Metal-Free Electrocyclization at Ambient Temperature: Synthesis of 1-Arylcarbazoles

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Abstract: An efficient novel protocol for the construction of an hyellazole-inspired compound collection is described. Starting from 2,6-diarylacetanilides, the desired products were obtained using hypervalent iodine promoted electrocyclization. The mechanism of product formation was investigated through intramolecular competition experiments.

Key words: alkaloids, heterocycles, electrocyclization, hypervalent iodine, biaryls

Natural products present a rich resource for the discovery of disease-modulating drug candidates.[1] Compounds having C–N bonds are widely occurring in nature and have ubiquitous applications in biological studies.[2] Among all the nitrogen-containing natural products, substances with the carbazole motif are highly interesting due to their versatile and unique physiological properties, and a variety of synthetic methods have been reported to date for the construction of this unique structural motif.[3] Herein, we report the development of a straightforward approach to 1-arylcarbazoles from simple chemicals using hypervalent iodine mediated C–H bond amination.

In continuation of our studies[4] on the direct functionalization of C–H bonds, we decided to examine a short synthetic route to a natural-product-like compound collection containing the 1-arylcarbazole scaffold. Hyellazole and 6-chlorohyellazole (Figure 1) are two unusual, nonbasic, marine carbazole alkaloids isolated by Moore and co-workers from the blue-green algae *Hyella caespitosa*.[5] These alkaloids possess structures that are entirely different from the carbazole alkaloids isolated from terrestrial plants. Various strategies have been developed over the years for the synthesis of these natural products since their isolation.[6] Significantly, Knölker and co-workers have developed a short and straightforward large-scale synthesis of hyellazole in eight steps with 63% yield and of 6-chlorohyellazole in 10 steps with 55% yield using iron complex chemistry.[6j] In both cases, the starting material used was the inexpensive and commercially available 2,6-dimethoxytoluene. Based on the limited knowledge on biological functions of this kind of natural product and the fact that known syntheses of these natural products are based on multiple steps, we decided to investigate the regioselective formation of 1-arylcarbazoles from 2,6-diarylated acetanilides using C–H bond amination as the key step toward the synthesis of the compound collection.

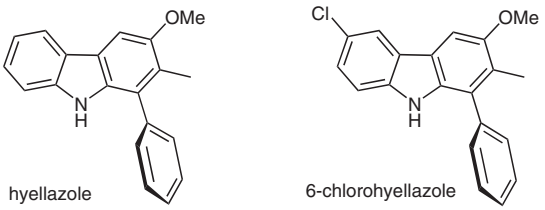
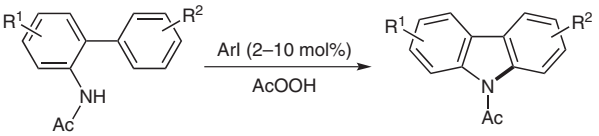


Figure 1 Natural products based on the 1-arylcarbazole scaffold

During our studies on the direct functionalization of unactivated C–H bonds, we developed an organocatalytic intramolecular oxidative method of C–N bond formation (Scheme 1). Using a substoichiometric amount of aryl iodide, the desired carbazoles were formed under ambient conditions in the presence of peracetic acid.[4a]



Scheme 1 Organocatalytic intramolecular oxidative amination

Our retrosynthetic plan was as shown in Scheme 2. The key reaction is a hypervalent iodine mediated intramolecular amination reaction on compound **1**. Compound **1** can be prepared from different inexpensive, commercially available anilines in two steps, acetylation followed by palladium-catalyzed diarylation, in 50–75% yield.[7] We commenced our study by examining the reactions of electronically variable 2,6-diarylated acetanilides **1** using a substoichiometric amount of aryl iodide at ambient temperature.

Using various differently substituted derivatives **1**, we realized that the use of (diacetoxyiodo)benzene [$PhI(OAc)_2$] as an oxidant in stoichiometric amounts led to better yields than the organocatalytic conditions (Table 1).[8,9]

Having conditions for the synthesis of the 1-arylcarbazole moiety in hand, we focused on an exploration of the scope of the reaction. We first examined a variety of symmetrical *N*-(1,1′:3′,1″-terphenyl-2′-yl)acetamides **1** with variations in the outer aryl parts, which we synthesized by a

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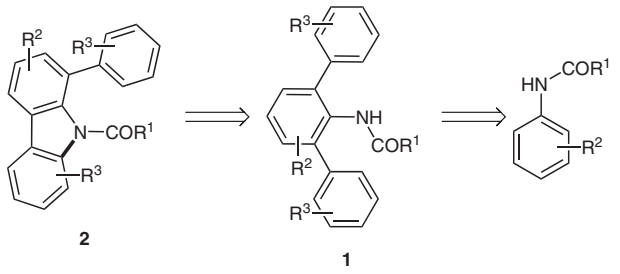
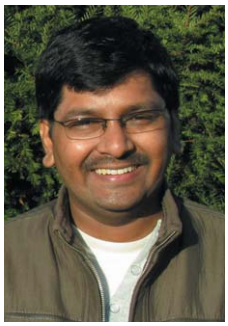


Scheme 2 Retrosynthetic approach

one-step procedure from the corresponding anilides.[7] To our delight, we found that the presence of substituents with different electronic and steric properties in various positions did not have an effect on the formation of the desired product (Scheme 3, products **2a**–**g**). In all cases, exclusive formation of carbazole was observed. Furthermore, in the case of the *meta*-substituted substrates **1e** and **1f**, the products, **2e** and **2f**, were obtained with a high regioisomeric ratio. In the case of **1g**, it was found that the addition of small amounts of mesitylene to 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) improved the yield of the desired polysubstituted product **2g** from 10% to 52%. We then tested reactants with a substituent in the middle aromatic part. In general, the examined substrates led to the formation of products in 56–88% yield (Scheme

Biographical Sketches



Rajarshi Samanta undertook his bachelors (2002) and masters (2004) studies in chemistry at the Jadavpur University, Kolkata, India. He obtained his PhD degree, working with Dr. T. K. Chakraborty, from the Indian Institute of Chemical Technology (Osmania University), Hyderabad, India in 2010. Since June, 2010 he has been a postdoctoral fellow in the group of Dr. A. P. Antonchick, Max Planck Institute of Molecular Physiology, Dortmund, Germany. His present research interests include metal and metal-free C–H functionalization, asymmetric synthesis and the total synthesis of natural products.

Katharina Kulikov was born in Uzbekistan in 1987. In 1996, she moved to Germany where she finished school in 2008 and started her course of studies in chemical biology at the TU Dortmund. In 2011, she finished her bachelor's thesis in the Antonchick group.

Carsten Strohmann studied chemistry (1982–1990) at the Universities of Braunschweig and Karlsruhe, Germany. He obtained his PhD degree, working with Prof. R. Tacke, in 1990. After postdoctoral study (1990–1991) with Prof. D. Seyferth as a DFG fellow at MIT in Cambridge (USA), he gained his habilitation (1992–1995) in the group of Prof. M. Veith at the University of Saarbrücken. In 1995 he was appointed Privatdozent at the University of Saarbrücken and in 1998 he was appointed Privatdozent at the University of Würzburg. Since 2008 he has been a Professor of Inorganic Chemistry, TU Dortmund.

Andrey P. Antonchick studied chemistry at Belarusian State University (Minsk, Belarus). He received a PhD in bioorganic chemistry from the Institute of Bioorganic Chemistry of the National Academy of Sciences of Belarus (Minsk, Belarus) and the Max Planck Institute for Chemical Ecology (Jena, Germany) under the guidance of Prof. V. A. Khripach and P.D. Dr. B. Schneider. After a postdoctoral appointment with Prof. M. Rueping at Frankfurt University, he joined the group of Prof. H. Waldmann at the Max Planck Institute of Molecular Physiology (Dortmund, Germany). In June 2010 he was appointed group leader at the Max Planck Institute of Molecular Physiology.

Table 1 Comparison of the Organocatalytic and Stoichiometric Conditions

R^1	R^2	R^3	Conditions[a]	Yield (%)
Cl	H	H	A	49 (**2b**)
Cl	H	H	B	73 (**2b**)
H	Me	H	A	60 (**2f**)
H	Me	H	B	71 (**2f**)
H	H	Cl	A	65 (**2h**)
H	H	Cl	B	88 (**2h**)
H	H	*i*-Pr	A	53 (**2i**)
H	H	*i*-Pr	B	61 (**2i**)

[a] A: **1** (1 equiv), ArI (10 mol%), AcOOH (2.2 equiv), HFIP–CH_2Cl_2 (1:1) (0.05 M), r.t.; B: **1** (1 equiv), $PhI(OAc)_2$ (1.5 equiv), HFIP (0.1 M), r.t.

3, products **2h**–**l**). In the presence of electron-donating or electron-withdrawing groups, product formation occurred smoothly. Finally, besides the application of various acetanilides, we demonstrated that a 2-methoxyacetamide derivative can also be used to obtain the product of oxidative amination (Scheme 3, product **2n**). We were able to obtain the crystal structure of **2b** which unequivocally confirmed the structure (Figure 2).[10]

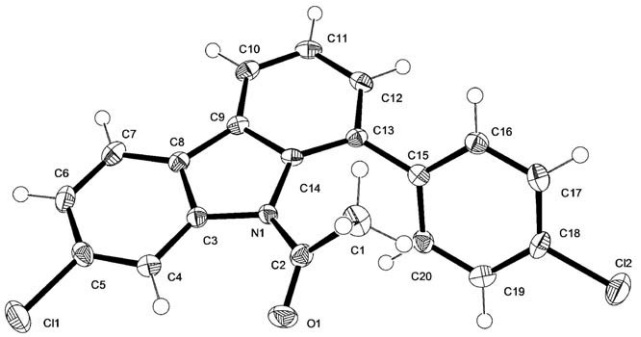
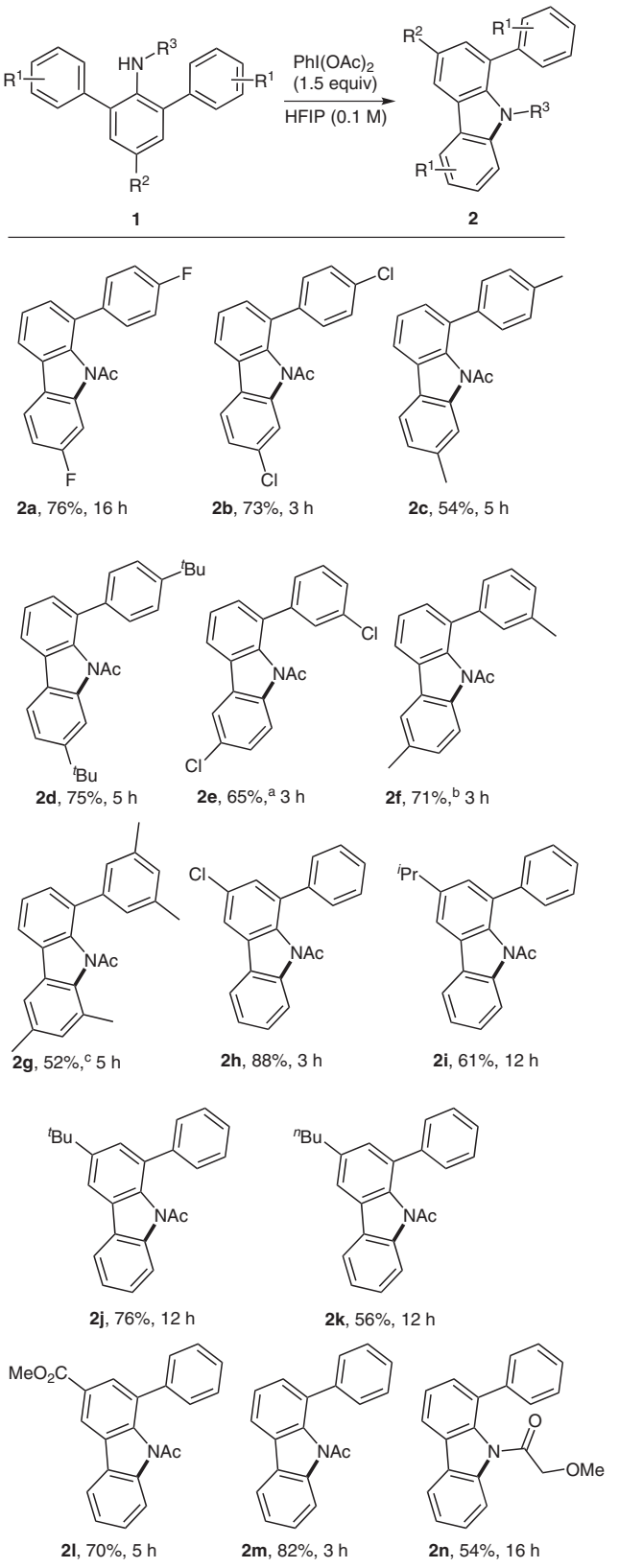


Figure 2 ORTEP plot of compound **2b** at the 50% probability level[10]

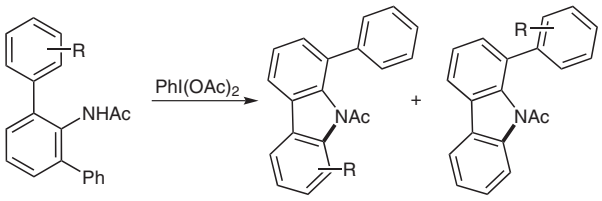
After intensive investigation of the symmetrical reactants, we focused on the application of nonsymmetrical substrates in the synthesis of 1-arylcarbazoles (Table 2). Substrates bearing a deactivating group such as fluorine or chlorine in the *para* position led to the formation of a mixture of nonseparable regioisomeric carbazole ring systems (Table 2, entries 1 and 2). The fluorine-containing derivative gave a 1:1 mixture, while the chlorine-containing reactant led to a 3:1 mixture, where the major product **4b** is derived from functionalization of the unsubstituted part of the molecule. Interestingly, the shift of chlorine to the *meta* position led to the completely selective formation of isomer **4c** in high yield (Table 2, entry 3). Furthermore, a derivative bearing an activating group (methyl) in the



Scheme 3 Reaction scope. Yields are for isolated products after column chromatography. [a] Major isomer is shown (ratio = 15:1). [b] Major isomer is shown (ratio = 10:1). [c] Using HFIP–mesitylene (7:1) as solvent.

para position resulted in **3d** (Table 2, entry 4). In this case, oxidative amination occurs by selective modification of the substituted part of the substrate.

Table 2 Investigation of Nonsymmetrical Reactants **1**[a]



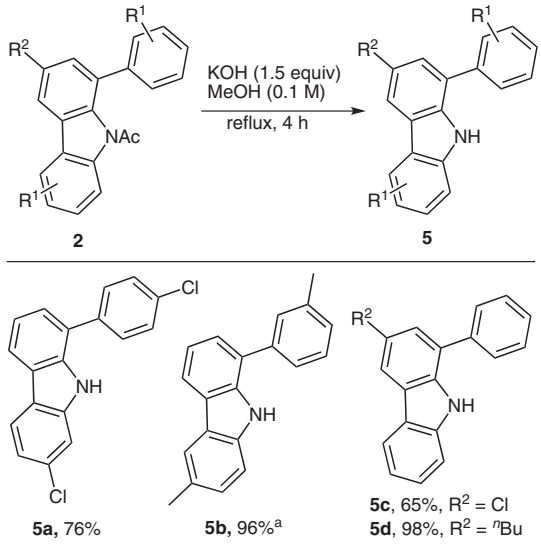
1 **3** **4**

Entry	R	Time (h)	Yield[b,c] (%) of **3**	Yield[b,c] (%) of **4**
1	*p*-F	2	22 (**3a**)	22 (**4a**)
2	*p*-Cl	2.5	22 (**3b**)	66 (**4b**)
3	*m*-Cl	3	n.d.	92 (**4c**)
4	*p*-Me	5	80 (**3d**)	n.d.

[a] Reaction conditions: **1** (1 equiv), $PhI(OAc)_2$ (1.5 equiv), HFIP (0.1 M), r.t.
[b] Isolated yields after column chromatography. In the case of nonselective formation of the product, the yields of the isomers were calculated based on ^1H NMR spectra of the product mixture.
[c] n.d. = not detected.

We successfully demonstrated that the protecting group on the nitrogen atom can be removed under basic conditions (Scheme 4). To our delight, we were able to synthesize the unprotected 1-arylcarbazoles **5** in good to excellent yields.

After the investigation of the generality of the developed transformation, we performed studies on the mechanism of the reaction. Initially, we performed experiments using



Scheme 4 Scope of the hydrolysis. Yields are for isolated products after column chromatography. [a] Major isomer is shown (ratio = 10:1).

deuterated substrate for the examination of a primary kinetic isotopic effect. Competition experiments under optimized oxidative conditions gave a kinetic isotopic effect of 1.04. Accordingly, if C–N bond formation and C–H bond cleavage occurred simultaneously, a primary kinetic isotope effect (KIE) would lead to the preferred reaction with the unlabeled substrate (KIE >1); however, the calculated KIE = 1.04 shows that C–H cleavage does not occur as the rate-determining step of the reaction and the formation of carbazole via a concerted mechanism is not taking place. Subsequently, we found that the presence of a radical scavenger does not affect formation of the desired carbazole. Therefore, reaction mechanisms with radical species cannot be taken into consideration.

To further examine the mechanism, a series of symmetrical *N*-(1,1′:3′,1″-terphenyl-2′-yl)acetamides **1** substituted with electron-donating or electron-withdrawing groups were screened as substrates in competition experiments to determine the electronic dependency of the formation of 1-arylcarbazoles. The product ratios obtained from a series of experiments were correlated with the Hammett constants. The results were analyzed using the Hammett equation to obtain hints on the reaction mechanism. First of all, we assumed formation of a nitrenium ion **B** via intermediate **A** by oxidation of acetamide **1** with (diacetoxyiodo)benzene (Scheme 5). The nitrenium ion **B** is then involved in electrophilic aromatic substitution leading to the formation of the carbocation **C** which subsequently rearomatizes to provide product **2** (Scheme 5, path A); however, this pathway was excluded based on the nonlinear correlation in the corresponding Hammett plot (see the Supporting Information for details). The best linear correlations in the corresponding Hammett plots were obtained for σ_p and σ^+ constants with goodness of the fit (R^2) 0.93 and 0.99, correspondingly (see Figure 3 and the Supporting Information for details). Linear correlations for σ_p constants correspond to an *ipso*-substitution pathway; however, this pathway can be excluded due to the unlikely formation of a conformationally strained four-membered-ring intermediate. The negative ρ value observed in the Hammett plot for σ^+ constants (ρ = –0.501) reveals that electron density is leaving the π-system in the rate-determining step. Taken together, those studies allowed us to

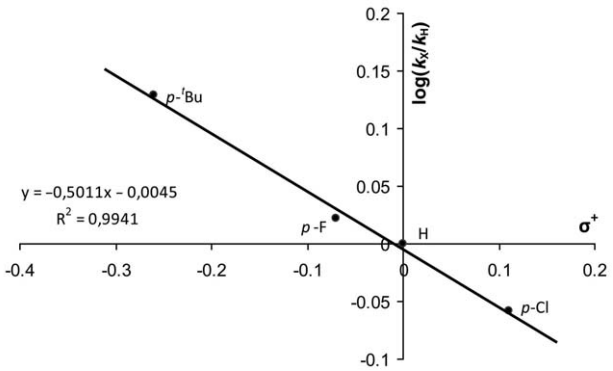
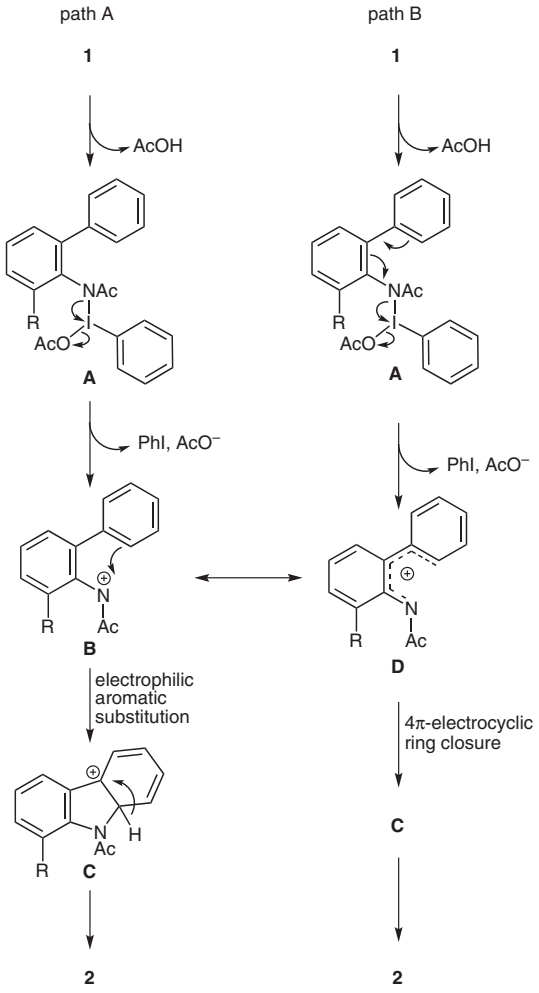


Figure 3 Hammett plot of $\log(k_X/k_H)$ versus σ^+

make a conclusion on the mechanism of formation of 1-phenylcarbazole. Oxidation of **1** with hypervalent iodine leads to formation of ion **D**, which is in resonance with ion **B**, via the intermediate **A** (Scheme 5, path B). Ion **D** undergoes a 4π-electron–5-atom electrocyclic ring closure to form carbocation **C** which, in a subsequent aromatization, leads to the formation of the desired product **2**.[11,12] Furthermore, a 4π-electron–5-atom electrocyclization mechanism correlates well with the results obtained for nonsymmetrical 2,6-diarylacetanilides (Table 2).



Scheme 5 Proposed mechanism of the formation of 1-phenylcarbazole

In conclusion, we have developed a highly efficient, general method for the preparation of a compound library based on the hyellazole scaffold. The mechanism of 1-arylcarbazole formation was examined. Our results suggest a 4π-electron–5-atom electrocyclization mechanism for hypervalent iodine mediated intramolecular oxidative amination of 2,6-diarylacetanilides.

Unless otherwise noted, all commercially available compounds were used as provided without further purification. Solvents for chromatography were technical grade and distilled prior to use. Column chromatography was performed using Merck silica gel 60 (particle size: 0.040–0.063 mm). Solvent mixtures are volume/volume. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker DRX400 (400 MHz), Bruker DRX500 (500 MHz) and Varian Inova 500 (500 MHz) spectrometers. High-resolution mass spectra were recorded on an LTQ Orbitrap mass spectrometer coupled to an Accela HPLC system (HPLC column: Hypersil GOLD, 50 mm × 1 mm, 1.9 μm). Fourier transform infrared (FT-IR) spectra were obtained with a Bruker Tensor 27 spectrometer (ATR, neat) and are reported in terms of frequency of absorption (cm^{-1}). Chemical yields refer to pure isolated substances.

N-Protected 1-Arylcarbazoles 2–4; General Procedure

A 2,6-diarylacetanilide **1** (0.1 mmol) was placed in a 4-mL screw-capped vial with 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP, 1 mL). Then, (diacetoxyiodo)benzene (0.15 mmol) was added to the stirred solution at r.t. The reaction mixture was stirred for 3–16 h. After completion of the reaction, the mixture was directly concentrated under reduced pressure and the N-protected 1-arylcarbazole product was purified by silica gel column chromatography (3–5% EtOAc in petroleum ether).

9-Acetyl-7-fluoro-1-(4-fluorophenyl)-9*H*-carbazole (2a)

White crystalline solid; yield: 25 mg (76%); mp 160–161 °C [petroleum ether (40–60 °C)].

FT-IR: 2924, 1707, 1512, 1439, 1313, 1267 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98–7.90 (m, 3 H), 7.60–7.54 (m, 2 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 7.41 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.24–7.17 (m, 2 H), 7.13 (td, *J* = 8.8, 2.3 Hz, 1 H), 1.79 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.28, 162.87 (d, *J* = 243.7 Hz), 162.38 (d, *J* = 248.5 Hz), 140.86 (d, *J* = 12.7 Hz), 137.14 (d, *J* = 1.9 Hz), 136.86 (d, *J* = 3.5 Hz), 129.52 (d, *J* = 7.9 Hz), 129.23, 128.81, 128.13, 124.73, 121.54, 120.68 (d, *J* = 10.1 Hz), 119.10, 116.88 (d, *J* = 21.5 Hz), 111.52 (d, *J* = 24.1 Hz), 102.78 (d, *J* = 28.8 Hz), 26.46.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{14}ONF_2$: 322.10380; found: 322.10378.

9-Acetyl-7-chloro-1-(4-chlorophenyl)-9*H*-carbazole (2b)

White crystalline solid; yield: 25.8 mg (73%); mp 224–225 °C [petroleum ether (40–60 °C)–EtOAc].

FT-IR: 2923, 1708, 1586, 1456, 1358, 1217 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 1.7 Hz, 1 H), 7.97 (dd, *J* = 8.2, 1.7 Hz, 1 H), 7.91 (d, *J* = 8.2 Hz, 1 H), 7.55–7.42 (m, 6 H), 7.38 (dd, *J* = 8.2, 1.8 Hz, 1 H), 1.81 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.08, 140.56, 139.16, 136.87, 134.00, 133.71, 130.08, 129.32, 129.09 (2 C), 127.94, 124.78, 124.16, 123.81, 120.61, 119.62, 115.34, 26.56.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{14}ON^{35}Cl_2$: 354.04470; found: 354.04483; *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{14}ON^{35}Cl^{37}Cl$: 356.04175; found: 356.04199; *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{14}ON^{37}Cl_2$: 358.03880; found: 358.03864.

9-Acetyl-7-methyl-1-*p*-tolyl-9*H*-carbazole (2c)

White crystalline solid; yield: 17 mg (54%); mp 151–152 °C [petroleum ether (40–60 °C)].

FT-IR: 2922, 1703, 1432, 1314, 1272, 1216 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (s, 1 H), 7.93 (dd, *J* = 7.8, 1.7 Hz, 1 H), 7.88 (d, *J* = 7.8 Hz, 1 H), 7.49 (d, *J* = 8.1 Hz, 2 H), 7.47–7.39 (m, 2 H), 7.30 (d, *J* = 7.8 Hz, 2 H), 7.22 (d, *J* = 7.8 Hz, 1 H), 2.54 (s, 3 H), 2.42 (s, 3 H), 1.74 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.99, 140.56, 138.26, 138.11, 137.60, 136.92, 130.45, 130.29, 128.66, 128.63, 127.74, 124.74, 124.31, 122.99, 119.42, 118.71, 115.22, 26.59, 22.35, 21.38.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{20}ON$: 314.15394; found: 314.15398.

9-Acetyl-7-*tert*-butyl-1-(4-*tert*-butylphenyl)-9*H*-carbazole (2d)
Light yellow oil; yield: 29.8 mg (75%).

FT-IR: 2959, 1704, 1361, 1276, 1244 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.34 (s, 1 H), 7.99–7.89 (m, 2 H), 7.57–7.41 (m, 7 H), 1.72 (s, 3 H), 1.45 (s, 9 H), 1.38 (s, 9 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 173.03, 151.78, 150.98, 140.64, 138.13, 137.28, 130.27, 128.71, 128.62, 127.58, 126.61, 124.32, 123.01, 121.27, 119.18, 118.80, 111.90, 35.59, 34.81, 31.86, 31.50, 26.51.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{28}H_{32}ON$: 398.24784; found: 398.24695.

9-Acetyl-6-chloro-1-(3-chlorophenyl)-9*H*-carbazole (2e) (Major Isomer)
White amorphous solid; yield: 23 mg (65%).

FT-IR: 2924, 1707, 1591, 1563, 1437, 1263, 1170 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8.8 Hz, 1 H), 8.00–7.95 (m, 2 H), 7.60 (s, 1 H), 7.52–7.36 (m, 6 H), 1.85 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.85, 142.53, 138.49, 137.07, 135.76, 130.97, 129.86, 129.26, 128.95, 128.06, 127.94, 127.86, 127.63, 126.64, 125.92, 124.71, 120.04, 119.72, 116.18, 26.49.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{20}H_{14}ON^{35}Cl_2$: 354.04470; found: 354.04470; *m/z* $[M + H]^+$ calcd for $C_{20}H_{14}ON^{35}Cl^{37}Cl$: 356.04175; found: 356.04169; *m/z* $[M + H]^+$ calcd for $C_{20}H_{14}ON^{37}Cl_2$: 358.03880; found: 358.03837.

9-Acetyl-6-methyl-1-*m*-tolyl-9*H*-carbazole (2f) (Major Isomer)
Light yellow oil; yield: 22.2 mg (71%).

FT-IR: 2923, 1702, 1393, 1361, 1274, 1196 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 8.4 Hz, 1 H), 7.98–7.93 (m, 1 H), 7.80 (s, 1 H), 7.48–7.35 (m, 5 H), 7.30 (dd, *J* = 8.4, 1.1 Hz, 1 H), 7.19 (d, *J* = 6.7 Hz, 1 H), 2.53 (s, 3 H), 2.42 (s, 3 H), 1.75 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.57, 141.02, 139.47, 138.44, 137.12, 133.15, 130.44, 129.64, 129.10, 128.94, 128.54, 128.49 (2 C), 125.47, 124.95, 124.23, 119.83, 119.06, 114.75, 26.43, 21.73, 21.47.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{22}H_{20}ON$: 314.15394; found: 314.15400.

9-Acetyl-8-(3,5-dimethylphenyl)-1,3-dimethyl-9*H*-carbazole (2g) (Major Isomer)
Light yellow oil; yield: 17.7 mg (52%).

FT-IR: 2922, 1731, 1702, 1601, 1454, 1393, 1361, 1240, 1203 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.86 (m, 1 H), 7.63 (s, 1 H), 7.42–7.37 (m, 2 H), 7.23 (s, 2 H), 7.08 (s, 1 H), 7.03 (s, 1 H), 2.52 (s, 3 H), 2.48 (s, 3 H), 2.38 (s, 6 H), 1.81 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 174.14, 140.43, 138.98, 138.88, 138.59, 132.99, 131.71, 130.41, 129.32, 128.81, 127.21, 126.35 (2 C), 126.16, 123.87, 118.79, 117.55, 27.32, 21.62, 21.58, 21.24.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{24}H_{24}ON$: 342.18524; found: 342.18535.

9-Acetyl-3-chloro-1-phenyl-9*H*-carbazole (2h)
Colorless oil; yield: 28 mg (88%).

FT-IR: 2924, 1707, 1470, 1388, 1271 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 8.3 Hz, 1 H), 7.99–7.95 (m, 2 H), 7.60–7.58 (m, 2 H), 7.55–7.48 (m, 3 H), 7.46 (d, *J* = 2.1 Hz, 1 H), 7.44–7.38 (m, 2 H), 1.74 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.19, 140.67, 139.80, 135.30, 131.41, 129.98, 129.88 (2 C), 128.83, 128.58, 128.36, 127.81, 124.40, 123.79, 120.00, 119.00, 115.08, 26.50.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{20}H_{15}ON^{35}Cl$: 320.08367; found: 320.08367; *m/z* $[M + H]^+$ calcd for $C_{20}H_{15}ON^{37}Cl$: 322.08072; found: 322.08065.

9-Acetyl-3-isopropyl-1-phenyl-9*H*-carbazole (2i)
Light yellow oil; yield: 19.9 mg (61%).

FT-IR: 2959, 1701, 1437, 1401, 1360, 1272 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.3 Hz, 1 H), 8.01 (d, *J* = 7.6 Hz, 1 H), 7.85 (d, *J* = 1.5 Hz, 1 H), 7.64–7.59 (m, 2 H), 7.54–7.45 (m, 3 H), 7.39 (t, *J* = 7.6 Hz, 2 H), 7.34 (d, *J* = 1.5 Hz, 1 H), 3.17–3.09 (m, 1 H), 1.75 (s, 3 H), 1.40 (d, *J* = 6.6 Hz, 6 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.54, 145.40, 141.35, 140.61, 135.30, 130.09, 129.72, 128.78, 128.15, 127.94, 127.73, 127.71, 125.58, 123.49, 119.66, 116.72, 115.17, 34.24, 26.43, 24.53.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{23}H_{22}ON$: 328.16959; found: 328.16954.

9-Acetyl-3-*tert*-butyl-1-phenyl-9*H*-carbazole (2j)
Light yellow oil; yield: 25.9 mg (76%).

FT-IR: 2958, 2926, 1702, 1479, 1394, 1271, 1195 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.2 Hz, 1 H), 8.03 (dd, *J* = 7.6, 0.5 Hz, 1 H), 8.00 (d, *J* = 1.9 Hz, 1 H), 7.64–7.60 (m, 2 H), 7.54–7.45 (m, 4 H), 7.42–7.37 (m, 2 H), 1.75 (s, 3 H), 1.48 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.54, 147.73, 141.55, 140.62, 134.97, 129.73 (2 C), 128.48, 127.99, 127.71, 127.68, 127.13, 125.72, 123.49, 119.61, 115.76, 115.18, 34.99, 31.88, 26.43.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{24}H_{24}ON$: 342.18524; found: 342.18541.

9-Acetyl-3-butyl-1-phenyl-9*H*-carbazole (2k)
Light yellow oil; yield: 19 mg (56%).

FT-IR: 2926, 1701, 1438, 1399, 1271 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.4 Hz, 1 H), 7.99 (d, *J* = 7.6 Hz, 1 H), 7.80 (s, 1 H), 7.60 (d, *J* = 7.6 Hz, 2 H), 7.53–7.44 (m, 3 H), 7.38 (dd, *J* = 10.8, 4.1 Hz, 2 H), 7.30 (d, *J* = 1.3 Hz, 1 H), 2.86–2.79 (m, 2 H), 1.80–1.70 (m, 5 H), 1.50–1.40 (m, 2 H), 0.98 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.54, 141.25, 140.59, 139.35, 135.22, 130.02, 129.90, 129.71, 128.78, 127.92, 127.72, 125.51, 123.49, 119.67, 118.80, 115.17, 35.67, 34.19, 26.42, 22.63, 14.17.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{24}H_{24}ON$: 342.18524; found: 342.18533.

Methyl 9-Acetyl-1-phenyl-9*H*-carbazole-3-carboxylate (2l)
White crystalline solid; yield: 24 mg (70%); mp 206–207 °C [petroleum ether (40–60 °C)–EtOAc].

FT-IR: 2924, 1728, 1701, 1432, 1356, 1272, 1224 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.70 (d, *J* = 1.1 Hz, 1 H), 8.21–8.16 (m, 2 H), 8.08 (d, *J* = 7.7 Hz, 1 H), 7.62 (d, *J* = 7.7 Hz, 2 H), 7.56–7.49 (m, 3 H), 7.47–7.39 (m, 2 H), 4.00 (s, 3 H), 1.77 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.35, 167.10, 140.58, 140.19, 139.60, 130.46, 129.88, 129.81, 128.48, 128.45, 128.24, 127.95, 126.20, 124.86, 123.93, 121.07, 120.17, 114.83, 52.44, 26.68.

HRMS: *m/z* $[M + H]^+$ calcd for $C_{22}H_{18}O_3N$: 344.12812; found: 344.12823.

9-Acetyl-1-phenyl-9*H*-carbazole (2m)
Colorless oil; yield: 23.4 mg (82%).

FT-IR: 2925, 1702, 1476, 1445, 1401, 1269 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 8.3 Hz, 1 H), 8.09–7.96 (m, 2 H), 7.64–7.58 (m, 2 H), 7.54–7.46 (m, 5 H), 7.45–7.36 (m, 2 H), 1.75 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 172.61, 141.01, 140.24, 136.88, 130.29, 129.77, 129.27, 128.57, 127.89 (2 C), 127.82, 125.35, 124.39, 123.57, 119.79, 119.29, 115.02, 26.45.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{16}ON$: 286.12264; found: 286.12266.

9-(Methoxyacetyl)-1-phenyl-9*H*-carbazole (2n)
Colorless oil; yield: 17 mg (54%).

FT-IR: 2926, 1704, 1502, 1446, 1266, 1122 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 8.3 Hz, 1 H), 8.04–7.98 (m, 2 H), 7.64 (d, *J* = 7.2 Hz, 2 H), 7.59–7.36 (m, 7 H), 3.61 (s, 2 H), 2.90 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 173.20, 140.43, 139.91, 136.35, 130.20, 129.96, 129.05, 128.46, 128.18, 127.98, 127.94, 125.58, 124.50, 123.76, 119.89, 119.34, 114.79, 74.23, 58.88.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{18}O_2N$: 316.13321; found: 316.13325.

9-Acetyl-7-methyl-1-phenyl-9*H*-carbazole (3d)
Light yellow oil; yield: 23.9 mg (80%).

FT-IR: 2923, 1703, 1429, 1396, 1314, 1272, 1216, 1175 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (s, 1 H), 7.95 (dd, *J* = 7.8, 1.7 Hz, 1 H), 7.88 (d, *J* = 7.8 Hz, 1 H), 7.62–7.59 (m, 2 H), 7.52–7.43 (m, 4 H), 7.41–7.36 (m, 1 H), 7.22 (dd, *J* = 7.8, 0.5 Hz, 1 H), 2.54 (s, 3 H), 1.74 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 172.75, 141.12, 140.62, 138.33, 136.91, 130.27, 129.76, 128.74, 128.73, 127.94, 127.78, 124.80, 124.34, 123.00, 119.44, 118.98, 115.28, 26.45, 22.35.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{18}ON$: 300.13829; found: 300.13829.

9-Acetyl-1-(3-chlorophenyl)-9*H*-carbazole (4c)
Light yellow oil; yield: 29.3 mg (92%).

FT-IR: 2923, 1704, 1591, 1562, 1448, 1393, 1268, 1219, 1196 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 8.3 Hz, 1 H), 8.05–8.00 (m, 2 H), 7.62 (t, *J* = 1.6 Hz, 1 H), 7.55–7.35 (m, 7 H), 1.88 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 171.99, 142.89, 140.14, 136.69, 135.63, 130.86, 129.17, 128.88, 128.70, 128.00, 127.86, 126.00, 125.93, 125.35, 124.47, 123.70, 119.91, 119.83, 115.00, 26.57.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{15}ON^{35}Cl$: 320.08367; found: 320.08374; *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{15}ON^{37}Cl$: 322.08072; found: 322.08067.

1-Arylcarbazoles 5 by Hydrolysis of *N*-Acetyl-1-arylcarbazoles 2; General Procedure
The *N*-acetyl-1-arylcarbazole **2** (0.1 mmol) was taken up in MeOH (1 mL) in a 4 mL screw-capped vial, and KOH pellets (1.5 mmol) were added. Then, the reaction mixture was heated to reflux under continuous stirring. After 4 h, the mixture was cooled and neutralized with sat. aq NH_4Cl soln, then extracted with CH_2Cl_2 (3 × 20 mL). The extracts were washed with H_2O (15 mL) and brine (10 mL), dried (anhyd Na_2SO_4), concentrated under reduced pressure and purified by silica gel column chromatography (2–3% EtOAc in petroleum ether).

7-Chloro-1-(4-chlorophenyl)-9*H*-carbazole (5a)
White amorphous solid; yield: 23.7 mg (76%).

FT-IR: 3443, 3061, 2925, 1622, 1595, 1502, 1484, 1442, 1423, 1390, 1334, 1312, 1293, 1177, 1132 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.18 (s, 1 H), 8.03 (d, *J* = 7.5 Hz, 1 H), 7.99 (d, *J* = 8.3 Hz, 1 H), 7.59 (d, *J* = 8.2 Hz, 2 H), 7.53 (d, *J* = 8.2 Hz, 2 H), 7.43–7.37 (m, 2 H), 7.33 (t, *J* = 7.5 Hz, 1 H), 7.23 (d, *J* = 8.2 Hz, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.06, 137.46, 137.25, 133.85, 131.86, 129.73, 129.66, 126.08, 124.15, 123.42, 122.27, 121.44, 120.63, 120.50, 119.87, 110.95.

GC-MS: *m*/*z* (%) = 313 (73) $[M^+]$, 311 (100), 275 (27), 241 (52), 213 (6), 155 (9), 137 (8), 119 (15).

6-Methyl-1-*m*-tolyl-9*H*-carbazole (5b) (Major Isomer)
Light green oil; yield: 26 mg (96%).

FT-IR: 3432, 3028, 2919, 2857, 1605, 1503, 1477, 1400, 1333, 1293, 1232 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.21 (s, 1 H), 8.05 (d, *J* = 7.7 Hz, 1 H), 7.92 (s, 1 H), 7.53–7.50 (m, 2 H), 7.48–7.41 (m, 2 H), 7.32 (d, *J* = 7.6 Hz, 2 H), 7.28–7.24 (m, 2 H), 2.56 (s, 3 H), 2.50 (s, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.25, 139.07, 137.83, 137.75, 129.25, 129.23, 128.93, 128.39, 127.40, 125.66, 125.52, 125.24, 123.88, 123.66, 120.49, 119.78, 119.42, 110.45, 21.75, 21.60.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{18}N$: 272.14338; found: 272.14328.

3-Chloro-1-phenyl-9*H*-carbazole (5c)
Colorless oil; yield: 18 mg (65%).

FT-IR: 3441, 3058, 2925, 1622, 1584, 1494, 1475, 1444, 1402, 1308, 1247, 1232, 1148, 1112 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 8.06 (d, *J* = 7.8 Hz, 1 H), 8.03 (d, *J* = 1.9 Hz, 1 H), 7.68–7.64 (m, 2 H), 7.57 (dd, *J* = 10.5, 4.9 Hz, 2 H), 7.50–7.38 (m, 4 H), 7.30–7.24 (m, 1 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 140.06, 137.93, 135.79, 129.53, 128.42, 128.22, 126.77, 126.30, 125.71, 125.50, 124.96, 122.87, 120.76, 120.05, 119.17, 111.04.

HRMS: *m*/*z* $[M^+]$ calcd for $C_{18}H_{12}N^{35}Cl$: 277.06528; found: 277.06525; *m*/*z* $[M^+]$ calcd for $C_{18}H_{12}N^{37}Cl$: 279.06233; found: 279.06253.

3-Butyl-1-phenyl-9*H*-carbazole (5d)
Light green oil; yield: 29.3 mg (98%).

FT-IR: 3432, 3055, 3030, 2925, 2854, 1605, 1497, 1449, 1411, 1389, 1315, 1258, 1234 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.22 (s, 1 H), 8.12 (d, *J* = 7.8 Hz, 1 H), 7.92 (d, *J* = 1.5 Hz, 1 H), 7.75–7.71 (m, 2 H), 7.61–7.55 (m, 2 H), 7.49–7.38 (m, 3 H), 7.32 (d, *J* = 1.5 Hz, 1 H), 7.29–7.24 (m, 1 H), 2.90–2.86 (m, 2 H), 1.83–1.74 (m, 2 H), 1.49 (dq, *J* = 14.7, 7.4 Hz, 2 H), 1.02 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 139.95, 139.42, 135.82, 134.74, 129.33, 128.50, 127.56, 126.75, 125.87, 124.80, 123.99, 123.66, 120.50, 119.45, 118.98, 110.77, 35.92, 34.68, 22.63, 14.21.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{22}N$: 300.17468; found: 300.17465.

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