Asian Journal of Chemistry; Vol. 34, No. 2 (2022), 432-436

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2022.23619

Acid Catalyzed Multicomponent One-Pot Synthesis of New Quinazolinone based Unsymmetrical C-N Linked *Bis* Heterocycles

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Received: 13 November 2021; *Accepted*: 28 December 2021; *Published online*: 11 January 2022; AJC-20670

A novel series of unsymmetrical C-N linked *bis* heterocycles bearing quinazolinone and acridinedione skeletons have been synthesized in an acid promoted one pot multicomponent reaction. A blend of 6-aminoquinazolin-4-(3*H*)-one, aromatic aldehydes and cyclohexane-1,3-dione in a simple and efficient condensation-cyclization reaction using hydrochloric acid in catalytic amount as catalyst afforded unsymmetrical *bis* hybrids in good to excellent yields. Multiheterocyclic hybrid compounds were also synthesized using heterocyclic ring containing aldehyde in three component reaction. The synthesized quinazolinone-acridindione hybrids were characterized using spectroscopic techniques such as a IR, ^{1}H NMR, ^{13}C NMR, ESI-mass and HRMS.

Keywords: Decahydroacridinedione, Unsymmetrical *bis* heterocycle, 6-Aminoquinazolin-4(3*H*)-one, Cyclohexanedione, Acid catalyst.

INTRODUCTION

Quinazolin-4(3*H*)-one core moiety containing heterocyclic compounds having prominent role in medicinal and pharmaceutical fields. Quinazolinone and their derivatives by varying substituents at 6-position showed diverse biological activities. This scaffold is associated with anticancer, antihypertensive, antimicrobial, anti-inflammatory and antimalarial properties [1-5]. Particularly, quinazolinone based C-N/N-C linked unsymmetrical *bis* aza heterocycles showed diverse medicinal properties.

Various C-N linked 2-/3-heterylquinazolin-4(3*H*)-one derivatives (heteryl moiety-substituted 1-pyrazolidinyl; substituted 2-thiazolidinyl; 4-quinazolinyl; substituted 2-thiadiazolidinyl; substituted 1-trazolyl) having wide range of medicinal properties such as antidepressant, anti-inflammatory ant tubercular, antibacterial, antifeedant, antiasthma activities [6-10]. C-N Linked 6-heterylquinazolinones are also pharmacologically important leads and exhibited diverse biological activities such as anti-inflammatory, bronchiodilatory, antitumour activities [11-13].

An important class of bioactive heterocyclic compounds having acridinedione as privileged skeleton, are exemplified for anticancer, antimalarial, antibacterial, anti-inflammatory, antimicrobial, antileishmanial, fungicidal, antimulti-drug resistant activities and multi-drug resistance (MDR) modifier to overcome MDR problems in breast cancer treatment [14-22]. In addition, acridinediones exhibit photochemical properties such as high fluorescence efficiency allowing them to be used as laser dyes [23,24].

The synthesis of acridine-1,8-dione derivatives was described either in two step reaction *via* the isolation of tetraketone intermediate [25] or in a multicomponent single step reaction using aromatic aldehyde, 1,3-cyclohexanedione and aryl amines as precursors. In recent past, the multicomponent reactions (MCRs) have been widely used as an efficient synthetic protocol towards the preparation of number of organic and pharmacological materials. The three components condensation of aldehydes, dimidione, amines as the most popular and classical approach was developed and offers a cost-effective and simple operational strategy to synthesize biologically active 1,8-dioxo-decahydroacridine derivatives. In literature, the diverse catalysts

were reported to catalyze this reaction such as proline [26], carbon-based solid acid (SBSA) [27], ceric ammonium nitrate [28], 4-dodecylbenzenesulfonic acid (DBSA) [29], *p*-TSA [30], triethylbenzylammonium chloride (TEBAC) [31], triethyl amine [14], $In(OTf)_3$ [32], $CuSO_4{\cdot}5H_2O$ [33], $[B(C_6F_5)_3]$ [34], nano TiO_2 [35], Cu-doped ZnO [36], SiO_2-Pr-SO_3H [37], water mediated oxalic acid [38], TPA NPs/PAA [39], Brønsted acidic imidazolium salts containing perfluoroalkyltails [40], [CMIM]-$[HSO_4]$ [41], MPTMS-functionalized silica immobilized with biphenyl-2,2′-dioic acid [42], Ru catalyzed [43] and USY-zeolite [44], *etc.*

Many protocols have been reported for the synthesis of acridine-1,8-dione derivatives, but most of the methods have certain limitations such as longer reaction time, use of expensive catalysts, hazardous solvents, poor yields, cumbersome workup and by products formation. Dorehgiraee *et al.* [45] reported the synthesis of acridone-1,8-derivatives with excellent yields in a simple single step three component reaction using hydrochloric acid in catalytic amount as catalyst.

Moreover, the synthesis of unsymmetrical heterocyclic hybrid compounds is a continuous trend in organic chemistry to increase their potentiality as drug leads or drug intermediates in pharmaceutical industry. To update, unsymmetrical N-C linked *bis* azaheterocycles having C-linked heterocycle at N-position of acridindione were not built in three component reaction and also few quinazolinone based C-N linked *bis*azaheterocycles were known in literature. Thus, we report the synthesis of a new series of unsymmetrical C-N linked *bis*azaheterocycles by incorporating the acridindione moiety at the 6-position of quinazolinone in one pot three components reaction.

EXPERIMENTAL

All the reagents and solvents were of analytical grade and commercially available which were used directly without further purification. Melting points were determined with Polmon digital melting point apparatus (Model No:MP-96) and are uncorrected. IR spectra were recorded on Bruker-27 in ATR method. The ^{1}H NMR and ^{13}C NMR spectra of the synthesized compounds using TMS as an internal standard in DMSO-d_6 solvent were recorded on JEOL JNM-ECZ500R/S1 instrument at 500 MHz and 125 MHz, respectively. LC-Mass spectra were obtained on Shimadzu instrument. ESI-HRMS spectra were recorded. TLC plates, an aluminium sheets precoated with silica gel 60 F_{254} were used to monitor the progress of the reaction.

General procedure: A mixture of 6-aminoquinazolin-4-(3*H*)-one (**5**) (1 mmol), 1,3-cyclohexane-dione (**6**) (2 mmol), appropriate substituted aromatic or heterocyclic aldehydes (**7**) (1 mmol) was taken in 3 mL of DMF and 2 drops of conc. HCl was added as a catalyst. The resulting mixture was refluxed for 6 h at 140 ºC. The completion of reaction was monitored by TLC. After completion of reaction, the mixture was poured into a crushed ice, the resulted solid was filtered. The crude product was purified by column chromatography using pet. ether-ethyl acetate as eluent to furnish the corresponding pure products **8**.

10-(3-Methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-9-phenyl-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (8a): Yield: 80%; m.p.: 144-145 ºC. IR (ATR, ν_{max}, cm^{-1}): 3025, 2945, 1674, 1634, 1229, 1180; ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 8.46 (s,1H), 7.93 (s, 1H), 7.81 (d, *J* = 9.0Hz, 1H), 7.29-7.20 (m, 5H), 7.09 (t, *J* = 7.2 Hz, 1H), 5.13 (s, 1H), 3.49 (s, 3H), 2.18-1.60 (m, 12H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.4, 160.1, 152.4, 152.0, 149.6, 148.2, 146.5, 136.6, 135.8, 135.0, 129.2, 128.6, 128.0, 127.3, 126.4, 125.7, 122.0, 113.9, 36.2, 33.7, 31.1, 27.7, 20.6; ESI-HRMS $[M+H]^+$ *m/z* calculated for $C_{28}H_{25}N_3O_3$: 452.19; found at *m/z* 452.1956.

9-(4-Methoxyphenyl)-10-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (8b): Yield: 79%; m.p.: 140-143 ºC. IR (ATR, ν_{max}, cm^{-1}): 2944,2835, 1669, 1630, 1364, 1231; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.50 (s, 1H), 7.97 (s, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.23 (m, 3H), 6.81 (d, *J* = 8.3 Hz, 2H), 5.10 (s, 1H), 3.71 (s, 3H), 3.53 (s, 3H), 2.21-1.60 (m, 12H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.5, 160.1, 157.3, 152.1, 151.7, 149.6, 148.2, 138.8, 136.6, 135.8, 134.8, 129.1, 128.6, 128.3, 127.4, 126.4, 122.1, 114.3, 113.4, 54.9, 36.2, 33.7, 30.2, 27.7, 20.7; LCMS: $[M+H]^+$ *m/z* calculated for $C_{29}H_{27}N_3O_3$: 482.50; found at *m/z* 482.43.

9-(4-Bromophenyl)-10-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (8c): Yield: 75%; m.p.: 141-142 ºC. IR (ATR, ν_{max}, cm^{-1}): 2957, 2882, 1636, 1609, 1231, 1182; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.46 (s, 1H), 7.93 (s,1H), 7.81 (d, *J* = 9.0 Hz, 1H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.6 Hz, 2H), 7.09 (t, *J* = 7.6 Hz, 1H), 5.13 (s, 1H), 3.49 (s, 3H), 2.18-1.60 (m, 12H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.4, 160.1, 152.6, 152.3, 149.6, 148.2, 145.9, 136.5, 136.4, 135.7, 135.0, 130.8, 129.8, 129.1, 128.6, 127.3, 126.6, 122.1, 118.8, 113.4, 36.1, 33.7, 31.1, 27.9, 27.8, 20.6; ESI-HRMS: $[M+H]^+$ *m/z* calculated for $C_{28}H_{24}BrN_3O_3$: 530.10; found at *m/z* 530.10397.

9-(4-Chlorophenyl)-10-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3,4,6,7,9,10-hexahydroacridine-1,8-(2*H*,5*H*)-dione (8d): Yield: 75%; m.p.: 139-143 ºC. IR (ATR, ν_{max}, cm^{-1}): 1654, 1633, 1274, 1178; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.35 (d, *J* = 2.5 Hz, 1H), 8.22 (s, 1H), 7.93 (d, *J* = 8.53 Hz, 1H), 7.61 (d, *J* = 8.53 Hz, 1H), 7.35 (d, *J* = 8.03 Hz, 2H), 7.22 (d, *J* = 8.03 Hz, 2H), 5.39 (s, 1H), 3.69 (s, 3H), 2.18-1.60 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.4, 160.2, 154.0, 153.8, 149.4, 148.2, 138.2, 137.6, 135.8, 133.2, 129.2, 128.3, 127.7, 127.2, 122.4, 121.4, 119.2, 110.9, 109.9, 36.2, 33.6, 32.7, 27.8, 20.8; ESI-MS $[M+H]^+$ *m/z* calculated for $C_{28}H_{24}BrN_3O_3$: 486.15; found at *m/z* 486.10.

9-(2,4-Dichlorophenyl)-10-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (8e): Yield: 80%; m.p.: 145-148 ºC. IR (ATR, ν_{max}, cm^{-1}): 3069, 2950, 1681, 1640, 1611,1485, 1362, 1232, 1185; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.50 (s, 1H), 8.20 (d, *J* = 2.6 Hz, 1H), 7.89-7.84 (m, 2H), 7.55 (dd, *J* = 8.3 Hz, *J* = 2.6 Hz, 1H), 7.39-7.30 (m, 2H), 5.29 (s, 1H), 3.54 (s, 3H), 2.19-1.60 (m, 12H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.1, 160.1, 152.8, 152.6, 149.6,148.2, 142.7, 136.7, 135.7, 135.2, 134.0, 133.8, 130.8, 128.8, 127.3, 126.7, 122.7, 112.9,

36.1, 33.7, 32.5, 28.2, 20.7; LCMS: $[M+H]^+$ *m/z* calculated for $C_{28}H_{23}Cl_2N_2O_3$: 520.41; found at *m/z* 520.37.

3-(10-(3-Methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-1,8-dioxo-1,2,3,4,5,6,7,8,9,10-decahydroacridin-9-yl)-benzonitrile (8f): Yield: 82%; m.p.: 132-135 ºC. IR (ATR, ν_{max}, cm^{-1}): 3073, 2932, 2219, 1673, 1641,1480, 1364,1269; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.49 (s, 1H), 8.22 (d, *J* = 2.6 Hz, 1H), 7.89-7.59 (m, 5H), 7.48 (t, *J* = 7.6 Hz, 1H), 5.16 (s, 1H), 3.53 (s, 3H), 2.21-1.60 (m, 12H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.5, 160.1, 153.0, 152.7, 149.6, 148.3, 148.0, 136.5, 135.7, 135.2, 132.8, 131.1, 129.7, 129.2, 128.6, 127.0, 122.1, 119.1, 112.9, 110.9, 36.0, 33.7, 32.0, 27.9, 20.6; LCMS: $[M+H]^+$ *m/z* calculated for $C_{29}H_{24}N_4O_3$: 477.42; found at *m/z* 477.42.

9-(3-Ethoxy-4-hydroxyphenyl)-10-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (8g): Yield: 75%; m.p.: 144-146 ºC. IR (ATR, ν_{max}, cm^{-1}): 3410, 2943, 2606, 1677, 1612, 1605, 1485, 1182; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 9.57 (s, 1H), 8.61 (s, 1H), 8.49 (s, 1H), 7.95 (s, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 6.82-6.66 (m, 3H), 5.06 (s, 1H), 4.01 (q, *J* = 6.2 Hz, 2H), 3.53 (s, 3H), 2.22-1.60 (m, 12H), 1.36 (t, *J* = 6.2 Hz, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.6, 160.1, 151.9, 149.6, 148.2, 146.2, 144.9, 137.6, 136.7, 135.8, 135.0 128.7, 126.6, 122.2, 119.3, 115.1, 114.4, 112.6, 63.6, 45.3, 36.3, 33.7, 30.1, 27.6, 20.7; LCMS: $[M+H]^+$ *m/z* calculated for $C_{30}H_{29}N_3O_5$: 512.45; found at *m/z* 512.45.

10-(3-Methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-9-(thiophen-2-yl)-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (8h): Yield: 72%; m.p.: 128-132 ºC. IR (ATR, ν_{max}, cm^{-1}): 3063, 2929, 1674, 1634; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.49 (s, 1H), 7.96-7.84 (m, 3H), 7.25 (s, 1H), 6.89-6.78 (m, 2H), 5.42 (s, 1H), 3.52 (s, 3H), 2.26-1.68 (m, 12H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 195.2, 160.0, 152.5, 152.2, 150.7, 149.6, 148.2, 136.4, 135.7, 134.7, 128.7, 127.3, 126.7, 126.3, 123.5, 122.9, 113.7, 36.1, 33.7, 27.5, 26.1, 20.7; LCMS: $[M+H]^+$ *m/z* calculated for $C_{26}H_{23}N_4O_3S$: 458.15; found at *m/z* 458.36.

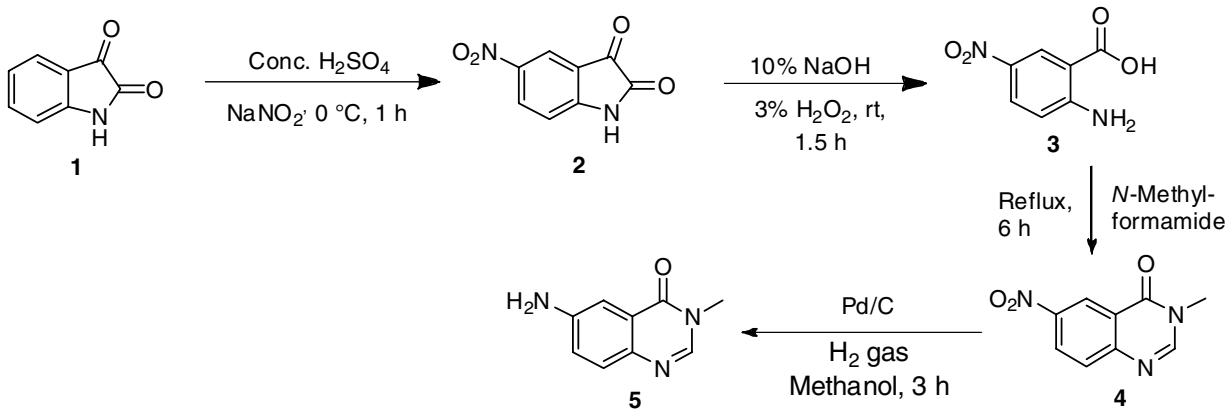
9-(2-Chloroquinolin-3-yl)-10-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3,4,6,7,9,10-hexahydro-acridine-1,8(2*H*,5*H*)-dione (8i): Yield: 78%; m.p.: 155-158 ºC. IR (ATR, ν_{max}, cm^{-1}): 3027, 2946, 1652, 1609, 1361, 1231, 1183; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.49 (s, 1H), 7.94-7.71 (m, 4H), 7.42 (d, *J* = 8.01Hz, 1H), 7.24-7.12 (m, 2H), 7.11 (t, *J* = 15.0Hz, 1H), 5.11 (s, 1H), 3.54 (s, 3H), 2.20-1.60 (m, 12H); ^{13}C NMR ($CDCl_3$, 125 MHz): δ 195.4, 160.2, 154.1, 153.9, 149.4, 148.1, 138.1, 137.6, 135.9, 135.3, 133.2, 129.3, 129.1, 128.3, 127.7, 127.3, 127.2, 122.4, 121.5, 119.2, 111.3, 109.9, 36.2, 33.7, 32.7, 27.7, 20.7; LCMS: $[M+H]^+$ *m/z* calculated for $C_{31}H_{25}ClN_4O_3$: 537.16; found at *m/z* 519.2.

9-(4-((1-(4-Methoxy-3-nitrophenyl)-1*H*-1,2,3-triazol-4-yl)methoxy)phenyl)-10-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (8j): Yield: 75%; m.p.: 161-163 ºC. IR (ATR, ν_{max}, cm^{-1}): 3027, 2946, 1672,1636, 1356, 1228, 1181; ^{1}H NMR (DMSO-d_6, 500 MHz): δ 8.78 (s, 1H), 8.50 (s, 1H), 8.09 (s, 1H), 8.01-7.82 (m, 5H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.26 (d, *J* = 8.3 Hz, 2H), 6.97 (d, *J* = 8.3 Hz, 2H), 5.21 (s, 2H), 5.16 (s, 1H), 4.03 (s, 3H), 3.53 (s, 3H), 2.22-1.64 (m, 12H); ^{13}C NMR (DMSO-d_6, 125 MHz): δ 196.4, 161.0, 157.0, 153.0, 152.7, 152.3, 150.5, 149.0, 148.4, 144.1, 140.2, 137.6, 136.6, 135.8, 131.3, 130.3, 129.3, 127.4, 127.0, 126.8, 126.4, 123.0, 117.1, 115.4, 115.1, 112.7, 109.2, 61.5, 58.0, 37.1, 34.6, 31.2, 28.6, 21.6; LCMS: $[M+H]^+$ *m/z* calculated for $C_{38}H_{33}N_7O_7$: 700.24; found at *m/z* 700.49.

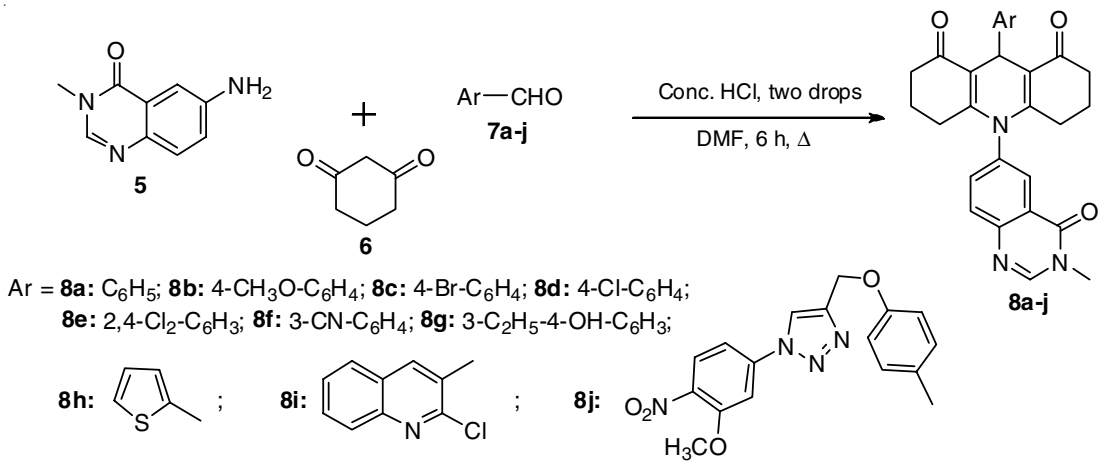
RESULTS AND DISCUSSION

6-Aminoquinazolinone (**5**) was chosen as amino precursor source in synthesizing the unsymmetrical *bis*azaheterocycles. Compound **5** was synthesized from isatin (**1**) *via* the intermediates **2-4** according to reported procedure [46] (**Scheme-I**). A blend of 6-aminoquinazolinone (**5**), 1,3-cyclohexanedione (**6**) and aromatic aldehyde 7 in 1:2:1 ratio underwent one pot conden-sationcyclization reaction to produce the corresponding acridindionylquinazolinones as unsymmetrical C-N linked *bis* heterocycles.

The synthesis of 9-phenyl-10-(3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)-3,4,6,7,9,10-hexahydroacridine-1,8(2*H*,5*H*)-dione (**8a**) was taken as a representative example to optimize the catalyzed three-component reaction conditions. Reactions using different catalysts revealed that the most suitable catalyst is the conc. HCl in catalytic amount in DMF solvent (**Scheme-II**, Table-1).



Scheme-I: Synthesis of 6-aminoquinazolinone



Scheme-II: Multi-component one-pot synthesis of new quinazolinone derivatives (all reactions were carried out using **5a** (1 mmol), **6** (2 mmol) and aromatic aldehyde **7** (1 mmol) in 3 mL of DMF under reflux for 6 h in an open air

TABLE-1
OPTIMIZATION OF CATALYST, SOLVENT AND CONDITION FOR ONE POT CONDENSATION-CYCLIZATION THREE COMPONENT REACTION OF 6-AMINOQUINAZOLINONE AND CYCLOHEXANEDIONE WITH BENZALDEHYDE[a]

Entry	Catalyst (mol%)	Solvent	Temperature (°C)	Time (h)	**8a** yield (%)[b]
1	$ZnCl_2$ (10/20)	Ethanol	80	24	NR[c]
2	$ZnCl_2$ (10/20)	DMF	140	24	NR[c]
3	I_2 (10/20)	Ethanol	80	12	NR[c]
4	I_2 (10/20)	DMF	140	12	NR[c]
5	*p*-TSA (10/20)	Ethanol	80	12	20
6	*p* -TSA (10/20)	DMF	140	12	40
7	Conc. HCl (two drops)	Ethanol	80	12	30
8	Conc. HCl (two drops)	DMF	140	6	80

[a]All reactions were carried out using **5a** (1 mmol), **6** (2 mmol) and benzaldehyde **7a** (1 mmol) in 3 mL of solvent under reflux in an open air; [b]Isolated yield; [c]NR = No reaction.

A cluster of 9-arylacridinedione derivatives **8b-g** bearing electron withdrawing or electron donating groups on phenyl ring were synthesized using substituted aromatic aldehydes **7b-g** under the standard protocol in a simple and three component method. The result showed that the electronic and substituent nature of the aryl moiety had no considerable effect on the reaction. The structure of the products was confirmed based on their IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. For example, compound **8a** showed a ketone and amide carbonyl absorption bands at 1674 and 1634 cm^{-1} in IR spectrum. The ^{1}H NMR spectrum showed characteristic singlet signals at δ 8.46, 7.93, 3.49 ppm due to quinazolinone C-2H, C-5H and N-CH_3 and at δ 5.13 ppm due to aliphatic methine protons. Remaining aromatic proton signals were observed in the range δ 7.81-7.09 ppm. Signals between δ 2.18 and 1.60 ppm were attributed to cyclohexanone twelve CH_2 protons. Ketone carbonyl and quinazolinone carbonyl carbons are indicated by the presence of peaks at δ 195.4, 160.1 ppm in ^{13}C NMR spectrum, in addition to the prominent aliphatic methyne, methyl, three methylene carbons peaks at δ 33.7, 31.1, 36.2, 27.7 and 20.6 ppm, respectively. Dihydropyridine olefinic carbons resonate at δ 152.4 and 113.9 ppm while aromatic 13 carbon peaks are observed at δ 152.0, 149.6, 148.2, 146.5, 136.6, 135.8, 135.0, 129.2, 128.6, 127.3, 126.4, 125.7 and 122.0 ppm. Along with other spectral data, the peak for $[M+H]^+$ at *m/z* 452.1956 in ESI-HRMS spectrum is in agreement with the proposed structure for the compound **8a**.

Further, the scope of this protocol was extended in synthesizing new multi-heterocyclic hybrid compounds **8h-j** using thiophene carbaldehyde (**7h**), quinoline aldehyde (**7i**) and triazole containing aromatic aldehyde **7j** in mulicomponent condensation-cyclization reaction with **5** and **6**. The structures of these hybrid compounds were deduced based on their spectral data.

Conclusion

A new series of unsymmetrical C-N-linked *bis* azaheterocycles containing quinazolinone as well as hexahydroacridine-1,8(2*H*,5*H*)-dione was synthesized in a simple and efficient one pot multicomponent reaction. A mixture of quinazolinone based amine, aromatic aldehydes and cyclohexane-1,3-dione underwent condensation-cyclization in three components one pot reaction in the presence of conc. HCl as catalyst to afford the corresponding unsymmetrical *bis* azaheterocycles in good to high yields. We have reported the one pot synthesis of *bis* compounds, wherein, heterocyclic moiety at N-position of acridinedione ring. Under the same protocol, multiheterocyclic hybrid compounds were synthesized using heterocycle containing aldehydes in three-component reaction.

ACKNOWLEDGEMENTS

One of the authors, Nagamani Rayala is thankful to the Osmania University for providing the UGC non-NET Fellow-

ship. The authors thank the Sapala Organic Pvt. Ltd., Hyderabad, India for providing NMR facilities. We thank Osmania University for NMR facility in CFRD and for the financial assistance under UGC-UPE FAR, SAP, OU-DST PURSE-II Programme.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. A.A. Radwan, F.K. Alanazi and A. Al-Dhfyan, *Drug Res.*, **63**, 129 (2013); https://doi.org/10.1055/s-0032-1333306
2. R. Karan, P. Agarwal, M. Sinha and N. Mahato, *ChemEngineering*, 5, 73 (2021); https://doi.org/10.3390/chemengineering5040073
3. I. Khan, S. Zaib, S. Batool, N. Abbas, Z. Ashraf, J. Iqbal and A. Saeed, *Bioorg. Med. Chem.*, **24**, 2361 (2016); https://doi.org/10.1016/j.bmc.2016.03.031
4. M.M. Ghorab, Z.H. Ismail, A.A. Radwan and M. Abdalla, *Acta Pharm.*, **63**, 1 (2013); https://doi.org/10.2478/acph-2013-0006
5. J.S. Negi, A.S. Bisht and D.K. Sharma, *Indian J. Pharm. Chem. Anal.*, **7**, 61 (2020); https://doi.org/10.18231/j.ijpca.2020.009
6. N. Gokhan-Kelekci, S. Koyunoglu, S. Yabanoglu, K. Yelekci, O. Ozgen, G. Ucar, K. Erol, E. Kendi and A. Yesilada, *Bioorg. Med. Chem.*, **17**, 675 (2009); https://doi.org/10.1016/j.bmc.2008.11.068
7. A. Yesilada, S. Koyunoglu, N. Saygilia, E. Kupeli, E. Yesilada, E. Bedir and I. Khanc, *Arch. Pharm.*, **337**, 96 (2004); https://doi.org/10.1002/ardp.200200752
8. F.A.M. Al-Omary, G.S. Hassan, S.M. El-Messery, M.N. Nagi, E.-S.E. Habib and H.I. El-Subbagh, *Eur. J. Med. Chem.*, **63**, 33 (2013); https://doi.org/10.1016/j.ejmech.2012.12.061
9. H. Panwar, S. Singh, A. Kumar, S. Singh, N. Singh and H. Singh, *Der Pharma Chem.*, **3**, 399 (2011).
10. P.S.N. Reddy, P.P. Reddy and T. Vasantha, *Indian J. Chem.*, **41B**, 1946 (2002).
11. D.P. Jindal, R.S. Bhatti, S. Ahlawat and R. Gupta, *Eur. J. Med. Chem.*, **37**, 419 (2002); https://doi.org/10.1016/S0223-5234(02)01345-4
12. A. Banerjee, M.Y. Pawar, S. Patil, P.S. Yadav, P.A. Kadam, V.G. Kattige, D.S. Deshpande, P.V. Pednekar, M.K. Pisat and L.A. Gharat, *Bioorg. Med. Chem. Lett.*, **24**, 4838 (2014); https://doi.org/10.1016/j.bmcl.2014.08.056
13. Z. Kilic-Kurt, F. Bakar and S. Olgen, *Arch. Pharm.*, **348**, 715 (2015); https://doi.org/10.1002/ardp.201500109
14. A. Naouri, A. Djemoui, M.R. Ouahrani, M.B. Lahrech, N. Lemouari, D.H.A. Rocha, H. Albuquerque, R.F. Mendes, F.A. Almeida Paz, L.A. Helguero, K. Bachari, O. Talhi and A.M.S. Silva, *J. Mol. Struct.*, **1217**, 128325 (2020); https://doi.org/10.1016/j.molstruc.2020.128325
15. J.S. Rupar, V.D. Dobricic, M.M. Aleksic, J.S. Brboric and O.A. Cudina, *Kragujevac J. Sci.*, **40**, 83 (2018).
16. N.P. Singh, R. Kumar, D.N. Pra, S. Sharma and O. Silakari, *Int. J. Biol. Chem.*, **5**, 193 (2011); https://doi.org/10.3923/ijbc.2011.193.199
17. S.M. Sondhi, J. Singh, R. Rani, P.P. Gupta, S.K. Agrawal and A.K. Saxena, *Eur. J. Med. Chem.*, **45**, 555 (2010); https://doi.org/10.1016/j.ejmech.2009.10.042
18. M.S. Baseer, G.K. Shankaraiah, V.M. Atul, G.M. Gajanan, S.C. Santosh and S.D. Bhaskar, *Der Pharma. Chem.*, **4**, 25 (2010).
19. D.G. Carole, D.M. Michel, C. Julien, D. Florence, N. Anna, J. Séverine, D. Gérard, T.-D. Pierre and G. Jean-Pierre, *Bioorg. Med. Chem.*, **13**, 5560 (2005); https://doi.org/10.1016/j.bmc.2005.06.045
20. A. Srivastava and Nizamuddin, *Indian J. Heterocycl. Chem.*, **13**, 261 (2004).
21. S. Gallo, S. Atifi, A. Mahamoud, C. Santelli-Rouvier, K. Wolfart, J. Molnar and J. Barbe, *Eur. J. Med. Chem.*, **38**, 19 (2003); https://doi.org/10.1016/S0223-5234(02)01422-8
22. S.A. Moallem, N. Dehghani, S. Mehri, S. Shahsavand, M. Alibolandi and F. Hadizadeh, *Res. Pharm. Sci.*, **10**, 214 (2015).
23. S. Balalaie, F. Chadegani, F. Darviche and H.R. Bijanzadeh, *Chin. J. Chem.*, **27**, 1953 (2009); https://doi.org/10.1002/cjoc.200990328
24. L.-B. Li, S.-J. Ji and Y. Liu, *Chin. J. Chem.*, **26**, 979 (2008); https://doi.org/10.1002/cjoc.200890208
25. F.-M. Wang, L. Zhou, J.-F. Li, D. Bao and L.-Z. Chen, *J. Heterocycl. Chem.*, **54**, 3120 (2017); https://doi.org/10.1002/jhet.2925
26. K. Venkatesan, S.S. Pujari and K.V. Srinivasan, *Synth. Commun.*, **39**, 228 (2008); https://doi.org/10.1080/00397910802044306
27. A. Davoodnia, A. Khojastehnezhad and N. Tavakoli-Hoseini, *Bull. Korean Chem. Soc.*, **32**, 656 (2011); https://doi.org/10.5012/bkcs.2011.32.2.656
28. M. Kidwai and D. Bhatnagar, *Tetrahedron Lett.*, **51**, 2700 (2010); https://doi.org/10.1016/j.tetlet.2010.03.033
29. T.-S. Jin, J.-S. Zhang, T.-T. Guo, A.-Q. Wang and T.-S. Li, *Synthesis*, 2001 (2004); https://doi.org/10.1055/s-2004-829151
30. N. Jazi, S. Fozooni and H. Hamidian, *J. Chem. Res.*, **42**, 80 (2018); https://doi.org/10.3184/174751918X15181752711035
31. X.-S. Wang, M.-M. Zhang, D.-Q. Shi, S.-J. Tu, X.-Y. Wei and Z.-M. Zong, *J. Chem. Res.*, 719 (2006); https://doi.org/10.3184/030823406779173352
32. Q.H. To, Y.-R. Lee and S.-H. Kim, *Bull. Korean Chem. Soc.*, **33**, 1170 (2012); https://doi.org/10.5012/bkcs.2012.33.4.1170
33. M.A. Pasha, R.-u.-R. Khan and K.B. Ramesh, *Can. Chem. Trans.*, **4**, 90 (2016).
34. S. Chandrasekhar, Y. Srinivasa Rao, L. Sreelakshmi, B. Mahipal and C. Raji Reddy, *Synthesis*, 1737 (2008); https://doi.org/10.1055/s-2008-1067039
35. A. Khazaei, A.R. Moosavi-Zare, Z. Mohammadi, V. Khakyzadeh and J. Afsar, *J. Chin. Chem. Soc.*, **63**, 165 (2016); https://doi.org/10.1002/jccs.201500384
36. H. Alinezhad and S.M. Tavakkoli, *Scient. World J.*, **2013**, 575636 (2013); https://doi.org/10.1155/2013/575636
37. G.M. Ziarani, A. Badiei, M. Hassanzadeh and S. Mousavi, *Arab. J. Chem.*, **7**, 335 (2014); https://doi.org/10.1016/j.arabjc.2011.01.037
38. J.N. Sangshetti, P.P. Dharmadhikari, R.S. Chouthe and B. Fatema, *Arab. J. Chem.*, **10**, S10 (2017); https://doi.org/10.1016/j.arabjc.2012.06.005
39. M. Nasr-Esfahani, Z. Rafiee and H. Kashi, *J. Iran. Chem. Soc.*, **13**, 1449 (2016); https://doi.org/10.1007/s13738-016-0860-8
40. W. Shen, L.-M. Wang, H. Tian, J. Tang and J. Yu, *J. Fluor. Chem.*, **130**, 522 (2009); https://doi.org/10.1016/j.jfluchem.2009.02.014
41. D. Kour, D.R. Patil, M.B. Deshmukh, V.K. Gupta and R. Kant, *Eur. Chem. Bull.*, **3**, 173 (2014).
42. R. Vaid, M. Gupta and V.K. Gupta, *J. Iran. Chem. Soc.*, **14**, 2199 (2017); https://doi.org/10.1007/s13738-017-1156-3
43. N. Biswas and D. Srimani, *J. Org. Chem.*, **86**, 9733 (2021); https://doi.org/10.1021/acs.joc.1c01075
44. L.H.R. Alponti, M. Picinini, E.A. Urquieta-Gonzalez and A.G. Corrêa, *J. Mol. Struct.*, **1227**, 129430 (2021); https://doi.org/10.1016/j.molstruc.2020.129430
45. A. Dorehgiraee, E. Tavakolinejad Kermani and H. Khabazzadeh, *J. Chem. Sci.*, **126**, 1039 (2014); https://doi.org/10.1007/s12039-014-0628-6
46. P. Shankaraiah, A.K.D. Bhavani, A.K. Kumar and K. Ramakrishna, *Russ. J. Gen. Chem.*, **90**, 720 (2020); https://doi.org/10.1134/S1070363220040246