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Scandium Pentafluorobenzoate-Catalyzed Unexpected Cascade Reaction of 2-Aminobenzaldehydes with Primary Amines: A Process for the Preparation of Ring-Fused Aminals

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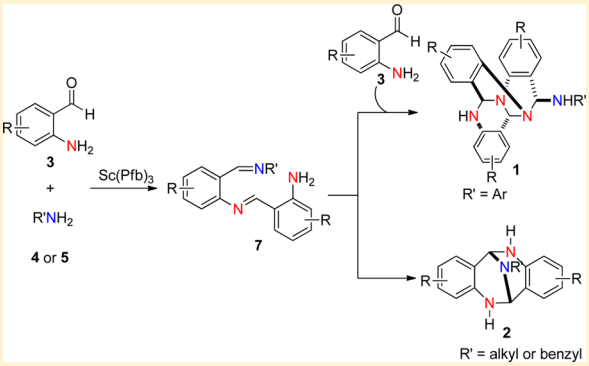
Supporting Information

ABSTRACT: An unexpected cascade reaction of 2-aminobenzaldehydes with arylamines catalyzed by scandium pentafluorobenzoate [$Sc(Pfb)_3$] was reported as a facile strategy for the efficient synthesis of a novel class of polycyclic ring-fused aminals *N*-substituted-6,7,11b,13-tetrahydro-6,12-[1,2]benzenoquinazolino[3,4-*a*]-quinazolin-13-amines **1**. Under similar conditions, a series of the analogues of Tröger's base, 13-substituted-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocines **2** were obtained when the arylamines were replaced by methanamines. A possible mechanism for the formation of **1** and **2** was proposed.

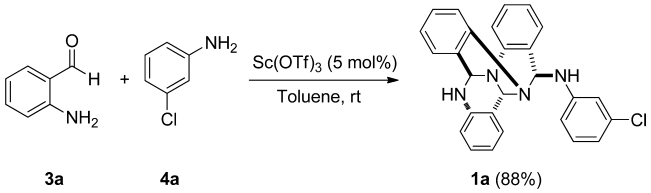


Nitrogen heterocycles are present in many compounds of enormous practical importance, ranging from pharmaceutical agents and biological probes to electroactive materials. Ring-fused aminals of nitrogen heterocycles found in numerous natural products[1] have attracted considerable attention as useful building blocks and potential drug candidates.[2] Consequently, the development of synthetic methods for the preparation of bridged polyfused aminals has received considerable attention. To date, various methods have been reported for the synthesis of ring-fused aminals. Traditionally, multistep synthesis procedures are required in most cases.[3−5] Recently, a number of ring-fused aminal-formed reactions have been reported through direct functionalization of heterocycles,[6−9] which is one of the best and shortest routes to these compounds. Nevertheless, bridged polyfused carbon and heteroatom networks cannot be achieved through this method. Therefore, the discovery of new reaction sequences able to produce valuable elaborated compounds constitutes a challenge from both academic and industrial points of view.

2-Aminobenzaldehydes are an important class of versatile and efficient synthetic platforms in the synthesis of nitrogen heterocycles due to their special chemical properties. For example, they are common starting materials for the synthesis of quinolones,[10−13] quinoxalines,[14] and indolines[12,15,16] and are also widely used in the synthesis of ring-fused aminals.[6,8,9] Due to the easy condensation between amine and aldehyde, several polycyclic ring-fused aminals have been formed through the simple self-condensation of 2-aminobenzaldehydes,[17,18] which, on the other hand, often inevitably became the byproducts in the 2-aminobenzaldehydes participant reactions. In most cases,[9,15,16] either the amino or the aldehyde group of the 2-aminobenzaldehydes is protected in case of self-condensation. To our knowledge, the reaction of unprotected 2-aminobenzaldehydes with primary amines has been rarely reported. To better understand the reactivity of 2-aminobenzaldehydes with amines and in conjunction with our continuing efforts for research on rare earth Lewis acids-catalyzed reactions,[19] we report our investigation on the reaction of 2-aminobenzaldehydes with varieties of primary amines catalyzed by an efficient Lewis acid, $Sc(Pfb)_3$,[20] affording a series of bridged, polyfused aminals.

The first experiment was carried out at room temperature, 2-aminobenzaldehyde **3a** and 3-chloroaniline **4a** were chosen as model substrates, and the frequently used Lewis acid, [$Sc(OTf)_3$], and toluene were employed. After 12 h the reaction was complete (TLC), and the main product was purified with 88% yield (Scheme 1). The structural elucidation of the isolated substance by the X-ray analysis[21] of its single

Scheme 1. Reaction of 2-Aminobenzaldehyde with 3-Chloroaniline Catalyzed by $Sc(OTf)_3$



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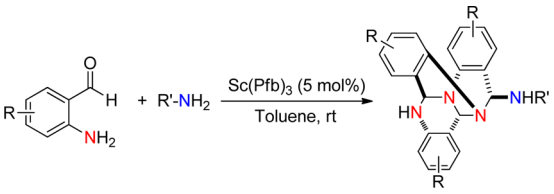
crystal revealed that a new, bridged, polyfused aminal, *N*-(3-chlorophenyl)-6,7,11b,13-tetrahydro-6,12-[1,2]benzenequinazolino[3,4-*a*]quinazolin-13-amine **1a** was obtained.

Further modification of the experimental procedure with respect to the catalyst, the solvent, and the reaction temperature revealed that, compared with Brønsted acids, traditional Lewis acids, and other rare earth metal Lewis acids, $Sc(Pfb)_3$ gave the best result, affording **1a** in 97% yield; toluene was the best solvent compared with H_2O, DMF, EtOH, THF, and 1,2-DCE; room temperature was suitable for this reaction (see Table S1 in the Supporting Information for a screen).

Using the optimized conditions (5 mol % $Sc(Pfb)_3$, toluene, air, rt), a library of novel and diverse ring-fused quinazoline derivatives **1a**–**n** (Table 1) were prepared from the respective

Table 1. $Sc(Pfb)_3$-Catalyzed 2-Aminobenzaldehydes Reacting with Arylamines[a]



3 4 1

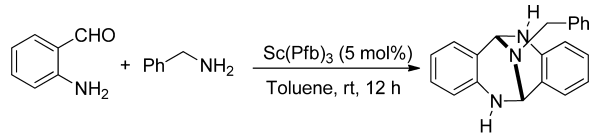
entry	R	R′	product **1a**–**n**	yield (%)[b]
1	H	3-Cl-C_6H_4	**1a**	97
2	H	2-Cl-C_6H_4	**1b**	69
3	H	4-Cl-CH_4	**1c**	71
4	H	2-Br-C_6H_4	**1d**	98
5	H	3-CH_3-C_6H_4	**1e**	90
6	H	4-CH_3-C_6H_4	**1f**	69
7	H	2-OH-C_6H_4	**1g**	88
8	H	3-OH-C_6H_4	**1h**	56
9	H	2-OH,4-Cl-C_6H_3	**1i**	97
10	H	3-CF_3,5-CF_3-C_6H_3	**1j**	62[c]
11	H	C_6H_5	**1k**	80[c]
12	5-OMe	3-Cl-C_6H_4	**1l**	81
13	5-OMe	2-Br-C_6H_4	**1m**	83
14	5-OMe	C_6H_5	**1n**	73[c]

[a]General conditions: **3** (1.5 mmol), **4** (0.5 mmol), $Sc(Pfb)_3$ (0.025 mmol), 1.0 mL of toluene at room temperature for 12 h, unless stated otherwise. [b]Isolated yields. [c]At 90 °C.

2-aminobenzaldehydes with arylamines. Halogenated arylamines reacted with 2-aminobenzaldehyde and 2-amino-5-methoxybenzaldehyde smoothly and formed the corresponding products (Table 1, entries 1–4, 12, 13), among which relatively low yields (Table 1, entries 2 and 3) were caused by self-condensation of 2-aminobenzaldehyde. Arylamines containing electron-donating substituents (−Me, −OH) also gave the products in moderate to excellent yields (Table 1, entries 5–9). In these reactions, the side reactions included not only self-condensation of 2-aminobenzaldehyde but also some others such as oxidation of the electron-rich aromatic ring and more complex condensations. Aniline and 3,5-bis(trifluoromethyl)-aniline which could not react with 2-aminobenzaldehydes at room temperature afforded the products **1k**, **1j**, and **1n** in good yields at 90 °C (Table 1, entries 10, 11, 14). Unfortunately, anilines with other strong electron-withdrawing groups, such as nitro- or sulfino-, were not tolerated in this procedure. In these reactions, what we obtained was the self-condensation products of 2-aminobenzaldehydes,[17,18] which might have resulted from the low reactivity of the electron-deficient arylamines.

Inspired by the substrate scope study that electron-rich amines could react well with 2-aminobenzaldehydes to afford **1**, we speculated that nonaromatic amines could be more suitable for this reaction. Thus, 2-aminobenzaldehyde reacting with benzylamine under the same conditions was explored (Scheme 2). Interestingly, compound **1** was not detected. Besides the

Scheme 2. Reaction of 2-Aminobenzaldehyde with Benzylamine



3a **5a** **2a** (56%)

self-condensation compounds of 2-aminobenzadehyde, another product, **2a**, was isolated in moderate yield. Through the X-ray analysis[22] of its single crystal, the structure of **2a** was established as 13-benzyl-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine.

The epiminodibenzo[*b*,*f*][1,5]diazocines, **2**, as an analogous scaffold of Tröger's base possesses not only most of the applications of Tröger's base[23] but also the possibility of exploiting the covalent (reactivity) and noncovalent (hydrogen-bonding) capabilities and the application in molecular recognition. They hold the extended interest of the synthesis of Tröger's base derivatives. However, strong acid conditions or multistep processes were always inevitable in the synthesis of the epiminodibenzo[*b*,*f*][1,5]diazocines **2**.[24] Herein, we provide a novel methodology for the convenient synthesis of **2** *via* the cascade reaction of 2-aminobenzaldehydes with methanamines catalyzed by a simple Lewis acid.

The reaction conditions were screened (Table S2, SI) to improve the yield of product **2a** as well. The result elucidated that $Sc(Pfb)_3$ and toluene were still the best catalyst and solvent for this reaction, but higher reaction temperature was required to improve the yield of **2a**. When it was increased to 90 °C, the product was obtained in 83% yield (Table S2, SI, entry 10).

With the optimal condition in hand, the generality of the synthetic approach was examined (Table 2). Benzylamines bearing different substituents reacted with 2-aminobenzaldehyde giving the products in moderate to excellent yields (47–98%, Table 2, entries 1–10). Aliphatic amines were also suitable substrates for this reaction, giving **2k**–**m** in relatively low yields (Table 2, entries 11–13). 2-Amino-5-methoxybenzaldehyde reacted with benzylamines, affording **2n** and **2o** in good yields as well (Table 2, entries 14 and 15). Interestingly, when the multisubstituted methanamine 1,2,3,4-tetrahydroisoquinoline was employed, the expected product was not detected, and the main isolated product was **1o** (Scheme 3). However, only the self-condensation products of 2-aminobenzaldehyde were detected when it reacted with other multisubstituted amines such as diethylamine.

As depicted in Scheme 4,[25] we proposed a reasonable mechanistic hypothesis. In the first step, the aldehyde-amine condensation between 2-aminobenzaldehyde and amine rapidly formed the intermediate **6**, and then imine **7** was formed through the reaction of intermediate **6** with another molecule of 2-aminobenzaldehyde, **3**. Next, there might be two competing routes. In route I, compounds **2** were formed

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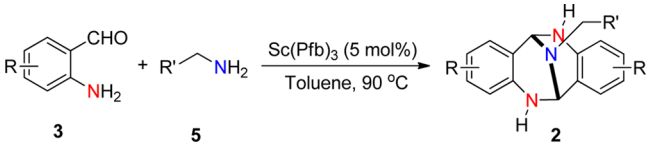
Table 2. 2-Aminobenzaldehydes Reacting with Different Methanamines[a]

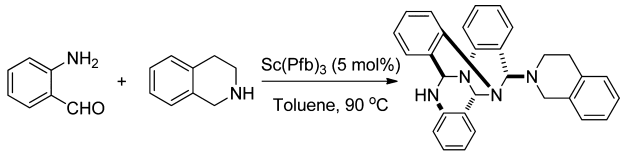


3 5 2

entry	R	R′	product **2a–o**	yield (%)[b]
1	H	C_6H_5	**2a**	83
2	H	3-F,4-F-C_6H_3	**2b**	98
3	H	3-F-C_6H_4	**2c**	90
4	H	2-F-C_6H_4	**2d**	89
5	H	4-F-C_6H_4	**2e**	84
6	H	4-NO_2-C_6H_4	**2f**	88
7	H	4-Cl-C_6H_4	**2g**	86
8	H	4-CH_3-C_6H_4	**2h**	63
9	H	4-CH_3O-C_6H_4	**2i**	74
10	H	C_6H_5-C_6H_4	**2j**	47
11	H	H	**2k**	70
12	H	C_3H_7	**2l**	64
13	H	$C_{15}H_{31}$	**2m**	54
14	5-OMe	C_6H_5	**2n**	70
15	5-OMe	2-F-C_6H_4	**2o**	90

[a]General conditions: **3** (0.5 mmol), **5** (0.25 mmol), $Sc(Pfb)_3$ (0.0125 mmol), 0.5 mL of toluene at 90 °C for 12 h. [b]Isolated yields.

Scheme 3. 2-Aminobenzaldehyde Reacting with 1,2,3,4-Tetrahydroisoquinoline



1o, 68% yield

immediately through the $Sc(Pfb)_3$-promoted intermolecular cascade imine addition of **7**. In route II, imine **7** went on reacting with 2-aminobenzaldehyde **3** to give intermediate **8**, and compounds **1** were finally formed through the intermolecular cascade imine addition of **8**. The activity of amines prompted the reaction to go through different routes, giving the corresponding products. The exceptional formation of **1o** through route II may have resulted from the similar reactivity of 1,2,3,4-tetrahydroisoquinoline with aniline due to the large steric hindrance, and the difficulty for the secondary amine to be a bridgehead nitrogen as a quaternary amine in compound **2**.

In summary, the reaction of 2-aminobenzaldehydes with primary amines catalyzed by the efficient Lewis acid $Sc(Pfb)_3$ was investigated, and a facile method for the preparation of polycyclic ring-fused aminals including the new compounds, aryl-bridged quinazolino[3,4-*a*]quinazolines, **1**, and the analogous scaffold of Tröger's base, epiminodibenzo[*b*,*f*][1,5]-diazocines, **2**, was developed. The activity of the amines played an important role in the reaction, and the more reactive methanamines favored the formation of epiminodibenzo[*b*,*f*]-[1,5]diazocines, **2**.

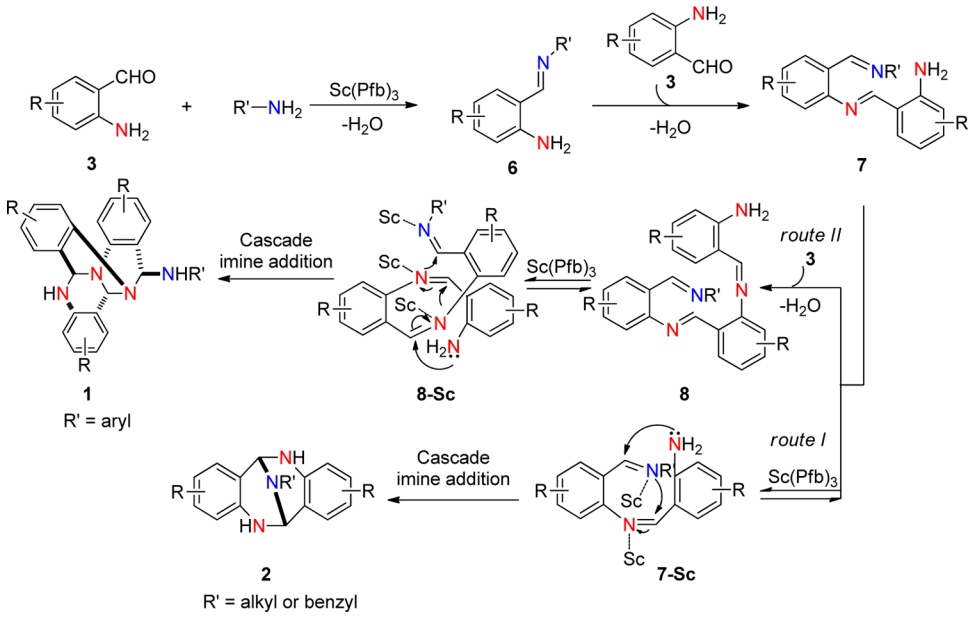
EXPERIMENTAL SECTION

General Information. ^1H NMR and ^{13}C NMR spectra were respectively recorded at 400 and 100 MHz, using tetramethylsilane as an internal reference. Chemical shifts (δ) and coupling constants (J) were expressed in parts per million and hertz, respectively. Melting points were uncorrected. Samples for IR were prepared as a thin film on a KBr plate. High-resolution mass spectrometry (HRMS) was performed on an ESI-TOF spectrometer. All reagents were obtained from commercial sources without further purification

General Procedure for the Synthesis of 1a–n. To a solution of 2-aminobenzaldehydes **3** (1.5 mmol) and arylamine **4** (0.5 mmol) in toluene (1.0 mL) was added $Sc(Pfb)_3$ (0.025 mmol). After being stirred at room temperature or 90 °C for 12 h, the mixture was evaporated under vacuum. The product was isolated by silica gel column chromatography with a hexane/ethyl acetate mixture as eluent.

***N*-(3-Chlorophenyl)-6,7,11b,13-tetrahydro-6,12-[1,2]-benzenoquinazolino[3,4-*a*]-quinazolin-13-amine (1a):** yellow

Scheme 4. Proposed Pathways for the Cascade Reactions



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solid; 211.5 mg, 97% yield; mp: 190−192 °C; IR (KBr) ν 3394, 3332, 3038, 2917, 2851, 1596, 1479, 1240, 1052, 753 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.32−7.22 (m, 4H), 7.19−7.15 (m, 2H), 7.12−6.99 (m, 4H), 7.00−6.94 (m, 2H), 6.88 (dd, J = 1.2, 8.0 Hz, 1H), 6.76−6.72 (m, 1H), 6.68 (d, J = 8.0 Hz, 1H), 5.64 (s, 1H), 5.57 (d, J = 4.4 Hz, 1H), 5.33 (s, 1H), 5.27 (s, 1H), 5.86 (br, 1H), 4.63 (d, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 147.6, 145.6, 143.3, 140.7, 135.0, 130.4, 129.6, 129.4, 129.1, 128.9, 128.7, 128.2, 127.6, 124.7, 124.6, 124.4, 123.6, 122.7, 120.2, 119.0, 117.2, 114.5, 112.7, 75.1, 70.6, 63.0. MS (m/z) 437 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{22}ClN_4$ 437.1533, found 437.1532.

***N*-(2-Chlorophenyl)-6,7,11b,13-tetrahydro-6,12-[1,2]-benzenoquinazolino[3,4-*a*]-quinazolin-13-amine (1b):** yellow solid; 150.7 mg, 69% yield; mp: 212−214 °C; IR (KBr) ν 3394, 3348, 3062, 3012, 2917, 2851, 1598, 1494, 1480, 1117, 755 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.87 (dd, J = 1.2, 8.0 Hz, 1H), 7.40 (dd, J = 1.2, 8.0 Hz, 1H), 7.37−7.28 (m, 4H), 7.24−7.22 (m, 1H), 7.16 (dt, J = 1.2 Hz, 7.6 Hz, 1H), 7.10−7.03 (m, 3H), 6.98−6.94 (m, 2H), 6.86 (dt, J = 1.2 Hz, 7.6 Hz, 1H), 6.74 (dt, J = 0.8 Hz, 7.6 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.70 (s, 1H), 5.63 (d, J = 4.8 Hz, 1H), 5.36 (s, 1H), 5.21 (d, J = 4.4 Hz, 1H), 4.88 (br, 1H); ^{13}C NMR ($CDCl_3$): δ 145.6, 143.3, 142.8, 140.7, 129.5, 129.4, 129.3, 129.2, 128.8, 128.7, 128.3, 128.0, 127.6, 124.7, 124.6, 124.4, 123.6, 122.8, 120.2, 120.1, 119.4, 117.3, 114.7, 75.4, 70.6, 62.9. MS (m/z) 437 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{22}ClN_4$ 437.1533, found 437.1539.

***N*-(4-Chlorophenyl)-6,7,11b,13-tetrahydro-6,12-[1,2]-benzenoquinazolino[3,4-*a*]-quinazolin-13-amine (1c):** yellow solid; 155.1 mg, 71% yield; mp: 180−182 °C; IR (KBr) ν 3369, 2959, 2922, 2847, 1597, 1508, 1491, 1480, 1133, 748 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.31−7.27 (m, 5H), 7.20−7.14 (m, 4H), 7.09−7.04 (m, 3H), 6.97 (t, J = 7.2 Hz, 2H), 6.75 (t, J = 7.2 Hz, 1H), 6.70 (d, J = 8.0 Hz, 1H), 5.66 (s, 1H), 5.57 (d, J = 4.4 Hz, 1H), 5.34 (s, 1H), 4.88 (br, 1H), 4.58 (d, J = 4.4 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 145.6, 145.0, 143.3, 140.7, 129.5, 129.4, 129.3, 129.1, 128.8, 128.8, 128.7, 128.3, 127.8, 124.7, 124.6, 124.3, 123.7, 123.6, 122.8, 120.2, 117.3, 115.8, 75.4, 70.6, 62.9. MS (m/z) 437 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{22}ClN_4$ 437.1533, found 437.1537.

***N*-(2-Bromophenyl)-6,7,11b,13-tetrahydro-6,12-[1,2]-benzenoquinazolino[3,4-*a*]quinazolin-13-amine (1d):** yellow solid; 235.9 mg, 98% yield; mp: 202−205 °C; IR (KBr) ν 3386, 3385, 3046, 3013, 2918, 2847, 1599, 1570, 1479, 1021, 754 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.86 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 8.0 Hz, 1H), 7.31−7.28 (m, 3H), 7.25−7.23 (m, 1H), 7.16 (t, J=8.0 Hz, 1H), 7.10−7.04 (m, 3H), 7.00−6.95 (m, 2H), 6.81 (t, J = 8.0 Hz, 1H), 6.75 (t, J = 7.2 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H), 5.70 (s, 1H), 5.63 (d, J = 4.8 Hz, 1H), 5.36 (s, 1H), 5.62 (d, J = 4.8 Hz, 1H), 4.90 (br, 1H); ^{13}C NMR ($CDCl_3$): δ 145.6, 143.9, 143.3, 140.7, 132.6, 129.5, 129.4, 129.2, 128.8, 128.8, 128.7, 128.3, 127.6, 124.7, 124.6, 124.4, 123.6, 122.8, 120.2, 120.0, 117.4, 114.9, 110.9, 75.6, 70.6, 63.0. MS (m/z) 481 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{22}BrN_4$ 481.1028, found 481.1028.

***N*-(*m*-Tolyl)-6,7,11b,13-tetrahydro-6,12-[1,2]benzeno-quinazolino[3,4-*a*]quinazolin-13-amine (1e):** yellow solid; 187.4 mg, 90% yield; mp: 175−177 °C; IR (KBr) ν 3390, 3328, 3046, 3013, 2922, 2851, 1605, 1591, 1479, 1450, 1058, 754 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.35 (d, J = 7.6 Hz, 1H), 7.27 (d, J = 7.6 Hz, 2H), 7.20−7.17 (m, 2H), 7.15−7.09 (m, 2H), 7.08−7.04 (m, 5H), 6.96 (dt, J = 0.8, 7.4 Hz, 1H), 6.76−6.72 (m, 2H), 6.70 (d, J = 8.0 Hz, 1H), 5.72 (s, 1H), 5.60 (d, J = 4.0 Hz, 1H), 5.34 (s, 1H), 4.88 (br, 1H), 4.51 (d, J = 4.0 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 146.6, 145.6, 143.5, 140.7, 129.6, 129.4, 129.2, 129.1, 128.7, 128.6, 128.2, 124.6, 124.5, 124.2, 123.7, 122.9, 120.2, 119.1, 117.2, 114.5, 75.5, 70.6, 62.8, 29.7. MS (m/z) 417 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{28}H_{25}N_4$ 417.2079, found 417.2073.

***N*-(*p*-Tolyl)-6,7,11b,13-tetrahydro-6,12-[1,2]benzeno-quinazolino[3,4-*a*]quinazolin-13-amine (1f):** yellow solid; 143.7 mg, 69% yield; mp: 175−177 °C; IR (KBr) ν 3357, 3013, 2909, 2851, 1611, 1514, 1478, 1451, 1241, 752 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.33 (d, J = 7.6 Hz, 1H), 7.26−7.24 (m, 2H), 7.20−7.13 (m, 6H), 7.08−7.02 (m, 4H), 7.00−6.93 (m, 1H), 6.73 (t, J = 7.6 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 5.72 (s, 1H), 5.57 (d, J = 4.4 Hz, 1H), 5.33 (s, 1H), 4.85 (br, 1H), 4.45 (d, J = 4.4 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 145.6, 144.4, 143.6, 140.7, 129.9, 129.6, 129.2, 128.7, 128.3, 128.2, 124.6, 124.5, 124.1, 123.7, 123.0, 120.2, 117.2, 114.7, 75.9, 70.6, 62.8, 20.7. MS (m/z) 417 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{28}H_{25}N_4$ 417.2079, found 417.2085.

2-((6,7,11b,13-Tetrahydro-6,12-[1,2]benzenoquinazolino-[3,4-*a*]quinazolin-13-yl)amino)phenol (1g): yellow solid; 184.1 mg, 88% yield; mp: 193−195 °C; IR (KBr) ν 3382, 3349, 2922, 2851, 1607, 1590, 1487, 1473, 1258, 760, 148 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.58 (s, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.30−7.25 (m, 3H), 7.17−7.11 (m, 3H), 7.06−7.03 (m, 2H), 6.99−6.91 (m, 2H), 6.86−6.83 (m, 2H), 6.73−6.68 (m, 2H), 6.61 (d, J = 8.0 Hz, 1H), 6.54 (t, J = 7.6 Hz, 1H), 5.64−5.63 (m, 1H), 5.55−5.53 (m, 2H), 5.36 (d, J = 8.0 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 150.8, 150.7, 148.7, 147.4, 140.3, 134.9, 134.6, 133.8, 133.6, 133.4, 133.3, 129.3, 128.9, 128.8, 128.5, 126.3, 124.9, 124.1, 122.6, 120.8, 120.5, 119.8, 80.1, 74.1, 67.3. MS (m/z) 419 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{23}N_4O$ 419.1872, found 419.1866.

3-((6,7,11b,13-Tetrahydro-6,12-[1,2]benzenoquinazolino-[3,4-*a*]quinazolin-13-yl)amino)phenol (1h): yellow solid; 117.2 mg, 56% yield; mp: 193−195 °C; IR (KBr) ν 3299, 2924, 2847, 1598, 1481, 1366, 1188, 1047, 964, 767, 752 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.17 (s, 1H), 7.26−7.23 (m, 3H), 7.20−7.13 (m, 3H), 7.04−6.99 (m, 3H), 6.97−6.89 (m, 3H), 6.70−6.66 (m, 2H), 6.62−6.53 (m, 3H), 6.17 (dd, J = 1.2, J = 8.0 Hz, 1H), 5.54 (s, 1H), 5.50 (d, J = 7.6 Hz, 1H), 5.36 (d, J = 4.0 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 158.0, 148.1, 145.5, 143.5, 142.1, 129.7, 129.5, 128.8, 128.4, 128.3, 128.1, 127.9, 123.8, 123.5, 123.4, 123.2, 121.2, 117.3, 115.5, 105.9, 104.8, 101.0, 73.8, 68.9, 62.3. MS (m/z) 419 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{23}N_4O$ 419.1872, found 419.1870.

5-Chloro-2-((6,7,11b,13-tetrahydro-6,12-[1,2]benzeno-quinazolino[3,4-*a*]quinazolin-13-yl)amino)phenol (1i): yellow solid; 219.6 mg, 97% yield; mp: 169−171 °C; IR (KBr) ν 3303, 3241, 2917, 2851, 1606, 1573, 1515, 1485, 1221, 1187, 1054, 958, 758 cm^{-1}; ^1H NMR (DMSO-d_6): δ 9.86 (s, 1H), 7.46 (d, J = 1.6 Hz, 1H), 7.29−7.24 (m, 3H), 7.18−7.11 (m, 3H), 7.06−7.02 (m, 2H), 7.01−6.93 (m, 2H), 6.83 (d, J = 8.4 Hz, 1H), 6.73−6.69 (m, 2H), 6.62 (d, J = 8.0 Hz, 1H), 6.57 (t, J = 3.6 Hz, 1H), 5.78 (d, J = 7.2 Hz, 1H), 5.67 (d, J = 7.2 Hz, 1H), 5.53 (s, 1H), 5.37 (d, J = 8.4 Hz, 1H); ^{13}C NMR (DMSO-d_6): δ 145.4, 144.4, 143.2, 142.2, 136.5, 129.8, 129.3, 128.7, 128.7, 128.5, 128.4, 128.2, 127.5, 124.0, 123.7, 123.0, 123.0, 121.0, 117.8, 117.4, 115.5, 115.3, 114.4, 74.2, 68.8, 62.1. MS (m/z) 453 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{22}ClN_4O$ 453.1482, found 453.1490.

***N*-(3,5-Bis(trifluoromethyl)phenyl)-6,7,11b,13-tetrahydro-6,12-[1,2]benzenoquinazolino[3,4-*a*]quinazolin-13-amine (1j):** yellow solid; 167.1 mg, 62% yield; mp: 208−210 °C; IR (KBr) ν 3390, 3067, 3017, 2926, 2851, 1611, 1480, 1390, 1277, 1168, 1125, 760 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.67 (s, 2H), 7.38 (s, 1H), 7.31−7.27(m, 2H), 7,25 (s, 1H), 7.22−7.17 (m, 2H), 7.10−7.04 (m, 3H), 7.01- 6.97 (m, 1H), 6.89 (d, J = 6.8 Hz, 1H), 6.73 (t, J = 7.2 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 6.63 (d, J = 4.4 Hz, 1H), 5.59 (s, 1H), 5.35 (s, 1H), 5.01 (d, J = 4.4 Hz, 1H), 4.94 (br, 1H); ^{13}C NMR ($CDCl_3$): δ 147.0, 145.6, 142.9, 140.6, 132.7, 132.4, 129.7, 129.4, 129.2, 129.0, 129.0, 128.8, 128.3, 126.8, 124.8, 123.3, 122.3, 120.2, 117.2, 113.9, 113.9, 112.0, 74.7, 70.6, 63.2. MS (m/z) 539 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{29}H_{21}N_4F_6$ 539.1670, found 539.1664.

***N*-Phenyl-6,7,11b,13-tetrahydro-6,12-[1,2]benzeno-quinazolino[3,4-*a*]quinazolin-13-amine (1k):** yellow solid; 161.0 mg, 80% yield; mp: 195−196 °C; IR (KBr) ν 3394, 3349, 3058, 3013, 2918, 2855, 1599, 1494, 1478, 1238, 1043, 756 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.38−7.34 (m, 3H), 7.28−7.25 (m, 4H), 7.21−7.14 (m, 2H), 7.09−7.00 (m, 4H), 6.98−6.90 (m, 2H), 6.73 (t, J = 7.6 Hz, 1H), 6.69 (d, J = 8.0 Hz, 1H), 5.71 (s, 1H), 6.62 (d, J = 4.0 Hz, 1H), 5.34 (s, 1H), 4.87 (br, 1H), 4.57 (d, J = 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 146.7, 145.6, 143.6, 140.7, 139.2, 129.6, 129.3, 129.2, 129.1, 128.7, 128.3, 128.2, 124.6, 124.1, 123.7, 123.0, 120.2, 120.0, 117.2, 115.4, 111.6, 75.6, 70.6, 62.8. MS (m/z) 403 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{23}N_4$ 403.1923, found 403.1926.

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***N*-(3-Chlorophenyl)-2,10,17-trimethoxy-6,7,11b,13-tetrahydro-6,12-[1,2]benzenequinazolino[3,4-*a*]quinazolin-13-amine (1l):** yellow solid; 213.5 mg, 81% yield; mp: 160−162 °C; IR (KBr) ν 3390, 3000, 2926, 2834, 1597, 1497, 1266, 1230, 1035 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.25−7.23 (m, 2H), 7.19 (t, J = 8.8 Hz, 1H), 7.07 (dd, J = 1.6, 8.4 Hz, 1H), 6.86−6.84 (m, 2H), 6.75 (dd, J = 2.8, 8.4 Hz, 1H), 6.66 (d, J = 2.8 Hz, 1H), 6.65 (d, J = 1.2 Hz, 1H), 6.61 (d, J = 2.8 Hz, 1H), 6.43 (s, 1H), 5.47 (d, J = 4.8 Hz, 1H), 5.18 (s, 1H), 4.22 (br, 2H), 3.70 (s, 3H), 3.66 (s, 3H), 3.56 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 156.5, 156.2, 154.0, 147.4, 138.1, 136.0, 134.9, 133.8, 130.3, 129.1, 128.1, 125.6, 124.6, 124.3, 119.5, 118.9, 116.5, 115.8, 115.6, 114.7, 113.2, 113.0, 112.5, 75.0, 71.3, 63.2, 55.5, 55.4, 55.3. MS (m/z) 527 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{30}H_{28}ClN_4O_3$ 527.1850, found 527.1857.

***N*-(2-Bromophenyl)-2,10,17-trimethoxy-6,7,11b,13-tetrahydro-6,12-[1,2]benzenoquinazolino[3,4-*a*]quinazolin-13-amine (1m):** yellow solid; 237.2 mg, 83% yield; mp: 142−144 °C; IR (KBr) ν 3399, 2988, 2926, 2822, 1661, 1615, 1590, 1496, 1464, 1264, 1229, 1035 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.82 (dd, J = 1.2, 8.4 Hz, 1H), 7.55 (dd, J = 1.2, 8.0 Hz, 1H), 7.37 (t, J = 7.6 Hz, 1H), 7.18 ((t, J = 8.8 Hz, 2H), 6.89 (dd, J = 2.8, 8.8 Hz, 1H), 6.81−6.72 (m, 3H), 6.67 (d, J = 1.6 Hz, 2H), 6.62 (d, J = 2.8 Hz, 1H), 6,46 (s, 1H), 5.55−5.53 (m, 2H), 5.20−5.18 (m, 2H), 3.89−3.88 (m, 1H), 3.74 (s, 3H), 3.68(s, 3H), 3.58(s, 3H); ^{13}C NMR ($CDCl_3$): δ 156.5, 156.2, 154.0, 143.9, 138.5, 136.2, 134.0, 132.5, 129.3, 128.5, 128.0, 125.5, 124.7, 124.3, 120.1, 119.5, 116.7, 115.6, 115.5, 113.3, 112.4, 112.3, 111.1 75.8, 71.2, 63.3, 55.5, 55.4, 55.3. MS (m/z) 571 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{30}H_{28}N_4O_3Br$ 571.1345, found 571.1336.

2,10,17-Trimethoxy-*N*-phenyl-6,7,11b,13-tetrahydro-6,12-[1,2]benzenoquinazolino[3,4-*a*]quinazolin-13-amine (1n): yellow solid; 179.8 mg, 73% yield; mp: 150−153 °C; IR (KBr) ν 3370, 2959, 2924, 2853, 1602, 1496, 1465, 1265, 1230, 1034 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.34 (t, J = 7.6 Hz, 2H), 7.23 (d, J = 8.4 Hz, 3H), 7.18 (d, J = 8.8 Hz, 1H), 6.92−6.84 (m, 2H), 6.75 (dd, J = 2.8, 8.8 Hz, 1H), 6.70 (d, J = 2.8 Hz, 1H), 6.66 (d, J = 1.6 Hz, 2H), 6.62 (d, J = 3.2 Hz, 1H), 6.47 (s, 1H), 5.54 (d, J = 13.2 Hz, 2H), 5.18 (s, 1H), 4.54 (br, 1H), 3.79−3.75 (m, 1H), 3.72 (s, 3H), 3.68 (s, 3H), 3.56 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 156.4, 156.1, 154.0, 146.4, 139.3, 138.4, 136.4, 134.0, 129.3, 129.2, 128.6, 125.5, 124.9, 124.4, 119.4, 119.1, 116.4, 115.7, 115.5, 114.8, 114.1, 113.4, 112.5, 112.4, 75.4, 71.3, 63.2, 55.4, 55.4, 55.3. MS (m/z) 493 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{30}H_{29}N_4O_3$ 493.2240, found 493.2242.

General Procedure for the Preparation of 2a−o. To a solution of 2-aminobenzaldehydes **3** (0.5 mmol) and methanamines **5** (0.25 mmol) in toluene (0.5 mL) was added $Sc(Pfb)_3$ (0.0125 mmol). After being stirred at 90 °C for 12 h, the mixture was evaporated under vacuum, and the residue was purified by column chromatography on silica gel.

13-Benzyl-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2a): yellow solid; 65 mg, 83% yield; mp: 146−149 °C; IR (KBr) ν 3372, 3025, 2926, 2839, 1606, 1494, 754 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.40−7.38 (m, 2H), 7.31−7.27 (m, 3H), 7.03−7.00 (m, 4H), 6.70 (t, J = 7.2 Hz, 2H), 6.55 (d, J = 8.0 Hz, 2H), 4.83 (s, 2H), 4.51 (br, 2H), 3.84 (d, J = 13.2 Hz, 1H), 3.67 (d, J = 13.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 141.1, 137.9, 129.3, 128.6, 128.5, 128.1, 127.4, 124.1, 118.7, 116.2, 65.7, 54.5; MS (m/z) 314 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{21}H_{20}N_3$ 314.1579, found 314.1580.

13-(3,4-Difluorobenzyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2b): pale-gray solid; 85.6 mg, 98% yield; mp: 162−164 °C; IR (KBr) ν 3394, 3071, 3050, 3017, 2942, 2897, 2847, 1608, 1514, 1498, 1276, 1112, 754 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.30−7.28 (m, 1H), 7.11−7.02 (m, 6H), 6.74 (t, J = 7.2 Hz, 2H), 6.60 (d, J = 8.0 Hz, 2H), 4.83 (s, 2H), 4.53 (br, 2H), 3.84 (d, J = 13.2 Hz, 1H), 3.63 (d, J = 13.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 150.0 (ddd, J = 12.7, 70.8, 246.5 Hz), 141.0, 135.0 (m), 128.7, 128.0, 124.9 (dt, J = 3.5 Hz, 6 Hz), 123.9, 118.8, 117.8 (d, J = 17.1 Hz), 117.1 (d, J = 16.8 Hz), 116.2, 65.7, 53.5. MS (m/z) 350 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{21}H_{18}N_3F_2$ 350.1469, found 350.1473.

13-(3-Fluorobenzyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2c): yellow solid; 74.6 mg, 90% yield; mp: 146−148 °C; IR (KBr) ν 3371, 3042, 2934, 2843, 1606, 1590, 1475, 1265, 753 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.30−7.24 (m, 1H), 7.18−7.15 (m, 2H), 7.07−7.02 (m, 4H), 6.96 (dt, J = 0.8 Hz, 8.0 Hz, 2H), 6.73 (dt, J = 0.8 Hz, 7.8 Hz, 2H), 6.60 (d, J = 8.0 Hz, 2H), 4.86 (s, 2H), 4.54 (br, 2H), 3.88 (d, J = 13.6 Hz, 1H), 3.69 (d, J = 13.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 163.1 (d, J = 244.2 Hz), 141.0, 140.7 (d, J = 7.1 Hz), 129.9 (d, J = 7.1 Hz), 128.6, 128.1, 124.6 (d, J = 2.7 Hz), 124.0, 118.8, 116.2, 115.9 (d, J = 21.3 Hz), 114.3 (d, J = 21.0 Hz), 65.7, 54.0. MS (m/z) 332 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{21}H_{19}N_3F$ 332.1563, found 332.1565.

13-(2-Fluorobenzyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2d): yellow solid; 73.7 mg, 89% yield; mp: 136−139 °C; IR (KBr) ν 3398, 3046, 3009, 2922, 2864, 1608, 1585, 1489, 1456, 1265, 1116, 749 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.56−7.52 (m, 1H), 7.27−7.22 (m, 1H), 7.13−7.00 (m, 6H), 6.73 (t, J = 7.6 Hz, 2H), 6.60 (d, J = 8.4 Hz, 2H), 4.91 (s, 2H), 4.57 (br, 2H), 3.98(d, J = 14.0 Hz, 1H), 3.71 (d, J = 14.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 161.5 (d, J = 245.4 Hz), 141.1, 131.2 (d, J = 4.3 Hz), 128.9 (d, J = 8.0 Hz), 128.6, 128.1, 125.1(d, J = 14.0 Hz), 124.2 (d, J = 3.4 Hz), 124.1, 118.8, 116.3, 115.4 (d, J = 21.6 Hz), 66.0, 47.3(d, J = 3.0 Hz). MS (m/z) 332 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{21}H_{19}N_3F$ 332.1555, found 332.1563.

13-(4-Fluorobenzyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2e): yellow solid; 69.6 mg, 84% yield; mp: 145−147 °C; IR (KBr) ν 3396, 3042, 2930, 2847, 1893, 1785, 1609, 1523, 1286, 1230, 756 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.40−7.36 (m, 2H), 7.07−6.98 (m, 6H), 6.73 (t, J = 7.6 Hz, 2H), 6.59 (d, J = 8.0 Hz, 2H), 4.84 (s, 2H), 4.53 (br, 2H), 3.84 (d, J = 13.2 Hz, 1H), 3.66 (d, J = 13.2 Hz, 1H) ; ^{13}C NMR ($CDCl_3$): δ 162.2 (d, J = 243.6 Hz), 141.1, 133.5(d, J = 3.1 Hz), 130.8 (d, J = 7.8 Hz), 128.6, 128.0, 124.0, 118.7, 116.1, 115.2 (d, J = 21.1 Hz), 65.6, 53.7. MS (m/z) 332 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{21}H_{19}N_3F$ 332.1567, found 332.1563.

13-(4-Nitrobenzyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2f): dark-yellow solid; 78.8 mg, 88% yield; mp: 156−158 °C; IR (KBr) ν 3390, 3316, 3017, 3054, 2951, 2022, 2847, 2743, 1621,1608, 1579, 1509, 1481, 1456, 753 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.26 (s, 1H), 8.14 (dd, J = 1.2, 8.0 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.49 (t, J = 8.0 Hz, 1H), 7.09−7.02 (m, 4H), 6.77−6.73 (m, 2H), 6.62 (d, J = 8.0 Hz, 2H), 4.84 (s, 2H), 4.59 (br, 2H), 4.00 (d, J = 13.6 Hz, 1H), 3.78 (d, J = 13.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 148.4, 140.9, 140.3, 135.3, 129.4, 128.7, 128.0, 123.9, 123.7, 122.5, 118.9, 116.2, 65.8, 53.7. MS (m/z) 359 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{21}H_{19}N_4O_2$ 359.1508, found 359.1506.

13-(4-Chlorobenzyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2g): yellow solid; 74.8 mg, 86% yield; mp: 136−138 °C; IR (KBr) ν 3398, 3349, 3274, 3042, 3000, 2930, 2834, 1901, 1785, 1607, 1509, 1089, 1013 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.36 (q, J = 8.4 Hz, 4H), 7.11−7.06 (m, 4H), 6.78 (t, J = 7.2 Hz, 2H), 6.64 (d, J = 7.6 Hz, 2H), 4.49 (s, 2H), 4.59 (br, 2H), 3.89 (d, J = 13.2 Hz, 1H), 3.70 (d, J = 13.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 141.0, 136.4, 133.1, 130.5, 128.6, 128.6, 128.0, 123.9, 118.8, 116.1, 65.7, 53.7. MS (m/z) 348 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{21}H_{19}N_3Cl$ 348.1268, found 348.1269.

13-(4-Methylbenzyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2h): pale-gray solid; 51.6 mg, 63% yield; mp: 157−158 °C; IR (KBr) ν 3394, 3358, 3046, 3017, 2918, 2839, 1906, 1607, 1483, 1264, 1115, 1009, 745 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.32 (d, J = 7.6 Hz, 2H), 7.15 (d, J = 7.6 Hz, 2H), 7.07−7.02 (m, 4H), 6.74 (t, J = 7.2 Hz, 2H), 6.60 (d, J = 8.0 Hz, 2H), 4.86 (s, 2H), 4.54(br, 2H), 3.84 (d, J = 13.2 Hz, 1H), 3.68 (d, J = 13.2 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 141.1, 137.0, 134.8, 129.2, 129.2, 128.5, 128.1, 124.1, 118.7, 116.2, 65.6, 54.2, 21.2. MS (m/z) 328 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{22}H_{22}N_3$ 328.1814, found 328.1812.

13-(4-Methoxybenzyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2i): yellow solid; 63.5 mg, 74% yield; mp: 157−159 °C; IR (KBr) ν 3393, 3336, 3267, 2925, 2832, 1609, 1495, 1232, 1026, 752 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.33 (d, J = 8.8 Hz, 2H), 7.06−7.01 (m, 4H), 6.86 (d, J = 8.8 Hz, 2H), 6.72 (dt, J = 0.8 Hz, 7.6 Hz, 2H), 6.59 (d, J = 8.0 Hz, 2H), 4.86 (s, 2H), 4.54 (br, 2H), 3.79 (d, J = 12.8 Hz, 1H), 3.64 (d, J = 12.8 Hz, 1H), 3.80 (s, 3H); ^{13}C

NMR ($CDCl_3$): δ 159.0, 141.1, 130.4, 129.8, 128.5, 128.0, 124.1, 118.6, 116.1, 113.8, 65.5, 55.3, 53.8. MS (*m*/*z*) 344 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{22}H_{22}N_3O$ 344.1763, found 344.1748.

13-([1,1′-Biphenyl]-4-ylmethyl)-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2j): yellow solid; 42.7 mg, 47% yield; mp: 111−113 °C; IR (KBr) ν 3396, 3021, 2922, 2851, 1897, 1806, 1607, 1500, 1263, 1115, 1007, 749, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.60−7.54 (m, 4H), 7.49−7.42 (m, 4H), 7.36−7.32 (m, 1H), 7.07−7.03 (m, 4H), 6.73 (t, *J* = 6.8 Hz, 2H), 6.60 (d, *J* = 7.6 Hz, 2H), 4.91 (s, 2H), 4.56 (br, 2H), 3.91 (d, *J* = 13.2 Hz, 1H), 3.74 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 141.1, 141.0, 140.3, 137.0, 129.6, 128.8, 128.6, 128.1, 127.3, 127.2, 127.1, 124.1, 118.7, 116.2, 65.7, 54.1. MS (*m*/*z*) 390 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{27}H_{24}N_3$ 390.1970, found 390.1971.

13-Methyl-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2k): yellow solid; 41.5 mg, 70% yield; mp: 166−168 °C; IR (KBr) ν 3382, 3354, 3304, 3038, 2942, 2922, 2884, 2851, 2793, 1609, 1473, 1004, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.07−7.01 (m, 4H), 6.73 (t, *J* = 7.2 Hz, 2H), 6.58 (d, *J* = 8.0 Hz, 2H), 4.84 (s, 2H), 4.56 (br, 2H), 2.52 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 140.6, 128.5, 128.0, 123.8, 118.7, 116.0, 67.4, 38.4. MS (*m*/*z*) 238 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{15}H_{16}N_3$ 238.1344, found 238.1344.

13-Butyl-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2l): yellow solid; 44.7 mg, 64% yield; mp: 125−127 °C; IR (KBr) ν 3399, 3042, 3017, 2932, 2929, 2855, 1608, 1509, 1266, 746 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.11−7.05 (m, 4H), 6.77 (t, *J* = 7.2 Hz, 2H), 6.61 (d, *J* = 8.0 Hz, 2H), 4.98 (s, 2H), 4.59 (br, 2H), 2.79−2.72 (m, 1H), 2.57−2.50 (m, 1H), 1.71−1.61 (m, 2H), 1.40−1.37 (m, 2H), 0.96 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 141.2, 128.4, 128.0, 124.3, 118.6, 116.1, 66.1, 50.0, 31.7, 22.7, 14.1. MS (*m*/*z*) 280 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{18}H_{22}N_3$ 280.1814, found 280.1816.

13-Hexadecyl-5,6,11,12-tetrahydro-6,12-epiminodibenzo-[*b*,*f*][1,5]diazocine (2m): oil, 60.4 mg, 54% yield; IR (KBr) ν 3392, 2915, 2851, 1609, 1494, 1468, 753 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.07−7.00 (m, 4H), 6.72 (t, *J* = 7.2 Hz, 2H), 6.57 (d, *J* = 8.0 Hz, 2H), 4.94 (s, 2H), 2.74−2.67 (m, 1H), 2.52−2.45 (m, 1H), 1.62 (br, 2H), 1.28−1.24 (m, 28H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$): δ 141.1, 128.4, 127.9, 124.2, 118.6, 116.1, 66.1, 50.3, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.4, 27.9, 27.5, 22.7, 14.1. MS (*m*/*z*) 448 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{30}H_{46}N_3$ 448.3692, found 448.3693.

13-Benzyl-3,9-dimethoxy-5,6,11,12-tetrahydro-6,12-epiminodibenzo[*b*,*f*][1,5]diazocine (2n): brown solid; 65.4 mg, 70% yield; mp: 150−153 °C; IR (KBr) ν 3369, 2925, 2851, 2830, 1661, 1607, 1504, 1453, 1261, 1224, 1154, 1033, 830 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.43−7.41 (m, 2H), 7.35−7.29 (m, 3H), 6.70−6.58 (m, 6H), 4.80 (s, 2H), 4.27 (br, 2H), 3.85 (d, *J* = 13.2 Hz, 1H), 3.72 (s, 6H), 3.67 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 153.1, 137.9, 134.4, 129.2, 128.4, 127.3, 125.3, 118.0, 115.1, 113.0, 66.0, 55.7, 54.2. MS (*m*/*z*) 374 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{23}H_{24}N_3O_2$ 374.1869, found 374.1867.

13-(2-Fluorobenzyl)-3,9-dimethoxy-5,6,11,12-tetrahydro-6,12-epiminodibenzo-[*b*,*f*][1,5]diazocine (2o): yellow solid; 88.1 mg, 90% yield; mp: 140−142 °C; IR (KBr) ν 3396, 2925, 1501, 1458, 1258, 1227, 1037 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.53 (t, *J* = 7.2 Hz, 1H), 7.26−7.21 (m, 1H), 7.10 (t, *J* = 7.2 Hz, 1H), 7.02 (t, *J* = 8.8 Hz, 1H), 6.69−6.57 (m, 6H), 4.82 (s, 2H), 4.22 (br, 2H), 3.94 (d, *J* = 13.6 Hz, 1H), 3.70 (s, 6H), 3.66 (d, *J* = 14.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 161.4 (d, *J* = 245.1 Hz), 153.2, 134.3, 131.2 (d, *J* = 4.3 Hz), 128.9 (d, *J* = 8.1 Hz), 125.2, 125.0 (d, *J* = 14.1 Hz), 124.1 (d, *J* = 3.5 Hz), 118.2, 115.4 (d, *J* = 21.7 Hz), 115.2, 113.0, 66.3, 55.7, 47.0. MS (*m*/*z*) 392 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{23}H_{23}FN_3O_2$ 392.1774, found 392.1782.

Procedure for the Synthesis of 1o. The same as the procedure for the preparation of **2a**−**o**.

13-(3,4-Dihydroisoquinolin-2(1*H*)-yl)-6,7,11b,13-tetrahydro-6,12-[1,2]benzenoquinazolino[3,4-*a*]quinazoline (1o): yellow solid; 75.2 mg, 68% yield; mp: 103−105 °C; IR (KBr) ν 3415, 3062, 3021, 2922, 1603, 1479, 1450, 1365, 1288, 1069, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.30−7.26 (m, 3H), 7.24−7.22 (m, 1H), 7.19−7.16 (m, 4H), 7.13−7.02 (m, 5H), 6.91 (dt, *J* = 1.2, 7.6 Hz, 1H), 6.79 (dt, *J* = 1.2, 7.6 Hz, 1H), 6.69 (d, *J* = 7.6 Hz, 1H), 5.71 (s, 1H), 5.33 (s, 1H), 4.88 (s, 1H), 4.65 (d, *J* = 15.2 Hz, 1H), 4.11 (d, *J* = 15.2 Hz, 1H), 3.65−3.60 (m, 1H), 3.20−3.15 (m, 1H), 3.08−3.01 (m, 1H), 2.95−2.89 (m, 1H); ^{13}C NMR ($CDCl_3$): δ 146.4, 145.0, 140.8, 135.5, 134.9, 130.4, 129.2, 129.1, 129.0, 128.8, 128.7, 128.6, 128.0, 126.8, 126.4, 126.2, 125.8, 124.4, 123.8, 123.7, 123.3, 120.0, 117.4, 84.6, 70.2, 65.2, 52.8, 46.6, 30.4. MS (*m*/*z*) 443 [(M + H)$^+$]; HRMS (ESI) Calcd for $C_{30}H_{27}N_4$ 443.2236, found 443.2239.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR spectral data and crystallographic information in CIF format for compounds **1a** and **2a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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