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doi.org/10.1002/open.202300009

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New Azacycles by One-Pot Three-Component Hantzsch-Like Synthesis of Tetra(hexa)azacyclopenta[*a*]anthracenes, Tetraazaindeno[5,4-*b*]fluorenes, and Oxatetraazacyclopenta[*m*]tetraphenes

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New Azacycles by One-Pot Three-Component Hantzsch-Like Synthesis of Tetra(hexa)azacyclopenta[*a*]anthracenes, Tetraazaindeno[5,4-*b*]fluorenes, and Oxatetraazacyclopenta[*m*]tetraphenes (H. Butenschön, I. A. Abdelhamid et al.) #OpenAccess

Multicomponent reactions (MCRs) are envisaged as an entry point for the synthesis of heterocyclic compounds with interesting biological activities. An efficient approach to annelated tetra(hexa)azacyclopenta[*a*]anthracenes, tetraazaindeno[5,4-*b*]fluorenes, and oxatetraazacyclopenta[*m*]tetraphene was accomplished using a three-component reaction involving 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5-one with aromatic aldehydes and the corresponding active 1,3-dicarbonyl compounds (namely, dimedone, 1,3-dimethylbarbituric acid, 1,3-indanedione, and 4-hydroxycoumarine). The reactions were conducted in glacial acetic acid at reflux for 5 h to give the desired products in good yields (62–83 %). The chemical constitutions of all new products were confirmed spectroscopically.

Introduction

Multicomponent reactions (MCRs) represent an attractive and efficient rapid access to important organic compounds.[1–5] Among these, the Hantzsch reaction is one of the most frequently used multicomponent reactions for producing 1,4-dihydropyridines (1,4-DHPs), which have a wide range of biological and pharmacological effects, including antituberculosis,[6] anticancer,[7] anticonvulsant,[8] antiviral,[9] anti-inflammatory,[10] anti-Alzheimer,[11] and anticonvulsant[12] activities. Numerous FDA-approved drugs based on the 1,4-dihydropyridine moiety like nisoldipine, amlodipine, and felodipine were introduced as calcium channel blockers for treatment of hypertension (Figure 1).[13] Besides, pyrazolo[1,5-*a*]pyrimidines indicated a wide range of biological activities that include CRF-1 receptor antagonists,[14] KDR kinase inhibitors,[15] antischistosomal,[16] and antiproliferative agents.[17] Zaleplone, an FDA-approved sedative/hypnotic for short term treatment of insomnia, is a pyrazolo[1,5-*a*]pyrimidine derivative (Figure 1).[18] In addition, due to their remarkable photophysical properties, pyrazolo[1,5-*a*]pyrimidines received noticeable interest in material science as promising fluorophores.[19–22] In continuation of our interest in enamine chemistry,[23,24] Hantzsch[25–28] and Michael addition reactions,[29–34] in this contribution, we describe the full details of our investigation on the syntheses of novel annelated tetra(hexa)azacyclopenta[*a*]anthracenes, tetra-

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Supporting information for this article is available on the WWW under https://doi.org/10.1002/open.202300009

This publication is part of a Special Collection of ChemistryOpen on "Multicomponent Reactions". Please visit http://chemistryopen.org/collections to view all contributions.

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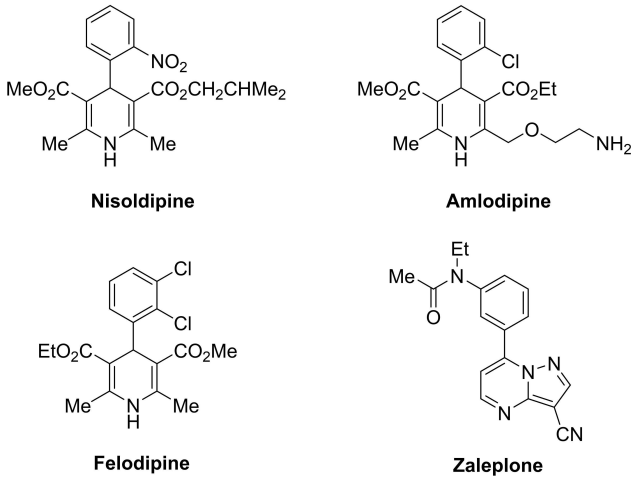

Figure 1. Some FDA-approved dihydropyridine[13] and pyrazolo[1,5-*a*]pyrimidine[18] based drugs.

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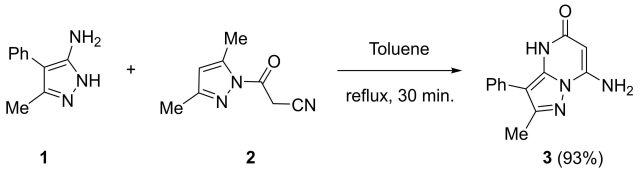
azaindeno[5,4-*b*]fluorenes, and oxatetraazacyclopenta[*m*]-tetraphene derivatives.

Results and Discussion

Recently, we reported the synthesis of 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5(4*H*)-one **3** from the reaction of 3-methyl-4-phenyl-1*H*-pyrazol-5-amine **1** with 3-(3,5-dimethyl-1*H*-pyrazol-1-yl)-3-oxopropanenitrile **2** in toluene under reflux conditions (Scheme 1).[23] Besides, we studied the utility of **3** as a precursor for the synthesis of the new symmetric ring system heptaza-dicyclopenta[*a,j*]anthracenes **I** (Figure 2).[23] In an effort to develop efficient syntheses of novel heterocycles, here, we show how compound **3** may be used as starting material for a novel series of aza-polycyclic aromatic compounds (**II**) through the unsymmetric Hantzsch reaction of one mole equivalent of **3** with one mole equivalent of both, aldehydes and active methylene compounds (Figure 2).

Initially, we conducted the reaction of the 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5-one **3** with aromatic aldehydes **4** and dimedone **5** in a trial to prepare a novel series of tetraazacyclopenta[*a*]anthracenes **6** (IUPAC name: pyrazolo[5′,1′:2,3]pyrimido[4,5-*b*]quinoline-5,7-diones). Thus, the



Scheme 1. Synthesis of 7-aminopyrazolo[1,5-*a*]pyrimidin-5(4*H*)-one **3**.[23]

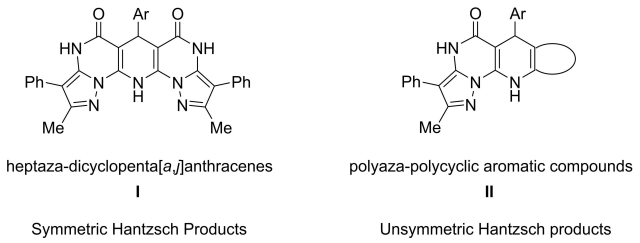
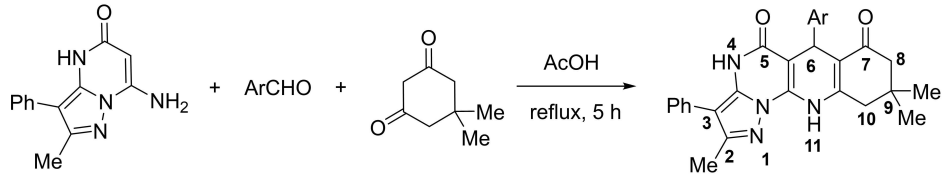


Figure 2. Structure of the targeted symmetric and unsymmetric Hantzsch products.[23]

cyclo-condensation reaction of the substituted aldehydes **4** with one mole equivalent of both 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5-one **3** and dimedone **5** in the presence of acetic acid directly leads to the formation of the target products **6a-d** in 66–78% yield (Scheme 2). As a representative example, the constitution of compound **6a** was confirmed on the basis of its spectral data. Thus, the IR spectra featured the presence of NH groups with a broad absorption band at $\tilde{\nu}$ 3266 cm^{-1}. In addition, the spectra indicated two sharp bands at $\tilde{\nu}$ 1653 and 1631 cm^{-1} corresponding to the ketonic and amidic carbonyl groups, respectively. The ^{1}H NMR spectrum of **6a** showed three singlets at δ 0.91, 1.03, and 2.33 ppm assigned to the three methyl groups. In addition, it indicated an AB line system as two pairs of doublets at δ 2.05–2.27 ppm ($J=-16.0$ Hz) and δ 2.59–2.78 ppm ($J=-17.5$ Hz) related to diastereotropic protons H10 and H8, respectively. In addition, it featured a singlet at δ 4.98 ppm assigned to H6. It also revealed signals assigned to the aryl protons as multiplets at δ 7.07–7.39 ppm. Absorptions of the two NH groups appeared as two broad signals at δ 10.30 and 11.80 ppm, respectively.

Replacing dimedone **5** with 1,3-dimethylbarbituric acid **7**, which has two additional nitrogen atoms, afforded the hexaazacyclopenta[*a*]anthracenes **8** in 75–82% yield. Thus, the three-component reaction of aldehydes **4**, 1,3-dimethylbarbituric acid **7** and 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5-one **3** in glacial acetic under reflux conditions gave 1,4,8,10,11,11b-hexaazacyclopenta[*a*]anthracene-5,7,9-triones **8a-c** (Scheme 3).

In contrast, the replacement of dimedone by 1,3-indanedione **9** leads to additional annulation to pentacyclic structure **10** (tetraazaindeno[5,4-*b*]fluorene). This finding warrants interest, because compounds with an indenopyridine moiety show a wide range of bioactivities including calcium antagonistic,[35] antidepressant,[36,37] and antihistamine activities.[36,37] They also act as NK-1 and dopamine receptor ligands.[38] Thus, under the same reaction conditions, the cyclocondensation reaction of aldehydes with both **3** and 1,3-indandione **9** proceeded smoothly, and a new series of indeno[2′,1′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7-diones **10** was obtained (Scheme 4). Surprisingly, in the presence of an electron-withdrawing nitro group in **4**, the reaction yields the non-oxidized product **10d** in high yield, while the other derivatives directly afford the readily oxidized products **10a-c**. It is noteworthy to



Scheme 2. Synthesis of pyrazolo[5′,1′:2,3]pyrimido[4,5-*b*]quinoline-5,7-diones **6a-d**.

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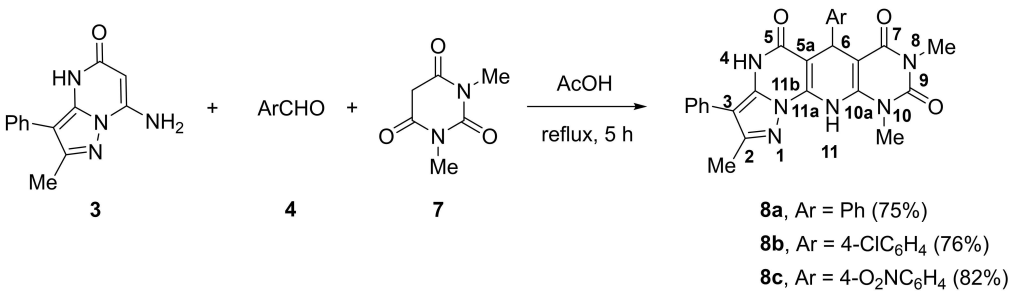
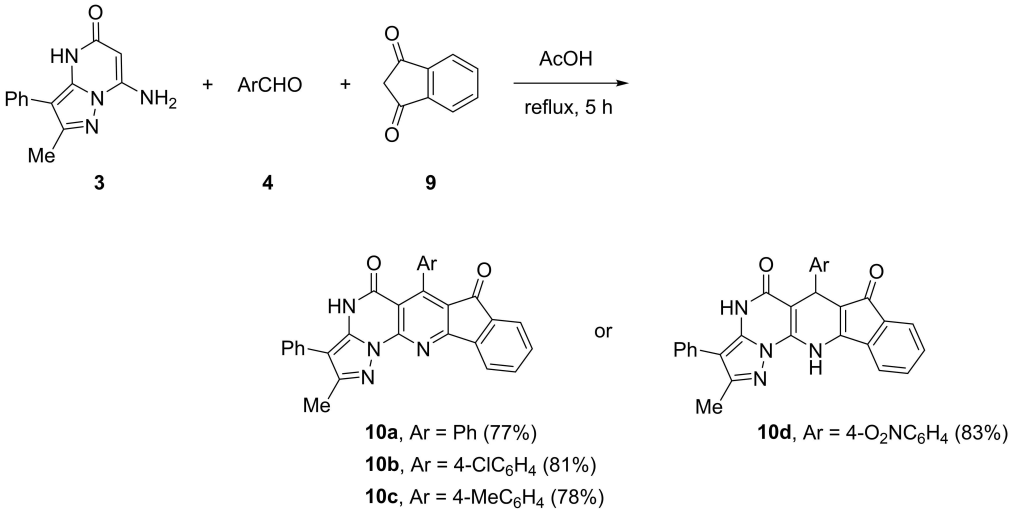


Scheme 3. Synthesis of 1,4,8,10,11,11b-hexaazacyclopenta[*a*]anthracene-5,7,9-triones **8 a-c**.

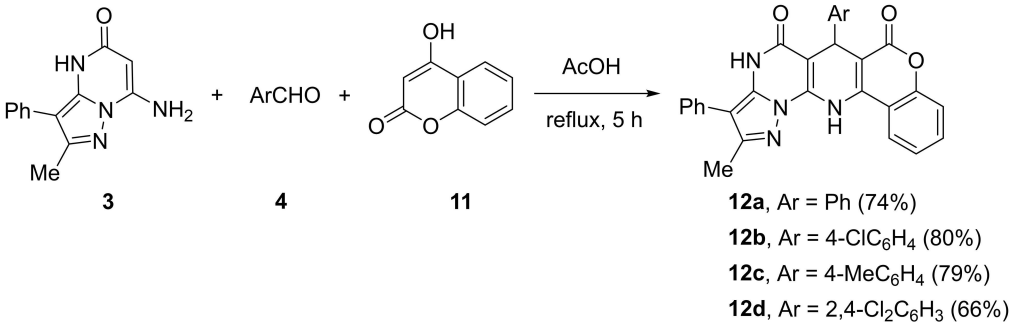


Scheme 4. Synthesis of indeno[2′,1′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7-diones **10 a-d**

mention that these compounds can be considered as 1,4,12,12b-tetraazaindeno[5,4-*b*]fluorene analogues.

Encouraged by the above results, our study was extended to include the synthesis of chromeno[3′,4′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7(4*H*)-dione derivatives **12** via the cyclocondensation of aldehydes **4** with both 4-hydroxycoumarin **11** and **3**. These ring systems can be regarded as 1,4,8,13,13b-oxatetraazacyclopenta[*m*]tetraphene analogues (Scheme 5). In contrast to the three-component reaction incorporating 1,3-indanedione (Scheme 4), only partially oxidized products **12 a-d** could be obtained under the same reaction condition even at prolonged reaction times under reflux conditions (up to 12 h).

As indicated in Scheme 6, we propose a plausible pathway for these transformations based on the Hantzsch reaction's classical mechanism. Generally, the reaction pathway involves the initial acid-catalyzed enamine addition of **3** to the aldehyde **4** to yield intermediate **13** which loses water to form the unstable ylidene **14**. The ylidene **14** then reacts with one equivalent of an active methylene compound (**5**, **7**, **9**, or **11**) yielding the intermediate **15**, which cyclizes into **16**. The intermediate **15** loses water and becomes deprotonated,



Scheme 5. Synthesis of chromeno[3′,4′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7(4*H*)-diones **12 a-d**.

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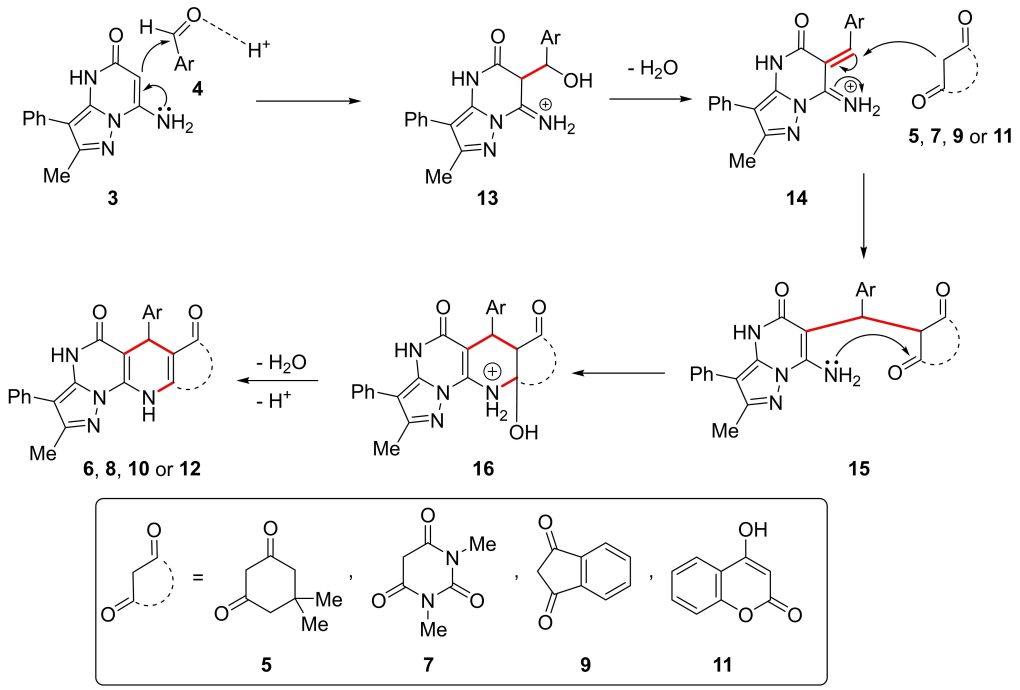
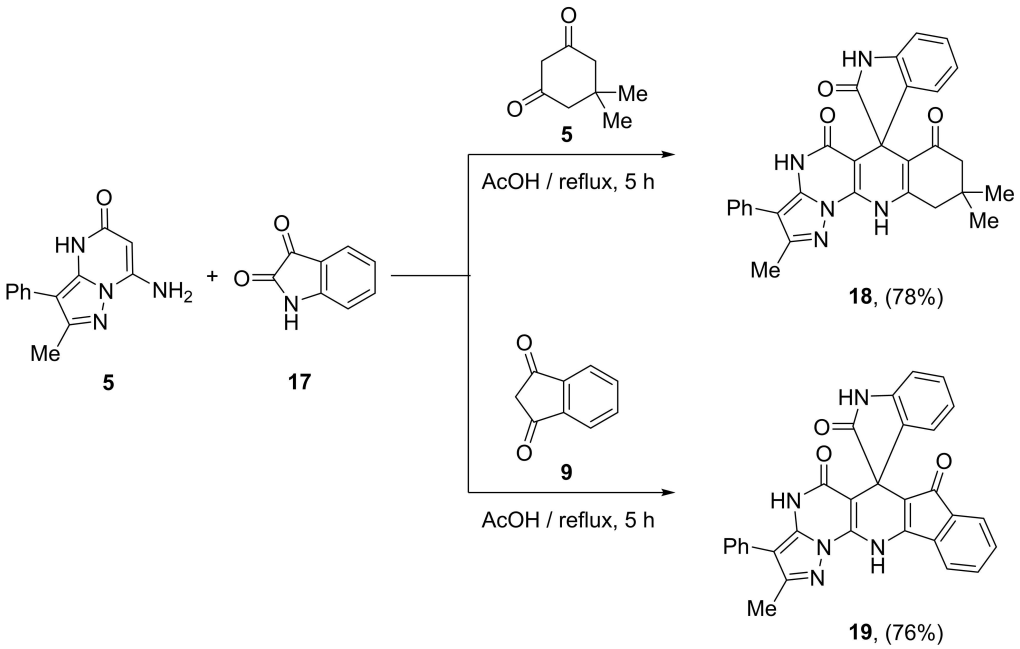


Scheme 6. A proposed mechanism for the synthesis of compounds **6**, **8**, **10**, and **12**.

producing the final isolable product **6**, **8**, **10**, or **12** respectively. (Scheme 6).

As a part of our sequential work on spirocyclic oxindoles,[39–45] we modified the structures by replacing the aldehydes with isatin **17** to achieve the concept of molecular hybridization[46] to improve their medicinal efficacy and overcome drug resistance.[47–50] Thus, the reaction of isatin **17** and 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5-one **3** with either dimedone **5** or indan-1,3-dione **9** leads to the formation of the spirocyclic oxindoles of the respective tetraazacyclopenta[*a*]anthracene **18** or tetraazaindeno[5,4-*b*]fluorene **19** (Scheme 7). The constitutions of the obtained products were confirmed by inspection of their spectral data.

We believe that more effort is still needed in order to further broaden the scope of reaction of 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5-one **3** especially in Hantzsch-



Scheme 7. Synthesis of spirocyclic compounds **18** and **19**.

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like reactions for the purpose of elaboration of interesting new ring systems. The bioactivity and the photophysical properties of the synthesized tetra(hexa)azacyclopenta[*a*]anthracenes **6** and **8**, tetraazaindeno[5,4-*b*]fluorenes **19**, and oxatetraazacyclopenta[*m*]tetraphene **12** derivatives as new ring systems are currently under investigation.

Conclusion

We have reported the first efficient route for the synthesis of new annelated ring systems including tetra(hexa)azacyclopenta[*a*]anthracenes **6** and **8**, tetraazaindeno[5,4-*b*]fluorenes **10**, and oxatetraazacyclopenta[*m*]tetraphene **12** derivatives using a three-component one pot reaction. The sequence involves the reaction of one mole equivalent of 7-aminopyrazolo[1,5-*a*]pyrimidin-5-one **3** with one mole equivalent of both aldehydes and active methylene reagents.

Experimental Section

General: Melting points were measured with a Stuart melting point apparatus and are uncorrected. The IR spectra were recorded using a FTIR Bruker–vector 22 spectrophotometer as KBr pellets. The ^{1}H and ^{13}C NMR spectra were recorded in DMSO–d_6 as solvent with a Bruker AVS 400 instrument (^{1}H: 400.1 MHz, ^{13}C: 100.6 MHz) or a Varian Gemini NMR spectrometer (^{1}H: 300 MHz, ^{13}C: 75 MHz). Chemical shifts δ refer to $\delta_{TMS} = 0.00$ ppm or to residual solvent signals. The multiplicities of the ^{13}C signals in some compounds were determined by ATP measurements. Due to poor solubilities, ^{13}C NMR spectral data for compounds **8a**, **8c**, **10a**, **10b**, **10c**, **12b**, and **12d** are not provided. Mass spectra were recorded with a Shimadzu GCMS–QP–1000 EX mass spectrometer in EI (70 eV) model. The elemental analyses were performed at the Micro-analytical center, Cairo University. All solvents and reagents was supplied by Sigma-Aldrich and used as received. 7-Amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5(4*H*)-one **3** was synthesized according to the reported literatures.[23]

General procedure (GP) for the synthesis of compounds 6, 8, 10, 12, 18 and 19: A mixture of 7-amino-2-methyl-3-phenylpyrazolo[1,5-*a*]pyrimidin-5(4*H*)-one **3**[23] (0.24 g, 1 mmol), aromatic aldehyde **4** (1 mmol) or isatin **17** (0.15 g, 1 mmol), and the cyclic 1,3-dicarbonyl compound (dimedone **5**, 1,3-dimethylbarbituric acid **7**, 1,3-indanedione **9**, or 4-hydroxycoumarine **11**) (1 mmol) was heated in glacial acetic acid (15 mL) at reflux for 5 h. The solvent was evaporated under reduced pressure and the residue was treated with aq. $NaHCO_3$ solution (2 N, 25 mL). The collected crude products were purified by crystallization from EtOH/dioxane mixture (2 : 1, *v*/*v*, 15 mL).

2,9,9-Trimethyl-3,6-diphenyl-6,9,10,11-tetrahydropyrazolo[5′,1′:2,3]pyrimido[4,5-*b*]quinoline-5,7(4*H*,8*H*)-dione (6 a): GP. Yellow powder (0.34 g, 75 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3266 (br, 2NH), 1663, 1631 (2CO) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.91 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.05–2.27 (AB line system, $^2J = -16.0$ Hz, 2H, CH_2), 2.49 (s, 3H, pyrazole CH_3), 2.59–2.78 (AB line system, $^2J = -17.5$ Hz, 2H, CH_2), 4.98 (s, 1H, C*H*), 7.07–7.42 (m, 10H, Ar*H*), 10.37 (br s, 1H, NH), 11.79 (br s, 1H, NH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.5 (CH_3), 27.1 (CH_3), 32.6 (CH_3), 34.1 (CH), 39.3 (CH_2), 50.6 (CH_2), 87.9 (C), 92.8 (C), 102.8 (C), 111.8 (C), 126.4 (CH), 127.0 (CH), 128.1 (CH), 128.2 (CH), 128.9 (CH), 129.6 (CH), 130.8 (C), 139.5 (C), 146.8 (C), 15.3 (C), 146.6 (C), 160.1 (CO), 173.4 (C), 195.0 (CO) ppm. MS (EI, 70 eV): *m/z* 450 [M]$^+$. Anal. calcd. for $C_{28}H_{26}N_4O_2$: C 74.65; H 5.82; N 12.44. Found: C 74.41; H 5.63; N 12.65.

2,9,9-Trimethyl-6-(4-nitrophenyl)-3-phenyl-6,9,10,11-tetrahydropyrazolo[5′,1′:2,3]pyrimido[4,5-*b*]quinoline-5,7(4*H*,8*H*)-dione (6 b): GP. Yellow powder (0.39 g, 78 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3346 (br, 2NH), 1667 (br, 2CO) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.91 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.05–2.28 (AB line system, $^2J = -17.8$ Hz, 2H, CH_2), 2.34 (s, 3H, CH_3), 2.62–2.78 (AB line system, $^2J = -17.6$ Hz, 2H, CH_2), 5.08 (s, 1H, C*H*), 7.30–8.11 (m, 9H, Ar*H*), 10.55 (br s, 1H, NH), 11.67 (br s, 1H, N*H*) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.5 (CH_3), 27.2 (CH_3), 29.3 (CH_3), 32.6 (C), 35.0 (CH), 40.6 (CH_2), 50.5 (CH_2), 86.5 (C), 100.9 (C), 110.9 (C), 123.6 (CH), 127.1 (CH), 128.9 (CH), 129.6 (CH), 129.7 (CH), 139.9 (C), 146.1 (C), 146.3 (C), 150.9 (C), 151.0 (C), 154.2 (C), 160.0 (CO), 169.9 (C), 195.1 (CO) ppm. MS (EI, 70 eV): *m/z* 495 [M]$^+$. Anal. calcd. for $C_{28}H_{25}N_5O_4$: C 67.87; H 5.09; N 14.13. Found: C 67.65; H 5.22; N,14.40.

6-(Benzo[*d*][1,3]dioxol-5-yl)-2,9,9-trimethyl-3-phenyl-6,9,10,11-tetrahydropyrazolo[5′,1′:2,3]pyrimido[4,5-*b*]quinoline-5,7(4*H*,8*H*)-dione (6 c): GP. Yellow powder (0.3 g, 66 %). Mp 270–272 °C. IR (KBr): $\tilde{\nu}$ 3419 (br, 2NH), 1627, 1592 (2CO) cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.94 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.07-2.26 (AB line system, $^2J = -17.6$ Hz, 2H, CH_2), 2.33 (s, 3H, pyrazole CH_3), 2.58–2.77 (AB line system, $^2J = -17.2$ Hz, 2H, CH_2), 4.90 (s, 1H, C*H*), 5.90 (s, 1H, OCH_2O), 6.67–7.43 (m, 8H, Ar*H*), 10.34 (br s, 1H, N*H*), 11.58 (br s, 1H, N*H*) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.5 (CH_3), 27.2 (CH_3), 29.4 (CH_3), 32.6 (C), 33.8 (CH), 40.6 (CH_2), 50.7 (CH_2), 92.9 (C), 101.1 (CH_2), 102.9 (C), 108.1 (CH), 108.9 (CH), 111.9 (C), 120.9 (CH), 127.0 (CH), 128.9 (CH), 129.7 (CH), 130.9 (C), 139.4 (C), 145.8 (C), 147.1 (C), 150.2 (C), 150.5 (C), 160.1 (C), 168.3 (C), 195.0 (CO) ppm. MS (EI, 70 eV): *m/z* 494 [M]$^+$. Anal. calcd. for $C_{29}H_{26}N_4O_4$: C 70.43; H 5.30; N 11.33. Found: C 70.20; H 5.62; N 11.15.

2,9,9-Trimethyl-3-phenyl-6-(*p*–tolyl)-6,9,10,11-tetrahydropyrazolo[5′,1′:2,3]pyrimido[4,5-*b*]quinoline-5,7(4*H*,8*H*)-dione (6 d): GP. Yellow powder (0.36 g, 77 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3444, 3414 (2NH), 1665, 1634 (2CO) cm^{-1}, ^{1}H NMR (400 MHz, DMSO-d_6): δ 0.91 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.04–2.22 (AB line system, $^2J = -15.9$ Hz, 2H, CH_2), 2.19 (s, 3H, tolyl CH_3), 2.34 (s, 3H, pyrazole CH_3), 2.50-2.72 (AB line system, $^2J = -17.0$ Hz, 2H, CH_2), 4.93 (s, 1H, CH), 6.98–7.42 (m, 9H, Ar*H*), 10.32 (br s, 1H, N*H*), 11.80 (br s, 1H, N*H*) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.4 (CH_3), 21.0 (CH_3), 21.5 (CH_3), 27.1 (CH_3), 29.5 (CH), 32.6 (C), 33.6 (CH), 40.8 (CH_2), 50.6 (CH_2), 102.8 (C), 112.0 (C), 126.9 (CH), 128.0 (CH), 128.8 (CH), 128.9 (CH), 129.6 (CH), 130.9 (C), 139.4 (C), 143.9 (C), 150.1 (C), 150.5 (C), 160.0 (C), 172.4 (CO), 195.0 (CO) ppm. MS (EI, 70 eV): *m/z* 464 [M]$^+$, Anal. calcd. for $C_{29}H_{28}N_4O_2$: C 74.98; H 6.08; N 12.06. Found: C 74.87; H 6.35; N 12.34.

2,8,10-Trimethyl-3,6-diphenyl-4,6,11,11 b-tetrahydro-1,4,8,10,11,11 b-hexaaza-5*H*-cyclopenta[*a*]anthracene-5,7,9(8*H*,10*H*)-trione (8 a): GP. Yellow powder (0.35 g, 75 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3360 (br, 2NH), 1647, 1579 (br, 3CO) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.91 (s, 3H, CH_3), 2.29 (s, 6H 2CH_3), 5.81 (s, 1H, C*H*), 7.10-7.40 (m, 10H, Ar*H*), 11.57 (br, 2H, 2N*H*) ppm. MS (EI, 70 eV): *m/z* 466 [M]$^+$. Anal. calcd. for $C_{26}H_{22}N_6O_3$: C 66.94; H 4.75; N 18.02. Found: C 66.68; H 4.51; N 17.83.

6-(4-Chlorophenyl)-2,8,10-trimethyl-3-phenyl-4,6,11,11 b-tetrahydro-1,4,8,10,11,11 b-hexaaza-5*H*-cyclopenta[*a*]anthracene-5,7,9(8*H*,10*H*)-trione (8 b): GP. Yellow powder (0.38 g, 76 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3404 (br, 2NH), 1653, 1581 (br, 3CO) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.90 (s, 3H, CH_3), 2.30 (s, 6H, 2CH_3), 5.81 (s, 1H, C*H*), 7.03-7.41 (m, 9H, Ar*H*), 11.60 (br s, 2H, 2N*H*) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ 12.9 (CH_3), 20.3 (CH_3), 20.8 (CH_3), 34.0 (CH), 79.7 (C), 87.9 (C), 101.6 (C), 126.2 (CH), 126.3 (CH), 128.2 (CH),

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128.3 (CH), 129.1 (CH), 130.5 (C), 133.6 (C), 135.8 (C), 136.1 (C), 149.4 (C), 148.8 (C), 151.4 (C), 160.9 (CO), 171.7 (CO), 173.9 (CO) ppm. MS (EI, 70 eV): *m/z* 500 $[M]^+$. Anal. calcd. for $C_{26}H_{21}ClN_6O_3$: C 62.34; H 4.23; N 16.78. Found: C 62.60; H 4.52; N 16.45.

2,8,10-Trimethyl-6-(4-nitrophenyl)-3-phenyl-4,6,11,11 b-tetrahydro-1,4,8,10,11,11 b-hexaaza-5*H*-cyclopenta[*a*]anthracene-5,7,9(8*H*,10*H*)-trione (8 c): GP. Yellow powder (0.42 g, 82 %). Mp 288–290 °C. IR (KBr): $\tilde{\nu}$ 3425, 3332 (2NH), 1690, 1646, 1611 (3CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 1.89 (s, 3H, CH_3), 2.30 (s, 6H, 2CH_3), 5.91 (s, 1H, C*H*), 7.28-8.12 (m, 9H, Ar*H*), 11.60 (br, 2H, 2N*H*) ppm. MS (EI, 70 eV): *m/z* 511 $[M]^+$. Anal. calcd. for $C_{26}H_{21}N_7O_5$: C 61.05; H 4.14; N 19.17. Found: C 61.27; H 4.39; N 18.98.

2-Methyl-3,6-diphenyl-4*H*-indeno[2′,1′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7-dione (10 a): GP. Yellow powder (0.35 g, 77 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3426 (NH), 1723, 1686 (2CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.35 (s, 3H, CH_3), 7.28-8.04 (m, 14H, Ar*H*), 11.80 (br s, 1H, N*H*) ppm. MS (EI, 70 eV): *m/z* 454 $[M]^+$. Anal. calcd. for $C_{29}H_{18}N_4O_2$: C 76.64; H 3.99; N 12.33. Found: C 76.95; H 4.16; N 12.57.

6-(4-Chlorophenyl)-2-methyl-3-phenyl-4*H*-indeno[2′,1′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7-dione (10 b): GP. Yellow powder (0.40 g, 81 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3447 (NH), 1675, 1617 (2CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.31 (s, 3H, CH_3), 7.33-8.00 (m, 13H, Ar*H*), 11.80 (br s, 1H, N*H*) ppm. MS (EI, 70 eV): *m/z* 488 $[M]^+$. Anal. calcd. for $C_{29}H_{17}ClN_4O_2$: C 71.24; H 3.50; N 11.46. Found: C 71.09; H 3.18; N 11.60.

2-Methyl-3-phenyl-6-(*p*–tolyl)-4*H*-indeno[2′,1′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7-dione (10 c): GP. Yellow powder (0.36 g, 78 %). Mp 238–240 °C. IR (KBr): $\tilde{\nu}$ 3408 (NH), 1658 (br, 2CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 2.42 (s, 3H, CH_3), 7.20–7.97 (m, 13H, Ar*H*), 11.60 (br s, 1H, N*H*) ppm. MS (EI, 70 eV): *m/z* 468 $[M]^+$. Anal. calcd. for $C_{30}H_{20}N_4O_2$: C 76.91; H 4.30; N 11.96. Found: C 76.75; H 4.51; N 11.73.

2-Methyl-6-(4-nitrophenyl)-3-phenyl-6,12-dihydro-4*H*-indeno[2′,1′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7-dione (10 d): GP. Orange powder (0.42 g, 83 %). Mp 292–294 °C. IR (KBr): $\tilde{\nu}$ 3397, 3344 (2NH), 1662 (br, 2CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.40 (s, 3H, CH_3), 5.02 (s, 1H, C*H*), 7.28-8.27 (m, 13H, Ar*H*) 11.80 (br, 2H, 2N*H*) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ 12.8 (CH_3), 34.6 (CH), 82.8 (C), 93.0 (C), 108.8 (C), 120.4 (CH), 121.4 (CH), 123.1 (CH), 126.5 (CH), 128.3 (CH), 129.1 (CH), 129.2 (CH), 130.1 (CH), 132.1 (C), 132.2 (CH), 135.7 (C), 136.0 (C), 140.5 (C), 145.5 (C), 145.9 (C), 150.5 (C), 152.4 (C), 154.1 (C), 159.1 (CO), 168.3 (CO) ppm. MS (EI, 70 eV): *m/z* 501 $[M]^+$. Anal. calcd. for $C_{29}H_{19}N_5O_4$: C 69.46; H 3.82; N 13.97. Found: C 69.22; H 3.52; N 13.71.

2-Methyl-3,6-diphenyl-6,13-dihydro-7*H*-chromeno[3′,4′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7(4*H*)-dione (12 a): GP. Yellow powder (0.35 g, 74 %). Mp 248–250 °C. IR (KBr): $\tilde{\nu}$ 3430, 3329 (2NH), 1656, 1615 (2CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.32 (s, 3H, CH_3), 5.81 (s, 1H, C*H*), 7.17-7.86 (m, 14H, Ar*H*), 12.10 (br s, 1H, NH), 14.6 (br s, 1H, N*H*) ppm.^{13}C NMR (75 MHz, DMSO-d_6): δ 12.9 (CH_3), 35.6 (CH), 49.2 (C), 71.9 (C), 88.1 (C), 104.5 (C), 116.0 (CH), 120.4 (CH), 120.5 (CH), 123.6 (CH), 124.1 (CH), 125.6 (CH), 126.3 (CH), 126.6 (CH), 128.0, (CH), 128.4 (CH), 129.3 (C), 130.0 (C), 132.2 (C), 135.6 (C), 138.1 (C), 149.2 (C), 150.6 (CO), 160.9 (CO), 163.5 (C) ppm. MS (EI, 70 eV): *m/z* 472 $[M]^+$. Anal. calcd. for $C_{29}H_{20}N_4O_3$: C 73.72; H 4.27; N 11.86. Found: C 73.40; H 4.50; N 11.65.

6-(4-Chlorophenyl)-2-methyl-3-phenyl-6,13-dihydro-7*H*-chromeno[3′,4′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7(4*H*)-dione (12 b): GP. Yellow powder (0.40 g, 80 %). Mp 292–294 °C. IR (KBr): $\tilde{\nu}$ 3407 (br, 2NH), 1644 (br, 2CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.35 (s, 3H, CH_3), 5.10 (s, 1H, C*H*), 7.50–8.46 (m, 13H, Ar*H*), 10.30 (br s, 1H, N*H*), 11.83 (br s, 1H, NH) ppm. MS (EI, 70 eV): *m/z* 506 $[M]^+$. Anal. calcd. for $C_{29}H_{19}ClN_4O_3$: C 68.71; H 3.78; N 11.05. Found: C 68.50; H 3.95; N 11.29.

2-Methyl-3-phenyl-6-(*p*–tolyl)-6,13-dihydro-7*H*-chromeno[3′,4′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7(4*H*)-dione (12 c): GP. Yellow powder (0.38 g, 79 %), Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3396 (NH), 1706, 1638 (2CO) cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6): δ 2.24 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 5.01 (s, 1H, C*H*), 7.07–8.86 (m, 14H, Ar*H* and NH), 11.80 (br s, 1H, N*H*) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 13.6 (CH_3), 21.0 (CH_3), 33.8 (CH), 93.5 (C), 103.2 (C), 103.8 (C), 113.3 (C), 126.9 (CH), 127.0 (CH), 128.2 (CH), 128.96 (CH), 128.98 (CH), 129.2 (CH), 129.65 (CH), 129.7 (CH), 129.8, (CH), 130.9 (C), 136.4 (C), 139.6 (C), 141.8 (C), 150.8 (C), 150.9 (C), 152.6 (C), 160.1 (CO), 160.4 (CO), 169.8 (C) ppm. MS (EI, 70 eV): *m/z* 486 $[M]^+$. Anal. calcd. for $C_{30}H_{22}N_4O_3$: C, 74.06; H, 4.56; N, 11.52. Found: C, 74.16; H, 4.43; N, 11.33.

6-(2,4-Dichlorophenyl)-2-methyl-3-phenyl-6,13-dihydro-7*H*-chromeno[3′,4′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-5,7(4*H*)-dione (12 d): GP. Off-white powder (0.36 g, 66 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3359, 3218 (2NH), 1723, 1655 (2CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.40 (s, 3H, CH_3), 4.60 (s, 1H, C*H*), 7.50–7.67 (m, 12H, Ar*H*), 11.26 (br s, 1H, N*H*), 11.90 (br s, 1H, NH) ppm. MS (EI, 70 eV): *m/z* 540 $[M]^+$. Anal. calcd. for $C_{29}H_{18}C_{l2}N_4O_3$: C 64.34; H 3.35; N 10.35. Found: C 64.12; H 3.60; N 10.67.

2′,9′,9′-Trimethyl-3′-phenyl-9′,10′-dihydro-4′*H*-spiro[indoline-3,6′-pyrazolo[5′,1′:2,3]pyrimido[4,5-*b*]quinoline]-2,5′,7′(8′*H*,11′*H*)-trione (18): GP. Red brown powder (0.38 g, 78 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3404, 3241 (br, 3NH), 1706, 1661 (br, 3CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 0.95 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 1.95 (m, 2H, CH_2), 2.14 (m, 2H, CH_2), 2.34 (s, 3H, pyrazole CH_3), 6.65–7.43 (m, 9H, Ar*H*), 10.14 (s, 1H, N*H*), 10.41 (s, 1H, N*H*), 11.46 (br s, 1H, NH) ppm. ^{13}C NMR (100 MHz, DMSO-d_6): δ 14.4 (CH_3), 27.0 (CH_3), 28.9 (CH_3), 32.4 (C), 42.8 (CH_2), 48.8 (CH_2), 51.1 (C), 87.2 (C), 103.4 (C), 108.4 (CH), 11.3 (C),120.9 (CH), 123.3 (CH), 127.3 (C), 127.8 (CH), 129.0 (CH), 129.7 (2CH), 136.4 (C), 139.8 (C), 144.1 (C), 150.9 (C), 151.1 (C), 163.4 (CO), 169.1 (C), 180.1 (CO), 194.0 (CO) ppm. MS (EI, 70 eV): *m/z* 491 $[M]^+$. Anal. calcd. for $C_{29}H_{25}N_5O_3$: C 70.86; H 5.13; N 14.25. Found: C 70.65; H 5.04; N 14.11.

2-Methyl-3-phenylspiro[indeno[2′,1′:5,6]pyrido[3,2-*e*]pyrazolo[1,5-*a*]pyrimidine-6,3′-indoline]-2′,5,7(4*H*,12*H*)-trione (19): GP. Red brown powder (0.36 g, 76 %). Mp > 300 °C. IR (KBr): $\tilde{\nu}$ 3450 (br), 3370 (3NH), 1698, 1658 (br, 3CO) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 2.38 (s, 3H, CH_3), 6.78–8.22 (m, 13H, Ar*H*), 10.45 (br s, 1H, N*H*), 11.52 (br s, 2H, 2N*H*) ppm. ^{13}C NMR (75 MHz, DMSO-d_6): δ 13.5 (CH_3), 51.4 (C), 87.3 (C), 108.4 (C), 109.0 (CH), 109.6 (CH), 110.7 (C), 120.4 (CH), 121.6 (CH), 123.9 (CH), 127.0 (CH), 127.2 (CH), 128.8 (CH), 129.0 (CH), 129.8 (C), 130.8 (CH), 131.1 (C), 133.0 (CH), 134.9 (C), 136.0 (C), 136.6 (C), 142.5 (C), 143.3 (C), 151.2 (C), 156.2 (CO), 159.6 (C), 179.0 (CO), 190.3 (CO) ppm. MS (EI, 70 eV): *m/z* 497 $[M]^+$. Anal. calcd. for $C_{29}H_{25}N_5O_3$: C 72.43; H 3.85; N 14.08. Found: C 72.29; H 3.67; N 14.02.

Supporting Information Summary

Copies of ^1H and ^{13}C NMR spectra of the synthesized compounds are available in the supplementary material.

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Acknowledgements

Amr M. Abdelmoniem and Ismail A. Abdelhamid acknowledge the Alexander von Humboldt Foundation for research fellowships.

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: heterocycles · multicomponent reactions · oxatetraaza-cyclopenta[*m*]tetraphene · polyaza-cyclopenta[*a*]anthracenes · tetraaza-indeno[5,4-*b*]fluorenes

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Manuscript received: January 29, 2023
Revised manuscript received: February 4, 2023

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