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Cite this: *Org. Biomol. Chem.*, 2022, **20**, 5543

A new approach to 10-arylated 5*H*-dibenzo[*b*,*f*]azepines using *syn*-selective hydrohalogenation of ethynylaniline†

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Received 19th May 2022,
Accepted 29th June 2022

DOI: 10.1039/d2ob00950a

rsc.li/obc

A new synthetic method for 10-arylated dibenzo[*b*,*f*]azepines was developed. The pseudo-intramolecular hydrohalogenation of 2-(2′-bromophenyl)ethynylaniline, which proceeded in a *syn*-selective manner without forming any detectable over-addition product, was a crucial step. All attempts of subsequent arylation *via* Suzuki–Miyaura cross coupling and construction of a seven membered ring *via* Ullmann-type intramolecular coupling were unsuccessful because of dehydrohalogenation or other side reactions. This problem was overcome by the *N*-acetylation of the amino group, which facilitated the abovementioned coupling reactions to afford the desired 10-arylated dibenzoazepines.

Introduction

Although alkynes are good electrophiles for nucleophilic addition, they are an inappropriate substrate for electrophilic addition because the generation of carbocations with highly electronegative sp carbon atoms is difficult. Furthermore, issues such as overaddition to form dihaloalkanes[1] and the difficulty in handling gaseous hydrogen chloride must be addressed.[2] Consequently, several efficient transition metal-catalyzed systems have been developed recently[3–5] for realizing the *anti*-[4] and *syn*-selective[5] hydrochlorination of alkynes.

We previously demonstrated an effective hydrohalogenation method that used 2-ethynylaniline as a substrate and involved a pseudo-intramolecular process.[6] The salt formation between an amino group and an acidic reagent was a crucial step to increase the proximity between the reactants, and this facilitated hydrochlorination even in the absence of a metal catalyst or special reagent, without the formation of any detectable overaddition products (Fig. 1). This reaction furnished the corresponding haloalkenes in a *syn*-selective and regioselective manner, with an amino group in the product. These structural features prompted us to investigate the synthesis of 10-aryldibenzo[*b*,*f*]azepines (10Ar-DBA).

Similar to carbamazepine, the dibenzoazepine (DBA) framework is often found in pharmaceuticals and agrochemicals, and numerous methods have been developed for their synthesis.[7] Despite the abundant synthetic methods, there are only a few reports on the synthesis of 10Ar-DBAs. This framework was first synthesized by Bergmann *et al.* *via* ring expansion and rearrangement using 9-(α-hydroxybenzyl)acridine.[8] Wang *et al.* constructed an azepine ring and a fused cyclohexane ring in a single step through Pd-catalyzed cyclization using *o*-ethynylaniline and cyclohexanone in the presence of trimethylsilyl cyanide; the subsequent oxidation reaction

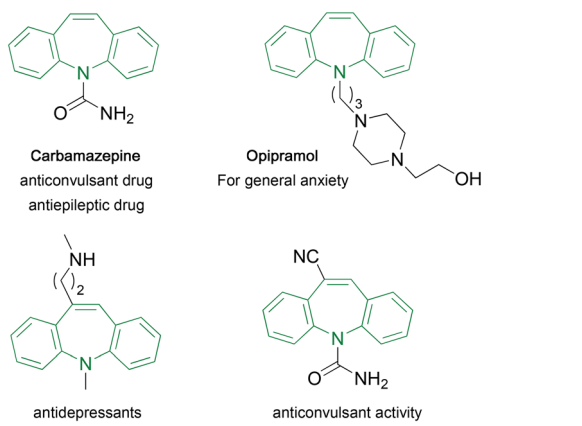

Fig. 1 Selected dibenzapine derivatives showing biological activity.

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†Electronic supplementary information (ESI) available: Copies of NMR spectra of compounds **2**, **5**, **9** and **10**, temperature-variable NMR spectra of **10a**, crystallographic data of **5**, **9a** and **10a**, and optimization of reaction conditions. CCDC 2150669–2150671. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d2ob00950a

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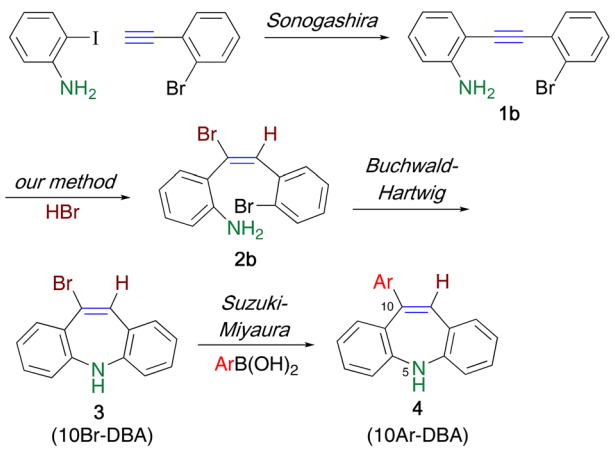
afforded the target 10Ar-DBA framework.[9] Recently, Dorta *et al.* used this framework as a planar chiral ligand by introducing phosphorous[10] or sulfur[11] atom on the ring nitrogen. They introduced a phenyl group at the 10-position through the Suzuki–Miyaura cross-coupling reaction using 10-bromo-5-(trifluoroacetyl)dibenzoazepine.[10] In 2019, Doucet *et al.* reported the Pd-catalyzed arylation at the 10-position; the bromo-substituted DBA was not necessary as the substrate for this reaction.[12] Although these methods are excellent for the construction of the DBA framework, the development of a facile synthetic method for 10Ar-DBAs is highly demanded. Herein, we report another synthetic method that involves our previously developed pseudo-intramolecular hydrohalogenation as a key step. The synthetic route (Scheme 1) consists of four steps: (1) preparation of an ethynylaniline by Sonogashira coupling, (2) pseudo-intramolecular hydrohalogenation, (3) construction of a dibenzazepine ring by Buchwald–Hartwig coupling, and (4) arylation at the 10-position by Suzuki–Miyaura coupling.

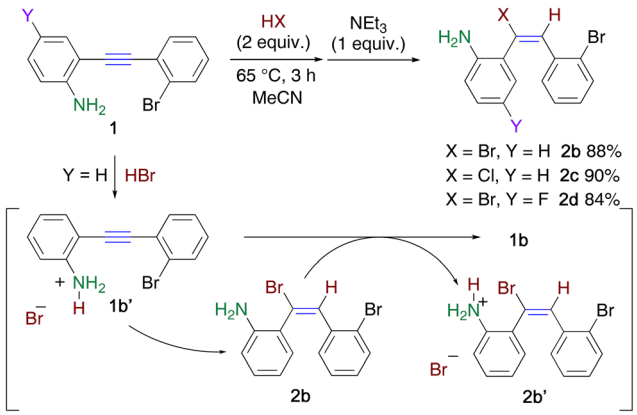
Results and discussion

2-Bromo-1-ethynylbenzene[13] was prepared in 86% yield by the Sonogashira cross-coupling[14] of 2-bromo-1-iodobenzene with (trimethylsilyl)ethyne, followed by desilylation upon treatment under basic conditions.[14] When the prepared ethynylbenzene was subjected to another Sonogashira coupling reaction with 2-iodoaniline, ethynylaniline **1b** [15] was furnished in 91% yield.

Ethynylaniline **1b** (Y = H) immediately precipitated as a yellow salt **1b′** in acetonitrile upon treatment with an equimolar amount of hydrobromic acid. When the suspension was heated at 65 °C for 3 h, the precipitate gradually disappeared. However, almost half of **1b** was recovered, along with the formation of hydrobromide **2b′**. This is because the less electronegative ethenyl group increased the basicity of the amino group in **2b**, which was converted to the deprotonated product **2b′** during the reaction (Scheme 2).[16] Hence, 2 equiv. of hydrobromic acid was necessary for the efficient hydrobromination of **1b**, and adduct **2b** was readily obtained in 88% yield upon



Scheme 1 Synthetic plan for 10Ar-DBA.

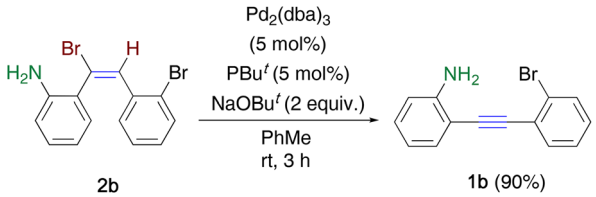


Scheme 2 Hydrohalogenation of ethynylaniline **1**.

the addition of triethylamine to the reaction mixture. Similarly, the hydrochlorination of **1b** using 2 equiv. of hydrochloric acid proceeded to afford **2c** in 90% yield. An electron-withdrawing fluoro group did not disturb the reaction, which leading to **2d** in 84% yield.

Next, the hydrobrominated product **2b** was subjected to the Buchwald–Hartwig coupling reaction according to a method reported in the literature;[17] however, a substantial amount of **2b** was recovered (Table S1†). Although **2b** was completely consumed upon heating at 90 °C or upon treatment with stronger base, it underwent dehydrobromination rather than ring closure to afford **1b** (Scheme 3). Dehydrohalogenation is seldom observed in the usual Pd-catalyzed reactions using haloalkenes. Indeed, the rection did not proceed when α-bromostilbene[18] was used under the same conditions. Hence, the *ortho*-amino group in **2b** possibly serves as a directing group to attract Pd^0 species and facilitate the oxidative addition and the subsequent base-induced dehydrobromination, which affords a triple bond.

To avoid undesirable dehydrohalogenation assisted by the *ortho*-amino group prevents the cross-coupling reaction, *N*-acetylation was conducted to decrease the coordinating ability of the amino group. When bromoalkene **5a** was subjected to the Buchwald–Hartwig coupling reaction under the conditions corresponding to Scheme 4, a complex mixture was obtained, with 61% recovery of **5**; 10Br-DBA **6** was not detected in the mixture (Scheme 4). However, it is worth noting that this reaction pathway did not involve dehydrobromination



Scheme 3 Dehydrobromination of **2b**.

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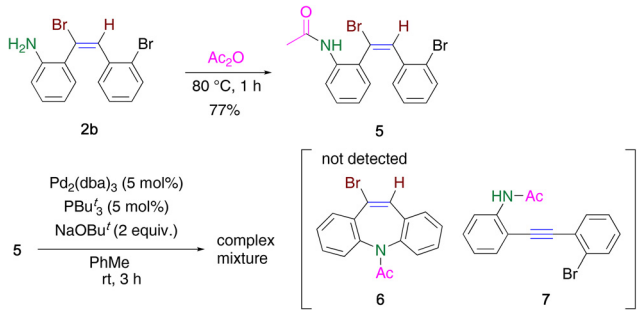
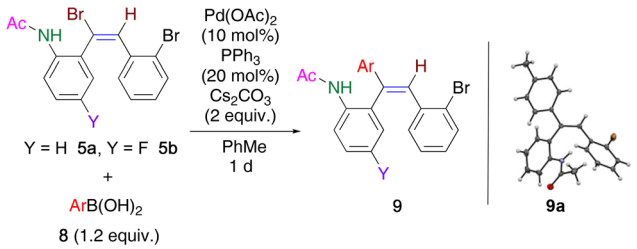


Scheme 4 Acetylation of **2b** and Pd-catalyzed reaction of **5**.

Table 1 Suzuki–Miyaura coupling using bromoalkene **5**



Entry	Y	Ar	Temp./°C	Product	Yield[a]/%
1	H	4-MeC$_6$H$_4$	rt	**9a**	92
2	H	4-MeOC$_6$H$_4$	rt	**9b**	26
3	H	4-ClC$_6$H$_4$	rt	**9c**	13
4[b]	H	4-MeOC$_6$H$_4$	rt	**9b**	88
5[b]	H	4-ClC$_6$H$_4$	rt	**9c**	89
6[b]	H	4-MeOCOC$_6$H$_4$	rt	**9d**	0
7	H	4-MeOCOC$_6$H$_4$	80	**9d**	21
8	F	4-MeC$_6$H$_4$	rt	**9e**	89

[a] Determined by ^{1}H NMR. [b] 10 equiv. of H_2O were added.

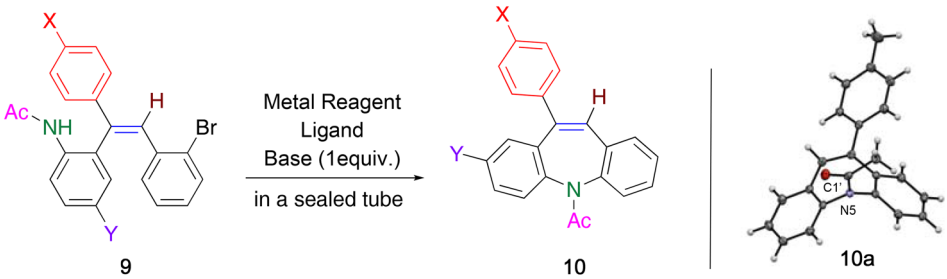
leading to **7**. Therefore, Suzuki–Miyaura coupling using *N*-acetylated bromoalkene **5** was effective.

Bromoalkene **5a** reacted with 4-methylphenylboronic acid **8a** to afford differently triarylated alkene **9a** in 92% yield, without any *E*/*Z* isomerization (Table 1, entry 1). When boronic acids **8b** and **8c** were used, the yields of coupling products **9b** and **9c** decreased considerably, presumably because of the formation of a trimer upon the dehydration of **8b** and **8c** (entries 2 and 3). This drawback was overcome by adding 10 equiv. of water to hydrolyze the trimer, which afforded **9b** and **9c** in high yields (entries 4 and 5). In the case of less reactive **8d**, heating the reaction mixture was more effective than adding water, and **9d** was obtained (entries 6 and 7). The Suzuki–Miyaura coupling efficiently proceeded even in the presence of a fluoro group to afford triarylalkene **9e** in 89% yield (entry 8).

Finally, the construction of an azepine ring was investigated (Table 2). When triarylalkene **9** was treated with a Pd catalyst,[19] cyclization proceeded to afford **10a** in 22% yield, along with 64% recovery of **9** (entry 1). Increasing the catalyst loading resulted in the complete consumption of **9**, and the yield of **10a** increased up to 53% (entry 2). However, the yield could not be improved further under the other reaction conditions tested. We next studied the intramolecular cross-coupling reaction using CuI, instead of a Pd catalyst.[20] Although it was necessary to use stoichiometric amounts of CuI (3 equiv.), 10Ar-DBA **10a** was obtained in higher yields than that obtained using a Pd catalyst (entries 3–5). Heating in a sealed tube for a longer time, instead of microwave heating, was also effective, and the reaction proceeded to furnish **10a** with 87% yield (entry 6).

Other triarylalkenes **9b–e** were converted to the corresponding products **10b–e**, respectively, in moderate yields,

Table 2 Synthesis of 10Ar-DBA **10**



Entry	Y	X		Metal reagent (equiv.)	Ligand (equiv.)	Base	Solv.	Temp./°C	Time/h	Yield/%
1	H	Me	**a**	Pd(OAc)$_2$ (0.05)	Xantphos (0.05)	Cs_2CO_3	1,4-Dioxane	100	24	22
2	H	Me	**a**	Pd(OAc)$_2$ (0.2)	Xantphos (0.2)	Cs_2CO_3	1,4-Dioxane	100	24	53
3	H	Me	**a**	CuI (1)	—	K_2CO_3	DMF	150[a]	3	13
4	H	Me	**a**	CuI (3)	—	K_2CO_3	DMF	150[a]	3	64
5	H	Me	**a**	CuI (3)	—	K_2CO_3	1,4-Dioxane	150	24	72
6	H	Me	**a**	CuI (3)	—	K_2CO_3	1,4-Dioxane	150	24	87
7	H	MeO	**b**	CuI (3)	—	K_2CO_3	1,4-Dioxane	150	24	33
8	H	Cl	**c**	CuI (3)	—	K_2CO_3	1,4-Dioxane	150	24	51
9	H	COOMe	**d**	CuI (3)	—	K_2CO_3	1,4-Dioxane	150	24	39
10	F	Me	**E**	CuI (3)	—	K_2CO_3	1,4-Dioxane	150	24	33

[a] Microwave heating was used.

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under the same conditions (entries 7–9). When the CuI-mediated ring closure reaction was employed for acetylated bromoalkene **5**, a complex reaction mixture was obtained, presumably because of the higher reactivity of the bromoalkene moiety than the bromobenzene moiety. Hence, the sequence of the Suzuki–Miyaura and Ullmann-type intramolecular coupling reactions was crucial for the synthesis of 10Ar-DBAs **10**.

In the ^{1}H NMR spectrum of **10a**, two types of signals were observed for each proton, indicating that **10a** existed in two isomeric forms. In the temperature-variable NMR spectra of **10a** acquired in DMSO-d_6, each type of signal coalesced (Fig. 2). X-ray crystallographic analysis of **10a** revealed that the N5–C1′ bond length (1.38 Å) was shorter than the usual N–C single bond length (1.47 Å), indicating double bond characteristics in the former. Consequently, rotation around this bond was prevented, facilitating the existence of stable atropisomers.[21]

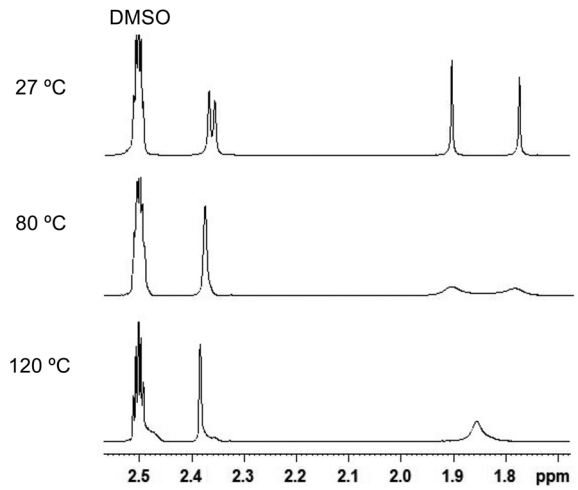
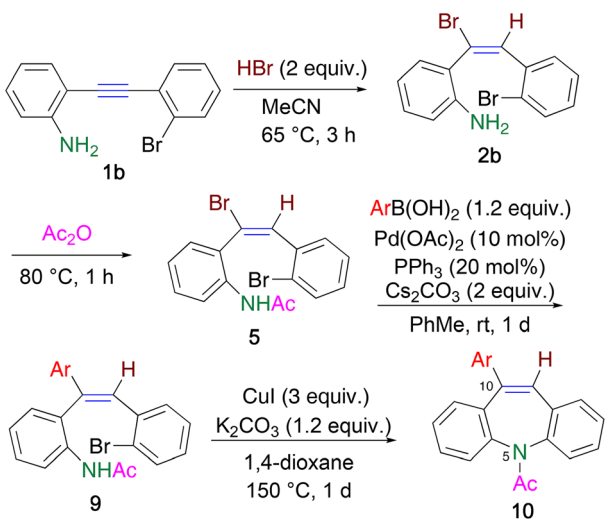


Fig. 2 Changes of methyl groups in the temperature-variable NMR spectra of **10a** (DMSO-d_6).



Scheme 5 Summary of the synthetic method for 10Ar-DBAs **10**.

Conclusions

5-Acetylated 10Ar-DBAs **10a–e** were successfully synthesized from the corresponding ethynylaniline **1b** and **1c** (Scheme 5). The developed *syn*-selective hydrobromination of **1b** efficiently afforded substrate **2b** for the successive Pd-catalyzed cross-coupling reactions. However, the elimination of hydrogen bromide, which was promoted by the presence of the *ortho*-amino group, proceeded predominantly. This undesirable reaction was suppressed by *N*-acetylation, and the subsequent Suzuki–Miyaura and Ullmann-type intramolecular coupling reactions were facilitated to afford 10Ar-DBAs **10**. This method will be useful for synthesizing new biologically active compounds because the 10-position of the DBA framework can be easily modified. Although 10Ar-DBA possessing an electron-withdrawing group at the 5-position could not be obtained by direct arylation,[11] it was possible to obtain this using our protocol. We believe that the modification of the substituents on 10Ar-DBAs will trigger further investigations on the butterfly-like dynamics of these compounds.[21]

Experimental

General

All reagents and dry solvents were purchased from commercial sources and used as received. ^{1}H, ^{13}C{^{1}H} and ^{19}F{^{1}H} NMR spectra were recorded on a Bruker DPX-400 spectrometer (400 MHz, 100 MHz, and 367.5 MHz, respectively) and a JEOL JMN-ECZ400S spectrometer (400 MHz and 100 MHz, respectively) in a deuterated solvent using TMS as an internal standard. For ^{19}F{^{1}H} NMR, the chemical shift of hexafluorobenzene (δ = −163.0 ppm in $CDCl_3$) was used as an external reference. The assignments of the ^{13}C{^{1}H} NMR were performed by DEPT experiments. In cases of 10Ar-DBAs **10**, NMR spectra were measured using a mixture of diastereomer A and B (A/B = 51/49–56/44). Hence, integral values of ^{1}H NMR were shown using H_A and H_B, which were belonged to isomer A and B, respectively. Assignments of ^{13}C NMR were also shown using C_A and C_B, which were belonged to isomer A and B, respectively. IR spectra were recorded on a JASCO FT/IR-4200 spectrometer equipped with an ATM detector. High-resolution mass spectra were obtained on an AB SCEIX Triplet TOF 4600 mass spectrometer. Melting points were recorded on an SRS-Optimelt automated melting point system and were uncorrected. Microwave heating was performed by Anton-Paar Microwave 300 (850 W, 2455 MHz) using 10 mL glass vessel.

X-ray crystallographic analysis

Diffraction data were collected at 93 K under a cold N_2-gas stream on a Rigaku XtaLAB Synergy-S/Mo system (λ = 0.71073 Å (Mo-Kα)). The integrated data were analyzed by

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using an Olex2 crystallographic software package.[22] The structures were solved with the ShelXT structure solution program[23] using Intrinsic Phasing and refined with the ShelXL refinement package[24] using the least-squares minimization. Anisotropic refinement was performed for all non-hydrogen atoms, and all the hydrogen atoms were put at calculated positions.

Hydrobromination of 1b

In a screw capped test tube, HBr aq. (d = 1.49, 48% (w/w), 116 μL, 1.0 mmol) was added to a solution of ethynylaniline **1b** (134 mg, 0.5 mmol) in MeCN (5 mL). Yellow solid immediately precipitated. When the mixture was heated at 65 °C, the yellow solid gradually decreased and completely disappeared after 3 h. After addition of NEt_3 (70 μL, 0.5 mmol), solvent was removed under vacuo, and the residue was dissolved in $CHCl_3$ (10 mL). The $CHCl_3$ solution was washed with H_2O (10 mL × 3), dried over $MgSO_4$, and evaporated to afford adduct **2b** (154 mg, 0.44 mmol, 88%) as a yellow solid. When HCl was used instead of HBr, reaction was conducted in a same way.

***E*-2-[1-Bromo-2-(2-bromophenyl)ethenyl]aniline (2b).** Yellow solid, mp 103.3–103.7 °C (dec). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, J = 7.6, 1.6 Hz, 1H), 7.41 (s, 1H), 7.10 (br d, J = 7.6 Hz, 1H), 7.09 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 7.02 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 6.97 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 6.91 (dd, J = 7.6, 1.6 Hz, 1H), 6.68 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 6.62 (dd, J = 7.6, 1.6 Hz, 1H), 4.4–1.2 (br, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.5 (C), 136.0 (C), 134.9 (CH), 132.6 (CH), 130.5 (CH), 130.2 (CH), 129.9 (CH), 129.3 (CH), 127.3 (CH), 123.8 (C), 123.5 (C), 123.2 (C), 118.6 (CH), 116.0 (CH); IR (KBr/cm^{-1}) 3475, 3384, 1616, 748; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{14}H_{12}Br_2N$: 351.9331, found: 351.9324.

***E*-2-[2-(2-Bromophenyl)-1-chloroethenyl]aniline (2c).** Yellow solid (139 mg, 0.45 mmol, 90%), mp 101.9–103.4 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, J = 7.6, 1.6 Hz, 1H), 7.16 (s, 1H), 7.11 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 7.11 (dd, J = 7.6, 1.6 Hz, 1H), 7.02 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 6.98 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 6.90 (dd, J = 7.6, 1.6 Hz, 1H), 6.68 (ddd, J = 7.6, 7.6, 0.8 Hz, 1H), 6.63 (dd, J = 7.6, 0.8 Hz, 1H), 4.0–3.8 (br, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 143.9 (C), 135.2 (C), 132.9 (C), 132.5 (CH), 130.5 (CH), 130.4 (CH), 130.3 (CH), 130.0 (CH), 129.2 (CH), 127.1 (CH), 123.7 (C), 122.0 (C), 118.4 (CH), 115.9 (CH); IR (KBr/cm^{-1}) 3487, 3395, 1618, 751; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{14}H_{12}BrClN$: 307.9836, found: 307.9841.

***E*-2-[2-(2-Bromophenyl)-1-bromoethenyl]-4-fluoroaniline (2d).** Pale yellow oil (eluted with hexane/EtOAc = 9/1, 143.3 mg, 0.39 mmol, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 7.6 Hz, 1H), 7.41 (s, 1H), 7.06 (ddd, J = 7.2, 1.2, 1.2 Hz, 1H), 7.01 (dd, J = 7.2, 7.2 Hz, 1H), 6.92 (dd, J = 7.2, 1.2 Hz, 1H), 6.85 (dd, J = 9.2, 2.8 Hz, 1H), 6.83 (ddd, J = 9.6, 8.0, 2.8 Hz, 1H), 6.56 (dd, J = 8.0, 4.8 Hz, 1H), 4.0–3.4 (br, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 155.5 (CF, J_{C-F} = 238.4 Hz), 139.9 (C), 135.7 (C), 135.6 (CH), 132.7 (CH), 129.8 (CH), 129.6 (CH), 127.4 (CH), 124.3 (C, J_{C-F} = 7.0 Hz), 123.5 (C), 121.4 (C), 117.5 (CH, J_{C-F} = 22.1 Hz), 117.1 (CH, J_{C-F} = 8.0 Hz), 116.2 (CH, J_{C-F} = 22.1 Hz); HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{14}H_{11}Br_2FN$: 369.9237, found: 369.9221.

Pd-Mediated dehydrobromination

To a mixture of bromoalkene **2b** (70.2 mg, 0.2 mmol), $Pd_2(dba)_3$ (10.7 mg, 0.01 mmol), PBu^t_3 (3.4 mg, 0.01 mmol), and $NaOBu^t$ (19.4 mg, 0.2 mmol), dry PhMe (2 mL) was added under Ar atmosphere. After stirring the resultant mixture at room temperature for 3 h, filtered through celite. The filtrate was evaporated to afford 2-[(2-bromophenyl)ethynyl]aniline (**1b**) (48.2 mg, 0.18 mmol, 90%) as a yellow oil.

N-Acetylation of bromoalkene 2b

A solution of bromoalkene **2b** (70.2 mg, 0.2 mmol) in Ac_2O (2 mL) was heated at 80 °C for 1 h. After concentration under reduced pressure, the residue was subjected to column chromatography on SiO_2 to afford *N*-acetylated product **5** (eluted with hexane/EtOAc = 7/3, 60.5 mg, 0.15 mmol, 77%) as a yellow solid. Single crystal was obtained by recrystallization from hexane.

***E*-1-(2-Acetylamino)phenyl-1-bromo-2-(2-bromophenyl)ethene (5a).** Yellow plates, mp 115.6–116.3 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (br d, J = 7.6 Hz, 1H), 7.53 (dd, J = 7.6, 1.2 Hz, 1H), 7.49 (s, 1H), 7.37 (dd, J = 7.6, 1.2 Hz, 1H), 7.30 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.28–7.19 (br, 1H), 7.11 (br dd, J = 7.6, 7.6 Hz, 1H), 7.05 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 6.96 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 6.76 (dd, J = 7.6, 1.2 Hz, 1H), 2.09 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.3 (C), 135.9 (CH), 135.3 (C), 134.4 (C), 132.7 (CH), 130.4 (CH), 130.3 (CH), 130.1 (CH), 128.0 (C), 127.7 (CH), 124.4 (CH), 123.2 (C), 121.8 (CH), 120.8 (C), 24.9 (CH_3); IR (KBr/cm^{-1}) 3410, 1676, 1519, 1445, 1296, 752; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{16}H_{14}Br_2NO$: 393.9437, found: 393.9455.

***E*-1-(2-Acetylamino-4-fluoro)phenyl-1-bromo-2-(2-bromophenyl)ethene (5b).** Colorless crystals, (eluted with hexane/EtOAc = 4/1, 52.0 mg, 0.126 mmol, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, J = 9.2, 5.2 Hz, 1H), 7.55 (dd, J = 8.0, 1.2 Hz, 1H), 7.49 (s, 1H), 7.103 (s, 1H), 7.099 (d, J = 8.0 Hz, 1H), 7.08 (dd, J = 5.2, 1.6 Hz 1H), 7.04–6.99 (m, 2H), 6.78 (dd, J = 8.0, 1.6 Hz, 1H), 2.08 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.0 (C), 161.9 (CF, J_{C-F} = 251.5 Hz), 138.2 (CH), 137.1 (C), 135.1 (CH), 134.2 (C), 132.8 (CH), 132.7 (CH), 131.0 (CH), 130.0 (C), 127.6 (CH, J_{C-F} = 10.1 Hz), 123.9 (C), 119.0 (CH, J_{C-F} = 23.1 Hz), 117.7 (C), 117.6 (CH, J_{C-F} = 22.1 Hz), 27.1 (CH_3); HRMS (ESI/TOF) calcd for [M + Na$^+$] $C_{16}H_{12}Br_2FNNaO$: 433.9162, found: 433.9150.

Synthesis of triarylalkene 9

To a mixture of bromoalkene **5** (79.0 mg, 0.2 mmol), 4-Me$C_6H_4B(OH)_2$ **8a** (32.6 mg, 0.24 mmol), PPh_3 (10.7 mg, 0.04 mmol), $Pd(OAc)_2$ (5.3 mg, 0.02 mmol), and Cs_2CO_3 (134.3 mg, 0.4 mmol), dry PhMe (1 mL) was added under Ar atmosphere. After stirring the resultant mixture at room temperature for 1 d, H_2O (10 mL) was added and extracted with $CHCl_3$ (10 mL × 3). The organic layer was dried over $MgSO_4$, and evaporated to afford yellow oil. The residue was treated by

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column chromatography on SiO_2 to furnish **9a** (eluted with hexane/EtOAc = 8/2, 78.2 mg, 0.184 mmol, 92%) as a yellow solid.

When other boronic acids **8b–d** were used, reactions were conducted in a similar way. In cases of **8b** and **8c**, 10 equiv. of H_2O were added to hydrolyze a trimer of boronic acid. In the case of **8d**, the reaction mixture was heated at 80 °C.

***Z*-2-(2-Bromophenyl)-1-(2-ethanoylamino)phenyl-1-(4-methylphenyl)ethene (9a).** Colorless plates (recrystallized from hexane), mp 125.8–126.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (br d, J = 7.6 Hz, 1H), 7.55 (dd, J = 7.6, 1.2 Hz, 1H), 7.31 (ddd, J = 7.6, 7.6, 2.0 Hz, 1H), 7.26 (s, 1H), 7.26 (d, J = 8.0 Hz, 2H), 7.21–7.16 (br, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.14 (dd, J = 7.6, 1.2 Hz, 1H), 7.08 (br dd, J = 7.6, 7.6 Hz, 1H), 7.01 (ddd, J = 7.6, 7.6, 2.0 Hz, 1H), 6.94 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 6.83 (dd, J = 7.6, 1.2 Hz, 1H), 2.38 (s, 3H), 1.92 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.4 (C), 139.5 (C), 138.8 (C), 138.3 (C), 136.8 (C), 135.6 (C), 132.5 (CH), 131.2 (CH), 130.5 (CH), 129.6 (CH), 129.2 (CH), 128.9 (CH), 128.8 (C), 128.6 (CH), 127.3 (CH), 127.3 (CH), 124.6 (C), 124.1 (CH), 121.4 (CH), 24.8 (CH_3), 21.3 (CH_3); IR (KBr/cm^{-1}) 3407, 1695, 1516, 1447, 1298, 769; HRMS (ESI/TOF) calcd for [M + Na$^+$] $C_{23}H_{20}BrNNaO$: 428.0621, found: 428.0616.

***Z*-2-(2-Bromophenyl)-1-(2-ethanoylamino)phenyl-1-(4-methoxyphenyl)ethene (9b).** Yellow solid (eluted with hexane/EtOAc = 7/3, 74.1 mg, 0.176 mmol, 88%), mp 112.1–114.8 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (br d, J = 8.0 Hz, 1H), 7.54 (dd, J = 8.0, 1.2 Hz, 1H), 7.33–7.28 (m, 1H), 7.30 (d, J = 8.8 Hz, 2H), 7.20 (s, 1H), 7.25–7.17 (br, 1H), 7.14 (dd, J = 7.6, 1.6 Hz, 1H), 7.08 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.00 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 6.93 (ddd, J = 7.6, 7.6, 1.6 Hz, 1H), 6.89 (d, J = 8.8 Hz, 2H), 6.82 (dd, J = 7.6, 1.6 Hz, 1H), 3.83 (s, 3H), 1.93 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.4 (C), 160.2 (C), 139.2 (C), 136.8 (C), 135.6 (C), 133.6 (C), 132.6 (CH), 131.3 (CH), 130.5 (CH), 129.1 (CH), 128.9 (CH), 128.8 (C), 128.7 (CH), 127.6 (CH), 127.3 (CH), 124.6 (C), 124.2 (CH), 121.4 (CH), 114.3 (CH), 55.5 (CH_3), 24.8 (CH_3); IR (KBr/cm^{-1}) 3403, 1695, 1509, 1445, 1298, 753; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{23}H_{21}BrNO_2$: 422.0750, found: 422.0740.

***Z*-2-(2-Bromophenyl)-1-(2-ethanoylamino)phenyl-1-(4-chlorophenyl)ethene (9c).** Yellow solid (eluted with hexane/EtOAc = 8/2, 75.7 mg, 0.178 mmol, 89%), mp 163.6–170.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (br d, J = 8.0 Hz, 1H), 7.56 (dd, J = 8.0, 1.2 Hz, 1H), 7.35–7.27 (m, 6H), 7.13–7.08 (m, 3H), 7.03 (ddd, J = 8.0, 8.0, 1.6 Hz, 1H), 6.96 (ddd, J = 8.0, 8.0, 1.2 Hz, 1H), 6.84 (dd, J = 8.0, 1.6 Hz, 1H), 1.94 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.4 (C), 139.7 (C), 138.6 (C), 136.4 (C), 135.5 (C), 134.7 (C), 132.7 (CH), 131.2 (CH), 130.5 (CH), 129.7 (CH), 129.6 (CH), 129.2 (CH), 129.1 (CH), 128.7 (CH), 128.4 (C), 127.4 (CH), 124.6 (C), 124.4 (CH), 121.8 (CH), 24.7 (CH_3); IR (KBr/cm^{-1}) 3410, 1683, 1519, 1445, 1299, 740; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{22}H_{18}BrClNO$: 426.0255, found: 426.0253.

***Z*-2-(2-Bromophenyl)-1-(2-ethanoylamino)phenyl-1-(4-methoxycarbonylphenyl)ethene (9d).** Yellow solid (eluted with hexane/EtOAc = 7/3, 18.9 mg, 0.04 mmol, 21%), mp 163.4–166.1 °C (dec). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (br d, J = 8.4 Hz, 1H), 8.08 (d, J = 8.4 Hz, 2H), 7.57 (dd, J = 8.0, 1.2 Hz, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.37 (s, 1H), 7.35–7.31 (m, 1H), 7.11–7.04 (m, 3H), 7.04 (dd, J = 8.0, 1.6 Hz, 1H), 6.97 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 6.86 (dd, J = 8.0, 1.2 Hz, 1H), 3.93 (s, 3H), 1.92 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.2 (C), 166.6 (C), 145.5 (C), 138.8 (C), 136.2 (C), 135.4 (C), 132.5 (CH), 131.1 (CH), 131.1 (CH), 130.4 (CH), 130.0 (CH), 130.0 (C), 129.7 (CH), 129.1 (CH), 128.3 (C), 127.2 (CH), 127.2 (CH), 124.5 (C), 124.4 (CH), 121.9 (CH), 52.2 (CH_3), 24.6 (CH_3); IR (KBr/cm^{-1}) 3410, 1720, 1519, 1436, 1281, 754; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{24}H_{21}BrNO_3$: 450.0699, found: 450.0690.

***Z*-2-(2-Bromophenyl)-1-(2-ethanoylamino-4-fluoro)phenyl-1-(4-methylphenyl)ethene (9e).** Pale yellow oil, (eluted with hexane/EtOAc = 2/1, 90.0 mg, 0.22 mmol, 89%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (dd, J = 9.2, 5.6 Hz, 1H), 7.56 (dd, J = 8.0, 1.6 Hz, 1H), 7.24 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 8.0 Hz, 2H), 7.10–6.96 (m, 5H), 6.87 (dd, J = 8.4, 3.2 Hz, 1H), 6.85 (dd, J = 8.4, 2.0 Hz, 1H), 2.39 (s, 3H), 1.92 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 168.4 (C), 159.0 (CF, J_{C-F} = 244.5 Hz), 139.1 (C), 138.6 (C), 137.7 (C), 136.4 (C), 132.7 (CH), 131.8 (C), 131.1 (C, J_{C-F} = 7.0 Hz), 130.5 (CH), 129.7 (CH), 129.6 (CH), 129.1 (CH), 127.4 (CH), 127.3 (CH), 124.5 (C), 123.5 (CH, J_{C-F} = 8.0 Hz), 117.6 (CH, J_{C-F} = 23.0 Hz), 115.6 (CH, J_{C-F} = 22.0 Hz), 24.6 (CH_3), 21.4 (CH_3); ^{19}F{^{1}H} NMR (376.5 MHz, $CDCl_3$) δ −117.8 (s); HRMS (ESI/TOF) calcd for [M + Na$^+$] $C_{23}H_{19}BrFNNaO$: 446.0526, found: 446.0501.

Synthesis of dibenzoazepine 10

In a screw capped test tube, to a solution of triarylalkene **9a** (81.5 mg, 0.2 mmol) in 1,4-dioxane (1 mL), CuI (114.3 mg, 0.6 mmol) and K_2CO_3 (27.6 mg, 0.2 mmol) were added and sealed. The resultant mixture was heated at 150 °C for 1 d. When microwave heating was used, the reaction mixture was added in 10 mL glass vessel, and put in the equipment and heated at 150 °C for 3 h. After cooling to room temperature, the reaction mixture was filtered through celite with washing by EtOAc. The filtrate was evaporated to afford yellow solid as a residue, in which production of 10ArDBA **10a** with 87% yield was confirmed by ^{1}H NMR. Further purification was performed by column chromatography on SiO_2 to furnish **10a** (eluted with hexane/EtOAc = 7/3, 47.1 mg, 0.145 mmol, 72%) as a pale yellow solid.

5-Ethanoyl-10-(4-methylphenyl)-5*H*-dibenzo[*b*,*f*]azepine (10a). Pale yellow solid, mp 168.8–169.2 °C. Isomeric ratio = 51/49. ^{1}H NMR (400 MHz, $CDCl_3$) isomers A and B δ 7.5–7.3 (m, 8H$_A$ + 8H$_B$), 7.3–7.1 (m, 4H$_A$ + 5H$_B$), 7.10 (s, 1H$_A$), 2.42 (s, 3H$_B$), 2.41 (s, 3H$_A$), 2.03 (s, 3H), 1.90 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) isomers A and B δ 170.7 (C$_A$), 170.2 (C$_B$), 144.0 (C), 142.3 (C), 142.3 (C), 141.5 (C), 141.5 (C), 141.2 (C), 139.9 (C), 139.7 (C), 137.9 (C), 137.9 (C), 136.6 (C), 135.6 (C), 135.2 (C), 133.9 (C), 130.8 (CH), 130.6 (CH), 129.7 (CH), 129.7 (CH), 129.5 (CH), 129.5 (CH), 129.3 (CH), 129.1 (CH), 129.0 (CH), 129.0 (CH), 128.9 (CH), 128.7 (CH), 128.0 (CH), 127.8 (CH), 127.8 (CH), 127.6 (CH), 127.4 (CH), 127.3 (CH), 127.1 (CH), 126.5 (CH), 22.2 (C$_B$H$_3$), 22.1 (C$_A$H$_3$), 21.2 (CH_3) three signals (CH × 2, CH_3 × 1) are lacked presumably due to overlap-

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ping; IR (KBr/cm^{-1}) 1675, 1372, 1330, 767; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{23}H_{20}NO$: 326.1539, found: 326.1529.

5-Ethanoyl-10-(4-methoxyphenyl)-5*H*-dibenzo[*b*,*f*]azepine (10b). White solid (eluted with hexane/EtOAc = 6/4, 22.5 mg, 0.066 mmol, 33%), mp 158.0–159.0 °C. Isomeric ratio = 54/46. ^{1}H NMR (400 MHz, $CDCl_3$) isomers A and B δ 7.5–7.3 (m, 8H$_A$ + 7H$_B$), 7.3–7.1 (m, 2H$_A$ + 3H$_B$), 7.13 (s, 1H$_A$), 7.07 (s, 1H$_B$), 6.95 (d, J = 8.8 Hz, 2H$_A$), 6.93 (d, J = 8.8 Hz, 2H$_B$), 3.87 (s, 3H$_B$), 3.85 (s, 3H$_A$), 2.02 (s, 3H$_B$), 1.90 (s, 3H$_A$); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) isomers A and B δ 170.7 (C$_B$), 170.2 (C$_A$), 159.6 (C$_A$), 159.5 (C$_B$), 143.6 (C), 142.3 (C), 142.2 (C), 141.5 (C), 141.2 (C), 141.1 (C), 136.6 (C), 135.7 (C), 135.2 (C), 135.2 (C), 135.0 (C), 134.0 (C), 130.8 (CH), 130.6 (CH), 130.3 (CH), 130.0 (CH), 129.7 (CH), 129.7 (CH), 129.5 (CH), 129.4 (CH), 128.8 (CH), 128.5 (CH), 128.0 (CH), 127.8 (CH), 127.6 (CH), 127.4 (CH), 127.3 (CH), 127.1 (CH), 126.1 (CH), 114.0 (C$_B$H), 113.8 (C$_A$H), 55.4 (CH$_3$), 22.2 (C$_B$H$_3$), 22.1 (C$_A$H$_3$) four signals (CH × 3, CH$_3$ × 1) are lacked presumably due to overlapping; IR (KBr/cm^{-1}) 1673, 1510, 1249, 768; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{23}H_{20}NO_2$: 342.1489, found: 342.1502.

5-Ethanoyl-10-(4-chlorophenyl)-5*H*-dibenzo[*b*,*f*]azepine (10c). Pale yellow solid (eluted with hexane/EtOAc = 7/3, 35.2 mg, 0.102 mmol, 51%), mp 165.2–166.4 °C. Isomeric ratio = 56/44. ^{1}H NMR (400 MHz, $CDCl_3$) isomers A and B δ 7.5–7.3 (m, 10H$_A$ + 10H$_B$), 7.3–7.2 (m, 1H$_A$ + 1H$_B$), 7.15 (s, 1H$_B$), 7.13 (dd, J = 7.2, 1.2 Hz, 1H$_B$), 7.08 (s, 1H$_A$), 7.07 (br d, J = 8.4 Hz, 1H$_A$), 2.02 (s, 3H$_B$), 1.89 (s, 3H$_A$); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) isomers A and B δ 170.7 (C$_A$), 170.2 (C$_B$), 142.9 (C), 142.4 (C), 141.6 (C), 141.2 (C), 141.1 (C), 141.0 (C), 140.3 (C), 136.0 (C), 135.1 (C), 134.8 (C), 134.0 (C), 134.0 (C), 133.6 (C), 130.5 (CH), 130.4 (CH), 130.3 (CH), 130.1 (CH), 130.0 (CH), 130.0 (CH), 129.8 (CH), 129.6 (CH), 129.6 (CH), 129.2 (CH), 128.8 (CH), 128.6 (CH), 128.1 (CH), 127.9 (CH), 127.9 (CH), 127.8 (CH), 127.5 (CH), 127.4 (CH), 127.3 (CH), 127.2 (CH), 22.2 (C$_B$H$_3$), 22.1 (C$_A$H$_3$) three signals (C × 1, CH × 2) are lacked presumably due to overlapping; IR (KBr/cm^{-1}) 1674, 1489, 1372, 1331, 768; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{22}H_{17}ClNO$: 346.0993, found: 346.1002.

5-Ethanoyl-10-(4-methoxycarbonylphenyl)-5*H*-dibenzo[*b*,*f*] azepine (10d). Pale yellow solid (eluted with hexane/EtOAc = 6/4, 28.8 mg, 0.078 mmol, 39%), mp = 143.5–144.5 °C. Isomeric ratio = 52/48. ^{1}H NMR (400 MHz, $CDCl_3$) isomers A and B δ 8.09 (d, J = 8.4 Hz, 2H$_B$), 8.06 (d, J = 8.4 Hz, 2H$_A$), 7.55 (d, J = 8.4 Hz, 2H$_A$), 7.51 (d, J = 8.4 Hz, 2H$_B$), 7.5–7.3 (m, 6H$_A$ + 6H$_B$), 7.3–7.2 (m, 1H$_A$ + 1H$_B$), 7.23 (s, 1H$_A$), 7.16 (s, 1H$_B$), 7.10 (dd, J = 7.2, 1.2 Hz, 1H$_B$), 7.04 (br d, J = 8.0 Hz, 1H$_A$), 3.96 (s, 3H$_B$), 3.95 (s, 3H$_A$), 2.04 (s, 3H$_B$), 1.90 (s, 3H$_A$); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) isomers A and B δ 170.7 (C$_A$), 170.2 (C$_B$), 166.9 (C$_A$), 166.8 (C$_B$), 147.2 (C$_A$), 147.0 (C$_B$), 143.1 (C), 142.5 (C), 141.6 (C), 141.3 (C), 140.6 (C), 135.9 (C), 134.9 (C), 134.7 (C), 133.5 (C), 130.6 (CH), 130.5 (CH), 130.3 (CH), 130.1 (CH), 130.0 (CH), 129.9 (CH), 129.7 (CH), 129.7 (CH), 129.6 (C), 129.6 (C), 129.4 (CH), 129.1 (CH), 128.8 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 128.0 (CH), 127.8 (CH), 127.5 (CH), 127.4 (CH), 127.3 (CH), 52.2 (C$_B$H$_3$), 52.2 (C$_A$H$_3$), 22.2 (C$_B$H$_3$), 22.1 (C$_A$H$_3$) four signals (C × 1, CH × 3) are lacked presumably due to overlapping; IR (KBr/cm^{-1}) 1720, 1674, 1372, 1280, 778, 732; HRMS (ESI/TOF) calcd for [M + H$^+$] $C_{24}H_{20}NO_3$: 370.1438, found: 370.1452.

5-Ethanoyl-2-fluoro-11-(4-methylphenyl)-5*H*-dibenzo[*b*,*f*] azepine (10e). White solid (eluted with hexane/Et_2O = 1/1, 19.4 mg, 0.057 mmol, 33%). Isomeric ratio = 56/44. ^{1}H NMR (400 MHz, $CDCl_3$) isomers A and B δ 7.49–7.29 (m, 7H$_A$ + 7H$_B$), 7.24 (d, J = 8.0 Hz, 2H$_A$), 7.22 (d, J = 8.0 Hz, 2H$_B$), 7.17–7.11 (m, 1H$_A$ + 1H$_B$), 7.17 (s, 1H$_B$), 7.11 (s, 1H$_A$), 6.86 (dd, J = 9.6, 2.8 Hz, 1H$_B$), 6.80 (dd, J = 9.6, 2.8 Hz, 1H$_A$), 2.42 (s, 3H$_B$), 2.40 (s, 3H$_A$), 2.02 (s, 3H$_B$), 1.70 (s, 3H$_A$); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) isomers A and B δ 171.0 (C$_A$), 170.5 (C$_B$), 162.5 (C$_B$F, J_{C-F} = 217.3 Hz), 161.5 (C$_A$F, J_{C-F} = 248.5 Hz), 143.2 (C), 141.5 (C), 141.3 (C), 140.7 (C), 139.2 (C), 139.0 (C), 138.7 (C$_B$, J_{C-F} = 8.0 Hz), 138.3 (C), 138.28 (C), 138.1 (C), 137.6 (C$_A$, J_{C-F} = 8.0 Hz), 137.56 (C), 135.0 (C), 133.7 (C), 130.0 (CH), 129.74 (CH), 129.69 (CH), 129.59 (CH), 129.5 (CH), 129.3 (CH), 129.2 (CH), 129.0 (CH), 128.7 (CH), 128.1 (CH), 127.7 (C$_B$H, J_{C-F} = 19.0 Hz), 127.4 (C$_A$H, J_{C-F} = 23.0 Hz), 117.0 (C$_A$H, J_{C-F} = 23.0 Hz), 116.5 (C$_B$H, J_{C-F} = 23.0 Hz), 22.24 (C$_B$H$_3$), 22.15 (C$_A$H$_3$), 21.3 (CH$_3$) three signals (CH × 6, CH$_3$ × 1) are lacked presumably due to overlapping; ^{19}F{^{1}H} NMR (376.5 MHz, $CDCl_3$) δ −113.0 (s), −114.4 (s); HRMS (ESI/TOF) calcd for [M + Na$^+$] $C_{23}H_{18}FNNaO$: 366.1265, found: 366.1249.

Author contributions

Dr Iwai mainly prepared the manuscript and performed experiments. Mr Mukaijo performed experiments. Dr Asahara and Prof. Nishiwaki participated in discussion about this project.

Conflicts of interest

There are no conflicts to declare.

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