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A CONCISE SYNTHESIS OF 6,7-DIHYDRO-5*H*-DIBENZ[*c*,*e*]AZEPIN-5-ONE‡

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Abstract – A concise and efficient strategy for the synthesis of dibenz[*c*,*e*]azepin-5-ones has been developed. The approach relies on a key transformation involving Suzuki-Miyaura coupling of 2-bromobenzyl azides with 2-(methoxycarbonyl)phenylboronic acid, followed by either a stepwise sequence involving Staudinger reaction and lactam formation or one-pot hydrogenation/base-mediated intramolecular lactam formation.

Natural products and natural product based substances play pivotal roles in modern drug discovery.[1] Consequently, the unique, often complex structural motifs of many drugs are inspired by or derived from those found in natural products. For example, the potent tubulin assembly inhibitors *N*-acetylcolchinol (**2**) and its prodrug ZD 6126 (**3**) have structural features that are found in the highly toxic natural product colchicine (**1**) (Figure 1).[2] In ongoing investigations, our efforts have focused on the development of substances whose designs are based on scaffolds found in the novel dibenzo[*a*,*c*]cycloheptene-5-one (**4**) and dibenz[*c*,*e*]azepin-5-one (**5**) natural products. Dibenzazepine derivatives are structural platforms for an interesting array of pharmacologically active substances, including those that possess anxiolytic[3] and hypolipidemic[4] activities, as well as inhibitors of tubulin assembly[5] and protein kinase C.[6]

Recent studies in our laboratory have concentrated on routes for the preparation of novel polycyclic substances that are based on Suzuki-Miyaura coupling and aldol condensation strategies.[7] Recently, we uncovered an efficient catalytic system for the preparation of dibenzo[*a*,*c*]cyclohepten-5-ones **4**.[8] In an extension of this protocol, we envisioned that the process could be used for the synthesis of

‡ This paper is dedicated to Prof. Akira Suzuki on the occasion of his 80th birthday.

dibenz[*c*,*e*]azepin-5-ones **5** which bear an amide moiety in the central 7-membered ring. Although a number of approaches for the synthesis of dibenz[*c*,*e*]azepin-5-ones have been reported,[9] the need for concise and rapid routes to access these compounds still exists. Herein, we describe a new route for the synthesis of dibenzazepines that employs a Suzuki-Miyaura coupling process between 2-bromobenzyl azides and 2-(methoxycarbonyl)phenylboronic acid, followed by either a one-pot hydrogenation/base-mediated intramolecular lactam formation process or a stepwise sequence involving Staudinger reaction and lactam formation.

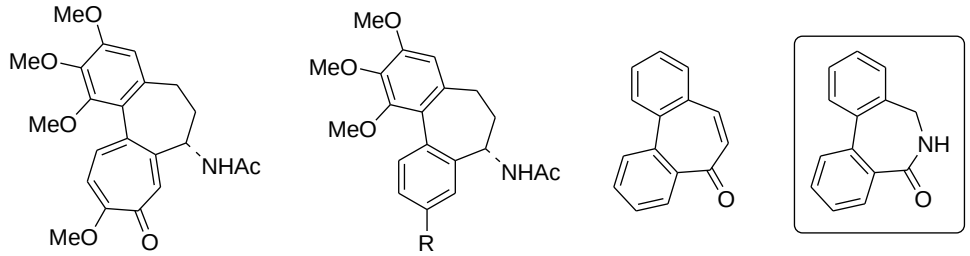
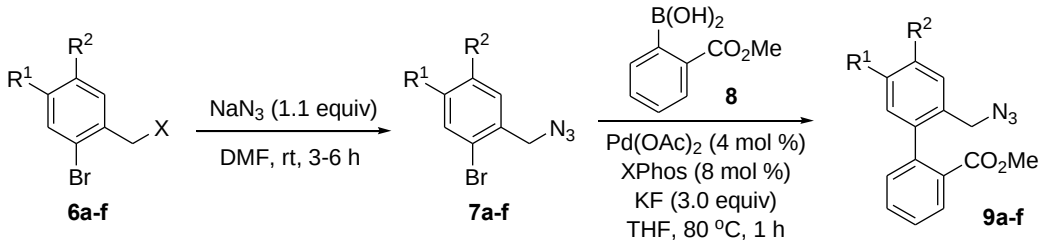


Figure 1. Tricyclic compounds possessing a central 7-membered ring such as colchicines (**1**), *N*-acetylcolchinol (**2**), ZD 6126 (**3**), dibenzo[*a*,*c*]cycloheptene-5-one (**4**) and dibenz[*c*,*e*]azepin-5-one (**5**) frameworks.

Table 1. Preparation of biaryl ester-azides **9a-f**



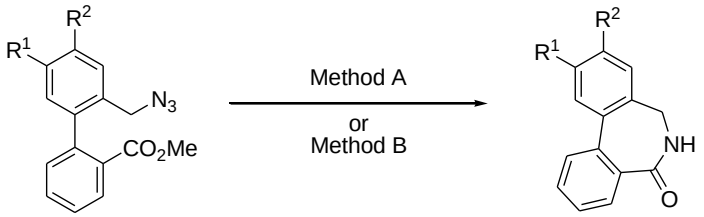
entry	R^1	R^2	X	**7** (yield, %)[a]	**9** (yield, %)[a]
1	H	H	Br	**7a** (94)	**9a** (99)
2	H	Cl	Br	**7b** (89)	**9b** (92)
3	H	F	Br	**7c** (86)	**9c** (94)
4	F	H	Br	**7d** (90)	**9d** (94)
5	CO_2Me	H	Br	**7e** (92)	**9e** (97)
6	OMe	OMe	Cl	**7f** (92)	**9f** (93)

[a]Isolated yield.

The 2-bromobenzyl azides **7a-f**, required for the synthetic pathway, were prepared by reactions of the corresponding benzyl halides **6a-f** with NaN_3 in DMF. These processes proceeded smoothly to furnish

7a-f in 86%-94% yields (Table 1). We next explored the Suzuki-Miyaura coupling reaction of **7a** with 2-(methoxycarbonyl)phenylboronic acid (**8**) in order to generate the biaryl ester-azide **9a**. A wide range of ligands (DavePhos, JohnPhos, SPhos, XPhos, Cyclohexyl JohnPhos, DPEPhos, XantPhos, and Cata*CX*ium PIntB), bases (Cs_2CO_3, K_3PO_4, Na_2CO_3, and KF), and solvents (dioxane, THF, toluene, DMF, and CH_3CN) were examined in order to develop optimum conditions of the coupling reaction (Table 1). This investigation led to the finding that the use of XPhos as ligand with KF as base in THF solvent provided an optimal yield for this process. It is noteworthy that in reactions with azides **7a-f**, both electron-withdrawing and –donating group substituted groups are well tolerated and the processes afford biaryl ester-azides **9a-f** in excellent yields.

Table 2. Synthesis of 6,7-dihydro-*5H*-dibenz[*c,e*]azepin-5-ones



9a-f **5a-f**

entry	R^1	R^2	product (**5**)	yield (%)[a]	
				Method A[b]	Method B[c]
1	H	H	**5a**	99	99
2	H	Cl	**5b**	90	30[d]
3	H	F	**5c**	92	94
4	F	H	**5d**	96	92
5	CO_2Me	H	**5e**	47[e]	70
6	OMe	OMe	**5f**	89	88

[a] Isolated yield. [b] Method A: i) PPh_3 (2 equiv), THF, rt, 10 h; ii) NaOMe (1.0 equiv), MeOH, rt, 6 h. [c] Method B: H_2 (1 atm), 10% Pd/C (20 wt %), NaOMe (1.0 equiv), MeOH, rt, 2 h. [d] Dechlorination occurred. [e] Although starting material **8e** was completely consumed (TLC monitoring), it was difficult to separate the by-product ($Ph_3P=O$) from the **4e** by column chromatography.

The availability of the biaryl ester-azides enabled us to investigate a method for the construction of dibenzazepines that employs reduction of the azide to produce the corresponding amine followed by lactam ring formation. Azides can be transformed to amines under mild conditions by using either hydrogenation processes or the Staudinger reaction. Indeed, treatment of ester-azide **9a** with PPh_3 under standard Staudinger conditions, followed by addition of NaOMe, led to the formation of the desired dibenzazepine **5a** in quantitative yield (Table 2, entry 1, Method A). The Staudinger based methodology

was applied to reaction of the other substituted biaryl ester-azides. In all but one case, reactions were found to take place efficiently to afford the desired products in excellent yields. The exception is reaction of **9e** that produces **5e** in a low yield owing to difficulties associated with chromatographic separation of the by-product Ph_3PO (Table 2, entry 5, Method A).

A one-pot procedure for preparation of dibenzazepines that relies on hydrogenation of biaryl ester-azides in MeOH solutions containing NaOMe was also explored (Table 2, Method B). By using this procedure, reactions of azides **9a** and **9c-f** resulted in efficient conversion to dibenzazepines **5a** and **5c-f**. Unfortunately, the chloroarene containing azide **9b** was found to undergo one-pot reaction to produce **5b** in very low yield (Table 2, entry 2, Method B).

In summary, the investigation described above has led to the development of a concise and efficient procedure to synthesize dibenz[*c*,*e*]azepin-5-ones, starting from 2-bromobenzyl halide. The key step in this approach involves Suzuki-Miyaura coupling of 2-bromobenzyl azides with 2-(methoxycarbonyl)phenylboronic acid, which is then followed by either stepwise Staudinger reaction and lactam formation or a one-pot hydrogenation/base-mediated lactam forming process. Further studies are in progress to probe applications of this protocol to the synthesis of pharmaceutically interesting dibenzazepines.

EXPERIMENTAL

Starting Materials. 2-Bromobenzyl bromide (**6a**) is commercially available. **6b**–**6e** were prepared by reaction of the corresponding 2-bromotoluenes with NBS in the presence of AIBN.[10] **6f** was synthesized from 2-bromo-4,5-dimethoxybenzyl alcohol following the literature method.[11]

General Procedure for preparation of 2-bromobezyl azides 7.[12] To a solution of benzyl bromide **6** (5.3 mmol) in DMF (5.5 mL) was added NaN_3 (377 mg, 5.8 mmol). The mixture was stirred at room temperature for 4–24 h, quenched with H_2O (200 mL), and extracted with CH_2Cl_2 (3 × 20 mL). The organic extracts were washed with brine (70 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by silica gel column chromatography to give benzyl azide **7**.

1-(Azidomethyl)-2-bromobenzene (7a).[13] rt 4 h, Yield 94%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (d, 1H, J = 8.0 Hz), 7.42–7.32 (m, 2H), 7.21 (td, 1H, J = 7.6, 1.5 Hz), 4.50 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.2, 133.29, 130.26, 128.02, 123.97, 104.99, 54.84; IR (neat) 3058, 2849, 2097, 1555, 1438 cm^{-1}; MS (EI) *m/z* 212 (M^+ + 2, 9), 210 (M^+, 7), 184 (66), 182 (62), 170 (52), 169 (40), 148 (19), 76 (88), 55 (100).

2-(Azidomethyl)-1-bromo-4-chlorobenzene (7b). rt 3 h, Yield 89%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, 1H, J = 8.5 Hz), 7.41 (d, 1H, J = 2.6 Hz), 7.19 (dd, 1H, J = 8.5, 2.6 Hz), 4.48 (s, 2H);

^{13}C NMR (75 MHz, $CDCl_3$) δ 137.0, 134.2, 134.1, 130.0, 129.9, 121.4, 54.4; IR (neat) 3075, 2853, 2100, 1459, 1393, 888, 811 cm^{-1}; MS (EI) *m/z* 247 (M^+ + 2, 23), 245 (M^+, 23), 189 (11), 155 (19), 149 (52), 111 (34), 83 (57), 71 (80), 57 (100).

2-(Azidomethyl)-1-bromo-4-fluorobenzene (7c). rt 3 h, Yield 86%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (dd, 1H, *J* = 8.8, 5.3 Hz), 7.17 (dd, 1H, *J* = 9.1, 3.0 Hz), 6.94 (td, 1H, *J* = 8.3, 3.0 Hz), 4.48 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1 (d, *J* = 246.5 Hz), 137.3 (d, *J* = 7.3 Hz), 134.1 (d, *J* = 8.0 Hz), 117.2 (d, *J* = 3.3 Hz), 116.9 (d, *J* = 4.5 Hz), 116.6 (d, *J* = 3.0 Hz), 54.2; IR (neat) 3080, 2097, 1584, 1437, 1271, 1236, 1044 cm^{-1}; MS (EI) *m/z* 231 (M^+ + 2, 83), 229 (M^+, 82), 201 (98), 199 (100), 186 (72), 120 (79), 94 (98), 74 (27).

1-(Azidomethyl)-2-bromo-4-fluorobenzene (7d). rt 3 h, Yield 90%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.34 (m, 2H), 7.07 (td, 1H, *J* = 8.2, 2.6 Hz), 4.47 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1 (d, *J* = 250.3 Hz), 131.09 (d, *J* = 3.4 Hz), 131.06 (d, *J* = 8.5 Hz), 123.9 (d, *J* = 9.7 Hz), 120.4 (d, *J* = 24.5 Hz), 114.9 (d, *J* = 20.9 Hz), 53.9; IR (neat) 3062, 2102, 1653, 1600, 1487, 1436, 1398, 1229, 1034, 861 cm^{-1}; MS (EI) *m/z* 231 (M^+ + 2, 30), 229 (M^+, 30), 201 (57), 188 (100), 148 (76), 121 (61), 110 (41), 94 (69), 85 (71), 71 (82), 56 (83).

Methyl 4-(azidomethyl)-3-bromobenzoate (7e). rt 24 h, Yield 92%, white solid; mp 64–67 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, 1H, *J* = 1.7 Hz), 8.01 (dd, 1H, *J* = 8.0, 1.7 Hz), 7.50 (d, 1H, *J* = 8.0 Hz), 4.55 (s, 2H), 3.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9, 137.4, 131.6, 129.1, 127.0, 126.4, 120.8, 51.9, 50.1; IR (neat) 3080, 2958, 2122, 1714, 1604, 1560, 1431, 1283, 1251, 1120 cm^{-1}; MS (EI) *m/z* 271 (M^+ + 2, 18), 269 (M^+, 18), 240 (25), 227 (51), 210 (100), 199 (28), 181 (27), 155 (31), 103 (57), 74 (40).

1-(Azidomethyl)-2-bromo-4,5-dimethoxybenzene (7f). 2-Bromo-4,5-dimethoxybenzyl chloride was used as a starting material. rt 5 h, Yield 92%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (s, 1H), 6.88 (s, 1H), 4.43 (s, 2H), 3.89 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6, 147.7, 125.9, 114.7, 113.1, 111.8, 55.3, 55.2, 53.5; IR (neat) 3005, 2935, 2093, 1601, 1504, 1438, 1384, 1258, 1219, 1163, 1029 cm^{-1}; MS (EI) *m/z* 273 (M^+ + 2, 21), 271 (M^+, 21), 231 (99), 199 (28), 184 (32), 120 (86), 105 (98), 92 (86), 79 (100), 62 (78).

General Procedure for preparation of azido-ester biaryls 9. To a vial (3 mL) were added benzyl azide **7** (0.47 mmol), boronic acid **8** (121 mg, 0.71 mmol), $Pd(OAc)_2$ (4.2 mg, 4.0 mol %), KF (82 mg, 1.4 mmol) , and X-Phos (17.9 mg, 8.0 mol %) sequentially. The mixture was suspended in THF (1.0 mL) and stirred at 80 °C for 1 h. After cooling to room temperature, the reaction mixture was purified by column chromatography (2% → 10% EtOAc/hexanes) to afford azido-ester biaryl **9**.

Methyl 6'-(azidomethyl)biphenyl-2-carboxylate (9a). Yield 99%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (dd, 1H, *J* = 7.8, 1.2 Hz), 7.57 (td, 1H, *J* = 7.5, 1.5 Hz), 7.47 (td, 1H, *J* = 7.6, 1.4 Hz),

7.42–7.33 (m, 3H), 7.28–7.26 (m, 1H), 7.16–7.14 (m, 1H), 4.14 (A of ABq, 1H, J = 13.7 Hz), 4.09 (B of ABq, 1H, J = 13.7 Hz), 3.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 141.7, 141.3, 133.1, 131.9, 131.3, 130.6, 130.5, 129.5, 128.8, 128.0, 127.9, 105.0, 52.9, 52.3; IR (neat) 2954, 2090, 1715, 1571, 1431, 1259, 1189 cm^{-1}; MS (EI) *m/z* 267 (M^+, 3), 180 (100), 164 (13), 152 (19), 105 (10).

Methyl 6'-(azidomethyl)-4'-chlorobiphenyl-2-carboxylate (9b). Yield 83%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.02 (dd, 1H, J = 7.8 Hz, 1.3 Hz), 7.58 (td, 1H, J = 7.5 Hz, 1.5 Hz), 7.49 (td, 1H, J = 7.2 Hz, 1.4 Hz), 7.44 (d, 1H, J = 2.2 Hz), 7.32 (dd, 1H, J = 8.2 Hz, 2.2 Hz), 7.22 (dd, 1H, J = 7.6 Hz, 1.3 Hz), 7.07 (d, 1H, J = 8.2 Hz), 4.12 (A of ABq, 1H, J = 14.1 Hz), 4.06 (B of ABq, 1H, J = 14.0 Hz), 3.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 138.9, 138.6, 133.9, 132.4, 130.8, 129.9, 129.4, 129.3, 128.9, 127.2, 127.1, 126.6, 51.1, 50.9; IR (neat) 3066, 2954, 2926, 2098, 1722, 1472, 1433, 1253, 764 cm^{-1}; MS (EI) *m/z* 301 (M^+, 0.1), 216 (24), 214 (100), 179 (20), 165 (22), 152 (42).

Methyl 6'-(azidomethyl)-4'-fluorobiphenyl-2-carboxylate (9c). Yield 94%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (dd, 1H, J = 7.7, 1.1 Hz), 7.57 (td, 1H, J = 7.5, 1.4 Hz), 7.48 (td, 1H, J = 7.6, 1.3 Hz), 7.26–7.04 (m, 4H), 4.13 (A of ABq, 1H, J = 14.1 Hz), 4.07 (B of ABq, 1H, J = 14.1 Hz), 3.64 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3, 162.1 (d, J = 245.2 Hz), 140.1, 137.0 (d, J = 3.4 Hz), 135.5 (d, J = 7.3 Hz), 131.8, 131.3, 130.7 (d, J = 7.9 Hz), 130.4, 130.5, 128.1, 115.1 (d, J = 22.3 Hz), 114.5 (d, J = 21.1 Hz), 52.3, 52.0; IR (neat) 3071, 2958, 2923, 2096, 1723, 1610, 1591, 1434, 1247 cm^{-1}; MS (EI) *m/z* 285 (M^+, 0.1), 256 (23), 224 (15), 198 (100), 183 (39), 170 (91), 151 (22).

Methyl 6'-(azidomethyl)-3'-fluorobiphenyl-2-carboxylate (9d). Yield 94%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (dd, 1H, J = 7.7, 1.1 Hz), 7.59 (td, 1H, J = 7.4, 1.4 Hz), 7.50 (td, 1H, J = 7.6, 1.2 Hz), 7.39 (dd, 1H, J = 8.4, 5.7 Hz), 7.26–7.24 (m, 1H), 7.09 (td, 1H, J = 8.4, 2.6 Hz), 6.89 (dd, 1H, J = 9.1, 2.6 Hz), 4.09 (A of ABq, 1H, J = 14.0 Hz), 4.04 (B of ABq, 1H, J = 14.0 Hz), 3.66 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.5, 160.3 (d, J = 246.3 Hz), 142.2 (d, J = 8.2 Hz), 138.4 (d, J = 1.6 Hz), 130.4, 129.4, 128.9, 128.8 (d, J = 8.6 Hz), 128.4, 127.5 (d, J = 3.3 Hz), 126.7, 114.8 (d, J = 21.9 Hz), 113.0, (d, J = 21.0 Hz), 50.53, 50.50; IR (neat) 3066, 2958, 2093, 1726, 1612, 1587, 1479, 1434, 1286, 1251 cm^{-1}; MS (EI) *m/z* 285 (M^+, 0.01), 256 (9), 198 (100), 183 (31), 169 (63), 151 (21), 85 (22), 59 (19).

Dimethyl 6'-(azidomethyl)biphenyl-2,3'-dicarboxylate (9e). Yield 97%, yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09–8.04 (m, 2H), 7.82 (d, 1H, J = 1.5 Hz), 7.60 (td, 1H, J = 7.5, 1.4 Hz), 7.53–7.48 (m, 2H), 7.26–7.23 (m, 1H), 4.20 (A of ABq, 1H, J = 14.2 Hz), 4.13 (B of ABq, 1H, J = 14.0 Hz), 3.90 (s, 3H), 3.63 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9, 166.6, 141.5, 140.3, 138.2, 132.1, 131.1, 130.6, 130.2, 129.8, 129.5, 128.9, 128.25, 128.21, 52.4, 52.1, 52.0; IR (neat) 3019, 2949, 2097, 1718, 1434, 1288, 1234 cm^{-1}; MS (EI) *m/z* 325 (M^+, 0.1), 296 (22), 269 (17), 238 (100), 211 (85), 179 (59), 165 (44), 151 (47), 139(22).

Methyl 6'-(azidomethyl)-3',4'-dimethoxybiphenyl-2-carboxylate (9f). Yield 93%, brown oil; ^{1}H NMR

(300 MHz, $CDCl_3$) δ 7.96 (dd, 1H, *J* = 7.7, 1.3 Hz), 7.56 (td, 1H, *J* = 7.5, 1.5 Hz), 7.46 (td, 1H, *J* = 7.6, 1.4 Hz), 7.29–7.26 (m, 1H), 6.92 (s, 1H), 6.66 (s, 1H), 4.10 (A of ABq, 1H, *J* = 13.9 Hz), 4.05 (A of ABq, 1H, *J* = 13.7 Hz), 3.96 (s, 3H), 3.84 (s, 3H), 3.65 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.6, 148.3, 148.1, 140.7, 133.8, 131.6, 131.5, 130.8, 130.1, 127.7, 125.2, 112.4, 111.6, 55.96, 55.95, 52.5, 52.1; IR (neat) 3080, 2932, 2092, 1715, 1607, 1516, 1440, 1249, 1237 cm^{-1}; MS (EI) *m/z* 327 (M^+, 5), 298 (10), 253 (9), 240 (100), 224 (14).

Method A: General Procedure for preparation of 6,7-dihydro-*5H*-dibenz[*c,e*]azepin-5-ones 5. To a solution of azido-ester biaryl **9** (0.18 mmol) in THF (18 mL) was added PPh_3 (94 mg, 0.36 mmol) and stirred at rt for 10 h. The solvent was evaporated in vacuo and dissolve in MeOH (18 mL). The resulting solution was treated with NaOMe (0.36 mL, 0.18 mmol, 0.5 M in MeOH) and stirred at rt for 6 h. The mixture was concentrated *in vacuo* and purified by column chromatography (50% EtOAc/hexanes) to afford dibenz[*c,e*]azepin-7-one **5**.

Method B: General Procedure for preparation of 6,7-dihydro-*5H*-dibenz[*c,e*]azepin-5-ones 5. To a solution of azido-ester biaryl **9** (0.37 mmol) in MeOH (37 mL) was added 10% Pd/C (20 mg, 20 wt%) and NaOMe (0.74 mL, 0.37 mmol, 0.5 M in MeOH). The suspension was stirred under H_2 (1 atm) for 2 h. The resulting mixture was filtered through a Celite pad while rinsing with EtOAc. The solution was concentrated *in vacuo* and purified by column chromatography (50% EtOAc/hexanes) to give dibenz[*c,e*]azepin-5-one **5**.

6,7-Dihydro-*5H*-dibenz[*c,e*]azepin-5-one (5a). Method A: 99%, Method B: 99%, white solid; mp 194–197 °C (lit.[9a] 190–191 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, 1H, *J* = 8.0 Hz), 7.69–7.56 (m, 3H), 7.53–7.48 (m, 1H), 7.45 (td, 1H, *J* = 7.6, 1.4 Hz), 7.37 (td, 1H, *J* = 7.4, 1.4 Hz), 7.29 (dd, 1H, *J* = 7.4, 1.2 Hz), 6.66 (brs, 1H), 4.25 (dd, 1H, *J* = 13.6, 6.1 Hz), 3.96 (dd, 1H, *J* = 14.7, 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.3, 139.2, 138.8, 137.7, 133.7, 131.2, 130.2, 129.4, 129.1, 128.5, 128.1, 127.9, 126.8, 44.9; IR (neat) 3282, 3167, 3022, 2918, 1642, 1599, 1452, 1404, 1346 cm^{-1}; MS (EI) *m/z* 209 (M^+, 39), 180 (100), 165 (6), 152 (30); HRMS (EI) calcd for $C_{14}H_{11}NO$ [M^+] 209.0841, found 209.0846.

9- Chloro-6,7-dihydro-*5H*-dibenz[*c,e*]azepin-5-one (5b). Method A: 90%, Method B: 30%, white solid; mp 195–197 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.01 (d, 1H, *J* = 7.4 Hz), 7.63–7.49 (m, 4H), 7.43 (dd, 1H, *J* = 8.3, 2.0 Hz), 7.30 (d, 1H, *J* = 1.8 Hz), 6.78 (brs, 1H), 4.21 (dd, 1H, *J* = 14.7, 5.9 Hz), 3.92 (dd, 1H, *J* = 14.8, 6.9 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 140.5, 137.3, 136.6, 134.1, 133.4, 131.4, 130.7, 130.3, 128.9, 128.6, 128.3, 126.8, 44.5; IR (neat) 3177, 3058, 2919, 1663, 1600, 1473, 1440, 1392, 774 cm^{-1}; MS (EI) *m/z* 243 (M^+, 100), 214 (88), 208 (28), 180 (30), 165 (12), 152 (64); HRMS (EI) calcd for $C_{14}H_{10}ClNO$ [M^+] 243.0451, found 243.0448.

9-Fluoro-6,7-dihydro-*5H*-dibenz[*c,e*]azepin-5-one (5c). Method A: 92%, Method B: 94%, white yellow

solid; mp 198–200 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, 1H, *J* = 7.8 Hz), 7.63–7.48 (m, 4H), 7.15 (td, 1H, *J* = 8.5 Hz, 2.6 Hz), 7.02 (dd, 1H, *J* = 8.4, 2.6 Hz), 6.85 (brs, 1H), 4.22 (dd, 1H, *J* = 14.7, 6.0 Hz), 3.99 (dd, 1H, *J* = 14.8, 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.9, 161.1 (d, *J* = 247.6 Hz), 139.7 (d, *J* = 7.2 Hz), 135.5, 133.6 (d, *J* = 3.3 Hz), 132.1, 130.1, 129.8 (d, *J* = 8.3 Hz), 128.9, 127.6, 126.7, 114.1 (d, *J* = 21.2 Hz), 112.5 (d, *J* = 21.7 Hz), 43.3; IR (neat) 3276, 2921, 1671, 1615, 1502, 1459, 1444, 1335, 1240, 1145, 970, 823 cm^{-1}; MS (EI) *m/z* 227 (M^+, 97), 198 (100), 169 (34), 98 (10); HRMS (EI) calcd for $C_{14}H_{10}FNO$ [M^+] 227.0746, found 227.0742.

10-Fluoro-6,7-dihydro-*5H*-dibenz[*c,e*]azepin-5-one (5d). Method A: 96%, Method B: 92%, white yellow solid; mp 198–200 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04–8.01 (m, 1H), 7.65–7.51 (m, 3H), 7.33–7.24 (m, 2H), 7.05 (td, 1H, *J* = 8.3, 2.6 Hz), 6.99 (brs, 1H), 4.19 (dd, 1H, *J* = 14.8, 6.0 Hz), 3.96 (dd, 1H, *J* = 14.8, 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.0, 162.6 (d, *J* = 244.6 Hz), 140.8 (d, *J* = 7.8 Hz), 136.7 (d, *J* = 1.9 Hz), 135.2 (d, *J* = 3.0 Hz), 133.7, 131.4, 130.3, 128.9, 128.5, 128.4 (d, *J* = 8.5 Hz), 116.2 (d, *J* = 22.5 Hz), 114.7 (d, *J* = 21.3 Hz), 44.1; IR (neat) 3288, 3171, 3058, 2921, 1657, 1561, 1392, 1264, 1177, 902, 890 cm^{-1}; MS (EI) *m/z* 227 (M^+, 100), 198 (97), 169 (36); HRMS (EI) calcd for $C_{14}H_{10}FNO$ [M^+] 227.0746, found 227.0749.

Methyl 7-oxo-6,7-dihydro-5*H*-dibenzo[*c,e*]azepine-2-carboxylate (5e). Method A: 47%, Method B: 70%, white solid; mp 264–266 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.06–8.02 (m, 2H), 7.64 (d, 2H, *J* = 4.0 Hz), 7.58–7.52 (m, 1H), 7.38 (d, 1H, *J* = 7.8 Hz), 7.01 (brs, 1H), 4.26 (dd, 1H, *J* = 14.8, 6.0 Hz), 4.03 (dd, 1H, *J* = 14.8, 6.9 Hz), 3.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 166.5, 143.3, 139.2, 136.7, 133.4, 131.5, 130.7, 130.6, 130.3, 129.3, 129.2, 128.6, 126.9, 52.3, 44.8; IR (neat) 3201, 3080, 1714, 1660, 1627, 1466, 1394, 1307, 1284, 1240, 1226 cm^{-1}; MS (EI) *m/z* 267 (M^+, 100), 238 (62), 208 (21), 180 (33), 165 (13), 150 (36); HRMS (EI) calcd for $C_{16}H_{13}NO_3$ [M^+] 267.0895, found 267.0898.

9,10-Dimethoxy-6,7-dihydro-*5H*-dibenz[*c,e*]azepin-5-one (5f). Method A: 89%, Method B: 88%, white solid; mp 256–259 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, 1H, *J* = 7.7 Hz), 7.61–7.53 (m, 2H), 7.47 (td, 1H, *J* = 7.3, 1.7 Hz), 7.10 (s, 1H), 6.88 (brs, 1H), 6.81 (s, 1H), 4.20 (dd, 1H, *J* = 14.6, 6.0 Hz), 3.95 (s, 3H), 3.94 (s, 3H), 3.87 (dd, 1H, *J* = 14.8, 7.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 149.0, 148.9, 137.8, 133.4, 131.9, 131.2, 131.1, 130.3, 128.6, 127.4, 112.6, 110.1, 56.2, 56.1, 44.7; IR (neat) 3161, 3010, 2923, 1649, 1599, 1512, 1465, 1435, 1390, 1272, 1141 cm^{-1}; MS (EI) *m/z* 269 (M^+, 100), 254 (32), 240 (44), 139 (34); HRMS (EI) calcd for $C_{16}H_{15}NO_3$ [M^+] 269.1052, found 269.1057.

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