Transition-Metal-Promoted Oxidative Cyclization To Give 1,2,4-Trisubstituted Carbazole Scaffolds

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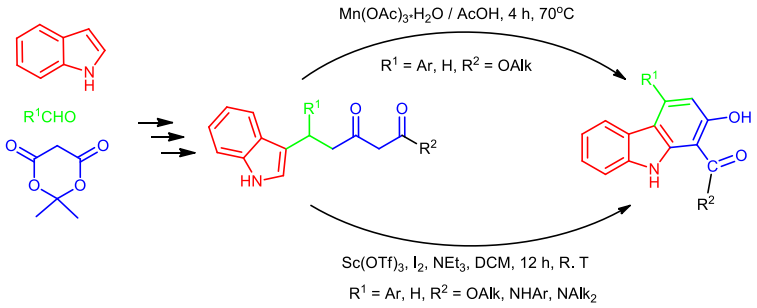

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Abstract Herein, we describe the synthesis of a 1,2,4-trisubstituted carbazole core from 5-(1H-indol-3-yl)-3-oxopentanoic acid esters or amides. For oxidative cyclization, we tested two different approaches. First, we used manganese triacetate as a conventional moderate oxidizer to ensure the radical course of reaction. Second, we independently tested, a more complicated oxidizing agent I_2/Me(OTf)$_3$. For both cases formation of a fused ring carbazole system having 2-hydroxyl and 1-carboxylic substituent were observed. In connection with the formation of an unexpected reaction intermediate, mechanistic aspects of the process were discussed.

Key words: carbazole, oxidative cyclization, indole, 3-oxoester, transition metals

In many biologically active compounds, the carbazole system and its structurally similar surrogate containing one saturated six-membered ring plays an important role as a scaffold. This structural motif can be found in various alkaloids,[1] such as pyrayaquinones,[2] murrayafolines;[3] in active compounds against human papillomavirus infections;[4] in HIV-integrase inhibitors;[5] α- and β-adrenoreceptor ligands;[6] in antagonists of the prostaglandin receptor;[7] and in antitumor agents such as aspidosperma alkaloids like vincristine and vinblastine;[8] and the anti-nausea drug ondansetron.[9]

Because of the broad application of compounds containing the carbazole group, a significant number of synthesis methods of this scaffold were developed. A frequently used approach requires the formation of a five-membered heterocyclic ring for the synthesis of carbazole derivatives thus, the most popular approaches are variations of the Fischer indole synthesis with the hydrazine derivative as a key intermediate,[6, 10] the closing of the pyrrole ring through the palladium-mediated Heck reaction,[11] and the formation of the central ring via oxidative coupling (Figure 1).[12] A less explored approach is the formation of the **A** ring on the existing indole moiety during the synthesis of carbazole-like compounds. In 1994, Chuang et al.

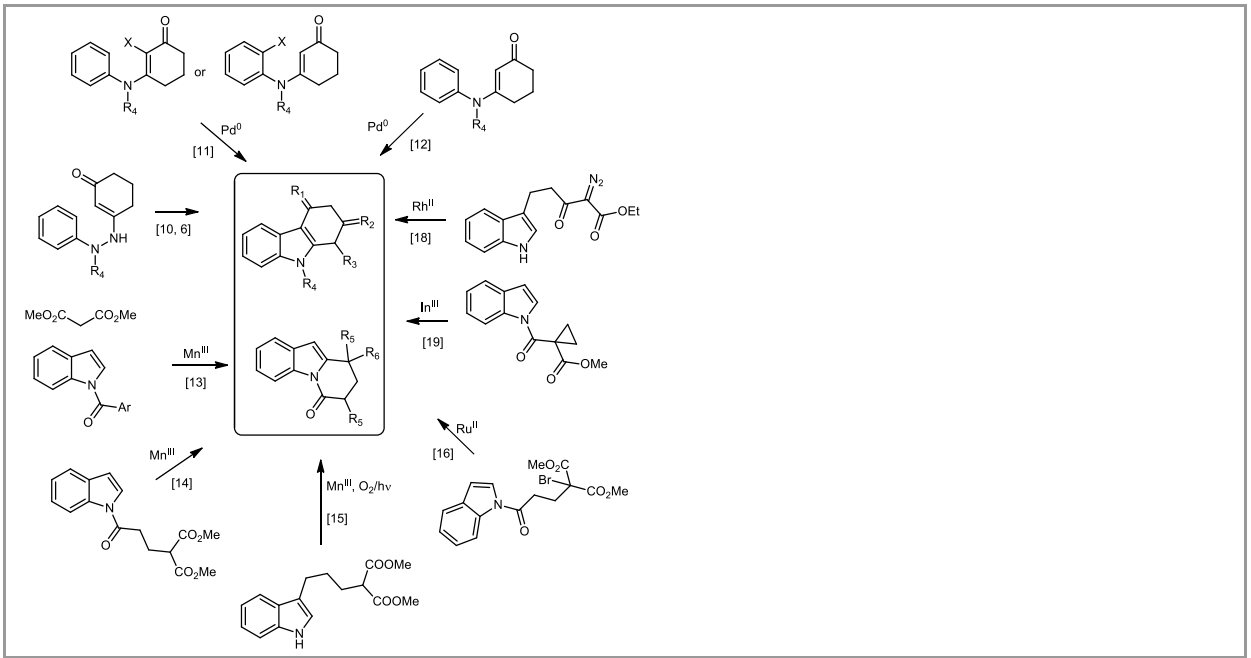
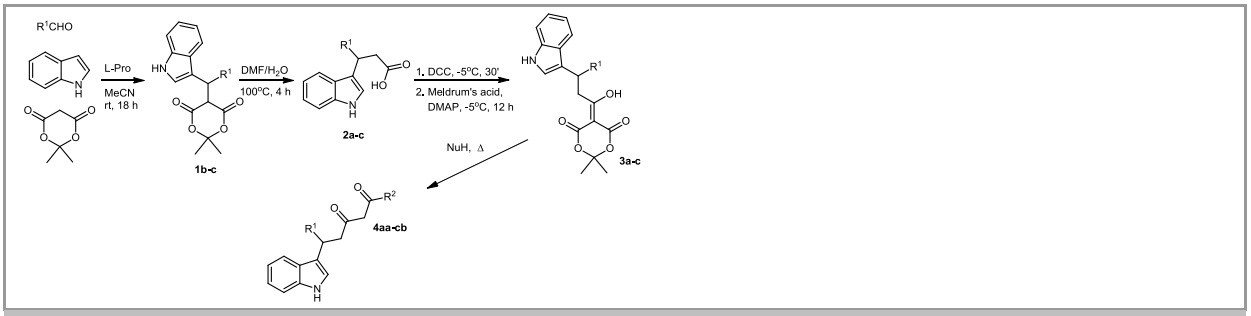


Figure 1 Carbazole derivatives formation methods - state of knowledge.

described oxidative radical cyclization using manganese (III) acetate and N-aroylindoles with the subsequent insertion of the malonic moiety into the newly formed ring.[13] Based on the results, Kerr et al. used N-acyl indoles containing 1,3-dicarbonyl moiety at the end of the alkyl side chain to perform oxidative radical cyclization, leading to the formation of mersicarpine and tronocarpine

alkaloids, also with manganese (III) acetate as an oxidizer.[14] Malonyl derivatives of indole were oxidized by the $Mn(acac)_3$ complex or in rare metal-free conditions using oxygen under UV irradiation in the presence of CaI_2.[15] Stephenson performed the cyclization of N-alkyl indoles using the



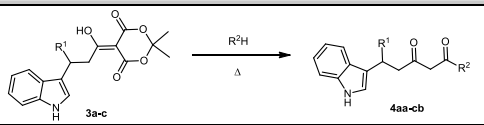
Scheme 1 Synthesis of intermediates for cyclization.

photocalyzed process in the presence of a ruthenium complex.[16] Moreover, 3-substituted and N-carboethoxy protected indoles were cyclized to (+)-subincanadine F alkaloid using CAN as an oxidizer.[17] Another approach for the cyclization of the third ring assumed the formation of carbenes as reactive intermediates via rhodium catalyzed decomposition of α-diazo-β-keto esters.[18] France et al. described a modification of this method, in which the α-diazo moiety was converted to the cyclopropyl ring. This ring then underwent cyclopropane ring opening when reacted with In (III) Lewis acid catalyst, followed by the subsequent Friedel-Crafts alkylation of the indole ring, leading to a six-membered new ring.[19]

In this study, we present an alternative approach for developing carbazoles and tetrahydro-carbazoles. We focused our research efforts on the cyclization of 5-(1H-indol-3-yl)-3-oxopentanoic acid (**4aa**-**ad**) and (5-(1H-indol-3-yl)-5-aryl-3-oxopentanoic acids derivatives (**4ba**-**cb**), which were easily accessible from acyl Meldrum's acid (**3a**-**c**) (Scheme 1).[20] In the case of **4aa**-**ad** with R^1 = H, the synthesis can be started from the commercially available 3-(1H-indol-3-yl)propanoic acid **2a**, whereas the 5-aryl substituted derivatives **4ba**-**cb** required a more complicated route with the preliminary formation of 5-((1H-indol-3-yl)(aryl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**1b**-**c**).[21] Table 1 lists the results of the synthesis of esters and amides **4aa**-**cb**.

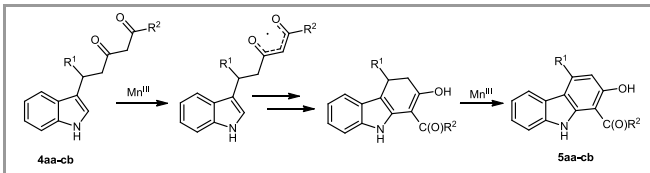
Because a compound containing a 1,3-dicarbonyl system can be easily oxidized to a radical using manganese (III) acetate,[22] we first performed trial cyclization experiments with the amides **4ac**, **ad** and **bd** or esters **4aa**-**cb** which were oxidized using manganese (III) acetate in acetic acid at 70°C for over 4h (Scheme 2). We assumed that the electrophilic radical generated from the 1,3-dicarbonyl moiety would easily attack the electron-rich indole π-system, which after subsequent oxidation with Mn(III) and abstraction of proton, would lead to the recovery of the aromatic system.

Table 1 Preparation of 3-oxoamides and 3-oxoesters 4aa-cb



Run	**4**	R^1	R^2	Yield [%]
1	**aa**	H	OMe	96
2	**ab**	H	OEt	75
3	**ac**	H	$O(CH_2CH_2)_2N$	98
4	**ad**	H	4-MeC_6H_4NH	88
5	**ba**	Ph	OMe	71
6	**bb**	Ph	OEt	67
7	**bc**	Ph	$O(CH_2CH_2)_2N$	70
8	**bd**	Ph	4-MeC_6H_4NH	75

9	**ca**	3-ClC_6H_4	OMe	66
10	**cb**	3-ClC_6H_4	OEt	57



Scheme 2 Key steps of the oxidative cyclization of 3-oxoesters 4aa-cb with manganese triacetate.

This approach was not successful in the case of 3-oxoamides **4ac**, **ad**, and **bd**, as well as in the case of morpholides of 3-(1H-indol-2-yl)-3-oxopropanoic acid **4d** and 4-(1H-indol-3-yl)-3- oxobutanoic **4e**. Despite the chain length or type of amides that were used (aliphatic or aromatic), we obtained a complicated mixture of oxidation products in all the cases.

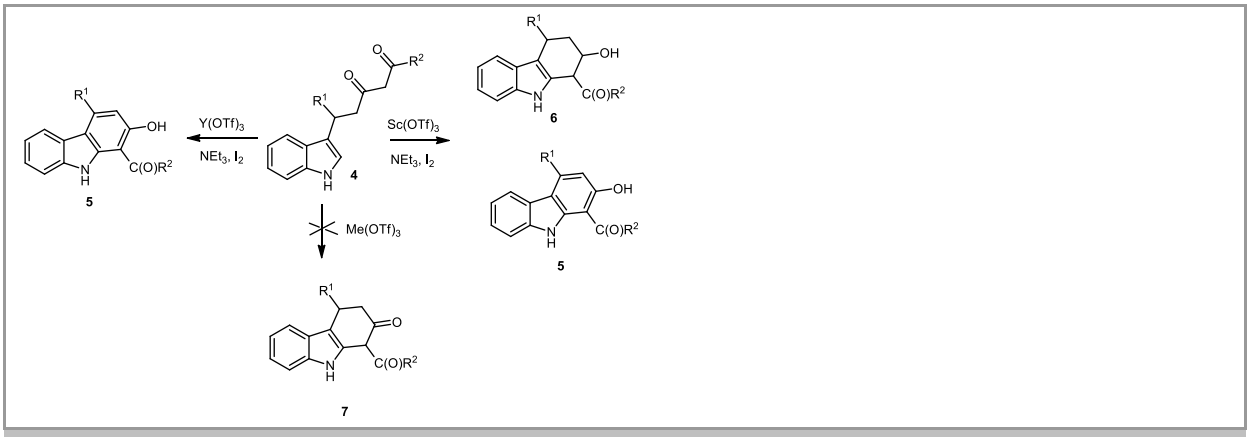
Moreover, the application of CAN as an alternative oxidizer for the oxidation of **4ad** amide in acetic acid led to identical results. Nevertheless in the case of esters **4aa**-**cb** oxidation with $Mn(OAc)_3$ allowed the formation of the cyclization product. From the reaction mixture, as the primary product, we isolated carbazole derivatives with the third aromatic ring **5aa**-**cb** because of subsequent oxidation. Thus, we expected that for the whole cyclization process and aromatization, 4 eq. of $Mn(OAc)_3$ might be required. Thus, we performed a series of experiments to determine the optimal ratio of the oxidizer. (Table 2). In most cases, the highest yields of **5aa**-**cb** were obtained with 2.5 eq of $Mn(OAc)_3$;moreover, a further increase in the amount of oxidizer led to a decrease the yield of products **5aa**-**cb**. We obtained moderate to good results with the oxidative cyclization of esters **4aa**-**cb**; however, it did not solve our problem with the cyclization of amides **4ad**-**bd**.

According to Sleiter,[23] who generated radicals from α-iodoesters or nitriles in the presence of H_2O_2/DMSO/Fe^{2+}, radicals can undergo addition to the pyrrole system with good yields. Therefore we anticipated that if our esters and amides contained the 1,3-dicarbonyl system, they would be very susceptible to the formation of moderately stable radicals. For our pilot experiment, we transformed the ester **4aa** into the α-iodo substituted ester using NIS in DMSO.[24] However, the treatment of the α-iodinated ester with $FeSO_4 \times 7H_2O/H_2O_2$/DMSO system did not lead to the formation of any desired carbazole derivative type of **5**.

Cheung et al. described the cyclopropanation of β-keto esters containing the unsaturated moiety in the presence I_2/Lewis acid/Et_3N.[25] They proposed a reaction mechanism in which, in the key step, alkene is converted to the iodonium cation, which then undergoes nucleophilic attack by chelated β-keto esters. It is a far analogy to our system, however we decided to check if our (1H-indoyl)-3-oxocarboxylic acids derivatives would react with iodine in the presence of Lewis acid catalysts.

Table 2 Results of oxidative cyclization of 3-oxoesters **4aa**-**cb** with $Mn(OAc)_3$

Run	**4**	R^1	R^2	Yield of **5** [%]		
				$Mn(OAc)_3$		
				1.6 eq	2.5 eq	3.2 eq
1	**aa**	H	OMe	33	31	31
2	**ab**	H	OEt	19	26	20
3	**ba**	Ph	OMe	29	32	12
4	**bb**	Ph	OEt	18	72	27
5	**ca**	3-ClC_6H_4	OMe	52	51	35
6	**cb**	3-ClC_6H_4	OEt	59	61	60



Scheme 3 Cyclization of 3-oxoesters and 3-oxoamides with transition metal triflates.

The most controversial issue is the behaviour of the indole π-excess system. We wanted to verify if the indole moiety could be only iodinated; if such a reaction occurred, it would finish before cyclization because aromatic substitution would be impossible in such a condition. The second option was the formation of a Wheland-type iodonium cation that would have a long enough lifetime to react with chelated β-keto esters, which would allow for the addition-elimination of the iodine atom.

To verify our hypothesis, we added 1 eq of $Sc(OTf)_3$ to methyl 5-(1H-indol-3-yl)-3-oxopentanoate (**4aa**) in the presence of 2.5 eq of Et_3N and 1.5 eq of I_2 in dichloromethane at RT. From the reaction mixture, we isolated the methyl 2-hydroxy-2,3,4,9-tetrahydro-1H-carbazole-1-carboxylate (**6aa**) with 43% yield. Considering the possible products of this reaction, we expected the 2-oxo **7** rather than the 2-hydroxy substituted product (Scheme 3).

After the first experiment, we attempted to test other transition metal triflates, and we used cupric triflate (Table 3, Run 2),but obtained the same product **6aa** with a lower yield. We performed a series of experiments using (5-(1H-indol-3-yl)-5-aryl-3-oxopentanoic acids esters **4aa**-**ca** with $Sc(OTf)_3$ or $Y(OTf)_3$. Note that in the case of 5-aryl substituted oxopentanoic acids esters, the only isolated product was carbazole **5aa**-**ca**; however, in the crude reaction mixture, we observed trace amount of alcohols **6aa**-**ca**. Thus, we hypothesized that products **5aa**-**ca** may be formed as a result of the subsequent oxidation of **6aa**-**ca**. In the independent experiments, we verified the stability of **6aa** to undergo oxidation with various oxidizers. Note that **6aa** was stirred at RT in DCM and separately treated with the following oxidizers: a) iodine; b) air; c) air in the presence of 2 eq of $Y(OTf)_3$; and d) the complete reaction set of I_2, NEt_3, and $Y(OTf)_3$. The reaction mixture was continuously monitored with TLC and the oxidation to product **5aa** was observed only in two cases. Note that I_2 allowed for the gradual formation of **5aa** with 50% yield after 7 days, and the application of the complete reaction set led to a fast and entire oxidation to **5aa** within one day.

In the case of $Y(OTf)_3$, the reaction of all the esters (5-aryl substituted or not) led to the formation of a fully aromatic products **5aa**-**cb** (Table 3, Runs 3-15).

Table 3 Cyclization of 3-oxoesters and 3-oxoamides with metal triflates **M** $(OTf)_3$

Run	**4, 5, 6**	**M**	R^1	R^2	Yield [%]	
					5	**6**
1	**aa**	Sc	H	OMe	-	43
2	**aa**	Cu	H	OMe	-	14
3	**aa**	Y	H	OMe	41	-
4	**aa**	Mg	H	OMe	27	-
5	**ab**	Sc	H	OEt	28	-
6	**ab**	Y	H	OEt	21	-
7	**ad**	Y	H	4-MeC_6H_4NH	42	-
8	**ba**	Sc	Ph	OMe	45	-
9	**ba**	Y	Ph	OMe	37	-
10	**bb**	Y	Ph	OEt	12	-

11	**bc**	Y	Ph	$O(CH_2CH_2)_2NH$	40	-
12	**bd**	Y	Ph	$4\text{-}MeC_6H_4NH$	42	-
13	**ca**	Sc	$3\text{-}ClC_6H_4$	OMe	16	-
14	**ca**	Y	$3\text{-}ClC_6H_4$	OMe	23	-
15	**cb**	Y	$3\text{-}ClC_6H_4$	OEt	11	-

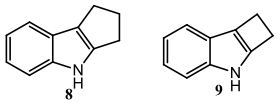
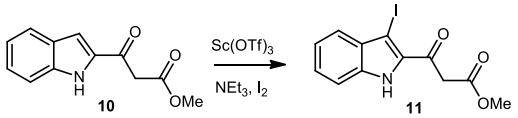


Figure 2 1,2,3,4-Tetrahydrocyclopenta[b]indole (**8**) and 2,3-dihydro-1H-cyclobuta[b]indole (**9**) scaffolds.

Encouraged by the cyclization of esters, we started to test the cyclization of amides. A series of amides **4ad**, **bc**, and **4bd** were tested in the reaction with $Y(OTf)_3$. From the reaction mixtures, we isolated a ring-closing product with the carbazole system **5ad**-**bd**.

We attempted to obtain derivatives of carbazoles with a smaller third ring, i.e., 1,2,3,4-tetrahydrocyclopenta[b]indole (**8**), and 2,3-dihydro-1H-cyclobuta[b]indole (**9**) scaffolds (Figure 2). However, during the synthesis of **8** and **9**, we were unable to isolate clean acylation products of Meldrum's acid with 2-(1H-indol-3-yl)acetic acid and 1H-indole-3-carboxylic acid respectively. Moreover, even the crude oily 5-(1-hydroxy-2-(1H-indol-3-yl)ethylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione or 5-(hydroxy(1H-indol-3-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione treated with methanol did not lead to the formation of the β-ketoester, which suggested the self-decomposition of the initially formed acyl Meldrum's acid.

Moreover, we attempted to prepare scaffold **9** via derivatives of 1H-indole-2-carboxylic acid. We treated methyl 3-(1H-indol-2-yl)-3-oxopropanoate (**10**) in the typical condition with 1 eq of $Sc(OTf)_3$ in the presence 2.5 eq of Et_3N and 1.5 eq of I_2 in dichloromethane at RT. From the reaction mixture, we isolated methyl 3-(3-iodo-1H-indol-2-yl)-3-oxopropanoate (**11**) (Scheme 4). The results may confirm the hypothesis that the Wheland type iodonium cation is formed, which can react with the chelated β-keto to form a cyclization product. Furthermore, after the elimination of HI it led to the recovery of the indole aromatic system. In the case of 2-substituted indole, the cyclization of iodonium cation was impossible. However we observed the formation of iodination product **11** with a yield 52 %.

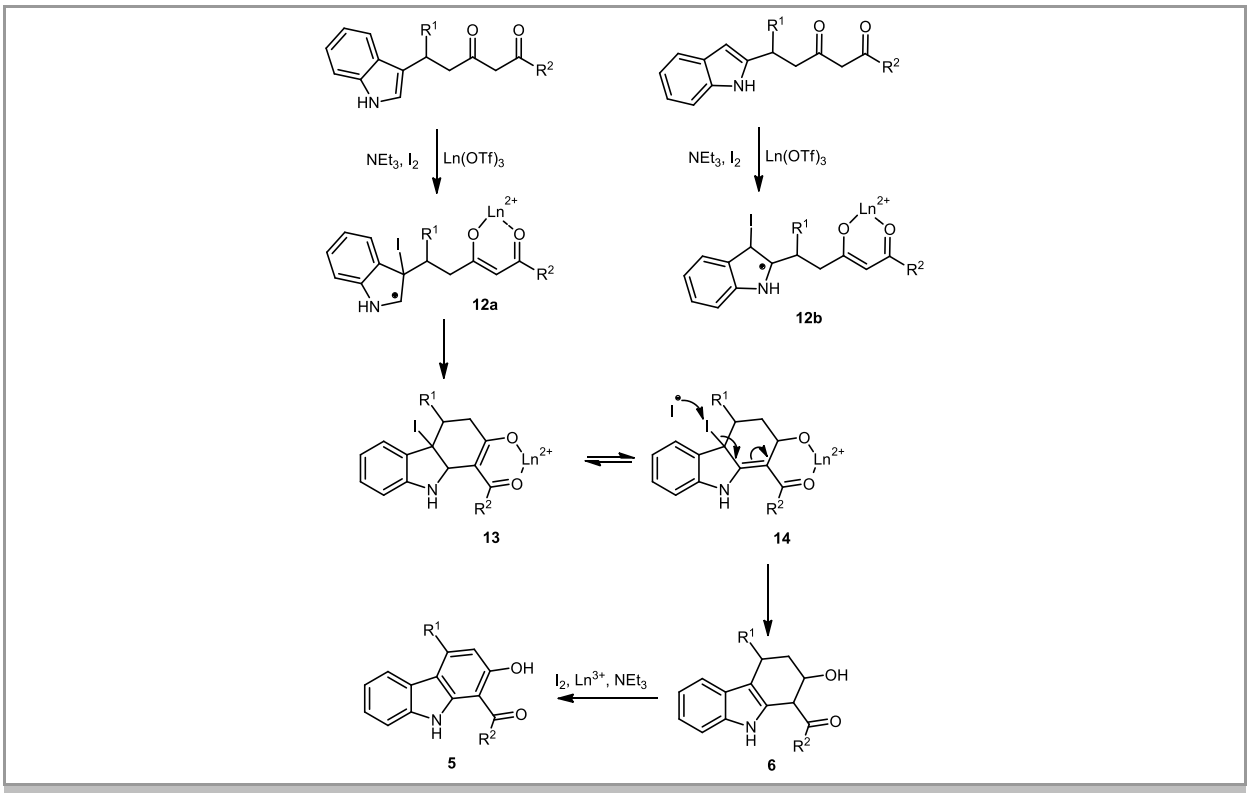


Scheme 4 Attempts to cyclize methyl 3-(1H-indol-2-yl)-3-oxopropanoate.

Based on the collected material and literature review,[24] we decided to propose a tentative mechanism of the investigated cyclization process using iodine in the presence of transition metal triflates (Scheme 5).

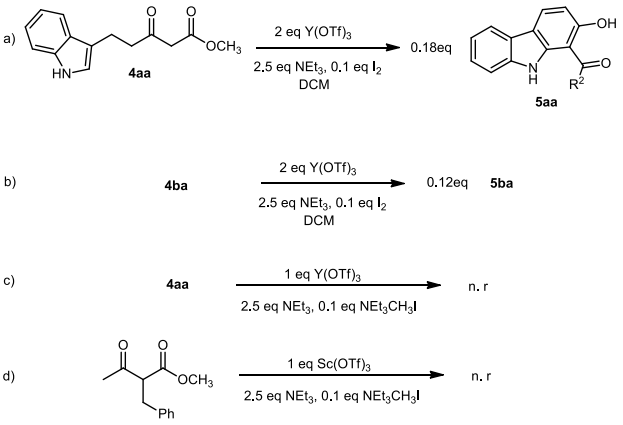
Regardless of the indole derivative's substitution position **2** or **3**, the first two steps were as follows: coordination to Lewis acid (such as Sc^{3+} and Y^{3+} etc.) and addition of iodine with the formation of a Wheland-type iodonium cation **12a**, **b**. In the case of **12a**, the nucleophilic ring closure is possible with the formation of the transition product **13**. The cyclization of **12b** would lead only to a spiro non-aromatic product, which indeed was not observed. At this moment, we would like to clarify the formation of a reduced alcohol **6**, we assumed that enol **13** complexed with scandium or yttrium underwent enol/allylic alcohol isomerization.[26] Iodinated compound **14** containing allylic moiety should undergo reductive elimination during an attack of the iodine anion and form the alcohol **6**, which would quickly oxidize with iodine in the presence of transition metal triflates to the carbazole **5**. To confirm our hypothesis about reductive elimination we had to find a proof for iodine

regeneration, therefore, we ran an experiment with a deficiency of iodine. The reaction of 1 eq of **4aa** with 2 eq of $Y(OTf)_3$, 2.5 eq of NEt_3 and only 0.1 eq I_2 in DCM at R.T through standard time of 12 h. From the reaction mixture, we isolated **5aa** in 18% yield, taking into account oxidation of **6** to the aromatic system. Note that such an amount of the product would require at least 0.54 eq of I_2, which indicates that iodine was recovered during the process (Scheme 6a). Similar result we obtained with **4ba** ester (Scheme 6b); however, increasing the amount of iodine to 4 eq did not increase the yield. To exclude the possibility of the oxidation of the iodine anion with traces of oxygen in the presence of Lewis acid, despite performing the reaction under argon, we performed a control experiment in which 1 eq of ester **4aa** was treated with 1 eq of $Y(OTf)_3$, 2.5 eq of NEt_3, and 1.5 eq of NEt_3CH_3I in DCM. As a result, we did not observe the formation of any cyclization product or even traces of I_2 (Scheme 6c). Furthermore, we excluded the possibility of the formation of the reduced alcohol in the reaction of the keto ester with the iodine anion in the presence of $Y(OTf)_3$. Moreover, we ran a similar experiment with methyl 2-benzyl-3-oxobutanoate, 1 eq $Sc(OTf)_3$, 2.5 eq of NEt_3, and 1.5 eq of NEt_3CH_3I in DCM. As a result, we did not observe the oxidation of the iodine anion or the reduction of keto ester to the hydroxyl ester (Scheme 6d).



Scheme 5 Tentative reaction mechanism of the cyclization of (5-(1H-indol-3-yl)-3-oxopentanoic acids.

In conclusion, we developed a new method for the synthesis of functionalized carbazoles and tetrahydro-carbazoles using (5-(1H-indol-3-yl)-5-aryl-3-oxopentanoic acids and (5-(1H-indol-3-yl)-3-oxopentanoic acid amides and esters as starting materials. Depending on the reaction conditions, it resulted in the formation of two products: reduced 2-hydroxy-2,3,4,9-tetrahydro-1H-carbazole-1-carboxylates and oxidized 2-hydroxy-9H-carbazole-1-carboxylates. Two different independent regents for oxidative cyclization (5-(1H-indol-3-yl)-5-aryl-3-oxopentanoic acids and (5-(1H-indol-3-yl)-3-oxopentanoic acids derivatives, i.e., Mn^{III} and I_2/Lewis acid, were tested and their complementarity was observed. A tentative mechanism has been described; however additional studies are necessary to clarify the exact mechanism.



Scheme 6 Control experiments for the elucidation of reaction mechanism.

Commercially available reagents were purchased from Sigma-Aldrich or Acros. Toluene was distilled in the presence of potassium under argon and stored over molecular sieves. DCM was distilled over P_4O_{10} and stored over molecular sieves. Commercially unavailable reagents such as 5-((1H-Indol-3-yl)(phenyl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (**1b**) and 5-((3-Chlorophenyl)(1H-indol-3-yl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (**1c**) were prepared according to previously reported procedures.[21] Analytical TLC was performed on aluminum sheets of UV-254 Merck silica gel. Flash chromatography was performed using 40–63 micron Zeochem silica gel. ^{1}H, ^{13}C NMR spectra were recorded on Bruker Avance III HD 400 MHz, and chemical shifts (δ) were recorded in ppm relative Me_4Si with the coupling constant *J* measured in Hz. High-resolution mass spectra (HRMS) were recorded on Agilent 6540 Q-TOF. Melting points were determined with Warsztat Elektromechaniczny W-wa apparatus and are not corrected.

3-(1H-indol-3-yl)-3-arylpropanoic acids (**2b-c**)**; General Procedure**

5-((1H-indol-3-yl)(aryl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (**1b-c**) (1 mmol) was dissolved in a mixture of DMF (10 mL) and water (1mL). The resulting solution was stirred and heated in an oil bath at 100°C for 4 h. After completion of the reaction, the solvent was removed under reduced pressure and the residue was dissolved in ethyl ether and extracted with $NaHCO_3$ (2 × 10mL, sat. aq). The water layer was acidified with conc. HCl. The resulting suspension was extracted with DCM (4 × 10mL). The organic extract was dried with $MgSO_4$ and filtered, and then the solvent was removed under reduced pressure to afford acids **2b-c**.

3-(1*H*-Indol-3-yl)-3-phenylpropanoic acid (**2b**)[27]

Yield: 0.119 g (45%); white amorphous solid.

^{1}H NMR (acetone-d_6, 400 MHz): δ = 10.13 (s, 1 H, OH), 7.98 (s, NH), 7.44-7.33 (m, 5 H, Ar-H), 7.28-7.24 (m, 2 H, Ar-H), 7.17-7.13 (m, 1 H, Ar-H), 7.08-7.04 (m, 1 H, Ar-H), 6.94-6.90 (m, 1 H, Ar-H), 4.80 (t, 1 H, *J* = 7.6, H-5), 3.20 (dd, 1 H, J^2 = 15.5, J^3 = 7.6, H-3), 3.06 (dd, 1 H, J^2 = 15.5, J^3 = 7.6, H-3).

^{13}C NMR (acetone-d_6, 100 MHz): δ = 172.7 (C-14), 145.1 (C-10), 137.3 (C-4), 128.4 (C-16, C-20), 128.0 (C-17, C-19), 126.3 (C-18), 121.8 (C-5), 121.7 (C-3), 121.6 (C-8), 119.2 (C-2), 118.8 (C-1), 111.5 (C-9), 111.4 (C-6), 40.9 (C-11), 39.4 (C-12).

HRMS (ESI+): *m/z* $[M + H]^+$ calcd for $C_{17}H_{16}NO_2$: 266.1180; found: 266.1139

3-(3-Chlorophenyl)-3-(1H-indol-3-yl)propanoic acid (**2c**)

Yield: 0.173 g (58%); white amorphous solid.

^{1}H NMR (acetone-d_6, 400 MHz): δ = 10.21 (s, 1 H, OH), 8.01 (s, NH), 7.51-7.39 (m, 5 H, Ar-H), 7.35-7.31 (m, 1 H, Ar-H), 7.31-7.27 (m, 1 H, Ar-H), 7.20-7.18 (m, 1 H, Ar-H), 7.10-7.06 (m, 1 H, Ar-H), 6.97-6.93 (m, 1 H, Ar-H), 4.81 (t, 1 H, J = 7.8, H-5), 3.21 (dd, 1 H, J^2 = 15.6, J^3 = 7.3, H-3), 3.10 (dd, 1 H, J^2 = 15.6, J^3 = 7.3, H-3).

^{13}C NMR (acetone-d_6,, 100 MHz): δ= 172.1 (C-1), 147.5 (C-6), 136.9 (C-14), 133.5 (C-11), 129.8 (C-12), 127.8 (C-8), 126.6 (C-13), 126.4 (C-9), 126.2 (C-10), 121.6 (C-16), 121.5 (C-19), 118.8 (C-18), 118.7 (C-17), 117.3 (C-7), 111.3 (C-20), 40.3 (C-3), 38.8 (C-5).

HRMS (ESI+): m/z $[M + H]^+$ calcd for $C_{17}H_{15}ClNO_2$: 300.0790; found: 300.0746.

5-(1-hydroxy-3-(1H-indol-3-yl)-propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3a**) **5-(1-hydroxy-3-(1H-indol-3-yl)-(3-aryl)-propylidene)-2,2-dimethyl-1,3-dioxane-4,6-diones** (**3b-c**) **and 5-(hydroxy(1H-indol-2-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione** (**3d**)**; General Procedure**

According to a typical DCC-mediated acylation of Meldrum's acid.[28] To a cooled (-10°C) solution of 3-(1H-indol-3-yl)-propanoic acid (**2a**-**c**) or 1H-indole-2-carboxylic acid **2d** 3 mmol in DCM 5mL, solution of DCC (0.74g, 3.6 mmol) in 5 mL DCM was added. After 30 min Meldrum's acid (0.43g, 3mmol) followed by solution of DMAP (0.55g, 4.5 mmol) in DCM 2mL were added. The reaction mixture was allowed to reach room temperature and stirred for 12 h. The precipitated DCU was filtered, and the resultant solution was washed with aq 10% $KHSO_4$ soln. (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried with anhydorus $MgSO_4$ and filtered and then the solvent was removed under reduced pressure. The residue was crystalized from ethyl ether.

5-(1-Hydroxy-3-(1H-indol-3-yl)propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3a**)

Yield: 0.822 g (87%); yellow crystalline solid; mp = 88-90°C.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 15.33 (s, 1 H), 8.05 (s,1 H), 7.75-7.70 (m, 1 H), 7.38-7.34 (m, 1 H), 7.24-7.18 (m, 1 H), 7.18-7.13 (m, 1 H), 7.10-7.07 (m, 1 H), 3.56-3.48 (m, 2 H), 3.26-3.18 (m, 2H), 1.65 (s, 6 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 197.1, 170.4, 160.3, 136.2, 127.1, 122.2, 121.9, 119.6, 118.8, 114.2, 111.1, 104.8, 91.8, 36.6, 26.7, 21.9.

HRMS (ESI-): m/z $[M - H]^-$ calcd for $C_{17}H_{16}NO_5$: 314.1028; found: 314.1022.

5-(1-Hydroxy-3-(1H-indol-3-yl)-3-phenylpropylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3b**)

Yield: 0.750 g (64%); yellow crystalline solid; mp = 55-57°C.

^{1}H NMR(DMSO, 400 MHz): δ= 10.95 (s, 1 H), 7.40-7.22 (m, 7 H), 7.19-7.12 (m, 1 H), 7.07-7.00 (m, 1 H), 6.93-6.87 (m, 1 H), 4.77 (t, J= 8.0 Hz, 1 H), 3.98-3.82 (m, 2 H), 1.52 (s, 6 H).

^{13}C NMR(DMSO, 100 MHz): δ= 199.62, 148.8, 141.6, 133.5, 133.3, 132.8, 132.7, 131.5, 131.3, 127.2, 126.3, 123.8, 123.6, 121.9, 116.7, 109.7, 97.9, 35.9, 35.3, 31.1.

HRMS (ESI-): m/z $[M - H]^-$ calcd for $C_{23}H_{20}NO_5$: 390.1341; found: 390.1314.

5-(3-(3-Chlorophenyl)-1-hydroxy-3-(1H-indol-3-yl)propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3c**)

Yield: 0.930 g (73%); yellow crystalline solid; mp = 107-109°C.

^{1}H NMR(DMSO-d_6, 400 MHz): δ= 11.00 (s, 1H), 7.41-7.27 (m, 6 H), 7.26-7.19 (m, 1 H), 7.09-7.00 (m, 1 H), 6.96-6.87(m, 1H), 4.80 (t, *J*= 8.0 Hz, 1 H), 3.95 (dd, *J*= 8.0 Hz, *J*= 14.4 Hz, 1 H), 3.85 (dd, *J*= 8.0 Hz, *J*= 14.4 Hz, 1 H), 1.56 (s, 6 H).

^{13}C NMR(DMSO-d_6, 100 MHz): δ= 177.2, 169.3, 161.8, 151.6, 141.6, 138.1, 135.4, 132.6, 131.6, 131.2, 127.5, 126.5, 123.8, 123.7, 121.2, 116.8, 109.7, 97.8, 38.6, 35.9, 31.1.

HRMS (ESI-): *m/z* [M - H]$^-$ calcd for $C_{23}H_{19}ClNO_5$: 424.0952; found: 424.0914.

5-(Hydroxy(1H-indol-2-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3d**)

Yield: 0.566 g (66%); yellow crystalline solid; mp = 111-113°C.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 16.03 (s, 1 H), 12.21 (s, 1 H), 7.87-7.82 (m, 1 H), 7.77-7.71 (m, 1 H), 7.52-7.47 (m, 1 H), 7.44-7.38 (m, 1 H), 7.21-7.16 (m, 1 H), 1.83 (s, 6 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 176.7, 171.8, 162.9, 139.1, 129.5, 127.8, 126.92, 123.0, 121.6, 116.1, 113.0, 104.9, 88.4, 26.5.

HRMS (ESI-): *m/z* [M - H]$^-$ calcd for $C_{15}H_{12}NO_5$: 286.0715; found: 286.0716.

5-(1H-indol-3-yl)-3-oxopentanoates (**4aa-ab**)**, 5-(1H-indol-3-yl)-3-oxo-5-arylpentanoates** (**4ba-cb**) **and methyl 3-(1H-indol-2-yl)-3-oxopropanoate** (**10**)**; General procedure**

5-(1-hydroxy-3-(1H-indol-3-yl)-propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3a**), 5-(1-hydroxy-3-(1H-indol-3-yl)-(3-phenyl)-propylidene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3b-c**) or 5-(hydroxy(1H-indol-2-yl)methylene)-2,2-dimethyl-1,3-dioxane-4,6-dione (**3d**) (1 mmol) was dissolved in methanol or ethanol (10mL). The resultant solution was refluxed for 24 h. After completion of the reaction, the solvent was removed under vacuum, and the residue was purified with flash chromatography as specified below.

Methyl 5-(1H-indol-3-yl)-3-oxopentanoate (**4aa**)

Purification by flash column chromatography, (EtOAc/Hex, 1:2). Yield: 0.235 g (96%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.04 (s, 1 H), 7.64-7.57 (m, 1 H), 7.43-7.35 (m, 1 H), 7.27-7.19 (m, 1 H), 7.19-7.11 (m, 1 H), 7.04-6.97 (m, 1 H), 3.72 (s, 3H), 3.46 (s, 2H), 3.15-3.05 (m, 2H), 3.02-2.93 (m, 2H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 202.5, 167.6, 136.3, 127.1, 122.1, 121.7, 119.4, 118.6, 114.6, 111.2, 52.3, 49.2, 43.5, 19.1.

Ethyl 5-(1H-indol-3-yl)-3-oxopentanoate (**4ab**)[15a]

Purification by flash column chromatography, (EtOAc/Hex, 1:2). Yield: 0.220 g (85%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.06 (s, 1 H), 7.62-7.60 (m, 1 H), 7.38-7.36 (m, 1 H), 7.24-7.20 (m, 1 H), 7.17-7.13 (m, 1 H), 7.02-6.97 (m, 1 H), 4.19 (q, 7.2 Hz, 2 H), 3.45 (s, 2 H), 3.12-3.09 (m, 2H), 2.99-2.96 (m, 2H), 1.27 (t, *J*=7.2 Hz, 3H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 202.7, 167.2, 136.3, 127.1, 122.1, 121.7, 119.3, 118.6, 114.7, 111.2, 61.4, 49.4, 43.5, 19.1, 14.1.

Methyl 5-(1H-indol-3-yl)-3-oxo-5-phenylpentanoate (**4ba**)

Purification by flash column chromatography, (EtOAc/Hex, 1:4). Yield: 0.282 g (88%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.09 (s, 1H), 7.45-7.43 (m, 1 H), 7.35-7.27 (m, 5 H), 7.23-7.16 (m, 2 H), 7.07-7.00 (m, 2 H), 4.88 (t, *J*=7.4 Hz, 1H), 3.68 (s, 3H), 3.45-3.28 (m, 4H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 201.4, 167.5, 143.6, 136.6, 128.5, 127.7, 126.5, 126.4, 122.2, 121.5, 119.5, 119.4, 118.4, 111.2, 52.3, 49.5, 49.4, 38.1.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{20}NO_3$: 322.1433; found: 322.1424.

Ethyl 5-(1H-indol-3-yl)-3-oxo-5-phenylpentanoate (**4bb**)

Purification by flash column chromatography, (EtOAc/Hex, 1:4). Yield: 0.224 g (67%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.05 (s, 1H), 7.46-7.42 (m, 1 H), 7.36-7.27 (m, 5 H), 7.22-7.15 (m, 2 H), 7.07-7.01 (m, 2 H), 4.87 (dd, *J* = 14.4; 7.2 Hz, 1H), 4.15 (q, 7.2 Hz, 2 H), 3.46-3.25 (m, 4H), 1.24 (t, *J*=7.1 Hz, 3H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 201.4, 167.1, 143.6, 136.6, 128.5, 127.7, 126.5, 126.4, 122.2, 121.5, 119.5, 119.4, 118.5, 111.2, 61.4, 49.6, 49.5, 38.1, 14.1.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{22}NO_3$: 336.1599; found: 336.1595.

Methyl 5-(3-chlorophenyl)-5-(1H-indol-3-yl)-3-oxopentanoate (**4ca**)

Purification by flash column chromatography, (EtOAc/Hex, 1:4). Yield: 0.234 g (66%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.12 (s, 1H), 7.43-7.41 (m, 1 H), 7.36-7.34 (m, 1 H), 7.30-7.28 (m, 1 H), 7.24-7.16 (m, 4 H), 7.08-7.01 (m, 1H), 7.04-6.99 (m, 1H), 4.86 (t, *J*=7.4 Hz, 1H), 3.69 (s, 3H), 3.45-3.26 (m, 4H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 200.8, 167.4, 145.8, 136.6, 134.3, 129.8, 127.8, 126.7, 126.2, 126.1, 122.4, 121.5, 119.6, 119.2, 117.7, 111.3, 52.4, 49.3, 49.2, 37.6.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{19}ClNO_3$: 356.1053; found: 356.1034.

Ethyl 5-(3-chlorophenyl)-5-(1H-indol-3-yl)-3-oxopentanoate (**4cb**)

Purification by flash column chromatography, (EtOAc/Hex, 1:4). Yield: 0.210 g (57%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.09 (s, 1H), 7.44-7.41 (m, 1 H), 7.39-7.32 (m, 1 H), 7.32-7.27 (m, 1 H), 7.27-7.14 (m, 4 H), 7.10-6.99 (m, 2H), 4.86 (dd, *J* = 14.4; 7.2 Hz, 1H), 4.16 (q, *J*= 7.1 Hz, 2 H), 3.45-3.14 (m, 4 H), 1.25 (t, *J*=7.1 Hz, 3H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 200.9, 167.0, 145.9, 136.6, 134.3, 129.8, 127.8, 126.7, 126.6, 126.1, 122.4, 121.5, 119.6, 119.2, 117.8, 111.2, 61.5, 49.6, 49.2, 37.6, 14.1.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{21}ClN_2O_3$: 370.1210; found: 370.1182.

Methyl 3-(1H-indol-2-yl)-3-oxopropanoate (**10**)[29]

Purification by flash column chromatography, (EtOAc/Hex, 1:5). Yield: 0.162 g (75%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 9.41 (s, 1 H), 7.77-7.69 (m, 1H) 7.51-7.44 (m, 1 H), 7.42-7.36 (m, 1 H), 7.31-7.26 (m, 1 H), 7.22-7.15 (m, 1 H), 4.02 (s, 2 H), 3.79 (s, 3 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 184.4, 167.7, 137.9, 134.3, 127.4, 127.01, 123.3, 121.2, 112.4, 111.09, 52.6, 45.2.

Morpholides 4ac, **bc** and **4d; General procedure**[20]

3a-d (0.66 mmol) was dissolved in benzene (5mL). Then, morpholine (113 mg, 1.3 mmol) and trimethylsilyl chloride (108 mg, 1 mmol) were added to the resulting solution. The mixture was then refluxed under argon for 4 h. After completion of the reaction, the solvent was removed under vacuum, and the residue was purified with flash chromatography as specified below.

5-(1H-Indol-3-yl)-1-morpholinopentane-1,3-dione (**4ac**)

Purification by flash column chromatography, (DCM/MeOH, 60:1). Yield: 0.294 g (98%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.13 (s, 1 H), 7.61 (d, *J* = 7.6 Hz, 1 H), 7.37 (dt, *J* = 8.0 Hz, *J* = 0.8 Hz, 1 H), 7.23-7.20 (m, 1 H), 7.16-7.12 (m, 1 H), 7.01 (s, 1 H), 3.65-3.47 (m, 8 H), 3.29-3.18 (m, 2H), 3.12-3.06 (m, 2 H), 3.06-2.93 (m, 2 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 204.1, 163.2, 136.3, 127.1, 122.1, 121.7, 119.4, 118.6, 111.2, 66.6, 66.5, 49.3, 46.7, 43.3, 42.2, 19.3.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{21}N_2O_3$: 301.1552; found: 301.1539.

5-(1H-Indol-3-yl)-1-morpholino-5-phenylpentane-1,3-dione (**4bc**)

Purification by flash column chromatography, (DCM/MeOH, 60:1). Yield: 0.263 g (70%); yellow oil.

^{1}H NMR(DMSO-d_6, 400 MHz): δ= 10.89 (s, 1 H), 7.42-7.40 (m, 1 H), 7.36-7.29 (m, 4 H), 7.26-7.22 (m, 2 H), 7.15-7.10 (m, 1 H), 7.05-7.01 (m, 1 H), 6.92-6.88 (m, 1 H), 4.70 (t, *J*= 7.6 Hz, 1H), 3.69 (d, *J*= 16.7 Hz, 1 H), 3.68 (d, *J* = 16.7 Hz, 1 H), 3.58-3.50 (m, 1 H), 3.48-3.37 (m, 5 H), 3.31-3.22 (m, 3 H), 2.99-2.97 (m, 1 H).

^{13}C NMR(DMSO-d_6, 100 MHz): δ= 203.9, 165.8, 145.3, 136.8, 128.6, 128.0, 126.7, 126.4, 122.4, 121.5, 119.1, 118.7, 117.9, 11.8, 66.4, 66.3, 49.2, 48.9, 46.3, 41.9, 37.7.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{25}N_2O_3$: 377.1865; found: 377.1875.

1-(1H-Indol-2-yl)-3-morpholinopropane-1,3-dione (**4d**)

Purification by flash column chromatography, (DCM/MeOH, 60:1). Yield: 0.204 g (75%); yellow oil.

^{1}H NMR(DMSO-d_6, 400 MHz): δ= 11.80 (s, 1H), 7.72-7.69 (m, 1 H), 7.46-7.41 (m, 2 H), 7.32-7.27 (m, 1 H), 7.11-7.05 (m, 1 H), 4.18 (s, 2 H), 3.62-3.56 (m, 4 H), 3.49-3.47 (m, 4 H).

^{13}C NMR(DMSO-d_6, 100 MHz): δ= 187.3, 166.2, 138.4, 135.6, 127.3, 126.1, 123.2, 120.8, 113.2, 110.8, 66.6, 66.5, 46.7, 44.7, 42.1.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{17}N_2O_3$: 273.1239; found: 273.1225.

5-(1H-indol-3-yl)-3-oxo-N-(p-tolyl)pentanamide (**4ad**) and **5-(1H-indol-3-yl)-3-oxo-5-aryl-N-(p-tolyl)pentanamide** (**4bd**); **General procedure**[20]

3a or **3b** (1 mmol) was dissolved in toluene (10mL). p-Toluidine (107 mg, 1.3 mmol) was added to the resulting solution. The mixture was stirred at 70°C for 18 h. After completion of the reaction, the solvent was removed under vacuum, and the residue was purified with flash chromatography as specified below.

5-(1H-Indol-3-yl)-3-oxo-N-(p-tolyl)pentanamide (**4ad**)

Purification by flash column chromatography, (EtOAc/Hex/AcOH, 1:2:0,01). Yield: 0.281 g (88%); yellow oil.

^{1}H NMR(DMSO-d_6, 400 MHz): δ= 10.8 (s, 1H), 10.0 (s, 1 H), 7.55-7.49 (m, 1 H), 7.49-7.44 (m, 2 H), 7.36-7.31 (m, 1 H), 7.15-7.03 (m, 4 H), 7.01-6.94 (m, 1 H), 3.58 (s, 2 H), 2.99-2.90 (m, 4 H), 2.26 (s, 3 H).

^{13}C NMR(DMSO-d_6, 100 MHz): δ= 204.9, 165.3, 136.9, 136.7, 132.8, 129.6, 127.4, 122.7, 121.4, 119.6, 118.7, 118.6, 113.8, 111.8, 51.9, 43.5, 20.9, 19.2.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{21}N_2O_2$: 321.1603; found: 321.1617.

5-(1H-Indol-3-yl)-3-oxo-5-phenyl-N-(p-tolyl)pentanamide (**4bd**)

Purification by flash column chromatography, (EtOAc/Hex/AcOH, 1:2:0,01). Yield: 0.297 g (75%); yellow oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.79 (s, 1 H), 8.10 (s, 1H), 7.46-7.44 (m, 1 H), 7.35-7.24 (m, 7 H), 7.21-7.16 (m, 2 H), 7.14-7.08 (m, 2 H), 7.08-7.02 (m, 1H), 7.01-6.96 (m, 1 H), 4.88 (t, *J*=7.6 Hz, 1H), 3.56-3.38 (m, 3 H), 3.34-3.24 (m, 1 H), 2.33 (s, 3 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 206.1, 143.3, 136.5, 134.8, 134.2, 129.4, 128.6,127.6, 126.7, 126.4, 122.4, 121.3, 120.3, 119.6, 119.3, 118.2, 111.3, 50.4, 49.7, 38.1, 20.9.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{25}N_2O_2$: 397.1916; found: 397.1889.

Oxidative cyclization of 3-oxoesters 4aa-cb with $Mn(OAc)_3$×2 H_2O; General procedure.

Ester **4aa**-**cb** (0.2 mmol) was dissolved in AcOH (4mL). To a resulted solution amount of $Mn(OAc)_3$×2 H_2O specified in the table 2 was added. The mixture was heated for 4 h at 70°C. After reaction completion, the solvent was removed under vacuum, and the residue was purified with flash chromatography as specified below.

Oxidative cyclization of 3-oxoesters and 3-oxoamides 4aa-cb and 4d with metal triflates; General procedure.

The ester or amide **4aa**-**cb** or **4d** (0.2 mmol) was dissolved in anhydrous DCM (4mL). To a resulted solution (0.2 mmol) of triflate specified in the table 3 was added, followed by I_2 (0.3 mmol) and NEt_3 (0.5 mmol, 69 µL). The mixture was then stirred for 12 h at R. T. After completion of the reaction, the residue was dissolved in DCM (30mL) and washed with aqueous sat. Na_2SO_3. The organic layer was dried with $MgSO_4$, the solvent was removed under vacuum, and the residue was purified with flash chromatography as specified below.

Methyl 2-hydroxy-9H-carbazole-1-carboxylate (**5aa**)

Purification by flash column chromatography, (DCM/Hex, 1:3). Yield: 0.019 g (41%); white amorphous solid.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 11.00 (s, 1H), 9.25 (s, 1H), 8.16-8.12 (m, 1H), 8.01-7.97 (m,1H), 7.52-7.47 (m, 1 H), 7.43-7.37 (m, 1 H), 7.31-7.24 (m, 1 H), 6.91-6.85 (m, 1 H), 4.19 (s, 3 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 170.5, 161.8, 138.9, 138.7, 127.9, 124.8, 123.0, 120.3, 119.2, 116.4, 110.7, 109.3, 96.5, 52.5.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{12}NO_3$: 242.0817; found: 242.0823.

Ethyl 2-hydroxy-9H-carbazole-1-carboxylate (**5ab**)[15a]

Purification by flash column chromatography, (DCM/Hex, 1:3). Yield: 0.014 g (28%); white amorphous solid.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 11.06 (s, 1 H), 9.25 (s, 1 H), 8.15-8.09 (m, 1H), 8.01-7.96 (m, 1 H), 7.51-7.45 (m, 1 H), 7.43-7.37 (m, 1 H), 7.31-7.23 (m, 1 H), 6.89-6.85 (m, 1 H), 4.66 (q, *J*= 7.1 Hz, 2 H), 1.61 (t, *J*=7.1 Hz, 3H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 170.0, 161.8, 139.1, 138.7, 127.8, 124.7, 123.1, 120.3, 119.2, 116.4, 110.7, 109.3, 96.7, 61.9, 14.7.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{14}NO_3$: 256.0974; found: 256.0978.

Methyl 2-hydroxy-4-phenyl-9H-carbazole-1-carboxylate (**5ba**)

Purification by flash column chromatography, (DCM/Hex, 1:3). Yield: 0.028 g (45%); white amorphous solid.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 11.03 (s, 1H), 9.45 (s, 1H), 7.64-7.60 (m, 2H), 7.58-7.53 (m,3H), 7.49-7.44 (m, 1 H), 7.35-7.31 (m, 2 H), 7.03-6.99 (m, 1 H), 6.78 (s, 1H), 4.21 (s, 3H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 170.4, 161.2, 145.5, 139.9, 139.5, 138.9, 128.7, 128.5, 128.3, 124.6, 122.7, 121.3, 119.9, 114.2, 110.9, 110.6, 95.4, 52.6.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{16}NO_3$: 318.1130; found: 318.1144.

Ethyl 2-hydroxy-4-phenyl-9H-carbazole-1-carboxylate (**5bb**)

Purification by flash column chromatography, (DCM/Hex, 1:2-1:1). Yield: 0.047 g (72%); white amorphous solid.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 11.05 (s, 1H), 9.48 (s, 1H), 7.65-7.59 (m, 2H), 7.58-7.51 (m,3H), 7.48-7.44 (m, 1 H), 7.34-7.30 (m, 2 H), 7.02-6.98 (m, 1 H), 6.78 (s, 1H), 4.69 (q, *J*= 7.1 Hz, 2 H), 1.63 (t, *J*=7.1 Hz, 3 H).

^{13}C NMR ($CDCl_3$, 100 MHz): δ= 169.6, 161.2, 145.3, 139.9, 139.7, 138.9, 128.7, 128.5, 128.3, 124.6, 122.7, 121.3, 119.9, 114.2, 110.9, 110.6, 95.6, 61.9, 14.7.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{18}NO_3$: 332.1287; found: 332.1295.

Methyl 4-(3-chlorophenyl)-2-hydroxy-9H-carbazole-1-carboxylate (**5ca**)

Purification by flash column chromatography, (DCM/Hex, 1:3). Yield: 0.036 g (52%); white amorphous solid.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 11.02 (s, 1H), 9.46 (s, 1H), 7.65-7.60 (m, 1H), 7.54-7.46 (m,4H), 7.38-7.29 (m, 2 H), 7.08-7.01 (m, 1 H), 6.75 (s, 1H), 4.21 (s, 3H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 170.3, 161.2, 143.6, 141.6, 139.5, 139.0, 134.4, 129.8, 128.8, 128.4, 126.9, 124.8, 122.4, 121.1, 120.1, 114.1, 110.8, 110.7, 95.7, 52.7.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{15}ClNO_3$: 352.0740; found: 352.0748.

Ethyl 4-(3-chlorophenyl)-2-hydroxy-9H-carbazole-1-carboxylate (**5cb**)

Purification by flash column chromatography, (DCM/Hex, 1:3). Yield: 0.044 g (61%); white amorphous solid.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 11.05 (s, 1 H), 9.49 (s, 1 H), 7.66-7.59 (m, 1 H), 7.56-7.45 (m, 4 H), 7.37-7.29 (m, 2 H), 7.10-7.01 (m, 1 H), 6.75 (s, 1 H), 4.69 (q, *J* = 7.1 Hz, 2 H), 1.63 (t, *J*=7.1 Hz, 3 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 169.8, 161.2, 143.4, 141.7, 139.7, 138.9, 134.4, 129.8, 128.8, 128.4, 127.0, 124.8, 122.4, 121.1, 120.1, 114.0, 110.8, 110.7, 95.9, 62.0, 14.7.

HRMS (ESI+): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{17}ClNO_3$: 366.0897; found: 366.0905.

2-Hydroxy-N-(p-tolyl)-9H-carbazole-1-carboxamide (**5ad**)

Purification by flash column chromatography, (EtOAc/Hex, 1:3). Yield: 0.026 g (42%); white amorphous solid.

^{1}H NMR(DMSO-d_6, 400 MHz): δ= 11.55 (s, 1 H), 11.48 (s, 1 H), 10.58 (s, 1 H), 8.12-8.10 (m, 1 H), 8.01-7.99 (m, 1 H), 7.70-7.67 (m, 3 H), 7.32-7.27 (m, 1 H), 7.21-7.19 (m, 2 H), 7.16-7.12 (m, 1 H), 6.90-6.88 (m, 1 H), 2.31 (s, 3 H).

^{13}C NMR(DMSO-d_6, 100 MHz): δ= 165.2, 155.3, 141.1, 140.2, 136.7, 133.0, 129.7, 124.9, 124.7, 122.4, 120.4, 119.5, 119.4, 117.1, 112.3, 108.6, 103.2, 20.9.

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{17}N_2O_2$: 317.1290; found: 317.1280.

(2-Hydroxy-4-phenyl-9H-carbazol-1-yl)(morpholino)methanone (**5bc**)

Purification by flash column chromatography, (EtOAc/Hex, 1:1). Yield: 0.030 g (40%); white amorphous solid.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.75 (s, 1 H), 7.54-7.46 (m, 6 H), 7.36-7.22 (m, 3 H), 6.96-6.92 (m, 1 H), 6.61 (s, 1 H), 3.83-3.73 (m, 6 H), 7.71-7.59 (m, 2 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 169.4, 154.6, 141.7, 139.9, 139.6, 138.5, 128.8, 128.4, 128.0, 124.8, 122.9, 121.3, 119.7, 114.9, 111.0, 110.5, 101.4, 67.1, 46.2.

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{21}N_2O_3$: 373.1552; found: 373.1536.

2-Hydroxy-4-phenyl-N-(p-tolyl)-9H-carbazole-1-carboxamide (**5bd**)

Purification by flash column chromatography, (EtOAc/Hex, 1:6). Yield: 0.033 g (42%); yellow amorphous solid.

^{1}H NMR(acetone-d_6, 400 MHz): δ= 11.54 (s, 1H), 10.79 (s, 1 H), 10.57 (s, 1 H), 7.77-7.72 (m, 3 H), 7.65-7.54 (m, 5 H), 7.33-7.29 (m, 2 H), 7.23-7.21 (m, 2 H), 6.96-6.91 (m, 1 H), 6.85 (s, 1 H), 2.34 (s, 3 H).

^{13}C NMR(acetone-d_6, 100 MHz): δ= 165.3, 154.2, 142.2, 141.8, 140.3, 136.6, 132.9, 129.3, 128.7, 128.6, 128.2, 124.6, 121.9, 120.8, 120.1, 120.0, 118.9, 115.2, 111.5, 109.5, 101.3, 20.90.

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{21}N_2O_2$: 393.1603; found: 393.1590.

Methyl 2-hydroxy-2,3,4,9-tetrahydro-1H-carbazole-1-carboxylate (**6aa**)

Purification by flash column chromatography, (EtOAc/Hex, 1:5). Yield: 0.021 g (43%); colorless oil.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 12.33 (s, 1 H), 7.14-7.05 (m, 2 H), 6.81-6.76 (m, 1 H), 6.74-6.70 (m, 1 H), 4.62 (d, J = 7.6 Hz, 1 H), 3.88 (s, 3 H), 3.53-3.28 (m, 1 H), 2.46-2.36 (m, 2 H), 2.03-1.87 (m, 2 H), 1.28 (brs, 1 H).

^{13}C NMR($CDCl_3$, 100 MHz): δ= 175.6, 172.7, 131.8, 128.5, 128.0, 123.6, 119.4, 110.4, 98.4, 56.8, 51.8, 40.3, 28.0, 23.7.

HRMS (ESI+): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{16}NO_3$: 246.1130; found: 246.1129.

Methyl 3-(3-iodo-1H-indol-2-yl)-3-oxopropanoate (**11**)

Purification by flash column chromatography, (EtOAc/Hex, 1:3). Yield: 0.035 g (52%); yellow amorphous solid.

^{1}H NMR($CDCl_3$, 400 MHz): δ= 9.60 (s, 1 H), 7.60-7.58 (m, 1 H), 7.46-7.39 (m, 2 H), 7.28-7.24 (m, 1 H), 4.35 (s, 2 H), 3.82 (s, 3 H).

Supporting Information

YES

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