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Synthesis of Dibenzazepinones by Palladium-Catalyzed Intramolecular Arylation of *o*-(2′-Bromophenyl)anilide Enolates

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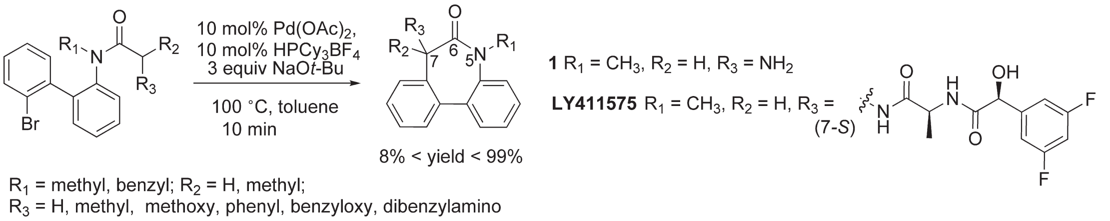

A new approach for the convenient synthesis of dibenzazepinones is reported. The key step is the formation of the seven-membered ring through palladium-catalyzed intramolecular arylation of an anilide enolate. The reactions were completed in 10 min at 100 °C with moderate to excellent yields. Aminodibenzazepinone **1**, the core structure in the γ-secretase inhibitor LY411575, can be prepared in five steps from 2-bromophenylboronic acid and 2-iodoaniline in 60% overall yield. The synthesis reported here compares favorably with presently available approaches to this interesting ring system.

Introduction

γ-Secretase inhibitor LY411575,[1,2] a potential drug candidate for Alzheimer's disease, is known to reduce brain and CSF levels of Aβ-peptides. As the core structure of LY411575, α-substituted dibenzazepinones have an interesting gear-like structure.[3,4] Prior syntheses of dibenzazepinones have been based upon Friedel−Crafts alkylation,[5a,b] palladium-catalyzed borylation−Suzuki reaction,[4] the cyclization of a hydroxylamide in neat trifluoromethanesulfonic acid,[5c] the intramolecular Staudinger−aza-Wittig reaction of an azido pentafluorophenyl ester,[5d] and the hydrogenation of methyl 2-nitro-2′-biphenylacetate.[5e] Some of these methods suffer from low yields or produce byproducts that are difficult to separate from the target molecule. The palladium-catalyzed intramolecular arylation of anilide enolates has been developed for the synthesis of oxindoles[6] and other five- and six-membered ring compounds.[7] We became interested in exploring the potential of this method for seven-member ring formation and its utility in the synthesis of aminodibenzazepinone **1**. In this paper, we describe the results of our investigations and detail a new synthesis of dibenzazepinones by the palladium-catalyzed intramolecular arylation of *o*-phenylanilide enolates.

Results and Discussion

Synthesis of Dibenzazepinone Precursors (Scheme 1). The Suzuki coupling of 2-bromophenylboronic acid and 2-iodoaniline afforded 2-amino-2′-bromobiphenyl **2** in 90% yield. Amidation of **2** with acyl chlorides or carboxylic acids gave amides **3**−**9** in generally excellent yields. Methylation of **3**−**9** with methyl iodide or benzylation of **3** with benzyl

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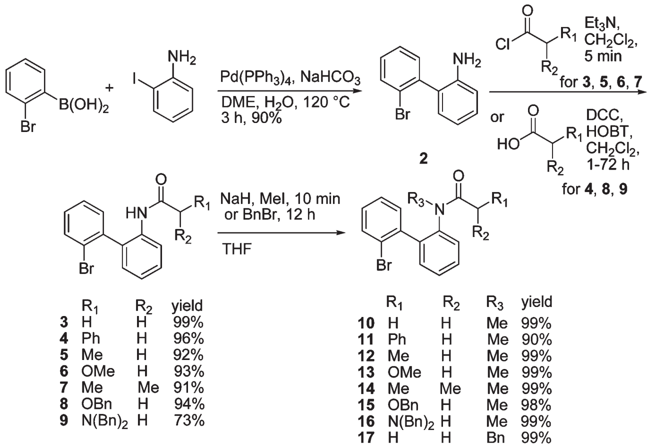
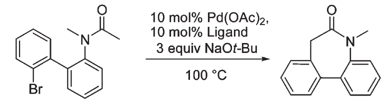
SCHEME 1. Synthesis of Amides 10−17



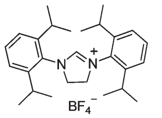
	R_1	R_2	yield
3	H	H	99%
4	Ph	H	96%
5	Me	H	92%
6	OMe	H	93%
7	Me	Me	91%
8	OBn	H	94%
9	N(Bn)$_2$	H	73%

	R_1	R_2	R_3	yield
10	H	H	Me	99%
11	Ph	H	Me	90%
12	Me	H	Me	99%
13	OMe	H	Me	99%
14	Me	Me	Me	99%
15	OBn	H	Me	98%
16	N(Bn)$_2$	H	Me	99%
17	H	H	Bn	99%

TABLE 1. Optimization of the Synthesis of Dibenzazepinone 19



10 **19**

entry	ligand precursor	solvent	time (min)	yield[a] (%)
1	 **18**	toluene	20	78
2	HPCy$_3$BF$_4$	toluene	10	90
3	HPCy$_3$BF$_4$	dioxane	10	45
4[b]	HPCy$_3$BF$_4$	toluene	10	61

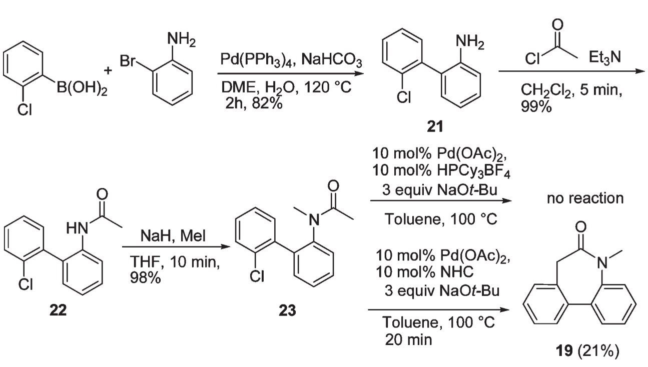
[a] Yield of **19** was calculated from isolated product after chromatography. [b] Reaction run with 5 mol % of the catalyst and 1.5 equiv of NaO*t*-Bu.

bromide provided the desired *N*-alkyl amides **10−17** as dibenzazepinone precursors in uniformly excellent yields.

Optimization of Reaction Conditions. As shown in Table 1, two general catalysis systems were screened with acetamide **10**. Treatment of **10** with *N*-heterocyclic carbene precursor **18**,[6] palladium acetate, and sodium *tert*-butoxide (NaO*t*-Bu) in toluene at 100 °C for 20 min gave dibenzazepinone **19** in 78% yield (entry 1). The use of tricyclohexylphosphonium tetrafluoroborate[7a] with palladium acetate increased the yield of **19** to 90% in 10 min (entry 2) and generated a byproduct identified as 9-methyl-9*H*-carbazole **20** (6% yield). This byproduct is presumed to arise by cleavage of the amide to the aniline by NaO*t*-Bu followed by the palladium-catalyzed intramolecular amination. Changing the solvent to dioxane decreased the yield of **19** to 45% (entry 3). To further explore the efficiency of the catalysis system of tricyclohexylphosphonium tetrafluoroborate, the catalytic loading was lowered to 5 mol % with 1.5 equiv of NaO*t*-Bu (entry 4). However, the yield of **19** dropped to 61%.

Exploration of the Reaction with Chloroaryl Substrates. For reasons related to materials cost, the possibility of using a chloroaryl substrate in place of the bromoaryl substrate was explored. As shown in Scheme 2, the synthesis of 2′-chloro-2-aminobiphenyl **21** from 2-chlorophenylboronic acid and 2-bromoaniline, which are less expensive starting materials, proceeded with the same efficiency as found for the bromoaryl analogue (82% yield). Following amidation of **21** with acetyl chloride and methylation of amide **22** with methyl iodide gave *N*-methyl amide **23** in quantitative overall yield. Unfortunately, with chloroaryl substrate **23**, the catalysis system of tricyclohexylphosphonium tetrafluoroborate provided no product; *N*-heterocyclic carbene ligand precursor **18** under the same conditions for 20 min gave **19** in only 21% yield.

SCHEME 2. Synthesis of Dibenzazepinone 19 from Chloroaryl Substrates



Exploration of the Substrate Scope. The optimized cyclization conditions were applied to seven more substrates (Table 2). A phenyl group in the α position of the amide was well tolerated; the yield of α-phenyldibenzazepinone **24** was almost quantitative (entry 2). In contrast, α-methyl and α-methoxy substrates **12** and **13** (entry 3 and 4) afforded relatively low yields of the dibenzazepinone and the product was accompanied by the byproduct 9-methyl-9*H*-carbazole. The incorporation of two methyl groups at the α position inhibited the reaction; α,α-dimethyldibenzazepinone **27** was formed in only 8% yield and 54% conversion (entry 5). The *N*-benzyl amide **17** was investigated as an alternative to *N*-methyl amide **10** because the product amide may be readily deprotected. The benzyl and methyl amides behaved similarly. *N*-Benzyl protected dibenzazepinone **28** was isolated in 84% yield along with 9-benzyl-9*H*-carbazole in 16% yield (entry 6).

Under the standard conditions using 3 equiv of base, an interesting byproduct was formed (54% yield) in the reaction of α-benzyloxyamide **15**. This side product was also produced by the reaction of product **29** with NaO*t*-Bu alone in toluene at 100 °C (Scheme 3) and therefore could be α-hydroxy-α-benzyl dibenzazepinone **30**, a 1,2-Wittig rearrangement product.[8] To confirm the structure of **30**, **29** was reduced to amine **31**(Scheme 3). Following debenzylation of **31**, Dess−Martin oxidation of alcohol **32** and treatment of aldehyde **33** with benzylmagnesium chloride afforded amine **34**, which was identical to the amide reduction product of **30**. The reaction conditions were then modified for the formation of **29**. α-Benzyloxydibenzazepinone **29** was formed in 81% yield with 4% **30** when the amount of NaO*t*-Bu was reduced to 1.5 equiv, and the reaction was run in toluene for 10 min (Table 2, entry 7).

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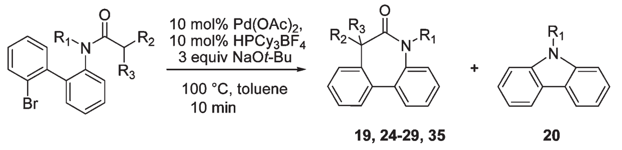
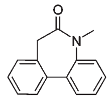
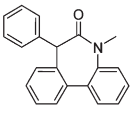
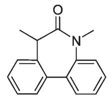
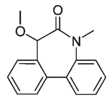
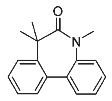
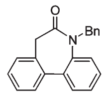
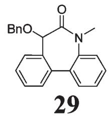
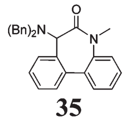
TABLE 2. Scope of the Intramolecular Arylation Pathway to Dibenzazepinones

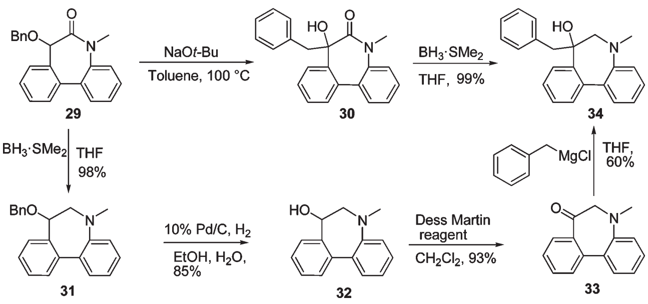


entry	reactant	product	yield[a] (%)	**20**[a] (%)	conversion[b] (%)
1	**10**	 **19**	90	6	96
2	**11**	 **24**	99	-	100
3	**12**	 **25**	45	34	80
4	**13**	 **26**	56	15	86
5	**14**	 **27**	8	15	54
6	**17**	 **28**	84	16	100
7[c]	**15**	 **29**	81	7	100
8	**16**	 **35**	93	-	100
9[d]	**16**	**35**	91	-	98

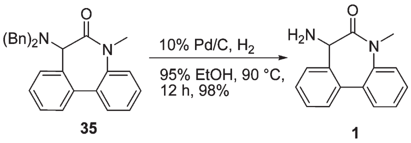
[a] Yield was calculated from isolated product after chromatography. [b] Conversion was based on the isolated starting material. [c] Reaction run with 1.5 equiv of NaO*t*-Bu. [d] Reaction run with 3 mol % of the catalyst for 15 min.

Because of our interest in the γ-secretase inhibitor, it was significant to find that α-dibenzylaminoamide **16** cyclized efficiently to afford α-dibenzylaminodibenzazepinone **35** in 93% yield (entry 8). Lowering the catalyst loading to 3 mol % had little effect and provided the desired product in 15 min in 91% yield (entry 9).

SCHEME 3. Rearrangement of α-Benzyloxydibenzazepinone 29



Completion of the Synthesis of α-Aminodibenzazepinone 1. α-Dibenzylaminodibenzazepinone **35** was debenzylated quantitatively through hydrogenolysis to afford α-aminodibenzazepinone **1** (eq 1). The complete synthesis of α-aminodibenzazepinone **1** by this approach requires five steps from 2-bromophenylboronic acid and 2-iodoaniline and proceeds in 60% overall yield. Significant increases in overall yield can be achieved by optimizing the step involving coupling of 2′-bromo-2-aminobiphenyl **2** with dibenzylaminoacetic acid.



(1)

Conclusion

The intramolecular α-arylation of amide enolates has been applied successfully to the formation of seven-membered ring compounds. These reactions provide a new route to the synthesis of substituted dibenzazepinones. The procedure is efficient and especially useful for the synthesis of α-aminodibenzazepinone. We anticipate that with the appropriate asymmetric ligand or chiral amino protecting group, α-aminodibenzazepinone may be made directly with high enantiomeric excess, thus eliminating the need for resolution of this important target.

Experimental Section

[1,1′-Biphenyl]-2-amine, 2′-Bromo- (2). A solution of 2-iodoaniline (3.48 g, 15.89 mmol), 2-bromophenylboronic acid (3.67 g, 18.27 mmol), $Pd(PPh_3)_4$ (550 mg, 0.48 mmol), and $NaHCO_3$ (4.0 g, 47.7 mmol) in DME (45 mL) was stirred at room temperature for 5 min. H_2O (23 mL) was added, and the resulting mixture was degassed by oil pump in a dry ice−acetone bath, sealed, and stirred at 120 °C for 3 h. After being cooled to room temperature, the mixture was extracted with Et_2O. The extracts were combined, dried over $MgSO_4$, and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **2** (3.53 g, 90%) as a pale yellow solid:[9] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 8.1 Hz, 1H), 7.47−7.31 (m, 2H), 7.27−7.19 (m, 2H), 7.06 (dd, J = 7.5, 1.5 Hz, 1H), 6.87 (td, J = 7.5, 0.9 Hz, 1H), 6.81 (dd, J = 8.1, 0.9 Hz, 1H), 3.54 (br, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7, 140.2, 133.3, 132.0, 130.4, 129.4, 129.3, 128.0, 127.3, 124.4, 118.4, 115.7.

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[1,1′-Biphenyl]-2-amine, 2′-Chloro- (21). A solution of 2-bromoaniline (516 mg, 3.0 mmol), 2-chlorophenylboronic acid (562 mg, 3.6 mmol), $Pd(PPh_3)_4$ (173 mg, 0.15 mmol), and $NaHCO_3$ (756 mg, 9.0 mmol) in DME (7 mL) was stirred at room temperature for 5 min. H_2O (7 mL) was added, and the resulting mixture was degassed by oil pump in a dry ice–acetone bath, sealed, and stirred at 120 °C for 2 h. After being cooled to room temperature, the mixture was extracted with Et_2O. The extracts were combined, dried over $MgSO_4$, and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to provide **21** (501 mg, 82%) as a white solid:[9] ^1H NMR (300 MHz, $CDCl_3$) δ 7.50 (m, 1H), 7.38–7.23 (m, 3H), 7.22 (t, J = 7.2 Hz, 1H), 7.05 (d, J = 7.5 Hz, 1H), 6.84 (t, J = 7.5 Hz, 1H), 6.77 (d, J = 8.1 Hz, 1H), 3.52 (br, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 138.1, 134.0, 133.1, 131.6, 131.0, 130.3, 129.5, 128.9, 128.4, 128.2, 128.1, 126.3, 125.4, 119.5, 117.3, 116.6, 114.6.

General Procedure for the Acylation of 2-Arylanilines with Acyl Chlorides. To a solution of 2-arylaniline (2.0 mmol) and Et_3N (0.34 mL, 2.4 mmol) in CH_2Cl_2 (10 mL) was added acyl chloride (2.4 mmol) slowly at 0 °C, and the mixture was stirred at room temperature for 5 min. Saturated NH_4Cl solution was added, and the resulting mixture was stirred for 10 min. The organic layer was separated, dried over $MgSO_4$, and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography.

[1,1′-Biphenyl]-2-acetamide, 2′-Bromo- (3). By the general procedure, **2** (1.0 g, 4.0 mmol), Et_3N (0.67 mL, 4.8 mmol), acetyl chloride (0.34 mL, 4.8 mmol) in CH_2Cl_2 (20 mL) for 5 min provided **3** (1.15 g, 99%) as an oil after flash chromatography (SiO_2, hexanes/EtOAc = 1/1): IR (cm^{-1}) 3421, 3286, 3056, 1670, 1520, 1442, 1369, 1294, 1027, 1005, 754; ^1H NMR (300 MHz, $CDCl_3$) δ 8.18 (d, J = 8.1 Hz, 1H), 7.71–7.69 (m, 1H), 7.42–7.37 (m, 2H), 7.29–7.25 (m, 2H), 7.21–7.13 (m, 2H), 6.86 (br, 1H), 1.96 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 138.9, 135.1, 133.3, 132.0, 130.1, 130.0, 129.3, 129.1, 128.1, 124.4, 124.0, 122.2, 24.6; HRMS (EI) *m*/*e* calcd for $C_{14}H_{12}NOBr$ (M^+) 289.0102, found 289.0101.

[1,1′-Biphenyl]-2-propionamide, 2′-Bromo- (5). By the general procedure, **2** (248 mg, 1.0 mmol), Et_3N (0.17 mL, 1.2 mmol), propionyl chloride (0.10 mL, 1.2 mmol) in CH_2Cl_2 (10 mL) for 5 min provided **5** (278 mg, 92%) as an oil after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3296, 2976, 1672, 1442, 754; ^1H NMR (300 MHz, $CDCl_3$) δ 8.21 (d, J = 7.8 Hz, 1H), 7.70–7.67 (m, 1H), 7.41–7.34 (m, 2H), 7.28–7.22 (m, 2H), 7.18–7.11(m, 2H), 6.92 (br, 1H), 2.20 (q, J = 7.5 Hz, 2H), 1.05 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 138.8, 135.1, 133.1, 131.9, 129.9, 129.0, 128.0, 124.1, 123.9, 121.9, 30.7, 9.5; HRMS (EI) *m*/*e* calcd for $C_{15}H_{14}NOBr$ (M^+) 303.0259, found 303.0270.

[1,1′-Biphenyl]-2-methoxyacetamide, 2′-Bromo- (6). By the general procedure, **2** (248 mg, 1.0 mmol), Et_3N (0.17 mL, 1.2 mmol), methoxyacetyl chloride (0.11 mL, 1.2 mmol) in CH_2Cl_2 (10 mL) for 5 min provided **6** (298 mg, 93%) as an oil after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3369, 2936, 1693, 1526, 1303, 1111, 757; ^1H NMR (300 MHz, $CDCl_3$) δ 8.37 (d, J = 8.1 Hz, 1H), 8.08 (br, 1H), 7.71–7.68 (m, 1H), 7.46–7.37 (m, 2H), 7.29–7.24 (m, 2H), 7.17–7.14 (m, 2H), 3.84 (d, J = 1.2 Hz, 2H), 3.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 138.5, 134.5, 133.0, 131.7, 131.5, 129.8, 129.7, 129.0, 127.9, 124.2, 124.0, 120.9, 72.1, 59.3; HRMS (EI) *m*/*e* calcd for $C_{15}H_{14}NO_2Br$ (M^+) 319.0208, found 319.0207.

[1,1′-Biphenyl]-2-isobutyramide, 2′-Bromo- (7). By the general procedure, **2** (248 mg, 1.0 mmol), Et_3N (0.17 mL, 1.2 mmol), isobutyryl chloride (0.13 mL, 1.2 mmol) in CH_2Cl_2 (10 mL) for 5 min provided **7** (289 mg, 91%) as an oil after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3424, 3298, 2968, 1676, 1517, 1285, 754; ^1H NMR (300 MHz, $CDCl_3$) δ 8.22 (d, J = 8.1 Hz, 1H), 7.72–7.67 (m, 1H), 7.43–7.36 (m, 2H), 7.29–7.24 (m, 2H), 7.19–7.12 (m, 2H), 6.92 (br, 1H), 2.36 (heptet, J = 6.9 Hz, 1H), 1.06 (d, J = 6.9 Hz, 3H), 1.03 (d, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.8, 138.8, 135.1, 133.1, 132.0, 131.9, 129.9, 129.7, 129.0, 128.0, 124.2, 123.9, 121.9, 36.5, 19.3; HRMS (EI) *m*/*e* calcd for $C_{16}H_{16}NOBr$ (M^+) 317.0415, found 317.0410.

[1,1′-Biphenyl]-2-acetamide, 2′-Chloro- (22). By the general procedure, **21** (475 mg, 2.33 mmol), Et_3N (0.39 mL, 2.8 mmol), acetyl chloride (0.2 mL, 2.8 mmol) in CH_2Cl_2 (10 mL) for 5 min provided **22** (570 mg, 99%) as an oil after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3421, 3283, 3058, 1670, 1521, 1442, 1293, 1036, 754; ^1H NMR (300 MHz, $CDCl_3$) δ 8.09 (d, J = 8.1 Hz, 1H), 7.49–7.46 (m, 1H), 7.39–7.23 (m, 4H), 7.18–7.15 (m, 2H), 7.10 (br, 1H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.4, 136.7, 135.2, 133.5, 131.9, 130.5, 130.2, 129.8, 129.6, 128.8, 127.3, 124.4, 122.5, 24.2; HRMS (EI) *m*/*e* calcd for $C_{14}H_{12}NOCl$ (M^+) 245.0607, found 245.0610.

[1,1′-Biphenyl]-2-phenylacetamide, 2′-Bromo- (4). To a solution of **2** (350 mg, 1.4 mmol), phenylacetic acid (209 mg, 1.54 mmol), and 1-hydroxybenzotriazole (HOBT) (209 mg, 1.54 mmol) in CH_2Cl_2 (10 mL) was added a solution of DCC (318 mg, 1.54 mmol) in CH_2Cl_2 (4 mL) slowly at room temperature in 1 h, and the mixture was stirred for 36 h and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **4** (490 mg, 96%) as an oil: IR (cm^{-1}) 3381, 3307, 3060, 1685, 1519, 1443, 1303, 754; ^1H NMR (300 MHz, $CDCl_3$) major conformer: δ 8.32 (d, J = 8.1 Hz, 1H), 7.48 (dd, J = 7.5, 1.5 Hz, 1H), 7.41 (td, J = 7.2, 1.5 Hz, 1H), 7.25–7.08 (m, 6H), 7.13–6.93 (m, 4H), 6.80 (br, 1H), 3.59 (s, 1H), 3.58 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 138.3, 135.0, 133.7, 133.2, 131.6, 131.2, 129.7, 129.4, 129.3, 129.1, 127.8, 127.6, 124.2, 123.8, 121.0, 45.1; HRMS (EI) *m*/*e* calcd for $C_{20}H_{16}NOBr$ (M^+) 365.0415, found 365.0410.

[1,1′-Biphenyl]-2-benzyloxyacetamide, 2′-Bromo- (8). To a solution of **2** (744 mg, 3.0 mmol), benzyloxyacetic acid (600 mg, 3.6 mmol) and HOBT (492 mg, 3.6 mmol) in CH_2Cl_2 (24 mL) was added a solution of DCC (750 mg, 3.6 mmol) in CH_2Cl_2 (6 mL) slowly at room temperature in 1 h, and the mixture was stirred for 1 h and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **8** (1.11 g, 94%) as an oil: IR (cm^{-1}) 3376, 3065, 2869, 1693, 1526, 1026, 738; ^1H NMR (300 MHz, $CDCl_3$) δ 8.41 (d, J = 8.1 Hz, 1H), 8.20 (br, 1H), 7.55 (dd, J = 8.1, 0.9 Hz, 1H), 7.44–7.37 (m, 1H), 7.33–7.09 (m, 8H), 7.06–6.98 (m, 2H), 4.39–4.29 (m, 2H), 4.03–3.91 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 138.5, 136.6, 134.6, 133.1, 131.7, 131.5, 129.9, 129.2, 128.5, 128.0, 127.9, 127.6, 124.3, 124.0, 120.9, 73.2, 69.7; HRMS (EI) *m*/*e* calcd for $C_{21}H_{18}NO_2Br$ (M^+) 395.0521, found 395.0538.

[1,1′-Biphenyl]-2-dibenzylaminoacetamide, 2′-Bromo- (9). To a solution of **2** (124 mg, 0.5 mmol), dibenzylaminoacetic acid (153 mg, 0.6 mmol) and HOBT (82 mg, 0.6 mmol) in CH_2Cl_2 (4 mL) was added a solution of DCC (125 mg, 0.6 mmol) in CH_2Cl_2 (1 mL) at room temperature in 1 h, and the mixture was stirred for 72 h and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **9** (176 mg, 73%) as an oil: IR (cm^{-1}) 3336, 3061, 3029, 2923, 2831, 2246, 1692, 1583, 1514, 1445, 910, 750; ^1H NMR (300 MHz, $CDCl_3$) δ 8.73 (s, 1H), 8.39 (d, J = 8.4 Hz, 1H), 7.82 (dd, J = 7.2, 0.6 Hz, 1H), 7.54 (td, J = 6.9, 1.2 Hz, 1H), 7.43–7.33 (m, 3H), 7.31–7.19 (m, 6H), 7.17–7.13 (m, 2H), 6.99–6.94 (m, 4H), 3.52 (d, J = 13.5 Hz, 2H), 3.44 (d, J = 13.5 Hz, 2H), 3.18 (d, J = 16.5 Hz, 1H), 3.04 (d, J = 16.5 Hz, 1H); ^{13}C NMR (75 MHz,

$CDCl_3$) δ 169.3, 139.4, 136.9, 135.2, 133.4, 132.1, 131.4, 130.3, 130.1, 129.2, 129.1, 128.7, 128.0, 127.6, 124.7, 124.1, 121.2, 58.9, 57.6; HRMS (EI) *m/e* calcd for $C_{28}H_{26}N_2OBr$ (MH$^+$) 485.1228, found 485.1217.

General Procedure for the Methylation of Amides with Methyl Iodide. A mixture of amide (1.0 mmol) and NaH (60% in mineral oil, 42 mg, 1.05 mmol) in THF (10 mL) was stirred at room temperature for 10 min. MeI (0.075 mL, 1.2 mmol) was added, and the resulting mixture was stirred for 10 min. After removal of volatile components from the mixture, the resulting crude product was purified by flash chromatography.

[1,1′-Biphenyl]-2-(*N*-methyl-acetamide), 2′-Bromo- (10). By the general procedure, **3** (1.01 g, 3.48 mmol), NaH 60% in mineral oil (147 mg, 3.65 mmol), MeI (593 mg, 4.18 mmol) in THF (25 mL) for 10 min afforded **10** (1.05 g, 99%) as a white solid after flash chromatography (SiO_2, hexanes/EtOAc = 1/1): IR (cm^{-1}) 3066, 1658, 1467, 1373, 757; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69−7.63 (m, 1H), 7.48−7.38 (m, 2H), 7.38−7.30 (m, 2H), 7.29−7.09 (m, 3H), 3.09 (s, 1.04H), 2.96 (s, 0.31H), 2.84 (s, 1.65H), 2.17 (s, 0.14H), 2.01 (s, 0.32H), 1.98 (s, 1.54H), 1.86 (s, 1.0H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 170.5, 142.7, 142.3, 142.0, 139.3, 138.8, 133.6, 133.3, 132.7, 132.5, 131.9, 131.4, 130.3, 129.7, 129.5, 129.4, 129.3, 128.7, 128.5, 128.4, 127.9, 127.7, 127.3, 123.5, 123.3, 77.43, 38.9, 38.4, 36.0, 31.1, 22.7, 22.0; HRMS (EI) *m/e* calcd for $C_{15}H_{14}NOBr$ (M$^+$) 303.0259, found 303.0268.

[1,1′-Biphenyl]-2-(*N*-methyl-phenylacetamide), 2′-Bromo- (11). By the general procedure, **4** (480 mg, 1.32 mmol), NaH 60% in mineral oil (53 mg, 1.32 mmol), MeI (225 mg, 1.59 mmol) in THF (5 mL) for 10 min afforded **11** (451 mg, 90%) as a white solid after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3060, 1658, 1373, 753; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71−7.58 (m, 1H), 7.45−7.09 (m, 11.4H), 6.85−6.80 (m, 0.6H), 3.70−3.50 (m, 1.6H), 3.37−3.32 (m, 0.4H), 3.15 (s, 1H), 2.99 (s, 0.3H), 2.86 (s, 1.7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.6, 170.9, 142.1, 142.0, 141.6, 139.1, 139.0, 138.9, 135.8, 135.3, 134.5, 133.8, 133.2, 132.9, 132.5, 131.7, 131.4, 130.4, 129.8, 129.7, 129.5, 129.4, 129.1, 129.0, 128.8, 128.7, 128.6, 128.4, 128.1, 127.9, 127.6, 127.5, 127.4, 127.0, 126.8, 126.6, 123.5, 123.3, 77.43, 41.1, 41.0, 38.9, 36.4; HRMS (EI) *m/e* calcd for $C_{21}H_{18}NOBr$ (M$^+$) 379.0572, found 379.0575.

[1,1′-Biphenyl]-2-(*N*-methyl-propionamide), 2′-Bromo- (12). By the general procedure, **5** (249 mg, 0.82 mmol), NaH 60% in mineral oil (35 mg, 0.86 mmol), MeI (140 mg, 0.99 mmol) in THF (10 mL) for 10 min afforded **12** (257 mg, 99%) as a white solid after flash chromatography (SiO_2, hexanes/EtOAc = 1/1): IR (cm^{-1}) 3058, 2974, 2936, 1660, 1464, 1378, 1285, 753; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67−7.60 (m, 1H), 7.45−7.37 (m, 2H), 7.37−7.28 (m, 2H), 7.27−7.05 (m, 3H), 3.11 (s, 1.08H), 2.97 (s, 0.35H), 2.85 (s, 1.57H), 2.35−2.18 (m, 0.7H), 2.18−2.04 (m, 1.3H), 1.14 (t, *J* = 7.2 Hz, 1.54H), 1.03 (t, *J* = 7.2 Hz, 0.40H), 0.95 (t, *J* = 6.9 Hz, 1.06H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 173.7, 142.3, 142.2, 141.7, 139.8, 139.1, 139.0, 138.7, 133.4, 133.1, 132.5, 132.3, 131.5, 131.2, 130.1, 129.5, 129.4, 129.2, 129.1, 128.5, 128.3, 128.2, 127.7, 127.4, 127.1, 127.0, 123.3, 123.1, 38.3, 38.0, 35.9, 27.6, 27.4, 26.9, 9.9, 9.7, 9.1; HRMS (EI) *m/e* calcd for $C_{16}H_{16}NOBr$ (M$^+$) 317.0415, found 317.0421.

[1,1′-Biphenyl]-2-(*N*-methyl-methoxyacetamide), 2′-Bromo- (13). By the general procedure, **6** (275 mg, 0.86 mmol), NaH 60% in mineral oil (36 mg, 0.90 mmol), MeI (147 mg, 1.03 mmol) in THF (8 mL) for 10 min afforded **13** (286 mg, 99%) as an oil after flash chromatography (SiO_2, hexanes/EtOAc = 1/1): IR (cm^{-1}) 3058, 2925, 2820,1676, 1465, 1330, 1103, 754; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68−7.63 (m, 1H), 7.48−7.40 (m, 2H), 7.39−7.17 (m, 5H), 4.09−3.93 (m, 0.75H), 3.88- 3.79 (m, 1.25H), 3.37 (s, 1.45H), 3.28 (s, 0.52H), 3.27 (s, 1.0H), 3.13 (s, 1.1H), 2.98 (s, 0.40H), 2.85 (s, 1.53H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.3, 168.7, 141.3, 140.3, 139.8, 139.5, 138.8, 138.6, 138.5, 138.4, 133.4, 133.0 132.6, 132.4, 131.4, 131.2, 131.0, 129.9, 129.5, 129.2, 129.1, 129.0, 128.6, 128.1, 128.0, 127.9, 127.4, 127.1, 126.9, 123.1, 122.8, 71.0, 70.6, 70.2, 59.1, 58.7, 38.2, 36.7, 35.7; HRMS (EI) *m/e* calcd for $C_{16}H_{16}NO_2Br$ (M$^+$) 333.0364, found 333.0377.

[1,1′-Biphenyl]-2-(*N*-methyl-isobutyramide), 2′-Bromo- (14). By the general procedure, **7** (260 mg, 0.82 mmol), NaH 60% in mineral oil (35 mg, 0.86 mmol), MeI (140 mg, 0.99 mmol) in THF (10 mL) for 10 min afforded **14** (268 mg, 99%) as a white solid after flash chromatography (SiO_2, hexanes/EtOAc = 1/1): IR (cm^{-1}) 2968, 1658, 1466, 1386, 1102, 752; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (m, 1H), 7.48−7.24 (m, 5H), 7.24−7.09 (m, 2H), 3.21 (s, 1.2H), 3.07 (s, 0.3H), 2.89 (s, 1.5H), 2.76 (heptet, *J* = 6.9 Hz, 0.1H), 2.62−2.46 (m, 0.9H), 1.13 (d, *J* = 6.6 Hz, 1.5H), 1.09 (d, *J* = 6.6 Hz, 1.5H), 0.94 (d, *J* = 6.6 Hz, 1.37H), 0.81 (d, *J* = 6.6 Hz, 0.35H), 0.69 (d, *J* = 6.6 Hz, 1.28H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.6, 177.2, 142.4, 142.2, 141.8, 139.8, 139.2, 138.9, 138.5, 133.5, 133.0, 132.8, 132.1,131.8, 131.3, 130.9, 130.6, 129.6, 129.4, 129.3, 129.1, 128.0, 127.8, 127.3, 127.2, 126.9, 123.3, 38.8, 37.9, 36.2, 31.5, 30.9, 30.3, 20.6, 20.1, 19.6,18.9,18.8, 18.7; HRMS (EI) *m/e* calcd for $C_{17}H_{18}NOBr$ (M$^+$) 331.0572, found 331.0565.

[1,1′-Biphenyl]-2-(*N*-methyl-benzyloxyacetamide), 2′-Bromo- (15). By the general procedure, **8** (1.04 g, 2.63 mmol), NaH 60% in mineral oil (110 mg, 2.77 mmol), MeI (448 mg, 3.16 mmol) in THF (30 mL) for 10 min afforded **15** (1.056 g, 98%) as an oil after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3060, 2925, 1673, 1026, 751; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.58 (m, 1H), 7.42−7.14 (m, 11.4H), 7.05 (dd, *J* = 7.2, 1.8 Hz, 0.6H), 4.63−4.33 (m, 2H), 4.14−3.87 (m, 2H), 3.12 (s, 1H), 3.00 (s, 0.4H), 2.86 (s, 1.6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.7, 169.0, 141.6, 140.6, 140.2, 139.8, 139.0, 138.9, 138.7, 138.6, 137.9, 137.5, 133.6, 133.1, 132.7, 132.5, 131.6, 131.5, 131.2, 130.3, 129.6, 129.4, 128.8, 128.4, 128.3, 128.1, 128.0, 127.9, 127.6, 127.4, 127.3, 127.2, 123.3, 123.1, 73.2, 73.0, 72.9, 69.0, 68.2, 38.5, 37.2, 36.0; HRMS (EI) *m/e* calcd for $C_{22}H_{20}NO_2NaBr$ (MNa$^+$) 432.0575, found 432.0548.

[1,1′-Biphenyl]-2-(*N*-methyl-dibenzylaminoacetamide), 2′-Bromo- (16). By the general procedure, **9** (166 mg, 0.34 mmol), NaH 60% in mineral oil (15 mg, 0.36 mmol), MeI (58 mg, 0.41 mmol) in THF (4 mL) for 10 min afforded **16** (170 mg, 99%) as an oil after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3060, 3027, 2919, 1664, 1464, 749; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.8 Hz, 0.5H), 7.48 (d, *J* = 8.1 Hz, 0.3H), 7.43−7.07 (m, 15.7H), 6.96−6.89 (m, 0.5H), 6.88 (d, *J* = 7.5 Hz, 0.5H), 6.60 (d, *J* = 7.2 Hz, 0.5H), 3.98−3.01 (m, 7.5H), 2.82 (s, 1.50H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 171.0, 170.7, 142.1, 141.3, 140.6, 140.1, 139.9, 139.8, 139.1, 138.9, 138.8, 138.7, 133.7, 133.1, 132.8, 132.3, 131.5, 131.0, 130.3, 130.1, 129.5, 129.4, 129.3, 129.0, 128.7, 128.5, 128.4, 128.3, 128.2, 127.8, 127.7, 127.6, 127.2, 127.1, 126.8, 123.4, 123.2, 123.0, 77.4, 58.3, 58.0, 57.4, 56.2, 53.5, 53.2, 38.7, 37.9, 35.9; HRMS (EI) *m/e* calcd for $C_{29}H_{28}N_2OBr$ (MH$^+$) 499.1385, found 499.1381.

[1,1′-Biphenyl]-2-(*N*-methyl-acetamide), 2′-Chloro- (23). By the general procedure, **22** (271 mg, 1.1 mmol), NaH 60% in mineral oil (47 mg, 1.155 mmol), MeI (188 mg, 1.32 mmol) in THF (7 mL) for 10 min afforded **23** (280 mg, 98%) as a white solid after flash chromatography (SiO_2, hexanes/EtOAc = 1/1): IR (cm^{-1}) 3069, 1658, 1373, 1031, 760; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48−7.33 (m, 5H), 7.33−7.23 (m, 3H), 7.15 (br, 1H), 3.04 (s, 1.15H), 2.96 (s, 0.44H), 2.85 (s, 1.41H), 2.01−2.00 (m, 0.25H), 1.94 (s, 1.50H), 1.86 (s, 1.25H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 170.3, 142.4, 142.0, 137.2, 136.9, 133.0, 132.2, 131.5, 131.2, 130.3, 129.9, 129.4, 129.1, 128.4, 128.2, 127.8, 127.2, 126.9, 126.5, 37.9, 35.9, 22.5, 22.2, 21.9; HRMS (EI) *m/e* calcd for $C_{15}H_{14}NOCl$ (M$^+$) 259.0764, found 259.0763.

[1,1′-Biphenyl]-2-(*N*-benzyl-acetamide), 2′-Bromo- (17). A mixture of **3** (290 mg, 1.0 mmol) and NaH (60% in mineral oil, 42 mg, 1.05 mmol) in THF (10 mL) was stirred at room temperature for 10 min. Benzyl bromide (205 mg, 1.2 mmol) was added, and the resulting mixture was stirred for 12 h. After removal of volatile components from the mixture, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 1/1) to give **17** (371 mg, 99%) as a white solid: IR (cm^{-1}) 3060, 1658, 1386, 751; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74−7.65 (m, 1H), 7.40−7.32 (m, 3H), 7.32−7.22 (m, 3H), 7.21−7.16 (m, 5H), 6.88 (d, J = 7.8 Hz, 0.24H), 6.75 (d, J = 7.8 Hz, 0.76H), 5.44 (d, J = 18.0 Hz, 0.22H), 5.27 (d, J = 14.1 Hz, 0.78H), 3.90 (d, J = 14.4 Hz, 0.22H), 3.45 (d, J = 14.4 Hz, 0.78H), 2.10 (s, 0.21H), 2.04 (s, 2.14H), 1.95 (s, 0.65H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.4, 139.9, 139.1, 138.7, 137.4, 133.6, 132.8, 131.4, 130.8, 130.4, 130.1, 129.8, 129.4, 129.1, 128.9, 128.5, 128.3, 128.0, 127.8, 127.4, 123.4, 52.9, 50.7, 23.4, 23.0; HRMS (EI) *m*/*e* calcd for $C_{21}H_{18}NOBr$ (M^+) 379.0572, found 379.0556.

General Procedure for the Palladium-Catalyzed Cyclization of Dibenzazepinones. A solution of $Pd(OAc)_2$ (3.4 mg, 0.015 mmol), $HPCy_3BF_4$ (5.6 mg, 0.015 mmol) and NaO*t*-Bu (44 mg, 0.45 mmol) in toluene (1 mL) was stirred at room temperature for 10 min and cooled in a dry ice−acetone bath. The amide as dibenzazepinone precursor (0.15 mmol) in toluene (0.5 mL) was added, and the resulting mixture was degassed by oil pump and refilled with argon. After being stirred at 100 °C for 10 min, the mixture was cooled to room temperature and purified by flash chromatography.

5-Phenyl-*N*-methyl-dibenzazepin-6-one (24). By the general procedure, **11** (57 mg, 0.15 mmol) gave **24** (44.5 mg, 99%) as a film after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 2920, 1662, 1366, 705; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73−7.70 (m, 0.7H), 7.66−7.59 (m, 1.3H), 7.53−7.46 (m, 2.4H), 7.46−7.28 (m, 3.6H), 7.21−7.18 (m, 0.4H), 7.10−7.04 (m, 0.6H), 6.99−6.87 (m, 3H), 6.71−6.66 (m, 1H), 5.35 (s, 0.6H), 4.65 (s, 0.4H), 3.40 (s, 1.9H), 3.36 (s, 1.1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 170.8, 142.2, 140.7, 139.3, 138.0, 136.7, 136.6, 136.0, 135.7, 134.6, 134.3, 131.8, 130.7, 130.3, 129.8, 129.4,128.9, 128.7, 128.6, 128.5, 128.2, 128.1, 127.9, 127.6, 127.3, 126.4, 126.2, 125.6, 125.0, 122.7, 122.4, 60.5, 51.5, 37.3, 36.7, 29.9; HRMS (EI) *m*/*e* calcd for $C_{21}H_{17}NO$ (M^+) 299.1310, found 299.1309.

5-Methoxy-*N*-methyl-dibenzazepin-6-one (26). By the general procedure, **13** (50 mg, 0.15 mmol) gave **26** (21 mg, 56%) as a film after flash chromatography (SiO_2, hexanes/EtOAc = 1/2): IR (cm^{-1}) 3066, 2926, 2831, 1680, 1440, 1212, 1092, 984, 767, 743; ^1H NMR (300 MHz, $CDCl_3$) δ 7.71 (d, J = 7.5 Hz, 1H), 7.63 (dd, J=7.8, 1.5 Hz, 1H), 7.58 (dd, J=7.5, 1.2 Hz, 1H), 7.54−7.32 (m, 5H), 5.03 (s, 0.05H), 4.54 (s, 0.95H), 3.56 (s, 2.86H), 3.42 (s, 0.14H), 3.35 (s, 2.86H), 3.03 (s, 0.14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 140.8, 137.3, 133.8, 133.5, 130.0, 129.5, 129.0, 128.9, 128.1, 127.9, 125.8, 122.9, 122.8, 78.7, 58.4, 36.5; HRMS (EI) *m*/*e* calcd for $C_{16}H_{15}NO_2$ (M^+) 253.1103, found 253.1100.

5,5-Dimethyl-*N*-methyl-dibenzazepin-6-one (27). By the general procedure, **14** (50 mg, 0.15 mmol) gave **27** (3 mg, 8%) as a film after flash chromatography (SiO_2, hexanes/EtOAc = 1/1): IR (cm^{-1}) 2926, 1651, 1598, 758, 735; ^1H NMR (300 MHz, $CDCl_3$) δ 7.58−7.52 (m, 3H), 7.45−7.38 (m, 3H), 7.29−7.24 (m, 2H), 3.37 (s, 3H), 1.79 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.4, 143.9, 141.9, 136.8, 135.4, 130.0, 129.9, 128.6, 128.5, 127.5, 125.3, 125.1, 122.0, 46.2, 38.5, 26.8, 23.2; HRMS (EI) *m*/*e* calcd for $C_{17}H_{17}NO$ (M^+) 251.1310, found 251.1305.

***N*-Benzyl-dibenzazepin-6-one (28).** By the general procedure, **17** (57 mg, 0.15 mmol) gave **28** (38 mg, 84%) as a film after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1})3063, 3029, 1669, 1440, 763, 738; 1H NMR (300 MHz, CDCl3) δ 7.52−7.48 (m, 2H), 7.43−7.37 (m, 3H), 7.37−7.20 (m, 3H), 7.14−7.08 (m, 3H), 6.92−6.87 (m, 2H), 5.19 (d, J = 15.6 Hz, 1H), 4.94 (d, J = 15.6 Hz, 1H), 3.68 (d, J = 12.3 Hz, 1H), 3.55 (d, J = 12.3 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 140.7, 137.6 137.5, 136.7, 135.5, 135.4, 135.1, 135.0, 134.9, 131.4, 131.3, 131.2, 130.1, 130.0, 129.6, 129.5, 129.2, 129.1, 129.0, 128.9, 128.2, 128.1, 128.0, 127.8, 127.5, 127.4, 127.0, 126.9, 126.8, 126.7, 126.0, 125.9, 124.9, 124.8, 124.7, 124.5, 124.4, 122.3, 122.2, 53.8, 51.9, 50.0, 44.1, 42.4, 42.3, 40.6; HRMS (EI) *m*/*e* calcd for $C_{21}H_{17}NO$ (M^+) 299.1310, found 299.1301.

5-Benzyloxy-*N*-methyl-dibenzazepin-6-one (29). By the general procedure, $Pd(OAc)_2$ (13.6 mg, 0.06 mmol), $HPCy_3BF_4$ (22.4 mg, 0.06 mmol), **15** (248 mg, 0.6 mmol) and NaO*t*-Bu (86.4 mg, 0.9 mmol) in toluene (6 mL) gave **29** (160 mg, 81%) as a film after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3063, 2926, 1680, 743; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, J = 7.8 Hz, 1H), 7.60−7.22 (m, 12H), 4.97 (d, J = 11.7 Hz, 1H), 4.75 (s, 1H), 4.59 (d, J = 11.7 Hz, 1H), 3.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 140.8, 138.0, 137.5, 133.8, 133.5, 130.0, 128.9, 128.9, 128.5, 128.0, 127.9, 127.9, 127.8, 125.8, 123.4, 122.8, 76.7, 72.2, 36.6; HRMS (EI) *m*/*e* calcd for $C_{22}H_{19}NO_2$ (M^+) 329.1416, found 329.1416.

5-Dibenzylamino-*N*-methyl-dibenzazepin-6-one (35). By the general procedure, **16** (75 mg, 0.15 mmol) gave **35** (58 mg, 93%) as a film after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3061, 3027, 2925, 2245, 1656, 732; ^1H NMR (300 MHz, $CDCl_3$) δ 7.58−7.24 (m, 7H), 7.17−7.08 (m, 7H), 6.73−6.67 (m, 4H), 4.67 (s, 1H), 3.42 (d, J = 14.1 Hz, 2H), 3.19 (s, 3H), 3.17 (d, J = 14.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 141.4, 137.1, 137.0, 136.4, 134.0, 130.4, 129.8, 129.7, 129.4, 129.0, 128.7, 128.0, 127.0, 124.6, 121.9, 77.9, 54.9, 37.5; HRMS (EI) *m*/*e* calcd for $C_{29}H_{26}N_2O$ (M^+) 418.2045, found 418.2042.

5-Benzyl-5-hydroxy-*N*-methyl-dibenzazepin-6-one (30). In the cyclization reaction of **15**, **30** (4% yield) was separated as a film after flash chromatography (SiO_2, hexanes/EtOAc = 3/1): IR (cm^{-1}) 3387, 2926, 1644, 1352, 763, 736; ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (m, 1H), 7.69 (dd, J = 7.5, 1.5 Hz, 1H), 7.60−7.41 (m, 4H), 7.41 (td, J = 8.1, 1.2 Hz, 2H), 7.17−7.12 (m, 3H), 6.91−6.86 (m, 2H), 5.27 (s, 1H), 3.39 (s, 3H), 2.73−2.60 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 143.0, 140.6, 136.6, 135.0, 134.0, 130.4, 130.0, 129.4, 128.9, 128.9, 128.4, 128.0, 126.8, 126.3, 125.6, 122.7, 78.2, 41.2, 38.6; HRMS (EI) *m*/*e* calcd for $C_{22}H_{19}NO_2$ (M^+) 329.1416, found 329.1409.

5-Benzyloxy-*N*-methyl-dihydrodibenzazepine (31). To a solution of **29** (160 mg, 0.486 mmol) in THF (6 mL) was added a solution of $BH_3 \cdot Me_2S$ in THF (2 M, 1 mL) at room temperature, and the mixturre was stirred for 2 h. NaOH solution in H_2O (1 M, 2 mL) was added, and the mixture was stirred for 10 min. THF was evaporated under reduced pressure, and the residue was extracted with Et_2O. The extracts were combined, dried over $MgSO_4$, and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **31** (150 mg, 98%) as an oil: IR (cm^{-1}) 3062, 2860, 1596, 1492, 1444, 1181, 755, 698; ^1H NMR (300 MHz, $CDCl_3$) δ 7.57−7.54 (m, 1H), 7.40−7.19 (m, 10H), 7.12 (td, J = 7.5, 1.8 Hz, 1H), 7.04 (dd, J = 7.8, 0.6 Hz, 1H), 4.55 (d, J = 11.4 Hz, 1H), 4.50 (m, 1H), 4.29 (d, J = 11.7 Hz, 1H), 3.62−3.47 (m, 2H), 2.71 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1, 139.2, 138.5, 138.4, 134.9, 129.0, 128.9, 128.7, 128.5, 127.8, 127.7, 127.5, 127.4, 123.6, 122.7, 118.3, 77.4, 71.8, 68.8, 41.8; HRMS (EI) *m*/*e* calcd for $C_{22}H_{21}NO$ (M^+) 315.1623, found 315.1609.

5-Hydroxy-*N*-methyl-dihydrodibenzazepine (32). To a solution of **31** (90 mg, 0.285 mmol) in 95% ethanol (3 mL) was added 10% palladium on carbon (30 mg, 0.0285 mmol), and the mixture was stirred at 80 °C under H_2 (1 atm) for 14 h. After being cooled to room temperature, the mixture was filtered through Celite. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **32** (54 mg, 85%) as an oil: IR (cm^{-1}) 3345, 2803, 1485, 1443, 1065, 756, 733;

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53−7.47 (m, 1H), 7.36−7.28 (m, 5H), 7.12 (td, *J* = 7.8, 1.5 Hz, 1H), 7.05 (dd, *J* = 8.1, 0.9 Hz, 1H), 4.71 (m, 1H), 3.51 (m, 1H), 3.38 (m, 1H), 2.71 (s, 3H), 2.18 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1, 141.3, 137.7, 134.7, 129.3, 129.0, 128.5, 127.8, 127.7, 122.9, 122.8, 118.4, 70.2, 70.0, 41.8; HRMS (EI) *m*/*e* calcd for $C_{15}H_{15}NO$ (M^+) 225.1154, found 225.1145.

***N*-Methyl-dibenzazepin-5-one** (**33**). To a solution of Dess−Martin reagent (122 mg, 0.289 mmol) in CH_2Cl_2 (3 mL) was added a solution of **32** (50 mg, 0.22 mmol) in CH_2Cl_2 (2 mL) at 0 °C, and the mixture was stirred for 30 min. NaOH solution in H_2O (1 M, 1 mL) was added, and the resulting mixture was stirred at room temperature for 5 min and extracted with EtOAc. The extracts were combined, dried over $MgSO_4$, and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **33** (46 mg, 93%) as a solid: IR (cm^{-1}) 3062, 2830, 1680, 1596, 1300, 757, 732; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86−7.82 (m, 1H), 7.64−7.58 (m, 1H), 7.52−7.36 (m, 4H), 7.23−7.16 (m 2H), 3.95 (s, 2H), 2.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.5, 150.2, 139.2, 137.4, 133.6, 133.0, 130.9, 130.3, 129.6, 128.6, 127.8, 124.3, 117.3, 72.2, 42.0; HRMS (EI) *m*/*e* calcd for $C_{15}H_{13}NO$ (M^+) 223.0997, found 223.0995.

5-Benzyl-5-hydroxy-*N*-methyl-dihydrodibenzazepine (**34**). The synthesis from **30**: to a solution of **30** (6 mg, 0.0183 mmol) in THF (0.5 mL) was added $BH_3 \cdot Me_2S$ (7.3 μL) at room temperature, and the mixture was stirred for 1.5 h. NaOH solution in H_2O (1 M, 1 drop) was added, and the mixture was stirred for 10 min. After removal of volatile components from the mixture, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **34** (5.7 mg, 99%) as an oil: IR (cm^{-1}) 3556, 2924, 1496, 1443, 761, 737; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, *J* = 4.8 Hz, 1H), 7.47 (dd, *J* = 4.5, 0.6 Hz, 1H), 7.42−7.39 (m, 2H), 7.37 (td, *J* = 5.1, 0.9 Hz, 1H), 7.31 (td, *J* = 4.8, 1.2 Hz, 1H), 7.16−7.11 (m, 4H), 7.08 (d, *J* = 4.8 Hz, 1H), 6.75−6.74 (m, 2H), 3.56 (d, *J* = 6.9 Hz, 1H), 3.37 (d, *J* = 6.9 Hz, 1H), 2.98 (d, *J* = 8.4 Hz, 1H), 2.78 (s, 3H), 2.69 (d, *J* = 8.1 Hz, 1H), 2.11 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.9, 143.0, 137.6, 136.4, 136.2, 130.7, 130.0, 129.2, 128.9, 128.3, 128.0, 127.5, 127.0, 124.6, 123.1, 118.0, 75.4, 74.2, 46.5, 42.1; HRMS (EI) *m*/*e* calcd for $C_{22}H_{22}NO$ (MH^+) 316.1701, found 316.1692.

The synthesis from **33**: to a solution of **33** (28 mg, 0.125 mmol) in THF (2 mL) was added a solution of benzylmagnesium chloride (2 M in THF, 69 μL, 0.138 mmol) slowly at rt, the mixture was stirred for 15 min, and a drop of H_2O was added. After removal of volatile components from the mixture, the resulting crude product was purified by flash chromatography (SiO_2, hexanes/EtOAc = 3/1) to give **34** (23.6 mg, 60%) as an oil.

5-Amino-*N*-methyl-dibenzazepin-6-one (**1**). A solution of **35** (30 mg, 0.072 mmol) and 10% palladium on carbon (6.5 mg, 0.0061 mmol) in ethanol (95%, 6 mL) was stirred under H_2 (1 atm, balloon) at 90 °C for 12 h. After being cooled to rt, the mixture was filtered, and the filtrate was extracted with Et_2O. The extracts were combined, dried over $MgSO_4$, and filtered. After removal of volatile components from the filtrate, the resulting crude product was purified by flash chromatography (SiO_2, Et_2O/EtOH = 10/1) to give **1** (16.7 mg, 98%) as an oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65−7.30 (m, 8H), 4.36 (s, 1H), 3.35 (s, 3H), 2.25 (br, 2H).

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Supporting Information Available: General experimental procedures and copies of ^{1}H/^{13}C NMR spectra for all products. This material is available free of charge via the Internet at http://pubs.acs.org.