Note

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Synthesis of Dibenzo[*b,e*]azepin-11-ones by Intramolecular Palladium-Catalyzed Acylation of Aryliodides with Aldehydes

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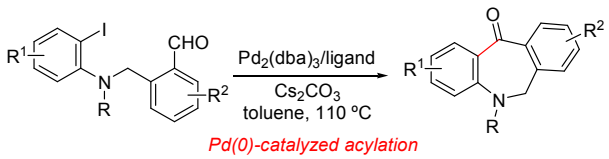


Abstract

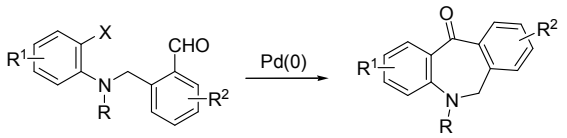
The paper describes an efficient methodology for the synthesis of diversely functionalized dihydrodibenzo[*b,e*]azepin-11-ones based on the Pd(0)-catalyzed intramolecular acylation of aryl iodides with aldehydes.

Palladium-catalyzed coupling reactions are well-established as reliable carbon-carbon bond-forming tools both in the research laboratory and in large-scale industrial production.[1] Among the variety of available cross-coupling processes, the palladium-catalyzed nucleophilic additions of aryl halides[2-8] and arylboronic acids[9-13] to carbon-heteroatom multiple bonds have been attracting increasing interest in recent years and are now emerging as powerful synthetic methodologies.

As part of our ongoing research on the synthesis of nitrogen heterocycles by means of palladium-catalyzed intramolecular coupling reactions of aryl halides and carbonyl compounds,[14] we have been studying the possibility of controlling the ambiphilic character of the σ-arylpalladium species involved in these reactions.[7,8,15,16] In this context, we have recently reported that when starting from (2-iodoanilino) aldehydes, both the enolate arylation and the acylation of the aryl halide can also be selectively promoted by Pd(0) with only a slight modification of the reaction conditions.[17] The latter acylation reaction seems to proceed through a mechanism involving a carbopalladation between the σ-arylpalladium(II) moiety and the carbonyl group, followed by a β-hydride elimination from the resulting Pd(II) alkoxide intermediate. Besides its mechanistic implications, this reaction has considerable synthetic interest because it could constitute an alternative to classical acylation methodologies such as the Friedel-Crafts reaction, whose intrinsic problems of regioselectivity often decrease its effectiveness in the synthesis of unsymmetrically substituted derivatives.[18] Moreover, it also provides an alternative to our previously reported palladium-catalyzed acylation of aryl halides by esters[7] and amides.[8] As these palladium-catalyzed reactions involve the nucleophilic attack of the σ-arylpalladium(II) species at the carbonyl group,

the use of the more electrophilic aldehydes as the acylating agents would result in a more efficient methodology.

To demonstrate the potential of the palladium-catalyzed acylation reaction with aldehydes,[3,19] we envisioned the synthesis of polycyclic compounds containing the dibenzo[*b,e*]azepine moiety (Scheme 1). The dibenzo[*b,e*]azepine system has attracted considerable attention due to its ubiquitous presence in the molecular structure of important bioactive compounds.[20] Therefore, the development of reliable methodologies for the construction of the dibenzo[*b,e*]azepine skeleton would be highly useful in the field of synthetic organic chemistry.[21] In particular, palladium-catalyzed annulation reactions have provided some attractive and valuable routes for the synthesis of dibenzo[*b,e*]azepine derivatives.[22]



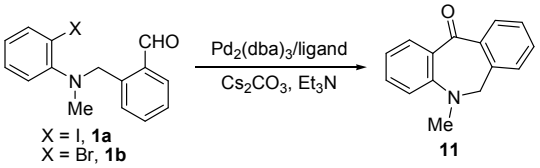
Scheme 1

We commenced our investigation by studying the acylation reactions of aldehydes **1a** and **1b** (Table 1). We were pleased to find that starting from iodoaniline **1a**, the acylation can be smoothly promoted by using 5 mol % of $Pd_2(dba)_3$, 10 mol % of the phosphine ligand, and Cs_2CO_3 as the base in toluene at high temperature. As also observed in our initial studies with (2-iodoanilino) aldehydes,[17] sterically hindered phosphines (i. e. dtpf, $^tBu_3P$ and (*o*-tolyl)$_3$P) proved to be highly efficient ligands for the acylation, and afforded dihydrodibenzo[*b,e*]azepin-11-one **11**[23] in 75% average yield (table 1, entries 1-3). The use of the same combination of catalyst and base in either acetonitrile or DMF was found to be less effective in promoting the acylation reaction (entries 4 and 5). Bromide **1b** was less efficient than iodide **1a** in the annulation

reaction, and longer reaction times were required to reach the total conversion of the starting material (entries 6-8).

Although the acylation can be carried out effectively in toluene under simple thermal heating, the long reaction times required for the full conversion of the starting material, especially when starting from bromide **1b**, prompted us to also explore the reaction under microwave irradiation (entries 9-13).

TABLE 1. Optimization of Acylation Reaction Conditions



X = I, **1a**
X = Br, **1b**

11

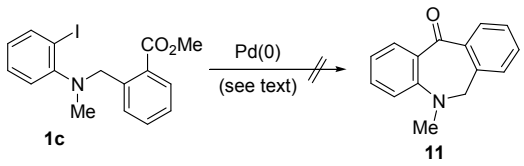
entry	aldehyde	ligand	solvent	time	^{1}H NMR ratio	yield (%)[a]
1	**1a**	dtpf	toluene[b]	24 h		**11** (77%)
2	**1a**	(^{t}Bu)$_3$P·HBF$_4$	toluene[b]	24 h		**11** (71%)
3	**1a**	(*o*-tolyl)$_3$P	toluene[b]	36 h		**11** (75%)
4	**1a**	dtpf	CH_3CN[b]	24 h		**11** (32%)
5	**1a**	dtpf	DMF[b]	24 h		**11** (34%)
6	**1b**	dtpf[c]	toluene[b]	36 h	**1b**:**11** (5:1)	
7	**1b**	(^{t}Bu)$_3$P·HBF$_4$[c]	toluene[b]	72 h	**1b**:**11** (1:1.1)	
8	**1b**	(*o*-tolyl)$_3$P[c]	toluene[b]	120 h		**11** (48%)
9	**1a**	dtpf	toluene[d]	60 min	**1a**:**11** (3:1)	
10	**1a**	dtpf	dioxane[d]	60 min	**1a**:**11** (3.5:1)	
11	**1a**	dtpf	DMF[d]	30 min		**11** (35%)
12	**1b**	dtpf	DMF[d]	30 min		**11** (37%)
13	**1b**	dtpf	CH_3CN[d]	30 min		**11** (34%)

[a] Yields refer to pure products isolated by flash chromatography. [b] The reactions were carried out using $Pd_2(dba)_3$ (0.05 equiv), ligand (0.1 equiv), Cs_2CO_3 (3 equiv) and Et_3N (6 equiv) in the indicated solvent at 110 ºC in a sealed tube. [c] 0.075 equiv of $Pd_2(dba)_3$ and 0.15 equiv of ligand were used. [d] The reactions were carried out using $Pd_2(dba)_3$ (0.05 equiv), ligand (0.1 equiv), Cs_2CO_3 (1 equiv) and Et_3N (3 equiv) in the indicated solvent at 120 ºC in a sealed vessel in a microwave reactor (fixed temperature, variable pressure).

Under microwave-mediated heating, the use of low absorbing solvents[24] such as toluene and dioxane resulted in poor conversions (entries 9-10). On the other hand, when using

DMF as the solvent, although the starting material was completely consumed in 30 min, dibenzoazepinone **11** was obtained in low yield (entries 11-12). Similar results were obtained when using K_3PO_4 or KOAc as the base instead of Cs_2CO_3, and (*o*-tolyl)$_3$P or ^{t}Bu$_3$P as the ligand (not shown in the table). Performing the reaction in acetonitrile also resulted in the complete conversion of the starting material, but **11** was again isolated only in modest yield (entry 13). It should be noted, however, that none of the experiments summarized in Table 1 yielded any observable products other than ketone **11** or the non-reacted starting material.

To compare the effectiveness of the palladium-catalyzed acylation with aldehydes with our previously reported procedure using esters as the acylating agents, we decided to prepare ester **1c** (Scheme 2). **1c** failed to undergo acylation reaction when submitted to the conditions optimized with esters [$Pd(PPh_3)_4$ and K_3PO_4 in toluene at 110 ºC][7] as well as to the new reaction conditions [$Pd_2(dba)_3$/ligand (dtpf, or (*o*-tolyl)$_3$P) and Cs_2CO_3 in toluene at 110 ºC]. In all the experiments only minor amounts of the hydrodehalogenation product[7] were observed together with the unreacted starting material.

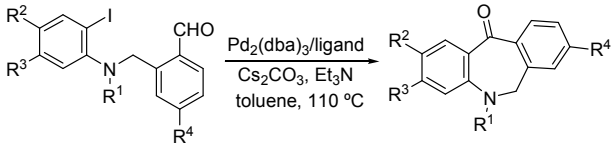


1c **11**

Scheme 2

As shown in Tables 2 and 3, a variety of diversely substituted substrates was investigated under the standard thermal heating conditions using toluene as the solvent.

TABLE 2. Synthesis of 5,6-dihydrodibenzo[*b,e*]azepin-11-ones[a]



R^1 = Bn, R^2 = Me, R^3 = R^4 = H, **2**	**12**
R^1 = Me, R^2 = MeO, R^3 = R^4 = H, **3**	**13**
R^1 = Me, R^2 = R^4 = H, R^3 = F, **4a**	**14a**
R^1 = Me, R^2 = R^4 = H, R^3 = Cl, **4b**	**14b**
R^1 = Me, R^2 = R^4 = H, R^3 = CH_2OH, **4c**	**14c**
R^1 = Me, R^2 = R^4 = H, R^3 =CHO, **4d**	**14d**
R^1 = Me, R^2 = R^4 = H, R^3 = CH_2OAc, **4e**	**14e**
R^1 = Me, R^2 = R^4 = H, R^3 = CH_2NMe_2, **4f**	**14f**
R^1 = Me, R^2 = R^3 = H, R^4 = F, **5**	**15**
R^1 = BOC, R^2 = R^3 = R^4 = H, **6**	

entry	aldehyde	ligand	time	yield (%)[b]
1	**2**	dtpf	24 h	**12** (91%)
2	**2**	$(^t\text{Bu})_3\text{P}\cdot\text{HBF}_4$	24 h	**12** (77%)[c]
3	**2**	$(o\text{-tolyl})_3\text{P}$	36 h	**12** (62%)
4	**3**	dtpf	36 h	**13** (60%)
5	**3**	$(^t\text{Bu})_3\text{P}\cdot\text{HBF}_4$	48 h	**13** (55%)
6	**3**	$(o\text{-tolyl})_3\text{P}$	48 h	**13** (51%)
7	**4a**	dtpf	48 h	**14a** (74%)
8	**4a**	$(^t\text{Bu})_3\text{P}\cdot\text{HBF}_4$	60 h	**14a** (71%)
9	**4b**	dtpf	36 h	**14b** (60%)[d]
10	**4b**	$(^t\text{Bu})_3\text{P}\cdot\text{HBF}_4$	72 h	**14b** (79%)
11	**4b**	$(o\text{-tolyl})_3\text{P}$	72 h	**14b** (65%)[d]
12	**4c**	dtpf	24 h	**14c** (71%)[e]
13	**4c**	$(^t\text{Bu})_3\text{P}\cdot\text{HBF}_4$	24 h	**14 c** (53%)[f]
14	**4d**	dtpf	36 h	**14d** (53%)
15	**4d**	$(^t\text{Bu})_3\text{P}\cdot\text{HBF}_4$	48 h	**14d** (46%)
16	**4e**	dtpf	24 h	**14e** (59%)
17	**4e**	$(^t\text{Bu})_3\text{P}\cdot\text{HBF}_4$	48 h	**14e** (67%)
18	**4f**	dtpf	24 h	**14f** (69%)
19	**5**	dtpf	36 h	**15** (87%)
20	**5**	$(^t\text{Bu})_3\text{P}\cdot\text{HBF}_4$	36 h	**15** (72%)
21	**5**	$(o\text{-tolyl})_3\text{P}$	36 h	**15** (55%)
22	**6**	dtpf	24 h	---
23	**6**	$(o\text{-tolyl})_3\text{P}$	24 h	---

[a] The reactions were carried out using $Pd_2(dba)_3$ (0.05 equiv), ligand (0.1 equiv), Cs_2CO_3 (3 equiv) and Et_3N (6 equiv) in toluene at 110 ºC in a sealed tube. [b] Yields refer to pure products isolated by flash chromatography. [c] Traces of **2** (≤ 5%) were also observed in the crude reaction mixture. [d] Traces of **5** (≤ 5%) were also observed in the crude reaction mixture. [e] **14d** (9%) was also isolated. [f] **14d** (15%) was also isolated.

In general, the introduction of substituents on the aniline ring (Table 1) had little effect on the success of the acylation reaction. Thus, the nucleophilicity of the aryl palladium intermediate does not appear to be significantly affected by the electronic properties of the substituent on the aromatic ring. Interestingly, the same behavior has also been observed in the closely related palladium-catalyzed acylation reaction with esters.[7] The functional group tolerance of the reaction is well illustrated by the fact that halides, ethers, esters, aldehydes, free hydroxyl and dimethylamino groups all were perfectly accommodated. I should be noted, however, that in the acylation reactions of **4c**, minor amounts of aldehyde **14d**, resulting from the palladium-catalyzed oxidation of alcohol **14c**,[17] were also isolated. The successful preparation of **14f** indicates that the Pd catalytic species are not deactivated by the presence of strong coordinating dialkylamino group.

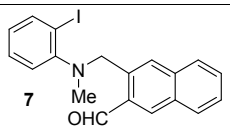
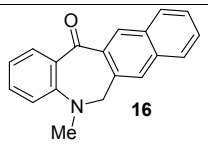
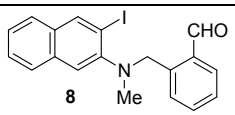
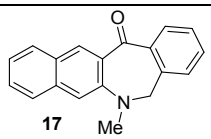
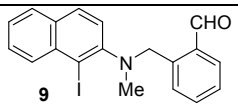
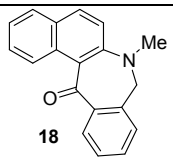
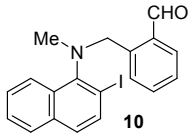
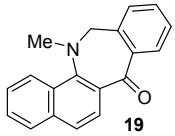
The effect of the substituent at the aniline nitrogen atom was also examined. While the methyl and benzyl groups were well tolerated in the acylation reaction, changing the substituent at the nitrogen from alkyl to the electron-withdrawing *tert*-butoxycarbonyl group resulted in the formation of complex reaction mixtures in which no acylation compound could be identified (entries 22 and 23).

The palladium-catalyzed acylation was also extended to the preparation of naphtho-fused derivatives, which are attractive for their potential antitumor activity.[20a] As can be seen in Table 3, both iodoanilines and iodonaphthylamines can be used for this purpose, although the acylation from the latter proceeded more slowly.

Regarding ligands, as shown in Tables 1-3, the three sterically hindered phosphines used in this work proved to be similarly effective in promoting the acylation reaction. On the whole, dtpf[25] seems to be the most versatile ligand, despite not always giving the

highest yield. On the other hand, the use of (*o*-tolyl)$_3$P as the ligand usually resulted in lower reaction rates, as reflected in the longer reaction times required for the complete consumption of the starting material.

TABLE 3. Synthesis of tetracyclic ketones[a]

entry	aldehyde	ligand	yield (%)[b]
	 **7**		 **16**
1	**7**	dtpf[c]	**16** (61%)
2	**7**	(^{t}Bu)$_3$P·HBF$_4$[c]	**16** (56%)
	 **8**		 **17**
3	**8**	dtpf[c]	**17** (58%)
4	**8**	(^{t}Bu)$_3$P·HBF$_4$	**17** (33%)
5	**8**	(*o*-tolyl)$_3$P	**17** (44%)
	 **9**		 **18**
6	**9**	dtpf	**18** (70%)
7	**9**	(^{t}Bu)$_3$P·HBF$_4$	**18** (87%)
8	**9**	(*o*-tolyl)$_3$P	**18** (90%)
	 **10**		 **19**
9	**10**	dtpf[c]	**19** (64%)
10	**10**	(^{t}Bu)$_3$P·HBF$_4$	**19** (63%)
11	**10**	(*o*-tolyl)$_3$P	**10** + **19** (1.5:1)[d]

[a] The reactions were carried out using $Pd_2(dba)_3$ (0.05 equiv), ligand (0.1 equiv), Cs_2CO_3 (3 equiv) and Et_3N (6 equiv) in toluene at 110 ºC for 72 h in a sealed tube. [b] Yields refer to pure products isolated by flash chromatography. [c] 24 h. [d] ^{1}H NMR ratio, yield not quantified.

In summary, we have demonstrated that the palladium-catalyzed intramolecular acylaton of aryl iodides with aldehydes constitutes an efficient methodology for the

synthesis of dihydrodibenzo[*b,e*]azepin-11-ones. The present reaction is a valuable synthetic alternative to our previously reported palladium-catalyzed acylation of aryl halides by esters and amides.

Experimental Section

General Methods. Chromatography refers to flash chromatography on silica gel. ^{1}H- and ^{13}C NMR spectra were recorded in $CDCl_3$ solution. Chemical shifts are reported in ppm downfield (δ) from Me_4Si.

2-[*N*-(2-Iodophenyl)-*N*-methylaminomethyl]benzaldehyde (1a). A mixture of 2-iodo-*N*-methylaniline[26] (0.25 g, 1.07 mmol), K_2CO_3 (0.23 g, 1.62 mmol), and 2-(bromomethyl)benzonitrile (0.21 g, 1.07 mmol) in acetonitrile (20 mL) was stirred at reflux for 120 h: every 24 h a new portion of 2-(bromomethyl)benzonitrile (0.1 g, 0.51 mmol) was added. The mixture was concentrated, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by chromatography (from hexanes to 97:3 hexanes-EtOAc) to give 2-[*N*-(2-iodophenyl)-*N*-methylaminomethyl]benzonitrile (315 mg, 85%).

To a cooled (0ºC) solution of 2-[*N*-(2-iodophenyl)-*N*-methylaminomethyl]benzonitrile (315 mg, 0.9 mmol) in CH_2Cl_2 (5 mL), a 1.0 M solution of DIBAL-H in hexanes (1.35 mL, 1.35 mmol) was added drop-wise under Argon. The resulting solution was stirred at room temperature for 3 h, cooled again, and poured into a mixture of ice and 6 N HCl. The mixture was vigorously stirred for 1 h and then extracted with CH_2Cl_2. The organic extracts were washed with 1 N $NaHCO_3$ aqueous solution, dried and concentrated. The residue was purified by chromatography (from hexanes to 97:3 hexanes-EtOAc) to give **1a** (140 mg, 44%) as a yellow oil. ^{1}H NMR (300 MHz) δ 2.67

(s, 3H), 4.57 (s, 2H), 6.81 (ddd, J = 7.8, 7.2, 1.5 Hz, 1H), 7.18 (dd, J = 8.1, 1.5 Hz, 1H), 7.32 (ddd, J = 7.8, 7.2, 1.5 Hz, 1H), 7.43 (t, J = 7.2 Hz, 1H), 7.58 (td, J = 7.5, 1.5 Hz, 1H), 7.77 (d, J = 7.5 Hz, 1H), 7.84-7.90 (m, 2H), 10.30 (s, 1H). ^{13}C NMR (75.4 MHz) δ 42.8, 57.2, 98.5, 122.4, 125.8, 127.5, 129.0, 130.4, 131.5, 133.5, 134.3, 140.1, 140.6, 153.7, 192.6. IR (NaCl) ν 1693 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{15}INO$: 352.0193 $[M+H]^+$; found: 352.0191.

2-[*N*-(2-Bromophenyl)-*N*-methylaminomethyl]benzaldehyde (1b). A mixture of 2-bromoaniline (0.5 g, 2.9 mmol), K_2CO_3 (0.6 g, 4.35 mmol), and 2-(bromomethyl)benzonitrile (0.57 g, 2.9 mmol) in acetonitrile (40 mL) was stirred at reflux for 24 h. The mixture was concentrated, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by chromatography (CH_2Cl_2) to give 2-[*N*-(2-bromophenyl)aminomethyl]benzonitrile (0.54 g, 65%).

A mixture of 2-[*N*-(2-bromophenyl)aminomethyl]benzonitrile (0.54 g, 1.88 mmol), K_2CO_3 (0.52 g, 3.76 mmol), and iodomethane (1.0 mL, 16.0 mmol) in acetonitrile (5 mL) was stirred at 80°C in a sealed tube for 2 days. The mixture was concentrated, and the residue was partitioned between water and CH_2Cl_2. The organic layer was dried and concentrated. The residue was purified by chromatography (from hexanes to 95:5 hexanes-EtOAc) to give 2-[*N*-(2-bromophenyl)-*N*-methylaminomethyl]benzonitrile (0.39 g, 69%).

1b (140 mg, 54%) was obtained starting from 2-[*N*-(2-bromophenyl)-*N*-methylaminomethyl]benzonitrile (0.26 g, 0.86 mmol) and operating as in the preparation of **1a**. Chromatography: from hexanes to 95:5 hexanes-EtOAc. Brown solid. ^{1}H NMR (400 MHz) δ 2.69 (s, 3H), 4.60 (s, 2H), 6.92 (ddd, J = 8.4, 7.6, 1.6 Hz, 1H),

7.16 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.26 (m, 1H), 7.43 (t, *J* = 8.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.58 (t, *J* = 7.6 Hz, 1H), 7.78 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 10.27 (s, 1H). ^{13}C NMR (100.5 MHz) δ 41.5, 57.0, 120.3, 122.3, 124.7, 127.4, 128.1, 129.9, 131.8, 133.6, 133.9, 134.3, 140.9, 150.9, 192.6. IR (NaCl) ν 1693 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{15}BrNO$: 304.0332 $[M+H]^+$; found: 304.0333.

Compounds **1c** and **2** were prepared according to the preparation of **1a**.

Methyl 2-[*N*-(2-iodophenyl)-*N*-methylaminomethyl]benzoate (1c). Chromatography: from hexanes to 95:5 hexanes-EtOAc. Pale yellow oil. ^{1}H NMR (300 MHz) δ 2.64 (s, 3H), 3.84 (s, 3H), 4.53 (s, 2H), 6.78 (ddd, *J* = 8.1, 7.5, 1.5 Hz, 1H), 7.15 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.25-7.34 (m, 2H), 7.51 (td, *J* = 7.5, 1.5 Hz, 1H), 7.83-7.91 (m, 3H). ^{13}C NMR (75.4 MHz) δ 42.5, 52.0, 58.4, 98.1, 122.2, 125.3, 126.6, 129.0, 129.7, 130.1, 130.4, 131.8, 140.0, 140.1, 154.4, 168.0. HRMS (ESI-TOF) cald for $C_{16}H_{17}INO_2$: 382.0304 $[M+H]^+$; found: 382.0306.

2-[*N*-Benzyl-*N*-(2-iodo-4-methylphenyl)aminomethyl]benzaldehyde (2). Chromatography: from hexanes to 9:1 hexanes-EtOAc. Colorless oil. ^{1}H NMR (300 MHz) δ 2.21 (s, 3H), 4.11 (s, 2H), 4.49 (s, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.98 (dd, *J* = 7.8, 2.1 Hz, 1H), 7.21-7.41 (m, 6H), 7.48 (td, *J* = 7.5, 1.5 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.67 (dd, *J* = 2.1, 0.6 Hz, 1H), 7.80 (dd, *J* = 7.8, 1.5 Hz, 1H), 10.13 (s, 1H). ^{13}C NMR (75.4 MHz) δ 20.2, 52.8, 59.0, 99.9, 124.2, 127.3, 127.4, 128.2, 129.1, 129.4, 130.8, 130.9, 133.3, 134.4, 136.2, 137.3, 140.3, 140.4, 148.2, 192.3. IR (NaCl) ν 1693 cm^{-1}. HRMS (ESI-TOF) cald for $C_{22}H_{21}INO$: 442.0662 $[M+H]^+$; found: 442.0655.

Compounds **3**, **4a-c**, **5** and **8-10** were prepared according to the preparation of **1b** starting from the corresponding *o*-iodoarylamines.[27-30]

2-[*N*-(2-Iodo-4-methoxyphenyl)-*N*-methylaminomethyl]benzaldehyde (3). Chromatography: CH_2Cl_2. Brown solid. ^{1}H NMR (300 MHz) δ 2.59 (s, 3H), 3.75 (s, 3H), 4.47 (s, 2H), 6.87 (dd, *J* = 8.7, 3.0 Hz, 1H), 7.10 (d, *J* = 8.7 Hz, 1H), 7.37 (d, *J* = 3.0 Hz, 1H), 7.41 (td, *J* = 7.5, 0.9 Hz, 1H), 7.54 (td, *J* = 7.5, 1.5 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.87 (dd, *J* = 7.5, 1.2 Hz, 1H), 10.34 (s, 1H). ^{13}C NMR (75.4 MHz) δ 43.4, 55.6, 57.5, 99.7, 114.8, 122.7, 124.6, 127.5, 130.6, 131.0, 133.4, 134.3, 140.7, 146.7, 158.7, 192.6. IR (NaCl) ν 1693 cm^{-1}. HRMS (ESI-TOF) cald for $C_{16}H_{17}INO_2$: 382.0298 $[M+H]^+$; found: 382.0290.

2-[*N*-(5-Fluoro-2-iodophenyl)-*N*-methylaminomethyl]benzaldehyde (4a). Chromatography: CH_2Cl_2. Yellow oil. ^{1}H NMR (300 MHz) δ 2.67 (s, 3H), 4.56 (s, 2H), 6.59 (ddd, *J* = 8.7, 7.8, 3.0 Hz, 1H), 6.90 (dd, *J* = 10.5, 3.0 Hz, 1H), 7.45 (td, *J* = 7.5, 1.2 Hz, 1H), 7.59 (td, *J* = 7.5, 1.5 Hz, 1H), 7.77 (dd, *J* = 8.7, 6.3 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.87 (dd, *J* = 7.5, 1.5 Hz, 1H), 10.27 (s, 1H). ^{13}C NMR (75.4 MHz) δ 42.5, 57.2, 90.3 (d, *J* = 4.1 Hz), 109.9 (d, *J* = 23.0 Hz), 112.8 (d, *J* = 21.9 Hz), 127.6, 130.2, 132.2, 133.6, 134.2, 140.1, 140.6 (d, *J* = 9.2 Hz), 155.5 (d, *J* = 8.1 Hz), 163.6 (d, *J* = 248.0 Hz), 192.7. IR (NaCl) ν 1692 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{14}FINO$: 370.0099 $[M+H]^+$; found: 370.0110.

2-[*N*-(5-Cloro-2-iodophenyl)-*N*-methylaminomethyl]benzaldehyde (4b). Chromatography: from hexanes to 95:5 hexanes-EtOAc. Yellow oil. ^{1}H NMR (300 MHz) δ 2.66 (s, 3H), 4.55 (s, 2H), 6.81 (dd, *J* = 8.1, 2.4 Hz, 1H), 7.14 (d, *J* = 2.4 Hz, 1H), 7.47 (td, *J* = 7.8, 1.2 Hz, 1H), 7.59 (td, *J* = 7.8, 1.5 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.5 Hz, 1H), 10.27 (s, 1H). ^{13}C NMR (75.4 MHz) δ 42.5, 57.2, 95.0, 122.8, 125.7, 127.6, 130.2, 132.2, 133.6, 134.2, 134.9,

140.2, 140.7, 155.1, 192.6. IR (NaCl) ν 1699 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{14}ClINO$: 385.9803 $[M+H]^+$; found: 385.9797.

2-[*N*-(5-Hydroxymethyl-2-iodophenyl)-*N*-methylaminomethyl]benzaldehyde (4c). Chromatography: from CH_2Cl_2 to CH_2Cl_2-MeOH 1%. Colorless oil. ^1H NMR (400 MHz) δ 1.98 (broad s, 1H), 2.65 (s, 3H), 4.55 (s, 2H), 4.63 (s, 2H), 6.81 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.19 (d, *J* = 2.0 Hz, 1H), 7.43 (td, *J* = 7.6, 0.8 Hz, 1H), 7.58 (td, *J* = 7.6, 1.6 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.86 (dd, *J* = 7.6, 1.6 Hz, 1H), 10.25 (s, 1H). ^{13}C NMR (100.5 MHz) δ 42.6, 57.2, 64.6, 96.9, 120.9, 124.3, 127.6, 130.5, 131.5, 133.5, 134.3, 140.1, 140.6, 142.3, 153.9, 192.6. IR (NaCl) ν 1682, 3400 cm^{-1}. HRMS (ESI-TOF) cald for $C_{16}H_{17}INO_2$: 382.0298 $[M+H]^+$; found: 382.0298.

2-[*N*-(5-Formyl-2-iodophenyl)-*N*-methylaminomethyl]benzaldehyde (4d) was prepared from **4c** (Swern oxidation). Chromatography: CH_2Cl_2. Yellow oil. ^1H NMR (400 MHz) δ 2.72 (s, 3H), 4.63 (s, 2H), 7.28 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.46 (td, *J* = 7.6, 0.8 Hz, 1H), 7.58 (td, *J* = 7.6, 1.6 Hz, 1H), 7.65 (d, *J* = 2.0 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.88 (dd, *J* = 7.6, 1.6 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 9.95 (s, 1H), 10.29 (s, 1H). ^{13}C NMR (100.5 MHz) δ 42.5, 57.3, 106.7, 121.5, 126.8, 127.7, 130.3, 132.1, 133.6, 134.2, 137.2, 140.0, 141.2, 154.9, 191.3, 192.6. IR (NaCl) ν 1681, 1704 cm^{-1}. HRMS (ESI-TOF) cald for $C_{16}H_{15}INO_2$: 380.0142 $[M+H]^+$; found: 380.0135.

2-[*N*-(5-Acetoxymethyl-2-iodophenyl)-*N*-methylaminomethyl]benzaldehyde (4e) was prepared from **4c** (AcCl). Chromatography: CH_2Cl_2. Pale yellow oil. ^1H NMR (400 MHz) δ 2.11 (s, 3H), 2.67 (s, 3H), 4.56 (s, 2H), 5.03 (s, 2H), 6.81 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.15 (d, *J* = 1.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.57 (td, *J* = 7.6, 1.6 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.82 (d, *J* = 8.0 Hz, 1H), 7.87 (dd, *J* = 7.6, 1.2 Hz, 1H), 10.28 (s, 1H). ^{13}C NMR (100.5 MHz) δ 20.9, 42.6, 57.2, 65.5, 97.8, 122.1, 125.5, 127.5,

130.4, 131.6, 133.5, 134.3, 137.2, 140.3, 140.4, 153.9, 170.6, 192.6. IR (NaCl) ν 1693, 1738 cm^{-1}. HRMS (ESI-TOF) cald for $C_{18}H_{19}INO_3$: 424.0404 $[M+H]^+$; found: 424.0394.

2-[*N*-(5-Dimethylaminomethyl-2-iodophenyl)-*N*-methylaminomethyl]benzaldehyde (4f) was prepared from **4c** (a. MsCl, b. Me_2NH). Chromatography: from CH_2Cl_2 to CH_2Cl_2-MeOH 8%. Brown oil. ^1H NMR (400 MHz) δ 2.29 (s, 6H), 2.68 (s, 3H), 3.46 (s, 2H), 4.58 (s, 2H), 6.77 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.22 (s, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.55 (td, *J* = 7.6, 1.6 Hz, 1H), 7.75 (d, *J* = 7.6 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.87 (dd, *J* = 7.6, 1.6 Hz, 1H), 10.32 (s, 1H). ^{13}C NMR (100.5 MHz) δ 42.8, 45.2, 57.1, 63.6, 96.5, 123.0, 126.5, 127.5, 130.5, 131.1, 133.4, 134.3, 139.8, 140.0, 140.7, 153.6, 192.5. IR (NaCl) ν 1693 cm^{-1}. HRMS (ESI-TOF) cald for $C_{18}H_{22}IN_2O$: 409.0771 $[M+H]^+$; found: 409.0774.

4-Fluoro-2-[*N*-(2-iodophenyl)-*N*-methylaminomethyl]benzaldehyde (5). Chromatography: CH_2Cl_2. Green oil. ^1H NMR (400 MHz) δ 2.69 (s, 3H), 4.57 (s, 2H), 6.82 (ddd, *J* = 8, 7.2, 1.6 Hz, 1H), 7.10 (td, *J* = 8, 2.8 Hz, 1H), 7.19 (dd, *J* = 8, 1.6 Hz, 1H), 7.32 (ddd, *J* = 8, 7.2, 1.6 Hz, 1H), 7.66 (dd, *J* = 10.4, 2.4 Hz, 1H), 7.87 (m, 2H), 10.18 (s, 1H). ^{13}C NMR (100.5 MHz) δ 42.7, 57.2 (d, *J* = 1.5 Hz), 98.4, 114.4 (d, *J* = 21.4 Hz), 117.4 (d, *J* = 22.9 Hz), 122.4, 126.0, 129.2, 130.6 (d, *J* = 2.3 Hz), 135.2 (d, *J* = 9.9 Hz), 140.2, 144.8 (d, *J* = 8.4 Hz), 153.6, 166.0 (d, *J* = 255.8 Hz), 191.1. IR (NaCl) ν 1694 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{14}FINO$: 370.0099 $[M+H]^+$; found: 370.0096.

2-[*N*-(*tert*-Butoxycarbonyl)-*N*-(2-iodophenyl)aminomethyl]benzaldehyde (6). A solution of *N*-(*tert*-butoxycarbonyl)-2-iodoaniline (0.4 g, 1.25 mmol) in THF (2 mL) was added at 0ºC under Argon to a suspension of NaH (60% in oil, 65 mg, 1.63 mmol)

in THF (8 mL). After 15 min at 25ºC, the mixture was cooled again to 0ºC. DMF (2 mL) and 2-(bromomethyl)benzaldehyde (325 mg, 1.63 mmol) were added and the mixture was stirred for 10 min at 0ºC and at 25ºC overnight. Saturated aqueous NH_4Cl was added and the mixture was extracted with EtOAc. The organic extracts were dried and concentrated. The residue was purified by chromatography (from hexanes to 8:2 hexanes-EtOAc) to give **6** (265 mg, 48%) as an orange oil. ^{1}H NMR (400 MHz, mixture of rotamers) δ 1.38 (s, 9H), 4.91 (d, *J* = 16 Hz, 1H), 5.48 (d, *J* = 16 Hz, 1H), 6.77-7.84 (m, 8H), 10.12 (s, 1H). ^{13}C NMR (100.5 MHz, major rotamer) δ 28.2, 48.6, 80.8, 100.3, 127.9, 128.6, 128.8, 129.8, 130.7, 130.9, 133.7, 134.3, 139.6, 143.5, 153.9, 192.1. HRMS (ESI-TOF) cald for $C_{19}H_{21}INO_3$: 438.0561 $[M+H]^+$; found: 438.0549.

3-[*N*-(2-Iodophenyl)-*N*-methylaminomethyl]-2-naphthaldehyde (7). A mixture of 2-iodo-*N*-methylaniline (150 g, 0.68 mmol), 3-(bromomethyl)-2-naphthaldehyde[31] (115 mg, 0.46 mmol) and 2,6-lutidine (80 μL ,0.68 mmol) was stirred at 100ºC for 6 h. The reaction mixture was partitioned between water and Et_2O. The organic layer was dried and concentrated. The residue was purified by chromatography (from hexanes to 95:5 hexanes-EtOAc) to give **7** (130 mg, 70%) as an orange oil. ^{1}H NMR (300 MHz) δ 2.72 (s, 3H), 4.70 (s, 2H), 6.80 (ddd, *J* = 7.8, 7.2, 1.5 Hz, 1H), 7.25 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.33 (ddd, *J* = 7.8, 7.2, 1.5 Hz, 1H), 7.54 (td, *J* = 7.2, 1.2 Hz, 1H), 7.62 (td, *J* = 7.2, 1.2 Hz, 1H), 7.86 (dd, *J* = 7.8, 1.5 Hz, 1H), 7.90 (d, *J* = 7.8 Hz, 1H), 7.97 (d, *J* = 7.8 Hz, 1H), 8.17 (s, 1H), 8.39 (s, 1H), 10.36 (s, 1H). ^{13}C NMR (75.4 MHz) δ 43.0, 57.8, 98.5, 122.4, 125.7, 126.7, 127.8, 129.1 (2 CH), 129.2, 129.4, 131.7, 132.7, 135.2, 135.3, 135.5, 140.1, 154.0, 192.9. IR (NaCl) ν 1692 cm^{-1}. HRMS (ESI-TOF) cald for $C_{19}H_{17}INO$: 402.0349 $[M+H]^+$; found: 402.0355.

2-[*N*-(3-Iodo-2-naphthyl)-*N*-methylaminomethyl]benzaldehyde (8).

Chromatography: from hexanes to 95:5 hexanes-EtOAc. Yellow solid. ^{1}H NMR (300 MHz) δ 2.73 (s, 3H), 4.66 (s, 2H), 7.35-7.48 (m, 3H), 7.52 (s, 1H), 7.57 (ddd, *J* = 7.8, 7.2, 1.5 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.87 (dd, *J* = 7.8, 1.2 Hz, 1H), 8.40 (s, 1H), 10.32 (s, 1H). ^{13}C NMR (75.4 MHz) δ 43.3, 57.5, 98.0, 119.0, 125.4, 126.4, 126.7, 127.0, 127.5, 130.4, 131.7, 132.1, 133.5, 133.6, 134.3, 139.7, 140.6, 150.5, 192.7. IR (NaCl) ν 1691 cm^{-1}. HRMS (ESI-TOF) cald for $C_{19}H_{17}INO$: 402.0349 $[M+H]^+$; found: 402.0342.

2-[*N*-(1-Iodo-2-naphthyl)-*N*-methylaminomethyl]benzaldehyde (9).

Chromatography: from hexanes to 1:1 hexanes-CH_2Cl_2. Yellow oil. ^{1}H NMR (400 MHz) δ 2.79 (s, 3H), 4.69 (s, 2H), 7.40-7.48 (m, 3H), 7.52-7.58 (m, 2H), 7.75 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.82 (d, *J* = 7.6 Hz, 1H), 7.89 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 10.40 (s, 1H). ^{13}C NMR (100.5 MHz) δ 43.6, 57.4, 103.5, 121.4, 125.7, 127.6, 127.8, 128.0, 129.8, 130.7, 131.5, 132.0, 132.9, 133.6, 134.3, 135.9, 140.7, 152.3, 192.8. IR (NaCl) ν 1692 cm^{-1}. HRMS (ESI-TOF) cald for $C_{19}H_{17}INO$: 402.0349 $[M+H]^+$; found: 402.0350.

2-[*N*-(2-Iodo-1-naphthyl)-*N*-methylaminomethyl]benzaldehyde (10).

Chromatography: from hexanes to 9:1 hexanes-EtOAc. Yellow oil. ^{1}H NMR (300 MHz) δ 3.02 (s, 3H), 4.91 (d, *J* = 13.5 Hz, 1H), 4.97 (d, *J* = 13.5 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 7.41-7.51 (m, 3H), 7.54 (td, *J* = 7.5, 1.5 Hz, 1H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.82 (m, 1H), 7.85 (d, *J* = 9 Hz, 1H), 7.87 (m, 1H), 8.05 (m, 1H), 20.21 (s, 1H). ^{13}C NMR (100.5 MHz) δ 40.6, 56.2, 97.3, 124.0, 126.2, 126.4, 127.5, 127.6, 128.5, 130.8, 131.2, 133.4, 133.6, 134.3, 134.6, 136.5, 141.6, 149.5, 192.1. IR (NaCl) ν 1691 cm^{-1}. HRMS (ESI-TOF) cald for $C_{19}H_{17}INO$: 402.0349 $[M+H]^+$; found: 402.0340.

Representative Procedure for the Pd(0)-Catalyzed Acylation (Table 1, Entry 1). A mixture of aldehyde **1a** (70 mg, 0.2 mmol), Cs_2CO_3 (195 mg, 0.6 mmol), Et_3N (0.17 mL, 1.2 mmol), $Pd_2(dba)_3$ (9 mg, 0.01 mmol), and dtpf (9.5 mg, 0.02 mmol) in toluene (8 mL) was stirred at 110°C in a sealed tube for 24 h. The reaction mixture was partitioned between water and Et_2O. The organic extracts were washed with brine, dried, and concentrated. The residue was purified by chromatography (from hexanes to hexanes-EtOAc 2.5%) to give **11** (34 mg, 77%).

6-Methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (11). Yellow solid: mp 109-110 ºC (recrystallized from Et_2O). ^{1}H NMR (300 MHz) δ 3.24 (s, 3H), 4.26 (s, 2H), 6.85 (m, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 7.24 (dd, *J* = 7.2, 1.5 Hz, 1H), 7.34-7.43 (m, 2H), 7.49 (td, *J* = 7.5, 1.5 Hz, 1H), 7.76 (dd, *J* = 7.5, 1.5 Hz, 1H), 8.30 (dd, *J* = 8.4, 1.5 Hz, 1H). ^{13}C NMR (75.4 MHz) δ 40.1, 58.4, 115.7, 117.5, 123.5, 125.6, 128.0, 128.9, 131.9, 132.3, 134.1, 136.9, 140.5, 150.9, 193.4. IR (NaCl) ν 1629 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{14}NO$: 224.1070 $[M+H]^+$; found: 224.1069.

6-Benzyl-9-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (12). Chromatography: from hexanes to hexanes-EtOAc 3%. Yellow solid: mp 85-90 ºC (recrystallized from Et_2O). Yield: 91% (48 mg). ^{1}H NMR (300 MHz) δ 2.30 (s, 3H), 4.30 (s, 2H), 4.70 (s, 2H), 6.80 (d, *J* = 8.4 Hz, 1H), 7.08 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.15 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.22 (d, *J* = 7.2 Hz, 2H), 7.30-7.43 (m, 4H), 7.46 (td, *J* = 7.5, 1.5 Hz, 1H), 7.78 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.12 (d, *J* = 1.2 Hz, 1H). ^{13}C NMR (75.4 MHz) δ 20.2, 55.4, 55.9, 117.2, 123.5, 125.9, 126.7, 127.3, 127.4, 128.0, 128.8, 129.0, 131.5, 131.8, 135.6, 136.7, 137.6, 140.7, 149.2, 193.6. IR (NaCl) ν 1633 cm^{-1}. HRMS (ESI-TOF) cald for $C_{22}H_{20}NO$: 314.1545 $[M+H]^+$; found: 314.1548.

9-Methoxy-6-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (13). Chromatography: from hexanes to hexanes-EtOAc 5%. Brown solid: mp 95-97 ºC (recrystallized from Et_2O). Yield: 60% (30 mg). ^{1}H NMR (300 MHz) δ 3.19 (s, 3H), 3.84 (s, 3H), 4.23 (s, 2H), 6.88 (d, *J* = 9.0 Hz, 1H), 7.08 (dd, *J* = 9.0, 3.3 Hz, 1H), 7.24 (d, *J* = 7.8 Hz, 1H), 7.38 (ddd, *J* = 7.8, 7.5, 1.2 Hz, 1H), 7.50 (dd, *J* = 7.8, 7.5, 1.5 Hz, 1H), 7.78 (d, *J* = 3.3 Hz, 1H), 7.79 (d, *J* = 7.8 Hz, 1H). ^{13}C NMR (75.4 MHz) δ 40.2, 55.6, 58.5, 112.1, 118.2, 123.7, 124.3, 125.8, 127.9, 129.1, 131.9, 137.0, 139.9, 146.5, 151.8, 192.7. IR (NaCl) ν 1630 cm^{-1}. HRMS (ESI-TOF) cald for $C_{16}H_{16}NO_2$: 254.1176 $[M+H]^+$; found: 254.1182.

8-Fluoro-6-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (14a). Chromatography: from hexanes to hexanes-EtOAc 10%. Yellow gum. Yield: 74% (36 mg). ^{1}H NMR (300 MHz) δ 3.23 (s, 3H), 4.28 (s, 2H), 6.51 (dd, *J* = 12.0, 2.4 Hz, 1H), 6.90 (ddd, *J* = 9.6, 7.5, 2.4 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.39 (td, *J* = 7.5, 1.2 Hz, 1H), 7.51 (td, *J* = 7.5, 1.5 Hz, 1H), 7.76 (dd, *J* = 7.5, 1.2 Hz, 1H), 8.32 (dd, *J* = 9.0, 7.5 Hz, 1H). ^{13}C NMR (75.4 MHz) δ 40.3, 58.5, 101.2 (d, *J* = 25.9 Hz), 106.0 (d, *J* = 23.0 Hz), 120.4, 125.7, 128.3, 129.0, 132.0, 135.4 (d, *J* = 11.5 Hz), 136.5, 140.3, 152.5 (d, *J* = 12.1 Hz), 166.7 (d, *J* = 252.5 Hz), 192.0. IR (NaCl) ν 1633 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{13}FNO$: 242.0976 $[M+H]^+$; found: 242.0981.

8-Cloro-6-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (14b). Chromatography: from hexanes to hexanes-EtOAc 8%. Brown solid: mp 86-88 ºC. Yield: 79% (35 mg). ^{1}H NMR (400 MHz) δ 3.24 (s, 3H), 4.26 (s, 2H), 6.82 (dd, *J* = 8.8, 2.0 Hz, 1H), 6.85 (s, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.39 (dd, *J* = 8.0, 7.2 Hz, 1H), 7.51 (ddd, *J* = 7.6, 7.2, 1.2 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 1H), 8.23 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (100.5 MHz) δ 40.2, 58.4, 115.1, 118.1, 122.0, 125.8, 128.3, 129.0, 132.2, 134.0, 136.6, 140.2, 140.3,

151.3, 192.3. IR (NaCl) ν 1630 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{13}ClNO$: 258.0680 $[M+H]^+$; found: 258.0678.

8-(Hydroxymethyl)-6-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (14c). Chromatography: from CH_2Cl_2 to CH_2Cl_2-MeOH 1%. Yellow oil. Yield: 71% (32 mg). ^1H NMR (400 MHz) δ 2.39 (broad s, 1H), 3.22 (s, 3H), 4.20 (s, 2H), 4.67 (s, 2H), 6.77 (dd, *J* = 8.0, 1.6 Hz, 1H), 6.89 (s, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.36 (td, *J* = 7.6, 1.2 Hz, 1H), 7.48 (td, *J* = 7.6, 1.2 Hz, 1H), 7.74 (dd, *J* = 7.2, 1.2 Hz, 1H), 8.24 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100.5 MHz) δ 40.1, 58.4, 64.7, 113.0, 115.8, 122.5, 125.7, 128.0, 128.8, 132.0, 132.7, 136.8, 140.3, 147.6, 151.1, 193.1. IR (NaCl) ν 1623, 3406 cm^{-1}. HRMS (ESI-TOF) cald for $C_{16}H_{16}NO_2$: 254.1176 $[M+H]^+$; found: 254.1166.

8-(Formyl)-6-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (14d). Chromatography: from hexanes to CH_2Cl_2. Yellow oil. Yield: 49% (22 mg). ^1H NMR (400 MHz) δ 3.35 (s, 3H), 4.32 (s, 2H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.32 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.40 (s, 1H), 7.41 (td, *J* = 7.6, 1.2 Hz, 1H), 7.55 (td, *J* = 7.6, 1.6 Hz, 1H), 7.75 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.43 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100.5 MHz) δ 40.3, 58.4, 117.2, 117.4, 125.9, 126.8, 128.4, 129.0, 132.5, 133.5, 136.7, 139.8, 140.2, 150.8, 192.4, 193.3. IR (NaCl) ν 1633, 1693 cm^{-1}. HRMS (ESI-TOF) cald for $C_{16}H_{14}NO_2$: 252.1019 $[M+H]^+$; found: 252.1016.

8-(Acetoxymethyl)-6-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (14e). Chromatography: from hexanes to CH_2Cl_2. Yellow oil. Yield: 69% (32 mg). ^1H NMR (400 MHz) δ 2.12 (s, 3H), 3.26 (s, 3H), 4.26 (s, 2H), 5.08 (s, 2H), 6.83 (d, *J* = 7.6 Hz, 1H), 6.85 (s, 1H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.38 (td, *J* = 7.6, 1.2 Hz, 1H), 7.50 (td, *J* = 7.6, 1.2 Hz, 1H), 7.75 (dd, *J* = 7.2, 1.2 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR (100.5 MHz) δ 20.9, 40.1, 58.4, 65.8, 114.8, 116.9, 123.1, 125.7, 128.1, 128.9, 132.0,

132.9, 136.8, 140.3, 142.1, 150.8, 170.7, 192.9. IR (NaCl) ν 1632, 1738 cm^{-1}. HRMS (ESI-TOF) cald for $C_{18}H_{18}NO_3$: 296.1281 $[M+H]^+$; found: 296.1276.

8-(Dimethylaminomethyl)-6-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (14f). Chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2-MeOH 3%). Yellow oil. Yield: 69% (28 mg). ^1H NMR (400 MHz) δ 2.27 (s, 6H), 3.27 (s, 3H), 3.44 (s, 2H), 4.26 (s, 2H), 6.81 (dd, *J* = 8.4, 1.6 Hz, 1H), 6.89 (s, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.38 (td, *J* = 7.6, 1.2 Hz, 1H), 7.49 (td, *J* = 7.6, 1.2 Hz, 1H), 7.76 (dd, *J* = 7.6, 1.2 Hz, 1H), 8.25 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (100.5 MHz) δ 40.2, 45.4, 58.4, 64.2, 115.8, 118.6, 122.7, 125.7, 128.0, 128.9, 131.9, 132.5, 136.9, 140.5, 145.1, 151.0, 193.0. IR (NaCl) ν 1633 cm^{-1}. HRMS (ESI-TOF) cald for $C_{18}H_{21}N_2O$: 281.1654 $[M+H]^+$; found: 281.1654.

4-Fluoro-6-methyl-5,6-dihydrodibenzo[*b,e*]azepin-11-one (15). Chromatography: from hexanes to hexanes-CH_2Cl_2 80%. Yellow solid: mp 82-84 ºC. Yield: 87% (34 mg). ^1H NMR (400 MHz) δ 3.24 (s, 3H), 4.23 (s, 2H), 6.88 (m, 2H), 6.95 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.07 (td, *J* = 8.8, 2.4 Hz, 1H), 7.41 (ddd, *J* = 8.8, 7.2, 1.2 Hz, 1H), 7.79 (dd, *J* = 8.8, 5.6 Hz, 1H), 8.31 (dd, *J* = 8.8, 1.2 Hz, 1H). ^{13}C NMR (100.5 MHz) δ 40.2, 58.0 (d, *J* = 1.5 Hz), 112.6 (d, *J* = 21.8 Hz), 115.1 (d, *J* = 21.0 Hz), 115.9, 117.9, 123.5, 131,7 (d, *J* = 9.2 Hz), 132.4, 134.2, 136.7 (d, *J* = 3.1 Hz), 139.3 (d, *J* = 7.0 Hz), 150.9, 165.0 (d, *J* = 252.8 Hz), 191.6. IR (NaCl) ν 1633 cm^{-1}. HRMS (ESI-TOF) cald for $C_{15}H_{13}FNO$: 242.0975 $[M+H]^+$; found: 242.0976.

5-Methyl-5,6-dihydrobenzo[*b*]naphtho[2,3-*e*]azepin-13-one (16). Chromatography: from hexanes to hexanes-EtOAc 8%. Yellow oil. Yield: 61% (21 mg). ^1H NMR (300 MHz) δ 3.25 (s, 3H), 4.43 (s, 2H), 6.84-6.91 (m, 2H), 7.40 (ddd, *J* = 8.7, 6.9, 1.5 Hz, 1H), 7.46-7.58 (m, 2H), 7.67 (s, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 8.29 (s, 1H), 8.35 (dd, *J* = 8.7, 1.5 Hz, 1H). ^{13}C NMR (75.4 MHz) δ 39.9, 58.8, 115.8,

117.6, 123.7, 123.9, 126.3, 127.3, 127.8, 129.2, 129.7, 132.3, 132.6, 134.1, 134.4, 134.9, 139.0, 151.2, 193.4. IR (NaCl) ν 1619, 1639 cm^{-1}. HRMS (ESI-TOF) cald for $C_{19}H_{16}NO$: 274.1226 $[M+H]^+$; found: 274.1223.

6-Methyl-6,7-dihydrobenzo[*e*]naphtho[2,3-*b*]azepin-12-one (17). Chromatography: from hexanes to 1:1 hexanes-CH_2Cl_2. Red oil. Yield: 58% (30 mg). ^1H NMR (300 MHz) δ 3.28 (s, 3H), 4.30 (s, 2H), 7.08 (s, 1H), 7.22 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.27 (dd, *J* = 7.5, 0.9 Hz, 1H), 7.36-7.45 (m, 2H), 7.51 (td, *J* = 7.5, 1.5 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.83 (d, *J* = 7.5 Hz, 1H), 7.84 (dd, *J* = 7.5, 3.3 Hz, 1H), 8.29 (s, 1H). ^{13}C NMR (75.4 MHz) δ 40.9, 58.5, 109.7, 123.0, 125.7, 125.9, 126.6, 126.8, 128.0, 128.8, 129.2, 129.8, 132.2, 134.5, 137.3, 138.2, 139.8, 147.4, 194.0. IR (NaCl) ν 1619, 1643 cm^{-1}. HRMS (ESI-TOF) cald for $C_{19}H_{16}NO$: 274.1226 $[M+H]^+$; found: 274.1224.

7-Methyl-7,8-dihydrobenzo[*e*]naphtho[2,1-*b*]azepin-13-one (18). Chromatography: from hexanes to 1:1 hexanes-EtOAc. Yellow oil. Yield: 90% (46 mg). ^1H NMR (400 MHz) δ 3.29 (s, 3H), 4.32 (s, 2H), 7.10 (d, *J* = 8.8 Hz, 1H), 7.24 (d, *J* = 7.2 Hz, 1H), 7.32 (ddd, *J* = 8.4, 7.2, 1.2 Hz, 1H), 7.37 (td, *J* = 7.6, 1.2 Hz, 1H), 7.46 (td, *J* = 7.6, 1.6 Hz, 1H), 7.58 (ddd, *J* = 8.8, 7.2, 1.2 Hz, 1H), 7.65 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.72 (d, *J* = 9.2 Hz, 1H), 7.82 (dd, *J* = 8.0, 1.2 Hz, 1H), 9.32 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (100.5 MHz) δ 39.7, 58.0, 114.4, 117.0, 123.4, 124.8, 126.9, 127.7, 128.1, 128.2, 128.6, 129.0, 130.8, 134.1, 135.1, 137.1, 142.1, 152.4, 191.9. IR (NaCl) ν 1603, 1635 cm^{-1}. HRMS (ESI-TOF) cald for $C_{19}H_{16}NO$: 274.1226 $[M+H]^+$; found: 274.1228.

13-Methyl-12,13-dihydrobenzo[*e*]naphtho[1,2-*b*]azepin-7-one (19). Chromatography: from hexanes to 1:1 hexanes-CH_2Cl_2. Yellow oil. Yield: 64% (30 mg). ^1H NMR (400 MHz) δ 2.93 (s, 3H), 4.60 (s, 2H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 1H), 7.49-7.59 (m, 4H), 7.80 (d, *J* = 7.6 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 1H),

8.36 (m, 2H). ^{13}C NMR (100.5 MHz) δ 41.4, 59.0, 123.5, 125.9, 126.7, 127.2, 127.5, 128.0, 128.2, 128.3, 128.5, 129.7, 130.5, 132.0, 137.5, 138.0, 139.9, 152.7, 192.4. IR (NaCl) ν 1615, 1633 cm^{-1}. HRMS (ESI-TOF) cald for $C_{19}H_{16}NO$: 274.1226 $[M+H]^+$; found: 274.1225.

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Supporting Information: ^{1}H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org/.

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