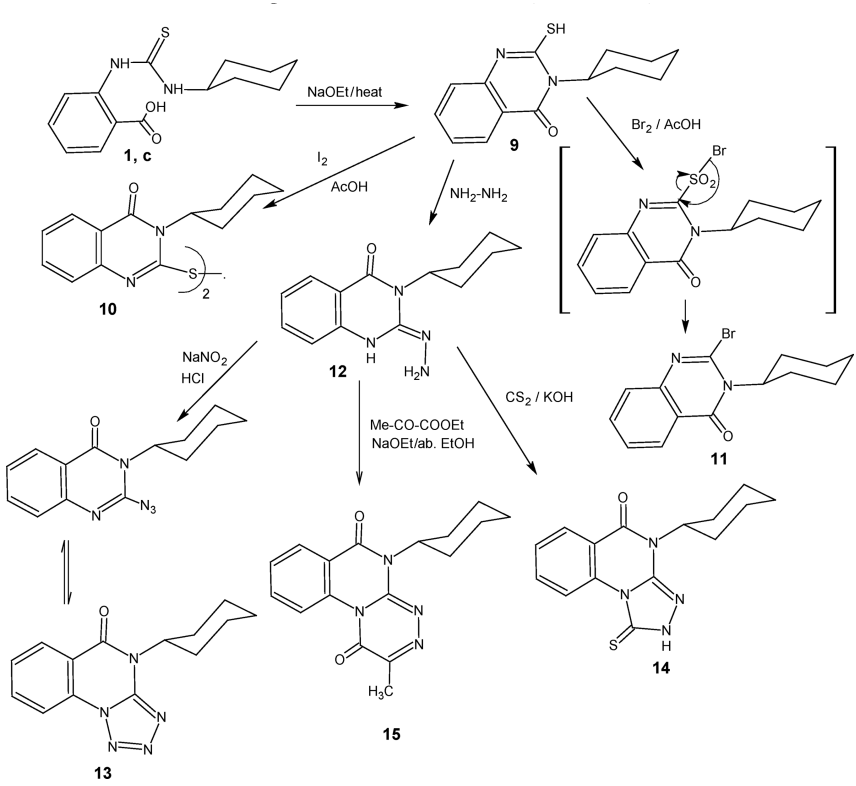


SCHEME 2

The reactivity of the carboxylic group in the ortho position to the thiourea moiety prompted us to synthesize 2-thioxoquinazolin-4-one.[11] Thus, refluxing compound **1c** with sodium ethoxide produced 3-cyclohexyl-2-mercaptoquinazolin-4(3*H*)-one (**9**). Compound **9** was used as starting material for further functionalization and heterocyclization; thus, the oxidation with I_2 solution produced the disulphide **10**. Also, compound **9** was reacted with Br_2 in glacial acetic acid to give 2-bromo-3-cyclohexylquinazolin-4(3*H*)-one (**11**). The bromination of compound **9** may proceed through the formation of qunazoline-2-sulphonyl bromide, which liberates SO_2 to give the final product (Scheme 3).

The full fused heterocyclic system tetrazoloquinazoline **13** and/or 3-thioxotriazoloquinazolinone **14** have been obtained from the hydrazinolysis of compound **9** using hydrazine hydrate-ethanol to give the hydrazono derivative **12** followed by diazodization using $NaNO_2$/HCl and/or worming with CS_2-sodium ethoxide.

The cyclocondensation of the 2-hydrazino derivative **12** with ethyl pyruvate afforded triazinoquinazoline **15** (Scheme 3).



SCHEME 3

EXPERIMENTAL

All experiments were carried out using anhydrous solvents. M.p.s are uncorrected. IR (KBr) was carried out on perkin–Elmer FTIR1600 spectrometer. ^{1}H and ^{13}C NMR (295K, internal reference TMS), was carried out on Brucker AC–250 spectrometer, and mass spectra were recorded on a gas chromatographic GCMSqp 1000ex Schimadzu instrument at 70 eV.

The Preparation of Asymmetrical *N,N′*-Disubstituted Thioureas 1a–d: General Procedure

A mixture of cyclohexyl isothiocyanate (10 mmol) and appropriate primary amines, such as *p*-toluidine, α-naphthylamine, anthranilic acid, and 4-aminoantipyrine (10 mmol), in dry dioxane (20 mL) were refluxed for 2 h, cooled, and evaporated under vacuum. The solid obtained was filtered off and crystallized from a suitable solvent.

N-Cyclohexyl-*N*′-*p*-tolylthiourea (1a)

Crystallized with ethanol to give colorless crystals (86% yield); m.p. = 100–102°C. IR (KBr): 1237 (NCSN), 1610 (C=N), and (br) 3270 cm^{-1} (NH). ^1H NMR: (DMSO-d_6) δ = 1.07–2.05 (m, 10 H, cyclohexyl), 2.35 (s, 3H, CH_3), 4.26 (m, 1H, N–C<u>H</u>–), 5.92 (br, 1H, NH-cyclohexyl), 7.08 (d, J = 8.2 Hz, 2H, Ar-H), 7.22 (d, J = 8.2 Hz, 2H, Ar-H), 8.40 (s, 1H, <u>H</u>N-aryl), ^{13}C NMR (DMSO-d_6): δ = 21.0, 24.7, 25.4, 32.5, 53.7 (CH_3 and cyclohexyl), 125.1, 130.6, 133.6, 137.0 (Ar-C) and 178.9 (C=S).

Calcd. for $C_{14}H_{20}N_2S$ (248.39): C, 67.70; H, 8.12; N, 11.28; S, 12.91. Found: C, 67.64; H, 8.05; N, 11.24; S, 12.88.

N-Cyclohexyl-*N*′-1-naphthylthiourea (1b)

Crystallized with ethanol to give colorless crystals (80% yield); m.p. = 136–138°C. M^+ = 284, base peak m/e = 143, IR (KBr): 1266 (NCSN), 1625 (C=N), 3297 and 3367 cm^{-1} (2NH). ^1H NMR: (DMSO-d_6) δ = 0.90–1.92 (m, 10 H, cyclohexyl), 4.24 (m, 1H, N–C<u>H</u>–), 5.53 (br, 1H, NH-cyclohexyl), 7.28–8.01 (m, 7H, Ar-H), 8.50 (s, 1H, <u>H</u>N-aryl), ^{13}C NMR (DMSO-d_6): δ = 24.6, 25.2, 32.4, 53.9 (cyclohexyl), 122.7, 124.9, 125.8, 127.0, 127.2, 128.4, 128.7, 129.7, 131.8, 134.6 (Ar-C) and 179.8 (C=S).

Calcd. for $C_{17}H_{20}N_2S$ (284.42): C, 71.79; H, 7.09; N, 9.85; S, 11.27. Found: C, 71.68; H, 7.05; N, 9.84; S, 11.28.

N-Cyclohexyl-*N*′-(2-carboxyphenyl)-thiourea (1c)

Crystallized from ethanol to give colorless crystals (60% yield); m.p. = 189–191°C. IR (KBr): 1258 (NCSN), 1611 (C=N), 1672 (C=O) 3100, 3234 (2NH) and 3303 cm^{-1} (OH). ^1H NMR: (DMSO-d_6) δ = 1.12–1.92 (m, 10 H, cyclohexyl), 3.45 (m, 1H, N–C<u>H</u>–), 6.48–8.41 (m, 4H, Ar-H), 8.63 (s, 1H, <u>H</u>N-cyclohexyl), 9.81 (s, 1H, <u>H</u>N-aryl), 13.70 (br, 1H, OH acid), ^{13}C NMR: (DMSO-d_6): δ = 24.6, 25.2, 30.4, 49.2 (cyclohexyl), 120.4, 120.9, 131.2, 131.7, 131.8, 140.5 (Ar-C), 167.6, 170.2 (C=O and C=S).

Calcd. for $C_{14}H_{18}N_2O_2S$ (278.37): C, 60.41; H, 6.52; N, 10.06; S, 11.52. Found: C, 60.37; H, 6.50; N, 10.00; S, 11.46.

N-Cyclohexyl-*N*′-(2,5-dihydro-2,3-dimethyl-5-oxo-1-phenyl-1*H*-pyrazol-4-yl)thiourea (1d)

Crystallized from ethanol to give colorless crystals (70% yield); m.p. = 130–132°C. M^+ = 344, base peak m/e = 56, IR (KBr): 1248 (NCSN), 1615 (C=N), 1715 (C=O), 3103 and 3282 cm^{-1} (2NH). ^1H NMR: (DMSO-d_6) δ = 1.13–1.91 (m, 10 H, cyclohexyl), 2.15 (s, 3H, CH_3), 2.97 (s, 1H,

NH-cyclohexyl), 3.06 (s, 3H, N—CH_3), 4.08 (m, 1H, N—CH cyclohexyl), 7.29–7.49 (m, 5H, Ar-H), 8.12 (s, 1H, NH-aryl). ^{13}C NMR: (DMSO-d_6): δ = 10.9, 24.4, 25.2, 32.0, 35.7, 52.9 (cyclohexyl, CH_3, N-CH_3), 109.0, 124.1, 126.4, 128.9, 135.4, 152.3 (Ar-C), 162.1, 181.8 (C=O and C=S).

Calcd. for $C_{18}H_{24}N_4OS$ (344.47): C, 62.76; H, 7.02; N, 16.26; S, 9.31. Found: C, 62.70; H, 7.00; N, 16.22; S, 9.28.

The Cyclization of Asymmetrical *N,N′*-Disubstituted Thioureas 2, 3, and 4: General Procedure

Appropriate asymmetrical *N,N′*-disubstituted thioureas (10 mmol) were dissolved in glacial acetic acid (20 mL); and Br_2 was added (10 mmol) and the mixture was stirred for 3 h. The color of Br_2 disappeared, and a colorless precipitate was formed, which was filtered off and crystallized from a proper solvent.

2-Cyclohexylamino-6-methylbenzo[d]thiazole (2)

Crystallized from DMF to give colorless crystals (85% yield); m.p. = 173–175°C. M^+ = 246, base peak m/e = 164, IR (KBr): 3172 cm^{-1} (NH). ^{1}H NMR: (DMSO-d_6) δ = 1.23–2.09 (m, 10 H, cyclohexyl), 2.10 (s, 3H, CH_3), 4.43 (m, 1H, N—CH), 7.31 (d, J = 8.2 Hz, 1H, Ar-H), 7.44 (s, 1H, Ar-H), 7.50 (d, J = 8.4 Hz, 1H, Ar-H), 9.90 (br, 1H, NH). ^{13}C NMR: (DMSO-d_6): δ = 21.0, 21.3, 24.8, 31.9, 56.1 (cyclohexyl, CH_3), 114.7, 121.6, 122.5, 128.4, 129.6, 135.2, 176.5 (Ar-C and C=N).

Calcd. for $C_{14}H_{18}N_2S$ (246.37): C, 68.25; H, 7.36; N, 11.37; S, 13.01. Found: C, 68.21; H, 7.35; N, 11.33; S, 12.95.

2-Cyclohexylaminonaphtho[2,1-d][1,3]thiazole (3)

Crystallized from DMF to give colorless crystals (88% yield); m.p. = 165–167°C. IR (KBr): 3218 cm^{-1} (NH). ^{1}H NMR: (DMSO-d_6) δ = 1.34–2.13 (m, 10H, cyclohexyl), 3.85 (m, 1H, N—CH), 7.61–8.26 (m, 6H, Ar-H), 8.47 (br, 1H, NH). ^{13}C NMR: (DMSO-d_6): δ = 23.9, 24.7, 31.6, 57.1, (cyclohexyl), 118.4, 121.8, 122.4, 122.9, 127.8, 128.2, 128.4, 130.4, 131.8, 133.6, 172.7 (Ar-C and C=N).

Calcd. for $C_{17}H_{18}N_2S$ (282.40): C, 72.30; H, 6.42; N, 9.92; S, 11.35 Found: C, 72.26; H, 6.38; N, 9.88; S, 11.31.

2-(Cyclohexylamino)-1,3-benzothiazole-4-carboxylic Acid (4)

Crystallized from DMF to give colorless crystals (83% yield); m.p. = 220–222°C. IR (KBr): 1698 (C=O), 3359 (NH), 3468 cm^{-1} (OH). ^{1}H

NMR: (DMSO-d_6) δ = 1.26–1.95 (m, 10 H, cyclohexyl), 3.58 (m, 1H, N—C<u>H</u>), 7.03 (d, J = 8.9, 1H, Ar-H), 7.49 (d, J = 8.9, 1H, Ar-H), 7.70 (m, 1H, Ar<u>H</u>), 7.89 (s, 1H, N<u>H</u>), 12.10 (s, 1H, O<u>H</u>), ^{13}C NMR: (DMSO-d_6): δ = 23.9, 24.7, 31.6, 57.1, (cyclohexyl), 104.8, 110.5, 113.2, 132.9, 138.2, 146.9 (Ar-C), 167.8, 171.7 (C=N and C=O).

Calcd. for $C_{14}H_{16}N_2O_2S$ (276.35): C, 60.85; H, 5.84; N, 10.14; S, 11.60. Found: C, 60.81; H, 5.80; N, 10.12; S, 11.53.

3-Cyclohexyl-2-(1-naphthylimino)-1,3-thiazolidin-4-one (5)

To a mixture of **1b** (10 mmol) and sodium ethoxide (prepared by dissolving 0.23 g of sodium metal in 20 mL of abs. ethanol), ethyl chloroacetate (10 mmol) was added, and the reaction mixture was refluxed for 4 h, diluted with water, and acidified. The solid thus separated was filtered and crystallized from ethanol to give colorless crystals (76% yield); m.p. = 210–212°C. M^+ = 324, base peak m/e = 163, IR (KBr): 1676 cm^{-1} (CO). ^{1}H NMR: (DMSO-d_6) δ = 1.15–1.93 (m, 10 H, cyclohexyl), 4.15 (m, 1H, N—C<u>H</u> cyclohexyl), 4.39 (s, 2H, CH_2), 6.99–7.91 (m, 7H, Ar-H), ^{13}C NMR: (DMSO-d_6): δ = 24.2, 24.4, 31.9, 52.5, 61.9, (cyclohexyl, CH_2), 117.7, 121.4, 122.7, 122.9, 124.7, 125.4, 128.0, 128.4, 133.8, 134.9, (Ar-C), 179.5, 181.1 (C=N and C=O).

Calcd. for $C_{19}H_{20}N_2OS$ (324.44): C, 70.34; H, 6.21; N, 8.63; S, 9.88. Found: C, 70.29; H, 6.18; N, 8.58; S, 9.84.

1-Cyclohexyl-3-(1-naphthyl)-2-thioxoimidazolidin-4,5-dione (6)

To a mixture of **1b** (10 mmol) and sodium ethoxide (prepared by dissolving 0.23 g of sodium metal in 20 mL of abs. ethanol), diethyl oxalate (10 mmol) was added, and the reaction mixture was refluxed for 4 h, diluted with water, and acidified with hydrochloric acid (3 mL, 60%). The solid thus separated was filtered and crystallized from ethanol to give colorless crystals (76% yield); m.p. = 115–117°C. IR (KBr): 1447 (C=S), 1660, 1670 cm^{-1} (2CO). ^{1}H NMR: (DMSO-d_6)δ = 1.06–1.88 (m, 10 H, cyclohexyl), 3.56 (m, 1H, N—C<u>H</u> cyclohexyl), 7.34–8.54 (m, 7H, Ar—H), ^{13}C NMR: (DMSO-d_6): δ = 24.2, 25.2, 32.9, 47.6, (cyclohexyl), 115.7, 121.2, 121.6, 125.2, 125.3, 125.6, 125.8, 125.9, 126.0, 133.6, 153.3, 154.6, 181.8 (Ar—C, 2C=O, and C=S).

Calcd. for $C_{19}H_{18}N_2O_2S$ (338.42): C, 67.43; H, 5.36; N, 8.28; S, 9.47. Found: C, 67.38; H, 5.35; N, 8.26; S, 9.46.

1-Cyclohexyl-3-(1-naphthyl)-2-thioxodihydropyrimidine-4,6(1*H*,5*H*)-dione (7)

To a mixture of **1b** (10 mmol) and sodium ethoxide (prepared by dissolving 0.23 g of sodium metal in 20 mL of abs. ethanol), diethyl malonate

(10 mmol) was added, and the reaction mixture was refluxed for 4 h, diluted with water, and acidified with hydrochloric acid (3 mL, 60%). The solid thus separated was filtered and crystallized from ethanol to give colorless crystals (76% yield); m.p. = 138–140°C. IR (KBr): 1490 (C=S), 1660, 1670 cm^{-1} (2CO). ^1H NMR: (DMSO-d_6): δ = 0.90–1.96 (m, 10 H, cyclohexyl), 4.26 (m, 1H, N—C<u>H</u> cyclohexyl), 5.53 (s, 2H, CH_2), 7.27–8.33 (m, 7H, Ar—H), ^{13}C NMR: (DMSO-d_6): δ = 24.6, 24.7, 25.2, 32.4, 32.6, (cyclohexyl, CH_2), 122.7, 125.0, 125.7, 127.0, 127.3, 128.4, 128.5, 128.8, 129.7, 131.7, 134.6, 179.7, 179.8 (Ar—C, 2C=O, and C=S).

Calcd. for $C_{20}H_{20}N_2O_2S$ (352.45): C, 68.16; H, 5.72; N, 7.95; S, 9.10. Found: C, 68.14; H, 5.70; N, 7.95; S, 9.07.

5-Cyclohexylamino-2,3-dimethyl-1-phenyl-2,4-dihydro-1*H*-pyrazolo[4,3-*e*][1,2,4]triazine (8)

A mixture of **1d** (10 mmol) and hydrazine hydrate (15 mmol) in ethanol (20 mL) was refluxed for 2 h. The precipitate obtained upon cooling was collected and crystallized from ethanol to give colorless crystals (63% yield); m.p. = 240–242°C. IR (KBr): 3103 and 3281 cm^{-1} (2NH). ^1H NMR: (DMSO-d_6) δ = 1.12–1.98 (m, 10 H, cyclohexyl), 2.15 (s, 3H, CH_3), 3.06 (s, 3H, N—CH_3), 4.09 (m, 1H, NH—CH), 7.15–7.67 (m, 5H, Ar—H), 8.12 (br, 2H, 2NH). ^{13}C NMR: (DMSO-d_6): δ = 10.9, 24.4, 25.2, 32.0, 35.7, 52.9 (cyclohexyl, CH_3, N—CH_3), 109.1, 124.1, 126.4, 128.9, 135.4, 152.3, 162.1, 181.8 (Ar—C and 2C=N).

Calcd. for $C_{18}H_{24}N_6$ (324.42): C, 66.64; H, 7.46; N, 25.90. Found: C, 66.59; H, 7.44; N, 25.87.

3-Cyclohexyl-2-mercaptoquinazolin-4(3*H*)-one (9)

A mixture of appropriate **1c** (10 mmol) and (10 mmol) sodium ethoxide (prepared by dissolving 0.23 g of sodium metal in 20 mL of abs. ethanol) was heated under reflux for 30 min. The precipitate formed after cooling and acidification with hydrochloric acid (3 mL, 60%) was collected and crystallized from ethanol to give colorless crystals (72% yield); m.p. = 220–222°C. IR (KBr): 1670 (CO), 2580 cm^{-1} (SH). ^1H NMR: (DMSO-d_6) δ = 1.08–2.46 (m, 10H, cyclohexyl), 3.50 (s, 1H, SH), 4.75 (m, 1H, N—CH of cyclohexyl), 7.15–7.90 (m, 4H, Ar—H), ^{13}C NMR (DMSO-d_6): δ = 25.1, 26.0, 28.5, 52.9 (cyclohexyl), 114.3, 114.7, 122.2, 127.4, 134.6, 139.5, 150.2, 162.3 (Ar—C, C=N, and C=O).

Calcd. for $C_{14}H_{16}N_2OS$ (260.35): C, 64.58; H, 6.19; N, 10.76; S, 12.32. Found: C, 64.55; H, 6.18; N, 10.73; S, 12.30.

Bis[3-cyclohexylquinazolin-4(3*H*)-one]-2-disulphide (10)

To a solution of **9** (10 mmol) in acetic acid (20 mL), iodine (10 mmol, 0.25 g in 10 mL of acetic acid) was added portionwise with stirring; the solid formed was collected by filtration and crystallized from ethanol to give yellow crystals (66% yield); m.p. = 263–265°C. $M^+ = 518$, base peak m/e = 280, IR (KBr): 1638 (N=C), 1680, 1690 cm^{-1} (2CO). ^1H NMR: (DMSO-d_6) $\delta = 1.09–2.46$ (m, 20H, 2cyclohexyl), 4.74 (m, 2H, N—C<u>H</u> of cyclohexyls), 7.14–7.90 (m, 8H, of 2Ar—H).

Calcd. for $C_{28}H_{30}N_4O_2S_2$ (518.69): C, 64.84; H, 5.83; N, 10.80; S, 12.36. Found: C, 64.82; H, 5.81; N, 10.79; S, 12.35.

2-Bromo-3-cyclohexylquinazolin-4(3*H*)-one (11)

To a solution of **9** (10 mmol) in acetic acid (20 mL), bromine (10 mmol, 0.16 g in 10 mL of acetic acid) was added portionwise with stirring; the solid formed was collected by filtration and crystallized from ethanol to give colorless crystals (83% yield); m.p. = 248–250°C. $M^{+2} = 309$, base peak m/e = 163, IR (KBr): 1643 (N=C), 1718 cm^{-1} (CO). ^1H NMR (DMSO-d_6): $\delta = 1.28–2.11$ (m, 10H, cyclohexyl), 3.38 (m, H, N—C<u>H</u> of cyclohexyl), 7.14–7.90 (m, 4H, Ar—H).

Calcd. for $C_{14}H_{15}BrN_2O$ (307.19): C, 54.74; H, 4.92; Br, 26.01; N, 9.12. Found: C, 54.72; H, 4.90; Br, 26.00; N, 9.09.

3-Cyclohexyl-2-hydrazono-2,3-dihydroquinazolin-4(1*H*)-one (12)

A mixture of **9** (10 mmol) and hydrazine hydrate 99% (10 mmol) in ethanol (30 mL) was refluxed for 3 h. The solid thus separated after cooling was collected by filtration and crystallized from ethanol to give colorless crystals (64% yield); m.p. = 268–270°C. IR (KBr): 1639 (C=N), 1715 (CO), 3132, 3220, 3286 cm^{-1} (NH and NH_2). ^1H NMR: (DMSO-d_6) $\delta = 1.10–2.51$ (m, 10H, cyclohexyl), 3.38 (s, 2H, NH_2), 4.74 (m, 1H, N—C<u>H</u> of cyclohexyl), 7.15–7.88 (m, 4H, Ar—H), 11.31 (br, 1H, NH).

Calcd. for $C_{14}H_{18}N_4O$ (258.32): C, 65.09; H, 7.02; N, 21.69. Found: C, 65.05; H, 7.00; N, 21.65.

4-Cyclohexyltetrazolo[1,5-*a*]quinazolin-5(4*H*)-one (13)

An aqueous solution of sodium nitrite (0.19 g, 2.79 mmol) in distilled water (2 mL) was added to a solution of **12** (10 mmol) in distilled water (5 mL) with stirring in an ice bath. On addition of glacial acetic acid (0.29 mL, 5.16 mmol) the solution turned dark red, and the

solid started to precipitate. Another molar equivalent of sodium nitrite (0.19 g, 2.79 mmol in 3 mL water) was added. The solid was filtered off, washed with water, and dried under vacuum to give a light orange solid, which crystallized from ethanol (10 mL), (60% yield); m.p. = 255–257°C. $M^+ = 269$, base peak m/e = 143, IR (KBr): 1639 (C=N), 1685 cm^{-1} (CO). ^1H NMR: (DMSO-d_6) δ = 1.16–2.52 (m, 10H, cyclohexyl), 4.73 (m, 1H, N—CH of cyclohexyl), 7.15–7.88 (m, 4H, Ar—H).

Calcd. for $C_{14}H_{15}N_5O$ (269.30): C, 62.44; H, 5.61; N, 26.01. Found: C, 62.40; H, 5.58; N, 25.97.

4-Cyclohexyl-1,2-dihydro-1-thioxo-[1,2,4]triazolo [4,3-a]quinazolin-5(4*H*)-one (14)

To a solution of potassium hydroxide (10%, 30 mL in ethanol), compound **12** (10 mmol) and carbon disulphide (10 mL) were added, and the reaction mixture was refluxed for 4 h, cooled, and poured into crushed ice-HCl (3 mL, 60%). The solid obtained was filtered off and crystallized from ethanol to give **14** (64% yield); m.p. = 234–236°C. IR (KBr): 1540 (C=S), 1638 (C=N), 1685 (CO), and 3220 cm^{-1} (NH). ^1H NMR: (DMSO-d_6) δ = 1.09–2.46 (m, 10H, cyclohexyl), 3.27 (s, 2H, NH_2), 4.74 (m, 1H, N—CH of cyclohexyl), 7.15–7.88 (m, 4H, Ar-H), 11.32 (br, 1H, NH).

Calcd. for $C_{15}H_{16}N_4OS$ (300.38): C, 59.98; H, 5.37; N, 18.65; S, 10.67. Found: C, 59.96; H, 5.35; N, 18.61; S, 10.62.

5-Cyclohexyl-2-methyl-1*H*-[1,2,4]triazino[4,3-*a*] quinazoline-1,6(5*H*)-dione (15)

A mixture of **12** (10 mmol) and ethyl pyruvate (10 mmol) in sodium ethoxide (20 mmol Na in 50 mL of abs. ethanol) was heated under reflux for 2 h, cooled, and poured into crushed ice. The solid obtained was filtered off and crystallized from ethanol (10 mL), (60 % yield); m.p. = 265–267°C. $M^+ = 310$, base peak m/e = 275, IR (KBr): 1638 (C=N), 1685 and 1699 cm^{-1} (2CO). ^1H NMR: (DMSO-d_6)δ = 1.16–2.51 (m, 10H, cyclohexyl), 3.39 (s, 3H, CH_3), 4.73 (m, 1H, N—CH of cyclohexyl), 7.14–7.90 (m, 4H, Ar—H).

Calcd. for $C_{17}H_{18}N_4O_2$ (310.35): C, 65.79; H, 5.85; N, 18.05. Found: C, 65.74; H, 5.80; N, 18.02.

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