SUCESSEFUL APPROACHE FOR THE SYNTHESIS OF NEWLY FUSED HETEROCYCLIC COMPOUNDS INCORBORATING PHENYLPERINAPHTHENONE AND NAPHRYDINE DERIVATIVES.

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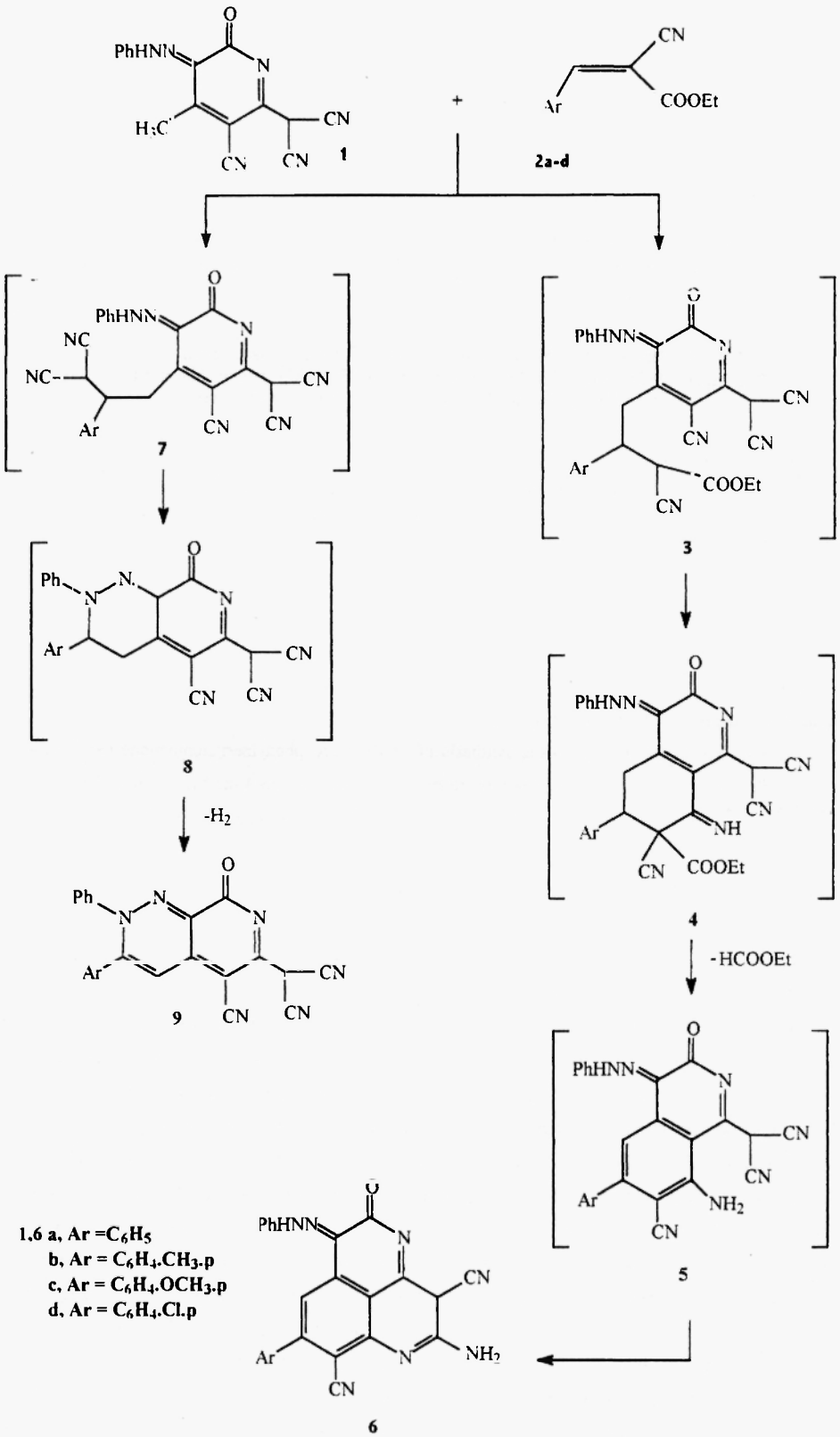
Abstract: The reaction of 3- cyano-4-methyl-6-oxo-5-phenylhydrazono-2-pyridinylmalono-nitrile **1** with a different substituted of α, β-unsaturated nitriles; hydrazines; hydroxylaminehydrochloride; phenylisocyanate; a mixture of hydrochloric / acetic acid and with sulfur afforded the corresponding newly fused heterocyclic azines. The structures of these compounds were established by analytical and spectral data.

The application of the substituted heteroaromatic compounds in various aspects is beyond estimation, and there are always continuos need for the discovery of new heterocyclic compounds in order to satisfy the great demand for these compounds in industrial and various biological fields [1,2].

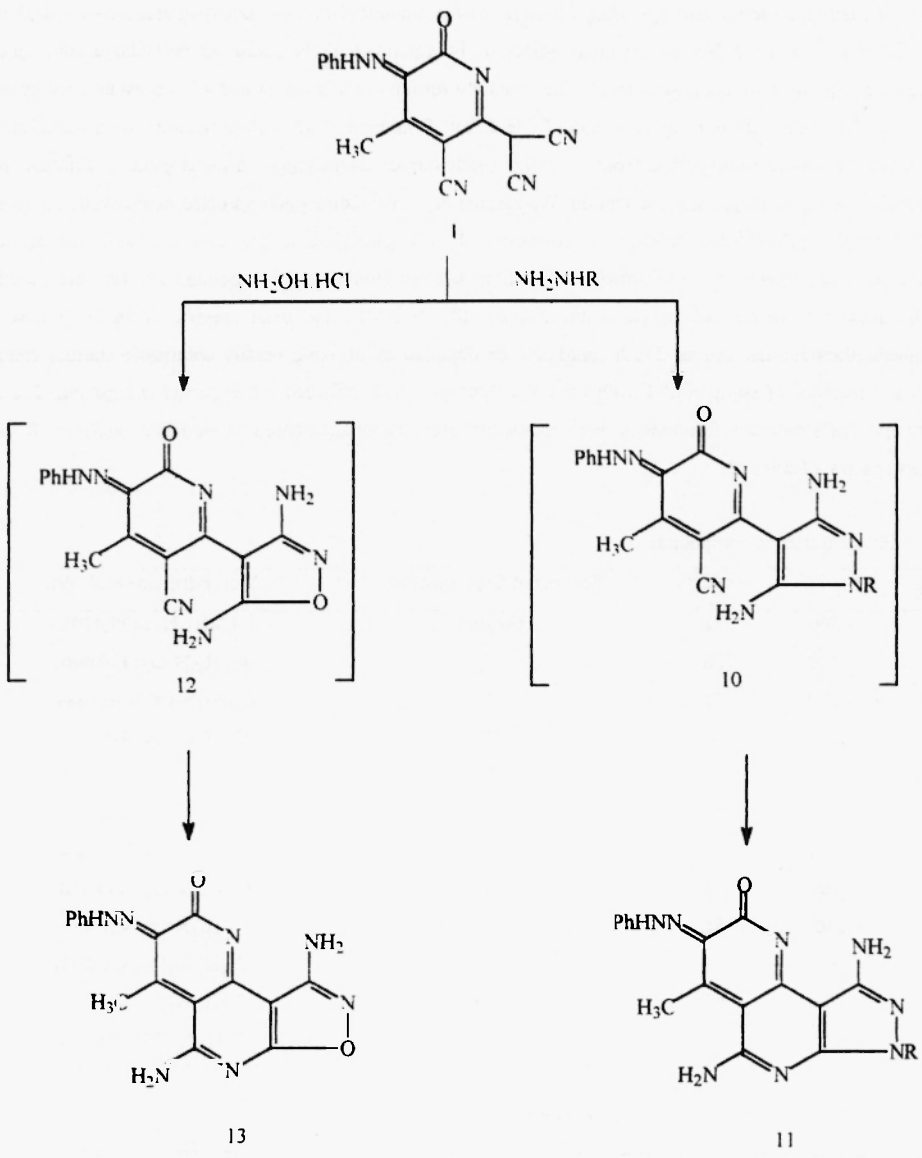
Within this respect, our initial strategy to the synthesis of newly fused phenylperinaphthenone (8) derivatives **6a-d** (Scheme-1) is planed according to the cycloaddition reaction between 3-cyano-4-methyl-6-oxo-5-phenylhydrazono-2-pyridinyl-malononitrile **1** with α, β-unsaturated nitrile derivatives **2a-d**. Our conception to the obvious cycloaddition reaction that it leads to the formation of pyrido[3,4-c]pyridazine derivative **7**. But the experimental evidence that depends on the different types of analysis of the reaction product, proofs that the cycloaddition reaction leads to the formation of phenylperinaphthenone(8) derivatives **6a-d**. (Table 1). The structure of these compound derivatives were established by elemental analysis, ^{1}H NMR, IR, and Mass spectral data (Tables 1, 2).

Formation of **6** is assumed to proceed through addition of **1** to **2** as to yield Michael adduct **3** which cyclizes into **4**. The later then aromatize by ethyl formate elimination affording **5**. Compound **5** furthercyclizes to the final isolable product **6**. Similar elimination have been observed before[3] . However, in the sterically crowded **4**, for the linear cyano group elimination of HCN has no means of reducing the steric hindrance, but the trigonal ethyl carbonyl group on the other hand should be cabable, by elimination of ethyl formate molecule. The structures of these compounds were confirmed by elemental analysis; IR; ^{1}H NMR and mass pectral data (Table 1,2). Furthermore, in the course of our studies on synthetization and reactions of the nitriloheterocyclic compounds[4-6], we have investigated the activity of the exocyclic malononitrile and carbonitrile at C2 and, C3 via the reaction of compound 1 with some electrophillic reagents such as substituted hydrazine and hydroxylamine hydrochloride where the corresponding pyrazolonaphthyridinone; isoxazolonnaphthyridinone derivatives **11**, and **13** (Scheme-2) were obtained respectively. The structures of these compounds were established by elemental analysis, IR, ^{1}H NMR, and mass spectral data (Table 1,2). The IR spectrum of the produced compounds **11a,b**; **13** refer to the construction nature of its structures were, no cyano group absorption bands were exhibited in the IR spectrum, but instead a characteristic band for amino group have been showed. Structures **11** and **13** were believed to be formed through the intermediacy of **10** and **12**, which, could not be isolated, then cyclized to the final rticyclic isolable product. Also, we exploit the reactivity of the adjacent methyl group at C4 with the carbonitrile group at C3 in compound 1 by the reaction with elemental sulfur in refluxing dioxane in the



1,6 a, Ar =C_6H_5
b, Ar = $C_6H_4.CH_3$.p
c, Ar = $C_6H_4.OCH_3$.p
d, Ar = C_6H_4.Cl.p

Scheme 1


PhHNN
O
N
H3C
CN
CN
CN
I
NH2OH.HCl
NH2NHR
PhHNN
O
N
NH2
H3C
CN
N
O
H2N
12
PhHNN
O
N
NH2
H3C
CN
N
NR
H2N
10
PhHNN
O
N
NH2
H3C
N
O
H2N
N
13
PhHNN
O
N
NH2
H3C
N
NR
H2N
N
11

Scheme 2

presence of triethylamine the corresponding Thiolo[2,3,4-fg](2-amino-3-cyano-6-phenylhydrazone)-1,4-naphthyridine-(5) 15 (Scheme-3) was yielded via the intermediacy of 14. Intermediate 14 could not be isolated either and further cyclized under the reaction conditions to 15. The structural formula of this compound 15 was established by elemental analysis, IR, ^{1}H NMR and mass spectral data (Table 1, 2)]. Treatment of 15 with acrylonitril does not afford a Diles Alder adduct as would be expected from a similar behaviour of thienoazines towared electron-deficient olefines , presumabily , owing to the former cyclization. We prepare the newly corresponding fused heterocyclic compounds, 18 and 19 through cycloaddition reaction of compound 1 with phenylisocyanate, and a mixture of acetic acid / hydrochloric acid respectively. The structural formulas of these synthesized compounds 18, 19 were confirmed by different analysis methods such as elemental analysis, IR, ^{1}H NMR, and mass spectra. (Table1). A new route to tetrazaphenanthrenone derivatives 21a,b could also be obtained by utilizing readily obtainable starting compound 1 through the reaction of compound 1 with urea and thiourea which afforded the expected compounds 21a and 21b respectively. The strucctural formulas of these compounds were established based on elemental analysis, IR, ^{1}H NMR, and mass spectra. (Table1, 2).

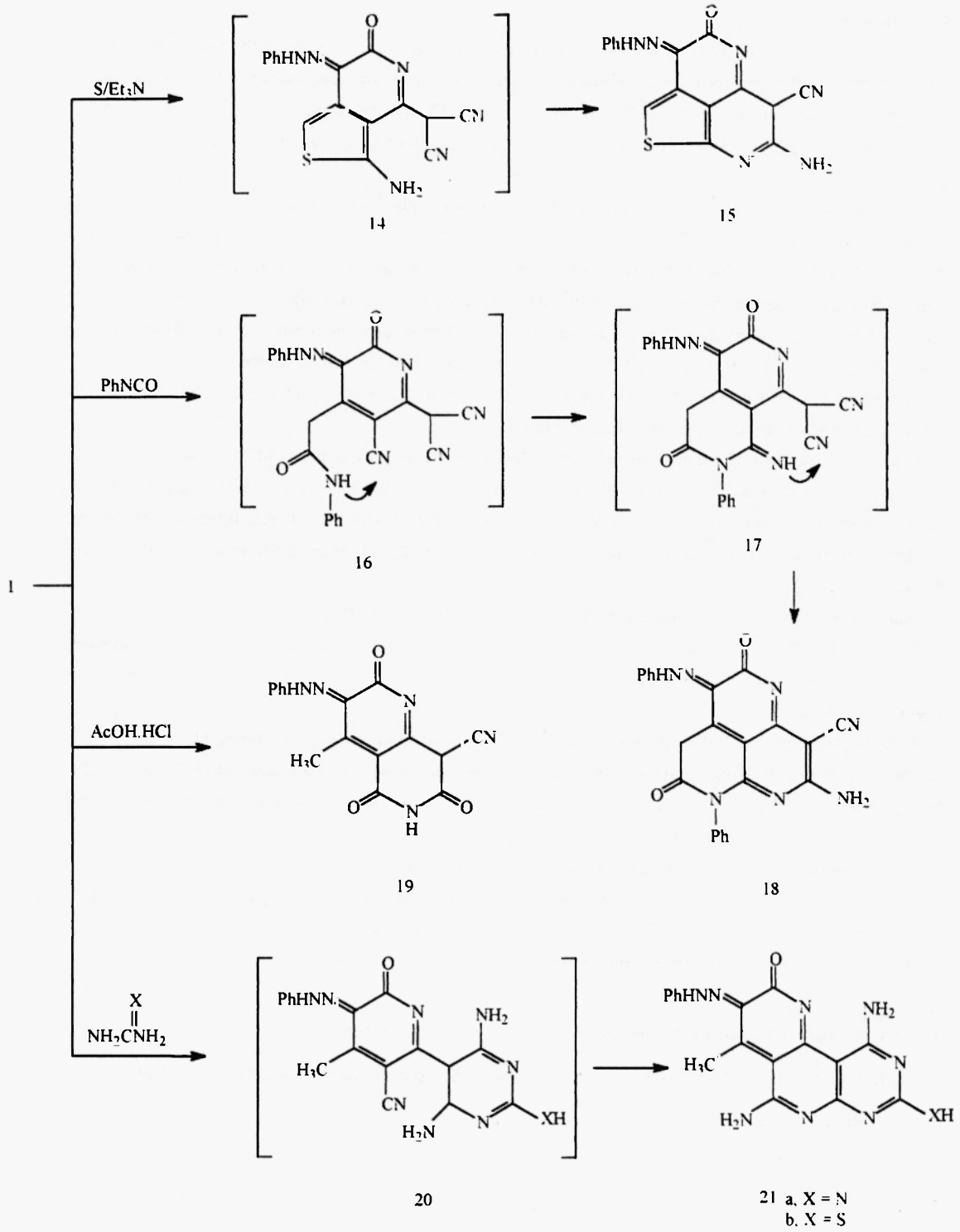
Table 1. Physical data of compounds.

Comp.	Mp °C	Yield %	Solvent of Crystallization	Mol. Formula (Mol. Wt)	MS
6a	>300	72	Ethanol	$C_{25}H_{15}N_7$ (429.439)	425
6b	>300	70	"	$C_{26}H_{17}N_7O_2$ (459.466)	459
6c	>300	72	"	$C_{25}H_{14}N_7OCl$ (463.884)	463
6d	230	66	"	$C_{23}H_{13}N_7O_3$ (419.401)	419
11a	250	70	"	$C_{22}H_{18}N_8O$ (410.347)	410
11b	>300	70	"	$C_{16}H_{14}N_8O$ (334.339)	334
13	>300	65	DMF	$C_{16}H_{13}N_7O_2$ (335.324)	335
15	>300	61	Ethanol	$C_{16}H_{10}N_6OS$ (334.358)	334
8	240	55	"	$C_{23}H_{15}N_7O_3$ (421.417)	421
19	>300	63	"	$C_{16}H_{11}N_5O_3$ (321.294)	321
21a	>300	67	Dioxane	$C_{17}H_{14}N_8O_3$ (362.339)	362
21b	>300	65	"	$C_{17}H_{14}N_8OS$ (378.406)	378

Table 2 ^{1}H NMR and IR spectral data of compounds

Comp.	^{1}H NMR ($CDCl_3$/TMS, 200MHz);δ	IR (KBr), ν (Cm^{-1})
6a	7.47(s, 2H, NH_2); 7.82-8.41(m, 12 H, Ar-H and NH)	3450-3210, 2220, 1710, 1610
11a	2.1(s, 3H,CH_3); 7.32(br 4H, 2NH_2); 7.6-8.6 (m, 8H, Ar-H and NH)	3460- 3310, 1715, 1612
13	2.1(s, 3H,CH_3); 7.2(br, 2H,NH_2); 7.6-8.1(m, 7H, Ar-H and NH)	3530-3350, 1695
15	7,1(br,2H,NH_2); 7.6-8.1(m, 8H, Ar-H and NH).	3450-3320, 2220, 1715, 1610
18	6.9(br, 2H,NH_2); 7.4-8.3(m,13H, Ar-H and NH).	3420-3000, 2222, 1695, 1600
19	2.11(s, 3H,CH_3); 7.6-8.1(m, 8H, Ar-Hand NH).	3480,3400, 2220, 1720, 1695
21	2.2 (s, 3H,CH3); 7.8-8.3 (m,7H, Ar-H and NH), 8.5 (br, 2H, NH_2), 8,7 (br, 2H, NH_2)	3455-3221, 1695,1610

Satisfied C, H, and N, analysis for all compounds were obtained


1
S/Et3N
PhNCO
AcOH.HCl
X
NH2CNH2
PhHNN
CN
NH2
H3C
XH
H2N
Ph
14
15
16
17
18
19
20
21 a, X = N
b, X = S

SCheme3

Experimental

All melting points are uncorrected. IR spectra were recorded (KBr) on a Shmadzu 408 and a Pye Unicam Spectrophtometer.[1] H NMR spectra; were recorded on a Varian EM 390 90 MHz spectrometer with DMSO as solvent and TMS as internal reference. chemical shifts are expressed in δ ppm. Mass spectra: were recorded on mass spectrometer MS 9 (AET) EI Mode. Elemental analysis was obtained from Microanalytical Center at Cairo University, Egypt.

2-aryl-5-amino-6-dicyano-9-phenylhydrazone-4,7-diazophenylperinaphth-enon(8)[6a-d].

A suspension of compound 1(3.02 g, 0.01 mol) in pyridine 20 ml was treated with arylidenethylacetoacetate derivatives 2a-d (0.01 mol). The reaction mixture was heated under reflux for 5 hours, then poured into ice water. The solid product was collected by filtration and crystallized from the proper solvent (cf. Table).

3-amino-1-N-substituted pyrazolo[3,4-b](8-amino-7-methyl-6-phenylhydraz-one)1,4-naphthyridine(5)[11a,b]. A mixture of equimolar amounts of compound 1(3.02 g, 0.01 mol) and phenyl hydrazine or hydrazine hydrate (0.01 mol) was heated on a water bath for 1 hour, then triturated with ethanol. The resulting solid product was collected by filtration and crystallized from the proper solvent (Table 1).

3-amino; Isoxazolo[5,4-b](8-amino-7-methyl-6-phenylhydrazone)1,4-napthy-ridinone(5)[13]. A suspension of 1 (3.02 g, 0.01 mol) in ethanol was treated with hydroxylamine hydrochloride (0.69 g, 0.01 mol) in the presence of catalytic amounts of sodium acetate. The reaction mixture was heated under reflux for 6h. then filtered while stile hot. The solvent evaporated under vacuum, and the solid product so formed was collected by filtration and crystallized from the proper solvent (Table 1).

Thiolo[2,3,4-fg](2-amino-3-cyano-6-phenylhydrazone)-1,4-naphthyridine-(5)[15].

A suspension of 1 (3.02 g, 0.01 mol) in pyridine 20 ml was treated with sulfur (3.02 g mol atom). The reaction mixture was heated under reflux for 3h., then poured into ice water. The solid product was collected by filtration and crystallized from proper solvent (Table1).

5-amino-6-cyano-3-phenyl-9-phenylhydrazone-3,4,7-triazaphenylperina-phthenone-2,8-dione[18]. A solution of 1 (3.02g, 0.01mol) in acetone was treated with phenylisocyanate, the reaction mixture was heated under reflux for 4h. The reaction mixture was filtered hot . The solvent evaporated under reduced pressure, the solid product was collected by filtration and crystallized from the proper solvent (c.f. table1).

3-cyano-7-methyl-6-phenylhydrazone-(1H)-1,4-naphtbylridine-2,5,8-thion-[19].

A solution of 1 (3.02g, 0.01 mol) in ethanol was treated with a mixture of acetic acid and hydrochloric acid (3:1). The reaction mixture was heated under reflux for 2 h. then poured into ice water . The solid product was collected by filtration and crystallized from proper solvent (Table1).

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