CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

Accepted Article

Title: Brønsted Acid-Catalyzed Tandem Cyclizations of Tryptamine-Ynamides Yielding 1H-Pyrrolo[2,3-d]carbazole Derivatives

Authors: Yanshi Wang, Jingsheng Lin, Xiaoyu Wang, Guanghui Wang, Xinhang Zhang, Bo Yao, Yuandong Zhao, Pengfei Yu, Bin Lin, Yongxiang Liu, and Maosheng Cheng

To be cited as: *Chem. Eur. J.* 10.1002/chem.201705189

Link to VoR: http://dx.doi.org/10.1002/chem.201705189

Supported by
ACES

WILEY-VCH

10.1002/chem.201705189

WILEY-VCH

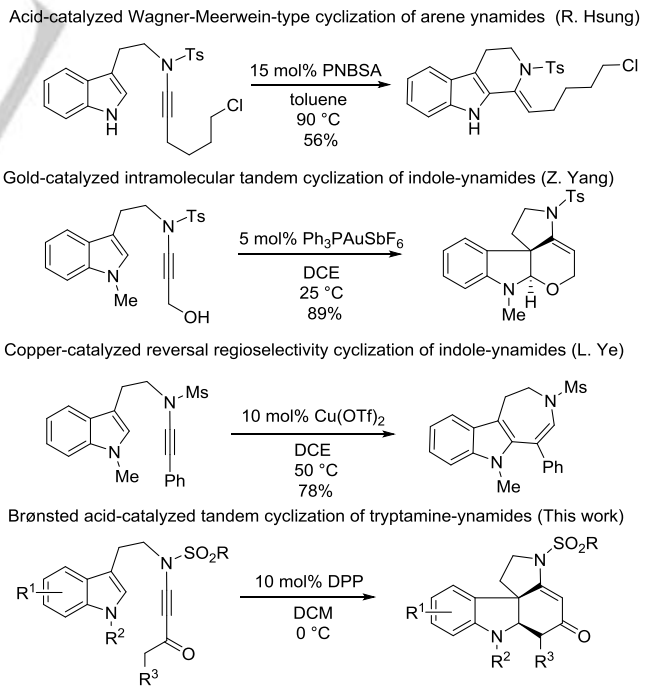
Brønsted Acid-Catalyzed Tandem Cyclizations of Tryptamine-Ynamides Yielding 1*H*-Pyrrolo[2,3-*d*]carbazole Derivatives

Yanshi Wang,[a,b] Jingsheng Lin,[a,b,c] Xiaoyu Wang,[a,b] Guanghui Wang,[a,b,c] Xinhang Zhang,[a,b,c] Bo Yao,[a,b] Yuandong Zhao,[a,b,c] Pengfei Yu,[d] Bin Lin,[a,b] Yongxiang Liu,*[a,b,c] and Maosheng Cheng*[a,b]

Abstract: Ynamide, as a versatile synthetic precursor has gained much attention from synthetic chemists and sparked the development of a number of methodologies in constructing various structures. The 1*H*-pyrrolo[2,3-*d*]carbazole was a core scaffold of a series of monoterpene indole alkaloids such as *Kopsia*, *Strychnos* and *Aspidosperma*. In this study, the 1*H*-pyrrolo[2,3-*d*]carbazole derivatives were synthesized via a Brønsted acid-catalyzed tandem cyclization from tryptamine-based ynamides. This strategy prevented Wagner-Meerwein rearrangement by an instantaneous intramolecular nucleophilic trap to indoleninium via *in situ* formed enol species induced by the formation of a more stable conjugate diene moiety. The functional group tolerances were investigated by a series of readily avalaible substrates. A plausible mechanism was proposed based on the evidence of the capturing of the hemiaminal intermediate. Lastly, a Büchi ketone, which is the pivotal intermediate in the synthesis of indole alkaloid vindorosine, was synthesized by utilizing our newly developed methodology.

Introduction

Ynamides have acted as significant building blocks in organic synthesis, and a number of synthetic methodologies on the basis of ynamides have been developed in the past decade, which afforded unique approaches to diverse structures.[1] Among them, the metal- or acid-catalyzed cycloisomerization of tryptamine-derived ynamide provided a straightforward and atom-economical strategy to prepare polycyclic indoline skeletons and was demonstrated by many pioneering works.[2] For example, Hsung and co-workers developed an acid-catalyzed Pictet-Spengler-type cyclization of arene-ynamides, which represented one of the first applications of ynamides in indole alkaloid synthesis.[2a] Yang and co-workers reported a gold-catalyzed intramolecular consecutive annulation of indole-ynamide to generate pyrrolidinoindoline by using alcohol as the nucleophile to capture the indoleninium.[2b] Recently, Ye and co-workers described a copper-catalyzed regioselectivity-reverse cyclization of arene-ynamide[2c] (Scheme 1). Such examples of tryptamine-derived ynamides cyclizations demonstrated that the substrates and conditions (i.e. the substitutions, the nucleophiles, the types of catalysts, etc.) had a profound influence on the cyclization pathways. In this study, we intended to synthesize 1*H*-pyrrolo[2,3-*d*]carbazoles by applying tryptamine-derived ynone substrates and to prevent Wagner-Meerwein rearrangement by capturing the spirocyclic indoleninium intermediate with *in situ* enolized ketone, which was promoted by the conjugation with the nearby enamide, through an intramolecular Mannich-type reaction via an acid-catalyzed tandem cyclization.



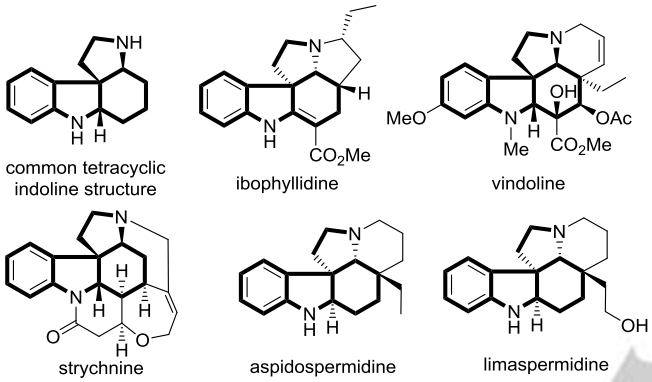
Scheme 1. Tryptamine-derived ynamide cyclizations.

The 1*H*-pyrrolo[2,3-*d*]carbazole scaffold was the core motif of a series of monoterpene indole alkaloids, such as *Kopsia*[3a,3c,3d]

[a] Y. Wang, J. Lin, X. Wang, G. Wang, X. Zhang, B. Yao, Y. Zhao, Prof. Dr. B. Lin, Prof. Dr. Y. Liu, Prof. Dr. M. Cheng
Key Laboratory of Structure-Based Drug Design and Discovery, Ministry of Education
Shenyang Pharmaceutical University
Shenyang 110016, P. R. China
E-mail: yongxiang.liu@syphu.edu.cn (Y. Liu)
mscheng@syphu.edu.cn (M. Cheng)
[b] Y. Wang, J. Lin, X. Wang, G. Wang, X. Zhang, B. Yao, Y. Zhao, Dr. B. Lin, Prof. Dr. Y. Liu, Prof. Dr. M. Cheng
Institute of Drug Research in Medicine Capital of China
Benxi, 117000, P. R. China
[c] J. Lin, G. Wang, X. Zhang, Y. Zhao, Prof. Dr. Y. Liu
Wuya College of Innovation
Shenyang Pharmaceutical University
Shenyang 110016, P. R. China
[d] Dr. P. Yu
State Key Laboratory of Hollow-fiber Membrane Materials and Membrane Processes
School of Environmental and Chemical Engineering, Tianjin Polytechnic University
Tianjin 300387, P. R. China

Supporting information for this article is given via a link at the end of the document.

Strychnos[3b-3e] and *Aspidosperma*[3c-3f] (Scheme 2).[3] The diverse bioactivities[4] (e.g. adrenergic blocking,[4a] anticancer,[4b,4c] antiarrhythmic[4b,4c] and anti-malarial[4d]) and intriguing molecular architectures of these indole alkaloids rendered them highly attractive targets for synthesis.[5] A variety of methodologies have been developed, especially in the construction of the tetracyclic indoline core structure,[6] such as Büchi's Robinson-type annulation,[6a] Padwa's [4+2]-cycloaddition/rearrangement,[6e] Macmillan's organocascade catalysis[6g] and Renaud's cascade radical cyclization.[6h] Herein, we proposed a new method giving access to the tetracyclic indoline core structure based on ynamide chemistry, a field booming in recent years (Scheme 3).

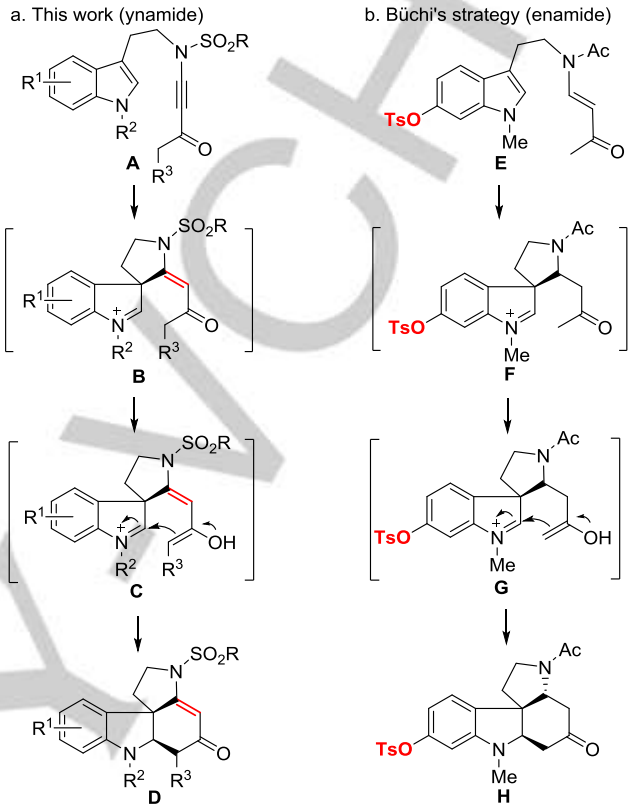


Scheme 2. 1*H*-pyrrolo[2,3-*d*]carbazole-containing indole alkaloids.

Results and Discussion

In the synthesis of the spiroindolines by the indoleninium intermediate, the inherent tendency of C-C bond migration through Wagner-Meerwein rearrangement to generate tricyclic fused ring system was the chief problem. Numerous efforts have been made to restrict such a high tendency to Wagner-Meerwein rearrangement,[6a,7] such as employing strongly nucleophilic intramolecular traps,[6a,7b] introducing electron-deficient groups on the indole and aliphatic nitrogen,[7a,7c] interrupting the Bischler-Napieralski reaction,[7d,7e] introducing electron-withdrawing group to the alkenes, etc.[7f−7j] In this study, we intended to prevent Wagner-Meerwein rearrangement by an instantaneous intramolecular nucleophilic trap to indoleninium as illustrated in Scheme 3a. In our strategy, the active spiroindoleninium intermediate of tryptamine-based ynamide would be trapped to afford a tetracyclic indoline by the easily *in situ* generated enol species, whose formation was facilitated by the presence of the enamide to produce a more stable conjugate diene moiety, and the Wagner-Meerwein rearrangement was prevented by the existence of the enone, which reduced the migratory aptitude of the alkene through electronic effects (Scheme 3a).[7f−7j] In contrast, in the absence of such an enamide, Büchi and his colleagues had to resort to a detour strategy by introducing an electron-withdrawing group (i.e. *p*-toluenesulfonyl) at the indole 6-position in order to ensure the formation of the tetracyclic system instead of a tricyclic product derived from Meerwein-Wagner rearrangement (Scheme 3b).[7a]

Later on, the tedious functional group transformation from a *p*-toluenesulfonyl (Ts) group to a methoxyl group had to be performed to achieve the synthesis of



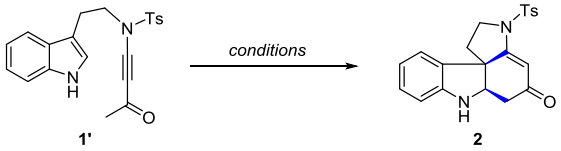
Scheme 3. Our tryptamine-based ynamide strategy and Büchi's tryptamine-based enamide strategy to tetracyclic indolines.

vindoline. Therefore, on the basis of ynamide cycloisomerization, we developed a unique and straightforward method to access Büchi-ketone-like tetracyclic indoline scaffold.[8]

Firstly, we screened the reaction conditions for the cyclization from ynesulfonamide substrate **1'** to 1*H*-pyrrolo[2,3-*d*]carbazole **2**. This substrate could be prepared easily by a copper-catalyzed coupling reaction of tryptamine derived sulfonamide with alkynyl bromide and sequential deprotection/oxidation procedures (see Supporting Information for the details).[9] In the condition screening of the cyclizations, a variety of Brønsted acids,[3a,10] including *p*-toluenesulfonic acid (TsOH), *p*-nitrobenzenesulfonic acid (PNBSA), camphorsulfonic acid (CSA), bis(trifluoromethanesulfonyl) imide ($HNTf_2$) and diphenyl phosphate (DPP) were examined, which led to the identification of DPP as the optimal catalyst in catalyzing this transformation (Table 1, entries 1-5). Decrease of reaction temperature to −10 °C resulted in a much lower yield for the same reaction time (Table 1, entry 6). When the reaction was performed at room temperature, a similar yield was obtained (Table 1, entry 7). Lowering the catalyst loading to 5 mol% gave a relatively lower yield (Table1, entry 8) and increasing of the catalyst loading to 20 mol% gave no obvious elevation to yield (Table 1, entry 9). As for the screening of solvents, several solvents such as toluene, dichloromethane (DCM), 1,2-dichloroethane (DCE), acetonitrile and tetrahydrofuran (THF) were examined, and DCM

was found to be the best solvent (Table 1, entries 10-13). Finally, the optimal conditions were determined as to stir the ketone in dichloromethane (DCM) at 0 °C for 30 minutes at the catalysis of 10 mol% diphenyl phosphate (DPP).

Table 1. Screening of cyclization conditions[a]

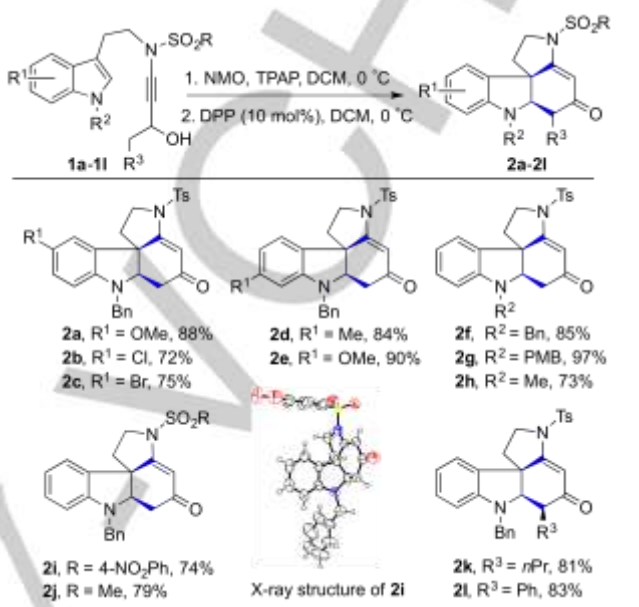


entry	catalyst	loading (mol%)	T (ºC)	solvent	yield (%)[b]
1	TsOH	10	0	DCM	49
2	PNBSA	10	0	DCM	61
3	CSA	10	0	DCM	64
4	$HNTf_2$	10	0	DCM	60
5	**DPP**	**10**	**0**	**DCM**	**69**
6	DPP	10	−10	DCM	37
7	DPP	10	23	DCM	67
8	DPP	5	0	DCM	54
9	DPP	20	0	DCM	70
10	DPP	10	0	toluene	60
11	DPP	10	0	DCE	66
12	DPP	10	0	CH_3CN	65
13	DPP	10	0	THF	33

[a] All reactions were carried out with 0.3 mmol of **1'** in 5.0 mL of solvent within 30 min. [b] Isolated yield.

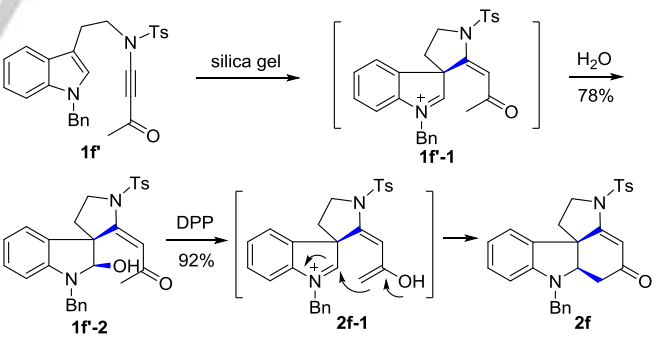
During the condition screening, we found that the ketone substrates were prone to decomposition in the isolation process. To address this issue, a two-step procedure was developed by performing the oxidation and tandem cyclizations in sequence with only one isolation operation afterward. Next, the scopes of this two-step transformation were examined with a variety of substrates in Scheme 4. The substrates with electron-donating substitutions on indoles gave better yields than those with electron-withdrawing groups (Scheme 4, **2a**-**2e**). The electron-donating substitutions on the nitrogens of indoles were necessary for the cyclization (Scheme 4, **2f**-**2h**). The substrates bearing 4-nitrobenzenesulfonyl (Ns) and methanesulfonyl (Ms) groups on the nitrogens of tryptamines were tested, which afforded similar results to those with Ts groups (Scheme 4, **2i**-**2j**). Substituents such as alkyl and phenyl on the α position of ketone could be tolerated well in the reaction conditions to provide satisfactory yields (Scheme 4, **2k**-**2l**). The structures of the tetracyclic indoline compounds were determined by 2D NMR spectra and a single crystal X-ray diffraction of **2i**.[11] The relative stereochemistry of **2k-2l** was confirmed by 2D NOE spectroscopy (see Supporting Information for the details).

To probe the mechanism of the tandem cyclizations, an intermediate capture experiment was conducted by exposing the substrate **1f'** into weak acid media silica gel, aiming to trap the spiroindoleninium **1f'-1** intermediate by certain nucleophiles. To our delight, water physisorbed in the silica gel could act as the



Scheme 4. Substrate scopes of the tetracyclic indolines.

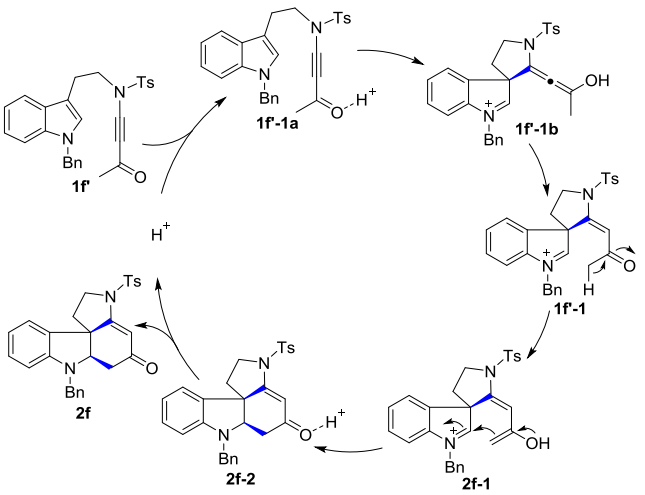
nucleophile to attack the spiroindoleninium to generate isolatable intermediate hemiaminal **1f'-2.** When the hemiaminal **1f'-2** was subjected to the standard acidic conditions, the iminium ion moiety in **2f-1** was generated, which was then captured by the *in situ* formed enol through an intramolecular Mannich-type reaction to give the desired cyclization product **2f** (Scheme 5).



Scheme 5. Intermediate capture experiments.

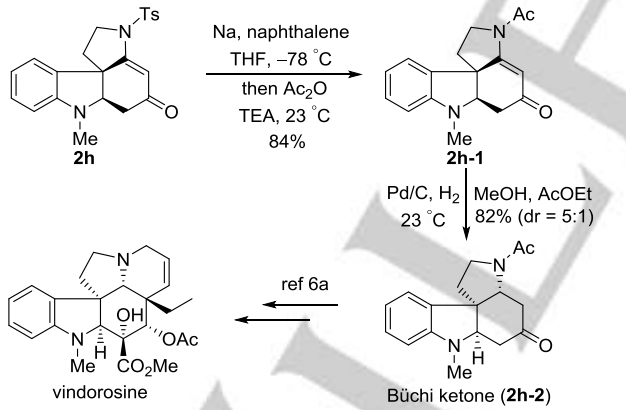
Based on these experimental results, a plausible mechanism was proposed in Scheme 6. Under the catalysis of a strong Brønsted acid, the activation of carbonyl in **1f'** by proton promoted a Michael addition of indole to ynone, providing the spiroindoleninium intermediate **1f'-1b** followed by an isomerization to afford **1f'-1**. The following enolization of the methyl ketone led to the formation of enol **2f-1**, which underwent a Mannich-type cyclization to generate **2f** after a proton transfer (Scheme 6). The structure of the intermediate **1f'-2** was

determined by 2D NMR specra (see Supporting Information for the details).



Scheme 6. Proposed mechanism for the formation of tetracyclic indoline.

The methodology developed so far can be utilized to construct important synthetic precursors for the syntheses of a number of indole alkaloids after some functional group manipulations.[6] As a demonstration, **2h** was transformed into Büchi ketone (**2h-2**), a key intermediate in the syntheses of many indole alkaloids such as vindorosine[6a] after several facile functional group transformations as depicted in Scheme 7.



Scheme 7. Synthesis of Büchi ketone from tetracyclic indoline **2h**.

Conclusions

In conclusion, an oxidation/Brønsted acid-catalyzed tryptamine-derived ynesulfonamide-based tandem cyclizations strategy to preparing tetracyclic indoline scaffolds has been developed, which represents a unique and straightforward method to access 1*H*-pyrrolo[2,3-*d*]carbazoles. The plausible mechanism of this tandem cyclization was probed by capturing the reaction intermediate. The applications of the methodology were demonstrated by the formal synthesis of vindorosine on the basis of the preparation of Büchi ketone intermediate. It is expected that such a methodology should find broad applications in the syntheses of various indole alkaloids with diverse structures.

Experimental Section

General Procedures for the Preparation of Tetracyclic Indolines 2, 2a-2l

To a solution of substrates **1**, **1a**-**1l** (0.2 mmol) in DCM (3 mL) were added 4 Å molecular sieves (30 mg) and NMO (35 mg, 0.30 mmol). The mixture was stirred at 0 °C for 5 min and TPAP (14 mg, 0.04 mmol) was added. The reaction was stirred at 0 °C for 30 min before filtered through a plug of calcined Celite (rinsed with 10% ethyl acetate/*n*-hexane). The filtrate was concentrated to give the crude ketone products, which were dissolved in anhydrous DCM (2.5 mL) at 0 °C under a N_2 atmosphere. A solution of diphenyl phosphate (5.0 mg, 0.020 mmol) in anhydrous DCM (0.2 mL) was added to the reaction mixture and the reaction was stirred at 0 °C for 30 min before TEA was added to quench the reaction. The solvents were removed *in vacuo* to give a residue, which was purified by a flash column chromatography on silica gel to provide the products **2**, **2a**-**2l**.

3-Tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]carbazol-5(6*H*)-one (2)

White solid (52 mg, 0.137 mmol, 69%); m.p. 231.0–232.8 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.94 (d, *J* = 8.2 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 6.99 (td, *J* = 7.8 Hz, 0.8, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 6.37 (t, *J* = 7.5 Hz, 1H), 5.91 – 5.88 (m, 3H), 4.05 (dd, *J* = 10.5, 8.4 Hz, 1H), 3.95 (dd, *J* = 9.8, 6.2 Hz, 1H), 3.72 (td, *J* = 10.5, 5.4 Hz, 1H), 2.46 (s, 3H), 2.41 (dd, *J* = 16.8, 6.2 Hz, 1H), 2.08 (td, *J* = 12.0, 8.4 Hz, 1H), 1.87 (dd, *J* = 16.8, 9.8 Hz, 1H), 1.82 (dd, *J* = 12.0, 5.4 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.5, 159.6, 148.9, 145.7, 134.2, 130.6, 129.9, 128.7, 127.2, 121.7, 117.9, 111.1, 105.3, 62.5, 54.4, 48.8, 40.3, 34.8, 21.2; IR (thin film, cm^{-1}): 3438, 3328, 2954, 2924, 2854, 1733, 1640, 1620, 1463, 1359, 1204, 1168, 1056; HRMS (ESI) (*m/z*) [M+H]$^+$: calcd. for $C_{21}H_{21}N_2O_3S$ 381.1267, found 381.1265.

7-Benzyl-10-methoxy-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2a)

White solid (88 mg, 0.176 mmol, 88%); m.p. 188.5–190.5 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.94 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 7.3 Hz, 2H), 7.34 (t, *J* = 7.4 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 6.60 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.33 (d, *J* = 8.5 Hz, 1H), 5.99 (s, 1H), 5.39 (d, *J* = 2.5 Hz, 1H), 4.24 (d, *J* = 15.1 Hz, 1H), 4.10 – 4.06 (m, 2H), 3.95 (dd, *J* = 9.9, 5.9 Hz, 1H), 3.73 (td, *J* = 10.7, 5.6 Hz, 1H), 3.47 (s, 3H), 2.46 – 2.41 (m, 4H), 2.20 (td, *J* = 11.8, 8.4 Hz, 1H), 2.01 – 1.99 (m, 1H), 1.89 (dd, *J* = 16.7, 10.0 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.3, 159.3, 152.6, 146.0, 142.3, 138.2, 134.1, 132.2, 130.7, 128.5, 127.4, 127.1, 127.0, 112.8, 109.4, 109.3, 105.6, 67.5, 55.5, 53.7, 49.0, 48.8, 35.0, 34.3, 21.2; IR (thin film, cm^{-1}): 3442, 2924, 2852, 1648, 1622, 1481, 1361, 1216, 1170, 1072, 1029; HRMS (ESI) (*m/z*) [M+H]$^+$: calcd. for $C_{29}H_{29}N_2O_4S$ 501.1843, found 501.1848.

7-Benzyl-10-chloro-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2b)

White solid (72 mg, 0.143 mmol, 72%); m.p. 217.1–219.1 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.95 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.38 – 7.33 (m, 4H), 7.29 – 7.25 (m, 1H), 7.02 (dd, J = 8.4, 2.1 Hz, 1H), 6.41 (d, J = 8.4 Hz, 1H), 6.06 (s, 1H), 5.42 (d, J = 2.1 Hz, 1H), 4.32 (d, J = 15.3 Hz, 1H), 4.17 (d, J = 15.3 Hz, 1H), 4.09 – 4.01 (m, 2H), 3.67 (td, J = 10.5, 5.6 Hz, 1H), 2.53 (d, J = 6.0 Hz, 1H), 2.45 (s, 3H), 2.22 (td, J = 11.8, 8.3 Hz, 1H), 2.03 – 1.97 (m, 1H), 1.90 (dd, J = 16.8, 9.9 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.0, 158.5, 147.1, 146.2, 137.7, 133.9, 132.9, 130.9, 128.63, 128.60, 127.4, 127.3, 126.9, 121. 4, 121.3, 110.1, 106.1, 67.3, 53.5, 48.6, 48.3, 35.5, 34.1, 21.4; IR (thin film, cm^{-1}): 3443, 2952, 2923, 2853, 1651, 1620, 1473, 1358, 1203, 1167, 1079, 1054; HRMS (ESI) (*m/z*) [M+Na]$^+$: calcd. for $C_{28}H_{27}ClN_2NaO_3S$ 527.1167, found 527.1151.

7-Benzyl-10-bromo-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2c)

White solid (82 mg, 0.149 mmol, 75% yield); m.p. 231.0–232.3 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.95 (d, J = 8.2 Hz, 2H), 7.58 (d, J = 8.2 Hz, 2H), 7.37 – 7.33 (m, 4H), 7.27 (t, J = 6.7 Hz, 1H), 7.15 (dd, J = 8.4, 1.9 Hz, 1H), 6.38 (d, J = 8.4 Hz, 1H), 6.05 (s, 1H), 5.62 (d, J = 1.8 Hz, 1H), 4.32 (d, J = 15.3 Hz, 1H), 4.17 (d, J = 15.3 Hz, 1H), 4.11 – 4.00 (m, 2H), 3.67 (td, J = 10.7, 5.5 Hz, 1H), 2.53 (d, J = 6.0 Hz, 1H), 2.46 (s, 3H), 2.23 (dt, J = 11.7, 8.4 Hz, 1H), 2.06 – 1.97 (m, 1H), 1.90 (dd, J = 16.8, 9.9 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.0, 158.5, 147.5, 146.2, 137.7, 133.9, 133.4, 131.5, 131.0, 128.6, 127.4, 127.3, 126.9, 123.9, 110.7, 108.8, 106.0, 67.2, 53.6, 48.6, 48.3, 35.5, 34.2, 21.5; IR (thin film, cm^{-1}): 3425, 3025, 2952, 2888, 2854, 1644, 1620, 1467, 1358, 1243, 1188, 1169, 1092, 1067, 1035; HRMS (ESI) (*m/z*) [M+Na]$^+$: calcd. for $C_{28}H_{25}BrN_2NaO_3S$ 571.0661, found 571.0638.

7-Benzyl-9-methyl-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2d)

White solid (81 mg, 0.167 mmol, 84%); m.p. 186.0–187.7 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.93 (d, J = 8.2 Hz, 2H), 7.56 (d, J = 8.2 Hz, 2H), 7.38 – 7.33 (m, 4H), 7.26 (t, J = 7.2 Hz, 1H), 6.28 (s, 1H), 6.21 (d, J = 7.2 Hz, 1H), 5.92 (s, 1H), 5.74 (d, J = 7.5 Hz, 1H), 4.33 (d, J = 15.3 Hz, 1H), 4.12 (d, J = 15.3 Hz, 1H), 4.05 (dd, J = 10.4, 8.3 Hz, 1H), 3.94 (dd, J = 9.8, 6.0 Hz, 1H), 3.71 (td, J = 10.4, 5.5 Hz, 1H), 2.49 – 2.44 (m, 4H), 2.15 – 2.09 (m, 4H), 1.94 (dd, J = 11.9, 5.5 Hz, 1H), 1.88 (dd, J = 16.7, 9.8 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.2, 159.6, 148.4, 145.8, 138.4, 138.1, 134.1, 130.6, 128.6, 128.1, 127.4, 127.2, 127.1, 121.1, 118.6, 109.7, 105.3, 67.0, 53.2, 48.9, 48.2, 35.5, 34.6, 21.3, 21.2; IR (thin film, cm^{-1}): 3437, 2955, 2922, 2853, 1650, 1623, 1456, 1382, 1360, 1207, 1169, 1076; HRMS (ESI) (*m/z*) [M+Na]$^+$: calcd. for $C_{29}H_{28}N_2NaO_3S$ 507.1713, found 507.1709.

7-Benzyl-9-methoxy-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2e)

White solid (90 mg, 0.180 mmol, 90%); m.p. 182.6–183.7 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.94 (d, J = 8.2 Hz, 2H), 7.56 (d, J = 8.2 Hz, 2H), 7.38 – 7.34 (m, 4H), 7.27 (t, J = 7.1 Hz, 1H), 6.04 (d, J = 2.2 Hz, 1H), 5.93 (dd, J = 8.1, 2.2 Hz, 1H), 5.89 (s, 1H), 5.80 (d, J = 8.1 Hz, 1H), 4.36 (d, J = 15.2 Hz, 1H), 4.13 (d, J = 15.2 Hz, 1H), 4.07 – 4.04 (m, 1H), 3.95 (dd, J = 9.8, 6.0 Hz, 1H), 3.72 (td, J = 10.5, 5.5 Hz, 1H), 3.59 (s, 3H), 2.48 (d, J = 10.5 Hz, 1H), 2.46 (s, 3H), 2.11 (td, J = 11.9, 8.3 Hz, 1H), 1.95 (dd, J = 11.9, 5.5 Hz, 1H), 1.90 (dd, J = 16.7, 9.8 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.1, 160.6, 159.6, 149.7, 145.7, 138.0, 134.1, 130.6, 128.5, 127.4, 127.2, 123.3, 121.8, 105.2, 102.0, 96.4, 67.2, 55.0, 52.8, 48.8, 48.1, 35.7, 34.7, 21.1; IR (thin film, cm^{-1}): 3425, 2924, 2170, 1697, 1650, 1622, 1491, 1454, 1358, 1254, 1168, 1073; HRMS (ESI) (*m/z*) [M+H]$^+$: calcd. for $C_{29}H_{29}N_2O_4S$ 501.1843, found 501.1841.

7-Benzyl-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]carbazol-5 (6*H*)-one (2f)

White solid (80 mg, 0.170 mmol, 85%); m.p. 165.8–167.5 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.95 (d, J = 8.2 Hz, 2H), 7.57 (d, J = 8.2 Hz, 2H), 7.41 – 7.32 (m, 4H), 7.28 – 7.25 (m, 1H), 7.01 (t, J = 7.5 Hz, 1H), 6.43 (d, J = 7.5 Hz, 1H), 6.40 (t, J = 7.3 Hz, 1H), 5.93 (s, 1H), 5.87 (d, J = 7.3 Hz, 1H), 4.33 (d, J = 15.3 Hz, 1H), 4.16 (d, J = 15.3 Hz, 1H), 4.07 (dd, J = 9.8, 8.4 Hz, 1H), 3.99 (dd, J = 9.8, 6.0 Hz, 1H), 3.74 (td, J = 10.7, 5.5 Hz, 1H), 2.46 (s, 3H), 2.16 (td, J = 12.0, 8.4 Hz, 1H), 1.98 (dd, J = 12.0, 5.5 Hz, 1H), 1.88 (dd, J = 16.7, 9.8 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195. 1, 159.4, 148.2, 145.8, 138.1, 134.1, 130.8, 130.6, 128.9, 128.5, 127.4, 127.2, 127.1, 121.4, 118.0, 109.0, 105.4, 67.0, 53.4, 48.8, 48.3, 35.4, 34.5, 21.1; IR (thin film, cm^{-1}): 3444, 2924, 2852, 1651, 1622, 1475, 1454, 1356, 1257, 1204, 1165; HRMS (ESI) (*m/z*) [M+Na]$^+$: calcd. for $C_{28}H_{26}N_2NaO_3S$ 493.1556, found 493.1555.

7-(4-Methoxybenzyl)-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2g)

White solid (97 mg, 0.194 mmol, 97%); m.p. 138.9–140.0 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.95 (d, J = 8.1 Hz, 2H), 7.57 (d, J = 8.1 Hz, 2H), 7.32 (d, J = 8.4 Hz, 2H), 7.03 (t, J = 7.7 Hz, 1H), 6.92 (d, J = 8.4 Hz, 2H), 6.49 (d, J = 7.7 Hz, 1H), 6.40 (t, J = 7.3 Hz, 1H), 5.94 (s, 1H), 5.86 (d, J = 7.3 Hz, 1H), 4.30 (d, J = 14.8 Hz, 1H), 4.08 – 4.04 (m, 2H), 3.94 (dd, J = 9.9, 6.0 Hz, 1H), 3.74 (s, 4H), 2.49 – 2.43 (m, 4H), 2.17 – 2.12 (m, 1H), 1.96 (dd, J = 11.9, 5.3 Hz, 1H), 1.88 (dd, J = 16.7, 9.9 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.1, 159.5, 158.4, 148.2, 145.7, 134.1, 130.8, 130.6, 129.6, 128.8, 128.7, 127.2, 121.3, 118.0, 113.9, 109. 0, 105.4, 66.8, 55.0, 53.4, 48.8, 47.7, 35.4, 34.5, 21.1; IR (thin film, cm^{-1}): 3441, 2899, 1625, 1517, 1475, 1347, 1258, 1215, 1161; HRMS (ESI) (*m/z*) [M+Na]$^+$: calcd. for $C_{29}H_{28}N_2NaO_4S$ 523.1662, found 523.1665.

7-Methyl-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]carbazol-5(6*H*)-one (2h)

White solid (58 mg, 0.147 mmol, 73%); m.p. 173.1–175.0 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.95 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.07 (td, J = 7.7, 1.2 Hz, 1H), 6.55 (d, J = 7.7 Hz, 1H), 6.40 (td, J = 7.5, 0.8 Hz, 1H), 5.93 (s, 1H), 5.85 (dd, J = 7.5, 0.8 Hz, 1H), 4.06 (dd, J = 10.2, 8.4 Hz, 1H), 4.00 (dd, J = 9.9, 6.0 Hz, 1H), 3.72 (td, J = 10.2, 5.6 Hz, 1H), 2.66 (s, 3H), 2.49 – 2.44 (m, 4H), 2.12 (td, J = 12.0, 8.4 Hz, 1H), 1.85 (dd, J = 12.0, 5.6 Hz, 1H), 1.74 (dd, J = 16.7, 9.9 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.3, 159.4, 149.0, 145.8, 134.1, 130.60, 130.57, 129.0, 127.2, 121.2, 117.9, 108.7, 105.5, 68.4, 53.4, 48.8, 34.62, 34.60, 31.4, 21.1; IR (thin film, cm^{-1}): 2959, 2923, 2896, 1648, 1619, 1477, 1359, 1255, 1169; HRMS (ESI) (*m/z*) [M+Na]$^+$: calcd. for $C_{22}H_{22}N_2NaO_3S$ 417.1243, found 417.1254.

7-Benzyl-3-((4-nitrophenyl)sulfonyl)-2,3,6a,7-tetrahydro-1*H*-pyrrolo [2,3-*d*]carbazol-5(6*H*)-one (2i)

Yellow solid (74 mg, 0.147 mmol, 74%); m.p. 181.7–182.7 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 8.51 (d, J = 8.8 Hz, 2H), 8.36 (d, J = 8.8 Hz, 2H), 7.39 – 7.38 (m, 2H), 7.35 (t, J = 7.6 Hz, 2H), 7.26 (t, J = 7.3 Hz, 1H), 7.04 (t, J = 7.7 Hz, 1H), 6.48 (dd, J = 15.5, 7.7 Hz, 2H), 6.16 (d, J = 7.3 Hz, 1H), 5.93 (s, 1H), 4.36 (d, J = 15.2 Hz, 1H), 4.19 – 4.11 (m, 2H), 4.00 (dd, J = 9.8, 5.9 Hz, 1H), 3.86 (td, J = 10.8, 5.6 Hz, 1H), 2.52 – 2.49 (m, 1H), 2.19 (td, J = 12.0, 8.6 Hz, 1H), 2.03 (dd, J = 12.0, 5.6 Hz, 1H), 1.93 (dd, J = 16.6, 9.8 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.1, 158.9, 151.0, 148.2, 141.9, 138. 0, 130.5, 129.0, 128.6, 127.4, 127.2, 125.3, 121.3, 118.2, 109.0, 105.9, 66.9, 53.4, 49.2, 48.3, 35.5, 34.6; IR

(thin film, cm^{-1}): 3450, 3104, 2925, 2853, 1652, 1624, 1532, 1476, 1382, 1351, 1202, 1172; HRMS (ESI) (*m/z*) $[M+H]^+$: calcd. for $C_{27}H_{24}N_3O_5S$ 502.1431, found 502.1433.

7-Benzyl-3-(methylsulfonyl)-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2j)

White solid (62 mg, 0.157 mmol, 79%); m.p. 159.3–161.3 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.43 (d, *J* = 7.5 Hz, 2H), 7.37 (t, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.3 Hz, 1H), 7.11 (t, *J* = 7.8 Hz, 1H), 7.03 (d, *J* = 7.1 Hz, 1H), 6.74 (t, *J* = 7.1 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 1H), 5.80 (s, 1H), 4.40 (d, *J* = 15.2 Hz, 1H), 4.22 (d, *J* = 15.2 Hz, 1H), 4.06 – 4.00 (m, 2H), 3.81 (td, *J* = 10.8, 5.5 Hz, 1H), 3.40 (s, 3H), 2.53 (dd, *J* = 16.5, 6.0 Hz, 1H), 2.23 (dt, *J* = 11.5, 8.7 Hz, 1H), 2.05 (dd, *J* = 11.5, 5.5 Hz, 1H), 1.99 (dd, *J* = 16.5, 9.9 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.0, 160.0, 148.2, 138.1, 130.6, 129.0, 128.6, 127.4, 127.2, 122.0, 118.5, 108.9, 104.4, 67.2, 53.5, 48.5, 48.4, 38.1, 35.5, 35.2; IR (thin film, cm^{-1}): 3441, 2957, 2923, 1619, 1476, 1453, 1384, 1354, 1205, 1167; HRMS (ESI) (*m/z*) $[M+H]^+$: calcd. for $C_{22}H_{23}N_2O_3S$ 395.1424, found 395.1424.

7-Benzyl-6-propyl-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2k)

White solid (83 mg, 0.162 mmol, 81%); m.p. 204.6–205.8 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.92 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.35 – 7.23 (m, 5H), 6.95 (td, *J* = 7.8 Hz, 1.1, 1H), 6.39 (d, *J* = 7.8 Hz, 1H), 6.34 (td, *J* = 7.5, 1.1 Hz, 1H), 6.07 (d, *J* = 7.5 Hz, 1H), 5.81 (s, 1H), 4.56 (d, *J* = 15.8 Hz, 1H), 4.30 (d, *J* = 15.8 Hz, 1H), 4.11 (t, *J* = 9.6 Hz, 1H), 3.87 (td, *J* = 10.8, 6.0 Hz, 1H), 3.82 (d, *J* = 5.3 Hz, 1H), 2.44 (s, 3H), 2.16 (dt, *J* = 7.3, 5.0 Hz, 1H), 2.08 (dt, *J* = 11.4, 9.0 Hz, 1H), 2.00 (dd, *J* = 12.2, 6.0 Hz, 1H), 1.49 (ddt, *J* = 13.4, 10.8, 5.0 Hz, 1H), 1.25 – 1.16 (m, 1H), 1.08 – 1.02 (m, 1H), 1.01 – 0.92 (m, 1H), 0.69 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 198.4, 157.9, 148.1, 145.6, 138.2, 133.8, 132.6, 130.4, 128.9, 128.5, 127.4, 127.3, 127.2, 121.6, 117.4, 108.1, 103.3, 68.9, 54.0, 49.7, 49.1, 47.7, 35.7, 32.9, 21.1, 19.2, 14.0; IR (thin film, cm^{-1}): 3438, 3289, 3089, 3051, 2956, 2924, 2858, 1726, 1652, 1629, 1596, 1482, 1456, 1355, 1299, 1165, 1089; HRMS (ESI) (*m/z*) $[M+Na]^+$: calcd. for $C_{31}H_{22}N_2NaO_3S$ 535.2026, found 535.2023.

7-Benzyl-6-phenyl-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*] carbazol-5(6*H*)-one (2l)

White solid (91 mg, 0.166 mmol, 83%); m.p. 109.0–110.9 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.99 (d, *J* = 8.2 Hz, 2H), 7.59 (d, *J* = 8.2 Hz, 2H), 7.31 – 7.26 (m, 3H), 7.20 – 7.10 (m, 5H), 6.99 (dd, *J* = 12.0, 4.3 Hz, 1H), 6.93 (d, *J* = 7.0 Hz, 2H), 6.38 – 6.36 (m, 2H), 6.05 (s, 1H), 5.87 (d, *J* = 7.4 Hz, 1H), 4.45 (d, *J* = 8.5 Hz, 1H), 4.11 (dd, *J* = 10.1, 8.5 Hz, 1H), 4.05 (d, *J* = 15.7 Hz, 1H), 3.74 (td, *J* = 10.7, 5.6 Hz, 1H), 3.45 (d, *J* = 15.7 Hz, 1H), 3.33 (d, *J* = 8.5 Hz, 1H), 2.48 (s, 3H), 2.32 (td, *J* = 11.8, 8.5 Hz, 1H), 1.93 (dd, *J* = 11.8, 5.5 Hz, 1H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 195.4, 158.6, 147.2, 145.8, 139.9, 138.1, 134.1, 131.0, 130.6, 129.9, 129.0, 128.30, 128.28, 127.3, 127.0, 126.8, 126.7, 121.2, 117.2, 107.9, 105.0, 73.4, 54.4, 54.0, 48.9, 48.5, 34.9, 21.2; IR (thin film, cm^{-1}): 3424, 3028, 2923, 2854, 1654, 1628, 1601, 1478, 1452, 1383, 1360, 1166; HRMS (ESI) (*m/z*) $[M+Na]^+$: calcd. for $C_{34}H_{30}N_2NaO_3S$ 569.1869, found 569.1859.

Intermediate Capture Experiment

(*E*)-1-(1-Benzyl-2-hydroxy-1'-tosylspiro[indoline-3,3'-pyrrolidin]-2'-ylidene)propan-2-one (1f'-2)

The ketone product **1f'** were prepared from substrates **1f** (235 mg, 0.481 mmol) according to the general procedure described in the synthesis of tetracyclic indolines **2**, **2a**-**2l**. The ketone product **1f'** was dissolved in DCM (2 mL) and silica gel (2.35 g, 200-300 mesh) was added. The solvent was removed *in vacuo* to afford yellow powder, then it was added H_2O (45 mg, 2.5 mmol) and stirred vigorously at room temperature for 2 h. TLC monitored the reaction till all the starting materials disappeared. The powder was filtered, rinsed with ethyl acetate. The filtrate was concentrated to a residue, which was recrystallized with *n*-hexane/ethyl acetate (5:1) to provide the product **1f'-2** as a yellow solid (183 mg, 0.375 mmol, 78%); m.p. 126.7–127.5 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.76 (d, *J* = 8.3 Hz, 2H), 7.33 – 7.27 (m, 6H), 7.25 – 7.22 (m, 1H), 7.03 (td, *J* = 7.7, 1.2 Hz, 1H), 6.89 (s, 1H), 6.79 (dd, *J* = 7.4, 0.9 Hz, 1H), 6.62 (td, *J* = 7.4, 0.7 Hz, 1H), 6.36 (d, *J* = 7.8 Hz, 1H), 6.08 (d, *J* = 12.2 Hz, 1H), 4.52 (dd, *J* = 82.2, 16.2 Hz, 2H), 4.43 (d, *J* = 12.2 Hz, 1H), 4.13 (dd, *J* = 9.9, 8.0 Hz, 1H), 3.54 (ddd, *J* = 12.1, 10.0, 5.7 Hz, 1H), 2.43 (s, 3H), 2.16 (dd, *J* = 13.0, 5.6 Hz, 1H), 2.10 – 2.05 (m, 1H), 2.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ = 200.2, 155.6, 149.1, 145.3, 138.9, 133.9, 130.0, 129.2, 128.8, 128.6, 127.7, 127.2, 127.1, 121.3, 118.0, 108.6, 106.3, 92.2, 62.7, 48.7, 46.9, 36.2, 30.8, 21.9; IR (thin film, cm^{-1}): 3421, 3027, 2923, 1661, 1582, 1493, 1455, 1383, 1351, 1230, 1166, 1149, 1093, 1058; HRMS (ESI) (*m/z*) $[M+K]^+$: calcd. for $C_{28}H_{28}KN_2O_4S$ 527.1401, found 527.1390.

(7-Benzyl-3-tosyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]carbazol-5 (6*H*)-one (2f)

1f'-2 (98 mg, 0.20 mmol) was dissolved in anhydrous DCM (2 mL) at 0 °C under a N_2 atmosphere. A solution of diphenyl phosphate (5 mg, 0.02 mmol) in anhydrous DCM (0.2 mL) was added to the reaction mixture and the reaction was stirred at 0 °C for 10 min before TEA was added to quench the reaction. The solvents were removed *in vacuo* to give a residue, which was purified by a flash column chromatography (petroleum ether/ethyl acetate = 5:1) on silica gel to provide the products **2f** as a white solid (86 mg, 0.183 mmol, 92%).

Synthesis of Büchi Ketone

3-Acetyl-7-methyl-2,3,6a,7-tetrahydro-1*H*-pyrrolo[2,3-*d*]carbazol-5 (6*H*)-one (2h-1)

Preparation of sodium naphthalenide solution: To a solution of naphthalene (256 mg, 2.00 mmol) in anhydrous THF (10 mL) was added freshly cut sodium pieces (92 mg, 4.0 mmol). The mixture was sonicated at room temperature for 20 min with occasional swirling to afford a dark green solution of sodium naphthalenide (0.2 M) in THF.

To a solution of **2h** (100 mg, 0.253 mmol) in anhydrous THF (10 mL) was added the freshly prepared sodium naphthalenide solution dropwise at –78 °C with swirling until the dark green color persisted (4 mL, 0.8 mmol). After confirmation of completion by TLC (30 min after dark green persistence), MeOH (1 mL) was added to quench the reaction and the mixture warmed to room temperature over 30 min. The mixture was concentrated *in vacuo* to afford the crude product, which was used without further purification.

To a stirred solution of the crude product obtained above in DCM (10 mL) was added Et_3N (0.17 mL, 1.3 mmol) at 0 °C followed by the addition of Ac_2O (0.090 mL, 0.95 mmol) in one portion. The mixture was warmed to room temperature. After 5 h, H_2O (2 mL) was added to the mixture and it was extracted with DCM (20 mL x 3). The combined organic layers were washed with brine (20 mL) and dried over anhydrous Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by a flash column chromatography on silica gel (petroleum ether/ethyl acetate = 5:1) to afford **2h-1** as a white solid (60 mg, 0.213 mmol, 84% yield); m.p. 178.8–179.6 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.16 (t, *J* = 7.6 Hz, 1H), 7.01 (d, *J* = 7.2 Hz, 1H), 6.69 (t, *J* = 7.2 Hz, 1H), 6.60 (d, *J* = 7.6 Hz, 1H), 6.56 (s, 1H), 4.04 (dd, *J* = 10.0, 6.0 Hz, 1H), 4.01 – 3.97 (m, 1H), 3.85 (td,

J = 10.9, 5.8 Hz, 1H), 2.73 (s, 3H), 2.53 (m, 1H), 2.33 (s, 3H), 2.14 (td, *J* = 11.7, 8.7 Hz, 1H), 1.92 – 1.85 (m, 2H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 197.0, 171.3, 159.9, 149.1, 131.1, 129.0, 122.1, 118.2, 108.8, 108.5, 68.7, 52.8, 47.5, 35.2, 35.0, 31.4, 24.9; IR (thin film, cm^{-1}): 3732, 3421, 2928, 2311, 1692, 1650, 1632, 1606, 1481, 1388, 1313, 1270, 1208, 1179, 1127, 1009; HRMS (ESI) (*m/z*) [M+Na]$^+$: calcd. for $C_{17}H_{18}N_2NaO_2$ 305.1260, found 305.1272.

3-Acetyl-7-methyl-2,3,3a,4,6a,7-hexahydro-1*H*-pyrrolo[2,3-*d*]carbazol-5(6*H*)-one (2h-2)

In a round-bottomed flask, **2h**-**1** (50 mg, 0.18 mmol) was dissolved in methanol (4 mL) and ethyl acetate (1 mL) at room temperature. Pd/C (38 mg, 0.036 mmol, palladium 10% on carbon) was added and the space above the solution was purged with nitrogen to remove the air. The reaction was stirred under a hydrogen atmosphere (hydrogen balloon) at room temperature for 12 h. The Pd catalyst was removed via filtration through a plug of silica gel. The filtrate was concentrated under reduced pressure, and the residue was chromatographed on silica gel (petroleum ether/acetone = 4:1) to afford **2h**-**2** as a white solid (42 mg, 0.148 mmol, 82% yield); m.p. 189.2–190.6 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO) δ = 7.16 (d, *J* = 7.3 Hz, 1H), 7.11 (td, *J* = 7.8, 1.0 Hz, 1H), 6.72 (t, *J* = 7.4 Hz, 1H), 6.59 (d, *J* = 7.8 Hz, 1H), 3.88 (dd, *J* = 5.2, 4.1 Hz, 1H), 3.82 – 3.77 (m, 1H), 3.72 (dt, *J* = 10.3, 7.4 Hz, 1H), 3.60 (t, *J* = 3.8 Hz, 1H), 2.94 (dd, *J* = 16.9, 5.7 Hz, 1H), 2.67 – 2.64 (m, 5H), 2.45 (dt, *J* = 12.6, 9.1 Hz, 1H), 2.22 – 2.14 (m, 2H), 2.00 (s, 3H); ^{13}C NMR (150 MHz, [D$_6$]DMSO) δ = 208.2, 169.2, 152.2, 132.3, 128.7, 122.6, 118.7, 108.2, 70.3, 62.8, 51.7, 46.5, 39.1, 36.2, 33.3, 23.1; IR (thin film, cm^{-1}): 3416, 2976, 2960, 2926, 2895, 2865, 1714, 1647, 1602, 1486, 1404, 1340, 1231, 1202, 1181, 1109; HRMS (ESI) (*m/z*) [M+Na]$^+$: calcd. for $C_{17}H_{20}N_2NaO_2$ 307.1417, found 307.1431.

Acknowledgements

This work was supported by the Natural Science Foundation of Liaoning Province of China (No. 20170540855) and Municipal Natural Science Foundation of Tianjin of China (No. 15JCQNJC13900). We acknowledged the program for innovative research team of the Ministry of Education and the program for Liaoning innovative research team in university.

Conflict of interest

The authors declare no conflict of interest.

Keywords: Büchi ketone • cyclization • synthetic methods • tetracyclic indoline • tryptamine-ynamide

[1] a) K. A. DeKorver, H. Li, A. G. Lohse, R. Hayashi, Z. Lu, Y. Zhang, R. P. Hsung, *Chem. Rev.* **2010**, *110*, 5064−5106; b) G. Evano, A. Coste, K. Jouvin, *Angew. Chem. Int. Ed.* **2010**, *49*, 2840−2859; *Angew. Chem.* **2010**, *122,* 2902−2921; c) G. Evano, K. Jouvin, A. Costeb, *Synthesis* **2013**, *45*, 17−26; d) X.-N. Wang, H.-S. Yeom, L.-C. Fang, S. He, Z.-X. Ma, B. L. Kedrowski, R. P. Hsung, *Acc. Chem. Res.* **2014**, *47*, 560−578; e) A. M. Cook, C. Wolf, *Tetrahedron Lett.* **2015**, *56*, 2377−2392; f) G. Evano, C. Theunissen, M. Lecomte, *Aldrichimica Acta* **2015**, *48*, 59−70; g) G. Evano, N Blanchard, G. Compain, A. Coste, C. Zhang, *Chem. Lett.* **2016**, *45*, 574−585; h) F. Pan, C. Shu, L.-W. Ye, *Org. Biomol. Chem.* **2016**, *14*, 9456−9465; i) G. Evano, B. Michelet, C. Zhang, *C. R. Chimie* **2017**, *20*, 648−664.

[2] a) Y. Zhang, R. P. Hsung, X. Zhang, J. Huang, B. W. Slafer, A. Davis, *Org. Lett.* **2005**, *7*, 1047−1050; b) N. Zheng, Y.-Y. Chang, L.-J. Zhang, J.-X. Gong, Z. Yang, *Chem. Asian J.* **2016**, *11*, 371−375; c) L. Li, X.-M. Chen, Z.-S. Wang, B. Zhou, X. Liu, X. Lu, L.-W. Ye, *ACS Catal.* **2017**, *7*, 4004−4010.

[3] a) T. Sévenet, L. Allorge, B. David, K. Awang, A. Hamid A. Hadi, C. Kan-Fan, J.-C. Quirion, F. Remy, H. Schaller, L. E. Teo, *J. Ethnopharmacol.* **1994**, *41*, 147−183; b) J. Bosch, J. Bonjoch, M. Amat, in *The Alkaloids*, *Vol. 48* (Ed.: G. A. Cordell), Academic Press, New York, **1996**, pp. 75−189; c) J. E. Saxton, *Nat. Prod. Rep.* **1997**, *14*, 559−590; d) J. Leonard, *Nat. Prod. Rep.* **1999**, *16*, 319−338; e) S. E. O'Connor, J. J. Maresh, *Nat. Prod. Rep.* **2006**, *23*, 532−547; f) J. M. Lopchuk, in *Progress in Heterocyclic Chemistry*, *Vol. 23* (Eds.: G. W. Gribble, J. A. Joule), Pergamon Press, Oxford, **2011**, pp. 1−25.

[4] a) H. F. Deutsch, M. A. Evenson, P. Drescher, C. Sparwasser, P. O. Madsen, *J. Pharm. Biomed. Anal.* **1994**, *12*, 1283−1287; b) J. E. Saxton, in *The Alkaloids*, *Vol. 50* (Ed.: G. A. Cordell), Academic Press, New York, **1998**, pp. 343−375; c) T. Kam, Y. Choo in *The Alkaloids*, *Vol. 63* (Ed.: G. A. Cordell), Academic Press, New York, **2006**, pp. 181−337; d) R. C. Paula, M. F. Dolabela, A. B. Oliveira, *Planta Med.* **2014**, *80*, 378−386.

[5] a) J. Bonjoch, D. Solé, *Chem. Rev.* **2000**, *100*, 3455−3482; b) S. A. Kozmin, T. Iwama, Y. Huang, V. H. Rawal, *J. Am. Chem. Soc.* **2002**, *124*, 4628−4641; c) J. P. Marino, M. B. Rubio, G. Cao, A. Dios, *J. Am. Chem. Soc.* **2002**, *124*, 13398−13399; d) E. L. Campbell, A. M. Zuhl, C. M. Liu, D. L. Boger, *J. Am. Chem. Soc.* **2010**, *132*, 3009−3012; e) Y. Sasaki, D. Kato, D. L. Boger, *J. Am. Chem. Soc.* **2010**, *132*, 13533−13544; f) Y. Han-ya, H. Tokuyama, T. Fukuyama, *Angew. Chem. Int. Ed.* **2011**, *50*, 4884−4887; *Angew. Chem.* **2011**, *123*, 4986−4989; g) J. S. Cannon, L. E. Overman, *Angew. Chem. Int. Ed.* **2012**, *51*, 4288−4311; *Angew. Chem.* **2012**, *124*, 4362−4386; h) O. Wagnières, Z. Xu, Q. Wang, J. Zhu, *J. Am. Chem. Soc.* **2014**, *136*, 15102−15108; i) M. Mewald, J. W. Medley, M. Movassaghi, *Angew. Chem. Int. Ed.* **2014**, *53*, 11634−11639; *Angew. Chem.* **2014**, *126*, 11818−11823.

[6] a) G. Büchi, K. E. Matsumoto, H. Nishimura, *J. Am. Chem. Soc.* **1971**, *93*, 3299−3301; b) S.-Z. Zhou, S. Bommezijn, J. A. Murphy, *Org. Lett.* **2002**, *4*, 443−445; c) N. Heureux, J. Wouters, I. E. Markó, *Org. Lett.* **2005**, *7*, 5245−5248; d) J. Pereira, M. Barlier, C. Guillou, *Org. Lett.* **2007**, *9*, 3101−3103; e) J. Boonsombat, H. Zhang, M. J. Chughtai, J. Hartung, A. Padwa, *J. Org. Chem.* **2008**, *73*, 3539−3550; f) R. Delgado, S. B. Blakey, *Eur. J. Org. Chem.* **2009**, *2009*, 1506−1510; g) S. B. Jones, B. Simmons, A. Mastracchio, D. W. C. MacMillan, *Nature* **2011**, *475*, 183−188; h) B. Wyler, F. Brucelle, P. Renaud, *Org. Lett.* **2016**, *18*, 1370−1373; i) A. Kong, D. E. Mancheno, N. Boudet, R. Delgado, E. S. Andreansky, S. B. Blakey, *Chem. Sci.* **2017**, *8*, 697−700.

[7] a) M. Ando, G. Büchi, T. Ohnuma, *J. Am. Chem. Soc.* **1975**, *97*, 6880−6881; b) F. He, Y. Bo, J. D. Altom, E. J. Corey, *J. Am. Chem. Soc.* **1999**, *121*, 6771−6772; c) M. Amat, M. M. M. Santos, A. M. Gomez, D. Jokic, E. Molins, J. Bosch, *Org. Lett.* **2007**, *9*, 2907−2910; d) J. W. Medley, M. Movassaghi, *Angew. Chem. Int. Ed.* **2012**, *51*, 4572−4576; *Angew. Chem.* **2012**, *124*, 4650−4654; e) J. W. Medley, M. Movassaghi, *Org. Lett.* **2013**, *15,* 3614−3617; f) M. J. James, J. D. Cuthbertson, P. O'Brien, R. J. K. Taylor, W. P. Unsworth, *Angew. Chem. Int. Ed.* **2015**, *54*, 7640−7643; *Angew. Chem.* **2015**, *127*, 7750−7753; g) M. J. James, R. E. Clubley, K. Y. Palate, T. J. Procter, A. C. Wyton, P. O'Brien, R. J. K. Taylor, W. P. Unsworth, *Org. Lett.* **2015**, *17*, 4372−4375; h) J. T. R. Liddon, M. J. James, A. K. Clarke, P. O'Brien, R. J. K. Taylor, W. P. Unsworth, *Chem. Eur. J.* **2016**, *22*, 8777−8780; i) A. K. Clarke, M. J. James, P. O'Brien, R. J. K. Taylor, W. P. Unsworth, *Angew. Chem. Int. Ed.* **2016**, *55*, 13798−13802; *Angew. Chem.* **2016**, *128*, 14002−14006; j)

J. T. R. Liddon, A. K. Clarke, R. J. K. Taylor, W. P. Unsworth, *Org. Lett.* **2016**, *18*, 6328−6331.

[8] a) C.-X. Zhuo, W. Zhang, S.-L. You, *Angew. Chem. Int. Ed.* **2012**, *51*, 12662−12686; *Angew. Chem.* **2012**, *124*, 12834−12858; b) S. P. Roche, J.-J. Y. Tendoung, B. Tréguier, *Tetrahedron*, **2015**, *71*, 3549−3591; c) M. J. James, P. O'Brien, R. J. K. Taylor, W. P. Unsworth, *Chem. Eur. J.* **2016**, *22*, 2856−2881; d) C. Zheng, S.-L. You, *Chem* **2016**, *1*, 830−857.

[9] Y. Zhang, R. P. Hsung, M. R. Tracey, K. C. M. Kurtz, E. L. Vera, *Org. Lett.* **2004**, *6*, 1151−1154.

[10] T. Akiyama, K. Mori, *Chem. Rev.* **2015**, *115*, 9277−9306.

[11] CCDC 1551696 contains the supplementary crystallographic data for **2i**. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

10.1002/chem.201705189

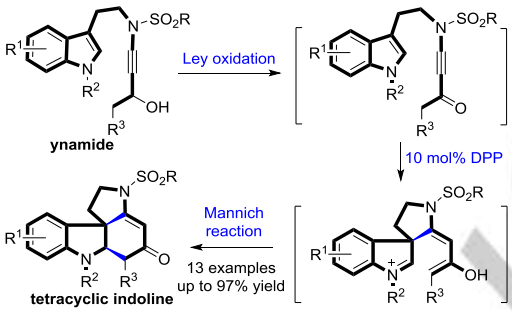
WILEY-VCH

Entry for the Table of Contents (Please choose one layout)

Layout 1:

FULL PAPER

A two-step transformation for the synthesis of 1*H*-pyrrolo[2,3-*d*]carbazole derivatives from tryptamine-based ynamides was developed and applied to the formal synthesis of vindorosine.



Y. Wang, J. Lin, X. Wang, G. Wang, X. Zhang, B. Yao, Y. Zhao, P. Yu, B. Lin, Y. Liu, M. Cheng**

Page No. – Page No.

Brønsted Acid-Catalyzed Tandem Cyclizations of Tryptamine-Ynamides Yielding 1*H*-Pyrrolo[2,3-*d*]carbazole Derivatives