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A Brønsted Acid Catalyzed Tandem Pinacol-Type Rearrangement for the Synthesis of *α*-(3-Indolyl) Ketones by Using *α*-Hydroxy Aldehydes

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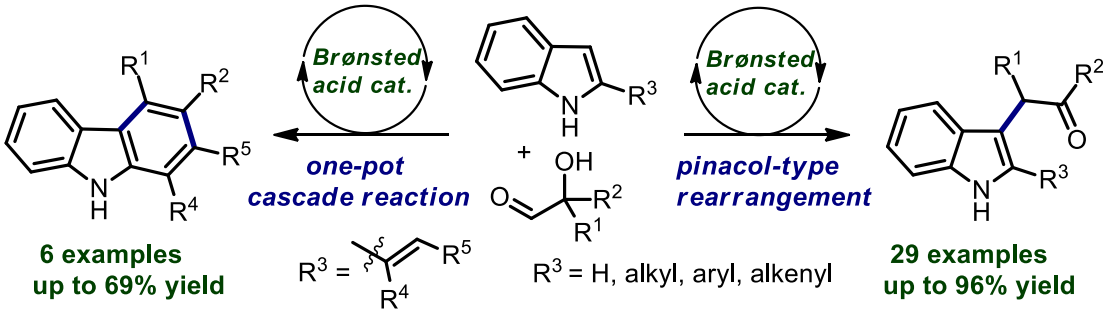


ABSTRACT

A Brønsted acid catalyzed Pinacol-type rearrangement pathway is reported here to synthesize various substituted *α*-(3-indolyl) ketones by employing unprotected indoles and α-hydroxy aldehydes as coupling partners. Utilization of economic and readily available Brønsted acid catalyst and use of simple starting precursors exemplifies the economic viability of this method. Under this developed protocol, selective migration of aryl over alkyl or a second aryl group is observed depending upon the migratory aptitude of the substituents. Applicability of this method was further demonstrated by synthesizing highly substituted carbazoles through a simple extension of this method to one-pot cascade annulation strategy.

KEYWORDS: *α*-Indolyl Ketones, Pinacol-Type Rearrangement, Indole, Brønsted Acid, Annulation

INTRODUCTION

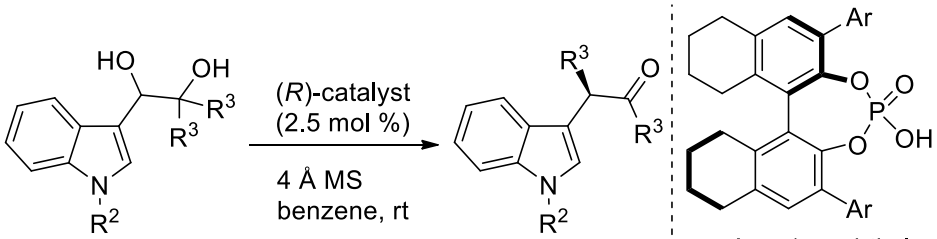
Over the past decades, pinacol and semipinacol rearrangements have emerged as powerful synthetic tools owing to their immense applicability in several fascinating organic transformations as well as capability to fine-tune the synthesis of several important complex molecular architectures.[1-2] Besides the advantages, the reported pinacol rearrangements have several major limitations, such as, poor regio- and diastereoselectivities, unpredictable side reactions, kinetic versus thermodynamic product formations, and mechanistically stepwise versus concerted pathways.[3] These drawbacks can be circumvented by designing reactions based on generation of the more predictable carbocation, thereby mitigating the regioselectivity issue and served as a profound route to several important classes of molecules.[4]

The construction of several indole based skeletons, particularly substituted α-(3-indolyl) ketones have acquired significant attention for the concise synthesis of several medicinally important compounds and alkaloids.[5] Most importantly, it is one of the key intermediates to achieve several important heterocycles like carbazoles, β-carbolines, spiroindolenines, and also tryptamine and tryptophols.[6-7] Despite their widespread applications, synthesis of this important scaffold is of considerable challenge as reported methods suffer from limitations such as low regio-selectivity for unsymmetrical ketones, multi-step synthesis, low yields, harsh reaction conditions, limited substrate scopes, utilization of expensive catalyst.[8-9]

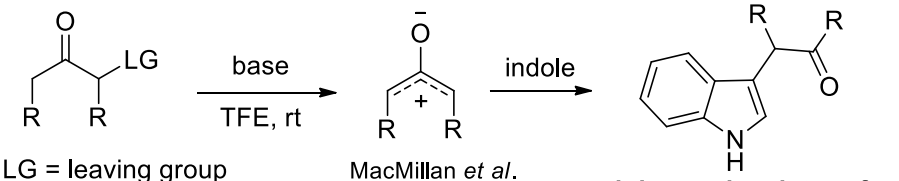
Scheme 1. Previous Reports and This Strategy

Previous Work

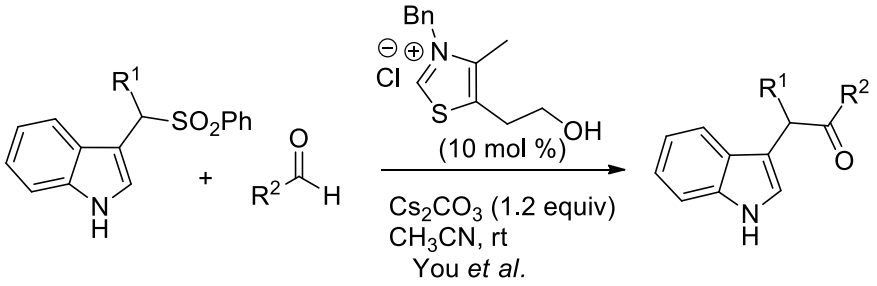
[a] Phosphoric acid catalyzed asymmetric pinacol rearrangement[9d]



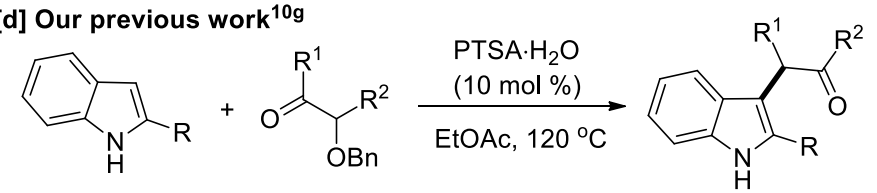
[b] Addition of indole to ketone via formation of oxy-allyl cation[8e]



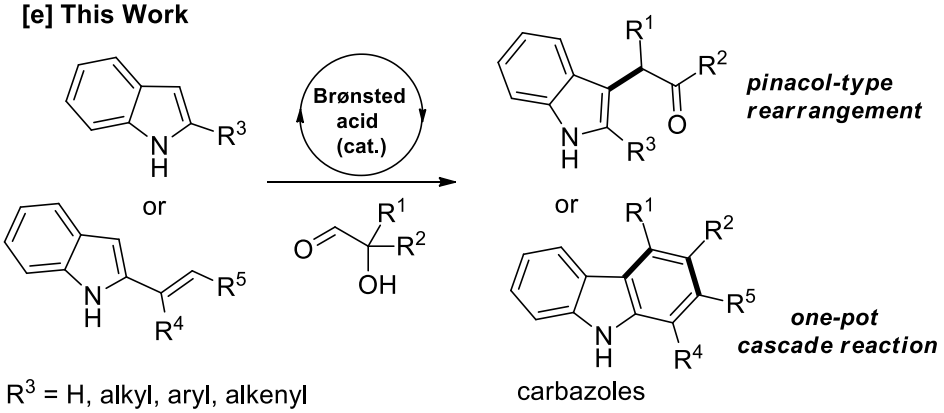
[c] Cross-coupling reaction using *N*-heterocyclic carbene catayst[9b]



[d] Our previous work[10g]

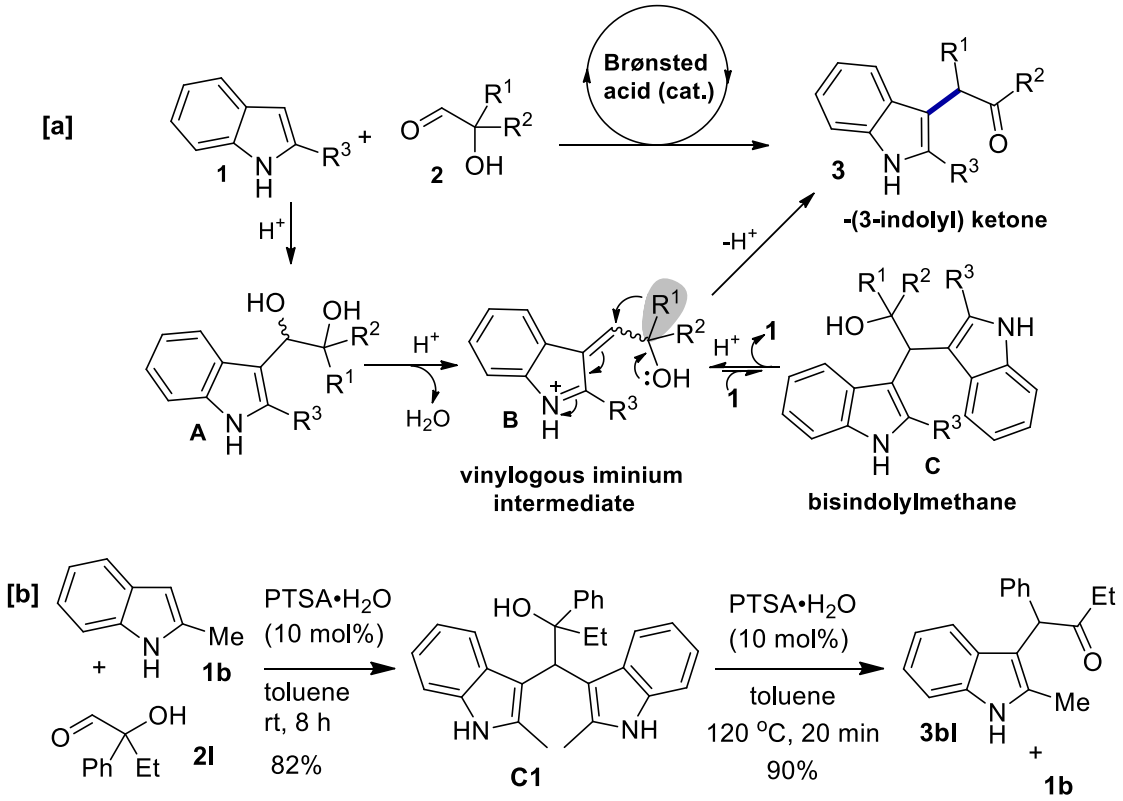


[e] This Work



In 2010, Antilla *et al.* developed an asymmetric version of the pinacol rearrangement to accomplish chiral *N*-protected α-(3-indolyl) ketones, starting from prefunctionalized indolyl diol derivatives (Scheme 1a).[9d] However, besides its advantages, this method was applicable only for identical migratory groups with limited substrate scope. Recently, Macmillan *et al.* documented an elegant method to access α-(3-indolyl) ketone *via* the generation of oxo-allyl cation intermediate, which is primarily applicable for the synthesis of symmetrical ketones (Scheme 1b).[8e] You *et al.* reported *N*-heterocyclic carbene catalyzed umpolung reaction between aryl-sulfonyl indoles and aldehydes to deliver aryl-substituted *α*-(3-indolyl) ketones (Scheme 1c).[9b] Very recently, we have developed a Brønsted acid catalyzed tandem reaction to achieve *α*-(3-indolyl) ketones by utilizing 2-benzyloxy aldehydes via the *in situ* generation of enol-ether intermediate (Scheme 1d).[10g]

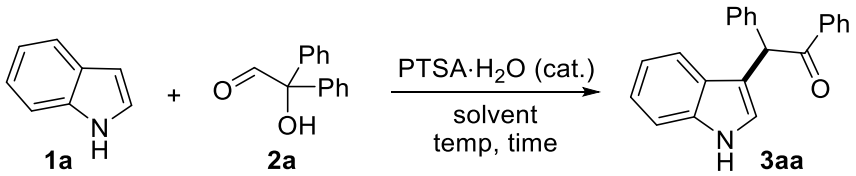
Scheme 2. Working Hypothesis



In our continuous efforts, to use *in situ* generated indolyl cations for the synthesis of functionalized indoles,[10] we envisioned that Brønsted acid catalyzed Pinacol-type rearrangement can also be achieved by employing unprotected indoles and α-hydroxy aldehydes[11] as coupling partners to accomplish diversely substituted α-(3-indolyl) ketones.[12] According to our hypothesis, in the presence of a Brønsted acid catalyst, first indole **1** would react with α-hydroxy aldehyde **2** to generate indolyl diol intermediate **A** which presumably would undergo dehydration to form the vinylogous iminium intermediate **B**. After that, migration of the alkyl or aryl group having greater migratory aptitude (R^1>R^2) *via* [1,2]-shift, would furnish the desired product **3** (Scheme 2a). It should be mentioned here that the vinylogous intermediate **B** will be in equilibrium with the bisindolylmethane **C**,[13] and the formation of desired product **3** would eventually shift the equilibrium towards **B**. So the generation of vinylogous intermediate **B** is the driving force to facilitate the Pinacol-type pathway. The advantages of this protocol are; i) direct use of unprotected indoles and easily available α-hydroxy aldehydes as coupling partners, ii) use of cheap readily available Brønsted acid as catalyst, iii) this may open the route to the carbazoles by one-pot cascade reactions, iv) easy to control the selective migration depending upon the migratory aptitude.

RESULTS AND DISCUSSION

Table 1: Optimization of Reaction Conditions[a] `



entry	cat. (mol %)	solvent	temp (°C)	time (h)	yield (%)[b]
1	10	EtOAc	60	60	10

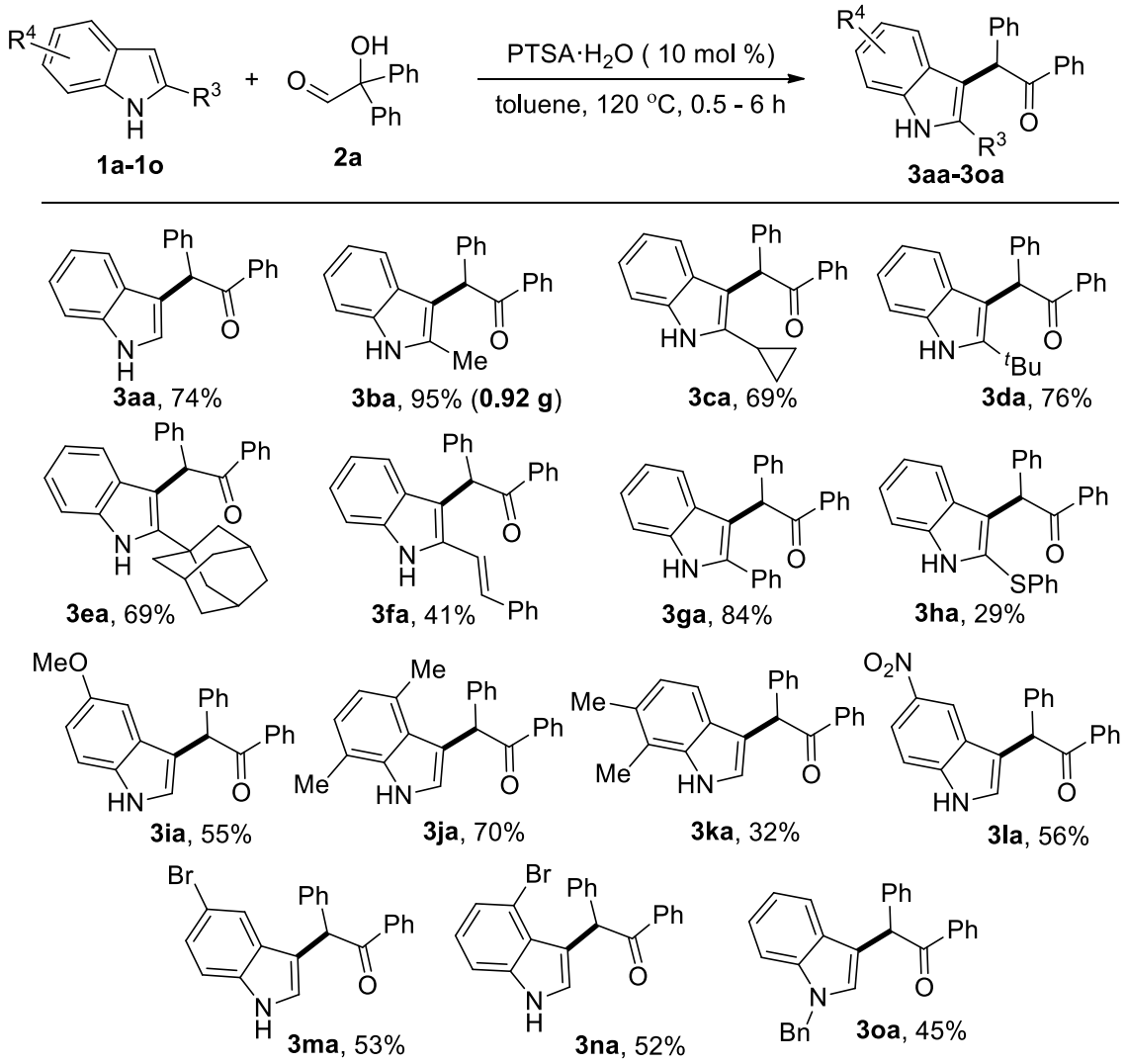
2	10	benzene	60	60	27
3	10	DCE	60	48	32
4	10	toluene	60	48	35
5	10	toluene	rt	24	ND
6	10	toluene	100	4.5	69
7	**10**	**toluene**	**120**	**2**	**74**
8	5	toluene	120	2	41
9	20	toluene	120	2	50
10[c]	10	toluene	120	2	74
11[d]	10	toluene	120	7	69

[a]Reaction Conditions: **1a** (0.2 mmol), **2a** (0.22 mmol). [b]Isolated yield. [c]0.30 mmol **2a** was used. [d]Diphenyl phosphate catalyst was used.

Keeping this synthetic strategy in mind, we focused on optimizing the reaction conditions by choosing commercially available indole **1a** (1.0 equiv) and *α*-hydroxy aldehyde **2a** (1.1 equiv) as model substrates. To our delight, commercially available and inexpensive PTSA·H_2O (0.1 euuiv) was an effective catalyst for this protocol. A brief optimization study revealed that toluene was the ideal solvent (Table 1, entries 1-4) for this reaction. During the course of this study, it has been observed that temperature plays a crucial role in this reaction as on increasing the temperature, yields improve remarkably along with enhanced reaction rate (entries 5-7). Yields of the reactions diminished drastically on either increasing or decreasing the catalyst loading (entries 8-9). Increasing the amount of **2a** did not provide a better result (entry 10). The reaction did not show any incremental effect on changing the catalyst from PTSA·H_2O to less acidic diphenyl phosphate (entry 11). Hence the conditions reported under entry 7 is the optimal reaction conditions (74%). It should be mentioned here that, in all the cases, reactions underwent through the partial formation of bis-indolylmethane intermediate as depicted in our working

hypothesis (Scheme 2a). To show the involvement of bisindolylmethane **C** (Scheme 2a) as one of the intermediate, first, the bisindolylmethane **C1** was isolated in 82% yield by conducting the reaction at room temperature using indole **1b** and aldehyde **2l** (Scheme 2b). Then upon treatment of the bisindolylmethane **C1** under the standard reaction conditions, the desired product **3bl** was isolated in 90% yield and the 2-methylindole **1b** was recovered in 84% yield.

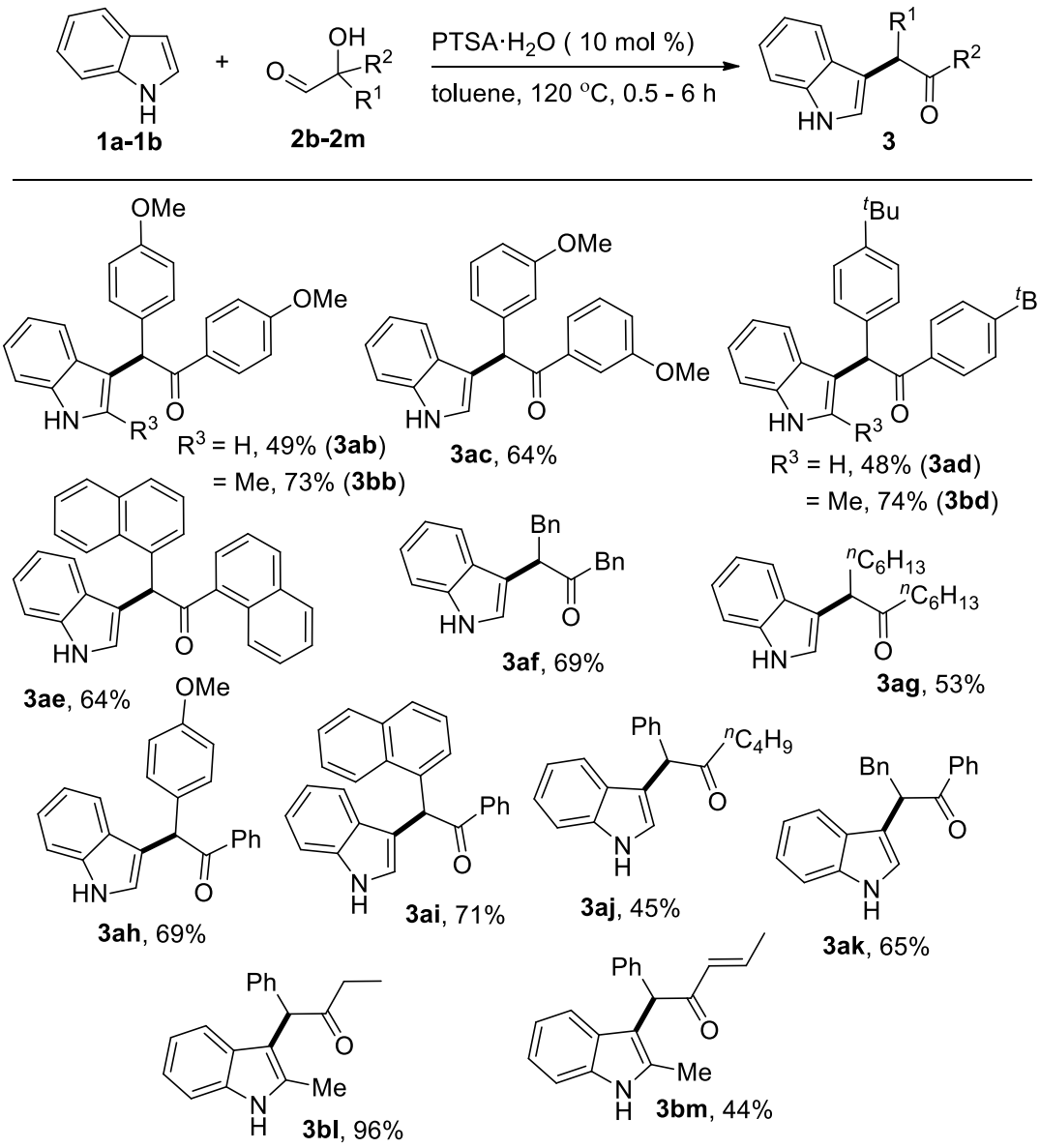
Scheme 3. Scope of Indoles for Pinacol-type Rearrangement[a]



[a]Reaction Conditions: **1a-1o** (0.2 mmol), **2a** (0.22 mmol), PTSA·H_2O (10 mol %), toluene, 120 °C; isolated yield.

With the optimized conditions in hand, the generality of this strategy was first investigated by treating various functionalized indoles with *α*-hydroxy aldehyde **2a** as a coupling partner. 2-Methyl and 2-cyclopropyl indoles reacted efficiently to generate the desired α-(3-indolyl) ketones in moderate to excellent yields (Scheme 3, **3ba**-**3ca**, 69-95%). Even bulky *tert*-butyl as well as adamantyl groups substituted indole did not hamper the reactivity and the corresponding products **3da**-**3ea** were isolated in 69-76% yields. Indoles bearing styryl-, phenyl-, thiophenyl-groups at C2 position successfully took part in reaction to deliver **3fa**-**3ha** in 29-84% yields. Indoles, bearing electron-donating or withdrawing functional groups at the benzene ring irrespective of their positions, underwent smooth conversion to provide the desired products in moderate to good yields (**3ia**-**3na**, 32-70%). Although the primary goal of this protocol was to employ NH free indoles, even the *N*-benzyl protected indole was also reactive enough to furnish the product **3oa** in 45% yield. Upon conducting the reaction on a gram scale, 0.92 g of the product **3ba** was isolated demonstrating the applicability of this method (95% yield). A sterically hindered substitution at the C2-position retard the first nucleophilic attack leading to the formation of products in low yields whereas in case of C2-unsubstituted one the formation of bisindolyl methane **C** was one of the major intermediate at the beginning of the reaction also leading to lower yield. In case of a sterically less demanding methyl substitution, an optimum result was obtained at higher temperature probably due to the direct conversion to products **3ba** and **3bl** through the intermediate **B**.

Scheme 4. Scope of Aldehydes for Pinacol-type Rearrangement[a]

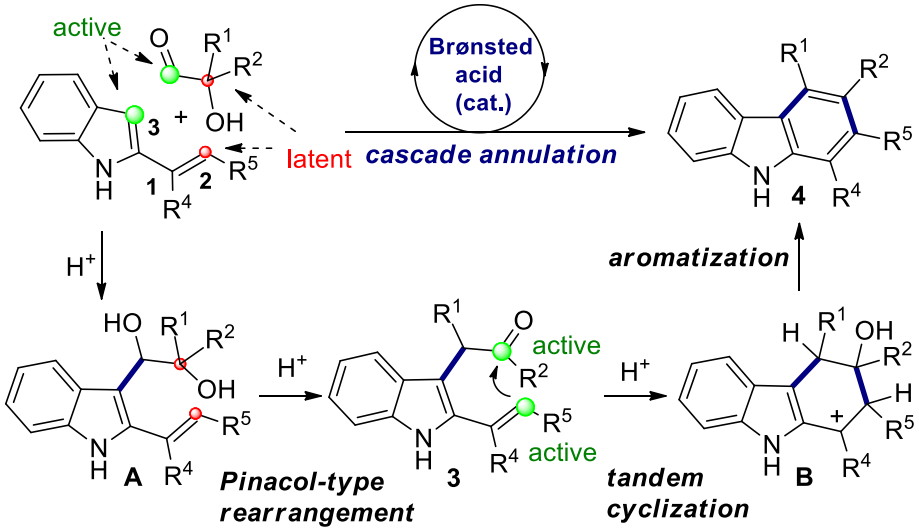


[a]Reaction Conditions: **1a-1b** (0.2 mmol), **2b-2m** (0.22 mmol), PTSA·H_2O (10 mol %), toluene, 120 °C; isolated yield.

To further check the versatility of this method, the scope of electrophiles was next explored by using indole (**1a**) or 2-methyl indole (**1b**) as model substrates. *α*-Hydroxy aldehydes bearing identical aryl groups at the *α*-position were found to be elegant coupling partners and the corresponding α-(3-indolyl) ketones were isolated in moderate to good yields (Scheme 4, **3ab-3ae**, **3bb**, **3bd**, 48-74%). Analogously, *α*-hydroxy aldehydes having similar alkyl substitutions at the *α*-position were also well-tolerated to obtain the products **3af-3ag** in 53-69% yields.

Pleasingly, when aldehydes bearing two different functional groups at the α-centre, were subjected to the optimized conditions, the group having greater migratory aptitude migrated selectively to furnish the single regioisomer exclusively in moderate to good yields (**3ah-3ak**, **3bl**, 45-96%). Analogously, preferential phenyl group migration over the allyl one, followed by subsequent double bond migration delivered **3bm** in 44% yield. Thus this present operationally simple protocol provides an elegant route to several valuable building blocks α-(3-indolyl) ketones in one step by employing simple precursors and catalyst.

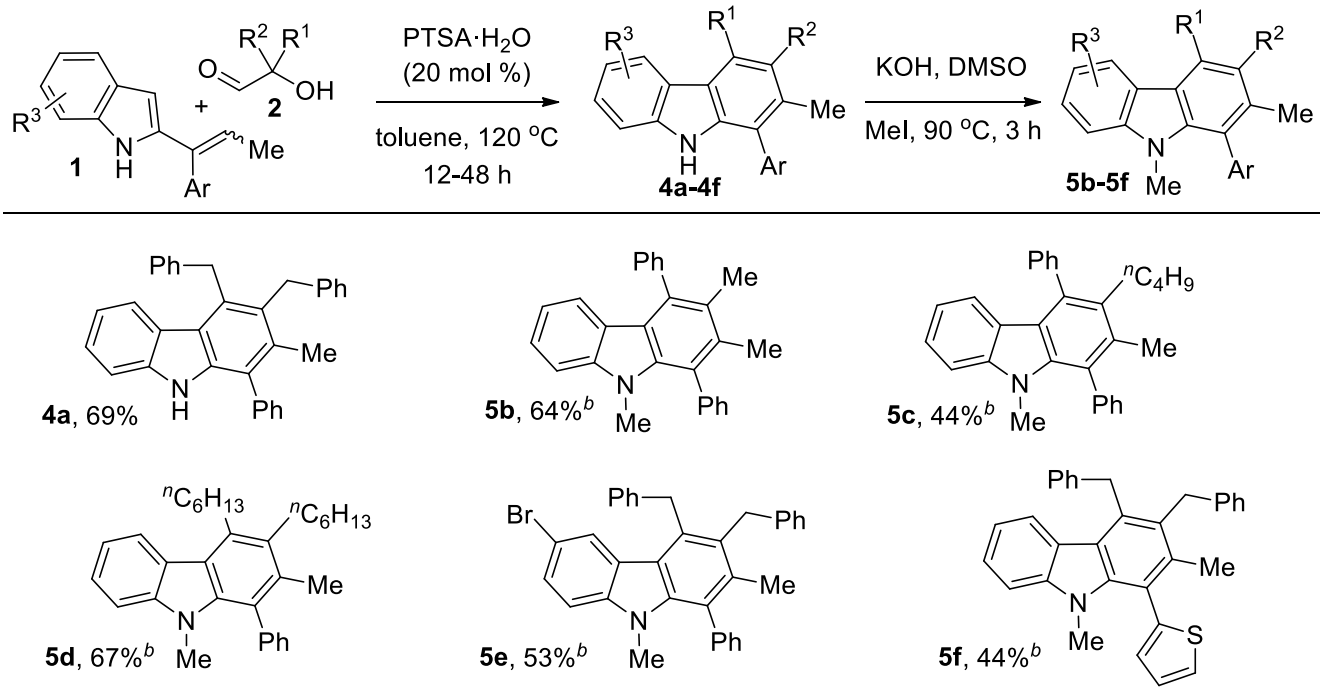
Scheme 5. Working Hypothesis for Cascade Annulation Strategy



After successfully accomplishing various structurally diverse α-(3-indolyl) ketones, next we intended to explore the applicability of this newly developed protocol by exploiting the carbonyl functionality *in situ* for the synthesis of highly substituted carbazoles through Brønsted acid catalyzed cascade annulation pathway. It is noteworthy to mention that carbazole is a privileged class of heterocycle present in various natural products and biologically active compounds.[6a] Beside this, it exhibits ubiquitous applications in medicinal as well as material chemistry. In order to execute our assumption, we planned to attach an alkene moiety at the C2 position of

indole. Due to superior nucleophilic character of the indole nucleus, first nucleophilic addition would occur *via* C3 position of indole generating α-(3-indolyl) ketone **3** through Pinacol-type rearrangement pathway *via* the formation of indolyl diol intermediate **A**. After that, the second nucleophilic addition would take place through the terminal C2′ position of alkene to generate the desired functionalized carbazole **4** *via* intermediate **B** (Scheme 5).

Scheme 6. Synthesis of Carbazole by Cascade Annulation[a]



[a]Reaction Conditions: **1** (0.2 mmol), **2** (0.22 mmol), PTSA·H_2O (20 mol %), toluene, 120 °C; isolated yield. [b]To isolate pure carbazoles, *N*-methylation was carried out.

With this synthetic strategy in hand, the scope of carbazoles was next investigated by choosing 2-alkenyl indole **1p** as a coupling partner with various aldehydes. Aldehyde bearing two benzyl groups at the *α*-position was successfully participated in the reaction (**4a**, 69%, Scheme 6). To our joy, aldehyde having two different substitutions at the α-centre also provided only one isomer of carbazoles **4b-4c** owing to the selective migration of the phenyl group over alkyl one. However, due to the difficulties associated with the purification of carbazoles **4b-4c**, probably

due to the impurities generated via side reactions of aldehydes, *N*-methylation was performed and pleasingly the carbazoles **5b-5c** were isolated in pure form in 44-64% yields over two steps. In a similar fashion, carbazoles **5d-5f** were also isolated in 44-67% yields. It should be noted that the presence of an aryl group at the C1′ position of alkene enhanced the nucleophilicity at the C2′ position and also stabilized the Prins-type intermediate, thereby facilitated the formation of carbazoles. Whereas, in case of 2-styryl indole **1f**, the presence of sterically hindered phenyl ring at the C2′ position prevents the intramolecular nucleophilic attack leading to the formation of **3fa**.

CONCLUSION

In conclusion, we have successfully developed a Brønsted acid catalyzed Pinacol-type rearrangement for the synthesis of indoles to various functionally diverse *α*-(3-indolyl) ketones by utilizing easily prepared α-hydroxy aldehydes and indoles as coupling partners. The method is operationally simple and scalable. Common bottle reagent PTSA·H_2O has been employed as catalyst rendering this protocol economically viable. Various key functional groups such as alkyl, aryl, alkenyl, thiophenyl, methoxy, nitro, and bromo are tolerated the reaction conditions demonstrating the generality of this method. Selective migration of aryl groups for differently substituted aldehydes eliminates the regioselectivity issue. The applicability of this strategy was further demonstrated by synthesizing densely functionalized carbazoles by employing one-pot cascade annulation strategy. The asymmetric version of this Pinacol-type rearrangement is currently undergoing in our laboratory.

EXPERIMENTAL SECTION

General Remarks. All reactions involving air or moisture-sensitive reagents were carried out in flame dried glassware under nitrogen/argon atmosphere. Ethylacetate was obtained from SRL

India. All other solvents were acquired from Merck India and were dried according to the standard literature procedure. Reactions were monitored by thin-layer chromatography (TLC) using Merck silica gel 60 F254 pre-coated plates (0.25 mm), and visualized under UV light or by dipping into $KMnO_4$ or DNP solution. Silica gel (particle size 100-200 mesh) was purchased from SRL India for performing column chromatography by using mixture of hexanes and ethylacetate eluent. The ^{1}H NMR spectroscopic data were recorded with a Bruker 400 or 500 or 600 MHz instruments. Proton decoupled ^{13}C NMR spectra ($^{13}C\{^1H\}$) were similarly recorded at 101 or 126 or 151 MHz instruments by using a broadband decoupled mode. Proton and carbon NMR chemical shifts (δ) are reported in parts per million (ppm) relative to residual proton or carbon signals in $CDCl_3$ (δ = 7.26, 77.16) or DMSO-d_6 (δ= 2.50, 39.52). Coupling constants (*J*) are reported in Hertz (Hz) and refer to apparent multiplicities. The following abbreviations are used for the multiplicities: s: singlet, d: doublet, t: triplet, q: quartet, dd: doublet of doublets, dt: doublet of triplet, m: multiplet, br: broad. Infrared (IR) spectra were recorded by Perkin Elmer FTIR spectrometer, and reported in terms of wave number (cm^{-1}). High resolution mass spectra (HRMS) were recorded in ESI (+ Ve) method using a time-of-flight (TOF) mass analyzer. Aldehydes[11b, 11c, 11d] and 2-alkenyl indoles[10b] were synthesized according to the reported methods.

Synthesis of α-(3-Indolyl) Ketones by Pinacol-type Rearrangement (GP I):

The indole **1** (0.2 mmol, 1.0 equiv) and *p*-toluenesulfonic acid·monohydrate (PTSA·H_2O, 0.02 mmol, 10 mol %) were charged into an oven dried culture tube containing a stirring bar. To this aldehyde **2** (0.22 mmol, 1.1 equiv, dissolved in 1.5 mL of toluene) was added dropwise at the room temperature while stirring. The resulting mixture was then heated at 120 °C in oil bath for 0.5 to 6.5 h. Upon completion of the reaction (as monitored by TLC), the reaction mixture was

transferred into a 25 mL round bottom flask by dissolving in ethyl acetate solvent and evaporated under vacuum. The crude residue was purified by silica gel column chromatography using ethyl acetate/hexane as an eluent to afford the desired products **3**.

*2-(1H-Indol-3-yl)-1,2-diphenylethan-1-one (**3aa**)*:[9b] The titled compound **3aa** was synthesized according to the **GP I** (reaction time: 2.5 h), the product **3aa** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (46 mg, 74% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.17 (br s, 1H), 8.08 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 7.3 Hz, 2H), 7.44 – 7.30 (m, 7H), 7.26 – 7.18 (m, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 2.3 Hz, 1H), 6.30 (s, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ (ppm) 198.6, 139.0, 137.0, 136.6, 133.1, 129.2, 129.0, 128.74, 128.67, 127.2, 126.7, 124.0, 122.5, 119.9, 118.9, 114.5, 111.5, 50.8.

*2-(2-Methyl-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3ba**)*:[9b] The titled compound **3ba** was synthesized according to the **GP I** (reaction time: 30 min), the product **3ba** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (0.92 g, 95% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.07 (d, *J* = 8.4 Hz, 2H), 8.01 (br s, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.7 Hz, 2H), 7.32 – 7.23 (m, 5H), 7.21 (d, *J* = 7.7 Hz, 1H), 7.15 – 7.08 (m, 2H), 6.25 (s, 1H), 2.27 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ (ppm) 199.1, 139.4, 137.2, 135.3, 132.9, 129.2, 128.62, 128.57, 128.4, 128.0, 126.8, 121.3, 119.8, 118.6, 110.5, 108.4, 50.9, 12.4.

*2-(2-Cyclopropyl-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3ca**):* The titled compound **3ca** was synthesized according to the **GP I** (reaction time: 2 h), the product **3ca** was isolated after column chromatography using 3-5% ethyl acetate/hexane as eluent (48 mg, 69% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.07 (d, *J* = 8.4 Hz, 2H), 7.81 (br s, 1H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.46 (t,

J = 7.4 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.30 – 7.21 (m, 6H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.38 (s, 1H), 2.07 – 2.00 (m, 1H), 1.03 – 0.89 (m, 2H), 0.77 – 0.71 (m, 1H), 0.67 – 0.61 (m, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ (ppm) 199.1, 139.5, 137.4, 134.9, 132.8, 129.3, 128.7, 128.5, 128.34, 128.25, 126.8, 121.6, 120.1, 119.3, 110.6, 110.1, 51.0, 7.9, 6.9, 6.6. **FTIR:** (neat)/ cm^{-1} = 3375, 2923, 2854, 1669, 1447. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{25}H_{22}NO$, 352.1696; found 352.1687.

*2-(2-(tert-Butyl)-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3da**):* The titled compound **3da** was synthesized according to the **GP I** (reaction time: 5 h), the product **3da** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (56 mg, 76% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.09 (br s, 1H), 8.00 (d, *J* = 7.5 Hz, 2H), 7.44 (dd, *J* = 7.9, 6.9 Hz, 1H), 7.37 – 7.32 (m, 3H), 7.27 – 7.22 (m, 4H), 7.18 (d, *J* = 7.3 Hz, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.91 (t, *J* = 7.5 Hz, 1H), 6.44 (s, 1H), 1.481–1.478 (m, 9H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 200.5, 142.4, 140.6, 138.3, 134.4, 132.6, 129.3, 129.2, 128.6, 128.5, 128.4, 126.7, 121.4, 120.9, 120.0, 110.4, 107.9, 52.7, 33.4, 30.9. **FTIR:** (neat)/ cm^{-1} = 3390, 3054, 2960, 1671, 1450, 1208. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{26}H_{26}NO$, 368.2009; found 368.2000.

*2-(2-((1s,3s)-Adamantan-1-yl)-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3ea**)*: The titled compound **3ea** was synthesized according to the **GP I** (reaction time: 6 h), the product **3ea** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (61 mg, 69% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.13 (br s, 1H), 8.01 (d, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.34 (t, *J* = 7.3 Hz, 3H), 7.25–7.17 (m, 6H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.90 (t, *J* = 7.5 Hz, 1H), 6.53 (s, 1H), 2.14 (s, 6H), 2.07 (s, 3H), 1.81–1.73 (m, 6H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$): δ (ppm) 200.6, 142.4, 140.7, 138.2, 134.3, 132.7, 129.20, 129.15, 128.7, 128.5, 128.3, 126.7, 121.3, 120.9, 119.8, 110.4, 107.9, 52.5, 42.1, 36.7, 35.8, 28.6. **FTIR:** (neat)/ cm^{-1} =

3404, 2902, 2851, 1671, 1448, 1199, 1007. **HRMS (ESI) *m*/*z*:** $[M + Na]^+$ calcd for $C_{32}H_{31}NNaO$, 468.2298; found 468.2273.

*(E)-1,2-Diphenyl-2-(2-styryl-1H-indol-3-yl)ethan-1-one (**3fa**):* The titled compound **3fa** was synthesized according to the **GP I** (reaction time: 4 h), the product **3fa** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (34 mg, 41% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.30 (br s, 1H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.43 (d, *J* = 7.3 Hz, 3H), 7.39 – 7.27 (m, 10H), 7.24 – 7.13 (m, 3H), 7.07 (t, *J* = 7.0 Hz, 2H), 6.84 (d, *J* = 16.6 Hz, 1H), 6.38 (s, 1H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 198.7, 139.3, 137.3, 136.9, 136.7, 133.8, 133.0, 129.4, 129.3, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 127.1, 126.6, 123.6, 120.6, 119.9, 117.1, 112.9, 110.8, 51.1. **FTIR:** (neat)/ cm^{-1} = 3365, 3058, 2924, 2854, 1673, 1447, 1260, 1017. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{30}H_{24}NO$, 414.1852; found 414.1847.

*1,2-Diphenyl-2-(2-phenyl-1H-indol-3-yl)ethan-1-one (**3ga**):*[9b] The titled compound **3ga** was synthesized according to the **GP I** (reaction time: 2 h), the product **3ga** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (65 mg, 84% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.35 (br s, 1H), 7.69 (d, *J* = 7.8 Hz, 2H), 7.63 (d, *J* = 8.0 Hz, 1H), 7.46 (br s, 5H), 7.37 – 7.29 (m, 7H), 7.20 – 7.15 (m, 3H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.30 (s, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ (ppm) 198.4, 140.0, 136.9, 136.8, 136.3, 132.7, 132.5, 129.4, 129.2, 128.7, 128.6, 128.6, 128.5, 128.3, 128.1, 126.9, 122.5, 121.4, 120.5, 111.0, 109.1, 51.2.

*1,2-Diphenyl-2-(2-(phenylthio)-1H-indol-3-yl)ethan-1-one (**3ha**):* The titled compound **3ha** was synthesized according to the **GP I** (reaction time: 2.5 h), the product **3ha** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (24 mg, 29% yield). **^{1}H NMR**

(400 MHz, DMSO-d_6): δ (ppm) 11.81 (br s, 1H), 7.86 (d, J = 7.2 Hz, 2H), 7.48 – 7.45 (m, 2H), 7.33 – 7.25 (m, 4H), 7.23 – 7.11 (m, 9H), 7.00 (d, J = 7.3 Hz, 2H), 6.56 (s, 1H). **^{13}C{^{1}H} NMR** (126 MHz, DMSO-d_6): δ (ppm) 198.2, 139.5, 137.4, 136.5, 135.8, 133.0, 130.0, 129.2, 129.1, 128.5, 128.3, 128.1, 127.0, 126.5, 126.2, 123.1, 122.9, 119.9, 119.7, 118.8, 111.7, 51.0. **FTIR:** (neat)/ cm^{-1} = 3386, 2923, 1678, 1447, 666, 612. **HRMS (ESI) *m*/*z*:** [M + H]$^+$ calcd for $C_{28}H_{22}NOS$, 420.1417; found 420.1398.

*2-(5-Methoxy-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3ia**):* The titled compound **3ia** was synthesized according to the **GP I** (reaction time: 6.5 h), the product **3ia** was isolated after column chromatography using 10% ethyl acetate/hexane as eluent (38 mg, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.05 (d, J = 7.3 Hz, 1H), 8.01 (br s, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.7 Hz, 2H), 7.37 (d, J = 7.5 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.26 – 7.22 (m, 2H), 7.00 (d, J = 2.5 Hz, 1H), 6.92 (d, J = 2.3 Hz, 1H), 6.86 (dd, J = 8.8, 2.4 Hz, 1H), 6.22 (s, 1H), 3.78 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 198.5, 154.5, 139.1, 137.2, 133.1, 131.8, 129.2, 129.0, 128.8, 128.7, 127.2, 127.2, 124.7, 114.3, 112.5, 112.1, 101.2, 56.1, 50.9. **FTIR:** (neat)/ cm^{-1} = 3357, 2923, 2854, 1675, 1580, 1448, 1266, 1209, 1102, 1020. **HRMS (ESI) *m*/*z*:** [M + Na]$^+$ calcd for $C_{23}H_{19}NNaO_2$, 364.1308; found 364.1302.

*2-(4,7-Dimethyl-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3ja**):* The titled compound **3ja** was synthesized according to the **GP I** (reaction time: 2.5 h), the product **3ja** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (47 mg, yield 70%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.03 (d, J = 7.8 Hz, 3H), 7.50 (t, J = 7.3 Hz, 1H), 7.39 (t, J = 7.3 Hz, 2H), 7.33 – 7.22 (m, 5H), 6.90 – 6.88 (m, 2H), 6.76 (d, J = 7.3 Hz, 1H), 6.59 (s, 1H), 2.56 (s, 3H), 2.42 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ (ppm) 198.8, 139.8, 137.0, 136.7, 132.9, 129.4, 129.2, 128.8, 128.7, 128.2, 127.1, 124.6, 124.3, 123.1, 121.8, 118.4, 115.0, 52.3, 20.4,

16.4. **FTIR:** (neat)/ cm^{-1} = 3856, 3753, 3651, 3358, 2931, 1718, 1673, 1425, 1259. **HRMS (ESI)** ***m*/*z*:** $[M + H]^+$ calcd for $C_{24}H_{22}NO$, 340.1696; found 340.1685.

*2-(6,7-Dimethyl-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3ka**):* The titled compound **3ka** was synthesized according to the **GP I** (reaction time: 5 h), the product **3ka** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (21 mg, 32% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.04 (d, *J* = 7.6 Hz, 2H), 7.94 (br s, 1H), 7.50 (t, *J* = 7.3 Hz, 1H), 7.41 – 7.34 (m, 4H), 7.30 (d, *J* = 7.1 Hz, 2H), 7.26 – 7.20 (m, 2H), 6.99 (s, 1H), 6.93 (d, *J* = 8.3 Hz, 1H), 6.25 (s, 1H), 2.38 (s, 3H), 2.36 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 198.5, 139.2, 137.29, 136.9, 133.0, 130.1, 129.2, 129.0, 128.7, 128.6, 127.1, 124.7, 123.2, 122.9, 118.4, 116.1, 115.0, 51.0, 19.3, 13.1. **FTIR:** (neat)/ cm^{-1} = 3374, 2916, 2849, 1674, 1447, 1250. **HRMS (ESI)** ***m*/*z*:** $[M + H]^+$ calcd for $C_{24}H_{22}NO$, 340.1696; found 340.1682.

*2-(5-Nitro-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3la**):* The titled compound **3la** was synthesized according to the **GP I** (reaction time: 6 h), the product **3la** was isolated after column chromatography using 20% ethyl acetate/hexane as eluent (40 mg, 56% yield). **^{1}H NMR** (500 MHz, DMSO-d_6): δ (ppm) 11.77 (br s, 1H), 8.61 (s, 1H), 8.16 (d, *J* = 7.6 Hz, 2H), 7.98 (d, *J* = 8.9 Hz, 1H), 7.59 (t, *J* = 7.3 Hz, 1H), 7.53 (d, *J* = 8.9 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.44 (d, *J* = 7.9 Hz, 2H), 7.42 (s, 1H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.21 (t, *J* = 6.9 Hz, 1H), 6.75 (s, 1H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO-d_6): δ (ppm) 197.9, 140.6, 139.4, 139.3, 136.2, 133.3, 128.9, 128.84, 128.77, 128.5, 128.2, 126.8, 125.7, 116.8, 116.2, 115.9, 112.1, 49.0. **FTIR:** (neat)/ cm^{-1} = 3294, 3062, 2923, 2853, 1674, 1469, 1277, 1198, 1093, 981. **HRMS (ESI)** ***m*/*z*:** $[M + H]^+$ calcd for $C_{22}H_{17}N_2O_3$, 357.1234; found 357.1231.

*2-(5-Bromo-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3ma**):* The titled compound **3ma** was synthesized according to the **GP I** (reaction time: 3 h), the product **3ma** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (41 mg, 53% yield). **^{1}H NMR** (400 MHz, $CDCl_3$); δ (ppm) 8.24 (br s, 1H), 8.05 (d, *J* = 8.6 Hz, 2H), 7.61 (d, *J* = 1.6 Hz, 1H), 7.54 (t, *J* = 8.4 Hz, 1H), 7.43 (t, *J* = 7.7 Hz, 2H), 7.36 – 7.29 (m, 4H), 7.27 – 7.23 (m, 2H), 7.19 (d, *J* = 8.6 Hz, 1H), 6.98 (d, *J* = 2.4 Hz, 1H), 6.21 (s, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ (ppm) 198.3, 138.6, 136.8, 135.2, 133.3, 129.04, 129.03, 128.9, 128.8, 128.4, 127.4, 125.5, 125.2, 121.4, 114.3, 113.3, 113.0, 50.6. **FTIR:** (neat)/ cm^{-1} = 3347, 2920, 2851, 1673, 1447, 793. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{22}H_{17}BrNO$, 390.0488; found 390.0477.

*2-(4-Bromo-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3na**):* The titled compound **3na** was synthesized according to the **GP I** (reaction time: 3 h), the product **3na** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (40 mg, 52% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.46 (br s, 1H), 8.10 (d, *J* = 7.7 Hz, 2H), 7.50 (t, *J* = 7.2 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.34 – 7.31 (m, 4H), 7.28 – 7.18 (m, 3H), 7.00 (s, 1H), 6.95 (t, *J* = 7.8 Hz, 1H), 6.64 (s, 1H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 198.8, 139.1, 138.1, 137.0, 132.9, 129.5, 129.4, 129.3, 128.9, 128.8, 128.7, 128.7, 127.2, 126.6, 124.6, 124.4, 123.2, 115.5, 114.0, 111.1, 51.1. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3334, 2923, 2853, 1676, 1596, 1335, 1182, 991, 909, 815. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{22}H_{17}BrNO$, 390.0488; found 390.0465.

*2-(1-Benzyl-1H-indol-3-yl)-1,2-diphenylethan-1-one (**3oa**):*[9d] The titled compound **3oa** was synthesized according to the **GP I** (reaction time: 2 h), the product **3oa** was isolated after column chromatography using 2% ethyl acetate/hexane as eluent (36 mg, 45% yield). **^{1}H NMR** (500 MHz, $CDCl_3$): δ (ppm) 8.08 (d, *J* = 7.3 Hz, 2H), 7.56 – 7.53 (m, 2H), 7.45 – 7.40 (m, 4H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.28 – 7.25 (m, 5H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.11 (t, *J* = 7.4 Hz, 1H), 7.05 –

7.04 (m, 3H), 6.33 (s, 1H), 5.29 (d, *J* = 4.4 Hz, 2H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 198.5, 139.1, 137.6, 137.2, 137.0, 133.0, 129.2, 129.0, 128.9, 128.73, 128.67, 128.2, 127.7, 127.5, 127.2, 126.7, 122.3, 119.8, 119.2, 113.6, 110.1, 50.9, 50.3.

*2-(1H-Indol-3-yl)-1,2-bis(4-methoxyphenyl)ethan-1-one (**3ab**):* The titled compound **3ab** was synthesized according to the **GP I** (reaction time: 6 h), the product **3ab** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (36 mg, 49% yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.10 (s, 1H), 8.05 (d, *J* = 8.9 Hz, 2H), 7.48 (d, *J* = 7.9 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 2.2 Hz, 1H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.18 (s, 1H), 3.83 (s, 3H), 3.76 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ (ppm) 197.3, 163.5, 158.7, 136.6, 131.4, 131.3, 130.2, 130.0, 126.8, 123.8, 122.5, 119.9, 119.0, 115.3, 114.1, 113.9, 111.4, 55.6, 55.4, 49.6. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3348, 2925, 1668, 1597, 1509, 1457, 1269, 1027, 804. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{24}H_{22}NO_3$, 372.1594; found 372.1595.

*1,2-bis(4-Methoxyphenyl)-2-(2-methyl-1H-indol-3-yl)ethan-1-one (**3bb**):* The titled compound **3bb** was synthesized according to the **GP I** (reaction time: 4 h), the product **3bb** was isolated after column chromatography using 10% ethyl acetate/hexane as eluent (56 mg, 73% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ (ppm) 7.97 (d, *J* = 9.0 Hz, 2H), 7.87 (br s, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 1H)., 7.14 (d, *J* = 8.6 Hz, 2H), 7.10 (t, *J* = 7.3 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.82–6.80 (m, 4H), 6.08 (s, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 2.32 (s, 1H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$): δ (ppm) 197.7, 163.3, 158.4, 135.3, 132.5, 131.8, 131.0, 130.22, 130.19, 128.2, 121.4, 119.9, 118.8, 113.8, 113.7, 110.4, 109.6, 55.5, 55.4, 49.8, 12.7. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3310, 3057, 2932, 2838, 1661, 1597, 1509, 1460, 1214. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{25}H_{24}NO_3$, 386.1751; found 386.1752.

*2-(1H-Indol-3-yl)-2-(3-methoxyphenyl)-1-(4-methoxyphenyl)ethan-1-one (**3ac**):* The titled compound **3ac** was synthesized according to the **GP I** (reaction time: 6 h), the product **3ac** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (48 mg, 64% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ (ppm) 8.15 (br s, 1H), 7.67 (d, *J* = 7.7 Hz, 1H), 7.61 (s, 1H), 7.53 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.33 (t, *J* = 7.9 Hz, 1H), 7.25 (t, *J* = 8 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.7 Hz, 1H), 7.09–7.07 (m, 1H), 7.04 (d, *J* = 2.2 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.95 (t, *J* = 1.8 Hz, 1H), 6.80 (dd, *J* = 8.3, 2.4 Hz, 1H), 6.25 (s, 1H), 3.81 (s, 3H), 3.76 (s, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$): δ (ppm) 198.2, 159.91, 159.88, 140.6, 138.4, 136.5, 129.7, 129.6, 126.7, 123.9, 122.6, 121.6, 120.0, 119.7, 118.9, 115.1, 114.5, 113.3, 112.5, 111.4, 55.5, 55.3, 50.9. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3354, 2925, 1675, 1597, 1456, 1335, 1246 1057, 850. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{24}H_{22}NO_3$, 372.1594; found 372.1591.

*1,2-bis(4-(tert-Butyl)phenyl)-2-(1H-indol-3-yl)ethan-1-one (**3ad**):* The titled compound **3ad** was synthesized according to the **GP I** (reaction time: 5 h), the product **3ad** was isolated after column chromatography using 2% ethyl acetate/hexane as eluent (36 mg, 48% yield). **^{1}H NMR** (500 MHz, $CDCl_3$): δ (ppm) 8.10 (br s, 1H), 8.00 (d, *J* = 8.4 Hz, 2H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.31 – 7.28 (m, 4H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 2.4 Hz, 1H), 6.25 (s, 1H), 1.30 (s, 9H), 1.27 (s, 9H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 198.3, 156.7, 149.8, 136.6, 136.1, 134.6, 129.0, 128.8, 126.8, 125.7, 125.6, 123.9, 122.5, 119.9, 119.0, 115.0, 111.4, 50.1, 35.2, 34.6, 31.5, 31.2. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3357, 2960, 1673, 1603, 1107, 997, 793. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{30}H_{34}NO$, 424.2635; found 424.2641.

*1,2-bis(4-(tert-Butyl)phenyl)-2-(2-methyl-1H-indol-3-yl)ethan-1-one (**3bd**):* The titled compound **3bd** was synthesized according to the **GP I** (reaction time: 1.5 h), the product **3bd** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (82 mg, 74% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ (ppm) 7.96 (d, *J* = 8.4 Hz, 2H), 7.91 (br s, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 1H), 7.17 (d, *J* = 8.3 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.17 (s, 1H), 2.37 (s, 3H), 1.30 (s, 9H), 1.29 (s, 9H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$): δ (ppm) 198.4, 156.3, 149.2, 136.4, 135.2, 134.6, 132.6, 128.7, 128.6, 128.2, 125.5, 125.2, 121.3, 119.8, 118.9, 110.2, 109.0, 50.1, 35.0, 34.4, 31.4, 31.1, 12.6. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3354, 2963, 1673, 1603, 1426, 1335, 1246, 1107. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{31}H_{36}NO$, 438.2791; found 438.2781.

*2-(1H-Indol-3-yl)-1,2-di(naphthalen-1-yl)ethan-1-one (**3ae**):* The titled compound **3ae** was synthesized according to the **GP I** (reaction time: 6 h), the product **3ae** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (52 mg, 64% yield). **^{1}H NMR** (500 MHz, $CDCl_3$): δ (ppm) 8.61 - 8.59 (m, 1H), 8.18 (br s, 1H), 8.10 (d, *J* = 7.2 Hz, 1H), 8.04 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 7.2 Hz, 1H), 7.87 – 7.85 (m, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.53 – 7.49 (m, 3H), 7.47 – 7.44 (m, 2H), 7.41 – 7.35 (m, 4H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 2.4 Hz, 1H), 7.04 (s, 1H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 202.3, 136.8, 135.7, 135.5, 134.3, 133.1, 131.8, 130.9, 129.2, 128.6, 128.4, 128.3, 128.2, 128.1, 127.2, 126.9, 126.63, 126.60, 126.2, 125.8, 125.7, 124.9, 124.6, 123.4, 122.7, 120.1, 119.1, 114.4, 111.5, 50.5. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3375, 3054, 2923, 2853, 1674, 1506, 1457, 1228, 1093, 907. **HRMS (ESI) *m*/*z*:** $[M + Na]^+$ calcd for $C_{30}H_{21}NNaO$, 434.1515; found 434.1503.

*3-(1H-Indol-3-yl)-1,4-diphenylbutan-2-one (**3af**):* The titled compound **3af** was synthesized according to the **GP I** (reaction time: 1.5 h), the product **3af** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (38 mg, 69% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ (ppm) 8.21 (br s, 1H), 7.64 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 8.1 Hz, 1H), 7.28 (d, *J* = 6.7 Hz, 1H), 7.29 – 7.19 (m, 8H), 7.09 (d, *J* = 7.2 Hz, 2H), 6.99 (s, 1H), 6.96 (d, *J* = 4.6 Hz, 2H), 4.37 (t, *J* = 7.3 Hz, 1H), 3.66 (dd, *J* = 36.6, 15.7 Hz, 2H), 3.51 (dd, *J* = 13.6, 8.2 Hz, 1H), 3.11 (dd, *J* = 13.7, 6.5 Hz, 1H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$): δ (ppm) 207.7, 140.2, 136.5, 134.3, 129.6, 129.1, 128.6, 128.3, 126.8, 126.5, 126.1, 123.1, 122.5, 120.0, 119.0, 113.0, 111.5, 51.0, 48.9, 38.1. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3369, 3029, 1704, 1454, 1321, 1095. **HRMS (ESI) *m*/*z*:** $[M + Na]^+$ calcd for $C_{24}H_{21}NNaO$, 362.1515; found 362.1512.

*8-(1H-Indol-3-yl)tetradecan-7-one (**3ag**):* The titled compound **3ag** was synthesized according to the **GP I** (reaction time: 1.5 h), the product **3ag** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (35 mg, 53% yield). **^{1}H NMR** (600 MHz, $CDCl_3$): δ (ppm) 8.14 (br s, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.20 (t, *J* = 7.5 Hz, 1H), 7.13 (t, *J* = 7.4 Hz, 1H), 7.06 (s, 1H), 3.90 (t, *J* = 7.4 Hz, 1H), 2.44 – 2.34 (m, 2H), 2.12 – 2.06 (m, 1H), 1.84 – 1.78 (m, 1H), 1.51 – 1.42 (m, 2H), 1.30 – 1.17 (m, 13H), 0.85 (t, *J* = 7.0 Hz, 3H), 0.80 (t, *J* = 7.2 Hz, 3H). **^{13}C{^{1}H} NMR** (151 MHz, $CDCl_3$): δ (ppm) 211.7, 136.3, 126.9, 122.3, 122.2, 119.7, 119.1, 114.3, 111.2, 50.0, 41.1, 31.7, 31.6, 31.5, 29.3, 28.76, 27.81, 23.9, 22.6, 22.4, 14.1, 14.0. **FTIR:** (neat)/ cm^{-1} = 3348, 2926, 2854, 1693, 1459, 1342, 1100, 1012. **HRMS (ESI) *m*/*z*:** $[M + Na]^+$ calcd for $C_{22}H_{33}NNaO$, 350.2454; found 350.2438.

*2-(1H-Indol-3-yl)-2-(4-methoxyphenyl)-1-phenylethan-1-one (**3ah**):*[9b] The titled compound **3ah** was synthesized according to the **GP I** (reaction time: 1.5 h), the product **3ah** was isolated after column chromatography using 10% ethyl acetate/hexane as eluent (47 mg, yield 69%). **^{1}H NMR**

(400 MHz, $CDCl_3$): δ (ppm) 8.10 (br s, 1H), 8.05 (d, *J* = 7.3 Hz, 2H), 7.53 – 7.48 (m, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.29–7.25 m, 2H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 2.3 Hz, 1H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.22 (s, 1H), 3.76 (s, 3H). **$^{13}C\{^1H\}$ NMR** (101 MHz, $CDCl_3$): δ (ppm) 198.8, 158.8, 137.1, 136.6, 133.1, 131.1, 130.2, 129.0, 128.7, 126.7, 123.8, 122.6, 120.0, 119.0, 115.1, 114.2, 111.4, 55.4, 50.0. **FTIR:** (neat)/ cm^{-1} = 3485, 3055, 2926, 2852, 1686, 1511, 1265.

*2-(1H-Indol-3-yl)-2-(naphthalen-1-yl)-1-phenylethan-1-one (**3ai**):* The titled compound **3ai** was synthesized according to the **GP I** (reaction time: 4.5 h), the product **3ai** was isolated after column chromatography using 10% ethyl acetate/hexane as eluent (51 mg, 71% yield). **^1H NMR** (500 MHz, $CDCl_3$): δ (ppm) 8.52 – 8.35 (m, 1H), 8.15 (br s, 1H), 7.97 (dd, *J* = 15.4, 7.7 Hz, 2H), 7.86– 7.84 (m, 1H), 7.53–7.48 (m, 3H), 7.45–7.42 (m, 3H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 2H), 7.25 – 7.22 (m, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 6.28 (s, 1H). **$^{13}C\{^1H\}$ NMR** (126 MHz, $CDCl_3$): δ (ppm) 202.5, 139.1, 136.8, 136.5, 134.1, 132.6, 130.7, 129.2, 128.8, 128.5, 128.0, 127.7, 127.3, 126.9, 126.6, 126.0, 124.6, 123.9, 122.6, 120.0, 119.1, 114.8, 111.4, 54.4. **FTIR:** ν_{max} (neat)/ cm^{-1} = 3410, 3058, 1678, 1508, 1457, 1230, 1093. **HRMS (ESI) *m/z*:** $[M + Na]^+$ calcd for $C_{26}H_{19}NNaO$, 384.1359; found 384.1360.

*1-(1H-Indol-3-yl)-1-phenylhexan-2-one (**3aj**):* The titled compound **3aj** was synthesized according to the **GP I** (reaction time: 30 min), the product **3aj** was isolated after column chromatography using 2% ethyl acetate/hexane as eluent (26 mg, yield 45%). **^1H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.17 (br s, 1H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.36–7.35 (m, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.26 (t, *J* = 7 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 2.3 Hz, 1H), 7.10 (t, *J* = 7.5 Hz, 1H), 5.38 (s, 1H), 2.64 (dt, *J* = 7.2, 3.1 Hz, 2H), 1.63 – 1.58 (m, 2H), 1.36 – 1.25 (m, 2H), 0.87 (t, *J* = 7.4 Hz, 3H). **$^{13}C\{^1H\}$ NMR** (126 MHz, $CDCl_3$): δ (ppm)

209.0, 138.8, 136.4, 129.0, 128.7, 127.2, 127.0, 123.4, 122.5, 119.9, 119.0, 114.0, 111.4, 55.8, 42.3, 26.4, 22.4, 13.9. **FTIR:** (neat)/ cm^{-1} = 3408, 2957, 2871, 1708, 1457, 1339, 1098. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{20}H_{22}NO$, 292.1696; found 292.1680.

*2-(1H-Indol-3-yl)-1,3-diphenylpropan-1-one (**3ak**):* The titled compound **3ak** was synthesized according to the **GP I** (reaction time: 1.5 h), the product **3ak** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (42 mg, yield 65%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.10 (br s, 1H), 7.93 (d, *J* = 8.6 Hz, 2H), 7.71 (d, *J* = 7.8 Hz, 1H), 7.44 – 7.40 (m, 1H), 7.34 – 7.29 (m, 3H), 7.23 – 7.13 (m, 7H), 6.97 (d, *J* = 2.5 Hz, 1H), 5.15 (dd, *J* = 8.2, 6.0 Hz, 1H), 3.65 (dd, *J* = 13.7, 8.3 Hz, 1H), 3.23 (dd, *J* = 13.7, 6.0 Hz, 1H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ (ppm) 199.8, 140.6, 137.0, 136.5, 132.8, 129.2, 128.6, 128.5, 128.4, 126.3, 126.2, 122.9, 122.4, 120.0, 118.9, 114.3, 111.5, 47.1, 39.3. **FTIR:** (neat)/ cm^{-1} =3372, 2928, 1667, 1446, 1341, 1266, 1181, 1103, 977, 931, 874. **HRMS (ESI) *m*/*z*:** $[M + Na]^+$ calcd for $C_{23}H_{19}NNaO$, 348.1359; found 348.1353.

*1,1-bis(2-Methyl-1H-indol-3-yl)-2-phenylbutan-2-ol (**C1**):* The 2-methylindole **1b** (0.2 mmol, 1.0 equiv) and *p*-toluenesulfonic acid·monohydrate (PTSA·H_2O, 0.02 mmol, 10 mol %) were charged into an oven dried culture tube containing a stirring bar. To this aldehyde **2l** (0.22 mmol, 1.1 equiv, dissolved in 1.5 mL of toluene) was added dropwise at the room temperature while stirring. The resulting mixture was then stirred for 8 h at the room temperature. Upon completion of the reaction (as monitored by TLC), the reaction mixture was transferred into a 25 mL round bottom flask by dissolving in ethyl acetate and evaporated under vacuum. The crude residue was purified by silica gel column chromatography using 5-10% ethyl acetate in hexane as an eluent to afford the desired bisindolylmethane product **C1** (67 mg, 82% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 10.66 (br s, 1H), 10.23 (br s, 1H), 8.05 (br s, 1H), 7.98 (br s, 1H), 7.48 (d, *J* = 6.6

Hz, 2H), 7.18 (d, *J* = 7.6 Hz, 1H), 7.11 (t, *J* = 7.5 Hz, 2H), 7.01 – 6.90 (m, 4H), 6.77 (t, *J* = 7.3 Hz, 1H), 6.70 (t, *J* = 7.2 Hz, 1H), 4.93 (br s, 1H), 4.48 (br s, 1H), 2.39 (s, 3H), 2.08 (s, 3H), 1.91 – 1.85 (m, 2H), 0.50 (t, *J* = 6.5 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, DMSO) δ (ppm) 151.2, 146.6, 135.1, 134.8, 133.2, 131.9, 128.6, 126.8, 126.2, 125.1, 121.1, 119.2, 118.8, 117.8, 117.1, 112.2, 111.9, 110.3, 109.9, 109.5, 80.5, 44.8, 34.7, 12.8, 8.1. **FTIR:** (neat)/ cm^{-1} = 3559, 3398, 2973, 1460, 1368, 1308, 1247, 1174, 1126, 1025, 904, 811. **HRMS (ESI) *m*/*z*:** $[M + Na]^+$ calcd for $C_{28}H_{28}N_2NaO$, 431.2094; found 431.2097.

*Synthesis of compound **3bl** from bisindolylmethane **C1**:* The compound **C1** (0.1 mmol, 1.0 equiv) and *p*-toluenesulfonic acid·monohydrate (PTSA·H_2O, 0.01 mmol, 10 mol %) were charged into an oven dried culture tube containing a stirring bar. To this 1.0 mL of toluene was added at the room temperature while stirring. The resulting mixture was then heated at 120 °C in oil bath for 20 min. Upon completion of the reaction (as monitored by TLC), the reaction mixture was transferred into a 25 mL round bottom flask by dissolving in ethyl acetate solvent and evaporated under vacuum. The crude residue was purified by silica gel column chromatography using 5% ethyl acetate/hexane as an eluent to afford the desired product **3bl** (25 mg, 90% yield). In a second fraction the indole **1b** was also isolated (11 mg, 84% yield).

*1-(2-methyl-1H-indol-3-yl)-1-phenylbutan-2-one (**3bl**):* The titled compound **3bl** was synthesized according to the **GP I** (reaction time: 30 min), the product **3bl** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (53 mg, yield 96%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.99 (br s, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 8.9 Hz, 1H), 7.27 – 7.25 (m, 2H), 7.23 – 7.17 (m, 3H), 7.13 (t, *J* = 8.1 Hz, 1H), 7.05 (t, *J* = 8.1 Hz, 1H), 5.30 (s, 1H), 2.63 – 2.46 (m, 2H), 2.36 (s, 3H), 1.04 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ (ppm) 210.0, 138.8, 135.4, 133.4, 129.0, 128.3, 128.1, 126.8, 121.5, 120.0, 119.1, 110.5, 108.4,

55.0, 35.3, 12.4, 8.4. **FTIR:** (neat)/ cm^{-1} =3350, 2922, 1699, 1461, 1310, 1247, 1115, 917, 842. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{19}H_{20}NO$, 278.1539; found 278.1538.

*(E)-1-(2-Methyl-1H-indol-3-yl)-1-phenylpent-3-en-2-one (**3bm**):* The titled compound **3bm** was synthesized according to the **GP I** (reaction time: 1 h), the product **3bm** was isolated after column chromatography using 5% ethyl acetate/hexane as eluent (25 mg, yield 44%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 8.04 (br s, 1H), 7.39 (dd, *J* = 11.4, 6.1 Hz, 1H), 7.29 (d, *J* = 7.3 Hz, 2H), 7.23 – 7.19 (m, 3H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 7.2 Hz, 1H), 6.97 (dd, *J* = 14.7, 7.7 Hz, 1H), 6.27 (dd, *J* = 15.3, 1.5 Hz, 1H), 5.40 (s, 1H), 2.33 (s, 3H), 1.78 (dd, *J* = 7.0, 1.5 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ (ppm) 197.6, 142.6, 138.7, 135.4, 133.5, 130.6, 129.2, 128.7, 128.4, 128.3, 127.1, 126.8, 121.5, 119.9, 119.0, 110.5, 107.7, 54.0, 18.3, 12.5. **FTIR:** (neat)/ cm^{-1} = 3348, 2922, 2852, 1685, 1625, 1459, 1291, 964. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{20}H_{20}NO$, 290.1539; found 290.1534.

Synthesis of Carbazoles by Formal [4+2] Benzannulation (GP II): The indole **1p** (0.2 mmol, 1.0 equiv) and *p*-toluenesulfonic acid·monohydrate (PTSA·H_2O, 0.04 mmol, 20 mol %) were charged into an oven dried culture tube containing a stirring bar. To this aldehyde **2** (0.22 mmol, 1.1 equiv, dissolved in 1.5 mL of toluene) was added dropwise at the room temperature while stirring. The resulting mixture was then heated at 120 ºC in oil bath over 24 to 48 h. Upon completion of the reaction (as monitored by TLC), the reaction mixture was transferred into a 25 mL round bottom flask using ethyl acetate solvent and evaporated under vacuum. The crude residue was purified by silica gel column chromatography using hexane as an eluent to afford the desired products **4a-4f**. As carbazoles **4b-4f** were isolated along with inseparable impurities, they were subjected to the *N*-methylation conditions to obtain pure *N*-methylated products **5b-5f** in 44-67% yields over two steps.

Procedure for *N*-Methylation Reaction: The carbazoles **4b-4f** (1.0 equiv) was dissolved in 3 mL dimethyl sulfoxide, solid potassium hydroxide (1.2 equiv) was added and the mixture was stirred for 30 min at room temperature. Then methyl iodide (1.5 equiv) was added at room temperature and heated at 90 ^{o}C in oil bath for 2 to 3 h. Upon completion of the reaction as indicated by TLC, water was added to the reaction mixture and extracted with ethyl acetate. The organic layers were dried over Na_2SO_4, evaporated under vacuum and purified by silica gel column chromatography using hexane as an eluent to afford the desired products **5b-5f**.

*3,4-Dibenzyl-2-methyl-1-phenyl-9H-carbazole (**4a**):* The titled compound **4a** was synthesized according to the **GP II** (reaction time: 24 h), the product **4a** was isolated after column chromatography using hexane as eluent (59 mg, yield 69%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 7.98 (d, *J* = 8.0 Hz, 1H), 7.81 (br s, 1H), 7.60 – 7.56 (m, 2H), 7.50 – 7.48 (m, 3H), 7.34 – 7.33 (m, 2H), 7.29 – 7.26 (m, 6H), 7.22 – 7.20 (m, 2H), 7.11–7.09 (m, 3H), 4.66 (s, 2H), 4.24 (s, 2H), 2.21 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ (ppm) 140.9, 139.8, 139.7, 138.6, 137.9, 133.3, 133.0, 130.4, 129.4, 129.2, 128.7, 128.5, 128.4, 128.0, 127.6, 126.1, 125.8, 125.0, 123.9, 123.8, 122.5, 120.7, 119.5, 110.5, 36.4, 35.0, 17.8. **FTIR:** (neat)/ cm^{-1} = 3421, 2915, 1600, 1451, 1328, 1254, 1103, 1028, 957. **HRMS (ESI) *m*/*z*:** $[M + H]^+$ calcd for $C_{33}H_{28}N$, 438.2216; found, 438.2199.

*2,3,9-Trimethyl-1,4-diphenyl-9H-carbazole (**5b**):* The titled compound **5b** was synthesized according to the **GP II** (reaction time: 24 h) and followed by subsequent methyl protection. The product **5b** was isolated along with its minor regioisomer (generated due to the migration of methyl group over phenyl one) in 3.5:1 ratio after column chromatography using hexane as eluent (46 mg, 64% combined yield). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 7.59 – 7.46 (m, 5H), 7.44 – 7.41 (m, 5H), 7.32 – 7.28 (m, 1H), 7.20 (d, *J* = 8.2 Hz, 1H), 6.83 (t, *J* = 7.5 Hz, 1H), 6.58

(d, *J* = 7.9 Hz, 1H), 3.13 (s, 3H), 2.18 (s, 3H), 2.17 (s, 3H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$): δ (ppm) 142.3, 141.7, 140.3, 137.3, 135.7, 133.6, 131.2, 130.6, 129.7, 129.0, 128.3, 127.5, 127.3, 125.6, 124.8, 124.5, 122.8, 122.0, 118.5, 108.3, 32.0, 18.0, 17.1. **FTIR:** (neat)/ cm^{-1} = 3054, 2923, 2854, 1573, 1463, 1388, 1311, 1070, 1024, 894, 846. **HRMS (ESI) *m/z*:** $[M + H]^+$ calcd for $C_{27}H_{24}N$, 362.1903; found 362.1900.

*3-Butyl-2,9-dimethyl-1,4-diphenyl-9H-carbazole (**5c**):* The titled compound **5c** was synthesized according to the **GP II** (reaction time: 32 h) and followed by subsequent methyl protection. The product **5c** was isolated after column chromatography using hexane as eluent (33 mg, yield 44% over two steps). **^{1}H NMR** (400 MHz, $CDCl_3$): δ (ppm) 7.57 – 7.47 (m, 5H), 7.46 – 7.42 (m, 5H), 7.28 –7.25 (m, 1H), 7.18 (d, *J* = 8.0 Hz, 1H), 6.81 (t, *J* = 7.5 Hz, 1H), 6.45 (d, *J* = 8.0 Hz, 1H), 3.12 (s, 3H), 2.60 – 2.57 (m, 2H), 2.21 (s, 3H), 1.49 – 1.41 (m, 2H), 1.26 – 1.17 (m, 2H), 0.77 (t, *J* = 7.3 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$): δ (ppm) 142.3, 141.4, 140.4, 137.2, 135.7, 133.0, 131.2, 130.7, 129.7, 128.8, 128.4, 127.4, 127.3, 124.83, 124.82, 122.9, 122.0, 120.2, 118.5, 108.2, 33.3, 32.0, 30.3, 23.2, 17.4, 13.9. **FTIR:** (neat)/ cm^{-1} = 3055, 2922, 2852, 1569, 1457, 1384, 1312, 1027. **HRMS (ESI) *m/z*:** $[M + H]^+$ calcd for $C_{30}H_{30}N$, 404.2373; found 404.2371.

*3,4-Dihexyl-2,9-dimethyl-1-phenyl-9H-carbazole (**5d**):* The titled compound **5d** was synthesized according to the **GP II** (reaction time: 48 h) and followed by subsequent methyl protection. The product **5d** was isolated after column chromatography using hexane as eluent (58 mg, 67% yield over two steps). **^{1}H NMR** (400 MHz, DMSO-d_6): δ (ppm) 8.00 (d, *J* = 7.8 Hz, 1H), 7.51 – 7.43 (m, 3H), 7.39 (d, *J* = 7.3 Hz, 1H), 7.35 (t, *J* = 8 Hz, 1H), 7.29 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.17 (dt, *J* = 6.5, 1.3 Hz 1H), 3.18 – 14 (m, 2H), 2.75 – 2.70 (m, 2H), 2.05 (s, 3H), 1.67 – 1.56 (m, 4H), 1.32 – 1.20 (m, 4H), 0.90 (t, *J* = 4.6 Hz, 3H), 0.87 (t, *J* = 4.8 Hz, 3H). **^{13}C{^{1}H} NMR** (101 MHz,

DMSO-d_6): δ (ppm) 141.7, 139.7, 137.1, 134.4, 132.3, 130.8, 129.7, 128.3, 127.4, 124.6, 123.2, 121.8, 121.5, 119.0, 118.9, 109.1, 31.7, 31.12, 31.07, 30.6, 29.8, 29.4, 29.4, 29.3, 28.9, 22.2, 22.1, 17.2, 14.0. **FTIR:** ν_{max} (neat)/ cm^{-1} = 2923, 2854, 1789, 1727, 1459, 1391, 1119, 1029, 972. **HRMS (ESI) *m/z*:** $[M + H]^+$ calcd for $C_{32}H_{42}N$, 440.3312; found 440.3307.

*3,4-dibenzyl-6-bromo-2,9-dimethyl-1-phenyl-9H-carbazole (**5e**):* The titled compound **5e** was synthesized according to the **GP II** (reaction time: 48 h) and followed by subsequent methyl protection. The product **5e** was isolated after column chromatography using hexane as eluent (56 mg, 53% yield over two steps). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 8.05 (d, *J* = 1.5 Hz, 1H), 7.51 – 7.38 (m, 6H), 7.29 – 7.17 (m, 8H), 7.14 (d, *J* = 8.7 Hz, 1H), 7.05 (d, *J* = 7.4 Hz, 2H), 4.59 (s, 2H), 4.20 (s, 2H), 3.13 (s, 3H), 2.05 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ (ppm) 141.0, 140.7, 139.9, 139.3, 138.7, 135.4, 133.1, 131.2, 129.3, 128.8, 128.5, 128.4, 128.3, 128.0, 127.60, 127.57, 126.3, 125.9, 125.0, 124.6, 124.3, 120.2, 111.8, 109.9, 36.3, 35.1, 32.3, 18.0. **FTIR:** (neat)/ cm^{-1} = 2923, 2855, 1577, 1493, 1443, 1385, 1292, 1181, 1084, 1028, 973, 918, 856, 795. **HRMS (ESI) *m/z*:** $[M + H]^+$ calcd for $C_{34}H_{29}BrN$, 532.1458; found 532.1452.

*3,4-dibenzyl-2,9-dimethyl-1-(thiophen-2-yl)-9H-carbazole (**5f**):* The titled compound **5f** was synthesized according to the **GP II** (reaction time: 48 h) and followed by subsequent methyl protection. The product **5f** was isolated after column chromatography using hexane as eluent (39 mg, 44% yield over two steps). **^{1}H NMR** (400 MHz, $CDCl_3$) δ (ppm) 7.95 (d, *J* = 8.0 Hz, 1H), 7.49 (dd, *J* = 5.2, 1.0 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.15 (m, 9H), 7.10 – 7.05 (m, 4H), 4.64 (s, 2H), 4.18 (s, 2H), 3.37 (s, 3H), 2.16 (s, 3H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ (ppm) 142.3, 140.9, 140.8, 139.5, 139.4, 137.1, 134.3, 129.3, 128.7, 128.5, 128.4, 128.0, 127.2, 126.5, 126.1, 125.9, 125.1, 122.50, 122.47, 121.3, 119.3, 115.6, 108.6, 36.4,

35.1, 31.2, 17.8. **FTIR:** (neat)/ cm^{-1} = 2924, 2853, 1574, 1449, 1388, 1292, 1180, 1078, 1028, 922, 845. **HRMS (ESI) *m/z*:** $[M + H/Na]^+$ calcd for $C_{32}H_{28}NS$, 458.1937; found 458.1945.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

NMR spectra (PDF).

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REFERENCES

(1) (a) Collins, C. J. The Pinacol Rearrangement. *Q. Rev. Chem. Soc.* **1960**, *14*, 357−377. (b) Alvarez-Manzaneda, E. J.; Chahboun, R.; Barranco, I.; Torres, E. C.; Alvarez, E.; Alvarez-Manzaneda, R. First Enantiospecific Synthesis of Marine Nor-Sesquiterpene (+)- Austrodoral from (-)-Sclareol. *Tetrahedron Letters*, **2005**, *46*, 5321−5324. (c) Zhang, X.-M.; Tu, Y.-Q.;

Zhang, F.-M.; Chen, Z.-H.; Wang, S.-H. Recent Applications of the 1,2-Carbon Atom Migration Strategy in Complex Natural Product Total Synthesis. *Chem. Soc. Rev.* **2017**, *46*, 2272−2305.

(2) (a) Song, Z.-L.; Fan, C.-A.; Tu, Y.-Q. Semipinacol Rearrangement in Natural Product Syntheis. *Chem. Rev.* **2011**, *111*, 7523−7556. (b) Snape, T. J. Recent Advances in the Semi-Pinacol Rearrangement of α-Hydroxy Epoxides and Related Compounds. *Chem. Soc. Rev.* **2007**, *36*, 1823−1842.

(3) (a) Nakamura, K.; Osamura, Y. Theoritical Study of the Reaction Mechanism and Migratory Aptitude of the Pinacol Rearrangement. *J. Am. Chem. Soc*. **1993**, *115*, 9112−9120. (b) Kurti, L.; Czakó, B. *Strategic Applications of Named Reactions in Organic Synthesis*, Academic Press/Elsevier, San Diego, **2005**, pp. 350 – 351.

(4) (a) Sugihara, Y.; Iimura, S.; Nakayama, J. Aza-Pinacol Rearrangement: Acid-Catalyzed Rearrangement of Aziridines to Imines. *Chem. Commun*. **2002**, 134−135. (b) Matsubara, S.; Yamamoto, H.; Oshima, K. Stereoselective Pinacol-Type Rearrangement of 2,3-Epoxy Alcohols with Retention of Configuration Mediated by Bis(iodozincio)methane. *Angew. Chem., Int. Ed.* **2002**, *41*, 2837−2839. (c) Hu, X.-D.; Fan, C.-A.; Zhang, F.-M.; Tu, Y. Q. A Tandem Semipinacol Rearrangement/Alkylation of α-Epoxy Alcohols: An Efficient and Stereoselective Approach to Multifunctional 1,3-Diols. *Angew. Chem., Int. Ed.* **2004**, *43*, 1702−1705. (d) Yang, M.; Wang, L.; He, Z.-H.; Wang, S.-H.; Zhang, S.-Y.; Tu, Y.-Q.; Zhang, F.-M. Tandem Semipinacol-Type 1,2-Carbon Migration/Aldol Reaction toward the Construction of [5-6-7] All-Carbon Tricyclic Core of Calyciphyline A-Type Alkaloids. *Org. Lett.* **2012**, *14*, 5114−5117. (e) Liu, Y.; Yeung, Y.-Y. Synthesis of Macrocyclic Ketones through Catalyst-Free Electrophilic

Halogen-Mediated Semipinacol Rearrangement: Application to the Total Synthesis of (±)-Muscone. *Org. Lett.* **2017**, *19*, 1422−1425.

(5) (a) Baran, P. S.; Richter, J. M.; Lin, D. W. Direct Coupling of Pyrroles with Carbonyl Compounds: Short Enantioselective Synthesis of (*S*)-Ketorolac. *Angew*. *Chem., Int. Ed.* **2005**, *44*, 609−612. (b) Cacchi, S.; Fabrizi, G. Synthesis of Functionalization of Indoles through Palladium-Catalyzed Reactions. *Chem. Rev.* **2005**, *105*, 2873−2920. (c) Humphrey, G. R.; Kuethe, J. T. Practical Methodologies for the Synthesis of Indoles. *Chem. Rev.* **2006**, *106*, 2875−2911. (d) Higuchi, K.; Kawasaki, T. Simple Indole Alkaloids and Those with a Nonrearranged Monoterpenoid Unit. *Nat. Prod. Rep.* **2007**, *24*, 843−868. (e) Bandini, M.; Eichholzer, A. Catalytic Functionalization of Indoles in a New Dimention. *Angew*. *Chem., Int. Ed.* **2009**, *48*, 9608−9644. (f) Shiri, M. Indoles in Multicomponent Processes (MCPs). *Chem. Rev.* **2012**, *112*, 3508−3549. (g) Zhang, M.-Z.; Chen, Q.; Yang, G.-F. A Review on Recent Developments of Indole-Containing Antiviral Agents. *Eur. J. Med. Chem.* **2015**, *89*, 421-441. (h) Zhang, M.-Z.; Chen, Q.; Xie, C.-H.; Mulholland, N.; Turner, S.; Irwin, D.; Gu, Y.-C.; Yang, G.-F.; Clough, J. Synthesis and Anifungal Activity of Novel Streptochlorin Analogues. *Eur. J. Med. Chem.* **2015**, *92*, 776-783. (i) Zhang, M.-Z.; Mulholland, N.; Beattie, D.; Irwin, D.; Gu, Y.-C.; Chen, Q.; Yang, G.-F.; Clough J. Synthesis and Antifungal Activity of 3-(1,3,4-Oxadiazol-5-yl)-Indolles and 3-(1,3,4-Oxadiazol-5-yl)Methyl-Indoles *Eur. J. Med. Chem.* **2013**, *63*, 22-32. (j) Zhang, M.-Z.; Chen, Q.; Mulholland, N.; Beattie, D.; Irwin, D.; Gu, Y.-C.; Yang, G.-F.; Clough J. Synthesis and Fungisidal Acitivity of Novel Pimprinine Analogues. *Eur. J. Med. Chem.* **2012**, *53*, 283-291.

(6) (a) Schmidt, A. W.; Reddy, K. R.; Knölker, H.-J. Occurrence, Biogenesis, and Synthesis of Biologically Active Carbazole Alkaloids. *Chem. Rev.* **2012**, *112*, 3193−3328. (b) James, M. J.;

Clubley, R. E.; Palate, K. Y.; Procter, T. J.; Wyton, A. C.; O'Brien, P.; Taylor, R. J. K.; Unsworth, W. P. Silver (I)-Catalyzed Dearomatization of Alkyne-Tethered Indoles: Divergent Synthesis of Spirocyclic Indolenines and Carbazoles. *Org. Lett.* **2015**, *17*, 4372−4375. (c) Fedoseev, P.; Van der Eycken, E. Temperature Switchable Brønsted Acid-Promoted Selective Syntheses of Spiro-Indolenines and Quinolines. *Chem. Commun.* **2017**, *53*, 7732−7735. (d) Wang, T.-T.; Zhang, D.; Liao, W.-W. Versatile Synthesis of Functionalized *β*- and *γ*-Carbolines *via* Pd-Catalyzed C-H Addition to Nitriles/Cyclization Sequences. *Chem. Commun.* **2018**, *54*, 2048−2051.

(7) (a) Nichols, D. E.; Lloyd, D. H.; Johnson, M. P.; Hoffman, A. J. Synthesis and Serotonin Receptor Affinities of a Series of Enantiomers of *α*-Methyltryptamines: Evidence for the Binding Conformation of Tryptamines at Serotonin 5-HT_{1B} Receptors. *J. Med. Chem.* **1988**, *31*, 1406−1412. (b) Garden, S. J.; da Silva, R. B.; Pinto, A. C. A Versatile Synthetic Methodology for the Synthesis of Tryptophols. *Tetrahedron* **2002**, *58*, 8399−8412. (c) Kochanowska-Karamyan, A. J.; Hamann, M. T. Marine Indole Alkaloids: Potential New Drug Leads for the Control of Depression and Anxiety. *Chem. Rev.* **2010**, *110*, 4489−4497.

(8) (a) Ezquerra, J.; Pedregal, C.; Lamas, C.; Pastor, A.; Alvarez, P.; Vaquero, J. J. Stereoselective Synthesis of 1,3,4-Substituted Tetrahydro-*β*-Carbolines from Indoles Based on Selective Transformations. *Tetrahedron* **1997**, *53*, 8237−8248. (b) Baran, P. S.; Richter, J. M. Direct Coupling of Indoles with Carbonyl Compounds: Short, Enantioselective, Gram-Scale Synthetic Entry into the Hapalindole and Fischerindole Alkaloid Families. *J. Am. Chem. Soc.* **2004**, *126*, 7450−7451. (c) Tang, Q.; Chen, X.; Tiwari, B.; Chi, Y. R. Addition of Indoles to Oxyallyl Cations for Facile Access to *α*-Indole Carbonyl Compounds. *Org. Lett.* **2012**, *14*, 1922−1925. (d) Chen, L.; Zhou, J. A Highly Efficient Friedel-Crafts Reaction of Tertiary *α*-

Hydroxyesters or α-Hydroxyketones to α-Quaternary Esters or Ketones. *Chem. Asian. J.* **2012**, *7*, 2510−2515. (e) Vander Wal, M. N.; Dilger, A. K.; MacMillan, D. W. C. Development of a Generic Activation Mode: Nucleophilic α- Substitution of Ketones *via* Oxy-Allyl Cations. *Chem. Sci.* **2013**, *4*, 3075−3079. (f) Kumar, A.; Singh, T. V.; Thomas, S. P.; Venugopalan, P. Friedel-Crafts Arylation of α-Hydroxy Ketones: Synthesis of 1,2,2,2-Tetraarylethanones. *Eur. J. Org. Chem.* **2015**, 1226−1234.

(9) (a) Palucki, M.; Buchwald, S. L. Palladium-Catalyzed α-Arylation of Ketones. *J. Am. Chem. Soc.* **1997**, *119*, 11108−11109. (b) Li, Y.; Shi, F.-Q.; He, Q.-L.; You, S.-L. *N*-Heterocyclic Carbene-Catalyzed Cross-Coupling of Aldehydes with Arylsulfonyl Indoles. *Org. Lett.* **2009**, *11*, 3182−3185. (c) Bellina, F.; Rossi, R. Transition Metal-Catalyzed Direct Arylation of Substrates with Activated sp^3-Hybridized C-H Bonds and Some of Their Synthetic Equivalents with Aryl Halides and Pseudohalides. *Chem. Rev.* **2010**, *110*, 1082−1146. (d) Liang, T.; Zhang, Z.; Antilla, J. C. Chiral Brønsted Acid Catalyzed Pinacol Rearrangement. *Angew. Chem., Int. Ed.* **2010**, *49*, 9734−9736. (e) Hu, Y. L.; Jiang, H.; Lu, M. Efficient and Convenient C3-Functionalization of Indoles through $Ce(OAc)_3$/TBHP-Mediated Oxidative C-H Bond Activation in the Presence of β-Cyclodextrin. *Green Chem.* **2011**, *13*, 3079−3087. (f) Suárez, A.; Martinez, F.; Sanz, R. Synthesis of α-Functionalized α-Indol-3-yl Carbonyls through Direct S_N Reactions of Indol-3-yl α-Acyoins. *Org. Bimol. Chem.* **2016**, *14*, 11212−11219. (g) Wang, J.-L.; Li, H.-J.; Wang, H.-S.; Wu, Y.-C. Regioselective 1,2-Diol Rearrangement by Controlling the Loading of $BF_3{\cdot}Et_2O$ and Its Application to the Synthesis of Related Nor-Sesquiterene- and Sesquiterene-Type Marine Natural Products. *Org. Lett.* **2017**, *19*, 3811−3814.

(10) (a) Sahu, S.; Banerjee, A.; Maji, M. S. Transition-Metal-Free Redox-Neutral One-Pot C3-Alkenylation of Indoles Using Aldehydes. *Org. Lett.* **2017**, *19*, 464−467. (b) Banerjee, A.; Sahu,

S.; Maji, M. S. Benzannulation of 2-Alkenylindoles using Aldehydes by Sequential Triple-Relay Catalysis: A Route to Carbazoles and Carbazole Alkaloids. *Adv. Synth. Catal.* **2017**, *359*, 1860−1866. (c) Sahu, S.; Das, B.; Maji, M. S. Stereodivergent Total Synthesis of Hapalindoles, Fisherindoles, Hapalonamide H, and Ambiguine H Alkaloids by Developing a Biomimetic, Redox-Neutral, Cascade Prins-Type Cyclization. *Org. Lett.* **2018**, *20*, 6485−6489. (d) Saha. S.; Banerjee, A.; Maji, M. S. Brønsted Acid Catalyzed One-Pot Benzannulation of 2-Alkenylindoles under Aerial Oxidation: A Route to Carbazoles and Indolo[2,3-a]carbazole Alkaloids. *Org. Lett.* **2018**, *20*, 6920−6924. (e) Sk, M. R.; Bera, S. S.; Maji, M. S. Weakly Coordinating Ketone-Directed Cp*Co(III)-Catalyzed C–H Allylation on Arenes and Indoles, *Org. Lett*. **2018**, *20*, 134−137. (f) Banerjee, A.; Guin, A.; Saha, S.; Mondal, A.; Maji, M. S. Formal [4+2] Benzannulation of 2-Alkenyl Indoles with Aldehydes: A Route to Structurally Diverse Carbazoles and Bis-Carbazoles. *Org. Bimol. Chem.* **2019**, *17*, 1822−1826. (g) Banerjee, A.; Maji, M. S. A Brønsted Acid Catalyzed Cascade Reaction for the Conversion of Indoles to a-(3-Indolyl) Ketones by Using 2-Benzyloxy Aldehydes. *Chem.−Eur. J.* **2019**, *25*, 11521−11527. (h) Sahu, S.; Roy, A.; Gorai, M.; Guria, S.; Maji, M. S. C3-Alkenylation between Pyrroles and Aldehydes Mediated by a Brønsted Acid and a Brønsted Base. *Eur. J. Org. Chem.* DOI: 10.1002/ejoc.201901228.

(11) (a) Liang, D.; Li, X.; Li, Y.; Yang, Y.; Gao, S.; Cheng, P. Br_2-Catalyzed Regioselective Dehydrative Coupling of Indoles with Acyloins: Direct Synthesis of *α*-(3-Indolyl) Ketones. *RSC Adv.* **2016**, *6*, 29020−29025. (b) Schlegel, M.; Schneider, C. Lewis Acid-Catalyzed Friedel–Crafts Reactions Toward Highly Versatile, *α*-Quaternary Oxime Ethers. *Chem. Commun*. **2018**, *54*, 11124−11127. (c) Zhang, X.; Staples, R. J.; Rheingold, A. L.; Wulff, W. D. Catalytic Asymmetric *α*-Iminol Rearrangement: New Chiral Platforms. *J. Am. Chem. Soc.* **2014**, *136*,

13971−13974. (d) Qin, B.; Liu, X.; Shi, J.; Zheng, K.; Zhao, H.; Feng, X. Enantioselective Cyanosilylation of *α*,*α*-Dialkoxy Ketones Catalyzed by Proline-Derived in-Situ-Prepared N-Oxide as Bifunctional Organocatalyst. *J. Org. Chem.* **2007**, *72*, 2374−2378.

(12) During preparation of this manuscript, a closely related work by F. Secci *et al.* is published: Turnu, F.; Luridiana, A.; Cocco, A.; Porcu, S.; Frongia, A.; Sarais, G.; Secci, F. Catalytic Tandem Friedel–Crafts Alkylation/C4–C3 Ring-Contraction Reaction: An Efficient Route for the Synthesis of Indolyl Cyclopropanecarbaldehydes and Ketones. *Org. Lett.* DOI: 10.1021/acs.orglett.9b02617.

(13) (a) Palmieri, A.; Petrini, M. Recent Advances in the Synthesis of Unsymmetrical Bisindolylmethane Derivatives. *Synthesis* **2019**, *51*, 829–841. (b) Abe, T.; Nakamura, S.; Yanada, R.; Choshi, T.; Hibino, S.; Ishikura, M. One-Pot Construction of 3,3′-Bisindolylmethanes through Bartoli Indole Synthesis. *Org. Lett.* **2013**, *15*, 3622-3625. (c) Guo, X.; Pan, S.; Liu, J.; Li, Z. One-Pot Synthesis of Symmetric and Unsymmetric 1,1-Bis-indolylmethanes via Tandem Iron-Catalyzed C-H Bond Oxidation and C-O Bond Cleavage. *J. Org. Chem.* **2009**, *74*, 8848–8851.