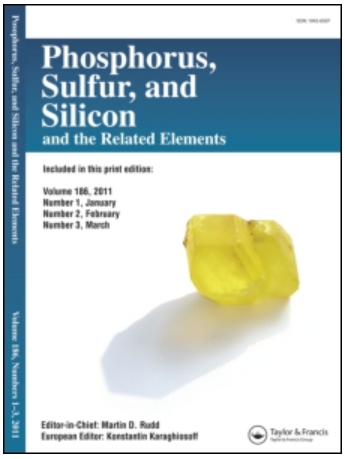

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Phthalazinone in Heterocyclic Synthesis: Synthesis of Some s-Triazole, s-Triazolothiadiazine, s-Triazolothiadiazine, and s-Triazolothiadiazole Derivatives as Pharmaceutical Interest

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PHTHALAZINONE IN HETEROCYCLIC SYNTHESIS: SYNTHESIS OF SOME s-TRIAZOLE, s-TRIAZOLOTHIADIAZINE, s-TRIAZOLOTHIADIAZINE, AND s-TRIAZOLOTHIADIAZOLE DERIVATIVES AS PHARMACEUTICAL INTEREST

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*1(2*H*)-Oxophthalazine-2-acetic acid ethyl ester was allowed to react with various reagents under different conditions to yield compounds 2-[(4-substituted-5-mercaptotriazol-3-yl) methyl]-1(2*H*)-oxophthalzines **5** and **7** which acted as starting materials for the preparation of some new s-triazolo[5,1-*b*][1,3]thiazine (**8**), s-triazolo[3,4-*b*][1,3,4]thiadiazine **9**,**12**,**14**,**20**, and s-triazolo[3,4-*b*][1,3,4]thiadiazole **18**,**21** derivatives.*

Keywords: 1(2H)Phthalazinone,2,4-dichloroanthraquinone; bromomalononitrile

Some phthalazine derivatives exhibit potent antihypertensive,[1] antipyretic,[2] and tuberculostatic[3] activities. Various s-triazoles, s-triazolo[3,4-*b*][1,3,4]thiadiazoles, and thiadiazines have been reported to possess diveres biological activities such as antifungal,[4] antibacterial,[5] antiinflammatory,[6] and herpicidal.[7,8] Also, the arylazo group is known to be important in pormoting antinewplastic activity.[9] In view of the aforesaid versatile benefits and in connection with our previous efforts directed toward the facile synthesis of heterocyclic ring systems,[10–13] we aimed at incorporating the phthalazinone moiety into a variety of s-triazoles, s-triazolo[3,4-*b*][1,3,4]thiadiazoles, and arylazo-s-triazolo[3,4-*b*][1,3,4]thiadizine moieties to obtain new

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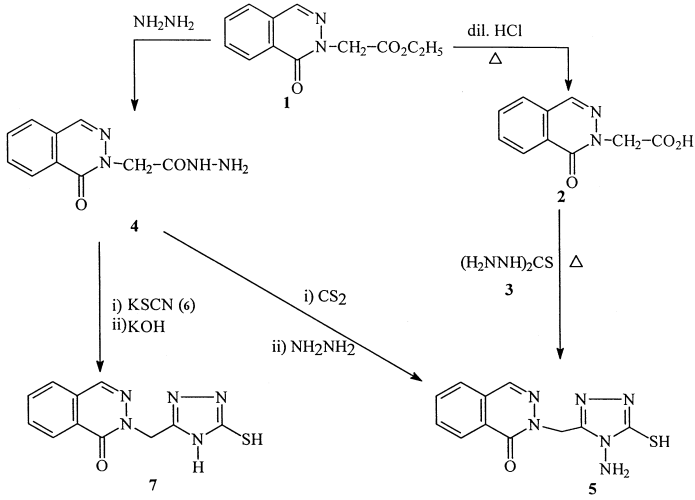
heterocyclic compounds with expected wide spectrum of potential applications.

The key precursor 1(2*H*)-oxophthalazin-2-acetic acid ethyl ester (**1**) was prepared according to the reported method.[14] Compound **1** underwent hydrolysis with HCl and hydrazinolysis with hydrazine hydrate and gave 1(2*H*)-oxophthalazine-2-acetic acid derivatives **2** and **4** respectively. Structure **2** was confirmed on the basis of its ^{1}H NMR spectrum which revealed, in addition to the expected signals, the absence of the ester group. Now we discribe a facile one step synthesis 2-[(4-amino-5-mercapto-s-triazol-3-yl)methyl]-1(2*H*)-oxophthalazine (**5**) via reaction of **2** with equimolar amounts of thiocarbohydrazide **3** under fusion conditions. This method led to higher yields and shorter working times in comparison with the reported method[15] via reaction of **4** with carbon disulfide and hydrazine hydrate.

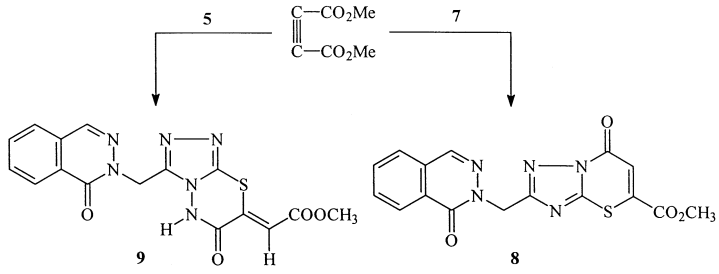


SCHEME 1

On the other hand, reaction of **4** with KSCN (**6**) in refluxing ethanol with drops of HCl gave the salt which was converted directly to **7** in poor yield by heating in aqueous KOH followed by acidification with HCl (Scheme 1).

Reaction of each **7** and **5** with dimethylacetylene dicarboxylate [DMAD] in refluxing methanol in the presence of a trace of acetic acid gave the corresponding 1:1 adducts. Such products were formulated as 2-[1(2*H*)-oxophthalizin-2-yl)methyl]-7-carbomethoxy-s-triazolo[5,1-*b*][1,3]thiazine derivatives **8** and **9** respectively. Both elemental and spectral data for **8** and **9** were consistent with the assigned structure.

Its assumed that the reaction proceeds via an addition followed by a cyclocondensation to yield **8** and **9**.

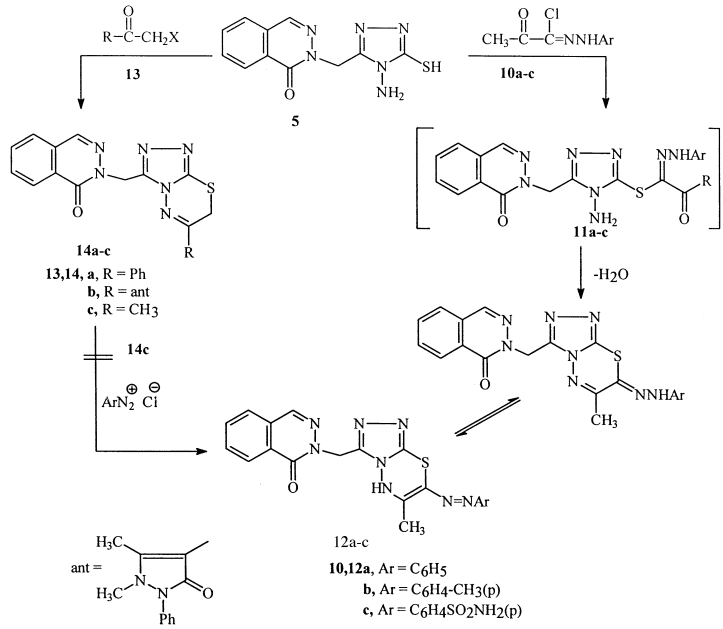


SCHEME 2

Similarly, compound **5** reacted with a variety of methyl N-aryl-2-oxopropanehydrazonyl chloride[10] (**10a–c**) in ethanol in the presence of $NaOC_2H_5$ to afford the respective 7-arylhydrazono-3 [(1(2*H*)-oxophthalazin-2-yl)methyl]-s-triazolo[3,4-*b*][1,3,4]thiadiazine **12** via an in situ dehydrative-cyclization of the initially formed thiohydrazonate **11a–c** under the reaction conditions (Scheme 2). The structures of **12a–c** were established on the basis of their elemental analysis and spectral data (MS, ^{1}H NMR, IR). Thus, the ^{1}H NMR of **12a–c** revealed in each case the presence of only one NH proton signal at δ 10.54, besides the expected signals. The molecular ion peak of **12a** [m/z = 416 (100%)] corresponded to the molecular formula $C_{20}H_{16}N_8OS$. The intermediate **5** condensed with alkyl halides such as 4-chloroacetyl antipyrine,[10] phenacylbromide, and chloroacetone **13a–c**, respectively, in refluxing ethanol in the presence of triethylamine as a catalyst to yield the corresponding s-triazolo[3,4-*b*][1,3,4]thiadiazines **14a–c** respectively. The analytical and spectral data of **14a–c** were in accordance with the proposed structures. The IR and ^{1}H NMR spectra of the dicycles show the absence of signals due to NH_2 or NH group, and the presence of signals in the region of δ 4.13–4.30 were attributed to the protons adjacent to sulfur atom, in addition to the expected signals. Coupling attempts of **14c** with aryldiazonium chlorides to obtain **12** were unsuccessful (Scheme 3).

The intermediate **5** reacted with arylisothiocyanates[14–18] **16a** in refluxing ethanol and **16b** in dry acetone to produce **18a**,**b**, respectively, via the nonisolable intermediate **17** by loss of one mole of H_2S. The proposed structure was in agreement with the analytical and spectral data (Scheme 4).

In addition, reaction of **5** with 2,3-dichloronaphthoquinone effected a cyclization to furnish the corresponding s-triazolo[3,4-*b*][1,3,



SCHEME 3

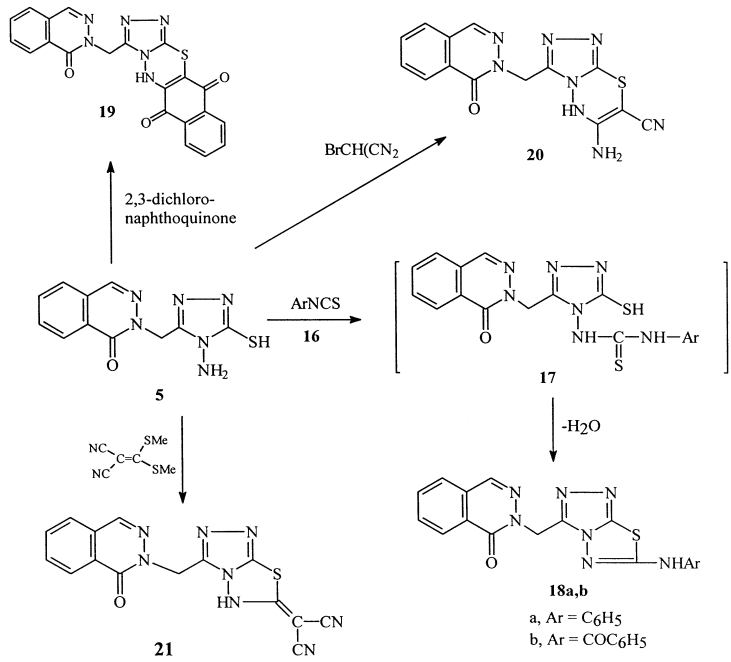
4]-thiadiazine derivative **19** via elimination of two mmol of HCl. Its IR spectrum showed bands at 3290 (NH), 1685 and 1668 (2 C=O). The mass spectrum of **19** revealed a molecular ion peak *m/z* 428 (M^+, 100%).

Furthermore, the triazolo[3,4-*b*][1,3,4]thiadiazine derivative **20** also was prepared by reaction of **5** with bromomalononitrile. Both elemental analysis and spectral data are consistent with the assigned structure. Thus, the IR spectrum showed bands at 3320, 3200 (NH, NH_2), and 2192 cm^{-1} (C≡N). The mass spectrum revealed *m/z* 338 (M^+, 100%) corresponding to the molecular formula $C_{14}H_{10}N_8OS$.

Finally, the dicyanotriazolothiadiazole derivative **21** was obtained by reaction of **5** with ketene dithioacetale.[11] The IR spectrum of **20** showed bands at 3380 (NH), 3219 (C≡N), and 1668 cm^{-1} (C=O) cm^{-1}. Its ^{1}H-NMR spectrum exhibited a singlet at δ 12.9 (NH) besides the expected signals.

Antimicrobial Activity

Preliminary biological activity screening of some synthesized compounds has been performed against microorganisms representing gram-positive bacteria (Bacillus subtills), gram-negative bacteria (E. coli), yeast (Candida albican), and fungi (Aspergillus niger), using the



SCHEME 4

bioassay technique of antibiotics[19] specified in U.S. pharmacopoeia. Ampicillin and chloramphenicol were used as standards. The results obtained are summarized in Table I.

EXPERIMENTALS

Melting points are uncorrected. IR spectra were recorded with a FTIR-8201 PC spectrophotometer Shimadzu. ^{1}H-NMR spectra were obtained

TABLE I Antimicrobial Activity of Some Newly Synthesized Compounds

Comp. no.	B. subtillis	E. coli	Candida albican	Asp. niger
7	+	+	+	−
12c	+	+	+	−
14a	+	+	+	+
19	+	+	+	+
Ampicillin	+	+	−	+
Chloramphenicol	+	+	−	+

on a Varian Germini 200 MHz spectrometer in DMSO-d_6 as solvent and TMS as an internal reference. Mass spectra were performed on a Shimadzu GCMS-QP-1000 EX using the direct inlet system and EI + QI MSLMRUPLR. Microanalysis were performed by the Microanalytical Unit at Cairo University. Thin layer chromatography was carried out on 5 × 20 cm sheets coated with silica gel GF 254 type 60, mesh size 50–250.

1(2*H*)-Oxophthalazine-2-acetic Acid (2)

A mixture of **1** (0.2 mmol) and HCl (200 ml, 5%) was refluxed for 2 h, and the solid obtained after cooling was filtered and recrystallized from acetic acid to yield pale yellow crystals, yield 80%, m.p. 248°C. IR: 3450 (OH), 1700 (C=O), 1658 (C=O) cm^{-1}. ^{1}HNMR (DMSO-d_6) δ 4.93 (s, 2H, CH_2), 7.41–7.93 (m, 5H, H—Ar + H4-phthalazine), 11.63 (br, 1H, OH) ppm.

MS: m/z 204 (M+, 45%). Anal. calcd. for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.92; N, 13.72; Found: C, 58.90; H, 3.80; N, 13.90.

1(2*H*)-Oxophthalazine-2-acetic Acid Hydrazide (4)

To a solution of 1-phthalazone-2-acetic acid ethyl ester (**1**), (0.01 mmol) in ethanol (30 ml) was added hydrazine hydrate (0.05 mmol). The reaction mixture was heated under reflux for 1 h. The precipitate obtained was filtered, dried, and recrystallized from DMF, to yield colorless crystals, m.p. 185°C; IR: 3300 (NH_2), 3160 (NH), 1685 (C=O), 16510 (C=O) cm^{-1}; MS: m/z = 218 (M^+, 82%), Anal. Calcd. for $C_{10}H_{10}N_4O_2$: C, 55.04; H, 4.58; N, 25.68. Found: C, 55.10; H, 4.60; N, 26.10.

2[(4-Amino-5-mercapto-s-triazol-3-yl)]methyl]-1(2*H*)-phthalazinone (5)

Method 1: The method of Reid and Heindel[15] was followed. The solid obtained was crystallized from ethanol, m.p. 243°C. IR: 3301 (NH_2), 2931 (CH_2), 2769 (SH), 1656 (CO) cm^{-1}; ^{1}H NMR (DMSO-*d*6) δ 5.10 (s, 2H, CH_2), 6.1 (s, 2H, NH_2), 7.2–7.91 (m, 5H, H—Ar + H4-phth) 13.46 (s, 1H, SH)ppm; MS: m/z 274 (62.4%, M^+), 132 (100), 89 (33). Anal. Calcd. for $C_{11}H_{10}N_6OS$: C, 48.17; H, 3.64; N, 30.65; S, 11.67. Found: C, 48.00; H, 3.60; N, 30.80; S, 11.60.

Method 2: A mixture of thiocarbohydrazide **3** (0.01 mmol) and **2** (0.01 mmol) was fused at 190–200°C in an oil bath for 15 min. After cooling, the reaction mixture was triturated with ethanol, and the solid

obtained was crystallized from ethanol to give a single product which was found to be identical in all aspects (m.p., mixed m.p. and IR data) with a product from Method 1.

2-[(5-Mercapto-s-triazol-3-yl)methyl]-1(2*H*)-phthalazinone (7)

A mixture of **4** (0.01 mmol) and KSCN **6** (0.05 mmol) was refluxed in 20 ml EtOH containing few drops of conc. HCl for 3 h. The precipitate formed was collected by filtration and dried to give the salt which was used without further purification. A mixture of the salt (0.01 mmol) and KOH (0.013 mmol) was refluxed in 25 ml of H_2O for 3 h. The reaction mixture was cooled and then acidified with HCl. The solid formed was collected and recrystallized from ethanol to give **7** (35%) as a white crystals, m.p. 280°C; IR (KBr): 3200 (NH), 1668 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 5.89 (s, 2H, CH_2), 7.84–7.97 (m, 5H, Ar—H + H4-phth.), 13.3 (s, 1H, NH), 13.91 (s, 1H, SH) ppm. Anal. Calcd. for $C_{11}H_9N_5OS$: C, 50.96; H, 3.47; N, 27.02. Found: C, 50.80; H, 3.60; N, 27.10.

2-[(1(2*H*)-Oxophthalazin-2-yl)methyl]-7-carbomethoxy-s-triazolo[5,1-*b*][1,3]thiazine-5-one (8)

To **7** (0.005 mmol) and DMAD (0.008 mmol) dissolved in methanol (30 ml) was added, a trace glacial acetic acid, and the mixture refluxed for 6 h. Upon cooling, a product separated out, was collected and recrystallized from methanol to give a white crystals, m.p. 193°C. IR: 1730 (C=O, ester), 1705 (C=O), 1663 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.72 (s, 3H, CH_3), 5.46 (s, 2H, CH_2), 7.1–8.01 (m, 6H, H—Ar + H4-phtha. + H-5-thiazole) ppm; MS: $m/z = 369$ (M^+, 80%). Anal. Calcd. for $C_{16}H_{11}N_5O_4S$: C, 52.03; H, 2.98; N, 18.97; S, 8.67. Found: C, 52.20; H, 3.10; N, 19.20; S 8.80.

2-[(1(2*H*)-Oxophthalazin-2-yl)methyl]-7-carbomethoxymethylene-s-triazolo[3,4-*b*][1,3]-thiadiazine-6-one (9)

This compound similarly prepared as mentioned in the previous experiment from **5** (0.005 mmol) and DMAD (0.008 mmol) and was isolated as white crystals, m.p. 265°C. IR: 3350 (OH), 1725 (C=O, ester), 1700 (C=O), 1662 (C=O) cm^{-1}; ^1H NMR (DMSO-d_6) δ: 3.81 (s, 3H, CH_3), 5.63 (s, 2H, CH_2), 7.10 (s, 1H, olefinic proton), 7.34–8.1 (m, 5H, H—Ar + H4-phtha.), 10.64 (s, 1H, NH) ppm; MS: $m/z = 384$ (M^+, 63%), Anal. Calcd.

for $C_{16}H_{12}N_6O_4S$: C, 50.00; H, 3.13; N, 21.87; S 8.33. Found: C, 50.10; H, 3.20; N, 22.10; S 8.60.

N-aryl-2-oxo-propanehydrazonyl Chlorides 10a—c were Prepared Accordance to Hassanien[10]

7-Arylhydrazono-3-[(1(2H)-oxophthalazin-2-yl)methyl]-6-methyl-5H-s-triazolo-[3,4-b][1,3,4]thiadiazines (12a–c)

General Procedure. To a mixture of equimolar quantities of the appropriate hydrazonyl chloride **10** and compound **5** (0.01 mmol) in absolute ethanol (30 ml) was added gradually triethyl amine (0.01 mmol). The reaction mixture was refluxed for 3–4 h. After cooling the solid product was filtered and recrystallized from EtOH.

7-Phenylhydrazino-3-[(1(2H)-oxophthalazin-2-yl)methyl]-6-methyl-5H-s-triazolo-[3,4-b][1,3,4]thiadiazines (12a)

M.p. 296.8°C. IR: 3178 (NH), 2954 (CH-aliph.), 1651 (CO) cm^{-1}; ^1H NMR (DMSO-*d*6) δ 1.2 (s, 3H, CH_3), 5.98 (s, 2H, CH_2), 7.10–7.89 (m, 10H, H—Ar + H4-phthala.), 10.5 (s, 1H, NH) ppm; MS: *m/z* 416 (100%, M^+), 283 (14%), 171 (25%), 132 (43.7%). Anal. Calcd. for $C_{20}H_{16}N_8OS$: C, 57.69; H, 3.84; N, 26.92; S, 7.69. Found: C, 57.50; H, 3.80; N, 27.10; S, 8.00.

7-(p-Tolyl)hydrazino-3-[(1(2H)-oxophthalazin-2-yl)-methyl]-6-methyl-5H-s-triazolo[3,4-b]-[1,3,4]thiadiazines (12b)

M.p. 305°C. IR: 3209 (NH), 2981 (CH-aliph.), 1655 (CO) cm^{-1}; ^1H NMR (DMSO-*d*6) δ 1.27 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 5.81 (s, 2H, CH_2), 7.01–7.84 (m, 9H, H—Ar + H4-phthal.), 10.61 (s, 1H, NH) ppm. Anal. Calcd. for $C_{21}H_{18}N_8OS$: C, 58.60; H, 4.18; N, 26.04; S, 7.44. Found: C, 58.30; H, 4.30; N, 25.80; S, 7.60.

7-(p-Sulphonamidophenyl)hydrazino-3-[(1(2H)-oxophthalazin-2-yl)methyl]-6-methyl-5H-s-triazolo[3,4-b]-[1,3,4]thiadiazines (12c)

M.p. 290°C. IR: 3302 (SO_2NH_2), 3180 (NH), 1656 (CO) cm^{-1}; ^1H NMR (DMSO-*d*6) δ 1.34 (s, 3H, CH_3), 5.91 (s, 2H, CH_2), 7.01–7.98 (m, 11H, H—Ar + SO_2NH_2 + H-4-phthala.), 10.63 (s, 1H, NH) ppm; MS: *m/z* (495, 100%), 418 (26%), 289 (30%). Anal. Calcd. for $C_{20}H_{17}N_9O_3S_2$: C, 48.48; H, 3.43; N, 25.45; S, 12.92. Found: C, 48.70; H, 3.60; N, 25.10; S, 13.20.

3-[(1(2*H*)-Oxophthalazin-2-yl)Methyl]-6-substituted-7*H*-s-triazolo[3,4-*b*][1,3,4]thiadiazines (14a—c)

A mixture of **5** (0.01 mmol), proper α-haloketones **13a–c** (0.01 mmol), and fused potassium carbonate (0.04 mmol) in absolute ethanol (80 ml) was refluxed for 8–10 h. After the removal of EtOH under reduced presseure, the resulting solid was washed with water, filtered, and recrystallized from EtOH.

3-[(1(2H)-Oxophthalazin-2-yl)Methyl]-6-phenyl-7H-s-triazolo[3,4-b][1,3,4]thiadiazines (14a)

M.p. 258°C. IR: 2981 (CH-aliph.), 1666 (C=O) 726 (C—S—C) cm^{-1}; ^1H NMR (DMSO-d_6) δ 4.39 (s, 2H, CH_2), 5.81 (s, 2H, CH_2), 7.41–8.48 (m, 10H, Ar—H) ppm; MS: *m/z* 374 (100%, M^+), 272 (24%), 216 (13%), 132 (77%), 77 (99.1%). Anal. Calcd. for $C_{19}H_{14}N_6OS$: C, 60.96; H, 3.74; N, 22.45; S, 8.55. Found: C, 61.30; H, 3.80; N, 22.50; S, 9.10.

3-[(1(2H)-Oxophthalazin-2-yl)Methyl]-6-(antipyrin-4yl)-7H-s-triazolo[3,4-b][1,3,4]thiadiazines (14b)

M.p. 315°C. IR: 2988 (CH-aliph.), 1665, 1657 (2CO) cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.36 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 4.13 (s, 2H, CH_2), 5.95 (s, $2H_2$, CH_2) 7.61–8.10 (m, 10H, H—Ar + H4-phth.) ppm. Anal. Calcd. for $C_{24}H_{20}N_8O_2S$: C, 59.50; H, 4.13; N, 23.14; S, 6.61. Found: C, 59.60; H, 4.30; N, 23.30; S, 6.70.

3-[(1(2H)-Oxophthalazin-2-yl)Methyl]-6-methyl-7H-s-triazolo[3,4-b][1,3,4]thiadiazines (14c)

M.p. 229°C. IR: 2980, 2895 (CH-aliph.), 1658, (C=O) cm^{-1}; ^1H-NMR (DMSO-*d*6) δ 1.12 (s, 3H, CH_3), 4.31 (s, 2H, CH_2), 5.64 (s, 2H, CH_2), 7.1–7.93 (m, 5H, H—Ar + H4-phth.). MS: *m/z* 312 (100%). Anal. Calcd. for $C_{14}H_{12}N_6OS$: C, 53.84; H, 3.84; N, 26.92; S, 10.25. Found: C, 54.10; H, 4.00; N, 27.10; S, 9.90.

6-Phenylamino-3-[(1(2*H*)-oxophthalazin-2-yl)methyl]-s-triazolo[3,4-*b*][1,3,4]thiadiazole (18a)

A mixture of **5** (0.01 mmol), arylisothiocyanates **16** (0.01 mmol) and absolute ethanol (30 ml) was refluxed for 7 h. The solid so formed was collected and crystallized from ethanol. m.p. 180°C. IR: 3425 (NH), 3047 (H—Ar), 1660 (C=O) cm^{-1}. ^1H NMR (DMSO-*d*6) δ 5.86 (s, 2H, CH_2), 7.61–7.98 (m, 10H, H—Ar + H4-phtha), 10.61 (s, 1H, NH) ppm; MS *m/z*: 375 (100%), 245 (89%), 118 (43%), 77 (49.7%). Anal. Calcd. for

$C_{18}H_{13}N_7OS$: C, 57.60; H, 3.46; N, 26.13; S, 8.53. Found: C, 57.90; H, 3.40; N, 26.30; S, 8.80.

6-Benzoylamino-3-[(1(2*H*)-oxophthalazin-2-yl)methyl]-s-triazolo[3,4-*b*][1,3,4]thiadiazole (18b)

To a solution of benzoylisothiocyanate [prepared from (1.5 ml, 0.01 mmol) benzoyl chloride, and (0.98 g, 0.01 mmol) potassium thiocyanate in dry acetone in situ] was added (0.01 mmol) of compound **5**, after boiling for 2 h, the reaction mixture was cooled, the solid was separated, and crystallized from ethanol to give pale yellow crystals, m.p. 193–5°C. IR: 3278 (NH), 1695, 1670 (2C=O) cm^{-1}; ^1H NMR (DMSO-*d*6) δ 5.69 (s, 2H, CH_2), 7.01–7.89 (m, 10H, H—Ar + H4-phtha), 12.5 (s, 1H, NH) ppm; MS: *m/z* 403 (100%), 217 (24%), 77 (43%). Anal. Calcd. for $C_{19}H_{13}N_7O_2S$: C, 56.57; H, 3.22; N, 24.31; S, 7.94. Found: C, 56.80; H, 3.10; N, 24.30; S, 8.10.

3-[(1(2*H*)-Oxophthalazin-2-yl)methyl]-6,11-dioxo-5H-naphtho[2,3-e]-s-triazolo[3,4-*b*][1,3,4]thiadiazine (19)

A mixture of **5** (0.01 mmol) and 2,3-dichloronaphthoquinone (0.01 mmol) in dimethylformamide (20 ml) containing (0.01 mmol) of triethylamine was refluxed for 18 h. The precipitate formed was collected by filtration and recrystallized from ethanol, m.p. > 300°C. IR: 3290 (NH), 1685, 1668 (C=O) cm^{-1}. ^1H NMR (DMSO-*d*6) δ 5.93 (s, 2H, CH_2), 7.01–8.1 (m, 9H, H—Ar + H4-phtha), 12.31 (s, 1H, NH) ppm; MS: *m/z* 428 (100%), 304 (24%), 246 (18%). Anal. Calcd. for $C_{21}H_{12}N_6O_3S$: C, 58.87; H, 2.80; N, 19.62; S, 7.47. Found: C, 58.90; H, 2.90; N, 19.90; S, 7.60.

3-[(1(2*H*)-Oxophthalazin-2-yl)methyl]-6-amino-5H-s-triazolo[3′,4′-*b*][1,3,4]thiadiazine-7-carbonitrile (20)

A mixture of **5** (0.01 mmol), bromomalononitrile (0.01 mmol), and potassium hydroxide (0.01 mmol) in ethanol (30 ml) was refluxed for 2 h. The solid obtained was collected by filtration and recrystallized from ethanol, m.p. 282°C. IR: 3320, 3290 (NH_2, NH), 2192 (C≡N) cm^{-1}; ^1H NMR (DMSO-*d*6) δ 5.81 (s, 2H, CH_2), 6.98 (br, 2H, NH_2), 7.41–7.89 (m, 5H, H—Ar + H4-phtha), 12.84 (s, 1H, NH) ppm; MS: *m/z* 338 (M^+, 100%), 248 (13%), 175 (33%), Anal. Calcd. for $C_{14}H_{10}N_8OS$: C, 49.70; H, 2.95; N, 33.13; S, 9.46. Found: C, 49.60; H, 3.10; N, 33.20; S, 9.60.

6-Dicyanoethylidine-3-[1(2*H*)-oxophthalazin-2-yl)-methyl]-5H-s-triazolo[3,4-*b*][1,3,4]thiadiazole (21)

A mixture of **5** (0.01 mmol), ketene dithioacetale (0.01 mmol), and triethylamine (0.01 mmol) in dimethylformamide (20 ml) was refluxed for 15 h. The obtained solid was collected by filtration and recrystallized from ethanol, m.p. 292°C. IR: 3380 (NH), 2219 (C≡N), 1668 (C═O) cm^{-1}; ^{1}H NMR (DMSO-*d*6) δ 5.78 (s, 2H, CH_2), 7.1–7.89 (m, 5H, H─Ar + H4-phtha), 12.9 (s, 1H, NH) ppm; Anal. Calcd. for $C_{15}H_8N_8OS$: C, 51.72; H, 2.29; N, 32.18; S, 9.19. Found: C, 51.90; H, 2.30; N, 32.20; S, 9.30.

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