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Synthesis of 5*H*-Dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones from Benzamides via Palladium-Catalyzed Double C−H Bond Activation

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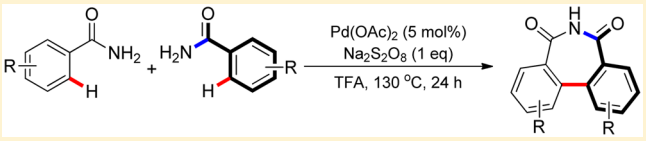
Supporting Information

ABSTRACT: A convenient and efficient method for the synthesis of 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones from simple and readily available benzamides is described in this work. The palladium-catalyzed homocoupling of benzamides occurred via ortho-selective double C−H bond activation using the simplest amide $CONH_2$ as a directing group. The subsequent intramolecular condensation reaction proceeded smoothly to produce 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones in satisfactory to excellent yields in one pot.



The transition-metal-catalyzed direct coupling between aromatic rings via double C−H bond activation has recently emerged as an extremely powerful tool for the synthesis of biaryl compounds.[1,2] An appropriate directing group is usually required to control regioselectivity in this type of C_{aryl}−C_{aryl} bond coupling reaction, which includes cross-coupling and homocoupling. Over the past few decades, various directing groups, such as heterocycles,[3] acyl groups,[4] carboxyl groups,[5] *N*-substituted amide groups,[6] and *N*-substituted acetamide groups,[7] have been successfully employed for this purpose. Among the myriad of directing groups utilized so far, *N*-substituted amide groups, including secondary and tertiary amide groups, have been frequently used not only for the C_{aryl}−C_{aryl} bond coupling reaction but also for other kinds of coupling reactions because of their unique reactivities in transition-metal-catalyzed C−H functionalizations.[8] In comparison with *N*-substituted amide groups, the free form, namely, primary amide group ($CONH_2$), has been rarely utilized as a directing group in the C−H functionalizations. Only two examples have been previously reported in the literature; such studies used primary amide as the directing group in the *ortho*-arylation of benzamides with aryl iodides[9] as well as in the benzylation of benzamides with benzyl bromides.[10] The primary amide-directing group is more easily functionalized after the desired operation. Therefore, the development of a new C−H functionalization method for the C_{aryl}−C_{aryl} bond coupling reaction, using primary amide as the directing group, is an important requirement. The direct homocoupling of benzamides can provide a new protocol with which to access 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones (Scheme 1).

5*H*-Dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones represent an interesting structural motif found frequently in biologically active compounds. As pharmaceuticals, 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-dione derivatives and their analogues exhibit remarkable properties, such as being actively antihyperlipidemic,[11] P-glycoprotein(P-gp)-mediated multidrug resistance (MDR) reversal agents,[12] hypolipidemic agents in rats,[13] histamine H3 receptor antagonists for the treatment of obesity,[14] potent inhibitors of the activity of human Tmolt4 T cell leukemia type IIIMP dehydrogenase (IMPDH),[15] and having antiepinephrine activity.[16] Therefore, the development of a convenient and efficient method for the synthesis of 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones has attracted considerable attention. The 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-dione skeleton is conventionally synthesized through a sequence of steps including aryl−aryl linkage through the homocoupling of 2-amino benzoic acids through azo intermediate, diphenicanhydride formation through intramolecular dehydrative condensation of diphenic acid, nucleophilic substitution of diphenicanhydride with ammonia, and intramolecular dehydrative cyclization (Scheme 1).[11]

Homocoupling products of benzamides have been observed as byproducts in small amounts in the palladium-catalyzed direct *ortho*-arylation of benzamides with aryl iodides.[9] This finding indicates that the diarylated benzamides might be obtained as major products after optimization of reaction conditions. On the basis of literature studies, the palladium-catalyzed direct homocoupling of benzamides is speculated to proceed through two different catalysis cycles (Scheme 2): one catalysis cycle involves Pd^0 and Pd^{II} species in the presence of a weak oxidant[17] and the other involves two sequential C−H activations at Pd^{II} and Pd^{IV}, respectively, in the presence of a strong oxidant.[18] Satisfactory yields of diarylated benzamides could not be obtained using a weak oxidant.[9] This observation encourages further examination of the palladium-catalyzed direct homocoupling of benzamides using a strong oxidant. The homocoupling of benzamides occurred, as expected, in the presence of a strong oxidant to produce 5*H*-dibenzo[*c*,*e*]-

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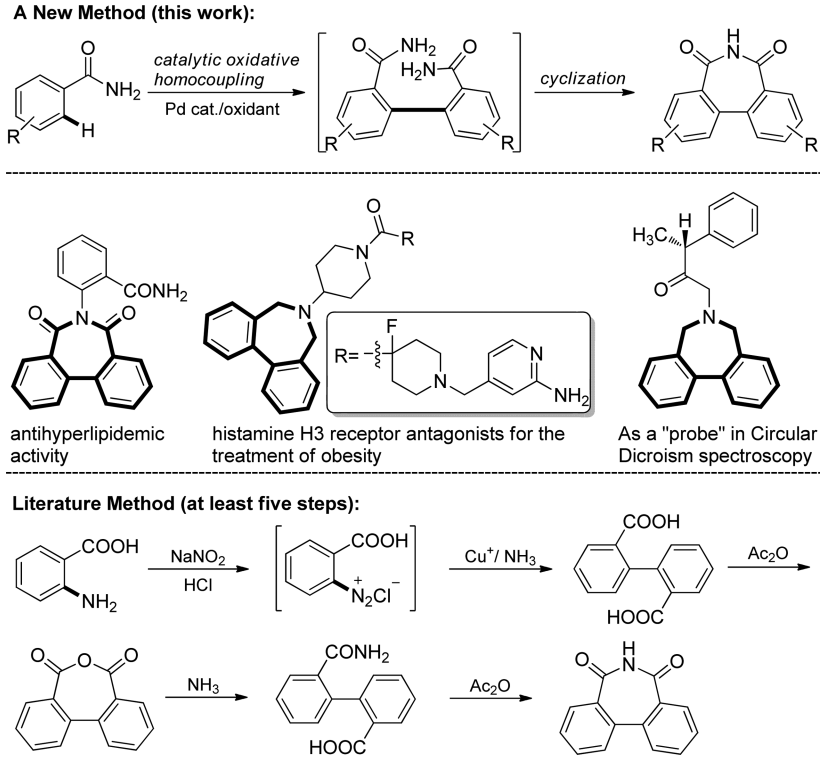
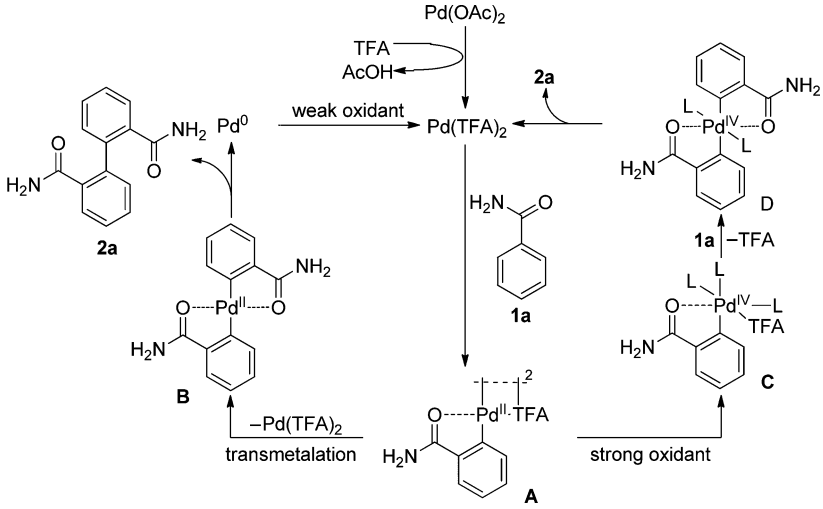
Scheme 1. Methods for the Synthesis of 5*H*-Dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones



Scheme 2. Proposed Reaction Mechanism for Palladium-Catalyzed Direct Homocoupling of Benzamides



azepine-5,7(6*H*)-diones in one pot. The results are reported in the current work.

The palladium-catalyzed homocoupling reaction of benzamide (**1a**) was selected as a model reaction to optimize the reaction conditions in the initial studies. The optimization included the selection of the most suitable precatalysts, oxidants, solvents, and reaction temperature as shown in Table 1. Several palladium precatalysts, including $Pd(OAc)_2$, $Pd(acac)_2$, $PdCl_2$, $Pd_2(dba)_3$, and $Pd(PPh_3)_2Cl_2$, were initially tested in the presence of a strong oxidant, potassium persulfate ($K_2S_2O_8$), in trifluoroacetic acid (TFA) at 130 °C (entries 1–5). The desired product, 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-dione (**3a**), was obtained in 43% yield using $Pd(OAc)_2$ as the precatalyst (entry 1), thus indicating that the homocoupling reaction of **1a** occurred as expected when a strong oxidant was utilized. The oxidants were subsequently screened using $Pd(OAc)_2$ as a precatalyst and TFA as a solvent. $Na_2S_2O_8$ proved to be the best among the tested oxidants, namely, $K_2S_2O_8$, ammonium persulfate [$(NH_4)_2S_2O_8$], 1,4-benzoquinone (BQ), 2-hydroperoxy-2-methylpropane (^{t}BuOOH), di-*tert*-butyl peroxide (DTBP), and sodium persulfate ($Na_2S_2O_8$) (entry 1 vs entries 6–10). The reaction time and temperature were subsequently screened using $Pd(OAc)_2$, $Na_2S_2O_8$, and TFA as the precatalyst, oxidant, and solvent, respectively. The **3a** yield decreased or did not change when the reaction time was shortened to 12 h or prolonged to 36 h (entry 10 vs entries 11 and 12); the **3a** yield was decreased to 52 or 60% when the model reaction was performed at 120 or 140 °C (entry 10 vs entries 13 and 14). TFA proved to be the best solvent after screening. Therefore, the subsequent double C–H activation

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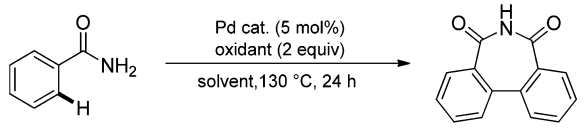
Table 1. Reaction Condition Screening[a]



1a 3a

entry	catalyst	oxidant	solvent	yield (%)
1	$Pd(OAc)_2$	$K_2S_2O_8$	TFA	43[b]
2	$Pd(acac)_2$	$K_2S_2O_8$	TFA	0[c]
3	$PdCl_2$	$K_2S_2O_8$	TFA	0[c]
4	$Pd_2(dba)_3$	$K_2S_2O_8$	TFA	0[c]
5	$Pd(PPh_3)_2Cl_2$	$K_2S_2O_8$	TFA	0[c]
6	$Pd(OAc)_2$	$(NH_4)_2S_2O_8$	TFA	trace[c]
7	$Pd(OAc)_2$	BQ	TFA	0[c]
8	$Pd(OAc)_2$	^{t}BuOOH	TFA	0[c]
9	$Pd(OAc)_2$	DTBP	TFA	0[c]
10	$Pd(OAc)_2$	$Na_2S_2O_8$	TFA	83
11	$Pd(OAc)_2$	$Na_2S_2O_8$	TFA	56[d]
12	$Pd(OAc)_2$	$Na_2S_2O_8$	TFA	83[e]
13	$Pd(OAc)_2$	$Na_2S_2O_8$	TFA	52[f]
14	$Pd(OAc)_2$	$Na_2S_2O_8$	TFA	60[g]
15	$Pd(OAc)_2$	$Na_2S_2O_8$	AcOH	trace[c]
16	$Pd(OAc)_2$	$Na_2S_2O_8$	dioxane	trace[c]

[a]Reaction conditions: **1a** (1.0 mmol, 121.1 mg), catalyst (5 mol %), and oxidant (1.0 mmol) in solvent (2.0 mL) at 130 °C for 24 h under air atmosphere. [b]^{1}H NMR yield; dibromomethane was used as an internal standard. [c]Starting material **1a** was recovered. [d]The reaction was performed for 12 h. [e]The reaction was performed for 36 h. [f]The reaction was performed at 120 °C. [g]The reaction was performed at 140 °C.

reactions of various benzamides were performed for 24 h in the presence of $Pd(OAc)_2$ as a precatalyst and $Na_2S_2O_8$ as an oxidant in TFA at 130 °C.

The scope and limitation of this type of double C−H activation reaction were determined under the optimal reaction conditions. The results are summarized in Table 2. The reaction of substrate **1b** bearing a methyl group on the para position of the benzene ring proceeded smoothly under the optimized conditions, like the simplest substrate **1a**, to offer an excellent yield (90%) of corresponding cyclic compound **3b** (entries 1 and 2). However, a methyl group linked on the meta position of benzamide substrate **1c** led to the formation of cyclic compound **3c** in a relatively low yield (entry 3, 73%). Furthermore, no reaction was observed when benzamide substrate **1d** bearing a methyl group on the ortho position of the benzene ring was examined (entry 4). The relatively low yield and nonreaction observed can be attributed to the steric hindrance caused by the *meta*- or *ortho*-methyl group linked on the benzene ring. Meanwhile, a moderate yield (64%) was observed when benzamide substrate **1e** bearing two methyl groups on the meta and para positions of the benzene ring was treated under the optimized conditions (entry 5). The reaction of benzamide substrate **1f** proceeded smoothly to produce desired cyclic compound **3f** in a good yield (87%) even though a bulky substituent (^{t}Bu) was linked on the para position of the benzene ring (entry 6). The steric effect of the methoxy group (MeO) on the reactivity of benzamide substrate was more evident than that of the methyl group (entry 7 vs entry 3). A low yield (46%) was observed in the reaction of *meta*-methoxy benzamide (**1g**). Low yields (40 and 37%, respectively) were observed in the reactions of benzamide substrates **1h** and **1i** containing an electron-withdrawing group (F) on the benzene ring (entries 8 and 9). The results indicated that the reactivity of benzamide substrate was lowered by a strong electron-withdrawing group, and the substituent position did not exert a significant influence on reactivity. The reaction of *para*-brominated benzamide **1j** or *para*-chlorinated benzamide **1l** resulted in excellent yields (91 and 93%, respectively) of the corresponding cyclic compounds **3j** or **3l** (entries 10 and 12, respectively). In addition, the desired product, **3k**, was obtained in a relatively low yield (43%) owing to the steric hindrance of the *meta*-bromine atom (entry 11). Br and Cl atoms linked to the benzene ring were notably maintained in the structures of products **3j**−**3l**, suggesting that further manipulation may produce more useful compounds. For the reaction scope to be explored further, the fused aromatic ring-containing substrates 2-naphthamide (**1m**) and 1-naphthamide (**1n**) were examined under the optimized reaction conditions. Desired product **3m** was obtained in 57% yield (entry 13). However, no reaction was observed when 1-naphthamide (**1n**) was examined (entry 14). This behavior was attributed to the steric hindrance caused in the substrate molecule. No reaction was observed again when 4-cyanobenzamide (**1o**) bearing a stronger electron-withdrawing group was treated under the optimal reaction conditions; starting material **1o** was recovered in 26% yield (entry 15).

Control experiments were conducted to gain insights into the mechanism of this type of double C−H bond activation reaction. The palladium-catalyzed double C−H activation reaction of benzylamide (**1a**) was conducted using $Na_2S_2O_8$ as the oxidant in TFA at 130 °C for 6 h. The formation of a small amount of intermediate **2a**, namely, the homocoupling product, was observed by HPLC-MS determination. The cyclic product, **3a**, was separated and produced in 28% yield, whereas no formation of *N*-benzoylbenzamide (**4**) was observed; starting material **1a** was recovered in 46% yield (Scheme 3, eq 1). Intermediates **2a** and **4** were prepared and treated under optimized reaction conditions to further confirm the reaction mechanism (Scheme 3, eqs 2 and 3). The target product, **3a**, was obtained in 95% yield through the intramolecular condensation of **2a**. No reaction was observed when **4** was treated under the same conditions. These results demonstrated that the desired cyclic products, 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones, were formed via homocoupling products of benzamides.

In summary, a convenient and efficient method has been developed for the synthesis of 5*H*-dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones through a palladium-catalyzed direct homocoupling reaction of benzamides and subsequent intramolecular condensation reaction in one pot. The simplest amide, $CONH_2$, is successfully used as a directing group for C_{aryl}−C_{aryl} bond coupling reaction in the presence of a strong oxidant for the first time. The wide availability of the starting materials and experimental simplicity could make the present method more useful in future organic synthesis applications.

EXPERIMENTAL SECTION

General Information. Solvents were purified by standard techniques without special instructions. ^{1}H and ^{13}C NMR spectra were recorded on a 400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C); DMSO-d_6 was used as the solvent. The chemical shifts are reported in ppm (δ), and the coupling constants J are given in Hz. The peak patterns are indicated as follows: s, singlet; d, doublet; m, multiplet. IR spectra were recorded on an FT-IR spectrometer. High-

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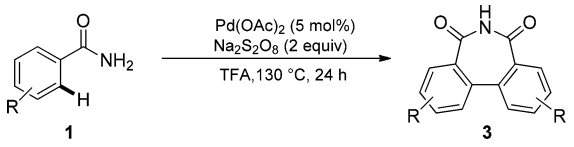
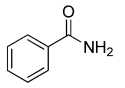
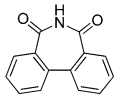
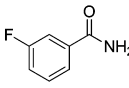
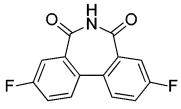
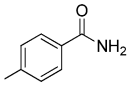
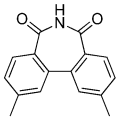
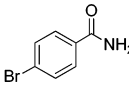
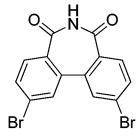
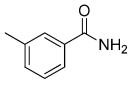
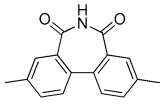
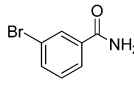
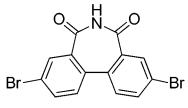
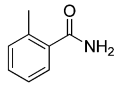
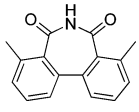
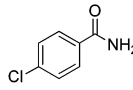
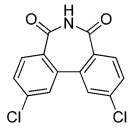
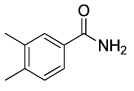
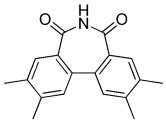
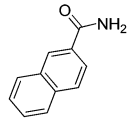
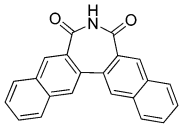
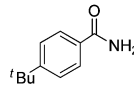
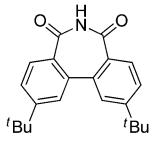
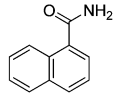
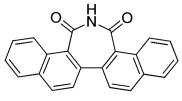
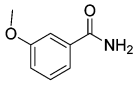
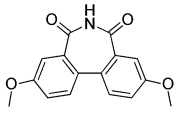
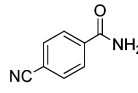
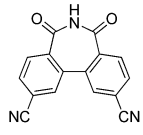
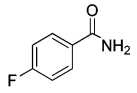
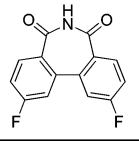
Table 2. Synthesis of 5*H*-Dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones from Various Benzamides[a]



entry	ketone **1**		product **3**		yield (%)	entry	ketone **1**		product **3**		yield (%)
1		**1a**		**3a**	83	9		**1i**		**3i**	37
2		**1b**		**3b**	90	10		**1j**		**3j**	91
3		**1c**		**3c**	73	11		**1k**		**3k**	43
4		**1d**		**3d**	0	12		**1l**		**3l**	93
5		**1e**		**3e**	64	13		**1m**		**3m**	57
6		**1f**		**3f**	87	14		**1n**		**3n**	0
7		**1g**		**3g**	46	15		**1o**		**3o**	0
8		**1h**		**3h**	40						

[a]Reaction conditions: benzamide (**1**, 1.0 mmol), $Pd(OAc)_2$ (11.2 mg, 5 mol %), and $Na_2S_2O_8$ (238.11 mg, 1.0 mmol) in TFA (2.0 mL) at 130 °C for 24 h under air atmosphere.

resolution mass spectra were recorded on either a Q-TOF mass spectrometer or a GC-TOF mass spectrometer. TLC was carried out on SiO_2, and the spots were located with UV light. Starting materials **1a**−**1o** are commercially available.

Procedure for the Preparation of 2,2′-Diphenyldicarboxamide. To diphenic acid (1.21 g, 5 mmol) was slowly added $SOCl_2$ (8.0 mL) at 0 °C. After the mixture was refluxed for 4 h, the excess $SOCl_2$ was removed under reduced pressure. Then, the crude product was treated with concentrated ammonia solution at 0 °C and stirred at room temperature for 2 h. The crude product was extracted with ethyl acetate (10 mL × 3), and the combined organic layers were washed with brine (10 mL × 2) and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified via silica gel chromatography (eluent: 5:1 petroleum ether/ethyl acetate) to afford desired product **2a** as a white solid (516 mg, 43% yield).

Representative Procedure for the Synthesis of 5*H*-Dibenzo[*c*,*e*]azepine-5,7(6*H*)-diones. A reaction flask was charged with a mixture of $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), $Na_2S_2O_8$ (238.1 mg, 1 mmol), benzamide (**1a**, 121.1 mg, 1 mmol), and trifluoroacetic acid (2 mL). The reaction mixture was stirred at 130 °C for 24 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the residue obtained was neutralized with Et_3N (1.0 mL). The crude product was dissolved in saturated $NaHCO_3$ solution followed by extraction with ether (10 mL × 3), and the combined organic layers were dried over anhydrous Na_2SO_4. The solvent was removed under vacuum. The crude product was purified by column chromatography (eluent: 5:1 petroleum ether/ethyl acetate) to afford **3a** as a white solid (92.5 mg, 83% yield).

*2,2′-Diphenyldicarboxamide (**2a**).*[19] White solid (516 mg, 43% yield); mp 208−210 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.97 (s, 2H), 7.55−7.46 (m, 2H), 7.46−7.37 (m, 4H), 7.31 (s, 2H), 7.11−7.01 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 171.6, 139.2, 137.1, 129.7, 129.4, 127.8, 127.5.

*5H-Dibenzo[c,e]azepine-5,7(6H)-dione (**3a**).*[20] White solid (92.5 mg, 83% yield); mp 184−186 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.71 (s, 1H), 7.93 (dd, J = 7.8, 1.2 Hz, 2H), 7.83 (d, J = 7.8 Hz, 2H),

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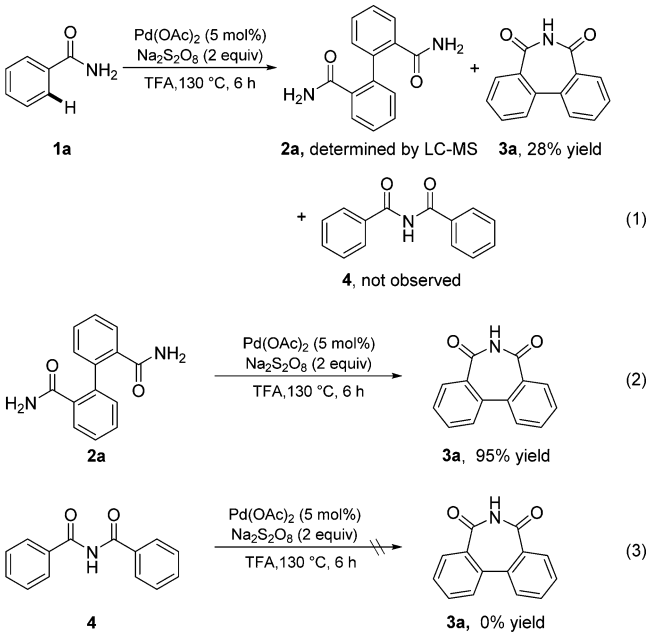
Scheme 3. Control Experiments



7.80–7.74 (m, 2H), 7.65–7.58 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.6, 135.4, 133.4, 133.3, 131.0, 130.5, 129.4; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{14}H_8NO_2$ 222.0561, found 222.0570.

2,10-Dimethyl-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3b**). Pale yellow solid (113.0 mg, 90% yield); mp 222–224 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.51 (s, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.65 (s, 2H), 7.40 (dd, J = 8.0, 0.8 Hz, 2H), 2.45 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.4, 143.6, 135.5, 131.2, 130.8, 130.6, 130.0, 21.5; IR (KBr) 3453.7, 1697.2, 1658.7, 1602.3, 1353.1, 1297.4, 1269.2, 1152.7, 657.0 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{16}H_{12}NO_2$ 250.0874, found 250.0870.

3,9-Dimethyl-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3c**). White solid (91.6 mg, 73% yield); mp 216–218 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.62 (s, 1H), 7.73 (d, J = 1.1 Hz, 2H), 7.70 (s, 1H), 7.68 (s, 1H), 7.56 (dd, J = 8.1, 1.4 Hz, 2H), 2.41 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.6, 138.8, 134.1, 132.8, 132.8, 131.6, 130.2, 20.9; IR (KBr) 3445.8, 1683.9, 1660.8, 1447.2, 1313.6, 823.0 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{16}H_{12}NO_2$ 250.0874, found 250.0869.

2,3,9,10-Tetramethyl-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3e**). White solid (89.28 mg, 64% yield); mp 233–235 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.44 (s, 1H), 7.70 (s, 2H), 7.62 (s, 2H), 2.37 (s, 6H), 2.32 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 167.9, 142.0, 137.1, 132.6, 131.3, 130.5, 129.9, 19.4, 18.8; IR (KBr) 3182.2, 3070.6, 1655.4, 1606.5, 1287.5 427.4 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{18}H_{16}NO_2$ 278.1187, found 278.1192.

2,10-Di-tert-butyl-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3f**). Dense yellow liquid (145.7 mg, 87%). ^1H NMR (400 MHz, DMSO-d_6) δ 11.53 (s, 1H), 7.89 (s, 1H), 7.87 (s, 1H), 7.71 (d, J = 1.7 Hz, 2H), 7.66 (dd, J = 8.3, 1.7 Hz, 2H), 1.37 (s, 18H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.3, 156.3, 135.7, 131.1, 130.7, 127.0, 126.5, 35.4, 31.1; IR (neat) 3336.4, 2961.9, 1678.9, 1158.6, 789.0, 700.0 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{22}H_{24}NO_2$ 334.1813, found 334.1814.

3,9-Dimethoxy-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3g**). White solid (65.1 mg, 46% yield); mp 217–219 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.67 (s, 1H), 7.73 (d, J = 8.7 Hz, 2H), 7.40 (d, J = 2.9 Hz, 2H), 7.33 (dd, J = 8.7, 2.9 Hz, 2H), 3.87 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.2, 159.2, 133.7, 131.9, 128.0, 120.1, 114.7, 56.0; IR (KBr) 3446.1, 3179.3, 2924.4, 1601.6. 1486.7, 1337.1, 1239.0, 1042.0, 818.8, 760.6, 624.3 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{16}H_{12}NO_4$ 282.0772, found 282.0780.

2,10-Difluoro-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3h**). White solid (51.8 mg, 40% yield); mp 246–248 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.76 (s, 1H), 7.99 (dd, J = 8.8, 6.1 Hz, 2H), 7.77 (dd, J = 10.5, 2.5 Hz, 2H), 7.52–7.44 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 166.8, 164.3 (d, J_{C-F} = 199.6 Hz), 136.5 (d, J_{C-F} = 7.2 Hz), 134.1 (d, J_{C-F} = 7.6 Hz), 129.4 (d, J_{C-F} = 2.2 Hz), 116.8 (d, J_{C-F} = 15.1 Hz), 116.7 (d, J_{C-F} = 13.3 Hz); IR (KBr) 3449.0, 2920.4, 1702.2, 1670.1, 1364.9, 1300.6, 1210.7, 860.2 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{14}H_6F_2NO_2$ 258.0372, found 258.0372.

3,9-Difluoro-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3i**). White solid (48.0 mg, 37% yield); mp 236–238 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.89 (dd, J = 8.6, 5.3 Hz, 2H), 7.74–7.58 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 166.5, 161.6 (d, J_{C-F} = 246.6 Hz), 134.5 (d, J_{C-F} = 7.5 Hz), 132.9 (d, J_{C-F} = 8.1 Hz), 130.7 (d, J_{C-F} = 3.4 Hz), 120.2 (d, J_{C-F} = 21.4 Hz), 116.8 (d, J_{C-F} = 24.0 Hz); IR (KBr) 3179.9, 3074.9, 1679.2, 1587.0, 1420.1, 1313.8, 830.7, 769.6 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{14}H_6F_2NO_2$ 258.0372, found 258.0365.

2,10-Dibromo-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3j**). White solid (173.3 mg, 91% yield); mp 288–290 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 8.11 (s, 2H), 7.84 (s, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 167.6, 135.8, 133.2, 133.0, 132.8, 132.5, 127.3; IR (KBr) 3434.4, 3335.5, 3252.6, 1692.7, 1584.7, 1382.0, 1347.8, 1302.0, 1147.2, 840.6 cm^{-1}; HRMS-ESI (m/z) [M − H]$^-$ calcd for $C_{14}H_6Br_2NO_2$ 379.8751, found 379.8750.

3,9-Dibromo-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3k**). White solid (82.0 mg, 43% yield); mp 306–308 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.96 (s, 1H), 8.02 (d, J = 2.2 Hz, 2H), 7.96 (dd, J = 8.5, 2.2 Hz, 2H), 7.79 (s, 1H), 7.77 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 166.9, 136.2, 134.8, 133.7, 133.3, 132.6, 122.9; IR (KBr) 3449.1, 3065.3, 2890.6, 1667.4, 1398.5, 1306.2, 822.1, 685.3 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{14}H_6Br_2NO_2$ 379.8751, found 379.8764.

2,10-Dichloro-5H-dibenzo[c,e]azepine-5,7(6H)-dione (**3l**). White solid (135.7 mg, 93% yield); mp 270–272 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.83 (s, 1H), 8.00 (d, J = 2.1 Hz, 2H), 7.94 (s, 1H), 7.92 (s, 1H), 7.71 (dd, J = 8.5, 2.1 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 167.4, 138.3, 135.9, 133.3, 132.1, 130.2, 129.7; IR (KBr) 3443.3, 3072.4, 1669.6, 1387.8, 1309.1, 871.5, 840.2 cm^{-1}; HRMS-APCI (m/z) [M − H]$^-$ calcd for $C_{14}H_7Cl_2NO_2$ 289.9781, found 289.9786.

6H-Dinaphtho[2,3-c:2′,3′-e]azepine-6,8(7H)-dione (**3m**).[21] White solid (92.0 mg, 57% yield); mp > 300 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 11.75 (s, 1H), 8.60 (s, 2H), 8.49 (s, 2H), 8.20–8.15 (m, 4H), 7.75–7.66 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 168.7, 135.1, 132.4, 132.1, 132.1, 131.5, 130.7, 129.4, 129.2, 128.6, 128.2.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b03087.

Copies of ^1H and ^{13}C NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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