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[4 + 3] Cycloaddition of Phthalazinium Dicyanomethanides with Azoalkenes Formed in Situ: Synthesis of Triazepine Derivatives

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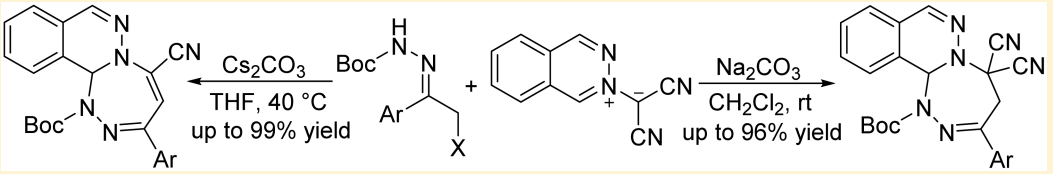
Supporting Information



ABSTRACT: [4 + 3] cycloaddition of phthalazinium dicyanomethanides with in situ formed azoalkenes was achieved, providing an access to various 1,2,4-triazepine derivatives in moderate to excellent yields.

INTRODUCTION

Nitrogen-containing seven-membered heterocyclic rings exist extensively in natural products and artificial bioactive pharmaceuticals. Thus, much efforts have been devoted to their synthesis.[1] As one of the important seven-membered heterocyclic compounds, triazepines possess various pharmacological activities, including psychotropic, antibacterial, antiviral, anticancer, antisecretory, CCK2 antagonist, analgesic, and anti-inflammatory activities.[2] For instance, the compound **I** showed the same antipsychotic activity as the reference drug clozapine.[2h] Compound **II** has analgesic activity in white mongrel mice.[2g] The compounds **III** and **IV** are excellent neuroleptic agents to treat psychotic disturbances.[2b] Compound **V** is a CCK2 receptor antagonist that shows better selectivity than CCK1 receptors.[2e] Compound **VI** shows moderate antisecretory activity in rats (Figure 1).[2c] Therefore, to explore reliable and practical methods to obtain triazepines is of great value.

Generally, 1,2,4-triazepines were prepared through the condensation of carbonyl compounds or carbon disulfides with (in situ) *o*-aminobenzohydrazides.[3] Other methods for this type of heterocyclic compounds have rarely been explored. In fact, a 1,3-dipolar cycloaddition reaction could be an ideal alternative for synthesis of 1,2,4-triazepines. The 1,3-dipolar cycloaddition is one of the most useful methods to construct nitrogen-containing heterocycles.[4] For synthesis of seven-memberd 1,2,4-triazepines, a formal [4 + 3] cycloaddition via stepwise reaction of a stable 1,3-dipole with four-membered dipolarophile is feasible. Azoalkenes (1,2-diaza-1,3-dienes),[5] which are readily generated in situ from α-halogeno hydrazones, often served as four-membered synthons to construct various five-,[6] six-,[7] or seven-membered[8−10] N-containing heterocyclic compounds. Recently, two [4 + 3] cycloaddition reactions of azoalkenes with stable 1,3-dipoles were achieved. In 2013, Hu and co-workers developed the first [4 + 3] cycloaddition of azoalkenes formed in situ with C,N-cyclic azomethine imines, giving tetrazepine derivatives (Scheme 1a).[9] During the preparation of this paper, Zhao and co-workers reported the [4 + 3] cycloaddition of azoalkenes with nitrones to afford oxatriazepines in excellent yield (Scheme 1b).[10] To the best of our knowledge, the C−N−C type of azomethine ylide has never been investigated in the [4 + 3] cycloaddition of azoalkenes. Its [4 + 3] cycloaddition reaction with azoalkenes will lead to a new synthesis of 1,2,4-triazepines (Scheme 1c). As part of our continuous efforts on 1,3-dipolar cycloaddition reactions,[11] herein, we present the first [4 + 3] cycloaddition of phthalazinium dicyanomethanides with azoalkenes formed in situ for the synthesis of 1,2,4-triazepines (Scheme 1c).

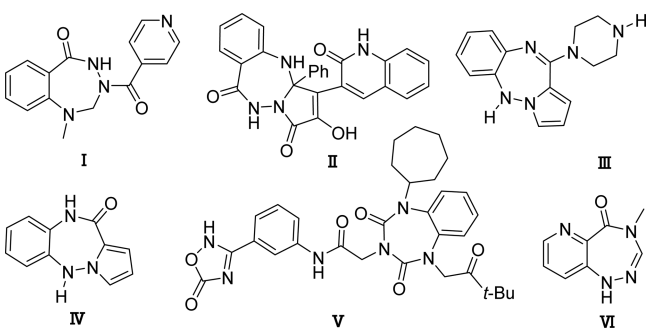


Figure 1. Biologically active triazepine derivatives.

RESULTS AND DISCUSSION

Initially, we performed the model reaction of *N*-Boc hydrazone **1a** with phthalazinium dicyanomethanide **2a** in the presence of sodium hydroxide in dichloromethane at room temperature. To our delight, the desired cycloaddition occurred, giving the [4 + 3] cycloaddition products 1,2,4-triazepine **3aa** and **4aa** as a mixture with a ratio of 1:1.3 in a 78% combined yield (Table 1,

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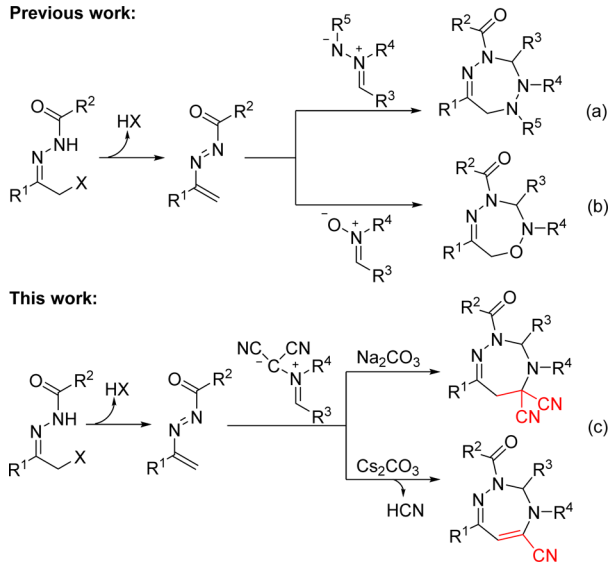
Scheme 1. [4 + 3] Cycloaddition Reactions of Azoalkenes with Stable 1,3-Dipoles

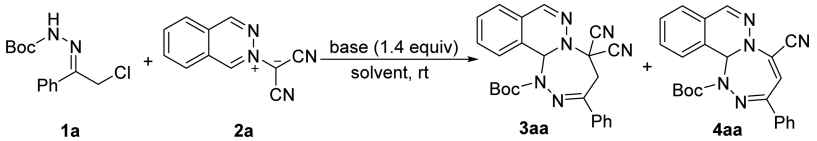


entry 1). Obviously, product **4aa** resulted from the elimination of HCN from product **3aa**. To improve the chemoselectivity and yield, we screened different bases (entries 2−6). The results showed that the choice of inorganic bases had a remarkable effect on the reaction. In comparison with NaOH, *t*-BuOK led to **4aa** as a single product in poor 26% yield (entry 1 vs 2). Interestingly, Na_2CO_3 resulted in **3aa** as a single product in 78% yield (entry 3). When both the amounts of Na_2CO_3 and *N*-Boc hydrazone **1a** were increased, the yield of **3aa** was increased to 96% (entry 4). The $NaHCO_3$ base did not promote this reaction (entry 5). In the presence of Cs_2CO_3, product **4aa** was obtained as the major product with a 7:1 ratio in 91% yield (entry 6). Next, further attempts to improve the yield and chemoselectivity toward the synthesis of **4aa** were carried out by switching solvents (entries 7−11). Gratifyingly, using THF, MeCN, and 1,4-dioxane as the solvent, product **4aa** was obtained as a single product in moderate to good yields (entries 9−11). When the reaction was performed in THF, product **3aa** was obtained as a single product in an acceptable 75% yield (entry 9). By increasing the reaction temperature to 40 °C, a satisfactory 84% yield was obtained (entry 12). The current reaction was quite robust, allowing the reaction to be scaled up. In the presence of Cs_2CO_3, 0.58 g (3 mmol) of phthalazinium dicyanomethanide **2a** reacted with *N*-Boc hydrazone **1a** to give the [4 + 3] cycloaddition product **4aa** in 74% yield. The structure of product **4aa** was confirmed by its X-ray crystallographic data.[12]

With the use of Na_2CO_3 as the base, we were able to selectively access formal [4 + 3] cycloaddition products **3**. Under the optimized reaction conditions, various *N*-Boc hydrazones were explored (Table 2). Substrates bearing fluoro, chloro, and bromo at different positions of the aryl reacted with **2a** well to give the products **3ba**−**3ea** in 69−87% yield (entries 2−5). The hydrazone containing two electron-poor substituents at the benzene ring displayed good activity in this reaction, providing the corresponding product **3fa** in 87% yield (entry 6). Different electron-rich aryl-substituted hydrazones showed similar reactivity to afford the corresponding 1,2,4-triazepines **3ia**−**3la** in 73−81% yield (entries 7−10). An aliphatic hydrazine **1m** has been attempted, but only a trace of product **3ma** was observed on the TLC (entry 11). The acetyl-protecting hydrazone **1n** displayed certain activity in the presence of $NaCO_3$, and product **3na** could be observed on the TLC. However, the product was not stable and decomposed in the silica gel column (entry 12). When Et_3N was used to neutralize the silica gel column, one molecule of HCN was eliminated to give another kind of product **4na** (see Table 3, entry 14).

With the use of Cs_2CO_3 as the base, under the standard conditions, we next investigated the scope of dicyanomethanide and hydrazones toward the synthesis of **4** (Table 3). It was found that a broad range of hydrazones bearing electron-neutral, electron-deficient, and electron-rich substituents at different positions on the aromatic ring reacted with

Table 1. Optimization of Reaction Conditions[a]



1a **2a** **3aa** **4aa**

entry	base	solvent	*t* (h)	yield (%)[b]	**3aa**/**4aa**[c]
1	NaOH	CH_2Cl_2	5	78	1:1.3
2	*t*-BuOK	CH_2Cl_2	5	26	<1:20
3	Na_2CO_3	CH_2Cl_2	16	78	>20:1
4[d]	Na_2CO_3	CH_2Cl_2	12	96	>20:1
5	$NaHCO_3$	CH_2Cl_2	48	trace	
6	Cs_2CO_3	CH_2Cl_2	12	91	1:7
7	Cs_2CO_3	toluene	48	trace	
8	Cs_2CO_3	DCE	20	69	1:1.5
9	Cs_2CO_3	THF	20	75	<1:20
10	Cs_2CO_3	MeCN	5	53	<1:20
11	Cs_2CO_3	1,4-dioxane	20	72	<1:20
12[e]	Cs_2CO_3	THF	5	84	<1:20

[a]Unless otherwise noted, reactions of **1a** (0.12 mmol) and **2a** (0.1 mmol) were performed in the presence of the base (0.14 mmol) in 2 mL of solvent at rt. [b]Combined yield of **3aa** and **4aa** after column chromatography. [c]Determined by HPLC analysis. [d]0.15 mmol of **1a** and 0.2 mmol of Na_2CO_3 were used. [e]The reaction was conducted at 40 °C.

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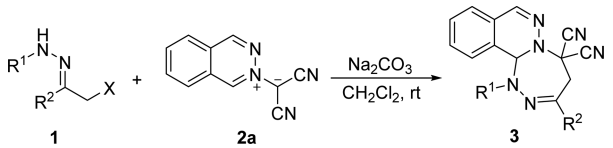
Table 2. Formal [4 + 3] Cycloaddition Reaction for Products 3[a]



entry	R^1	X	R^2	t (h)	3	yield (%)
1	Boc	Cl	Ph (**1a**)	12	**3aa**	96
2	Boc	Cl	4-FC_6H_4 (**1b**)	14	**3ba**	69
3	Boc	Cl	4-ClC_6H_4 (**1c**)	12	**3ca**	77
4	Boc	Br	3-BrC_6H_4 (**1d**)	12	**3da**	82
5	Boc	Br	4-BrC_6H_4 (**1e**)	14	**3ea**	65
6	Boc	Cl	3,4-$Cl_2C_6H_3$ (**1f**)	12	**3fa**	87
7	Boc	Br	3-$MeOC_6H_4$ (**1i**)	14	**3ia**	81
8	Boc	Br	4-$MeOC_6H_4$ (**1j**)	14	**3ja**	74
9	Boc	Br	4-MeC_6H_4 (**1k**)	14	**3ka**	73
10	Boc	Cl	4-*t*-BuC_6H_4 (**1l**)	36	**3la**	76
11	Boc	Cl	*t*-Bu (**1m**)	48	**3ma**	trace
12	Ac	Br	Ph (**1n**)	48	**3na**	decompose

[a]Reactions were conducted with 1.5 equiv of **1**, 1 equiv of **2a**, and 2 equiv of Na_2CO_3 in CH_2Cl_2 (2 mL) at a scale of 0.1 mmol at 25 °C.

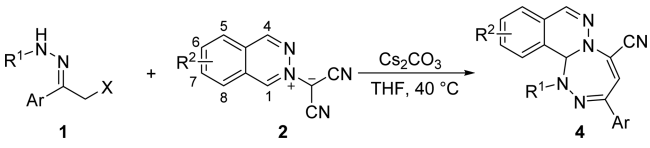
phthalazinium dicyanomethanide **2a** to form a variety of 1,2,4-triazepines in excellent yields (**4aa**−**4la**, entries 1−12). In contrast, the *N*-Boc hydrazone with *o*,*p*-dichloro and *o*-methoxy substituents displayed weak reactivity, providing the corresponding 1,2,4-triazepines in 53 and 62% yield (**4ga** and **4ha**), respectively (entries 7 and 8). The aliphatic hydrazine **1m** also underwent the cycloaddition reaction at 40 °C, and a mixture of the products **3ma** and **4ma** with a 1:1 ratio (determined by ^{1}H NMR analysis) was obtained in 67% yield (entry 13). Unfortunately, the mixture could not be separated by flash column chromatography. Furthermore, the *N*-acetyl hydrazone **1n** could give rise to the [4 + 3] cycloaddition product **4na** in 85% yield (entry 14). Encouraged by these results, the scope of phthalazine dicyanomethanide was then briefly examined. The results indicated that phthalazine-derived dicyanomethanides also proved to be tolerable in this reaction (**4ab** and **4ac**, entries 15 and 16).

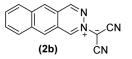
Under the optimized conditions, other kinds of azomethine ylides such as isoquinolinium dicyanomethylide and pyridazinium dicyanomethanide were also explored (Scheme 2). Unfortunately, Na_2CO_3-mediated [4 + 3] cycloaddition did not tolerate other C−N−C type of azomethine ylides. In contrast, Cs_2CO_3-mediated 1,3-dipolar cycloaddition had a broader substrate scope. In the presence of Cs_2CO_3, the reaction of azomethine ylides **5** and **7** with *N*-Boc hydrazone **1a** worked well, giving the biologically interesting products **6** and **8** in 97 and 48% yield, respectively.

CONCLUSIONS

In summary, we have developed a new and efficient approach to diverse 1,2,4-triazepine derivatives through a catalyst-free [4 + 3] cycloaddition reaction between phthalazinium dicyanomethanides and in situ formed azoalkenes. A variety of phthalazinium dicyanomethanides and *N*-Boc hydrazones were compatible under the mild reaction conditions, affording the 1,2,4-triazepine derivatives in moderate to excellent yields. The base-controlled [4 + 3] cycloaddition greatly enriched the diversiy of 1,2,4-triazepine products. Moreover, this reaction could be scaled up, thus allowing the reaction to be a practical approach to heterocyclic compounds.

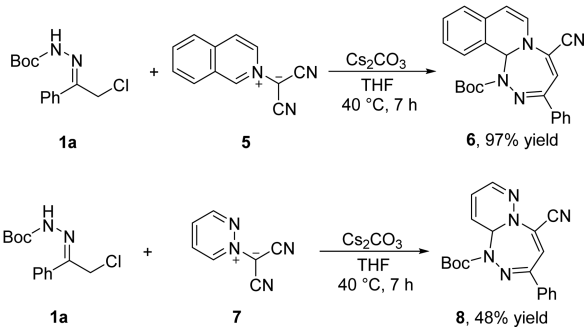
Table 3. Formal [4 + 3] Cycloaddition Reaction for Products 4[a]



entry	R^1	X	Ar	R^2	t (h)	4	yield (%)
1	Boc	Cl	Ph (**1a**)	H (**2a**)	5	**4aa**	84
2	Boc	Cl	4-FC_6H_4 (**1b**)	H (**2a**)	5	**4ba**	92
3	Boc	Cl	4-ClC_6H_4 (**1c**)	H (**2a**)	5	**4ca**	85
4	Boc	Br	3-BrC_6H_4 (**1d**)	H (**2a**)	5	**4da**	90
5	Boc	Br	4-BrC_6H_4 (**1e**)	H (**2a**)	5	**4ea**	90
6	Boc	Cl	3,4-$Cl_2C_6H_3$ (**1f**)	H (**2a**)	5	**4fa**	95
7	Boc	Cl	2,4-$Cl_2C_6H_3$ (**1g**)	H (**2a**)	3	**4ga**	53
8	Boc	Br	2-$MeOC_6H_4$ (**1h**)	H (**2a**)	6	**4ha**	62
9	Boc	Br	3-$MeOC_6H_4$ (**1i**)	H (**2a**)	5	**4ia**	95
10	Boc	Br	4-$MeOC_6H_4$ (**1j**)	H (**2a**)	6	**4ja**	86
11	Boc	Br	4-MeC_6H_4 (**1k**)	H (**2a**)	5	**4ka**	78
12	Boc	Cl	4-*t*-BuC_6H_4 (**1l**)	H (**2a**)	14	**4la**	99
13	Boc	Cl	*t*-Bu (**1m**)	H (**2a**)	**7**	**4ma**[b]	67[b]
14	Ac	Br	Ph (**1n**)	H (**2a**)	8	**4na**	85
15[c]	Boc	Cl	Ph (**1a**)	 (**2b**)	7	**4ab**	98
16[c]	Boc	Cl	Ph (**1a**)	6,7-2Me (**2c**)	5	**4ac**	69

[a]Unless otherwise noted, reactions were conducted with 1.2 equiv of **1**, 1 equiv of **2**, and 1.4 equiv of Cs_2CO_3 in THF (2 mL) at a scale of 0.1 mmol at 40 °C. [b]A mixture of **3ma** and **4ma** with a 1:1 ratio (determined by ^{1}H NMR analysis) was obtained in 67% yield. [c]At a scale of 0.15 mmol in THF (3 mL).

Scheme 2. [4 + 3] Cycloaddition Reactions of Dicyanomethylide with *N*-Boc Hydrazone



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EXPERIMENTAL SECTION

General Information. All reactions were performed under N_2 atmosphere in oven-dried glassware with magnetic stirring. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. All solvents were purified and dried according to standard methods prior to use. Organic solutions were concentrated under reduced pressure on a rotary evaporator or an oil pump. Reactions were monitored through thin-ayer chromatography (TLC) on silica gel-precoated glass plates. Chromatograms were visualized by fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed using flash silica gel (200−300 mesh). Infrared spectra were recorded using an FT-IR spectrophotometer and are reported as cm^{-1}. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 using a 300 MHz NMR instrument. Accurate mass measurements were performed on an electrospray ionization (ESI) apparatus using time-of-flight (TOF) mass spectrometry. Melting points were determined on a SMP3 melting apparatus. X-ray crystallographic data were collected using a MM007HF Saturn724+. Phthalazinium dicyanomethanides **2**,[13] isoquinolinium dicyanomethylide **5**,[14] pyridazinium dicyanomethanide **7**,[15] and *N*-Boc and *N*-acetyl hydrazones **1**[16] were prepared according to the literature procedures.

General Procedure for Formal [4 + 3] Cycloaddition Reaction for Products 3. Under a nitrogen atmosphere, to a mixture of *N*-Boc hydrazones (0.15 mmol, 1.5 equiv), phthalazinium dicyanomethanides (0.1 mmol, 1.0 equiv), and Na_2CO_3 (0.2 mmol, 21.2 mg, 2.0 equiv) was added CH_2Cl_2 (2 mL) via a syringe. Then the reaction mixture was vigorously stirred at room temperature. Once starting material was consumed through monitoring by TLC, the mixture was directly purified by column chromatography on silica gel to furnish the corresponding product **3** (petroleum ether/EtOAc 15:1−7:1).

*tert-Butyl 5,5-Dicyano-3-phenyl-4,5-dihydro-[1,2,4]triazepino-[3,4-a]phthalazine-1(12bH)-carboxylate (**3aa**):* White solid (40.9 mg, 96% yield); mp 128−129 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86−7.80 (m, 2H), 7.73 (s, 1H), 7.59−7.40 (m, 6H), 7.39−7.33 (m, 1H), 6.53 (s, 1H), 4.15−3.92 (m, 2H), 1.32 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.9, 141.7, 135.7, 132.1, 131.3, 130.1, 128.9, 128.3, 127.0, 126.7, 126.3, 125.0, 113.7, 113.6, 83.4, 70.2, 55.2, 40.0, 28.0; IR (film) ν_{max} 3058, 2982, 2933, 2239, 1727, 1591, 1577, 1565, 1521, 1456, 1412, 1369, 1283, 1249, 1155, 1113, 1074, 1048, 1007, 975, 918, 900, 880, 866, 850, 795, 761, 737, 696 cm^{-1}; HRMS calcd for $C_{24}H_{22}N_6O_2$ $[M + H]^+$ 427.1877, found 427.1874.

*tert-Butyl 5,5-Dicyano-3-(4-fluorophenyl)-4,5-dihydro-[1,2,4]-triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**3ba**):* White solid (28.9 mg, 65% yield); mp 153−154 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.89−7.78 (m, 2H), 7.71 (s, 1H), 7.59−7.46 (m, 2H), 7.45−7.32 (m, 2H), 7.16−7.11 (t, J = 8.6 Hz, 2H), 6.50 (s, 1H), 4.01 (q, J = 17.4 Hz, 2H), 1.30 (s, 9H); $^{13}C\{^1H\}$ NMR (76 MHz, $CDCl_3$) δ164.7 (d, $^1J_{C-F}$ = 252.3 Hz), 150.9, 141.8, 132.1, 131.8, 130.2, 129.3 (d, $^2J_{C-F}$ = 8.8 Hz), 128.3, 126.7, 126.3, 125.0, 116.2, 115.9, 113.6 (d, $^2J_{C-F}$ = 5.8 Hz), 83.5, 70.2, 55.0, 40.0, 28.0; IR (film) ν_{max} 3069, 2981, 2931, 2238, 1709, 1602, 1512, 1478, 1456, 1418, 1369, 1310, 1283, 1250, 1157, 1112, 1074, 1047, 1006, 918, 842, 819, 805, 763, 736 cm^{-1}; HRMS calcd for $C_{24}H_{21}FN_6O_2$ $[M + H]^+$ 445.1783, found 445.1780.

*tert-Butyl 3-(4-Chlorophenyl)-5,5-dicyano-4,5-dihydro-[1,2,4]-triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**3ca**):* Semisolid (35.4 mg, 77% yield); ^1H NMR (300 MHz, DMSO-d_6) δ 8.00 (s, 1H), 7.96−7.89 (m, 2H), 7.63−7.52 (m, 5H), 7.40−7.33 (m, 1H), 6.85 (s, 1H), 4.62 (d, J = 18.4 Hz, 1H), 4.41 (d, J = 18.4 Hz, 1H), 1.05 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 151.4, 151.0, 142.2, 135.9, 135.6, 132.2, 130.2, 129.4, 128.9, 128.8, 127.3, 126.8, 125.5, 114.9, 114.6, 81.9, 69.3, 56.8, 37.4, 27.9; IR (film) ν_{max} 3057, 2979, 2927, 2238, 1716, 1590, 1575, 1522, 1456, 1408, 1369, 1287, 1259, 1146, 1047, 905, 871, 764, 698, 658 cm^{-1}; HRMS calcd for $C_{24}H_{21}ClN_6O_2$ $[M + H]^+$ 461.1487, found 461.1482.

*tert-Butyl 3-(3-Bromophenyl)-5,5-dicyano-4,5-dihydro-[1,2,4]-triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**3da**):* White solid (41.3 mg, 82% yield); mp 144−145 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (t, J = 1.8 Hz, 1H), 7.75−7.68 (m, 2H), 7.63−7.60 (m, 1H), 7.56−7.50 (m, 2H), 7.40−7.30 (m, 3H), 6.47 (s, 1H), 4.00 (q, J = 17.7 Hz, 2H), 1.27 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 150.7, 141.7, 137.7, 134.1, 132.0, 130.3, 130.2, 129.9, 128.0, 126.7, 126.3, 125.4, 125.0, 123.1, 113.6, 113.3, 83.6, 70.3, 55.3, 39.6, 27.9; IR (film) ν_{max} 3064, 2982, 2931, 2239, 1723, 1559, 1476, 1455, 1407, 1369, 1282, 1258, 1155, 1074, 1047, 1016, 918, 868, 837, 796, 763, 735, 677, 667 cm^{-1}; HRMS calcd for $C_{24}H_{21}BrN_6O_2$ $[M + H]^+$ 505.0982, found 505.0980.

*tert-Butyl 3-(4-Bromophenyl)-5,5-dicyano-4,5-dihydro-[1,2,4]-triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**3ea**):* White solid (30.5 mg, 61% yield); mp 146−147 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.75−7.66 (m, 3H), 7.61−7.49 (m, 4H), 7.44−7.32 (m, 2H), 6.49 (s, 1H), 4.00 (q, J = 17.6 Hz, 2H), 1.28 (s, 9H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 150.8, 141.8, 134.6, 132.2, 130.2, 128.5, 128.1, 126.7, 126.3, 126.0, 125.0, 113.6, 113.4, 83.6, 70.2, 55.1, 39.8, 28.0; IR (film) ν_{max} 3056, 2980, 2929, 2238, 1932, 1722, 1588, 1489, 1456, 1413, 1396, 1369, 1280, 1260, 1155, 1074, 1004, 917, 880, 838, 763, 676 cm^{-1}; HRMS calcd for $C_{24}H_{21}BrN_6O_2$ $[M + H]^+$ 505.0982, found 505.0980.

*tert-Butyl 5,5-Dicyano-3-(3,4-dichlorophenyl)-5,5-dihydro-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**3fa**):* Semisolid (43.0 mg, 87% yield); ^1H NMR (300 MHz, DMSO-d_6) δ 8.16 (d, J = 2.0 Hz, 1H), 8.00 (s, 1H), 7.91−7.87 (m, 1H), 7.77−7.74 (m, 1H), 7.61−7.54 (m, 3H), 7.43−7.35 (m, 1H), 6.87 (s, 1H), 4.64 (d, J = 18.5 Hz, 1H), 4.39 (d, J = 18.5 Hz, 1H), 1.05 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 150.9, 150.2, 142.2, 137.6, 133.5, 132.2, 131.9, 131.1, 130.2, 129.5, 128.7, 127.8, 127.3, 126.8, 125.5, 114.7, 114.5, 82.0, 69.2, 56.7, 37.3, 27.8; IR (film) ν_{max} 3192, 2978, 2932, 2253, 2126, 1733, 1595, 1518, 1472, 1392, 1369, 1260, 1151, 1028, 821, 763, 701, 628, 592 cm^{-1}; HRMS calcd for $C_{24}H_{20}Cl_2N_6O_2$ $[M + H]^+$ 495.1098, found 495.1097.

*tert-Butyl 5,5-Dicyano-3-(3-methoxyphenyl)-4,5-dihydro-[1,2,4]-triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**3ia**):* Semisolid (37.1 mg, 81% yield); ^1H NMR (300 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.55−7.49 (m, 2H), 7.43−7.34 (m, 5H), 7.05−7.01 (m, 1H), 6.49 (s, 1H), 4.10−3.93 (m, 2H), 3.85 (s, 3H), 1.30 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.2, 159.8, 151.1, 138.6, 137.2, 131.8, 129.8, 129.7, 128.9, 128.9, 127.1, 126.3, 124.2, 120.3, 116.6, 114.2, 112.8, 106.4, 82.7, 72.8, 60.5, 55.5, 27.9; IR (film) ν_{max} 3356, 2981, 2931, 2238, 1725, 1579, 1489, 1455, 1412, 1369, 1287, 1155, 1046, 920, 845, 795, 763, 737, 692 cm^{-1}; HRMS calcd for $C_{25}H_{24}N_6O_3$ $[M + H]^+$ 457.19826, found 457.19827.

*tert-Butyl 5,5-Dicyano-3-(4-methoxyphenyl)-4,5-dihydro-[1,2,4]-triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**3ja**):* White solid (31.4 mg, 69% yield); mp 140−141 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80−7.77 (m, 2H), 7.68 (s, 1H), 7.54−7.41 (m, 3H), 7.36−7.29 (m, 1H), 6.95−6.93 (m, 2H), 6.53 (s, 1H), 3.98 (s, 2H), 3.86 (s, 3H), 1.33 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 162.3, 151.0, 141.7, 132.1, 130.0, 128.90, 128.5, 127.82, 126.58, 126.15, 124.97, 114.25, 113.68, 83.21, 69.94, 55.56, 54.89, 39.95, 28.08; IR (film) ν_{max} 3056, 2980, 2933, 2239, 1716, 1608, 1515, 1456, 1418, 1369, 1255, 1157, 1074, 1032, 918, 840, 763, 737 cm^{-1}; HRMS calcd for $C_{25}H_{24}N_6O_3$ $[M + H]^+$ 457.1982, found 457.1976.

*tert-Butyl 5,5-Dicyano-3-(p-tolyl)-4,5-dihydro-[1,2,4]triazepino-[3,4-a]phthalazine-1(12bH)-carboxylate (**3ka**).* Semisolid (31.9 mg, 73% yield); ^1H NMR (300 MHz, DMSO-d_6) δ 7.98 (s, 1H), 7.82−7.79 (m, 2H), 7.61−7.54 (m, 3H), 7.36−7.28 (m, 3H), 6.81 (s, 1H), 4.59 (d, J = 18.4 Hz, 1H), 4.38 (d, J = 18.4 Hz, 1H), 2.36 (s, 3H), 1.05 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, DMSO-d_6) δ 152.7, 151.1, 142.0, 140.7, 134.2, 132.2, 130.1, 129.4, 128.9, 127.6, 127.2, 126.8, 125.6, 115.0, 114.7, 81.7, 69.3, 56.8, 37.5, 27.9, 21.4; IR (film) ν_{max} 3398, 2964, 2926, 2251, 1716, 1607, 1456, 1417, 1368, 1261, 1158, 1097, 1028, 918, 800, 764, 677, 667, 539 cm^{-1}; HRMS calcd for $C_{25}H_{24}N_6O_2$ $[M + H]^+$ 441.2033, found 441.2030.

*tert-Butyl 3-(4-(tert-Butyl)phenyl)-5,5-dicyano-4,5-dihydro-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**3la**):* White solid (36.8 mg, 76% yield); mp 161−162 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80−7.74 (m, 2H), 7.70 (s, 1H), 7.53−7.42 (m, 5H), 7.37−7.30 (m, 1H), 6.52 (s, 1H), 4.01 (s, 2H), 1.34−1.32 (m, 18H);

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$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 155.0, 150.9, 141.7, 136.9, 132.6, 132.0, 130.0, 128.4, 126.9, 126.5, 126.1, 125.8, 125.0, 113.6, 113.5, 83.1, 70.0, 40.0, 35.0, 31.1, 28.0; IR (film) ν_{max} 3057, 2967, 2871, 2239, 1716, 1608, 1512, 1477, 1456, 1411, 1368, 1283, 1250, 1158, 1113, 1073, 1046, 1021, 1002, 918, 880, 844, 763, 739 cm^{-1}; HRMS calcd for $C_{28}H_{30}N_6O_2$ $[M + H]^+$ 483.2503, found 483.2496.

General Procedure for Formal [4 + 3] Cycloaddition Reaction for Products 4. Under a nitrogen atmosphere, to a mixture of *N*-Boc hydrazones (0.12 mmol, 1.2 equiv), phthalazinium dicyanomethanides (0.1 mmol, 1.0 equiv), and Cs_2CO_3 (0.14 mmol, 45.5 mg, 1.4 equiv) was added THF (2 mL) via a syringe. Then the reaction solution was vigorously stirred at 40 °C. Once starting material was consumed through monitoring by TLC, the mixture was directly purified by column chromatography on silica gel to furnish the corresponding product **4** (petroleum ether/EtOAc 15:1−7:1).

*tert-Butyl 5-Cyano-3-phenyl-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4aa**):* Yellow solid (33.5 mg, 84% yield); mp 170−171 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.86−7.82 (m, 2H), 7.69 (s, 1H), 7.57−7.47 (m, 7H), 6.27 (s, 1H), 5.69 (s, 1H), 1.15 (s, 9H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 160.0, 150.8, 136.9, 131.5, 130.1, 129.4, 128.8, 128.7, 128.5, 127.5, 126.8, 126.1, 124.0, 114.0, 106.1, 82.4, 72.6, 27.7; IR (film) ν_{max} 3057, 2982, 2238, 1715, 1591, 1577, 1564, 1522, 1495, 1464, 1407, 1369, 1295, 1142, 1113, 1054, 1013, 928, 899, 851, 762, 736, 698 cm^{-1}; HRMS calcd for $C_{23}H_{21}N_5O_2$ $[M + H]^+$ 400.1768, found 400.1765.

*tert-Butyl 5-Cyano-3-(4-fluorophenyl)-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4ba**):* Semisolid (38.2 mg, 92% yield); ^1H NMR (300 MHz, $CDCl_3$) δ 7.88−7.79 (m, 2H), 7.69 (s, 1H), 7.59−7.43 (m, 4H), 7.18−7.08 (m, 2H), 6.20 (s, 1H), 5.67 (s, 1H), 1.12 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ164.2 (d, $^1J_{C-F}$ = 250.9 Hz), 159.3, 151.0, 137.3, 133.3 (d, $^2J_{C-F}$ = 3.1 Hz), 131.8, 129.9, 129.8 (d, $^2J_{C-F}$ = 2.5 Hz), 129.2, 128.9, 127.1, 126.3, 124.2, 115.9, 115.7, 114.2, 105.9, 82.8, 72.9, 27.9; IR (film) ν_{max} 2980, 2931, 2239, 1716, 1601, 1584, 1566, 1512, 1462, 1415, 1369, 1303, 1241, 1142, 1047, 927, 900, 850, 815, 761, 682 cm^{-1}; HRMS calcd for $C_{23}H_{20}FN_5O_2$ $[M + H]^+$ 418.1674, found 418.1671.

*tert-Butyl 3-(4-Chlorophenyl)-5-cyano-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4ca**):* Yellow solid (37.0 mg, 85% yield); mp 185−186 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.82−7.74 (m, 2H), 7.69 (s, 1H), 7.59−7.37 (m, 6H), 6.19 (s, 1H), 5.66 (s, 1H), 1.12 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.8, 150.9, 137.3, 136.5, 135.6, 131.8, 129.7, 129.2, 129.0, 128.9, 128.7, 127.1, 126.2, 124.1, 114.1, 105.7, 82.8, 72.8, 27.8; IR (film) ν_{max} 2980, 2931, 2239, 1716, 1601, 1584, 1566, 1512, 1462, 1415, 1369, 1303, 1241, 1142, 1047, 927, 900, 850, 815, 761, 682 cm^{-1}; HRMS calcd for $C_{23}H_{20}ClN_5O_2$ $[M + H]^+$ 434.1378, found 434.1381.

*tert-Butyl 3-(3-Bromophenyl)-5-cyano-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4da**):* Yellow solid (42.7 mg, 90% yield); mp 167−168 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.01−8.00 (m, 1H), 7.74 (d, J = 7.9 Hz, 1H), 7.70 (s, 1H), 7.62−7.44 (m, 5H), 7.32 (t, J = 7.9 Hz, 1H), 6.18 (s, 1H), 5.65 (s, 1H), 1.12 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.4, 150.9, 139.1, 137.4, 133.2, 131.8, 130.7, 130.2, 129.8, 129.3, 128.7, 127.1, 126.3, 126.2, 124.1, 122.9, 114.0, 105.6, 82.9, 72.9, 27.8; IR (film) ν_{max} 3058, 2981, 2239, 1715, 1586, 1561, 1520, 1463, 1395, 1369, 1291, 1142, 1113, 1052, 928, 907, 867, 790, 762, 737, 706, 637, 581 cm^{-1}; HRMS calcd for $C_{23}H_{20}BrN_5O_2$ $[M + H]^+$ 478.0873, found 478.0882.

*tert-Butyl 3-(4-Bromophenyl)-5-cyano-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4ea**):* Yellow solid (43.1 mg, 90% yield); mp 182−183 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.75−7.67 (m, 3H), 7.61−7.43 (m, 6H), 6.19 (s, 1H), 5.66 (s, 1H), 1.12 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.8, 150.9, 137.3, 136.0, 131.8, 131.8, 129.8, 129.3, 128.7, 127.1, 126.2, 124.8, 124.1, 114.1, 105.6, 82.8, 72.8, 27.8; IR (film) ν_{max} 3054, 2980, 2930, 2238, 1715, 1588, 1561, 1520, 1491, 1462, 1406, 1392, 1368, 1292, 1242, 1142, 1073, 1007, 927, 899, 811, 761, 735, 682, 581 cm^{-1}; HRMS calcd for $C_{23}H_{20}BrN_5O_2$ $[M + H]^+$ 478.0873, found 478.0890.

*tert-Butyl 5-Cyano-3-(3,4-dichlorophenyl)-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4fa**):* Yellow solid (44.2 mg, 95% yield); mp 160−161 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 2.1 Hz, 1H), 7.71 (s, 1H), 7.68−7.64 (m, 1H), 7.60−7.44 (m, 5H), 6.15 (s, 1H), 5.65 (s, 1H), 1.11 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.4, 150.8, 137.5, 137.0, 134.6, 133.0, 131.9, 130.6, 129.8, 129.6, 129.5, 128.6, 127.2, 126.8, 126.2, 124.1, 113.9, 105.1, 83.1, 72.9, 27.8; IR (film) ν_{max} 3060, 2980, 2931, 2239, 1932, 1716, 1587, 1477, 1407, 1370, 1250, 1138, 1031, 928, 869, 785, 735, 681, 664, 582 cm^{-1}; HRMS calcd for $C_{23}H_{19}Cl_2N_5O_2$ $[M + H]^+$ 468.0989, found 468.0994.

*tert-Butyl 5-Cyano-3-(2,4-dichlorophenyl)-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4ga**):* Yellow solid (24.9 mg, 53% yield); mp 143−144 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.61−7.55 (m, 2H), 7.55−7.47 (m, 4H), 7.35−7.32 (m, 1H), 5.92 (s, 1H), 5.73 (s, 1H), 1.13 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.7, 150.8, 137.4, 136.2, 135.5, 133.5, 131.9, 131.8, 129.8, 129.8, 128.8, 128.2, 127.6, 127.1, 126.3, 124.1, 113.8, 108.2, 82.9, 73.0, 27.8; IR (film) ν_{max} 3057, 2980, 2929, 2854, 2238, 1717, 1588, 1525, 1474, 1394, 1302, 1250, 1142, 1071, 1014, 928, 903, 866, 762, 737, 683, 581 cm^{-1}; HRMS calcd for $C_{23}H_{19}Cl_2N_5O_2$ $[M + H]^+$ 468.0989, found 468.0996.

*tert-Butyl 5-Cyano-3-(2-methoxyphenyl)-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4ha**):* Yellow solid (26.5 mg, 62% yield); mp 121−122 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.63−7.44 (m, 6H), 7.10−6.97 (m, 2H), 6.17 (s, 1H), 5.73 (s, 1H), 3.93 (s, 3H), 1.18 (s, 9H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 159.4, 156.9, 150.7, 136.4, 131.1, 131.0, 130.6, 129.1, 128.7, 126.6, 126.5, 126.4, 125.9, 124.0, 120.6, 114.1, 110.9, 109.7, 82.0, 72.4, 55.3, 27.5; IR (film) ν_{max} 3056, 2980, 2933, 2236, 1720, 1561, 1517, 1491, 1462, 1406, 1392, 1368, 1292, 1242, 1142, 1073, 1005, 923, 896, 811, 761, 746, 592 cm^{-1}; HRMS calcd for $C_{24}H_{23}N_5O_3$ $[M + H]^+$ 430.1874, found 430.1881.

*tert-Butyl 5-Cyano-3-(3-methoxyphenyl)-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4ia**):* Semisolid (40.9 mg, 95% yield); ^1H NMR (300 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.58−7.44 (m, 4H), 7.40−7.31 (m, 3H), 7.05−6.96 (m, 1H), 6.23 (s, 1H), 5.66 (s, 1H), 3.86 (s, 3H), 1.14 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.2, 159.8, 151.1, 138.6, 137.2, 131.8, 129.8, 129.7, 129.0, 128.9, 127.1, 126.3, 124.2, 120.3, 116.6, 114.2, 112.8, 106.4, 82.7, 72.8, 55.5, 28.0; IR (film) ν_{max} 3057, 2981, 2934, 2239, 1724, 1580, 1489, 1455, 1411, 1369, 1288, 1252, 1221, 1155, 1074, 1046, 1017, 920, 876, 845, 824, 795, 762, 736, 692 cm^{-1}; HRMS calcd for $C_{24}H_{23}N_5O_3$ $[M + H]^+$ 430.1874, found 430.1876.

*tert-Butyl 5-Cyano-3-(4-methoxyphenyl)-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4ja**):* Yellow solid (36.8 mg, 86% yield); mp 165−166 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.84−7.75 (m, 2H), 7.66 (s, 1H), 7.57−7.41 (m, 4H), 7.00−6.89 (m, 2H), 6.24 (s, 1H), 5.67 (s, 1H), 3.86 (s, 3H), 1.12 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 161.4, 160.3, 151.1, 137.0, 131.7, 129.6, 129.5, 129.3, 128.9, 128.8, 126.9, 126.3, 124.1, 114.0, 106.3, 82.5, 72.8, 55.4, 27.9; IR (film) ν_{max} 3054, 2980, 2935, 2840, 2238, 1714, 1606, 1592, 1515, 1459, 1416, 1368, 1301, 1254, 1173, 1142, 1030, 926, 899, 829, 762, 702, 683, 667, 611, 581 cm^{-1}; HRMS calcd for $C_{24}H_{23}N_5O_3$ $[M + H]^+$ 430.1874, found 430.1873.

*tert-Butyl 5-Cyano-3-(p-tolyl)-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4ka**):* Yellow solid (32.1 mg, 78% yield); mp 173−174 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.75−7.72 (m, 2H), 7.68 (s, 1H), 7.60−7.43 (m, 4H), 7.26−7.24 (m, 2H), 6.25 (s, 1H), 5.67 (s, 1H), 2.41 (s, 3H), 1.13 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.4, 151.0, 140.6, 137.0, 134.2, 131.7, 129.6, 129.4, 128.9, 128.8, 127.6, 126.9, 126.3, 124.2, 114.3, 106.4, 82.5, 72.8, 27.9, 21.4; IR (film) ν_{max} 3054, 2980, 2930, 2239, 1715, 1589, 1564, 1516, 1463, 1410, 1369, 1296, 1142, 1113, 1013, 927, 900, 852, 811, 761, 735, 702, 682, 655, 608, 581 cm^{-1}; HRMS calcd for $C_{24}H_{23}N_5O_2$ $[M + H]^+$ 414.1925, found 414.1920.

*tert-Butyl 3-(4-(tert-Butyl)phenyl)-5-cyano-[1,2,4]triazepino[3,4-a]phthalazine-1(12bH)-carboxylate (**4la**):* Yellow solid (45.3 mg, 99% yield); mp 175−176 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.82−7.74 (m, 2H), 7.68 (s, 1H), 7.59−7.53 (m, 2H), 7.51−7.43 (m, 4H), 6.27 (s, 1H), 5.66 (s, 1H), 1.35 (s, 9H), 1.14 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.4, 153.8, 151.0, 137.0, 134.2, 131.7, 129.6, 128.9, 128.8, 127.5, 127.0, 126.2, 125.6, 124.1, 114.3, 106.4, 82.5, 72.8, 34.9, 31.2, 27.9; IR (film) ν_{max} 3053, 2965, 2870, 2238, 1716, 1588,

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1561, 1518, 1462, 1394, 1368, 1298, 1142, 1010, 927, 901, 848, 761, 682, 581, 560 cm^{-1}; HRMS calcd for $C_{27}H_{29}N_5O_2$ $[M + H]^+$ 456.2394, found 456.2396.

*1-Acetyl-3-phenyl-1,12b-dihydro-[1,2,4]triazepino[3,4-a]-phthalazine-5-carbonitrile (**4na**):* Yellow solid (29.0 mg, 85% yield); mp 163−164 °C ^1H NMR (300 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.76 (s, 1H), 7.56−7.39 (m, 7H), 6.22 (s, 1H), 5.55 (s, 1H), 2.22 (s, 3H); $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$) δ 168.0, 160.6, 138.2, 136.7, 131.4, 130.3, 129.2, 129.1, 128.5, 128.4, 127.1, 126.6, 125.1, 123.6, 113.6, 104.5, 71.3, 22.5; IR (film) ν_{max} 3056.64, 2238.46, 1680.94, 1589.45, 1562.94, 1519.07, 1468.68, 1404.37, 1361.83, 1297.78, 1240.59, 1150.56, 1118.6, 1048.8, 1013.71, 926.41, 895.93, 853.85, 768.68, 734.17, 717.62, 696.27, 579.72, 552.39 cm^{-1}; HRMS calcd for $C_{20}H_{15}N_5O$ $[M + H]^+$ 342.1352, found 342.1349.

*tert-Butyl 5-Cyano-3-phenylbenzo[g][1,2,4]triazepino[3,4-a]-phthalazine-1(14bH)-carboxylate (**4ab**):* Semisolid (66.4 mg, 98% yield); ^1H NMR (300 MHz, $CDCl_3$) δ 8.02−7.92 (m, 3H), 7.88−7.80 (m, 4H), 7.64−7.54 (m, 2H), 7.52−7.42 (m, 3H), 6.22 (s, 1H), 5.87 (s, 1H), 1.04 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.9, 150.9, 137.7, 137.0, 134.5, 133.1, 130.4, 129.2, 128.8, 128.7, 128.4, 128.0, 127.7, 127.1, 125.8, 125.5, 121.5, 114.3, 105.7, 82.6, 72.9, 27.8; IR (film) ν_{max} 3058, 2980, 2238, 1714, 1590, 1568, 1523, 1457, 1407, 1368, 1347, 1284, 1143, 1050, 1012, 959, 908, 868, 750, 699, 667, 616, 477 cm^{-1}; HRMS calcd for $C_{27}H_{23}N_5O_2$ $[M + H]^+$ 450.1925, found 450.1928.

*tert-Butyl 5-Cyano-10,11-dimethyl-3-phenyl-[1,2,4]triazepino-[3,4-a]phthalazine-1(12bH)-carboxylate (**4ac**):* Yellow solid (44.5 mg, 69% yield); mp 162−163 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85−7.82 (m, 2H), 7.61 (s, 1H), 7.48−7.40 (m, 3H), 7.26−7.22 (m, 2H), 6.21 (s, 1H), 5.61 (s, 1H), 2.35 (s, 3H), 2.30 (s, 3H), 1.14 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 160.2, 151.2, 141.6, 138.5, 137.4, 137.2, 130.2, 129.0, 128.6, 127.8, 127.7, 127.0, 126.4, 121.9, 114.3, 105.7, 82.4, 73.1, 27.8, 20.0, 19.7; IR (film) ν_{max} 3340, 2979, 2927, 2238, 1716, 1590, 1575, 1522, 1456, 1408, 1369, 1287, 1259, 1146, 1047, 905, 871, 848, 802, 764, 698, 658, 608 cm^{-1}; HRMS calcd for $C_{25}H_{25}N_5O_2$ $[M + H]^+$ 428.2081, found 428.2080.

*tert-Butyl 5-Cyano-3-phenyl-[1,2,4]triazepino[3,4-a]isoquinoline-1(12bH)-carboxylate (**6**):* Yellow solid (58.5 mg, 98% yield); mp 69−70 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.85−7.82 (m, 2H), 7.48−7.42 (m, 3H), 7.41−7.32 (m, 2H), 7.30−7.27 (m, 1H), 7.26−7.23 (m, 1H), 7.21 (d, J = 7.7 Hz, 1H), 6.27 (s, 1H), 6.04 (d, J = 7.7 Hz, 1H), 5.55 (s, 1H), 1.12 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 157.7, 151.4, 137.4, 130.6, 130.0, 129.0, 128.6, 128.4, 127.7, 127.2, 126.2, 125.9, 124.3, 124.2, 114.2, 107.6, 105.6, 82.5, 76.4, 27.8; IR (film) ν_{max} 3059, 2981, 2932, 2232, 1724, 1639, 1589, 1566, 1521, 1495, 1464, 1435, 1405, 1367, 1290, 1247, 1144, 1118, 1028, 1010, 938, 904, 850, 772, 689, 563 cm^{-1}; HRMS calcd for $C_{24}H_{22}N_4O_2$ $[M + H]^+$ 399.1816, found 399.1814.

*tert-Butyl 5-Cyano-3-phenylpyridazino[6,1-c][1,2,4]triazepine-1-(10aH)-carboxylate (**8**):* Yellow solid (24.1 mg, 46% yield); mp 130−131 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80−7.72 (m, 2H), 7.48−7.40 (m, 3H), 7.25−7.24 (m, 1H), 6.61−6.36 (m, 2H), 6.27 (s, 1H), 4.90 (dd, J = 4.7, 1.5 Hz, 1H), 1.50 (s, 9H); $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 158.9, 152.3, 137.3, 134.1, 130.2, 128.7, 128.6, 127.6, 127.1, 118.8, 114.0, 106.3, 83.1, 71.8, 28.3; IR (film) ν_{max} 3060, 2980, 2932, 2239, 1711, 1591, 1576, 1546, 1455, 1395, 1369, 1286, 1250, 1147, 1072, 1022, 1000, 949, 862, 757, 697, 658 cm^{-1}; HRMS calcd for $C_{19}H_{19}N_5O_2$ $[M + H]^+$ 350.1612, found 350.1617.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01296.

^1H and $^{13}C\{^1H\}$ NMR spectra for all products (PDF)

X-ray data for compound **4aa** (CIF)

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Notes

The authors declare no competing financial interest.

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