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Manganese Chloride as an Efficient Catalyst for Selective Transformations of Indoles in the Presence of a Keto Carbonyl Group

Minghao Li,[a,c] Jie Yang,[a,c] and Yanlong Gu[a,b,*]

[a] Institute of Physical Chemistry and Industrial Catalysis, Hubei Key Laboratory of Material Chemistry and Service Failure, School of Chemistry and Chemical Engineering, Huazhong University of Sciences and Technology, 1037 Luoyu Road, Hongshan Division, Wuhan, Hubei Province 430074, People's Republic of China
Fax: (+86)-(0)27-8754-4532; e-mail: klgyl@hust.edu.cn
[b] State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Lanzhou 730000, People's Republic of China
[c] M. Li and J. Yang contributed equally to this work.

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Abstract: Catalysis by manganese chloride tetrahydrate was found to be effective for the selective transformation of indoles, with which the desired acid-catalyzed reaction could be promoted and, at the same time, a side reaction that also needs assistance of acid, the electrophilic reaction of indole with the co-existing keto carbonyl group, does not occur. Some acid-catalyzed reactions, such as the ring-opening reaction of 2-alkoxy-3,4-dihydropyran with indole, and transesterification of β-keto ester with an alcohol that contains a C-3 unsubstituted indole fragment, could be performed smoothly by using manganese chloride as catalyst. A new multicomponent reaction of indole, 3,4-dihydropyran and β-keto ester was also developed with catalysis by manganese chloride.

Keywords: acid catalysis; indoles; manganese chloride; selective transformations; tandem reactions

Introduction

In the context of green chemistry, the implementation of methodologies giving selective access to elaborate scaffolds, while combining molecular diversity with eco-compatibility, is a great challenge for organic chemists.[1] Many research projects have, therefore, been driven forward by one particular motivation: easy access of complex molecules in combination with the potential to site-selectively introduce chemical functionalities.[2] The importance of this area has been well documented by one of the twelve principles of green chemistry, reduce derivatives. Although many methodologies for chemoselective control in various reactions have been well established by means of catalysis with enzymes or organic and organometallic compounds, the reported methods often involve practical difficulties due to high costs of catalyst, limited substrate scope or lack of green properties.[3] Therefore, new catalytic systems are being continuously explored in search of improved efficiencies and cost-effectiveness.

The indole ring system exists ubiquitously in naturally occurring products, and many indole-containing compounds exhibit important biological and pharmaceutical activities.[4] The synthesis and derivatization of indoles has, therefore, been a major area of focus for organic chemists over the years.[5] As an electron-rich heteroaromatic system, indole has often been used as a model substrate in electrophilic aromatic substitutions. Generally, the most reactive position of indole in these reactions is the C-3 site. Although the high reactivity can render indoles readily applicable in many reactions, when an electrophile that contains two or more reactive sites was used, how to control the reaction selectivity has become a great challenge.

In this paper, we report an efficient catalyst for catalytic selective transformations of indoles in the presence of a keto carbonyl group. It is well known that, in the presence of acid catalyst, the keto carbonyl group will undergo an electrophilic reaction with

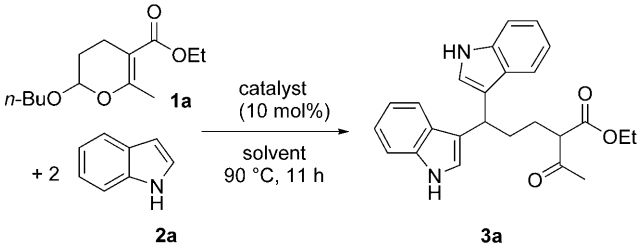
indole to form diindolylmethane derivatives. This reaction is particularly favorable to C-3 unsubstituted indoles that contain an electron-donating group. As a result, derivatization of C-3 unsubstituted indole in the presence of a keto carbonyl group is not easy, and generally cannot be performed in the presence of acid. However, we found unexpectedly that $MnCl_2$ can be used, in the presence of a keto carbonyl group, as a highly selective catalyst for transformations of indoles by means of three acid-catalyzed reactions: (i) ring-opening reaction of 2-alkoxy-3,4-dihydropyran with indole; (ii) transesterification of β-keto ester with an alcohol that contains a C-3 unsubstituted indole fragment; and (iii) an "ABCC"-type four-component reaction of β-keto ester, 3,4-dihydropyran and indole. While the desired reactions proceed well, the keto carbonyl groups involved in the structure of substrates or products remain unaltered although a highly reactive C-3 unsubstituted indole was also involved in the reaction system.

Results and Discussion

Initially, the reaction of 2-alkoxy-3,4-dihydropyran **1a** and indole **2a** was investigated. This type of electrophilic ring-opening reaction of 2-alkoxy-3,4-dohydropyran has just been reported by us by using thiols or thiophenols as nucleophiles.[6] Although the reactions of thiol or thiophenol proceeded very well in the presence of many Lewis acid catalysts, when indole was used as nucleophile, control of the reaction selectivity is not easy. For example, the ring-opening reaction of 2-aryl-3,4-dihydropyran with indole can only be performed by using manganese chloride tetrahydrate as catalyst, and other acids were proved to be inappropriate for this reaction.[7] Inspired by this specific observation, we thus decided to explore the application of this catalyst in organic synthesis. In fact, manganese chloride has been rarely used before as a catalyst in organic synthesis.[8] For this reason, we wanted to know what this catalyst can contribute for improving current organic synthesis.

Although the reaction of indole with 2-aryl-3,4-dihydropyran has been reported by us,[7] the ring-opening reaction of 2-alkoxy-3,4-dihydropyran with indole has not been reported yet. Importantly, the latter reaction might be able to generate a double substituted product that is inaccessible with our previous reaction. As indole is a very reactive nucleophile, and also considering the fact that reactivity of 2-alkoxy-3,4-dihydropyran is quite high, it may not easy to control the selectivity of this ring-opening reaction. Therefore, our investigation was started from the reaction of 2-butoxy-3,4-dihydropyran **1a** and an indole **2a**. As shown in Table 1, no reaction occurs in the absence of catalyst (entry 1). When some conventional acids, such as *p*-toluenesulfonic acid (TsOH), $Sc(OTf)_3$, $InCl_3$ and $FeCl_3$ were used as catalysts, **1a** was almost completely consumed at the end of the reaction, and a di(indolyl)methane derivative **3a** was obtained from a messy mixture in poor yields (entries 2 to 5). In order to control the reaction selectivity, a weak acid, boric acid, was then examined. And it was found that the starting materials, **1a** and **2a**, remained unaltered in these cases, as a result, only small amount of **3a** was detected (entry 6). Solid acids, such as montmorillonite K10 and Amberlyst 15, were also used in this reaction and no selectivity was observed (entries 7 and 8). Many other acid catalysts were also examined and no positive results were obtained (see Supporting Information). In a later study, anhydrous $MnCl_2$ was used, and the yield of **3a** reached to 40% (entry 9). Owing to the fact that **1a** was completely consumed in this case, efforts to further improve the reaction yield were in vain. Other manganese salts, such as $Mn(OAc)_2$ and $MnBr_2$, were also examined and the yields are rather poor (entries 10 and 11). Encouraged by the promising result obtained with anhydrous $MnCl_2$, manganese chloride tetrahydrate was then ex-

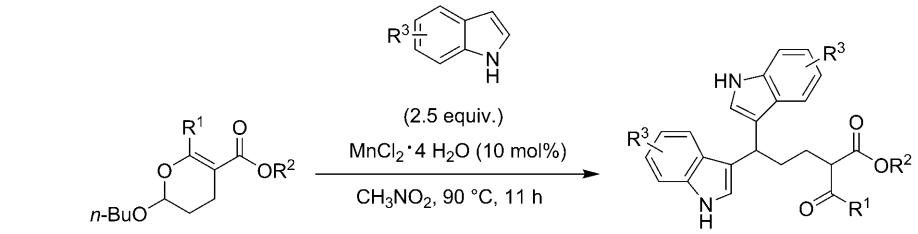
Table 1. Electrophilic ring-opening reaction of dihydropyran **1a** with indole **2a**.[a]

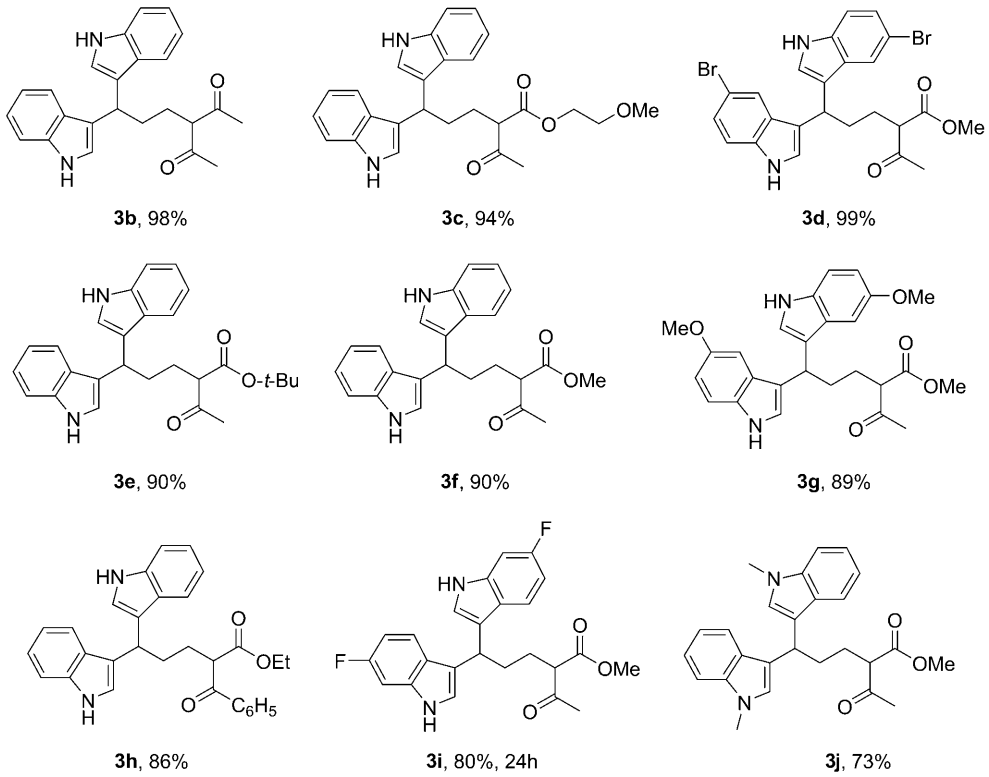


Entry	Catalyst	Solvent	Yield [%][b]
1	–	CH_3NO_2	0
2	TsOH	CH_3NO_2	28 (23)
3	$Sc(OTf)_3$	CH_3NO_2	31 (22)
4	$InCl_3$	CH_3NO_2	25 (26)
5	$FeCl_3$	CH_3NO_2	10
6	H_3BO_3	CH_3NO_2	21 (17)
7	montmorillonite K10	CH_3NO_2	20
8	Amberlyst-15	CH_3NO_2	16
9	$MnCl_2$	CH_3NO_2	40 (**81**)
10	$Mn(OAc)_2{\cdot}4H_2O$	CH_3NO_2	trace
11	$MnBr_2$	CH_3NO_2	30 (34)
12	$MnCl_2{\cdot}4H_2O$	CH_3NO_2	**82**
13	$MnCl_2{\cdot}4H_2O$	toluene	trace
14	$MnCl_2{\cdot}4H_2O$	1,4-dioxane	trace
15	$MnCl_2{\cdot}4H_2O$	CH_3CN	31
16	$MnCl_2{\cdot}4H_2O$	$ClCH_2CH_2Cl$	39
17	$MnCl_2{\cdot}4H_2O$	water	trace
18	$MnCl_2{\cdot}4H_2O$	–	59

[a] Solvent: 1.0 mL, **1a**: 0.25 mmol, **2a**: 0.63 mmol.
[b] Yield in brackets was obtained in the presence of 0.8 equiv. water.

Table 2. Electrophilic ring-opening reaction of the dihydropyrans with indoles catalyzed by $MnCl_2$ tetrahydrate.

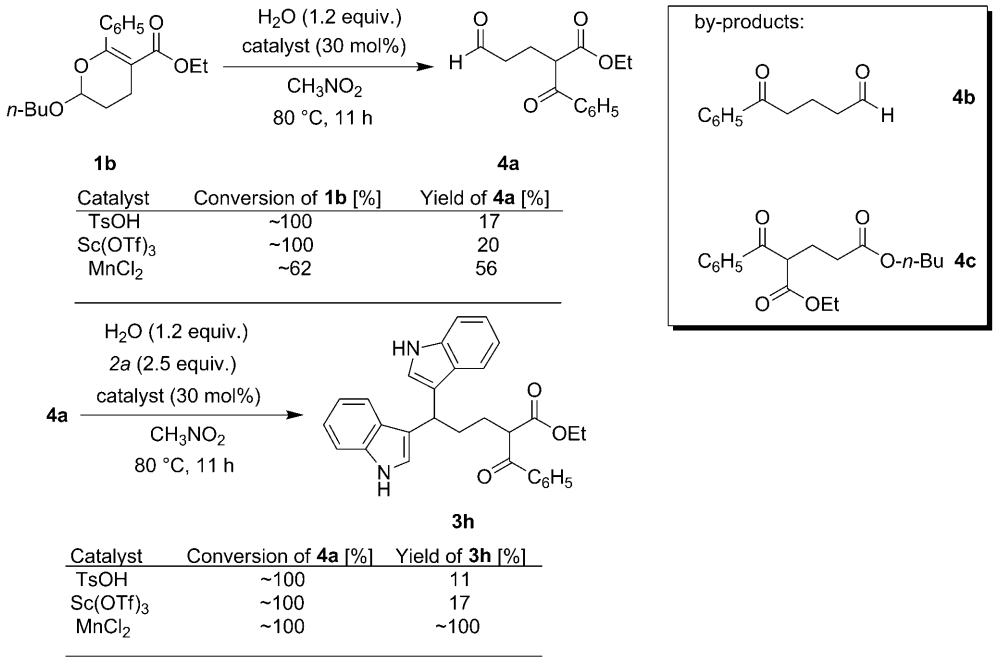




amined. And to our great delight, an 82% of yield was obtained in this case (entry 12). This result implies that a small amount of water is helpful for the progress of the model reaction. We therefore re-examined some of the other catalysts by adding small amount of waters into the reaction system, and as shown in Table 1, nearly the same performances were observed with the exception of anhydrous $MnCl_2$, which gives an 81% yield with the aid of water (entry 9). Therefore, at this stage, the best catalyst for the model reaction is $MnCl_2$ tetrahydrate. The solvent also plays a crucial role for the occurrence of the model reaction, and nitromethane was found to be the best one among all the examined solvents in Table 1 (entries 13 to 18).

Having these results in hand, we then examined the substrate generality of the $MnCl_2 \cdot 4H_2O$-catalyzed electrophilic ring-opening of **1a**-type dihydropyrans with indoles. And as shown in Table 2, many indoles and dihydropyrans are applicable in this system, and the desired products were obtained in good to excellent yields. It should be noted that the skeleton of the obtained product contains not only a fragment of di-(indolyl)methane, which is, sometimes, biologically active and pharmaceutically interesting,[9] but also a moiety of a β-dicarbonyl compound that has been widely used in organic synthesis. Although the product could be theoretically synthesized by (i) enolate alkylation or (ii) Michael addition of β-dicarbonyl compound to acrolein and the following selective electrophilic reaction of the formyl group of the product with indole (see Supporting Information), our present method exhibits some advantages including minimization of wastes, simplified operation procedure and easy control of reaction selectivity.

To probe the mechanism of the model reaction, we treated an analogous dihydropyran, **1b**, in nitromethane with 30 mol% of $MnCl_2$ tetrahydrate in the ab-

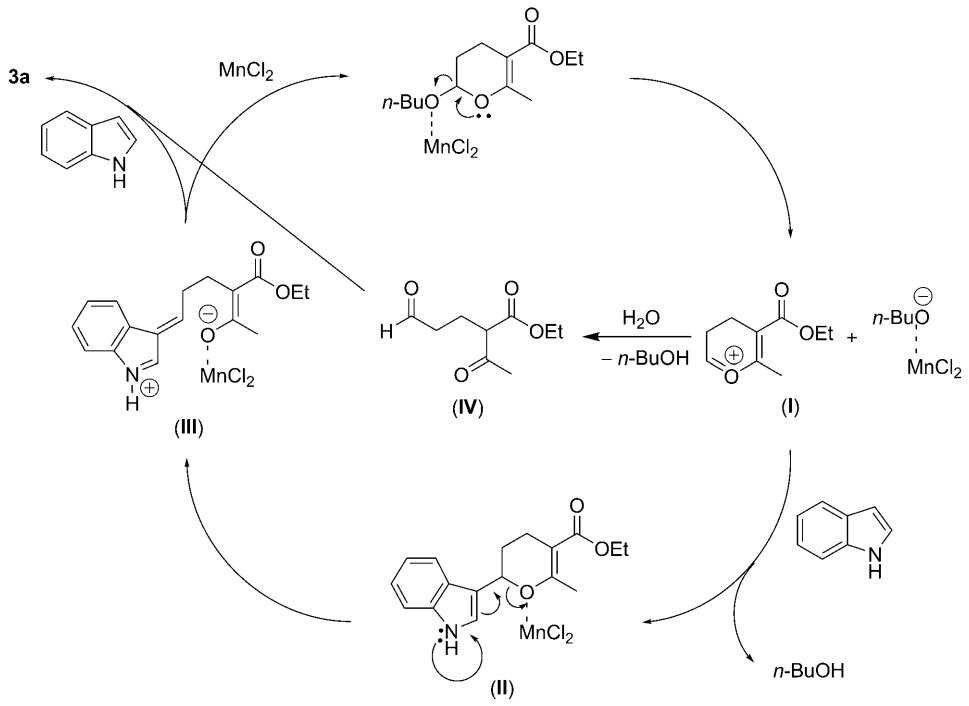


Scheme 1. Subdivisions of the model reaction and the by-products identified in the reaction systems.

sence of indole. As shown in Scheme 1, an aldehyde, **4a**, was obtained in 56% of yield after 11 h of reaction at 80 °C. It should be noted that **4a** is the only product in this reaction, and the moderate yield mainly resulted from incomplete conversion of **1b**. Following treatment of **4a** with **2a** in the presence of 30 mol% of $MnCl_2$ tetrahydrate resulted in the quantitative formation of **3i**. Two other acids, TsOH and $Sc(OTf)_3$, were also examined in this procedure in the presence of 1.2 equivalents of water. It was found that **1b** was completely consumed in the first step, but, however, **4a** was obtained only in a small amount (yield $<20\%$). Two by-products, **4b** and **4c** were isolated with nearly 30% overall yield from the obtained messy mixture. There are some other by-products that are difficult to isolate in the reaction mixture. Furthermore, TsOH and $Sc(OTf)_3$ were proved to be non-selective for the formation of **3i** in the second step because a messy mixture was formed in these cases.

On the basis of these results, we can conclude that the model reaction is susceptible to both catalyst and water. Kobayashi and his co-workers have accomplished a classification of many Lewis acids according to their activities in organic reactions.[10] In the ranking of Kobayashi, anhydrous $MnCl_2$ was considered as an inactive one. Therefore, we believe that the acid strength of $MnCl_2$ might be responsible for the high selectivity. When water was added into the reaction system, it might play two functions involving (i) facilitating the formation of reaction intermediate, and (ii) tuning the Lewis acidity of $MnCl_2$ to be suitable for the reaction. Out of these considerations, we thus proposed a possible mechanism for the model reaction in Scheme 2. In the beginning of the reaction, the dihydropyran substrate **1a** was activated with the aid of $MnCl_2$ catalyst to form a cyclic oxocarbenium ion intermediate (**I**). This step was generally catalyzed by a Lewis acid.[11] Although formation of a linear oxocarbenium ion might be also possible through a cleavage of the C–O bond in the ring, but compared with the cyclic one, it should be much less stable because of the lack of a conjugation effect. Once (**I**) was formed, it tended to react with water to form an aldehyde (**IV**) that can further interact with indole to generate **3a**. In view of the fact that 40% of the yield was obtained under anhydrous conditions, we thus suspect that the other way to **3a** is also possible, in which water was not involved. Out of this consideration, another reaction pathway was also proposed in Scheme 2. Interaction of (**I**) with indole might form an intermediate (**II**).[12] In the presence of $MnCl_2$, (**II**) underwent cleavage of the C-2–O bond to form a ring-opening intermediate (**III**) that tended to react with the next indole to generate the final product **3a**.[13]

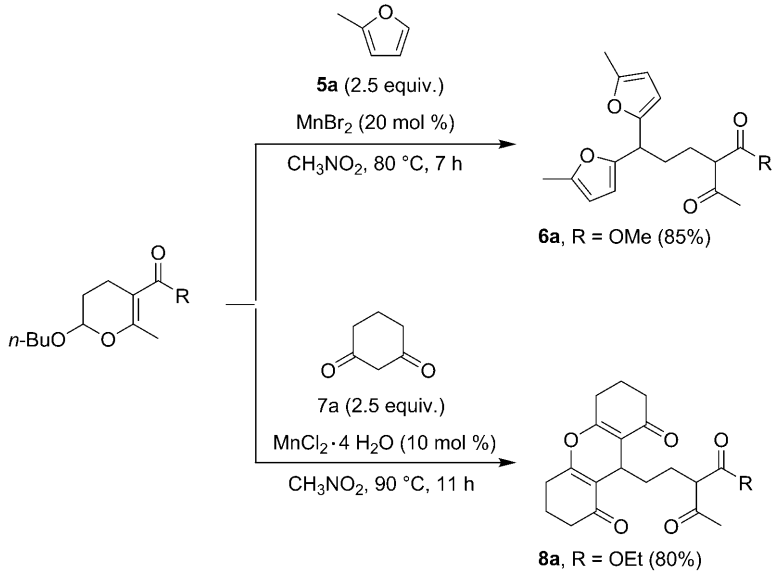
It should be noted that mechanism of the present ring-opening reaction is different from that of our previous report in which a monotransthioacetalization occurs and the aldehyde intermediate might not be formed.[6] No matter what kind of mechanism the reaction follows, we can confirm at this stage that manganese chloride tetrahydrate has indeed a specific ability for distinguishing the reactivity difference be-



Scheme 2. Plausible mechanism for the model reaction.

tween three kinds of carbonyl groups including aldehyde-carbonyl, ketone-carbonyl and ester-carbonyl, and thus is capable of controlling the reaction selectivity. Inspired by this fact, we suspect that other nucleophiles that are able to react with an aldehyde could also be used in this type of reaction. As shown in Scheme 3, in the presence of catalytic amount of $MnBr_2$ or $MnCl_2$, 1,3-cyclohexanedione and 2-methylfuran could react readily with a **1a**-type dihydropyran. Particularly, in the case of 1,3-cyclohexanedione, the generated products underwent a dehydration step to form a cyclized skeleton.

The above-mentioned ring-opening reactions have demonstrated that manganese chloride tetrahydrate has a specific ability for selectively promoting the transformation of indole. In order to further extend the use of this specific ability of manganese chloride tetrahydrate, we then investigated other organic reac-



Scheme 3. Ring-opening of the dihydropyran with other nucleophiles.

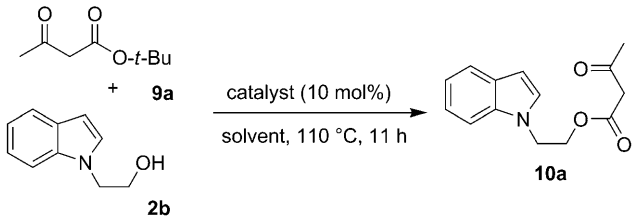
tions. The transesterification of β-keto esters with an alcohol has been extensively investigated by using acids or bases as catalysts.[14] When acid catalysts were used, extra efforts have to be made for inhibiting some side reactions because the keto carbonyl groups in β-keto esters are normally reactive under acidic conditions toward some nucleophiles.[15] Particularly, when *N*-(2-hydroxy)ethylindole **9a** was used as an alcohol, as the generated product **10a** contains both a keto carbonyl group and a reactive C-3 unsubstituted indole fragment, controlling of the reaction selectivity could be a hard task for us. As we expected, various conventional acids, such as H_2SO_4, TsOH, $Sc(OTf)_3$, $Bi(OTf)_3$, $Y(OTf)_3$, $SnCl_4$, $FeCl_3$, $InCl_3$ and $ZnCl_2$, were found to be ineffective for this transesterification although substrate **2b** was almost completely consumed in the most cases (Table 3, entries 1 to 9). The poor efficiencies of these catalysts mainly resulted from a lack of selectivity to **10a**. Solid catalysts, such as montmorillonite K10 and Amberlyst 15, were also used, and no clear selectivity was obtained (entries 10 and 11).

In the later study, $MnCl_2{\cdot}4H_2O$ was used as catalyst, and in this case, the yield of **10a** reached 90% (entry 12). This result implies that $MnCl_2{\cdot}4H_2O$ has a unique ability to catalyze the reaction of **9a** and **2b** without affecting the chemical stability of the keto carbonyl group of **10a** or **2b**. Other manganese salts, such as $Mn(OAc)_2$ and $MnBr_2$, were also examined, and only moderate yields were obtained (entries 13 and 14). Anhydrous $MnCl_2$ also worked well, but the yield of **10a** was slightly inferior to that of $MnCl_2{\cdot}4H_2O$ (entry 15). Interestingly, by adding 0.4 equivalents of water into the anhydrous $MnCl_2$ system, the reaction yield could be improved to the level of that with $MnCl_2{\cdot}4H_2O$. Further investigations revealed that, like in the case of the first model reaction, the solvent also plays a key role in controlling the reaction selectivity, and the best result was obtained by using toluene as medium (entries 16 to 20). It should be noted that, during the reaction, both anhydrous $MnCl_2$ and $MnCl_2{\cdot}4H_2O$ are soluble in toluene at the reaction temperature. Therefore, the role of water here is not facilitating formation of a crystal of the catalyst. Although the acid strength of manganese chloride tetrahydrate is not strong, a small amount of water here might play a role in tuning the acid strength of the manganese catalyst to be suitable for the reaction. This point deserves further investigation.

Other β-keto esters were also examined in the transesterification of **2b**, and the results are listed in Table 4. All the examined β-keto esters can selectively react with **9a** to afford the corresponding products in good to excellent yields. It should be noted that the same reactions under the identical conditionws over two conventional acids, TsOH and $Sc(OTf)_3$, afforded only small amount of products. In these cases, most of the substrates were consumed at the end of the reaction, and many spots were observed on TLC detection. These results indicated that (i) controlling of the selectivity is the key to render the reaction possible; (ii) the high selectivity of $MnCl_2{\cdot}4H_2O$ for catalyzing the model reaction is not an individual phenomenon, and is efficient for the synthesis of many **10a**-type indole derivatives.

In view of the unique ability of $MnCl_2{\cdot}4H_2O$ for both acting as a mild acid catalyst and preventing the electrophilic reaction of the keto carbonyl group with indoles, this catalyst might be capable of promoting the reactions of many keto carbonyl-containing compounds and C-3 unsubstituted indoles. We then investigated a novel multicomponent reaction of **9a**, 3,4-dihydropyran (**11a**) and indoles using $MnCl_2{\cdot}4H_2O$ as

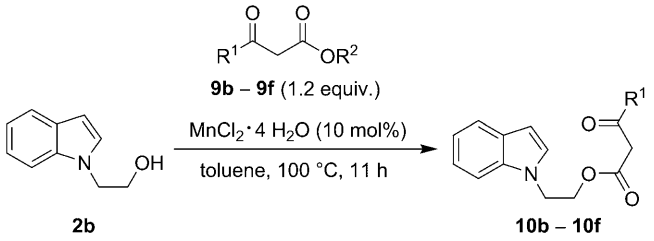
Table 3. Transesterification of **9a** with **2b** in different conditions.[a]

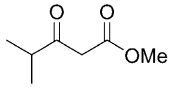
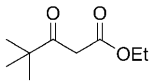
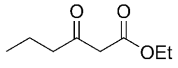
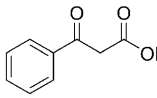
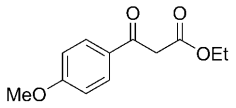


Entry	Catalyst	Solvent	Recovery rate of **2b** [%]	Yield of **10a** [%]
1	H_2SO_4	toluene	12	<5
2	TsOH	toluene	11	<5
3	$Sc(OTf)_3$	toluene	<5	<5
4	$Bi(OTf)_3$	toluene	<5	<5
5	$Y(OTf)_3$	toluene	13	25
6	$SnCl_4$	toluene	<5	<5
7	$FeCl_3$	toluene	16	8
8	$InCl_3$	toluene	10	6
9	$ZnCl_2$	toluene	18	<5
10[b]	montmorillonite K10	toluene	22	20
11[c]	Amberlyst 15	toluene	17	13
12	$MnCl_2{\cdot}4H_2O$	toluene	6	90
13	$Mn(OAc)_2$	toluene	20	55
14	$MnBr_2$	toluene	22	40
15	$MnCl_2$	toluene	10	80 (89)[e]
16	$MnCl_2{\cdot}4H_2O$	–	31	41
17[d]	$MnCl_2{\cdot}4H_2O$	CH_3NO_2	40	34
18[d]	$MnCl_2{\cdot}4H_2O$	dioxane	51	30
19	$MnCl_2{\cdot}4H_2O$	DMF	<5	20
20	$MnCl_2{\cdot}4H_2O$	DMSO	<5	15

[a] Solvent: 2.5 mL, **9a**: 1.2 mmol, **2b**: 1.0 mmol.
[b] 20.0 mg solid catalyst were used.
[c] Proton exchange ability is 4.7 mmol g^{-1}.
[d] 100 °C.
[e] Yield in brackets was obtained by adding 0.4 equiv. water.

Table 4. Reaction of **2b** with different β-keto esters catalyzed by $MnCl_2 \cdot 4H_2O$.[a]



Entry	β-Keto ester	Time [h]	Product	Catalyst[d]	Yield (%)
1[b]		**9b**	**10b**	$MnCl_2$	82
				$Sc(OTf)_3$	<5
				TsOH	6
2		**9c**	**10c**	$MnCl_2$	86
				$Sc(OTf)_3$	15
				TsOH	38
3[c]		**9d**	**10d**	$MnCl_2$	87
				$Sc(OTf)_3$	10
				TsOH	16
4		**9e**	**10e**	$MnCl_2$	81
				$Sc(OTf)_3$	8
				TsOH	<5
5		**9f**	**10f**	$MnCl_2$	88
				$Sc(OTf)_3$	<5
				TsOH	<5

[a] Toluene: 2.5 mL, β-keto ester: 1.2 mmol, **2b**: 1.0 mmol.
[b] β-Keto ester/**2b** = 1/3.
[c] Reaction time: 14 h.
[d] The catalyst was used with hydrate.

catalyst (Table 5). The reaction proceeded in a cascade pathway involving (i) electrophilic ring-opening reaction of **11a** with indole, and (ii) transesterification of the generated hydroxy-functionalized diindolylmethane with **9a**. The first step has been investigated by Yadav and his co-workers by using $InCl_3$ as catalyst.[16] However, for the model multicomponent reaction, $InCl_3$ was proved to be ineffective due to extensive formation of many by-products (entry 1). Other acids, such as TsOH, $Sc(OTf)_3$, $Bi(OTf)_3$, Amberlyst-15, montmorillonite K10 and H_3BO_3 were also examined, and no yield >40% was obtained (entries 2 to 7). To our delight, the same reaction over $MnCl_2 \cdot 4H_2O$ catalyst proceeded well and the desired product **12a** was obtained in 82% yield (entry 8). Anhydrous $MnCl_2$ was also examined, and the result is the same as that observed in the first reaction, the yield obtained was slightly inferior (entry 9). Investigation of the substrate scope revealed that many indoles could be used in this reaction, and the corresponding products were obtained in moderate to good yields (entries 10 to 14).

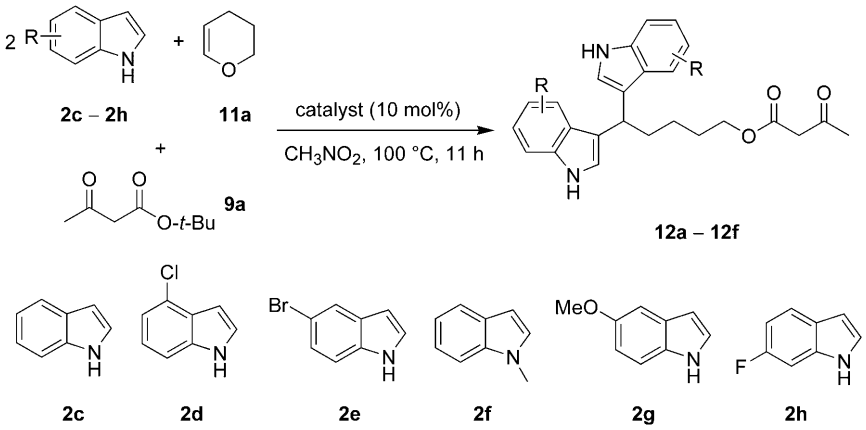
In order to shed light on the reaction mechanism, a ring-opening reaction of **11a** with indole was also examined, and it was found that the reaction proceeded very well in the presence of catalytic amount of $MnCl_2 \cdot 4H_2O$. Importantly, subsequeent treatment of the obtained ring-opening product with **9a** afforded **12a** in an excellent yield (see Supporting Information). These results imply that the reaction might proceed indeed through a cascade ring-opening and transesterification pathway. It should also be noted that this multicomponent reaction has never been reported before. This demonstrated that $MnCl_2 \cdot 4H_2O$ can really be used as an effective catalyst for selective organic synthesis.

Having these promising results in hand, our interest is naturally moved to how to use the product that was obtained with the manganese chloride tetrahydrate catalyst. In the first model reaction, we are able to synthesize a 1,3-dicarbonyl compound with a fragment of a di(indolyl)methane moiety. It is known that 2-(3-arylpropyl)-β-diketones can undergo a radical cyclization to form the skeleton of tetrahydronaphthalene.[17] This type of cyclization reaction has been utilized by us for converting the ring-opening product of 2-aryl-3,4-dihydropyran with indole to a valuable product.[6] Inspired by our previous result, we suspected that this oxidative cyclization reaction should also be effective for converting the **3a**-type product. In order to confirm our hypothesis and to verify both of the usefulness of **3a**-type products and the effectiveness of manganese chloride tetrahydrate as a catalyst, we thus started a three-step synthesis involving: (i) a domino Knoevenagel/oxo-Diels–Alder reaction of butyl vinyl ether (**13a**), acetylacetone (**14a**) and aqueous formaldehyde that generated a dihydropyran **1c** in 87% yield; (ii) $MnCl_2 \cdot 4H_2O$-catalyzed electrophilic ring-opening of **1c** with indole that generated the corresponding product, **3b**, in 98% yield, and (iii) $Mn(OAc)_3$-promoted radical cyclization of **3b** in acetic acid to afford a novel 2,3,4,9-tetrahydro-1*H*-carbazole derivative **15a** in 48% yield. The molecular skeleton of **15a** was known to possess antiangiogenic activity.[18] Although the method of accessing this skeleton is available, it only works for the synthesis of the unsubstituted one,[19] but how to modify the skeleton with substituent groups is still a big challenge. The method in Scheme 4 not only offers an alterative route for the synthesis of this skeleton, but is also capable of modifying the structure, and thus is valuable for organic synthesis.

Conclusions

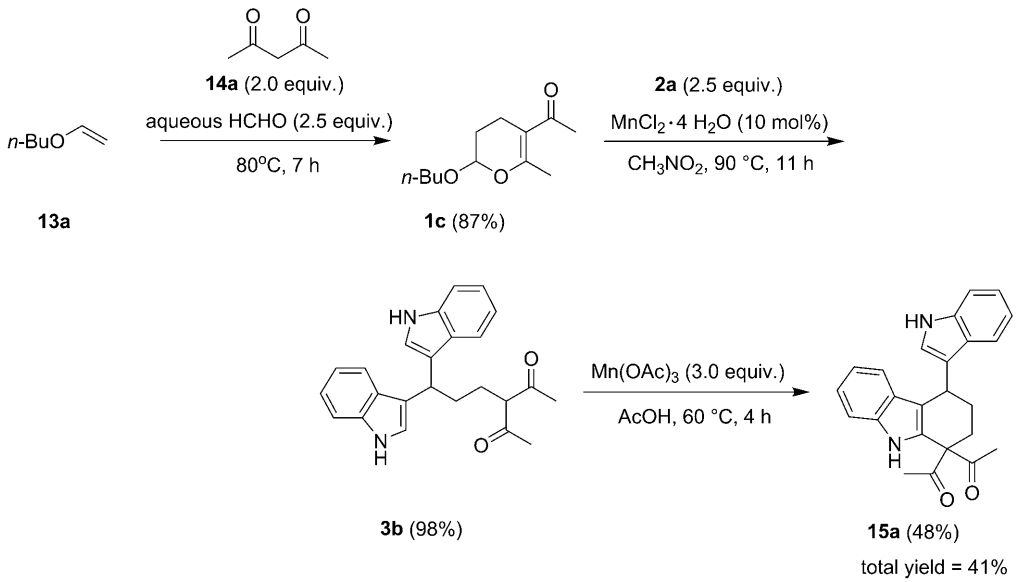
In conclusion, $MnCl_2$ tetrahydrate was proved to be an effective catalyst for selective transformations of indoles in the presence of a keto carbonyl group. Al-

Table 5. Multicomponent reactions of indoles **2c**–**h**, **9a** and **11a**.[a]



Entry	Indole	Catalyst	Product	Yield [%]
1	**2c**	$InCl_3$	**12a**	<5
2	**2c**	$Sc(OTf)_3$	**12a**	<5
3	**2c**	$Bi(OTf)_3$	**12a**	<5
4	**2c**	TsOH	**12a**	<5
5	**2c**	Amberlyst 15	**12a**	32
6	**2c**	montmorillonite K10	**12a**	29
7	**2c**	H_3BO_3	**12a**	38
8	**2c**	$MnCl_2{\cdot}4H_2O$	**12a**	82
9	**2c**	$MnCl_2$	**12a**	74
10	**2d**	$MnCl_2{\cdot}4H_2O$	**12b**	58
11[b]	**2e**	$MnCl_2{\cdot}4H_2O$	**12c**	68
12	**2f**	$MnCl_2{\cdot}4H_2O$	**12d**	73
13	**2g**	$MnCl_2{\cdot}4H_2O$	**12e**	72
14	**2h**	$MnCl_2{\cdot}4H_2O$	**12f**	63

[a] Nitromethane, 1.5 mL, **9a**: 2.0 mmol, indole: 2.5 mmol, **11a**: 1.0 mmol.
[b] Reaction time: 17 h.



Scheme 4. Synthesis of 2,3,4,9-tetrahydro-1*H*-carbazole **15a**.

though the side reaction between the keto carbonyl and C-3 unsubstituted indole is normally catalyzed by acid, some acid-catalyzed reactions, such as the ring-opening reaction of 2-butoxy-3,4-dihydropyran with indole and transesterification of a β-keto ester with an alcohol that contains a C-3 unsubstituted indole fragment, could be performed smoothly by using $MnCl_2 \cdot 4H_2O$ as catalyst. A new multicomponent reaction of indole, 3,4-dihydropyran and **9a** was also developed with catalysis of $MnCl_2 \cdot 4H_2O$. This work also indicated to us that $MnCl_2$ might be able to play a more important role in homogeneous catalysis than we have expected before. In spite of these promising results, the reasons for the obtained high selectivity by using $MnCl_2$ as catalyst are still unknown at this stage, this should be the next topic of our study.

Experimental Section

All the chemicals were used as it was received. 2-butoxy-3,4-dihydropyrans were prepared in water according to our reported method starting from olefins, 1,3-dicarbonyl compounds and formaldehyde aqueous solution.[20] *N*-(2-Hydroxyethyl)indole was prepared in DMSO from indole and 2-chloroethanol according to a literature method.[21] All reactions were conducted in a 10-mL V-type flask equipped with triangle magnetic stirring.

Typical Procedure for Electrophilic Ring-Opening Reaction of Dihydropyran 1a with Indole

In a typical reaction, nitromethane (1.0 mL) was mixed with **1a** (60.5 mg, 0.25 mmol), **2a** (73.0 mg, 0.63 mmol) and $MnCl_2 \cdot 4H_2O$ (5.0 mg, 10 mol%) under air. The mixture was stirred for 11 h at 90 °C. After reaction, the mixture was cooled to room temperature and the desired product, **3a**, was obtained by preparative TLC using a mixed solution of ethyl acetate and petroleum ether as eluting solvent (the ratio of ethyl acetate/petroleum ether is 1/2); yield: 82.2 mg (82%).

Tests for substrate scope and the reactions with other nucleophiles were all performed according to an analogous procedure with above mentioned.

Procedure for Mechanism Study

In a typical reaction, nitromethane (1.0 mL) was mixed with **1b** (152.2 mg, 0.5 mmol) and $MnCl_2 \cdot 4H_2O$ (15.0 mg, 30 mol%) under air. The mixture was stirred for 11 h at 80 °C. After reaction, the mixture was cooled to room temperature and the desired product, **4a**, was obtained by preparative TLC using a mixed solution of ethyl acetate and petroleum ether as eluting solvent (the ratio of ethyl acetate/petroleum ether is 1/4); yield: 69.5 mg (56%).

Then, the obtained **4a** was mixed with nitromethane (1.0 mL), indole (81.9 mg, 0.7 mmol) and $MnCl_2 \cdot 4H_2O$ (18.5 mg, 30 mol%). The mixture was then heated at 80 °C for 11 h. After reaction, the mixture was cooled to room temperature and the desired product, **3h**, was formed in quantitative yield.

Tests for the other catalyst were all performed according to an analogous procedure with above mentioned.

Procedure for Transesterification of 2b

In a typical reaction, toluene (2.5 mL) was mixed with *tert*-butyl acetylacetate (189.6 mg, 1.2 mmol), $MnCl_2 \cdot 4H_2O$ (19.8 mg, 0.1 mmol) and *N*-(2-hydroxyethyl)indole **2b** (161.0 mg, 1.0 mmol) under air. The mixture was stirred for 11 h at 110 °C. After reaction, the mixture was mixed with ethyl acetate (6.0 mL), petroleum ether (6.0 mL) and brine (12 mL). After 15 min of stirring at room temperature, the organic phases were combined together and dried with Na_2SO_4. Then, through preparative TLC, the product **3a** was obtained in 90% yield.

The other reactions were performed as an analogous procedure.

Procedure for Three-Component Reaction of 2c, 9a and 11a

In a typical reaction, nitromethane (1.5 mL) was mixed with **9a** (316.4 mg, 2.0 mmol), **11a** (84.1 mg, 1.0 mmol), **2c** (293.0 mg, 2.5 mmol) and $MnCl_2 \cdot 4H_2O$ (19.8 mg, 0.1 mmol) under air. The mixture was stirred for 10 h at 100 °C. After reaction, the mixture was mixed with ethyl acetate (6.0 mL), petroluem ethers (6.0 mL) and brine (12 mL). After 15 min of stirring at room temperature, the organic phases were combined together and dried with Na_2SO_4. Then, through preparative TLC, the product **5a** was obtained in 82% yield.

The other reactions were performed as an analogous procedure.

Procedure for Synthesis of 15a

The synthesis was started from the preparation of dihydropyran **1c**. In a U-type reaction flask equipped with magnetic stirring, vinyl *n*-butyl ether, **9a** (100.0 mg, 1.0 mmol), was mixed with acetylacetone (**10a**, 200.1 mg, 2.0 mmol) and formaldehyde aqueous solution (37 wt%, 202.8 mg, 2.5 mmol) under air. The mixture was stirred at 80 °C for 7 h. After reaction, the reaction mixture was cooled to room temperature. After addition of brine (5.0 mL), the aqueous phase was extracted with a mixture of ethyl acetate and heptane (v/v = 1/1, 5.0 mL × 3). The obtained organic phases were then combined together and dried with anhydrous Na_2SO_4. After evaporation under reduced pressure, the desired product **1c** was obtained by silica gel column chromatography using a mixed solution of ethyl acetate and petroleum ether as eluting solvent (the ratio of ethyl acetate/petroleum ether is 1/20); yield: 184.6 mg (87%).

The synthesis of **3b** was performed according to the procedure described in the part of ring-opening reaction. Finally, **3b** was obtained in 98% yield (317.3 mg).

Radical cyclization of **3b** was performed in acetic acid using a V-type flask as reactor. Thus, acetic acid (2.5 mL) was added into the flask that contain the obtained **3b** (0.85 mmol), and then, manganese triacetate dihydrate (559.6 mg, 2.1 mmol) was added. The mixture was then stirred at 60 °C for 4 h. After reaction, aqueous Na_2CO_3 solution (2 N, 15 mL) was added and then the mixture was extracted with a mixture of ethyl acetate and heptane (v/v = 1/1, 20 mL × 3). The obtained organic phases were combined

together and dried with anhydrous Na_2SO_4. After evaporation under reduced pressure, **11a** was obtained through a preparative TLC isolation using a mixed solution of ethyl acetate and petroleum ether as eluting solvent (the ratio of ethyl acetate/petroether is 1/5); yield: 151.5 mg (0.41 mmol, 48%).

Characterization Data of Newly Synthesized Products

***Ethyl 2-butoxy-6-methyl-3,4-dihydro-2H-pyran-5-carboxylate* (1a):** Colorless liquid; ^{1}H NMR ($CDCl_3$): δ = 0.91 (t, J = 7.6 Hz, 3H), 1.28 (t, J = 7.2 Hz, 3H), 1.36 (sext, J = 7.6 Hz, 2H), 1.53–1.61 (m, 2H), 1.70–1.80 (m, 1H), 1.81–1.90 (m, 1H), 2.24 (t, J = 1.6 Hz, 3H), 2.26–2.43 (m, 2H), 3.53 (td, J_a = 6.8 Hz, J_b = 9.6 Hz, 1H), 3.80 (td, J_a = 6.4 Hz, J_b = 9.6 Hz, 1H), 4.15 (q, J = 6.8 Hz, 2H), 5.02 (dd, J_a = 2.8 Hz, J_b = 4.0 Hz, 1H); ^{13}C NMR: δ = 13.6, 14.3, 17.7, 19.1, 19.8, 26.0, 31.6, 59.5, 68.3, 97.8, 101.9, 161.4, 168.1; IR: ν = 2929, 2935, 2872, 1706, 1629, 1456, 1378, 1456, 1378, 1337, 1272, 1237, 1192, 1170, 1119, 1075, 1011, 984, 863, 769, 600 cm^{-1}; HR-MS (ESI): m/z = 242.1529, calcd. for $C_{13}H_{22}O_4$ $[M]^+$: 242.1518.

***Ethyl 2-butoxy-6-phenyl-3,4-dihydro-2H-pyran-5-carboxylate* (1b):** Colorless liquid; ^{1}H NMR ($CDCl_3$): δ = 0.91 (q, J = 7.2 Hz, 6H), 1.39 (sext, J = 7.6 Hz, 2H), 1.56–1.64 (m, 2H), 1.81–1.90 (m, 1H), 1.93–2.00 (m, 1H), 2.52 (J_a = 6.0 Hz, J_b = 8.8 Hz, 2H), 3.59 (dt, J_a = 6.4 Hz, J_b = 9.2 Hz, 1H), 3.87–3.95 (m, 3H), 5.18 (dd, J_a = 2.4 Hz, J_b = 3.6 Hz, 1H), 7.32 (s, 5H); ^{13}C NMR: δ = 13.7, 13.9, 18.4, 19.3, 26.0, 31.7, 59.7, 68.5, 98.3, 104.5, 127.6, 128.5, 128.7, 137.2, 159.7, 168.2; IR: ν = 3082, 3026, 2935, 2872, 1692, 1634, 1446, 1371, 1339, 1292, 1246, 1153, 1125, 1057, 952, 761, 697 cm^{-1}; HR-MS (ESI): m/z = 327.1567, calcd. for $C_{18}H_{24}NaO_4$ $[M+Na]^+$: 327.1572.

***1-(2-Butoxy-6-methyl-3,4-dihydro-2H-pyran-5-yl)ethanone* (1c):** Colorless liquid; ^{1}H NMR ($CDCl_3$): δ = 0.90 (t, J = 7.6 Hz, 3H), 1.35 (sext, J = 7.6 Hz, 2H), 1.55 (quint, J = 6.8 Hz, 2H), 1.71–1.84 (m, 1H), 1.85–1.97 (m, 1H), 2.17 (s, 3H), 2.18 (s, 3H), 2.25–2.35 (m, 1H), 2.41–2.52 (m, 1H), 3.53 (td, J_a = 6.4 Hz, J_b = 9.6 Hz, 1H), 3.78 (td, J_a = 6.8 Hz, J_b = 9.6 Hz, 1H), 5.04 (t, J = 3.2 Hz, 1H); ^{13}C NMR: δ = 13.3, 18.5, 18.8, 20.0, 25.8, 28.8, 31.3, 67.8, 97.0, 109.9, 160.3, 197.7; IR: ν = 2959 ,2935, 2872, 1676, 1586, 1454, 1428, 1378, 1355, 1278, 1235, 1218, 1171, 1118, 1063, 1009, 963, 932, 863, 659, 581 cm^{-1}; HR-MS (ESI): m/z = 212.1309, calcd. for $C_{12}H_{20}NaO_3$ $[M+Na]^+$: 212.1310.

***Methyl 2-butoxy-6-methyl-3,4-dihydro-2H-pyran-5-carboxylate* (1d):** Colorless liquid; ^{1}H NMR ($CDCl_3$): δ = 0.91 (t, J = 7.6 Hz, 3H), 1.35 (sext, J = 7.6 Hz, 2H), 1.51–1.60 (m, 2H), 1.69–1.79 (m, 1H), 1.81–1.90 (m, 1H), 2.24 (t, J = 1.6 Hz, 3H), 2.26–2.41 (m, 2H), 3.53 (td, J_a = 6.4 Hz, J_b = 9.6 Hz, 1H), 3.68 (s, 3H), 3.78 (dt, J_a = 6.8 Hz, J_b = 9.6 Hz, 1H), 5.03 (dd, J_a = 2.4 Hz, J_b = 3.6 Hz, 1H); ^{13}C NMR: δ = 13.6, 17.5, 19.1, 19.6, 25.9, 31.5, 50.6, 68.1, 97.7, 101.6, 161.6, 168.3; IR: ν = 2957, 2872, 1710, 1630, 1435, 1380, 1339, 1276, 1119, 1079, 1011, 860, 769 cm^{-1}; HR-MS (ESI): m/z = 251.1243, calcd. for $C_{12}H_{20}NaO_4$ $[M+Na]^+$: 251.1259.

***tert-Butyl 2-butoxy-6-methyl-3,4-dihydro-2H-pyran-5-carboxylate* (1e):** Colorless liquid; ^{1}H NMR ($CDCl_3$): δ = 0.83 (t, J = 7.2 Hz, 3H), 1.28 (sext, J = 8.0 Hz, J = 2H), 1.40 (s, 9H), 1.49 (quint, J = 8.0 Hz, 2H), 1.60–1.70 (m, 1H), 1.71–1.80 (m, 1H), 2.12 (s, 3H), 2.15–2.30 (m, 2H), 3.44 (td, J_a = 6.8 Hz, J_b = 9.6 Hz, 1H), 3.71 (td, J_a = 6.8 Hz, J_b = 9.6 Hz, 1H), 4.91 (dd, J_a = 2.4 Hz, J_b = 4.0 Hz, 1H); ^{13}C NMR: δ = 13.7, 18.1, 19.1, 19.8, 26.2, 28.2, 31.6, 68.3, 79.2, 97.8, 103.4, 160.3, 167.7; IR: ν = 2962, 2934, 2873, 1703, 1630, 1456, 1366, 1339, 1299, 1283, 1247, 1175, 1119, 1076, 1011, 865, 771 cm^{-1}; HR-MS (ESI): m/z = 270.1822, calcd. for $C_{15}H_{26}O_4$ $[M]^+$: 270.1831.

***2-Methoxyethyl 2-butoxy-6-methyl-3,4-dihydro-2H-pyran-5-carboxylate* (1f):** Colorless liquid; ^{1}H NMR ($CDCl_3$): δ = 0.91 (t, J = 7.2 Hz, 3H), 1.35 (sext, J = 7.2 Hz, 2H), 1.56 (quint, J = 6.8 Hz, 2H), 1.69–1.79 (m, 1H), 1.81–1.89 (m, 1H), 2.24 (s, 3H), 2.28–2.39 (m, 2H), 3.37 (s, 3H), 3.52 (td, J_a = 6.8 Hz, J_b = 9.6 Hz, 1H), 3.61 (t, J = 4.8 Hz, 2H), 3.79 (td, J_a = 6.4 Hz, J_b = 9.2 Hz, 1H), 4.23 (dt, J_a = 0.8 Hz, J_b = 4.0 Hz, 2H), 5.03 (dd, J_a = 2.8 Hz, J_b = 3.6 Hz, 1H); ^{13}C NMR: δ = 13.7, 17.7, 19.1, 19.9, 25.9, 31.6, 58.8, 62.7, 68.3, 70.6, 97.9, 101.7, 162.0, 168.0; IR: ν = 2958, 2935, 2874, 2819, 1707, 1628, 1454, 1403, 1379, 1338, 1289, 1272, 1237, 1196, 1119, 1077, 1011, 984, 863, 768, 539, 496 cm^{-1}; HR-MS (ESI): m/z = 295.1525, calcd. for $C_{14}H_{24}NaO_5$ $[M+Na]^+$: 295.1521.

***Ethyl 2-acetyl-5,5-di(1H-indol-3-yl)pentanoate* (3a):** Yellow solid; mp 44–46 °C; ^{1}H NMR ($CDCl_3$): δ = 1.17 (t, J = 6.8 Hz, 3H), 1.84–2.00 (m, 2H), 2.06 (s, 3H), 2.09–2.22 (m, 2H), 3.41 (t, J = 7.2 Hz, 1H), 4.10 (q, J = 6.8 Hz, 2H), 4.43 (t, J = 7.2 Hz, 1H), 6.75 (dd, J_a = 2.0 Hz, J_b = 5.2 Hz, 2H), 6.99 (t, J = 7.2 Hz, 2H), 7.09 (t, J = 7.2 Hz, 2H), 7.18 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.88 (s, 2H); ^{13}C NMR: δ = 14.1, 14.3, 27.1, 28.9, 33.3, 34.0, 60.0, 61.5, 111.4, 119.1, 119.1, 119.3, 119.5, 121.7, 122.0, 126.9, 127.0, 136.7, 170.1, 204.0; IR: ν = 3412, 3118, 3055, 2977, 2932, 2868, 1731, 1707, 1617, 1484, 1455, 1420, 1358, 1339, 1272, 1219, 1150, 1094, 1013, 734, 587 cm^{-1}; HR-MS (ESI): m/z = 425.1822, calcd. for $C_{25}H_{26}N_2O_3$ $[M+Na]^+$: 425.1841.

***3-[3,3-Di(1H-indol-3-yl)propyl]pentane-2,4-dione and (E)-3-(1-hydroxyethylidene)-6,6-di(1H-indol-3-yl)hexan-2-one* (3b):** Yellow solid; mp 76–78 °C; ^{1}H NMR ($CDCl_3$): δ = 1.85 (s, 2H), 1.93 (s, 4H), 1.94–2.10 (m, 2.6H), 2.14–2.24 (m, 1.4H), 3.50 (t, J = 6.8 Hz, 0.7H), 4.37 (t, J = 7.2 Hz, 1H), 6.68 (d, J = 1.4 Hz, 2H), 6.78 (d, J = 1.6 Hz, 0.6H), 6.94–7.03 (m, 2H), 7.06 (t, J = 7.2 Hz, 2H), 7.10–7.19 (m, 2H), 7.49 (d, J = 8.0 Hz, 1.4H), 7.55 (d, J = 8.0 Hz, 0.6H), 7.84 (s, 1.4H), 7.96 (s, 0.6H); ^{13}C NMR: δ = 22.8, 26.5, 27.2, 29.4, 33.4, 34.2, 36.8, 68.6, 110.7, 111.5, 111.6, 119.1, 119.2, 119.2, 119.2, 119.5, 119.6, 121.8, 121.9, 122.0, 122.0, 126.9, 127.0, 136.7, 136.7, 191.5, 205.4; IR: ν = 3411, 2922, 1721, 1693, 1618, 1549, 1513, 1487, 1455, 1419, 1357, 1339, 1275, 1244, 1223, 1125, 1095, 1010, 743, 600, 586, 508 cm^{-1}; HR-MS (ESI): m/z = 395.1722, calcd. for $C_{24}H_{24}N_2NaO_2$ $[M+Na]^+$: 395.1735.

***2-Methoxyethyl 2-acetyl-5,5-di(1H-indol-3-yl)pentanoate* (3c):** Yellow solid; mp 71–73 °C; ^{1}H NMR ($CDCl_3$): δ = 1.80–1.99 (m, 2H), 2.01 (s, 3H), 2.05–2.20 (m, 2H), 3.23 (s, 3H), 3.40 (d, J = 7.6 Hz, 1H), 3.42–3.46 (m, 2H), 4.15–4.21 (m, 2H), 4.40 (t, J = 6.8 Hz, 1H), 6.72 (dd, J_a = 2.0 Hz, J_b = 9.6 Hz, 2H), 6.97 (t, J = 7.2 Hz, 2H), 7.07 (t, J = 7.6 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.50 (d, J = 8.0 Hz, 2H), 7.95 (bs, 2H); ^{13}C NMR: δ = 27.1, 28.9, 33.3, 34.0, 58.9, 59.7, 64.2, 70.2, 111.4, 119.0, 119.1, 119.2, 119.5, 121.7, 122.0, 126.9, 127.0, 136.7, 170.1, 203.9; IR: ν = 3411, 3115, 3055, 2931, 2871, 1735, 1711, 1642, 1618, 1548, 1487, 1456, 1421, 1370, 1357, 1339, 1245, 1222, 1201, 1151, 1126, 1096, 1042, 1030,

1012, 744, 597, 425 cm^{-1}; HR-MS (ESI): m/z = 455.1944, calcd. for $C_{26}H_{28}N_2NaO_4$ $[M+Na]^+$: 455.1947.

***Methyl 2-acetyl-5,5-bis(5-bromo-1H-indol-3-yl)pentanoate* (3d):** Yellow solid; mp 60–62 °C; ^1H NMR ($CDCl_3$): δ = 1.81–1.99 (m, 2H), 2.05–2.13 (m, 2H), 2.14 (s, 3H), 3.49 (t, J = 6.8 Hz, 1H), 3.68 (s, 3H), 4.28 (t, J = 7.2 Hz, 1H), 6.88 (d, J = 12.0 Hz, 2H), 7.10 (d, J = 8.8 Hz, 2H), 7.16 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 4.8 Hz, 2H), 8.23 (bs, 2H); ^{13}C NMR: δ = 26.9, 29.2, 32.7, 33.9, 52.7, 59.5, 112.3, 113.0, 118.1, 118.3, 121.7, 121.8, 123.1, 124.7, 128.4, 128.4, 135.3, 170.5, 203.8; IR: ν = 3421, 3401, 3125, 2938, 2869, 1733, 1713, 1566, 1460, 1374, 1360, 1340, 1274, 1219, 1152, 1100, 1049, 885, 797, 648, 586 cm^{-1}; HR-MS: (ESI): m/z = 566.9867, calcd. for $C_{24}H_{22}Br_2N_2NaO_3$ $[M+Na]^+$: 566.9895.

***tert-Butyl 2-acetyl-5,5-di(1H-indol-3-yl)pentanoate* (3e):** Yellow solid; mp 64–66 °C; ^1H NMR ($CDCl_3$): δ = 1.40 (s, 9H), 1.72–2.00 (m, 2H), 2.06 (s, 3H), 2.09–2.26 (m, 2H), 3.33 (t, J = 7.2 Hz, 1H), 4.42 (t, J = 7.2 Hz, 1H), 6.73 (s, 2H), 6.99 (t, J = 7.2 Hz, 2H), 7.09 (t, J = 6.8 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 8.0 Hz, 2H), 7.86 (bs, 2H); ^{13}C NMR: δ = 27.0, 28.0, 28.9, 33.2, 34.1, 61.1, 82.1, 111.4, 119.0, 119.2, 119.2, 119.5, 121.7, 122.0, 127.0, 136.7, 169.4, 204.4; IR: ν = 3413, 3055, 2976, 2932, 2866, 1729, 1705, 1620, 1549, 1484, 1456, 1420, 1393, 1376, 1339, 1281, 1248, 1142, 1096, 1011, 929, 814, 743, 597 cm^{-1}; HR-MS (ESI): m/z = 453.2137, calcd. for $C_{27}H_{30}N_2NaO_3$ $[M+Na]^+$: 453.2154.

***Methyl 2-acetyl-5,5-di(1H-indol-3-yl)pentanoate* (3f):** Yellow solid; mp 98–100 °C; ^1H NMR ($CDCl_3$): δ = 1.80–1.95 (m, 2H), 1.98 (s, 3H), 2.02–2.16 (m, 2H), 3.39 (t, J = 7.2 Hz, 1H), 3.55 (s, 3H), 4.39 (t, J = 7.2 Hz, 1H), 6.66 (dd, J_a = 2.0 Hz, J_b = 9.2 Hz, 2H), 6.96 (t, J = 7.6 Hz, 2H), 7.05 (t, J = 7.2 Hz, 2H), 7.10 (d, J = 8.0 Hz, 2H), 7.50 (dd, J_a = 2.4 Hz, J_b = 7.6 Hz, 2H), 7.84 (s, 2H); ^{13}C NMR: δ = 27.2, 29.1, 33.3, 34.1, 52.6, 59.7, 111.6, 119.0, 119.1, 119.2, 119.5, 121.8, 122.1, 126.9, 127.0, 136.7, 170.7, 204.3; IR: ν = 3410, 3055, 3008, 2953, 2929, 2864, 1735, 1708, 1618, 1487, 1455, 1430, 1357, 1340. 1278, 1243, 1220, 1151, 1095, 1011, 744, 585 cm^{-1}; HR-MS (ESI): m/z = 411.1661, calcd. for $C_{24}H_{24}N_2NaO_3$ $[M+Na]^+$: 411.1685.

***Methyl 2-acetyl-5,5-bis(5-methoxy-1H-indol-3-yl)pentanoate* (3g):** Red liquid; ^1H NMR($CDCl_3$): δ = 1.87–2.01 (m, 2H), 2.07 (d, J = 2.4 Hz, 3H), 2.10–2.22 (m, 2H), 3.46 (q, J = 6.4 Hz, 1H), 3.62 (d, J = 1.6 Hz, 3H), 3.74 (d, J = 2.8 Hz, 6H), 4.35 (q, J = 6.4 Hz, 1H), 6.74–6.79 (m, 2H), 6.79–6.84 (m, 2H), 6.99–7.05 (m, 2H), 7.08 (d, J = 8.8 Hz, 2H), 8.04 (bs, 1H), 8.09 (bs, 1H); ^{13}C NMR ($CDCl_3$): δ = 27.1, 28.9, 33.0, 34.1, 52.5, 56.0, 59.6, 101.7, 101.7, 111.6, 111.7, 112.1, 118.7, 118.8, 122.8, 122.8, 127.3, 132.0, 153.6, 170.6, 203.9, 204.0; HR-MS (ESI): m/z = 471.1892, calcd. for $C_{26}H_{28}N_2NaO_5$ $[M+Na]^+$: 471.1896.

***Ethyl 2-benzoyl-5,5-di(1H-indol-3-yl)pentanoate* (3h):** Yellow solid; mp 74–76 °C; ^1H NMR ($CDCl_3$): δ = 1.05 (t, J = 7.2 Hz, 3H), 2.05–2.18 (m, 2H), 2.18–2.29 (m, 2H), 4.05 (q, J = 7.2 Hz, 2H), 4.31 (t, J = 6.8 Hz, 1H), 4.46 (t, J = 7.2 Hz, 1H), 6.71 (d, J = 2,0 Hz, 2H), 6.97 (q, J = 7.2 Hz, 2H), 7.06 (t, J = 7.2 Hz, 2H), 7.15 (d, J = 8.0 Hz, 2H), 7.29 (t, J = 7.6 Hz, 2H), 7.44 (t, J = 7.2 Hz, 1H), 7.51 (t, J = 8.4 Hz, 2H), 7.81 (d, J = 7.6 Hz, 2H), 7.86 (s, 2H); ^{13}C NMR: δ = 14.1, 28.0, 33.4, 34.0, 54.4, 61.6, 111.5, 119.1, 119.3, 119.5, 119.5, 121.8, 122.2, 127.0, 127.0, 128.7, 128.8, 133.7, 136.2, 136.7, 136.7, 170.4, 196.0; IR: ν = 3408, 3055, 2977, 2962, 2932, 2863, 1728, 1678, 1595, 1453, 1453, 1420, 1340, 1279, 1224, 1187, 1154, 1094, 1012, 743, 691, 588, 489, 420 cm^{-1}; HR-MS (ESI): m/z = 487.2000, calcd. for $C_{30}H_{28}N_2NaO_3$ $[M+Na]^+$: 487.1998.

***Methyl 2-acetyl-5,5-bis(6-fluoro-1H-indol-3-yl)pentanoate* (3i):** Yellow solid; mp 80–82 °C; ^1H NMR ($CDCl_3$): δ = 1.86–2.23 (m, 2H), 2.08–2.20 (m, 5H), 3.49 (t, J = 7.2 Hz, 1H), 3.66 (s, 3H), 4.36 (t, J = 7.6 Hz, 1H), 6.75 (dt, J_a = 0.8 Hz, J_b = 9.6 Hz, 2H), 6.86 (d, J = 2.0 Hz, 1H), 6.88 (d, J = 2.0 Hz, 1H), 6.90 (d, J = 2.0 Hz, 1H), 6.93 (d, J = 2.4 Hz, 1H), 7.35–7.41 (m, 2H), 8.17 (bs, 2H); ^{13}C NMR: ^{13}C NMR: δ = 27.0, 29.1, 33.0, 34.0, 52.6, 59.6, 97.5, 97.7, 107.7, 107.9, 119.0, 119.1, 120.0, 120.1, 122.0, 122.1, 123.4, 123.4, 136.5, 136.6, 158.6, 161.0, 170.5, 204.1; IR: 3417, 3126, 3068, 2954, 2934, 2865, 1733, 1711, 1625, 1550, 1497, 1455, 1343, 1303, 1251, 1216, 1140, 1121, 1092, 1045, 951, 837, 805, 606, 478 cm^{-1}; HR-MS (ESI): m/z = 447.1512, calcd. for $C_{24}H_{22}F_2N_2NaO_3$ $[M+Na]^+$: 447.1496.

***Methyl 2-acetyl-5,5-bis(1-methyl-1H-indol-3-yl)pentanoate* (3j):** Red liquid; ^1H NMR ($CDCl_3$): δ = 1.86–2.06 (m, 2H), 2.08 (t, J = 1.6 Hz, 3H), 2.12–2.30 (m, 2H), 3.40–3.48 (m, 1H), 3.60 (s, 3H), 3.61 (s, 3H), 3.64 (t, J = 1.6 Hz, 3H), 4.43–4.53 (m, 1H), 6.83 (td, J_a = 1.6 Hz, J_b = 7.6 Hz, 2H), 6.98–7.08 (m, 2H), 7.12–7.19 (m, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.58 (q, J = 2.8 Hz, 2H); ^{13}C NMR: δ = 27.3, 29.0, 32.8, 33.8, 34.0, 52.5, 59.8, 109.4, 118.1, 118.3, 118.7, 119.7, 121.5, 126.5, 127.4, 127.5, 137.4, 170.5, 203.5; IR: ν = 3051, 2948, 2877, 2824, 1739, 1714, 1613, 1547, 1483, 1471, 1425, 1371, 1358, 1328, 1242, 1208, 1153, 1077, 1012, 986, 909, 738, 800, 738, 647, 630, 585, 557, 512 cm^{-1}; HR-MS (ESI): m/z = 439.1975, calcd. for $C_{26}H_{28}N_2NaO_3$ $[M+Na]^+$: 439.1998.

***Ethyl β-oxo-α-(3-oxopropyl)benzenepropanoate* (4a):** Colorless liquid; ^1H NMR ($CDCl_3$): δ = 1.06 (t, J = 7.2 Hz, 3H), 2.12–2.28 (m, 2H), 2.45–2.62 (m, 2H), 4.04 (dq, J_a = 1.2 Hz, J_b = 7.2 Hz, 2H), 4.35 (t, J = 7.2 Hz, 1H), 7.39 (t, J = 7.6 Hz, 2H), 7.50 (t, J = 7.6 Hz, 1H), 7.20 (dd, J_a = 1.2 Hz, J_b = 7.2 Hz, 2H), 9.67 (s, 1H); ^{13}C NMR: δ = 13.9, 21.2, 41.1, 52.6, 61.5, 128.6, 128.8, 133.7, 135.8, 169.6, 194.9, 201.3; IR: ν = 3063, 2981, 2938, 2872, 2831, 2728, 1731, 1685, 1594, 1447, 1369, 1247, 1192, 1164, 1096, 1074, 1024, 1004, 910, 851, 781, 736, 692, 597, 518, 495 cm^{-1}.

***5-Oxo-5-phenylpentanal* (4b):** Colorless liquid; ^1H NMR ($CDCl_3$): δ = 2.08 (t, J = 7.2 Hz, 2H), 2.60 (dt, J_a = 1.2 Hz, J_b = 6.8 Hz, 2H), 3.06 (t, J = 6.8 Hz, 2H), 7.46 (t, J = 8.0 Hz, 2H), 7.56 (tt, J_a = 2.0 Hz, J_b = 7.2 Hz, 1H), 7.95 (dd, J_a = 1.6 Hz, J_b = 8.8 Hz, 2H); ^{13}C NMR: δ = 16.5, 37.3, 43.1, 128.0, 128.7, 133.2, 136.7, 199.4, 202.0; IR: ν = 3058, 2963, 2940, 2725, 1726, 1689, 1595, 1448, 1410, 1372, 1292, 1257, 1231, 1197, 1182, 1098, 1072, 1054, 1029, 999, 938, 917, 735, 691, 567 cm^{-1}.

***5-n-Butyl 1-ethyl 2-benzoylpentanedioate* (4c):** Colorless liquid; ^1H NMR ($CDCl_3$): δ = 0.92 (t, J = 7.2 Hz, 3H), 1.18 (t, J = 7.2 Hz, 3H), 1.35 (sext, J = 7.6 Hz, 2H), 1.59 (quint, J = 7.2 Hz, 2H), 2.30 (dq, J_a = 2.0 Hz, J_b = 6.4 Hz, 2H), 2.45 (dt, J_a = 3.2 Hz, J_b = 6.4 Hz, 2H), 4.08 (t, J = 6.8 Hz, 2H), 4.14 (dt, J_a = 1.2 Hz, J_b = 7.2 Hz, 2H), 4.50 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.60 (tt, J_a = 1.2 Hz, J_b = 7.6 Hz, 1H), 8.03 (dd, J_a = 1.2 Hz, J_b = 8.4 Hz, 2H); ^{13}C NMR: δ = 13.7, 14.0, 19.1, 24.0, 30.6, 31.5, 52.8, 61.5, 64.5, 128.7, 128.8, 133.6, 136.0, 169.6, 172.9, 195.0; IR: ν = 3063, 2961, 2935, 2873, 1734, 1686, 1638, 1594, 1449, 1370, 1251, 1184, 1156, 1069, 1025, 980, 876, 854, 781, 740, 693, 597 cm^{-1}; HR-MS (ESI): m/z = 320.1629, calcd. for $C_{18}H_{24}O_5$ $[M]^+$: 320.1624.

***Methyl 2-acetyl-5,5-bis(5-methylfuran-2-yl)pentanoate* (6a):** Colorless liquid; ^{1}H NMR ($CDCl_3$): δ = 1.70–1.95 (m, 4H), 2.13 (s, 3H), 2.18 (s, 6H), 3.36 (t, J = 7.2 Hz, 1H), 3.66 (s, 3H), 3.88 (t, J = 7.2 Hz, 1H), 5.80 (s, 2H), 5.87 (d, J = 2.8 Hz, 2H); ^{13}C NMR: δ = 13.5, 26.0, 28.7, 30.5, 38.7, 52.3, 59.3, 106.0, 106.5, 150.8, 153.0, 170.0, 202.8; IR: ν = 3105, 2952, 2923, 2872, 1743, 1716, 1613, 1564, 1450, 1436, 1358, 1245, 1217, 1148, 1021, 949, 783 cm^{-1}; HR-MS (ESI): m/z = 341.1357, calcd. for $C_{18}H_{22}NaO_5$ $[M]^+$: 341.1365.

***Ethyl 2-acetyl-4-(1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)butanoate* (8a):** Yellow liquid; ^{1}H NMR ($CDCl_3$): δ = 1.27 (t, J = 7.2 Hz, 3H), 1.64–1.75 (m, 2H), 1.77–2.02 (m, 6H), 2.21 (s, 3H), 2.25–2.37 (m, 4H), 2.45–2.56 (m, 4H), 3.36 (t, J = 7.2 Hz, 1H), 3.87 (t, J = 8.0 Hz, 1H), 4.19 (q, J = 7.2 Hz, 2H); ^{13}C NMR: δ = 14.1, 19.9, 27.0, 27.2, 28.9, 29.9, 32.8, 33.5, 59.5, 61.5, 117.1, 117.2, 169.6, 191.1, 192.0, 203.0; IR: ν = 3071, 2957, 2873, 1722, 1650, 1610, 1460, 1426, 1401, 1371, 1328, 1275, 1221, 1183, 1136, 1075, 1017, 955, 914, 863, 826, 759, 744, 607, 523, 502 cm^{-1}; HR-MS (ESI): m/z = 374.1723, calcd. for $C_{21}H_{26}O_6$ $[M]^+$: 374.1729.

***2-(1H-1-Indolyl)ethyl acetoacetate* (10a):** Brown liquid; ^{1}H NMR ($CDCl_3$): δ = 2.05 (s, 3H), 3.29 (s, 2H), 4.30 (t, J = 5.2 Hz, 2H), 4.38 (t, J = 4.8 Hz, 2H), 6.48 (dd, J_a = 0.8 Hz, J_b = 3.2 Hz, 1H), 7.05 (d, J = 4.8 Hz, 1H), 7.09 (dt, J_a = 1.2 Hz, J_b = 8.0 Hz, 1H), 7.19 (dt, J_a = 0.8 Hz, J_b = 6.8 Hz, 1H), 7.29 (dd, J_a = 0.4 Hz, J_b = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 30.2, 44.8, 49.7, 63.9, 102.0, 109.2, 119.7, 121.2, 121.9, 128.1, 128.7, 136.1, 166.8, 200.4; IR: ν = 3102, 3054, 2957, 1745, 1716, 1656, 1614, 1513, 1464, 1444, 1403, 1362, 1334, 1315, 1262, 1249, 1203, 1174, 1150, 1051, 1012, 764, 745, 694, 596, 541, 428 cm^{-1}; HR-MS (ESI): m/z = 268.0938, calcd. for $C_{14}H_{15}NNaO_3$ $[M+Na]^+$: 268.0950.

***2-(1H-1-Indolyl)ethyl isobutyrylacetate* (10b):** Brown liquid; ^{1}H NMR ($CDCl_3$): δ = 1.03 (s, 3H), 1.04 (s, 3H), 2.53 (sept, 6.8 Hz, 1H), 3.37 (s, 2H), 4.30 (t, J = 7.6 Hz, 2H), 4.39 (dt, J_a = 0.8 Hz, J_b = 6.0 Hz, 2H), 6.48 (J_a = 0.4 Hz, J_b = 3.2 Hz, 1H), 7.06 (d, J = 3.2 Hz, 1H), 7.08 (dt, J_a = 0.8 Hz, J_b = 8.0 Hz, 1H), 7.19 (dt, J_a = 1.2 Hz, J_b = 7.2 Hz, 1H), 7.30 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 17.9, 41.3, 44.9, 46.7, 63.8, 101.9, 109.2, 119.7, 121.1, 121.8, 128.1, 128.7, 136.1, 167.2, 206.4; IR: ν = 3103, 3055, 2972, 2935, 2876, 1748, 1712, 1651, 1618, 1514, 1464, 1363, 1335, 1315, 1102, 1083, 1046, 1011, 969, 764, 744, 720, 695, 421 cm^{-1}; HR-MS (ESI): m/z = 296.1250, calcd. for $C_{16}H_{19}NNaO_3$ $[M+Na]^+$: 296.1263.

***2-(1H-1-Indolyl)ethyl pivaloylacetate* (10c):** Brown liquid; ^{1}H NMR ($CDCl_3$): δ = 1.09 (s, 7.3H), 1.13 (s, 1.7H), 3.43 (s, 2H), 4.31 (t, J = 5.2 Hz, 2H), 4.39 (t, J = 5.6 Hz, 2H), 6.47 (d, J = 3.2 Hz, 1H), 7.07 (d, J = 2.8 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.18 (t, J = 8.4 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 26.0, 43.7, 44.8, 44.9, 63.7, 101.9, 109.3, 119.6, 121.1, 121.8, 128.2, 128.7, 136.1, 167.6, 208.0; IR: ν = 3102, 3055, 2969, 2937, 2909, 2872, 1748, 1706, 1646, 1614, 1513, 1479, 1464, 1400, 1366, 1334, 1316, 1269, 1240, 1203, 1146, 1101, 1082, 1065, 1049, 1009, 932, 909, 765, 743, 720, 566, 553, 424 cm^{-1}; HR-MS (ESI): m/z = 310.1406, calcd. for $C_{17}H_{21}NNaO_3$ $[M+Na]^+$: 310.1419.

***2-(1H-1-Indolyl)ethyl butyroacetate* (10d):** Brown liquid; ^{1}H NMR ($CDCl_3$): δ = 0.79 (t, J = 7.6 Hz, 3H), 1.44 (sext, J = 7.6 Hz, 2H), 2.17 (t, J = 7.2 Hz, 2H), 3.16 (s, 2H), 4.14 (t, J = 5.6 Hz, 2H), 4.25 (t, J = 5.2 Hz, 2H), 6.43 (d, J = 3.2 Hz, 1H), 6.97 (d, J = 3.2 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 7.14 (t, J = 7.2 Hz, 1H), 7.21 (d, J = 4.4 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 13.6, 17.0, 44.8, 48.8, 63.8, 101.9, 109.4, 119.7, 121.2, 121.8, 128.3, 128.8, 136.2, 167.1, 202.8; IR: ν = 3103, 3030, 2964, 2953, 2876, 1747, 1714, 1649, 1618, 1513, 1463, 1403, 1364, 1334, 1316, 1260, 1226, 1205, 1154, 1126, 1073, 1047,764, 743, 720, 583, 570, 423 cm^{-1}; HR-MS (ESI): m/z = 296.1247, calcd. for $C_{16}H_{19}NNaO_3$ $[M+Na]^+$: 296.1263.

***2-(1H-1-Indolyl)ethyl 2-benzoylacetate* (10e):** Brown liquid; ^{1}H NMR ($CDCl_3$): δ = 3.83 (s, 2H), 4.26 (t, J = 5.2 Hz, 2H), 4.38 (t, J = 5.6 Hz, 2H), 6.44 (q, J = 1.2 Hz, 1H), 6.99 (d, J = 3.2 Hz, 1H), 7.08 (dt, J_a = 1.2 Hz, J_b = 6.8 Hz, 1H), 7.16 (t, J = 8.0 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 7.31–7.42 (m, 2H), 7.51 (t, J = 6.8 Hz, 1H), 7.59 (d, J = 8.0 Hz, 1H), 7.77 (dd, J_a = 1.6 Hz, J_b = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 44.9, 45.6, 64.0, 102.0, 109.3, 119.7, 121.2, 121.8, 128.2, 128.6, 128.9, 134.0, 135.8, 136.1, 167.4, 192.4; IR: ν = 3056, 2954, 1745, 1685, 1617, 1600, 1462, 1451, 1411, 1362, 1333, 1316, 1266, 1208, 1188, 1146, 1102, 1082, 1048, 1012, 1001, 744, 723, 689, 427 cm^{-1}; HR-MS (ESI): m/z = 330.1095, calcd. for $C_{19}H_{17}NNaO_3$ $[M+Na]^+$: 330.1106.

***2-(1H-1-Indolyl)ethyl 2-(4-methoxybenzoyl)acetate* (10f):** Brown liquid; ^{1}H NMR ($CDCl_3$): δ = 3.79 (s, 3H), 3.81 (s, 2H), 4.30 (t, J = 5.6 Hz, 2H), 4.40 (t, J = 5.6 Hz, 2H), 6.44 (d, J = 2.8 Hz, 1H), 6.83 (td, J_a = 2.0 Hz, J_b = 9.2 Hz, 2H), 7.02 (d, J = 3.2 Hz, 1H), 7.09 (t, J = 8.0 Hz, 1H), 7.17 (t, J = 8.4 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.75 (td, J_a = 2.0 Hz, J_b = 8.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 44.9, 45.4, 55.6, 63.9, 101.9, 109.2, 114.1, 119.7, 121.1, 121.8, 128.2, 128.7, 128.9, 130.9, 136.1, 164.1, 167.6, 190.8; IR: ν = 3102, 3055, 3009, 2958, 2937, 2841, 1744, 1676, 1601, 1577, 1512, 1463, 1421, 1362, 1318, 1263, 1217, 1174, 1148, 1117, 1083, 1026, 994, 838, 810, 765, 745, 639, 609, 569, 445, 425 cm^{-1}; HR-MS (ESI): m/z = 360.1206, calcd. for $C_{20}H_{19}NNaO_4$ $[M+Na]^+$: 360.1212.

***ε-(1H-Indol-3-yl)-1H-indole-3-pentyl acetoacetate* (12a):** Brown liquid; ^{1}H NMR ($CDCl_3$): δ = 1.34–1.43 (m, 2H), 1.63 (quint, J = 6.8 Hz, 2H), 2.09 (s, 3H), 2.16 (dd, J_a = 7.6 Hz, J_b = 15.6 Hz, 2H), 3.30 (s, 2H), 4.03 (t, J = 6.8 Hz, 2H), 4.40 (t, J = 7.6 Hz, 1H), 6.79 (d, J = 2.4 Hz, 2H), 7.00 (dt, J_a = 0.8 Hz, J_b = 7.6 Hz, 2H), 7.10 (dt, J_a = 0.8 Hz, J_b = 7.6 Hz, 2H), 7.20 (d, J = 8.4 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.88 (s, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.4, 28.4, 30.1, 33.8, 35.2, 49.9, 65.4, 111.2, 118.9, 119.4, 119.8, 121.6, 121.6, 126.9, 136.5, 167.3, 201.2; IR: ν = 3417, 3056, 2934, 1713, 1618, 1454, 1421, 1338, 1294, 1244, 1221, 1151, 1125, 1094, 1046, 930, 909, 739, 596, 585, 420 cm^{-1}; HR-MS (ESI): m/z = 425.1827, calcd. for $C_{25}H_{26}N_2NaO_3$ $[M+Na]^+$: 425.1841.

***ε-[1H-(4-Chloro)indol-3-yl]-1H-(4-chloro)indole-3-pentyl acetoacetate* (12b):** Brown liquid; ^{1}H NMR ($CDCl_3$): δ = 1.50–1.60 (m, 2H), 1.66 (quint, J = 6.8 Hz, 2H), 1.99 (q, J = 7.6 Hz, 2H), 2.15 (s, 3H), 3.37 (s, 2H), 4.08 (t, J = 6.4 Hz, 2H), 5.64 (t, 6.4 Hz, 1H), 6.58 (d, J = 2.4 Hz, 2H), 6.97 (dd, J_a = 5.6 Hz, J_b = 7.6 Hz, 4H), 7.10 (dd, J_a = 2.6 Hz, J_b = 6.8 Hz, 2H), 8.21 (d, J = 2.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.3, 28.4, 30.2, 33.3, 37.8, 50.0, 65.5, 110.0, 120.3, 121.1, 122.1, 123.1, 123.6, 126.3, 138.1, 167.4, 201.6; IR: ν = 3420, 3176, 3127, 3065, 2939, 2865, 1740, 1715, 1618, 1558, 1477, 1427, 1362, 1338, 1188, 1149, 1040, 982, 938, 911, 819, 779,

746, 555, 547, 492, 475, 411 cm^{-1}; HR-MS (ESI): m/z = 493.1053, calcd. for $C_{25}H_{24}Cl_2N_2NaO_3$ $[M+Na]^+$: 493.1062.

ε-[1H-(5-Bromo)indol-3-yl]-1H-(5-bromo)indole-3-pentyl acetoacetate **(12c):** Brown liquid; ^1H NMR ($CDCl_3$): δ = 1.27–1.38 (m, 2H), 1.60 (quint, J = 6.8 Hz, 2H), 2.04–2.12 (m, 2H), 2.15 (s, 3H), 3.38 (s, 2H), 4.03 (t, J = 6.8 Hz, 2H), 4.22 (t, J = 7.6 Hz, 1H), 6.88 (d, J = 2.0 Hz, 2H), 7.10 (d, J = 8.4 Hz, 2H), 7.16 (dd, J_a = 1.6 Hz, J_b = 8.4 Hz, 2H), 7.61 (d, J = 1.6 Hz, 2H), 8.20 (d, J = 2.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.3, 28.2, 30.2, 33.8, 34.6, 50.0, 65.4, 112.2, 112.8, 118.9, 121.8, 122.9, 124.5, 128.5, 135.2, 167.3, 201.4; IR: ν = 3418, 3123, 3075, 2936, 2862, 1732, 1716, 1642, 1622, 1566, 1455, 1415, 1359, 1317, 1277, 1268, 1175, 1151, 1097, 1037, 883, 866, 795, 766, 755, 584, 421 cm^{-1}; HR-MS (ESI): m/z = 581.0025, calcd. for $C_{25}H_{24}Br_2N_2NaO_3$ $[M+Na]^+$: 581.0051.

ε-[1H-(1-Methyl)indol-3-yl]-1H-(1-methyl)indole-3-pentyl acetoacetate **(12d):** Brown liquid; ^1H NMR ($CDCl_3$): δ = 1.38–1.50 (m, 2H), 1.68 (quint, J = 6.8 Hz, 2H), 2.11 (s, 3H), 2.20 (dd, Ja = 7.6 Hz, Jb = 15.6 Hz, 2H), 3.29 (s, 2H), 3.63 (s, 6H), 4.07 (t, J = 6.8 Hz, 2H), 4.44 (t, J = 7.6 Hz, 1H), 6.82 (s, 2H), 7.01 (dt, J_a = 0.8 Hz, J_b = 8.0 Hz, 2H), 7.15 (dt, J_a = 0.8 Hz, J_b = 8.0 Hz, 2H), 7.22 (d, J = 8.0 Hz, 2H), 7.58 (d, J = 8.0 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.7, 28.7, 30.2, 32.7, 33.9, 36.0, 50.1, 65.5, 109.3, 118.6, 118.9, 119.7, 121.4, 126.3, 127.6, 137.4, 167.3, 200.9; IR: ν = 3054, 3026, 2935, 2865, 2825, 1740, 1716, 1622, 1548, 1471, 1421, 1372, 1327, 1242, 1151, 1098, 1039, 1013, 972, 911, 945, 798, 737, 549, 539, 418, 410 cm^{-1}; HR-MS (ESI): m/z = 453.2159, calcd. for $C_{27}H_{30}N_2NaO_3$ $[M+Na]^+$: 453.2154.

ε-[1H-(5-Methoxy)indol-3-yl]-1H-(5-methoxy)indole-3-pentyl acetoacetate **(12e):** Brown liquid; ^1H NMR ($CDCl_3$): δ = 1.36–1.47 (m, 2H), 1.61–1.71 (m, 2H), 2.13 (s, 3H), 2.14–2.20 (m, 2H), 3.33 (s, 2H), 3.74 (s, 6H), 4.06 (t, J = 6.8 Hz, 2H), 4.32 (t, J = 7.6 Hz, 1H), 6.77 (dd, J_a = 2.4 Hz, J_b = 8.4 Hz, 2H), 6.87 (d, J = 2.0 Hz, 2H), 7.01 (d, J = 2.4 Hz, 2H), 7.13 (d, J = 8.8 Hz, 2H), 8.04 (s, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.4, 28.4, 30.1, 33.8, 34.9, 50.0, 55.9, 65.4, 101.8, 111.3, 111.8, 119.4, 122.5, 127.4, 131.8, 153.4, 167.3, 201.2; IR: ν = 3417, 2937, 2860, 2831, 1736, 1716, 1622, 1585, 1477, 1452, 1415, 1359, 1210, 1171, 1104, 1038, 921, 835, 799, 773, 750, 733, 628, 543, 415 cm^{-1}; HR-MS (ESI): m/z = 485.2043, calcd. for $C_{27}H_{30}N_2NaO_5$ $[M+Na]^+$: 485.2052.

ε-[1H-(6-Fluoro)indol-3-yl]-1H-(6-fluoro)indole-3-pentyl acetoacetate **(12f):** Brown liquid; ^1H NMR ($CDCl_3$): δ = 1.32–1.43 (m, 2H), 1.58–1.70 (m, 2H), 2.08–2.18 (m, 5H), 3.36 (s, 2H), 4.05 (t, J = 6.8 Hz, 2H), 4.32 (t, J = 7.6 Hz, 1H), 6.74 (dt, J_a = 2.4 Hz, J_b = 9.6 Hz, 2H), 6.88 (d, J = 2.4 Hz, 2H), 6.92 (dd, J_a = 2.4 Hz, J_b = 9.6 Hz, 2H), 7.38 (dd, J_a = 5.2 Hz, J_b = 8.8 Hz, 2H), 8.12 (d, J = 1.6 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 24.3, 28.4, 30.1, 33.8, 34.9, 50.0, 65.4, 97.3, 97.6, 107.5, 107.8, 119.7, 120.0, 120.1, 121.7, 121.8, 123.5, 136.4, 136.5, 158.6, 160.9, 167.3, 201.4; IR: ν = 3417, 3217, 3125, 3066, 2938, 2862, 1735, 1715, 1622, 1552, 1495, 1454, 1410, 1140, 1092, 1036, 952, 910, 837, 801, 732, 605, 486, 477, 420 cm^{-1}; HR-MS (ESI): m/z = 461.1658, calcd. for $C_{25}H_{24}F_2N_2NaO_3$ $[M+Na]^+$: 461.1653.

1,1′-(4-(1H-indol-3-yl)-2,3,4,9-tetrahydro-1H-carbazole-1,1-diyl)diethanone **(15a):** Yellow solid, mp 100–102 °C; ^1H NMR ($CDCl_3$): δ = 2.19–2.25 (m, 2H), 2.27 (s, 3H), 2.29 (s, 3H), 2.34–2.44 (m, 1H), 2.47–2.55 (m, 1H), 4.66 (t, J = 4.8 Hz, 1H), 6.51 (d, J = 2.0 Hz, 1H), 6.93 (t, J = 7.6 Hz, 1H), 7.19 (sept, J = 6.4 Hz, 4H), 7.38 (d, J = 8.4 Hz,1H), 7.41 (d, J = 8.0 Hz, 1H), 7.68 (d, J = 7.6 Hz, 1H), 7.87 (bs, 1H), 8.95 (bs, 1H); ^{13}C NMR: δ = 27.6, 27.9, 28.4, 28.6, 29.3, 67.9, 111.2, 111.3, 115.4, 118.9, 119.2, 119.4, 119.4, 119.9, 122.0, 122.5, 123.0, 126.5, 126.6, 130.1, 136.6, 136.7, 206.4, 207.3;IR: ν = 3416, 3053, 2936, 2856, 1715, 1688, 1617, 1489, 1456, 1419, 1356, 1291, 1223, 1179, 1142, 1090, 1010, 973, 750. 694, 592 cm^{-1}; HR-MS (ESI): m/z = 393.1588, calcd. for $C_{24}H_{22}N_2NaO_2$ $[M+Na]^+$: 393.1579.

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