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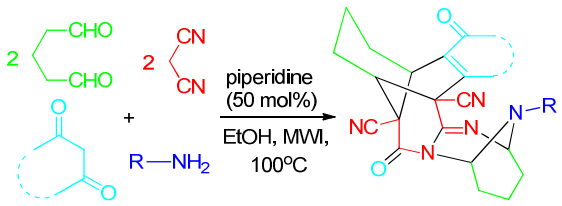

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Paper

High Efficient Construction of Bridged Pentacyclic Skeleton *via* Six-component Domino Reaction under Microwave Irradiation

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A novel bridged pentacyclic skeleton has been constructed via the six-component domino reactions of glutaraldehyde, malononitrile, cyclic 1,3-dicarbonyl compounds and amines under microwave irradiation. In this one-pot transformation, 11 new bonds and five new rings have been formed. The main advantages of this protocol are short reaction time (within 30 min), practical simplicity, high regioselectivity, benign solvents, atom-economy, and environmental friendliness.

The creation of diverse and complex molecules from readily available starting materials is a challenging theme in modern organic synthesis.[1,2] Multicomponent domino reactions (MDRs), in which multiple reactions are combined in a single synthetic operation, have been extensively used in the total synthesis of natural products and synthetic building blocks.[3,4] In these reactions, multiple stereocenters are generated with step economy, and purification of various precursors and tedious protection and deprotection of functional groups are avoided.[5,6] The design of new MDRs for the construction of complex molecules is therefore a continuing challenge at the forefront of organic synthesis.[7] Microwave-assisted organic synthesis has received much attention because of its faster chemistry and formation of cleaner products compared with conventional heating. This technology has recently been used in MDRs.[8]

Nitrogen-containing bridged polyheterocyclic skeletons are present in most natural and synthetic molecules with important biological activities.[9] Among them, aloperine and sparteine (Figure 1) which contain a bridged tetracyclic skeleton are useful quinolizidine alkaloids.[10] This alkaloid family has attracted significant attention because these compounds display potent anti-inflammatory, antipyretic, anticancer and antiviral activities.[11] These compounds have limited availability in nature and thus, the development of practical synthetic strategies from readily available starting materials is an interesting challenge. There have been several studies on the construction of these tetracyclic alkaloids and other bridged compounds,[12] but most of them are long and complex reaction sequences. Thus, there is a need for the development of synthetic protocols for the construction of this complex tetracyclic alkaloid skeleton using inexpensive and practical methodologies. Recently, we have been developing a series of MDRs that offer easy access to nitrogen-containing heterocyclic skeletons of chemical and pharmaceutical interest.[13]

In the current paper, we would report a novel multi-component domino reaction for the construction of a bridged pentacyclic skeleton under microwave irradiation. The attractive features of the current domino reaction include the formation of up to 11 new bonds and five new rings (pentacyclic 6–6–6–6–6 skeletons, i.e., cyclohexane, cyclohexene, two pyridines, and pyrimidine) in one-pot procedure.

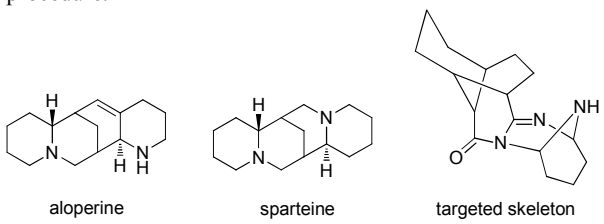

Figure 1. The structures of quinolizidine alkaloids and the targeted skeleton

Glutaraldehyde (**1**), which contains 1,5-biselectrophilic centers, is an important building block for the construction of some important polycyclic skeletons.[14] The two formyl groups in **1** can undergo double condensation with two malononitrile (**2**) molecules and subsequent double nucleophilic addition with a enaminone to construct a 1,8-naphthyridine skeleton.[12e] Because the enaminones were prepared previously from the reaction of 1,3-dicarbonyl compounds with anilines, we thought enaminones might no need prior preparation, but could be formed in the reaction system. So the four-component reaction of glutaraldehyde (**1**), malononitrile (**2**), dimedone (**3a**) and *p*-toluidine (**4a**) was carried in ethanol for 10 min under microwave irradiation. It was suprising that the desired products 1,8-naphthyridine derivative (**5a'**) was not obtained. HPLC analysis of the products mixture, however, indicated that most of the starting materials have been consumed by the reaction with the formation of a new product, which was subsequently identified as 9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino [1,2-*a*][1,3]diazocine derivative (**5a**) (Scheme 1). This result showed that the reaction proceeded in a different direction when the reaction components were changed. In this six-component domino reaction 11 new bonds and five new rings have been formed.

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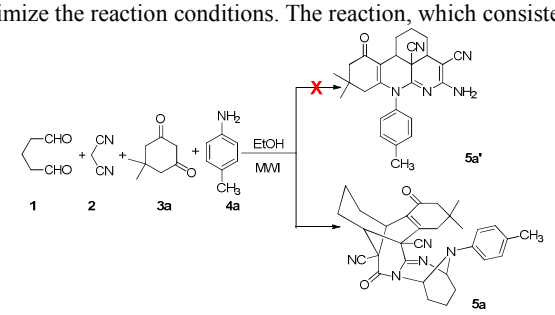
Encouraged by this result, we then selected the six-component domino reaction of glutaraldehyde (**1**), malononitrile (**2**), dimedone (**3a**) and *p*-toluidine (**4a**) as the model reaction to optimize the reaction conditions. The reaction, which consisted of



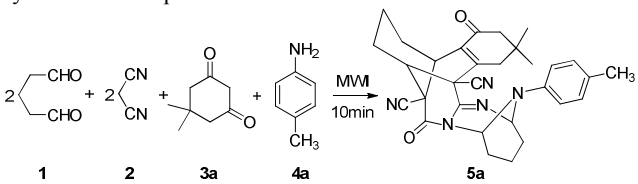
Scheme 1. New six-component domino reaction.

a 2:2:1:1 (ratio of mol) mixture of **1**, **2**, **3a**, and **4a**, was conducted under a variety of conditions (Table 1). The desired product **5a** was obtained in 31% yield when the reaction was carried out in ethanol under microwave irradiation and catalyst-free conditions (Table 1, entry 1). Several catalysts were evaluated, including acetic acid, potassium carbonate, sodium hydroxide, piperidine, triethyl amine, 1,4-diazabicyclo [2.2.2]octane (DABCO), 4-dimethylaminopyridine (DMAP), pyridine and *L*-proline. A catalyst (10 mol%) was added to all the reactions, which were carried out in ethanol at 100 °C under microwave irradiation conditions. The results of these screening experiments revealed that piperidine provided superior catalytic efficiency compared with all of the other catalysts tested (Table 1, entries 2-10). Various solvents were also evaluated to determine the impact of the solvent on the outcome of the reaction (Table 1, entries 5 and 11-16). The results of these screening experiments revealed that ethanol provided the best results all of the solvents tested.

Having identified piperidine as the best catalyst for this reaction, we proceeded to evaluate the amount of piperidine required to achieve optimium conversion. The results of these screening experiments showed that a 50 mol% charge of piperidine was sufficient to promote this reaction (Table 1, entries 5 and 17-22). The reaction was then conducted at a variety of temperatures, including 80, 90, 100 and 110°C, to determine the optimum temperature for the transformation. All of these experiments were carried out under microwave irradiation in ethanol catalyzed by 50 mol% piperidine, with the desired product **5a** being formed in yields of 54, 67, 72 and 63%, respectively (Table 1, entries 20 and 23-25). Therefore, the 100°C was chosen for this reaction. Based on all of these experiments, the optimum reaction conditions were determined to be 50 mol% piperidine in ethanol at 100°C under microwave irradiation.

With the optimized conditions in hand, we examined the scope of this synthesis using various starting materials. As shown in Table 2, a range of substituted 9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine derivatives **5a–v** were generated in moderate yields. The reaction is easy to perform, simply by mixing **1**, **2**, **4**, and a substituted cyclohexane-1,3-dione **3** in ethanol in the presence of piperidine (50 mol%) under microwave irradiation. As the data in Table 2 shown, aliphatic amines, aromatic amines with either electron-donating or electron-withdrawing groups, and heterocyclic aromatic amines were tolerated under the reaction conditions, leading to the final products in satisfactory yields.

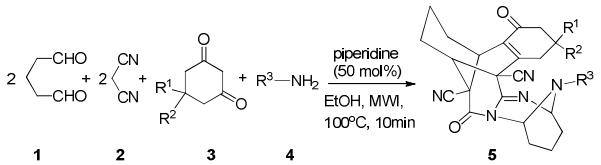
Table 1 Optimization of the reaction conditions for the synthesis of compound **5a**.



Entry	Solvent	Catalyst (mol%)	T (°C)	Yield (%)[a]
1	EtOH	——	100	31
2	EtOH	HOAc (10)	100	33
3	EtOH	K_2CO_3 (10)	100	37
4	EtOH	NaOH (10)	100	34
5	EtOH	Piperidine (10)	100	56
6	EtOH	Et_3N (10)	100	30
7	EtOH	DABCO (10)	100	27
8	EtOH	DMAP (10)	100	35
9	EtOH	Pyridine (10)	100	39
10	EtOH	*L*-proline (10)	100	36
11	CH_3CN	Piperidine (10)	100	42
12	THF	Piperidine (10)	100	29
13	Toluene	Piperidine (10)	100	18
14	DMF	Piperidine (10)	100	26
15	H_2O	Piperidine (10)	100	4
16	$HOCH_2CH_2OH$	Piperidine (10)	100	13
17	EtOH	Piperidine (20)	100	58
18	EtOH	Piperidine (30)	100	60
19	EtOH	Piperidine (40)	100	67
20	EtOH	Piperidine (50)	100	72
21	EtOH	Piperidine (60)	100	63
22	EtOH	Piperidine (70)	100	62
23	EtOH	Piperidine (50)	80	54
24	EtOH	Piperidine (50)	90	67
25	EtOH	Piperidine (50)	110	63

[a]yields were determined by HPLC-MS

Table 2 Synthesis of compounds **5** under microwave irradiation



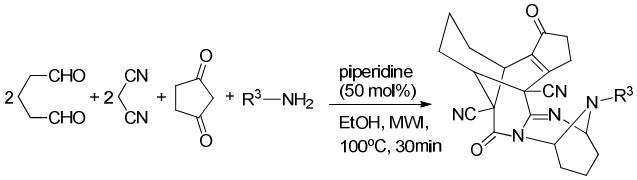
Entry	R^1	R^2	R^3	Product	Yield (%)[a]
1	CH_3	CH_3	4-MeC_6H_4	**5a**	64
2	CH_3	CH_3	4-$MeOC_6H_4$	**5b**	62
3	CH_3	CH_3	4-$EtOC_6H_4$	**5c**	59
4	CH_3	CH_3	4-*t*-BuC_6H_4	**5d**	57
5	CH_3	CH_3	3-*i*-PrC_6H_4	**5e**	54
6	CH_3	CH_3	2-EtC_6H_4	**5f**	50
7	CH_3	CH_3	4-ClC_6H_4	**5g**	54
8	CH_3	CH_3	3-Cl-4-MeC_6H_3	**5h**	52
9	CH_3	CH_3	*n*-C_4H_9	**5i**	44
10	CH_3	CH_3	Pyridine-2-yl	**5j**	59
11	CH_3	CH_3	Pyridine-3-yl	**5k**	56
12	H	H	C_6H_5	**5l**	62
13	H	H	4-MeC_6H_4	**5m**	60
14	H	H	4-$MeOC_6H_4$	**5n**	63
15	H	H	4-$EtOC_6H_4$	**5o**	61
16	H	H	2,3-$Me_2C_6H_3$	**5p**	55
17	H	H	3,5-$Me_2C_6H_3$	**5q**	54
18	H	H	4-ClC_6H_4	**5r**	50
19	H	H	*n*-C_4H_9	**5s**	47
20	H	CH_3	4-MeC_6H_4	**5t**	63
21	H	CH_3	4-ClC_6H_4	**5u**	55
22	H	C_6H_5	C_6H_5	**5v**	52

[a] isolated yield

To further explore the versatility of this protocol, other cyclic 1,3-dicarbonyl compounds, such as cyclopentane-1,3-dione (**6**) and 4-hydroxycoumarin (**8**) were used instead of the substituted cyclohexane-1,3-dione (**3**). These reactions provided the desired 9,14,10-(epibutane[1,1,4]triyl)-2,6-epiminocyclopenta[4,5]azocino[1,2-*a*][1,3]diazocine derivatives (**7**) and 9,17,10-(epibutane[1,1,4]triyl)-2,6-epiminochromeno[4',3':4,5]azocino[1,2-*a*][1,3]diazocine derivatives (**9**) smoothly under microwave irradiation (Table 3 and 4).

When cyclic 1,3-dicarbonyl compounds were replaced by acyclic 1,3-dicarbonyl compounds such as acetylacetone **10a**, the desired products **11a** was obtained only in 41% yield (Table 5). While when other acyclic 1,3-dicarbonyl compounds such as 1,3-diphenylpropane-1,3-dione (**10b**) and ethyl acetoacetate (**10c**) were used, the desired products were not obtained.

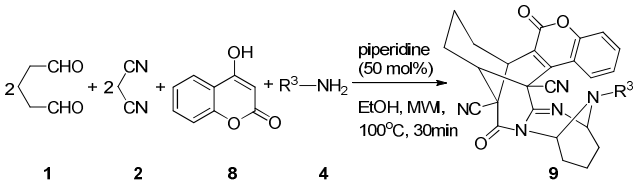
Table 3 Synthesis of compounds **7** under microwave irradiation



1 **2** **6** **4** **7**

Entry	R^3	Product	Isolated yield (%)
1	4-$MeOC_6H_4$	**7a**	62
2	3-*i*-PrC_6H_4	**7b**	51
3	3-ClC_6H_4	**7c**	54
4	3,5-$Me_2C_6H_3$	**7d**	57
5	*n*-C_4H_9	**7e**	49

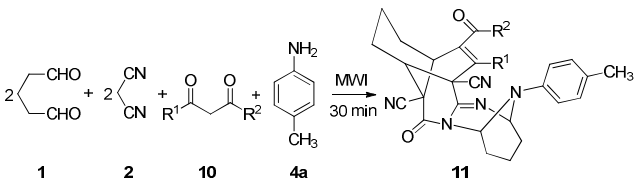
Table 4 Synthesis of compounds **9** under microwave irradiation



1 **2** **8** **4** **9**

Entry	R^3	Product	Isolated yield (%)
1	4-MeC_6H_4	**9a**	64
2	4-ClC_6H_4	**9b**	53
3	3-MeC_6H_4	**9c**	61
4	3-BrC_6H_4	**9d**	57
5	2,3-$Me_2C_6H_3$	**9e**	62
6	3-Cl-4-MeC_6H_3	**9f**	58

Table 5 Synthesis of compounds **11** under microwave irradiation



1 **2** **10** **4a** **11**

Entry	R^1	R^2	Product	Isolated yield (%)
1	CH_3	CH_3	**11a**	41
2	Ph	Ph	**11b**	no reaction
3	CH_3	OEt	**11c**	no reaction

These results are interesting, and unusual in organic synthesis. Furthermore, both these new MDRs are fast, and all the reactions are complete within 30 min. Water is almost the only by-product, which makes these reactions atom economical and environmentally friendly.

Structural elucidation assignments of compounds **5**, **7**, **9** and **11** were performed using ^1H NMR and ^{13}C NMR spectroscopies. The structures of compounds **5a** and **7b** were further confirmed by X-ray diffraction analysis. Figures 2 and 3 showed the structures of product **5a** and **7b**, respectively.

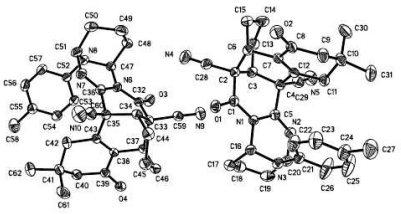


Figure 2 The crystal structure of compound **5a**

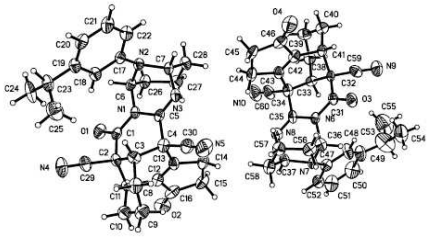
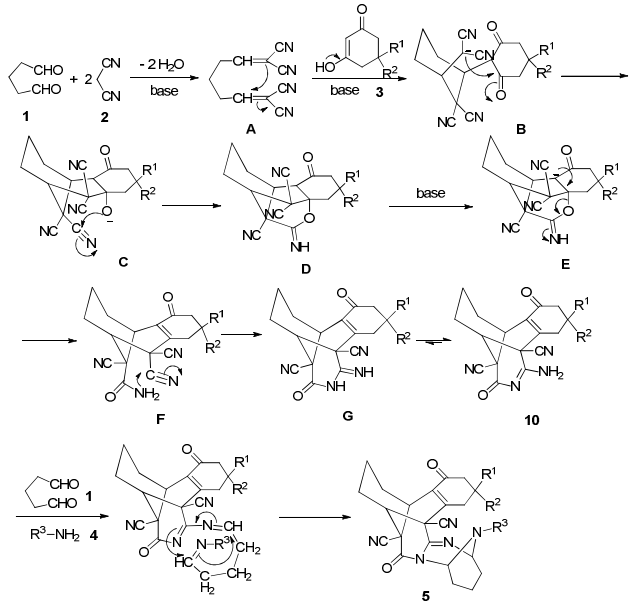


Figure 3 The crystal structues of compound **7b**

The proposed mechanism for these new multicomponent domino reactions is shown in Scheme 2. An initial Knoevenagel condensation of **1** with two molecules of **2** gives the intermediate **A**. Intermediate **B** is formed by Michael addition of a cyclohexane-1,3-dione **3** to intermediate **A** catalyzed by base. Intermediate **D** is produced by intramolecular cyclization from intermediate **B**. Intermediate **D** undergoes ring-opening reaction catalyzed by base to give intermediate **F**, which participates in an intramolecular cyclization and imine–enamine tautomerization to give the intermediate product **10**. Product **5** can be obtained by a three-component reaction of **10**, **1**, and an amine **4**. The latter reaction was confirmed experimentally. The intermediate product **10a** was obtained when the four-component reaction of **1**, two molecules of **2** and **3a** were carried out in ethanol in the presence of piperidine (50 mol%) under microwave irradiation. Furthermore, when the three-component reaction of **10a**, **1** and *p*-toluidine (**4a**) was performed under the above conditions, the desired product **5a** was obtained.

In summary, we have successfully established the first six-component domino reactions of glutaraldehyde, malononitrile, cyclic 1,3-dicarbonyl compounds and amines leading to the construction of new bridged pentacyclic skeletons with multiple stereocenters. These reactions are easy to perform, simply by mixing four readily available reactants and a base (piperidine) in ethanol under microwave irradiation. This protocol has the advantages of mild reaction conditions, convenient one-pot operation, short reaction time, excellent regio-selectivity, atom-economy, and environmental friendliness.



Scheme 2. Proposed mechanism for the formation of compound **5**

Experimental Section

Melting points were measured using a XT-4 micro melting point apparatus and were uncorrected. IR spectra were recorded with a Varian F-1000 spectrometer using KBr disks; absorptions are reported as cm^{-1}. ^1H NMR and ^{13}C NMR spectra were obtained in DMSO-d_6 solution, using a Agilent Vnmrs-300 MHz, Agilent Inova-400 MHz, Bruker Avance III-400 MHz, Agilent DD2-600 MHz spectrometer. *J* values are reported in hertz and chemical shifts are expressed in parts per million downfield from TMS as the internal standard. HRMS analyses were carried out using a Bruker micrOTOF-QII mass spectrometer with ESI resource. X-Ray diffraction analysis was recorded on a Smart-1000 diffractometer. Microwave irradiation was carried out with Initiator 2.5 Microwave Synthesizers from Biotage, Uppsala, Sweden. The reaction temperatures were measured by infrared detector during microwave heating.

General procedure for the synthesis of 5, 7, 9 and 11.

Glutaraldehyde (**1**) (2.0 mmol), malononitrile (**2**) (2.0 mmol), 1,3-dicarbonyl compounds (**3**, **6**, **8** or **10**) (1 mmol) and amines (**4**) (1.0 mmol) were introduced in a 5 mL initiator microwave reaction vial, and 50 mol% piperidine as well as ethanol (2 mL) were then successively added. Subsequently, the reaction vial was closed and then prestirred for 10 s. The mixture was irradiated at 100°C for 10-30 min with Initiator 2.5 Microwave Synthesizer. The reaction was monitored by TLC. After the completion, the reaction mixture was then cooled to room temperature. The precipitate was collected and purified by column chromatography (petroleum ether:acetone = 12:1) to give the crude products. The crude products were further purified by recrystallization from DMF and water to give the products **5, 7, 9** or **11.**

13,13-Dimethyl-8,11-dioxo-20-(*p*-tolyl)-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10- (epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (**5a**). Isolated as a white solid; mp 216–218°C; IR (KBr, *v*, cm^{-1}): 2924, 2869, 2249, 1695, 1636, 1509, 1461, 1346, 1261, 1236, 1090, 836; ^1H NMR (400 MHz, DMSO-d_6) δ_H: 7.01 (d, *J* = 8.4 Hz, 2H, ArH), 6.76 (d, *J* = 8.4 Hz, 2H, ArH), 6.12 (s, 1H, CH), 5.76 (s, 1H, CH), 3.55 (s, 1H, CH), 3.28 (s, 1H, CH), 2.17 (s, 3H, CH_3), 2.10 (t, *J* = 16.0 Hz, 3H, 3 × CH), 1.99–1.83 (m, 6H, 6 × CH), 1.69 (d, *J* = 16.4 Hz, 1H, CH), 1.65–1.53 (m, 4H, 4 × CH), 1.24 (d, *J* = 18.0 Hz, 1H, CH), 1.13–1.03 (m, 1H, CH), 0.78 (s, 3H, CH_3), 0.64 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.4, 164.7, 147.3, 147.2, 145.1, 131.7, 130.6, 118.5, 117.8, 116.5, 115.3, 68.9, 63.7, 52.8, 49.6, 48.1, 34.6, 34.4, 32.1, 29.4, 29.3, 29.0, 25.4, 25.0, 20.3, 15.8, 14.1; HRMS calcd for $C_{31}H_{32}N_5O_2$ $[M-H]^-$: 506.2556, found: 506.2556.

20-(4-Methoxyphenyl)-13,13-dimethyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (**5b**): Isolated as a white solid; mp 218–220 °C; IR (KBr, *v*, cm^{-1}): 2953, 2905, 2252, 1696, 1639, 1513, 1451, 1374, 1252, 1035, 934, 837; ^1H NMR (400 MHz, DMSO-d_6) δ_H: 6.80 (s, 4H, ArH), 6.07 (s, 1H, CH), 5.70 (s, 1H, CH), 3.66 (s, 3H, CH_3O), 3.55 (s, 1H, CH), 3.28 (s, 1H, CH), 2.17–2.08 (m, 3H, 3 × CH), 1.98–1.80 (m, 7H, 7 × CH), 1.64–1.59 (m, 4H, 4 × CH), 1.29 (d, *J* = 18.0 Hz, 1H, CH), 1.14–1.05 (m, 1H, CH), 0.79 (s, 3H, CH_3), 0.65 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 164.8, 154.3, 147.2, 140.9, 131.7, 117.8, 115.3, 69.2, 64.2, 55.6, 52.9, 49.9, 48.2, 34.7, 34.5, 32.3, 29.6, 29.4, 29.1, 25.5, 25.0, 15.8, 14.1; HRMS calcd for $C_{31}H_{32}N_5O_3$ $[M-H]^-$: 522.2505, found: 522.2492.

20-(4-Ethoxyphenyl)-13,13-dimethyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (**5c**): Isolated as a white solid; mp 220–222 °C; IR (KBr, *v*, cm^{-1}): 2952, 2871, 2249, 1707, 1649, 1515, 1394, 1004, 963, 938, 803; ^1H NMR (400 MHz, DMSO-d_6) δ_H: 6.78 (s, 4H, ArH), 6.06 (s, 1H, CH), 5.68 (s, 1H, CH), 3.92–3.88 (m, 2H, CH_2O), 3.53 (s, 1H, CH), 3.29 (s, 1H, CH), 2.18–2.08 (m, 3H, 3 × CH), 2.03–1.82 (m, 7H, 7 × CH), 1.64–1.59 (m, 4H, 4 × CH), 1.33 (s, 1H, CH), 1.27 (t, *J* = 6.8 Hz, 3H, CH_3), 1.18–1.08 (m, 1H, CH), 0.79 (s, 3H, CH_3), 0.66 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 164.8, 153.6, 147.2, 140.8, 131.7, 117.8, 115.7, 115.4, 69.2, 64.2, 63.6, 52.9, 49.9, 48.2, 34.8, 34.5, 32.2, 29.6, 29.2, 25.5, 25.0, 15.8, 15.2, 14.1; HRMS calcd for $C_{32}H_{36}N_5O_3$ $[M+H]^+$: 538.2818, found: 538.2803.

20-(4-(Tert-butyl)phenyl)-13,13-dimethyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5d): Isolated as a white solid; mp 240–242 °C; IR (KBr, *v*, cm^{-1}): 2950, 2870, 2250, 1692, 1640, 1519, 1367, 1345, 1255, 1093, 820, 746, 691; ^1H NMR (400 MHz, DMSO-d_6) δ_H: 7.31 (d, *J* = 8.4 Hz, 2H, ArH), 6.87 (d, *J* = 8.4 Hz, 2H, ArH), 5.73 (s, 1H, CH), 5.43 (s, 1H, CH), 2.78–2.72 (m, 2H, 2 × CH), 2.47–2.41 (m, 1H, CH), 2.45 (d, *J* = 15.6 Hz, 1H, CH), 2.26 (d, *J* = 15.6 Hz, 1H, CH), 2.07–1.84 (m, 8H, 8 × CH), 1.67–1.56 (m, 3H, 3 × CH), 1.34–1.29 (m, 1H, CH), 1.24 (s, 9H, $(CH_3)_3C$), 1.20–1.15 (m, 1H, CH), 1.04 (s, 3H, CH_3), 0.97 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 196.1, 164.3, 147.6, 146.5, 145.1, 132.4, 129.8, 126.3, 120.3, 118.4, 117.4, 114.9, 67.7, 67.3, 52.3, 50.5, 48.0, 36.8, 34.7, 32.8, 29.9, 28.2, 25.9, 24.9, 15.7, 14.8; HRMS calcd for $C_{34}H_{40}N_5O_2$ $[M+H]^+$: 550.3182, found: 550.3177.

20-(3-Isopropylphenyl)-13,13-dimethyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]

triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5e): Isolated as a white solid; mp 232–234 °C; IR (KBr, *v*, cm^{-1}): 2956, 2870, 2250, 1690, 1638, 1513, 1457, 1365, 1243, 1088, 935, 826, 765; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.07 (t, *J* = 8.0 Hz, 1H, ArH), 6.93 (s, 1H, ArH), 6.79 (d, *J* = 7.6 Hz, 1H, ArH), 6.45 (d, *J* = 8.0 Hz, 1H, ArH), 6.18 (s, 1H, CH), 5.85 (s, 1H, CH), 3.54 (s, 1H, CH), 3.27 (s, 1H, CH), 2.78–2.71 (m, 1H, CH), 2.15 (d, *J* = 18.0 Hz, 1H, CH), 2.07–1.94 (m, 6H, 6 × CH), 1.92–1.87 (m, 2H, 2 × CH), 1.66–1.51 (m, 5H, 5 × CH), 1.32 (d, *J* = 18.4 Hz, 1H, CH), 1.12 (d, *J* = 6.8 Hz, 3H, CH_3), 1.10 (d, *J* = 7.2 Hz, 3H, CH_3), 1.07–1.03 (m, 1H, CH), 0.76 (s, 3H, CH_3), 0.57 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 164.6, 147.2, 145.3, 141.6, 131.6, 127.9, 127.7, 118.7, 117.8, 116.6, 115.4, 68.7, 64.0, 52.8, 49.9, 48.1, 34.6 34.4, 32.9, 32.2, 29.7, 29.1, 25.4, 25.0, 24.4, 24.3, 15.7, 14.1; HRMS calcd for $C_{33}H_{38}N_5O_2$ $[M+H]^+$: 536.3026, found: 536.3035.

20-(2-Ethylphenyl)-13,13-dimethyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5f): Isolated as a white solid; mp 224–226 °C; IR (KBr, *v*, cm^{-1}): 2933, 2869, 2250, 1693, 1637, 1511, 1468, 1356, 1253, 1236, 1090, 836; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.27 (d, *J* = 7.2 Hz, 1H, ArH), 7.08-7.01 (m, 2H, ArH), 6.36 (d, *J* = 7.2 Hz, 1H, ArH), 5.67 (s, 1H, CH), 4.98 (s, 1H, CH), 3.57 (s, 1H, CH), 3.35 (s, 1H, CH), 2.69–2.57 (m, 2H, 2 × CH), 2.36 (d, *J* = 18.4 Hz, 1H, CH), 2.26 (s, 2H, CH_2), 2.16–2.07 (m, 3H, 3 × CH), 2.02–1.91 (m, 5H, 5 × CH), 1.82 (d, *J* = 12.4 Hz, 1H, CH), 1.66 (s, 4H, 4 × CH), 1.19 (t, *J* = 7.2 Hz, 3H, CH_3), 0.88 (s, 3H, CH_3), 0.81 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 164.3, 147.3, 146.9, 146.3, 145.2, 138.6, 137.7, 132.2, 130.1, 127.6, 127.1, 125.6, 124.6, 121.0, 118.3, 69.7, 67.8, 53.1, 52.5, 48.3, 48.0, 36.6, 35.3, 34.8, 34.5, 32.6, 30.2, 29.2, 28.2, 25.6, 23.7, 14.7; HRMS calcd for $C_{32}H_{34}N_5O_2$ $[M-H]^-$: 520.2713, found: 520.2694.

20-(4-Chlorophenyl)-13,13-dimethyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5g): Isolated as a white solid; mp 272–274 °C; IR (KBr, *v*, cm^{-1}): 2953, 2870, 2256, 1694, 1635, 1496, 1371, 1349, 1242, 1090, 1006, 939, 833, 818, 745; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.28 (d, *J* = 8.8 Hz, 2H, ArH), 6.93 (d, *J* = 7.2 Hz, 2H, ArH), 6.15 (s, 1H, CH), 5.80 (s, 1H, CH), 3.56 (s, 1H, CH), 3.28 (s, 1H, CH), 2.20–2.07 (m, 3H, 3 × CH), 1.99–1.88 (m, 6H, 6 × CH), 1.70 (d, *J* = 16.4 Hz, 1H, CH), 1.64–1.52 (m, 4H, 4 × CH), 1.27 (d, *J* = 17.6 Hz, 1H, CH), 1.14–1.04 (m, 1H, CH), 0.80 (s, 3H, CH_3), 0.66 (s, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C: 196.1, 164.2, 147.3, 145.2, 145.0, 132.3, 126.5, 118.3, 117.3, 114.9, 68.3, 67.4, 52.3, 50.5, 48.0, 37.0, 34.7, 34.3, 32.8, 31.6, 28.2, 15.7, 14.9; HRMS calcd for $C_{30}H_{29}ClN_5O_2$ $[M-H]^-$: 526.2010, found: 526.1996.

20-(3-Chloro-4-methylphenyl)-13,13-dimethyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5h): Isolated as a white solid; mp 276–278 °C; IR (KBr, *v*, cm^{-1}): 2953, 2871, 2252, 1696, 1639, 1513, 1451, 1373, 1252, 1184, 1126, 1089, 1035, 934, 837; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.19 (s, 1H, ArH), 6.94 (s, 1H, ArH), 6.80 (s, 1H, ArH), 6.17 (s, 1H, CH), 5.85 (s, 1H, CH), 3.57 (s, 1H, CH), 3.28 (s, 1H, CH), 2.19 (s, 3H, CH_3), 2.10–1.87 (m, 9H, 9 × CH), 1.61–1.53 (m, 5H, 5 × CH), 1.25–1.05 (m, 2H, 2 × CH), 0.79 (s, 3H, CH_3), 0.60 (s, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 195.2, 164.9, 147.3, 147.1, 146.7, 134.7, 132.5, 131.8, 128.3, 117.8, 116.8, 115.3, 115.2, 68.6, 63.4, 52.7, 49.7, 48.1, 34.5, 34.4, 32.1, 29.3, 28.9, 25.5, 25.4, 24.9, 18.9, 15.7, 13.9; HRMS calcd for $C_{31}H_{31}ClN_5O_2$ $[M-H]^-$: 540.2166, found: 540.2169.

20-Butyl-13,13-dimethyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5i): Isolated as a white solid; mp 216–218 °C; IR (KBr, *v*, cm^{-1}): 2955, 2872, 2248, 1697, 1638, 1465, 1374, 1333, 1264, 1233, 1148, 1089, 1054, 865, 844, 772, 738; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 5.17 (s, 1H, CH), 4.60 (s, 1H, CH), 3.47 (s, 1H, CH), 3.28 (s, 1H, CH), 2.45–2.38 (m, 2H, CH_2), 2.20–2.10 (m, 4H, 4 × CH), 2.03–1.93 (m, 2H, 2 × CH), 1.79–1.67 (m, 4H, 4 × CH), 1.59–1.47 (m, 4H, 4 × CH), 1.35–1.28 (m, 3H, 3 × CH), 1.24–1.16 (m, 2H, 2 × CH), 1.03 (s, 1H, CH), 1.00 (s, 3H, CH_3), 0.95 (s, 3H, CH_3), 0.82 (t, *J* = 8.0 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 200.9, 169.6, 151.5, 150.3, 137.0, 122.8, 120.4, 74.8, 73.7, 57.5, 57.2, 55.3, 53.1, 39.9, 39.2, 37.3, 34.8, 34.4, 34.0, 32.3, 30.4, 29.9, 25.0, 20.7, 19.0; HRMS calcd for $C_{28}H_{34}N_5O_2$ $[M-H]^-$: 472.2713, found: 472.2750.

13,13-Dimethyl-8,11-dioxo-20-(pyridin-2-yl)-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5j): Isolated as a white solid; mp 264–265 °C; IR (KBr, *v*, cm^{-1}): 2956, 2870, 2248, 1696, 1638, 1472, 1434, 1369, 1344, 1265, 1092, 1069; 786, 741; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.08 (s, 1H, ArH), 7.68 (t, *J* = 8.0 Hz, 1H, ArH), 7.15 (d, *J* = 8.8 Hz, 1H, ArH), 6.88 (t, *J* = 5.6 Hz, 1H, ArH), 6.80 (s, 1H, CH), 6.09 (s, 1H, CH), 3.56 (s, 1H, CH), 3.23 (s, 1H, CH), 2.24 (d, *J* = 18.0 Hz, 1H, CH), 2.15–2.06 (m, 2H, 2 × CH), 2.00–1.89 (m, 5H, 5 × CH), 1.83–1.75 (m, 1H, CH), 1.63–1.49 (m, 5H, 5 × CH), 1.33 (d, *J* = 18.0 Hz, 1H, CH), 1.21–1.11 (m, 1H, CH), 0.78 (s, 3H, CH_3), 0.49 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 164.1, 157.3, 148.3, 147.7, 146.8, 139.2, 131.6, 117.9, 117.2, 115.3, 110.3, 66.5, 61.3, 52.7, 49.9, 48.2, 34.6, 34.2, 28.8, 28.6, 26.2, 25.5, 25.0, 15.7, 14.5; HRMS calcd for $C_{29}H_{31}N_6O_2$ $[M+H]^+$: 495.2508, found: 495.2511.

13,13-Dimethyl-8,11-dioxo-20-(pyridin-3-yl)-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5k): Isolated as a white solid; mp 270–271 °C; IR (KBr, *v*, cm^{-1}): 2959, 2872, 2246, 1694, 1667, 1632, 1486, 1466, 1365, 1337, 1270, 1246, 1091, 1021, 805, 710; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.17–8.16 (m, 1H, ArH), 8.02 (s, 1H, ArH), 7.46 (d, *J* = 7.2 Hz, 1H, ArH), 7.33–7.30 (m, 1H, ArH), 6.21 (s, 1H, CH), 5.79 (s, 1H, CH), 3.59 (s, 1H, CH), 3.29 (s, 1H, CH), 2.20 (d, *J* = 18.0 Hz, 1H, CH), 2.09 (d, *J* = 16.4 Hz, 2H, 2 × CH), 2.00–1.83 (m, 7H, 7 × CH), 1.62–1.54 (m, 4H, 4 × CH), 1.26 (d, *J* = 18.0 Hz, 1H, CH), 1.18–1.10 (m, 1H, CH), 0.79 (s, 3H, CH_3), 0.61 (s, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.6, 164.7, 162.8, 147.4, 146.8, 143.6, 143.3, 140.8, 138.4, 131.8, 125.3, 124.8, 124.5, 117.7, 115.2, 68.8, 63.6, 52.8, 52.3, 49.6, 48.1, 48.0, 34.6, 32.1, 29.5, 25.6, 15.7, 13.9; HRMS calcd for $C_{29}H_{31}N_6O_2$ $[M+H]^+$: 495.2508, found: 495.2525.

8,11-Dioxo-20-phenyl-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5l): Isolated as a white solid; mp 224–226 °C; IR (KBr, *v*, cm^{-1}): 2954, 2871, 2249, 1693, 1637, 1496, 1460, 1334, 1238, 1094, 760, 696;

^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.19 (t, J = 7.2 Hz, 2H, ArH), 6.90 (d, J = 7.2 Hz, 1H, ArH), 6.85 (d, J = 8.4 Hz, 2H, ArH), 6.14 (s, 1H, CH), 5.70 (s, 1H, CH), 3.52 (s, 1H, CH), 3.29 (s, 1H, CH), 2.50–2.44 (m, 1H, CH), 2.34–2.26 (m, 1H, CH), 2.09 (d, J = 14.4 Hz, 1H, CH), 2.00–1.81 (m, 8H, 8 × CH), 1.62–1.46 (m, 5H, 5 × CH), 1.34–1.24 (m, 1H, CH), 0.82 (s, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.2, 164.7, 149.5, 147.3, 147.1, 132.2, 130.0, 121.9, 118.5, 117.9, 117.1, 115.3, 68.5, 64.6, 52.1, 48.1, 36.8, 34.3, 29.5, 29.2, 25.9, 25.4, 25.0, 21.1, 15.4, 14.1; HRMS calcd for $C_{28}H_{26}N_5O_2$ $[M\text{-}H]^-$: 464.2087, found: 464.2127.

8,11-Dioxo-20-(*p*-tolyl)-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5m): Isolated as a white solid; mp 230–232 °C; IR (KBr, ν, cm^{-1}): 2952, 2871, 2249, 1694, 1641, 1512, 1451, 1381, 1342, 1262, 1112, 1094, 751, 705; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.98 (d, J = 8.4 Hz, 2H, ArH), 6.73 (d, J = 8.4 Hz, 2H, ArH), 6.08 (s, 1H, CH), 5.65 (s, 1H, CH), 3.51 (s, 1H, CH), 3.28 (s, 1H, CH), 2.46–2.40 (m, 1H, CH), 2.35–2.28 (m, 1H, CH), 2.16 (s, 3H, CH_3), 2.08–2.05 (m, 1H, CH), 1.98–1.75 (m, 8H, 8 × CH), 1.59 (s, 3H, 3 × CH), 1.53–1.45 (m, 2H, 2 × CH), 1.33–1.25 (m, 1H, CH), 0.84 (s, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.2, 164.6, 149.5, 146.9, 144.9, 132.2, 130.8, 130.3, 117.9, 117.0, 115.3, 68.5, 64.6, 52.1, 48.0, 36.7, 34.2, 29.4, 29.1, 25.8, 25.4, 25.0, 20.9, 20.3, 15.4, 14.1; HRMS calcd for $C_{29}H_{30}N_5O_2$ $[M+H]^+$: 480.2400, found: 480.2368.

20-(4-Methoxyphenyl)-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5n): Isolated as a white solid; mp 190–192 °C; IR (KBr, ν, cm^{-1}): 2940, 2870, 2255, 1683, 1635, 1512, 1454, 1365, 1254, 1096, 1035, 968, 835; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.77 (s, 4H, ArH), 6.03 (s, 1H, CH), 5.57 (s, 1H, CH), 3.64 (s, 3H, CH_3O), 3.50 (s, 1H, CH), 3.29 (s, 1H, CH), 2.50–2.46 (m, 1H, CH), 2.36–2.30 (m, 1H, CH), 2.10–2.06 (m, 1H, CH), 1.97–1.87 (m, 8H, 8 × CH), 1.66–1.50 (m, 5H, 5 × CH), 1.34–1.24 (m, 1H, CH), 0.94 (s, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.3, 164.7, 154.5, 149.5, 147.0, 140.9, 132.3, 118.4, 117.9, 115.3, 115.2, 68.8, 65.3, 55.8, 52.2, 48.1, 36.9, 34.4, 34.3, 29.6, 29.3, 26.0, 25.5, 25.0, 21.1, 15.5, 14.1; HRMS calcd for $C_{29}H_{28}N_5O_3$ $[M\text{-}H]^-$: 494.2192, found: 494.2227.

20-(4-Ethoxyphenyl)-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5o): Isolated as a white solid; mp 218–220 °C; IR (KBr, ν, cm^{-1}): 2950, 2875, 2248, 1699, 1647, 1513, 1449, 1379, 1237, 1039, 945, 820; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.75 (s, 4H, ArH), 6.02 (s, 1H, CH), 5.56 (s, 1H, CH), 3.92–3.86 (m, 2H, CH_2O), 3.51 (s, 1H, CH), 3.28 (s, 1H, CH), 2.38–2.30 (m, 1H, CH), 2.10–2.06 (m, 1H, CH), 1.97–1.86 (m, 9H, 9 × CH), 1.67–1.59 (m, 3H, 3 × CH), 1.50 (t, J = 13.6 Hz, 2H, 2 × CH), 1.30 (d, J = 6.8 Hz, 1H, CH), 1.25 (t, J = 7.2 Hz, 3H, CH_3), 0.96 (s, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.3, 164.7, 153.7, 149.5, 146.9, 140.8, 132.3, 120.3, 118.4, 115.8, 68.8, 65.3, 63.7, 52.2, 48.1, 36.9, 34.3, 29.6, 29.3, 26.0, 25.5, 25.1, 21.2, 15.5, 15.2, 14.1; HRMS calcd for $C_{30}H_{30}N_5O_3$ $[M\text{-}H]^-$: 508.2349, found: 508.2389.

20-(2,3-Dimethylphenyl)-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5p): Isolated as a white solid; mp 226–228 °C; IR (KBr, ν, cm^{-1}): 2948, 2874, 2248, 1696, 1679, 1641, 1471, 1375, 1339, 1270, 1093, 788, 725; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.08 (t, J = 8.0 Hz, 1H, ArH), 6.07 (d, J = 7.6 Hz, 1H, ArH), 6.68 (d, J = 8.0 Hz, 1H, ArH), 5.13 (s, 1H, CH), 4.95 (s, 1H, CH), 3.30 (s, 1H, CH), 3.02 (s, 1H, CH), 2.90–2.82 (m, 1H, CH), 2.61–2.57 (m, 2H, 2 × CH), 2.39–2.35 (m, 1H, CH), 2.23 (s, 3H, CH_3), 2.16 (s, 3H, CH_3), 2.12–2.01 (m, 4H, 4 × CH), 1.96–1.82 (m, 5H, 5 × CH), 1.70 (d, J = 14.0 Hz, 1H, CH), 1.58–1.52 (m, 2H, 2 × CH), 1.43–1.33 (m, 1H, CH), 1.10 (s, 1H, CH); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 195.7, 164.0, 148.6, 147.4, 147.2, 138.8, 133.0, 131.2, 126.9, 126.8, 118.1, 117.7, 115.1, 69.7, 68.7, 52.0, 48.2, 37.3, 36.0, 34.9, 30.4, 29.9, 26.4, 26.2, 25.1, 22.2, 21.0, 15.7, 14.7, 14.6; HRMS calcd for $C_{30}H_{31}N_5O_2$ $[M]^+$: 493.2478, found: 493.2473.

20-(3,5-Dimethylphenyl)-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5q): Isolated as a white solid; mp 226–228 °C; IR (KBr, ν, cm^{-1}): 2924, 2865, 2245, 1690, 1640, 1592, 1461, 1364, 1267, 1196, 1177, 883, 832, 754; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.53 (s, 1H, ArH), 6.43 (s, 2H, ArH), 6.08 (s, 1H, CH), 5.65 (s, 1H, CH), 3.53 (s, 1H, CH), 3.30 (s, 1H, CH), 2.35 (t, J = 12.0 Hz, 1H, CH), 2.10 (s, 6H, 2 × CH_3), 2.06 (s, 1H, CH), 1.96–1.86 (m, 9H, 9 × CH), 1.61 (s, 3H, 3 × CH), 1.49 (t, J = 17.6 Hz, 2H, 2 × CH), 1.35–1.29 (m, 1H, CH), 0.76 (s, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.4, 164.6, 149.7, 147.4, 146.8 139.0, 132.1, 123.5, 118.0, 115.3, 115.0, 68.6, 64.6, 51.9, 48.1, 37.0, 34.2, 34.1, 29.6, 29.2, 26.0, 25.4, 25.0, 21.6, 21.1, 15.4, 14.2; HRMS calcd for $C_{30}H_{30}N_5O_2$ $[M\text{-}H]^-$: 492.2400, found: 492.2395.

20-(4-Chlorophenyl)-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5r): Isolated as a white solid; mp 256–258 °C; IR (KBr, ν, cm^{-1}): 2942, 2870, 2248, 1698, 1679, 1639, 1495, 1345, 1246, 1092, 1005, 944, 820, 745, 705; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.34 (d, J = 8.8 Hz, 2H, ArH), 6.99 (d, J = 8.8 Hz, 2H, ArH), 5.79 (s, 1H, CH), 5.48 (s, 1H, CH), 3.31 (s, 1H, CH), 2.91 (s, 1H, CH), 2.87–2.79 (m, 1H, CH), 2.59–2.52 (m, 2H, 2 × CH), 2.38–2.34 (m, 1H, CH), 2.10–2.04 (m, 2H, 2 × CH), 1.99–1.97 (m, 3H, 3 × CH), 1.91–1.79 (m, 4H, 4 × CH), 1.67–1.49 (m, 3H, 3 × CH), 1.40–1.30 (m, 1H, CH), 1.07 (s, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.5, 164.0, 148.4, 147.4, 146.6, 132.9, 129.7, 126.3, 120.3, 117.5, 114.9, 67.7, 67.0, 51.7, 47.9, 37.2, 35.8, 34.8, 29.8, 26.2, 25.9, 24.9, 22.1, 15.5, 14.4; HRMS calcd for $C_{28}H_{27}ClN_5O_2$ $[M+H]^+$: 500.1853, found: 500.1831.

20-Butyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5s): Isolated as a white solid; mp 246–248 °C; IR (KBr, ν, cm^{-1}): 2945, 2867, 2250, 1682, 1637, 1495, 1342, 1255, 1092, 1003, 822, 745, 704; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 4.91 (s, 1H, CH), 4.58 (s, 1H, CH), 3.46 (s, 1H, CH), 3.29 (s, 1H, CH), 2.83–2.77 (m, 1H, CH), 2.59–2.55 (m, 1H, CH), 2.39–2.31 (m, 1H, CH), 2.10–2.04 (m, 3H, 3 × CH), 1.92–1.70 (m, 8H, 8 × CH), 1.57–1.54 (m, 3H, 3 × CH), 1.37–1.26 (m, 6H, 6 × CH), 0.97–0.91 (m, 1H, CH), 0.87 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 195.6, 164.2, 148.9, 146.6, 132.7, 118.0, 115.3, 69.2, 68.2, 51.9, 51.8, 48.2, 37.2, 35.4, 34.8, 30.2, 29.8, 26.2, 25.9, 25.1, 22.1, 20.2, 15.6, 14.6, 14.3; HRMS calcd for $C_{26}H_{32}N_5O_2$ $[M+H]^+$: 446.2556, found: 446.2521.

13-Methyl-8,11-dioxo-20-(*p*-tolyl)-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5t): Isolated as a white solid; mp 246–247 °C; IR (KBr, *v*, cm^{-1}): 2937, 2870, 2246, 1702, 1680, 1640, 1513, 1336, 1249, 1235, 1124, 1089, 906, 871, 821, 735; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.99 (d, J = 8.0 Hz, 2H, ArH), 6.75 (d, J = 8.4 Hz, 2H, ArH), 6.12 (s, 1H, CH), 5.76 (s, 1H, CH), 3.51 (s, 1H, CH), 3.30 (s, 1H, CH), 2.34–2.22 (m, 2H, 2 × CH), 2.18 (s, 3H, CH_3), 2.07 (d, J = 14.4 Hz, 1H, CH), 1.98–1.88 (m, 7H, 7 × CH), 1.59–1.46 (m, 4H, 4 × CH), 1.42–1.34 (m, 1H, CH), 1.28–1.18 (m, 1H, CH), 0.93–0.85 (m, 1H, CH), 0.67 (d, J = 6.4 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 195.3, 164.8, 149.2, 147.1 145.0, 132.3, 130.6, 130.3, 117.9, 116.5, 116.5, 115.6, 68.8, 63.7, 52.9, 48.1, 44.3, 34.5, 34.2, 33.8, 29.2, 29.0, 28.3, 25.4, 25.0, 20.8, 20.3, 15.2, 14.1; HRMS calcd for $C_{30}H_{32}N_5O_2$ $[M+H]^+$: 494.2556, found: 494.2537.

20-(4-Chlorophenyl)-13-methyl-8,11-dioxo-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5u): Isolated as a white solid; mp 217–219 °C; IR (KBr, *v*, cm^{-1}): 2950, 2868, 2248, 1690, 1635, 1497, 1451, 1336, 1239, 1090, 937, 829, 745; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.26 (d, J = 8.8 Hz, 2H, ArH), 6.92 (d, J = 8.8 Hz, 2H, ArH), 6.15 (s, 1H, CH), 5.81 (s, 1H, CH), 3.54 (s, 1H, CH), 3.29 (s, 1H, CH), 2.37–2.26 (m, 2H, 2 × CH), 2.08–1.89 (m, 8H, 8 × CH), 1.59–1.51 (m, 4H, 4 × CH), 1.37 (t, J = 14.4 Hz, 1H, CH), 1.29–1.20 (m, 1H, CH), 0.92–0.85 (m, 1H, CH), 0.71 (d, J = 6.4 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 195.2, 164.7, 148.8, 147.3, 146.3, 132.4, 129.8, 125.6, 118.4, 117.8, 115.5, 68.6, 63.6, 52.8, 48.1, 44.4, 34.4, 34.3, 33.8, 29.1, 28.9, 28.3, 25.4, 25.0, 20.8, 15.2, 13.9; HRMS calcd for $C_{29}H_{29}ClN_5O_2$ $[M+H]^+$: 514.2010, found: 514.1988.

8,11-Dioxo-13,20-diphenyl-3,4,5,6,8,9,10,11,12,13,14,15-dodecahydro-2*H*-9,15,10-(epibutane[1,1,4]triyl)-2,6-epiminobenzo[4,5]azocino[1,2-*a*][1,3]diazocine-9,15-dicarbonitrile (5v): Isolated as a white solid; mp 220–224 °C; IR (KBr, ν, cm^{-1}): 2943, 2873, 2383, 1697, 1637, 1598, 1497, 1454, 1342, 1246, 1091, 1006, 758, 700; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.40–7.36 (m, 2H, ArH), 7.31–7.28 (m, 5H, ArH), 6.99–6.94 (m, 3H, ArH), 5.81 (s, 1H, CH), 5.44 (s, 1H, CH), 3.39 (s, 1H, CH), 3.12–3.02 (m, 1H, CH), 2.88–2.55 (m, 4H, 4 × CH), 2.09–1.91 (m, 6H, 6 × CH), 1.87–1.79 (m, 1H, CH), 1.70–1.45 (m, 4H, 4 × CH), 1.23–1.06 (m, 2H, 2 × CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C: 195.2, 163.9, 147.6, 147.3, 146.5, 143.2, 143.1, 132.8, 129.9, 129.3, 129.3, 127.6, 127.1, 122.6, 118.5, 118.4, 117.4, 115.3, 67.9, 67.1, 52.7, 48.0, 43.4, 38.3, 36.6, 34.9, 34.8, 30.0, 29.9, 15.3, 14.7; HRMS calcd for $C_{34}H_{32}N_5O_2$ $[M+H]^+$: 542.2556, found: 542.2522.

19-(4-Methoxyphenyl)-8,11-dioxo-2,3,4,5,6,8,9,10,11,12,13,14-dodecahydro-9,14,10-(epibutane[1,1,4]triyl)-2,6-epimino-cyclopenta[4,5]azocino[1,2-*a*][1,3]diazocine-9,14-dicarbonitrile (7a): Isolated as a white solid; mp 218–220 °C; IR (KBr, *v*, cm^{-1}): 2958, 2870, 2361, 1715, 1691, 1646, 1597, 1492, 1445, 1384, 1342, 1247, 1092, 1014, 960, 875, 867, 792, 706; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.73–6.66 (m, 4H, ArH), 5.99–5.98 (m, 1H, CH), 5.59–5.58 (m, 1H, CH), 3.69–3.66 (m, 4H, CH_3 and CH), 3.11 (s, 1H, CH), 2.55–2.50 (m, 1H, CH), 2.39–2.32 (m, 1H, CH), 2.04–1.87 (m, 7H, 7 × CH), 1.66–1.49 (m, 6H, 6 × CH), 1.22–1.84 (m, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 203.8, 164.5, 164.3, 154.3, 146.2, 140.8, 138.6, 118.3, 114.8, 69.6, 64.9, 55.6, 50.0, 48.0, 34.9, 34.3, 34.1, 29.3, 29.0, 25.4, 24.7, 24.2, 15.2, 14.0; HRMS calcd for $C_{28}H_{27}N_5NaO_3$ $[M+Na]^+$: 504.2012, found: 504.2000.

19-(3-Isopropylphenyl)-8,11-dioxo-2,3,4,5,6,8,9,10,11,12,13,14-dodecahydro-9,14,10-(epibutane[1,1,4]triyl)-2,6-epimino-cyclopenta[4,5]azocino[1,2-*a*][1,3]diazocine-9,14-dicarbonitrile (7b): Isolated as a white solid; mp 218–219 °C; IR (KBr, *v*, cm^{-1}): 2963, 2344, 1716, 1692, 1641, 1492, 1443, 1384, 1342, 1243, 1093, 959, 875, 790, 705; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.00 (t, J = 8.0 Hz, 1H, ArH), 6.88 (s, 1H, ArH), 6.78 (d, J = 7.6 Hz, 1H, ArH), 6.41–6.39 (m, 1H, CH), 6.16–6.15 (m, 1H, CH), 5.82–5.81 (m, 1H, CH), 3.68 (s, 1H, CH), 3.10 (s, 1H, CH), 2.77–2.73 (m, 1H, CH), 2.51–2.45 (m, 1H, CH), 2.29–2.23 (m, 1H, CH), 2.01–1.96 (m, 4H, 4 × CH), 1.95–1.83 (m, 3H, 3 × CH), 1.62–1.57 (m, 2H, 2 × CH), 1.56–1.45 (m, 4H, 4 × CH), 1.19–1.17 (m, 1H, CH), 1.14 (d, J = 6.8 Hz, 3H, CH_3), 1.11 (d, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 203.8, 164.4, 150.5, 147.2, 146.3, 138.5, 129.4, 119.8, 117.8, 115.6, 114.6, 113.0, 68.7, 63.9, 49.9 48.0, 34.8, 34.2, 34.0, 29.3, 28.9, 25.3, 24.7, 24.1, 15.2, 14.0; HRMS calcd for $C_{30}H_{32}N_5O_2$ $[M+H]^+$: 494.2556, found: 494.2559.

19-(3-Chlorophenyl)-8,11-dioxo-2,3,4,5,6,8,9,10,11,12,13,14-dodecahydro-9,14,10-(epibutane[1,1,4]triyl)-2,6-epiminocyclo penta[4,5]azocino[1,2-*a*][1,3]diazocine-9,14-dicarbonitrile (7c): Isolated as a white solid; mp 236–237 °C; IR (KBr, *v*, cm^{-1}): 2936, 2864, 2251, 1716, 1641, 1473, 1439, 1340, 1258, 1235, 1094, 1012, 874, 751; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 7.66–7.63 (m, 1H, ArH), 7.18–7.14 (m, 1H, ArH), 7.03–6.99 (m, 1H, ArH), 6.37–6.35 (m, 1H, CH), 5.81–5.80 (m, 1H, CH), 5.24–5.23 (m, 1H, CH), 3.72 (s, 1H, CH), 3.16 (s, 1H, CH), 2.82–2.76 (m, 1H, CH), 2.23–1.92 (m, 9H, 9 × CH), 1.86–1.83 (m, 1H, CH), 1.72–1.53 (m, 4H, 4 × CH), 1.33–1.25 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C: 204.2, 163.7, 162.9, 147.0, 145.9, 139.1, 134.2, 129.8, 126.7, 123.0, 119.4, 117.4, 114.5, 69.1, 68.1, 49.9, 48.0, 35.5, 35.1, 34.5, 30.5, 29.2, 26.3, 25.1, 24.2, 15.2, 14.3; HRMS calcd for $C_{27}H_{25}ClN_5O_2$ $[M+H]^+$: 486.1697, found: 486.1692.

19-(3,5-Dimethylphenyl)-8,11-dioxo-2,3,4,5,6,8,9,10,11,12,13,14-dodecahydro-9,14,10-(epibutane[1,1,4]triyl)-2,6-epiminocyclopenta[4,5]azocino[1,2-*a*][1,3]diazocine-9,14-dicarbonitrile (7d): Isolated as a white solid; mp 220–222 °C; IR (KBr, *v*, cm^{-1}): 2952, 2861, 2246, 1715, 1693, 1641, 1593, 1445, 1389, 1343, 1251, 1199, 1094, 1006, 859, 833, 700; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.54 (s, 1H, ArH), 6.38 (s, 2H, ArH), 6.07–6.06 (m, 1H, CH), 5.73–5.72 (m, 1H, CH), 3.67 (s, 1H, CH), 3.13 (s, 1H, CH), 2.55–2.51 (m, 1H, CH), 2.36–2.30 (m, 1H, CH), 2.10 (s, 6H, 2 × CH_3), 2.05–1.80 (m, 8H, 8 × CH), 1.62–1.60 (m, 2H, 2 × CH), 1.56–1.51 (m, 3H, 3 × CH), 1.22–1.19 (m, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 209.0, 169.5, 169.3, 152.2, 151.1, 143.8, 143.4, 128.3, 122.6, 119.4, 74.1, 69.0, 54.8, 52.9, 39.7, 39.1, 39.0, 34.1, 33.8, 30.4, 29.6, 29.0, 26.4, 20.0, 18.9; HRMS calcd for $C_{29}H_{30}N_5O_2$ $[M+H]^+$: 480.2400, found: 480.2392.

19-Butyl-8,11-dioxo-2,3,4,5,6,8,9,10,11,12,13,14-dodeca-hydro-9,14,10-(epibutane[1,1,4]triyl)-2,6-epiminocyclopenta [4,5]azocino[1,2-*a*][1,3]diazocine-9,14-dicarbonitrile (7e): Isolated as a white solid; mp 206–207 °C; IR (KBr, *v*, cm^{-1}): 2933, 2857, 2249, 1720, 1638, 1465, 1384, 1341, 1250, 1109, 1089, 1012, 851; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 5.16–5.15 (m, 1H, CH), 4.61–4.60 (m, 1H, CH), 3.63 (s, 1H, CH), 3.11 (s, 1H, CH), 2.96–2.90 (m, 1H, CH), 2.65–2.57 (m, 2H, 2 × CH), 2.31–2.24

(m, 1H, CH), 2.09–2.00 (m, 3H, 3 × CH), 1.98–1.89 (m, 2H, 2 × CH), 1.83–1.75 (m, 2H, 2 × CH), 1.73–1.69 (m, 2H, 2 × CH), 1.61–1.48 (m, 4H, 4 × CH), 1.35–1.24 (m, 3H, 3 × CH), 1.22–1.14 (m, 2H, 2 × CH), 0.79 (t, J = 7.2 Hz, 3H, CH_3); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C: 204.1, 164.5, 163.4, 145.7, 139.2, 117.9, 114.8, 70.2, 68.5, 51.7, 50.2, 48.2, 35.1, 34.6, 34.1, 29.4, 29.3, 26.1, 24.8, 24.2, 20.1, 15.3, 14.1; HRMS calcd for $[M+H]^+$: $C_{25}H_{30}N_5O_2$ 432.2400, found: 432.2396.

8,11-Dioxo-22-(*p*-tolyl)-2,3,4,5,6,8,9,10,11,17-decahydro-9, 17,10-(epibutane[1,1,4]triyl)-2,6-epiminochromeno[4',3':4,5] azocino[1,2-*a*][1,3]diazocine-9,17-dicarbonitrile (9a): Isolated as a white solid; mp 224–226 °C; IR (KBr, v, cm^{-1}): 2952, 2865, 2246, 1729, 1648, 1569, 1491, 1457, 1382, 1326, 1248, 1176, 1092, 953, 785; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.56 (d, J = 8.4 Hz, 1H, ArH), 7.65 (t, J = 7.6 Hz, 1H, ArH), 7.46–7.40 (m, 2H, ArH), 7.08 (d, J = 8.0 Hz, 2H, ArH), 6.81 (d, J = 8.0 Hz, 2H, ArH), 5.66 (s, 1H, CH), 5.44 (s, 1H, CH), 3.54 (s, 1H, CH), 2.92 (s, 1H, CH), 2.19 (s, 3H, CH_3), 2.17–2.12 (m, 1H, CH), 1.99–1.94 (m, 2H, 2 × CH), 1.88–1.75 (m, 3H, 3 × CH), 1.72–1.65 (m, 2H, 2 × CH), 1.52–1.49 (m, 1H, CH), 1.34–1.27 (m, 1H, CH), 1.02–0.98 (m, 1H, CH), 0.28–0.25 (m, 1H, CH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 163.5, 158.2, 152.8, 147.2, 145.4, 139.1, 133.0, 131.6, 130.5, 126.6, 125.4, 124.4, 118.4, 117.9, 117.1, 115.7, 115.5, 68.3, 67.2, 48.3, 48.0, 38.0, 36.7, 29.6, 26.3, 24.4, 20.6, 15.6, 13.6; HRMS calcd for $C_{32}H_{28}N_5O_3$ $[M+H]^+$: 530.2192, found: 530.2163.

22-(4-Chlorophenyl)-8,11-dioxo-2,3,4,5,6,8,9,10,11,17-deca-hydro-9,17,10-(epibutane[1,1,4]triyl)-2,6-epiminochromeno [4',3':4,5]azocino[1,2-*a*][1,3]diazocine-9,17-dicarbonitrile (9b): Isolated as a white solid; mp 242–243 °C; IR (KBr, v, cm^{-1}): 2949, 2861, 2350, 1727, 1693, 1642, 1494, 1453, 1318, 1272, 1241, 1101, 877, 829, 755; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.20 (d, J = 8.4 Hz, 1H, ArH), 7.51 (t, J = 8.0 Hz, 1H, ArH), 7.29 (d, J = 8.4 Hz, 1H, ArH), 7.06 (t, J = 7.6 Hz, 1H, ArH), 6.56 (d, J = 8.8 Hz, 2H, ArH), 6.42 (d, J = 8.8 Hz, 2H, ArH), 5.90 (s, 1H, CH), 5.57 (s, 1H, CH), 3.80 (s, 1H, CH), 3.61 (s, 1H, CH), 2.26–2.22 (m, 1H, CH), 2.12–1.98 (m, 4H, 4 × CH), 1.94–1.90 (m, 2H, 2 × CH), 1.87–1.82 (m, 1H, CH), 1.62–1.54 (m, 3H, 3 × CH), 1.32–1.29 (m, 1H, CH); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 164.1, 157.9, 152.2, 146.9, 145.5, 140.6, 132.4, 129.7, 128.5, 126.3, 126.0, 124.1, 124.0, 120.1, 118.6, 117.4, 117.2, 115.7, 115.1, 70.4, 65.3, 48.4, 47.9, 36.7, 36.1, 29.0, 25.7, 24.6, 15.4, 14.1; HRMS calcd for $C_{31}H_{25}ClN_5O_3$ $[M+H]^+$: 550.1646, found: 550.1675.

8,11-Dioxo-22-(*m*-tolyl)-2,3,4,5,6,8,9,10,11,17-decahydro-9, 17,10-(epibutane[1,1,4]triyl)-2,6-epiminochromeno[4',3':4,5] azocino[1,2-*a*][1,3]diazocine-9,17-dicarbonitrile (9c): Isolated as a white solid; mp 228–229 °C; IR (KBr, v, cm^{-1}): 2952, 2867, 2245, 1723, 1691, 1650, 1606, 1569, 1492, 1451, 1384, 1327, 1245, 1174, 1126, 1097, 1064, 953, 856, 760, 697; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.28–8.25 (m, 1H, ArH), 7.50–7.45 (m, 1H, ArH), 7.27–7.24 (m, 1H, ArH), 7.12–7.08 (m, 1H, ArH), 6.45 (t, J = 8.0 Hz, 1H, ArH), 6.22 (s, 1H, ArH), 6.19–6.12 (m, 2H, ArH), 5.95–5.94 (m, 1H, CH), 5.59–5.58 (m, 1H, CH), 3.82 (s, 1H, CH), 3.63–3.62 (m, 1H, CH), 2.29–2.22 (s, 1H, CH), 2.13–1.97 (m, 4H, 4 × CH), 1.92–1.91 (m, 1H, CH), 1.89 (s, 3H, CH_3), 1.85–1.55 (m, 5H, 5 × CH), 1.35–1.25 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C: 164.2, 158.0, 152.2, 146.6, 146.5, 140.8, 138.1, 132.5, 128.3, 126.1, 124.0, 123.6, 123.0, 117.5, 117.4, 117.1, 115.9, 115.0, 113.6, 70.3, 65.0, 48.3, 47.8, 36.5, 35.8, 29.1, 28.9, 25.6, 24.6, 21.5, 15.4, 14.3; HRMS calcd for $C_{32}H_{28}N_5O_3$ $[M+H]^+$: 530.2192, found: 530.2163.

22-(3-Bromophenyl)-8,11-dioxo-2,3,4,5,6,8,9,10,11,17-deca-hydro-9,17,10-(epibutane[1,1,4]triyl)-2,6-epiminochromeno [4',3':4,5]azocino[1,2-*a*][1,3]diazocine-9,17-dicarbonitrile (9d): Isolated as a white solid; mp 246–247 °C; IR (KBr, v, cm^{-1}): 2949, 2861, 2359, 1727, 1693, 1641, 1589, 1564, 1477, 1449, 1322, 1269, 1239, 1127, 1100, 1063, 949, 879, 860, 766, 686; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.62–8.60 (m, 1H, ArH), 7.72–7.68 (m, 1H, ArH), 7.51–7.46 (m, 2H, ArH), 7.27 (t, J = 8.0 Hz, 1H, ArH), 7.24–7.23 (m, 1H, ArH), 7.17–7.15 (m, 1H, ArH), 6.96–6.94 (m, 1H, ArH), 5.84 (s, 1H, CH), 5.64 (s, 1H, CH), 3.59 (s, 1H, CH), 3.11 (s, 1H, CH), 2.22–2.18 (m, 1H, CH), 2.09–1.82 (m, 5H, 5 × CH), 1.76 (s, 2H, 2 × CH), 1.59–1.55 (m, 1H, CH), 1.43–1.36 (m, 1H, CH), 1.07–1.03 (m, 1H, CH), 0.34–0.27 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C: 163.5, 158.2, 152.8, 149.1, 147.3, 139.0, 133.0, 131.8, 126.6, 125.4, 125.0, 124.3, 123.1, 121.0, 117.9, 117.1, 116.7, 115.7, 115.5, 67.8, 66.1, 48.2, 47.9, 37.7, 36.7, 29.4, 26.2, 24.4, 15.6, 13.4; HRMS calcd for $C_{31}H_{24}BrN_5NaO_3$ $[M+Na]^+$: 616.0960, found: 616.0967.

22-(2,3-Dimethylphenyl)-8,11-dioxo-2,3,4,5,6,8,9,10,11,17-decahydro-9,17,10-(epibutane[1,1,4]triyl)-2,6-epimino chromeno[4',3':4,5]azocino[1,2-*a*][1,3]diazocine-9,17-dicarbonitrile (9e): Isolated as a white solid; mp 238–239 °C; IR (KBr, v, cm^{-1}): 2945, 2871, 2345, 1697, 1640, 1502, 1385, 1327, 1253, 1228, 1118, 1094, 761; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.56–8.53 (m, 1H, ArH), 7.65–7.61 (m, 1H, ArH), 7.48–7.46 (m, 1H, ArH), 7.31–7.27 (m, 1H, ArH), 6.48 (d, J = 8.4 Hz, 1H, ArH), 5.76 (t, J = 8.0 Hz, 1H, CH), 5.57 (d, J = 7.6 Hz, 1H, CH), 5.43–5.42 (m, 1H, CH), 4.88–4.87 (m, 1H, CH), 3.83 (s, 1H, CH), 3.56 (s, 1H, CH), 2.32–2.28 (m, 1H, CH), 2.14–2.09 (m, 2H, 2 × CH), 2.05–2.04 (m, 6H, 2 × CH_3), 2.02–1.92 (m, 4H, 4 × CH), 1.85–1.82 (m, 1H, CH), 1.75–1.71 (m, 2H, 2 × CH), 1.61–1.58 (m, 1H, CH), 1.44–1.38 (m, 1H, CH); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 163.9, 158.1, 152.8, 146.9, 146.2, 139.9, 138.1, 133.0, 130.0, 126.7, 125.6, 124.5, 124.1, 117.8, 117.5, 116.8, 116.1, 115.8, 70.4, 69.1, 48.4, 48.0, 36.3, 36.2, 29.5, 29.3, 25.8, 24.7, 20.6, 15.4, 14.6, 14.4; HRMS calcd for $C_{33}H_{30}N_5O_3$ $[M+H]^+$: 544.2349, found: 544.2363.

22-(3-Chloro-4-methylphenyl)-8,11-dioxo-2,3,4,5,6,8,9,10,11, 17-decahydro-9,17,10-(epibutane[1,1,4]triyl)-2,6-epimino chromeno[4',3':4,5]azocino[1,2-*a*][1,3]diazocine-9,17-dicarbonitrile (9f): Isolated as a white solid; mp 260–261 °C; IR (KBr, v, cm^{-1}): 2955, 2864, 2365, 1724, 1641, 1608, 1501, 1340, 1243, 1125, 1093, 1065, 856, 802, 759; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.16–8.13 (m, 1H, ArH), 7.49–7.45 (m, 1H, ArH), 7.30–7.28 (m, 1H, ArH), 7.03–7.00 (m, 1H, ArH), 6.52 (d, J = 8.8 Hz, 1H, ArH), 6.37–6.36 (m, 1H, ArH), 6.31–6.29 (m, 1H, ArH), 5.93–5.92 (m, 1H, CH), 5.64–5.63 (m, 1H, CH), 3.82 (s, 1H, CH), 3.64–3.63 (m, 1H, CH), 2.26–1.95 (m, 7H, 7 × CH), 1.91 (s, 3H, CH_3), 1.86–1.81 (m, 1H, CH), 1.63–1.55 (m, 3H, 3 × CH), 1.32–1.29 (m, 1H, CH); ^{13}C NMR (150 MHz, DMSO-d_6) δ_C: 164.4, 157.9, 152.1, 146.7, 146.0, 140.8, 133.4, 132.2, 131.1, 128.4, 126.0, 124.0, 123.9, 117.4, 117.1, 116.8, 115.7, 115.5, 114.9, 70.8, 64.6, 48.3, 47.8, 36.7, 35.8, 28.8, 25.6, 24.5, 19.0, 15.4, 14.1; HRMS calcd for $C_{32}H_{26}ClN_5NaO_3$ $[M+Na]^+$: 586.1622, found: 586.1617.

15-Acetyl-14-methyl-8-oxo-16-(*p*-tolyl)-3,4,5,6,8,8a,9, 10, 11, 12,12a,13-dodecahydro-2*H*-2,6-epimino-9,13-etheno[1,3]diazo cino[1,2-*b*]isoquinoline-8a,13-dicarbonitrile (11a): Isolated as a white solid; mp 209–210 °C; IR (KBr, v, cm^{-1}): 2926, 2866, 2246,

1695, 1637, 1557, 1539, 1460, 1396, 1376, 1295, 1253, 1112, 1086, 1019, 925, 896; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.94 (d J = 8.4 Hz, 2H, ArH), 6.70 (d, J = 8.4 Hz, 2H, ArH), 6.03 (s, 1H, CH), 5.55 (s, 1H, CH), 3.46 (s, 1H, CH), 3.25 (s, 1H, CH), 2.16 (s, 3H, CH_3), 2.12–2.09 (m, 1H, CH), 2.06 (s, 3H, CH_3), 1.99–1.88 (m, 6H, 6 × CH), 1.61–1.56 (m, 4H, 4 × CH), 1.32 (s, 3H, CH_3), 1.23 (s, 1H, CH); ^{13}C NMR (75 MHz, DMSO-d_6) δ_C: 201.6, 164.7, 147.1, 145.2, 137.3, 131.1, 129.9, 117.9, 117.7, 115.8, 69.5, 65.1, 52.3, 47.8, 39.1, 37.7, 34.0, 30.2, 29.4, 29.1, 25.5, 25.0, 20.5, 16.0, 15.1, 14.1; HRMS calcd for $C_{28}H_{30}N_5O_2$ $[M+H]^+$: 468.2400, found: 468.2396.

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