Synthesis J. C. F. Barcellos et al. Paper

Synthesis of 11a-*N*-Arylsulfonyl-5-carbapterocarpans (Tetrahydro-5*H*-benzo[*a*]carbazoles) by Azaarylation of Dihydronaphthalenes with *o*-Iodo-*N*-(Arylsulfonyl)anilines in Poly(ethylene glycol)

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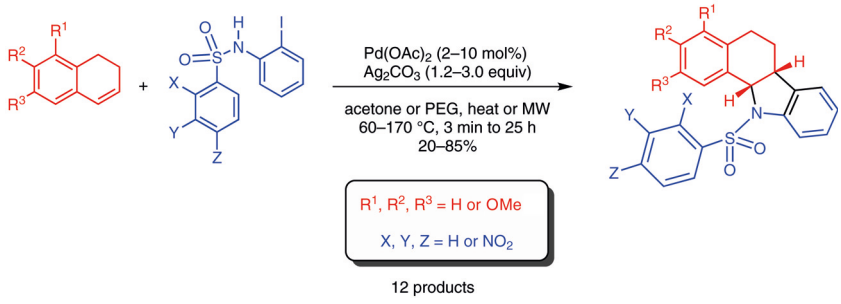

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Abstract 11a-*N*-Arylsulfonyl-5-carbapterocarpans (tetrahydro-5*H*-benzo[*a*]carbazoles) were synthesized by palladium-catalyzed azaarylation of dihydronaphthalenes with *o*-iodo-*N*-(arylsulfonyl)anilines in poly(ethylene glycol) (PEG-400). Better chemical yields (moderate to good) and shorter reaction times (a few minutes at 130–170 °C) were observed in PEG-400 compared with the corresponding reactions in acetone.

Key words arylations, sulfonamides, cyclizations, heterocyclic compounds, polycyclic compounds, indolines, solvent effects, catalysis, palladium

Crotonates undergo tandem Heck lactamizations with arylpalladium species bearing an amine group or an *N*-protected derivative at the *ortho*-position to give six-membered heterocycles such as quinolones[1a] or naphthyridinones.[1b] In contrast, indolines are obtained by azaarylation reactions when cyclohexadiene,[2a] acyclic dienes,[2a] indene,[2b] norbornadiene,[2c] dihydronaphthalene,[2b,c] allenes,[2d] or [60]fullerene[2e] are used as olefins. A stereoselective arylpalladium-catalyzed cyclopentannulation of diazabicyclic alkenes with *ortho*-functionalized aryl halides under microwave irradiation has also been reported.[2f]

As part of a program to identify new compounds with antineoplastic properties based on a modification of the chemical structures of isoflavonoids, we previously synthesized LQB-226, a 11a-*N*-tosylpterocarpan and its 5-carba analogue LQB-223 (**3a**) by azaarylation of chromene or dihydronaphthalene, respectively, with *N*-(2-iodophenyl)-4-toluenesulfonamide (Figure 1).[3a]

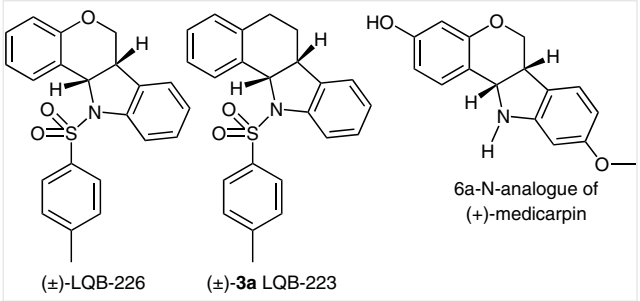


Figure 1 11a-N-Pterocarpans and a carba analogue

LQB-223 (**3a**) displayed antineoplastic activities against a series of cancer cells lines[3a] (including leukemias with the multidrug-resistant phenotype),[3b] antileishmanial activity in culture,[3a] and antimalarial activity in mice.[3c] Interestingly, in 2013 the first example of a natural 11a-N-pterocarpan, an analogue of medicarpin isolated from the roots of *Robinia pseudoacacia*, was reported in the literature.[4] The pharmacological properties of LQB-223 (**3a**) encouraged us to study the scope of the azaarylation reactions of a group of dihydronaphthalenes and *N*-(arylsulfonyl)-*o*-iodoanilines. We surmised that poly(ethylene glycol) with a molecular weight of 400 (PEG-400) might be useful as a solvent for these reactions, as it has been used as a green solvent for palladium-catalyzed Heck reactions and Stille, Sonogashira, and Suzuki–Miyaura cross-coupling reactions.[5] Moreover, Liu and co-workers[5e] and Razler et al.[5i] had shown that PEG-400 and PEG-2000, respectively, promote the formation of palladium nanoparticles, increasing the efficiency of the catalyst in Suzuki coupling reactions. We report rapid, li-

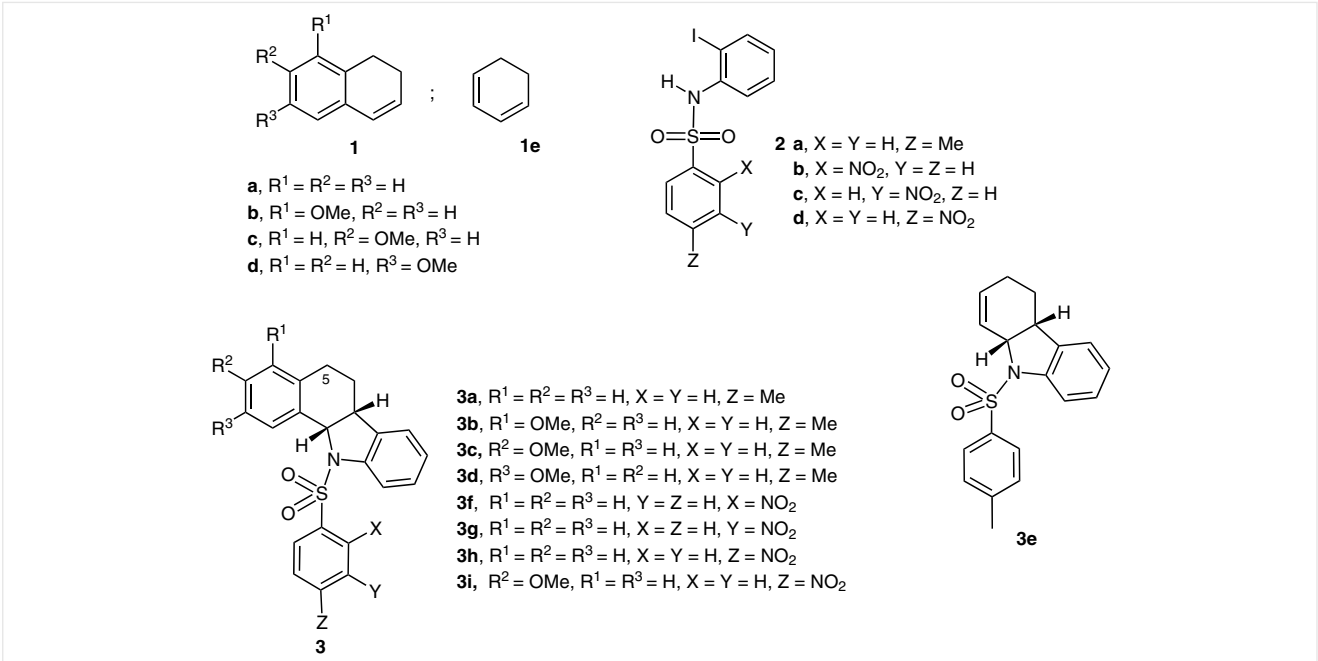
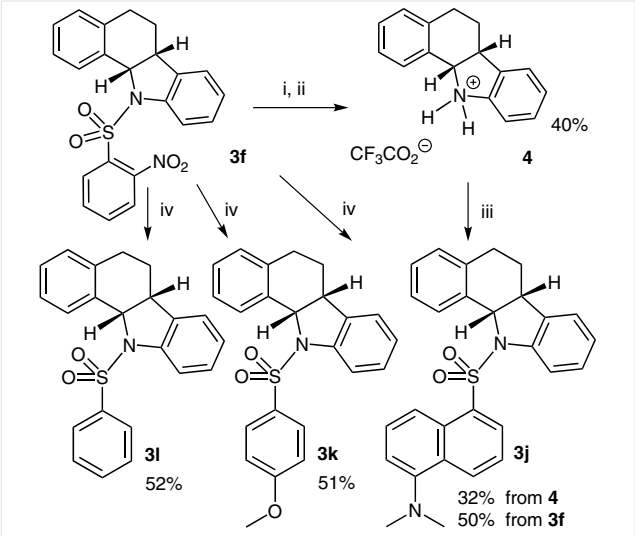


Figure 2 Olefins **1a**–**e**, *N*-(phenylsulfonyl)-*o*-iodoanilines **2a**–**d**, and tetrahydro(benzo)carbazoles **3a**–**i**

gand-free, azaarylations of 1,2-dihydronaphthalene (**1a**), its oxygenated derivatives **1b**–**d**, and cyclohexa-1,3-diene (**1e**) with *N*-(2-iodophenyl)-4-toluenesulfonamide (**2a**) or its nitro derivatives **2b**–**d** in the presence of palladium(II) acetate as a precatalyst, silver(I) carbonate as a base, and PEG-400 as the solvent to give the tetrahydro(benzo)carbazoles **3a**–**i** (Figure 2).

As previously described,[3] tetrahydrobenzocarbazole **3a** was obtained in good yield by palladium-catalyzed [10 mol% $Pd(OAc)_2$] azaarylation of 1,2-dihydronaphthalene (**1a**) with sulfonamide **2a** in refluxing acetone containing three equivalents of silver carbonate (Table 1, entry 1). The same yield was obtained when 1.2 equivalents of silver carbonate were used, although the reaction time increased from 12 hours to 20 hours (entry 2). With microwave irradiation (200 W, 120 °C) in acetone, the reaction was faster, but the yield fell from 85% to 70% (entry 3). We then examined the use of PEG-400 as solvent and, after some experimentation, we decided to use 10 mol% of palladium(II) acetate and 1.2 equivalents of silver carbonate at 170 °C (entry 4); under these conditions, compound **3a** was obtained in 80% yield after only three minutes. Similar yields were obtained when 5 or 2.5 mol% of palladium(II) acetate was used as the precatalyst (entries 6 and 7, respectively), although longer reaction times of 25 and 40 minutes, respectively, were required. A moderate yield was obtained in the presence of 1 mol% of palladium(II) acetate after two hours of reaction (entry 7). In contrast with acetone, the reaction in PEG-400 was clean, and the crude products could be readily purified by flash chromatography and subsequent crystallization.

To examine further the scope of this reaction, we selected the methoxylated dihydronaphthalenes **1b**–**d** as olefins. These compounds were prepared from the corresponding commercially available α-tetralones by carbonyl-group re-



Scheme 1 Synthetic approaches to sulfonamides **3j**, **3k**, and **3l**. *Reaction conditions*: (i) PhSH (5% in DMF), K_2CO_3, r.t., 5 min; (ii) TFA, Et_2O, r.t., 5 min; (iii) RSO_2Cl, py, $CHCl_3$, 40 °C, 20 h; (iv) (i) then (iii) (N–H intermediate used without purification).

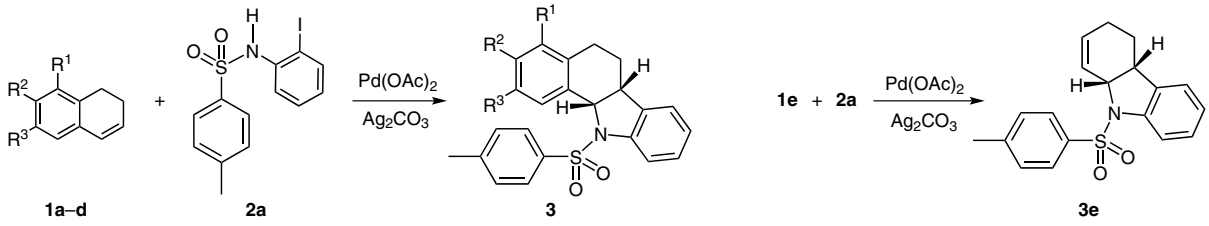
duction followed by elimination of water from the resulting alcohols.[6] Cyclohexa-1,3-diene (**1e**) is commercially available.

The substituted dihydronaphthalene **1b** was as reactive as **1a**, but the reactions were less clean and gave lower yields of tetrahydrobenzocarbazole **3a** (Table 1; entries 8–10). In acetone, **3b** was obtained in 45% yield, after 20 hours of reaction (entry 8). Extensive degradation was observed when olefin **1b** was allowed to react with sulfonamide **2a** in PEG-400 at 170 °C; however, when the temperature was decreased to 130 °C, product **3b** was obtained in the same yield after 10 minutes of reaction (entry 9). The yield in PEG-400 decreased when 5 mol% of palladium(II) acetate was used as the precatalyst (entry 10). The same trend was observed for the other azaarylations reactions studied, and adducts **3c** and **3d** were obtained in shorter reaction times and in better chemical yields in the presence of 5 or 10 mol% of palladium(II) diacetate in PEG-400 than for the corresponding reactions in acetone (entries 11–16). As in the case of **1b**, the reactions of **1c** and **1d** were also performed at 130 °C to minimize the formation of byproducts.

When cyclohexadiene reacted with sulfonamide **2a** in acetone, extensive degradation was observed and, after 4 hours, all the starting materials were consumed and adduct **3e** obtained in only 20% yield (entry 17). Interestingly, adduct **3e** was obtained in 41% yield in PEG-400, but 25 hours at 100 °C was necessary to ensure complete consumption of **1e**, demonstrating the low reactivity of this conjugate diene (entry 18).

As the antineoplastic action of compounds this type is dependent on the type of substituent on the nitrogen atom, we examined the azaarylation of **1a** and **1c** with sulfonamides **2b–d** to give tetrahydrobenzocarbazoles **3f–i** (Table 2).

Table 1 Azaarylation of 1,2-Dihydronaphthalenes **1a–d** with *N*-(2-Iodophenyl)-4-toluenesulfonamide (**2a**)

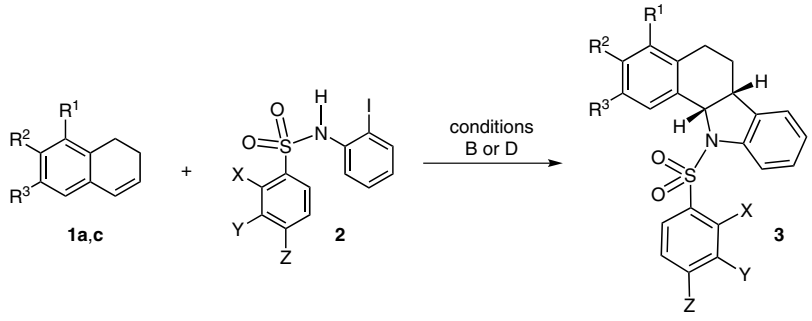


1a–d **2a** **3** **3e**

Entry	1	R^1	R^2	R^3	Conditions[a]	$Pd(OAc)_2$ (mol%)	Temp (°C)	Time	Product	Yield (%)
1	**1a**	H	H	H	A	10	60	12 h	**3a**	85
2	**1a**	H	H	H	B	10	60	20 h	**3a**	85
3	**1a**	H	H	H	C	10	120	20 min	**3a**	70
4	**1a**	H	H	H	D	10	170	3 min	**3a**	80
5	**1a**	H	H	H	D	5	170	25 min	**3a**	80
6	**1a**	H	H	H	D	2.5	170	40 min	**3a**	73
7	**1a**	H	H	H	D	1	170	2 h	**3a**	45
8	**1b**	OMe	H	H	B	10	60	20 h	**3b**	45
9	**1b**	OMe	H	H	D	10	130	10 min	**3b**	45
10	**1b**	OMe	H	H	D	5	130	10 min	**3b**	35
11	**1c**	H	OMe	H	B	10	60	20 h	**3c**	35
12	**1c**	H	OMe	H	D	10	130	10 min	**3c**	55
13	**1c**	H	OMe	H	D	5	130	40 min	**3c**	50
14	**1d**	H	H	OMe	B	10	60	20	**3d**	24
15	**1d**	H	H	OMe	D	10	130	30 min	**3d**	42
16	**1d**	H	H	OMe	D	5	130	50 min	**3d**	30
17	**1e**	cyclohexa-1,3-diene			B	10	60	4 h	**3e**	20
18	**1e**	cyclohexa-1,3-diene			E	10	100	25 h	**3e**	41

[a] Conditions A: $Pd(OAc)_2$, Ag_2CO_3 (3 equiv), acetone, reflux. Conditions B: $Pd(OAc)_2$, Ag_2CO_3 (1.2 equiv), acetone, reflux. Conditions C: $Pd(OAc)_2$, Ag_2CO_3 (1.1 equiv), acetone, MW (200 W), 120 °C, 20 min. Conditions D: $Pd(OAc)_2$, Ag_2CO_3 (1.2 equiv), PEG-400; E: $Pd(OAc)_2$, Ag_2CO_3 (2 equiv), PEG-400.
[b] Yield after crystallization of the crude product (MeOH–hexane).
[c] Ag_2CO_3 (2 equiv).

Table 2 Azaarylation of Dihydronaphthalenes **1a** and **1c** with Sulfonamides **2b–d**



Entry	1	R^1	R^2	R^3	2	X	Y	Z	Conditions[a]	Time (h)	Product	Yield (%)
1	**1a**	H	H	H	**2b**	NO_2	H	H	B	20	**3f**	46
2	**1a**	H	H	H	**2b**	H	H	H	D	1	**3f**	60
3	**1a**	H	H	H	**2c**	H	NO_2	H	B	20	**3g**	30
4	**1a**	H	H	H	**2c**	H	NO_2	H	D	1.5	**3g**	43
5	**1a**	H	H	H	**2d**	H	H	NO_2	B	20	**3h**	35
6	**1a**	H	H	H	**2d**	H	H	NO_2	D	1	**3h**	60
7	**1c**	H	OMe	H	**2d**	H	H	NO_2	B	20	**3i**	40
8	**1c**	H	OMe	H	**2d**	H	H	NO_2	D	2	**3i**	41

[a] Conditions B: $Pd(OAc)_2$ (10 mol%), Ag_2CO_3(1.2 equiv), acetone, reflux. Conditions D: $Pd(OAc)_2$ (10 mol%), Ag_2CO_3 (1.2 equiv), PEG-400, 100 °C.

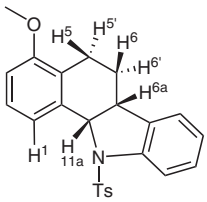
As observed for **2a**, shorter reaction times were required in PEG-400 at 100 °C than in refluxing acetone (Table 2). Azaarylation of **1a** with **2b–d** gave the corresponding tetrahydrobenzocarbazoles **3f–h** in moderate yields in PEG-400 (Conditions D; Table 2, entries 2, 4, and 6), but in low yields in acetone (Conditions B; entries 1, 3, and 5). Azaarylation of olefin **1c** with **2d** under Conditions B and D gave adduct **3i** in similar moderate yields (entries 7 and 8).

The relative configuration of H6a and H11a in compounds **3a–i** and **4** was determined by ^{1}H NMR spectroscopy. The presence of doublets for H11a (δ = 5.2–5.5 ppm) with $J_{H11a,6a}$ = 8.0–8.9 Hz in each of their spectra is in agreement with the proposed *cis*-stereochemistry;[3] this configuration was confirmed by a NOESY experiment; Table 3 shows the NOESY interactions for adduct **3b** as an example.

An additional possibility for the introduction of chemical diversity at the nitrogen atom is the removal of the *N*-arylsulfonyl group (Scheme 1). The use of thiophenol to cleave an *o*-nitroarylsulfonyl group in the corresponding sulfonamide had been reported,[7] and we therefore tried using these conditions. The reaction of tetrahydrobenzocarbazole **3f** was very rapid, and the resulting amine was obtained in pure form by dissolving the crude product in diethyl ether and adding trifluoroacetic acid to precipitate the corresponding trifluoroacetate salt **4.** As expected, neither **3g** nor **3h** gave **4** when treated under similar conditions.[7c]

Compound **4** was used in an alternative approach to prepare other *N*-(arylsulfonyl)-5-carbapterocarpans (Scheme 1). Treatment of the isolated salt **4** with dansyl chloride [5-(dimethylamino)naphthalene-1-sulfonyl chloride] in pyridine gave the dansyl derivative **3j** in 32% yield.[5] To increase the efficiency of this process, we decided to investigate the use of the unpurified free amino derivative intermediate obtained from **3f**. Under these conditions, sulfonamides **3j**, **3k**, and **3l** were obtained in yields of about 50%. The dansyl group is fluorescent, and its chloride reacts with basic amino acids of proteins, permitting studies of the cellular localization of the resulting marked proteins.[8]

Table 3 Chemical Shifts in $CDCl_3$ and NOESY Interactions for Adduct **3b**



3b

H atom	δ (ppm)	NOESY
H1	7.61	H-11a
H6	2.15	H-6a, H-5
H6a	3.01	H-11a, H-6, H-5
H11a	5.41	H-6a, H-1

In conclusion, the use of PEG-400 as solvent permitted the desired transformations to be carried out in the absence of ligands within 10–60 minutes at 130–170 °C. Protection of the nitrogen atom with a (2-nitrobenzenesulfonyl) group provides an alternative approach to the preparation of the target compounds. The pharmacological properties of these new compounds and their derivatives are under investigation.

Starting materials (dihydronaphthalene, 1,3-cyclohexadiene, methoxylated tetralones and 2-iodoaniline) and PEG-400 were purchased from Sigma-Aldrich®.

Microwave irradiation experiments described herein were performed using a single-mode Discover Labmate System from CEM Corp. using standard Pyrex vessels (capacity 10 mL).

Melting points measurements were determinated in a Thomas Hoover capillary melting point apparatus.

The ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini-200 (400 MHz and 500 MHz). The coupling constants (*J*) are in hertz (Hz). The chemical shifts are reported in ppm downfield to TMS (δ = 0.00) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 76.90) for ^{13}C NMR, and the relative areas of peaks obtained by electronic integration. Spectra apodization (exponential filter with LB = –0.1–0.5 Hz, Gaussian with LB = 0.1–0.4 GB [Hz], Sine Bell with LB = 4–10 Deg, Sine Square with LB = 90–50 Deg) was realized through MestReNova program version 6.0.2-5475, copyright 2009 Mestrelab Research S. L.

ESI-HRMS analyses were realized in a Bruker MicrOTOF II instrument. Solvents were evaporated under reduced pressure and controlled temperature in an IKA RV 10 control rotary evaporator and IKA HB 10 control water bath. The flash chromatographic separations were performed on silica gel columns using Merck granulation 0.040 to 0.063 mm. The monitoring of chromatographic separations and reaction processes were performed in SiliCycle Twin Layer Chromatography aluminum silica gel 60 F_{254} leaves, visualized by irradiation with UV at 254 nm, I_2 or 7% phosphomolybdic acid in ethanol, followed by heating.

Tetrahydro(benzo)carbazoles 3; General Procedure

A mixture of the appropriate dihydronaphthalene **1a**–**e** (1.0 mmol), sulfonamide **2a**–**d** (1.2 mmol),[9] $Pd(OAc)_2$ (1–10 mol%), and Ag_2CO_3 (1.2 mmol) in PEG-400 (1 mL) was immersed in a preheated graphite bath and stirred for the times and temperatures shown in Tables 1 and 2. EtOAc (10 mL) and brine (50 mL) were then added, and the mixture was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, dried (Na_2SO_4), and concentrated. The crude mixture was pre-purified by flash chromatography [silica gel, 20% EtOAc–hexane] to give brute **3a**–**i** as oils. For **3a**–**d**, the oil was dissolved in a minimal volume of a warm MeOH (~5 mL) and cold hexane (~5 mL) was added. The mixture was allowed to stand overnight in a freezer, and then the pure products were collected as solids by filtration. For adducts **3f**–**i**, the oils were dissolved in a minimal volume of warm 5% CH_2Cl_2–EtOH solution (~5 mL), cold EtOH (~5 mL) was added, and the products were collected by filtration. The product **3e** was obtained pure directly from the flash chromatography.

11-Tosyl-6,6a,11,11a-tetrahydro-5*H*-benzo[*a*]carbazole (3a)

White solid; yield: 318.7 mg (85%); mp 165 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 7.8 Hz, 1 H), 7.59 (d, *J* = 8.0 Hz, 1 H), 7.48 (d, *J* = 8.3 Hz, 2 H), 7.28–7.06 (m, 6 H), 7.02 (d, *J* = 7.4 Hz, 1 H), 6.91 (d, *J* = 7.6 Hz, 1 H), 5.38 (d, *J* = 8.5 Hz, 1 H), 3.10–3.04 (m, 1 H), 2.50–2.44 (m, 2 H), 2.35 (s, 3 H), 2.16–1.90 (m, 2 H).

^{13}C NMR (APT; 101 MHz, $CDCl_3$): δ = 152.15, 137.57, 136.24, 135.60, 134.37, 130.49, 129.56, 127.97, 127.86, 127.34, 127.07, 126.82, 125.71, 123.39, 119.96, 64.01, 39.45, 24.85, 23.64, 21.553.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{21}NNaO_2S$: 398.1185; found: 398.1187.

4-Methoxy-11-tosyl-6,6a,11,11a-tetrahydro-5*H*-benzo[*a*]carbazole (3b)

White solid; yield: 182.3 mg (45%); mp 205–208 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 7.62–7.56 (m, 2 H), 7.49 (d, *J* = 7.8 Hz, 2 H), 7.27–6.96 (m, 6 H), 6.66 (d, *J* = 8.0 Hz, 1 H), 5.41 (d, *J* = 8.1 Hz, 1 H), 3.70 (s, 3 H), 3.03–2.97 (m, 1 H), 2.69 (d, *J* = 17.6 Hz, 1 H), 2.34 (s, 3 H), 2.19–2.13 (m, 2 H), 1.90–1.84 (m, 1 H).

^{13}C NMR (HSQC; 100 MHz, $CDCl_3$): δ = 155.77, 143.81, 142.03, 136.12, 135.63, 135.31, 129.56, 127.78, 127.00, 126.82, 126.63, 125.68, 123.30, 122.58, 120.11, 108.39, 64.06, 55.27, 38.95, 22.28, 21.57, 17.28.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{24}H_{23}NNaO_3S$: 428.1291; found: 428.1280.

3-Methoxy-11-tosyl-6,6a,11,11a-tetrahydro-5*H*-benzo[α]carbazole (3c)

White solid; yield: 222.7 mg (55%); mp 168–169 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.7 Hz, 1 H), 7.59 (d, *J* = 7.9 Hz, 1 H), 7.49 (d, *J* = 8.1 Hz, 2 H), 7.23–6.97 (m, 5 H), 6.82 (dd, *J* = 8.6, 2.0 Hz, 1 H), 6.43 (s, 1 H), 5.38 (d, *J* = 8.5 Hz, 1 H), 3.72 (s, 3 H), 3.21–2.96 (m, 1 H), 2.60–2.28 (m, 5 H), 2.15–2.07 (m, 1 H), 2.00–1.91 (m, 1 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 158.61, 143.79, 138.94, 136.10, 131.95, 129.55, 127.86, 127.00, 126.46, 125.64, 123.36, 119.95, 113.08, 112.45, 63.80, 55.15, 39.36, 25.01, 23.53, 21.57.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{24}H_{23}NNaO_3S$: 428.1291; found: 428.1283.

4-Methoxy-11-tosyl-6,6a,11,11a-tetrahydro-5*H*-benzo[α]carbazole (3d)

White solid; yield: 169.5 mg (42%); mp 177°C.

^{1}H NMR (COSY; 500 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.0 Hz, 1 H), 7.55 (d, *J* = 1.7 Hz, 1 H), 7.50 (d, *J* = 8.1 Hz, 2 H), 7.20 (t, *J* = 7.7 Hz, 1 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 7.10 (t, *J* = 7.4 Hz, 1 H), 7.03 (d, *J* = 7.4 Hz, 1 H), 6.82 (d, *J* = 8.4 Hz, 1 H), 6.71 (dd, *J* = 8.3, 2.2 Hz, 1 H), 5.36 (d, *J* = 8.5 Hz, 1 H), 3.85 (s, 3 H), 3.13–2.99 (m, 1 H), 2.50–2.30 (m, 5 H), 2.16–2.05 (m, 1 H), 2.02–1.91 (m, 1 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 158.41, 143.83, 142.10, 136.13, 135.59, 135.28, 129.61, 129.56, 128.97, 127.85, 127.03, 125.66, 123.33, 119.96, 114.93, 113.75, 64.18, 55.34, 39.31, 23.91, 23.73, 21.55.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{24}H_{23}NNaO_3S$: 428.1291; found: 428.1284.

9-Tosyl-4,4a,9,9a-tetrahydro-3*H*-carbazole (3e)

Yellow solid; 133.3 mg (41%); mp 134°C.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.0 Hz, 1 H), 7.57 (d, *J* = 8.1 Hz, 2 H), 7.21 (t, *J* = 7.7 Hz, 1 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 7.06 (t, *J* = 7.4 Hz, 1 H), 7.01 (d, *J* = 7.3 Hz, 1 H), 5.88–5.84 (m, 2 H), 4.71 (d, *J* = 8.0 Hz, 1 H), 3.08–3.04 (m, 1 H), 2.35 (s, 3 H), 1.97–1.82 (m, 4 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 143.70, 141.66, 135.69, 135.05, 131.26, 129.55, 127.84, 126.92, 126.11, 124.69, 123.38, 118.06, 61.45, 38.62, 22.66, 21.51, 20.08.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{19}H_{19}NNaO_2S$: 348.1029; found: 348.1022.

11-[(2-Nitrophenyl)sulfonyl]-6,6a,11,11a-tetrahydro-5*H*-benzo[*a*]carbazole (3f)

Yellow solid; yield: 244.0 mg (60%); mp 124–126 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 7.8 Hz, 1 H), 7.64–7.48 (m, 4 H), 7.44 –7.36 (m, 1 H), 7.28–7.08 (m, 5 H), 6.93 (d, *J* = 7.5 Hz, 1 H), 5.81 (d, *J* = 8.3 Hz, 1 H), 3.76–3.54 (m, 1 H), 2.63–2.42 (m, 2 H), 2.27–2.06 (m, 2 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 148.12, 140.88, 137.80, 135.89, 133.97, 131.25, 131.05, 130.77, 130.39, 128.16, 127.99, 127.53, 126.84, 125.97, 123.94, 123.81, 118.69, 64.67, 39.71, 24.80, 23.63.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{22}H_{18}N_2NaO_4S$: 429.0879; found: 429.0871.

11-[(3-Nitrophenyl)sulfonyl]-6,6a,11,11a-tetrahydro-5*H*-benzo[*a*]carbazole (3g)

Yellow solid; yield: 174.6 mg (43%); mp 154–156 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 8.47 (t, *J* = 1.8 Hz, 1 H), 8.35 (dd, *J* = 8.2, 2.2 Hz, 1 H), 7.95–7.86 (m, 2 H), 7.61 (d, *J* = 8.0 Hz, 1 H), 7.56 (t, *J* = 8.0 Hz, 1 H), 7.30–7.22 (m, 2 H), 7.17–7.10 (m, 2 H), 7.05 (d, *J* = 7.5 Hz, 1 H), 6.92 (d, *J* = 7.5 Hz, 1 H), 5.49 (d, *J* = 8.6 Hz, 1 H), 3.15–3.09 (m, 1 H), 2.50–2.44 (m, 2 H), 2.12–2.08 (m, 1 H), 2.07–1.95 (m, 1 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 148.06, 141.18, 140.62, 137.78, 135.75, 133.43, 132.34, 130.49, 130.46, 130.29, 130.24, 128.33, 128.14, 127.72, 127.37, 126.93, 126.38, 123.85, 119.42, 64.55, 39.63, 24.72, 23.96.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{22}H_{18}N_2NaO_4S$: 429.0879; found: 429.0878.

11-[(4-Nitrophenyl)sulfonyl]-6,6a,11,11a-tetrahydro-5*H*-benzo[*a*]carbazole (3h)

Yellow solid; yield: 243.7 mg (60%); mp 97–100 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 8.21 (d, *J* = 8.8 Hz, 2 H), 7.94 (d, *J* = 7.8 Hz, 1 H), 7.81 (d, *J* = 8.8 Hz, 2 H), 7.62 (d, *J* = 8.0 Hz, 1 H), 7.29–7.25 (m, 2 H), 7.18–7.14 (m, 2 H), 7.08 (d, *J* = 7.5 Hz, 1 H), 6.94 (d, *J* = 7.6 Hz, 1 H), 5.47 (d, *J* = 8.5 Hz, 1 H), 3.18–3.07 (m, 1 H), 2.55–2.44 (m, 2 H), 2.19–1.94 (m, 2 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 150.20, 144.14, 141.07, 137.68, 135.83, 133.41, 130.40, 128.26, 128.21, 128.18, 127.71, 126.93, 126.41, 124.13, 123.86, 119.62, 64.47, 39.52, 29.70, 24.64, 23.64.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{22}H_{18}N_2NaO_4S$: 429.0879; found: 429.0882.

3-Methoxy-11-[(4-nitrophenyl)sulfonyl]-6,6a,11,11a-tetrahydro-5*H*-benzo[*a*]carbazole (3i)

Yellow solid; yield: 178.8 mg (41%); mp 167–168 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 8.6 Hz, 2 H), 7.82–7.80 (m, 3 H), 7.59 (d, *J* = 7.9 Hz, 1 H), 7.26–7.18 (m, 1 H), 7.13 (t, *J* = 7.4 Hz, 1 H), 7.06 (d, *J* = 7.4 Hz, 1 H), 6.82 (dd, *J* = 8.6, 2.4 Hz, 1 H), 6.43 (d, *J* = 2.02 Hz, 1 H), 5.44 (d, *J* = 8.5 Hz, 1 H), 3.73 (s, 3 H), 3.14–3.04 (m, 1 H), 2.52–2.32 (m, 2 H), 2.16–2.07 (m, 1 H), 2.01–1.88 (m, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.85, 150.16, 144.26, 141.03, 139.14, 135.74, 131.87, 128.25, 128.16, 126.32, 125.48, 124.11, 123.84, 119.54, 113.18, 112.58, 64.33, 55.17, 39.47, 24.86, 23.62.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{20}N_2NaO_5S$: 459.0985; found: 459.0986.

6,6a,11,11a-Tetrahydro-5*H*-benzo[*a*]carbazolium Trifluoroacetate (4)

A solution of PhSH (28 mg, 0.25 mmol) in DMF (0.5 mL) was added to a mixture of sulfonamide **3f** (100 mg, 0.25 mmol) and K_2CO_3 (52 mg, 0.38 mmol), and the mixture was stirred for 5 min. EtOAc (2 mL) was added and the mixture was washed with brine (3 × 3 mL). The organic layer was dried (Na_2SO_4) and concentrated under vacuum. The crude product was filtered through silica gel with hexane as eluent to give a yellow oil (58 mg) that was dissolved Et_2O (1 mL) and treated with TFA (23 µL, 0.3 mmol). The precipitate was collected by filtration to give a white crystal; yield: 22.1 mg (40%); mp 157 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 8.82 (s, 2 H), 7.62–7.50 (m, 1 H), 7.46–7.17 (m, 7 H), 5.21 (d, *J* = 7.6 Hz, 1 H), 3.76–3.56 (m, 1 H), 3.00–2.69 (m, 2 H), 2.14 (dq, *J* = 14.0, 4.7 Hz, 1 H), 1.96 (dtd, *J* = 15.2, 10.5, 4.7 Hz, 1 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 138.79, 138.20, 137.37, 129.72, 129.26, 128.64, 129.02, 128.69, 127.05, 124.95, 118.64, 60.55, 41.48, 28.19, 26.68.

HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{18}H_{16}N$: 222.1277; found: 222.1271.

N,*N*-Dimethyl-5-(5,6,6a,11a-tetrahydro-11*H*-benzo[*a*]carbazol-11-ylsulfonyl)naphthalen-1-amine (3j)

Anhydrous pyridine (28 µL) was added to a mixture of TFA salt **4** (62.5 mg, 0.28 mmol) and dansyl chloride (91.5 mg, 0.34 mmol) in anhydrous chloroform (0.28 mL) under argon, and the mixture was kept for 20 h at 40 °C. The crude product was purified by chromatography (silica gel, 10% EtOAc–hexane) to give **3j** as a yellow oil; yield: 40.5 mg (32%).

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 8.49 (d, *J* = 8.5 Hz, 1 H), 8.24 (d, *J* = 8.7 Hz, 1 H), 8.16 (d, *J* = 7.4 Hz, 1 H), 8.01 (d, *J* = 7.8 Hz, 1 H), 7.55 (d, *J* = 8.0 Hz, 1 H), 7.40 (t, *J* = 8.0 Hz, 1 H), 7.30–7.01 (m, 6 H), 6.90 (t, *J* = 7.1 Hz, 2 H), 5.56 (d, *J* = 8.3 Hz, 1 H), 3.04–2.94 (m, 1 H), 2.84 (s, 6 H), 2.56–2.44 (m, 1 H), 2.41 (m, 1 H), 2.06–1.96 (m, 1 H), 1.92–1.84 (m, 1 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 151.31, 142.20, 137.75, 135.95, 134.80, 134.35, 130.53, 130.47, 130.37, 130.25, 129.80, 128.04, 127.72, 127.59, 127.39, 126.70, 125.47, 123.42, 123.12, 119.79, 119.46, 115.16, 64.19, 45.37, 39.58, 24.86, 23.57.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{28}H_{26}N_2NaO_2S$: 477.1607; found: 477.1611.

11-(Arylsulfonyl)-6,6a,11,11a-tetrahydro-5*H*-benzo[*a*]carbazoles (3j–l); General Procedure

A solution of PhSH (56 mg, 0.5 mmol) in DMF (1.0 mL) was added to a mixture of sulfonamide **3f** (200 mg, 0.5 mmol) and K_2CO_3 (152 mg, 1.2 mmol), and the mixture was stirred for 5 min. EtOAc (3 mL) was added, and the mixture was washed with brine (3 × 3 mL). The organ-

ic layer was dried (Na_2SO_4) and concentrated under vacuum, and the crude product was filtered through silica gel (5% EtOAc–hexane eluent). The resulting yellow oil (189.5 mg) was dissolved in anhydrous CH_2Cl_2 (0.4 mL) and the appropriate sulfonyl chloride (0.5 mmol) and anhydrous pyridine (40 µL, 0.5 mmol) were added under argon. The mixture was kept for 20 h at 40 °C and then purified by chromatography (silica gel; 10% EtOAc–hexane).

_N,N_-Dimethyl-5-(5,6,6a,11a-tetrahydro-11_H_-benzo[_a_]carbazol-11-ylsulfonyl)naphthalen-1-amine (3j)

Yellow oil; yield: 112.9 mg (50%); for spectroscopic details, see above.

11-(Phenylsulfonyl)-6,6a,11,11a-tetrahydro-5_H_-benzo[_a_]carbazole (3k)

White solid; yield: 94.0 mg (52%); mp 167–169 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 7.8 Hz, 1 H), 7.93–7.87 (m, 3 H), 7.81–7.75 (m, 1 H), 7.66–7.59 (m, 2 H), 7.57–7.51 (m, 1 H), 7.50–7.44 (m, 1 H), 7.41–7.37 (m, 2 H), 7.31 (d, *J* = 7.5 Hz, 1 H), 7.19 (d, *J* = 7.6 Hz, 1 H), 5.72 (d, *J* = 8.6 Hz, 1 H), 3.40–3.32 (m, 1 H), 2.85–2.67 (m, 2 H), 2.42–2.21 (m, 2 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 141.96, 138.35, 137.64, 136.23, 134.26, 133.11, 130.49, 129.00, 128.08, 127.91, 127.41, 127.01, 126.81, 125.90, 123.51, 119.90, 64.11, 39.42, 24.80, 23.57.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{22}H_{19}NNaO_2S$: 384.1029; found: 384.1037.

11-[(4-Methoxyphenyl)sulfonyl]-6,6a,11,11a-tetrahydro-5_H_-benzo[_a_]carbazole (3l)

White solid; yield: 99.5 mg (51%); mp 154–155 °C.

^{1}H NMR (COSY; 400 MHz, $CDCl_3$): δ = 8.55 (d, *J* = 7.8 Hz, 1 H), 8.16 (d, *J* = 7.9 Hz, 1 H), 8.11 (d, *J* = 8.8 Hz, 2 H), 7.82 (t, *J* = 7.5 Hz, 1 H), 7.75 (t, *J* = 7.5 Hz, 1 H), 7.71–7.65 (m, 2 H), 7.60 (d, *J* = 7.4 Hz, 1 H), 7.48 (d, *J* = 7.5 Hz, 1 H), 7.38 (d, *J* = 8.7 Hz, 2 H), 5.96 (d, *J* = 8.5 Hz, 1 H), 4.36 (s, 3 H), 3.74–3.62 (m, 1 H), 3.16–2.95 (m, 2 H), 2.72–2.51 (m, 2 H).

^{13}C NMR (HSQC; 101 MHz, $CDCl_3$): δ = 163.14, 142.19, 137.54, 136.29, 134.38, 130.48, 130.12, 129.09, 127.97, 127.83, 127.31, 126.79, 125.72, 123.39, 120.05, 114.08, 77.36, 77.04, 76.72, 63.95, 55.52, 39.46, 24.81, 23.62.

HRMS (ESI): *m/z* [M + Na]$^+$ calcd for $C_{23}H_{21}NNaO_3S$: 414.1134; found: 414.1137.

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Supporting Information

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