catalysts

MDPI

Article

Synthesis of Polysubstituted 1,2-Dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones through Domino Palladium-Catalyzed Reactions of Indol-2-ylmethyl Acetates with 1,3-Dicarbonyl Derivatives

Antonia Iazzetti [1], Antonio Arcadi [2], Stefano Dessalvi [3], Giancarlo Fabrizi [3], Antonella Goggiamani [3,*], Federico Marrone [3], Andrea Serraiocco [3], Alessio Sferrazza [3,*] and Karim Ullah [3]

1 Department of Basic Biotechnological Sciences, Intensivological and Perioperative Clinics, Catholic University of Sacred Heart, L.go F. Vito 1, 00168 Rome, Italy
2 Dipartimento di Ingegneria e Scienze dell'Informazione e Matematica, Università degli Studi di L'Aquila, Via Vetoio, 67100 L'Aquila, Italy
3 Department of Chemistry and Technologies of Drug, Sapienza, University of Rome, P.le A. Moro 5, 00185 Rome, Italy
* Correspondence: antonella.goggiamani@uniroma1.it (A.G.); a.sferrazza@irbm.com (A.S.)

Abstract: A straightforward assembly of polysubstituted 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones through a domino palladium-catalyzed reaction of indol-2-ylmethyl acetates with 1,3-dicarbonyl derivatives is described. The key role of the features of the 1,3-dicarbonyls on the reaction outcome has been explored. The employment of 2-methylcyclohexan-1,3-dione as the dicarbonyl source could allow further challenging indole nucleus functionalizations.

Keywords: 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones; indolyl methides; palladium catalysis; domino reactions

Citation: Iazzetti, A.; Arcadi, A.; Dessalvi, S.; Fabrizi, G.; Goggiamani, A.; Marrone, F.; Serraiocco, A.; Sferrazza, A.; Ullah, K. Synthesis of Polysubstituted 1,2-Dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones through Domino Palladium-Catalyzed Reactions of Indol-2-ylmethyl Acetates with 1,3-Dicarbonyl Derivatives. *Catalysts* **2022**, *12*, 1516. https://doi.org/10.3390/catal12121516

Academic Editor: Leonarda Liotta

Received: 4 November 2022
Accepted: 22 November 2022
Published: 25 November 2022

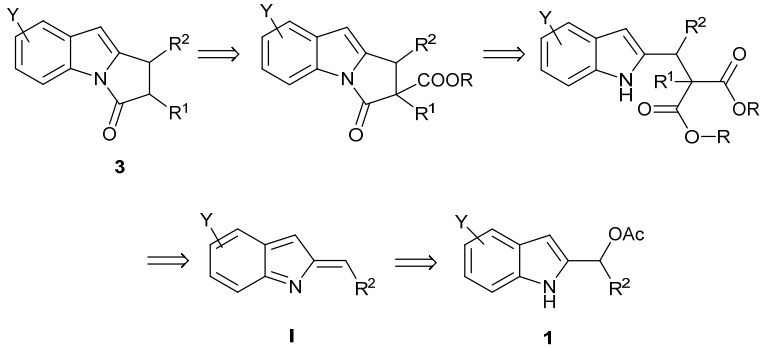
1. Introduction

The tricyclic 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]-indole core and its oxidized derivatives represent an important structural motif found in many biologically active natural products and drug candidates [1–3]. For example, flinderole C exhibits excellent antimalarial activity against the Plasmodium falciparum parasite [4–6] and mitomycin C is an effective antitumor agent [7,8]. Moreover, the antiviral [9,10] as well as antinociceptive [11] and psychotropic [12] properties of these derivatives boosted the development of effective strategies for their rapid construction. In 1983, Danishefsky described the formation of the 2-methyl-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one through the palladium-catalyzed cyclization of the *N*-(2-allylphenyl)acrylamide; [13] subsequently, various cascade reactions have been used as powerful tools to construct the 2,3-dihydro-1*H*-pyrrolo[1,2-*a*]-indoles in a pot fashion, achieving also remarkable progress in the rapid construction of enantioenriched pyrroloindolones [14–21].

Indeed, because of the problems of chemical sustainability of resources, the application of efficient methods for the concise synthesis of valuable scaffolds by avoiding a step-by-step approach, which involves tedious isolation processes, has attracted a great deal of attention from the synthetic community [22].

During our studies in the field of the synthesis of heterocyclic compounds, great interest has been devoted to the formation/functionalization of indole/benzofuran rings and the construction of indole-fused polycyclic systems through simple domino processes [23–26]. Nevertheless, the diversity-oriented synthesis of polysubstituted 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones through straightforward one-pot approaches from easily available building blocks would be particularly significant considering the structural variety of the biologically

active derivatives. From all possible retrosynthetic schemes of 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones, a simple one requires one C-C bond and one C-N disconnection. It was plausible to suppose that the reaction of 2-indolylmethyl acetates **1** with various common active methylene compounds **2** should achieve a general entry into the title target through the in situ generation of 2-methide-2*H*-indole intermediate **I**/nucleophile Michael addition/cyclization/decarboxylation cascade reaction (Scheme 1).



Scheme 1. Retrosynthetic approach to the 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one scaffold.

The sequential addition/annulation reaction of Meldrum's acid, malononitrile, and 1,3-dicarbonyls with *ortho*-quinone methides generated in situ under basic conditions was previously reported to achieve the one-pot synthesis of 3,4-dihydrocoumarins, 4H-chromenes, and xanthenones [27]. Moreover, the in situ-generated aza-ortho-quinone methydes from *o*-aminobenzyl alcohol derivatives were reacted with Meldrum's acid to afford dihydroquinolinones [28].

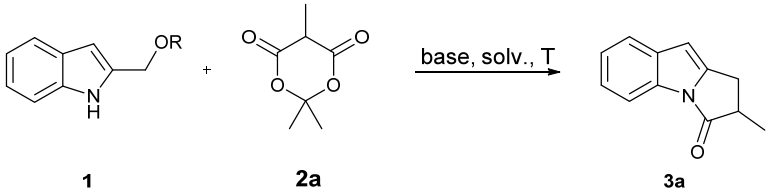
In the literature, methodologies are also reported to easily obtain indolo[1,2-*a*]indoles derivatives from 1*H*-indol-2-yl carbinols via the in situ generation of 2-methide-2*H*-indoles intermediates. Particularly, the enantioselective Brønsted acid catalyzed [3 + 2]-cycloaddition of cyclic enamides and organocatalyzed asymmetric (4 + 3) cycloaddition with dienolsilanes to bicyclo[3.2.2]cyclohepta[*b*]indoles have been described [29–32]. In addition, recently, we observed the formation of reactive indole-methides under basic conditions, starting from indolylmethyl acetates [33].

In the following, we describe the scope and limitations of this approach to the synthesis of the 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones 3.

2. Results and Discussions

We started our investigation by examining the reaction of (1H-indol-2-yl)methyl acetate **1a** with (1H-indol-2-yl)methyl ethyl carbonate **1b** with the 2,2,5-trimethyl-1,3-dioxane-4,6-dione **2a** under basic conditions as the model system. Pleasingly, the desired 2-methyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one **3a** was isolated in 55% yield by reacting **1a** with **2a** in DMSO at 100 °C in the presence of K_2CO_3 as the base (Table 1, entry 1).

Table 1. Optimization studies for the reaction of **1** with methyl Meldrum's acid **3a**. [a]



1a R = Ac; **1b** R = CO_2Et

Table 1. *Cont.*

Entry	1	Catalyst	Base	Solvent	T (°C)	t (h)	Yield 3a (%) [b]
1	**1a**	/	K_2CO_3	DMSO	100	7	55
2	**1b**	/	NaH	DMSO	100	72	42(17) [c]
3	**1b**	$Pd_2(dba)_3/PPh_3$	K_2CO_3	MeCN	70	5.5	68
4	**1b**	$Pd_2(dba)_3/PPh_3$	K_2CO_3	MeCN	80	7	68
5	**1b**	$Pd_2(dba)_3/PPh_3$	K_2CO_3	DMSO	80	1.5	75
6	**1b**	$Pd_2(dba)_3/P(2\text{-furyl})_3$	K_2CO_3	DMSO	80	1	78
7	**1b**	$Pd_2(dba)_3$/dppf	K_2CO_3	DMSO	80	1.5	85
8	**1b**	$Pd_2(dba)_3$/dppf	/	DMSO	80	24	(30) [c]
9	**1a**	$Pd_2(dba)_3/PPh_3$	K_2CO_3	MeCN	100	40	67
10	**1a**	$Pd_2(dba)_3/PPh_3$	K_2CO_3	DMSO	100	5.5	75
11	**1a**	$Pd_2(dba)_3$/dppf	K_2CO_3	DMSO	100	2	88
12	**1a**	$Pd_2(dba)_3$/dppf	K_2CO_3	DMSO	100	2	/(/) [c,d]

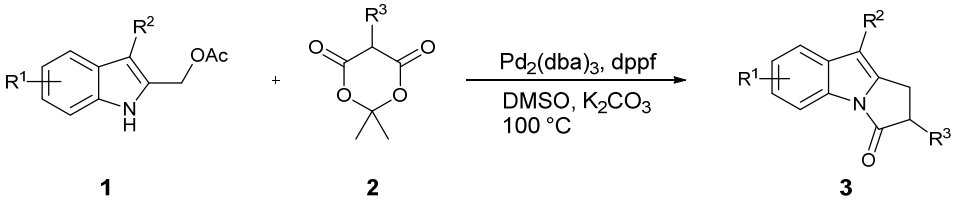
[a] Unless otherwise stated, reactions were carried out on a 0.35 mmol scale under an argon atmosphere using 0.02 equiv. of $Pd_2(dba)_3$, 0.04 equiv. of dppf or 0.08 mmol of PPh_3 or $P(2\text{-furyl})_3$, 1.5 equiv. of **2a**, 1.5 equiv. of K_2CO_3 in 1.5 mL of DMSO. [b] Yields are given for isolated products. [c] Numbers in brackets refer to the percentage of the recovered **1**. [d] The reaction was carried out without **2a**.

A poorer result was observed by reacting **1b** under the same reaction conditions in the presence of the stronger base NaH (Table 1, entry 2).

The advantages of the palladium catalysis in the reaction of benzofuran-2-ylmethyl acetates with nucleophiles [34] prompted us to explore the palladium-catalyzed version of the same reaction using different ligands and solvents, as shown in Table 1. The palladium-catalyzed reaction of indolemethyl acetates **1** with boronic acid to afford the corresponding indole-containing diarhylmethanes has been previously investigated [35]. The formation of the target **3a** occurred in good-to-high yields in DMSO or MeCN, both in the presence of a palladium complex containing a monodentate phosphine ligand (Table 1, entries 3–6 and 9–10) or bidentate phosphine one (Table 1, entries 7–8, 11–12). The best result was obtained by carrying out the reaction in DMSO at 100 °C in the presence of $Pd_2(dba)_3$/dppf as the catalyst (Table 1, entry 11). In previous studies on palladium-catalyzed benzylic substitution reactions, it was shown that the yields of the benzylation products were strongly affected by the bite angle of the bidentate bisphosphine ligand on the palladium catalyst [36–38]. The ligands dppf and DPEPhos were preferred for the benzylation of stabilized carbanions and amines, respectively. A complex mixture was observed when the reaction was performed without **2a** and the starting material **1a** was not recovered.

The exploration of the substrate scope of the procedure under the optimized condition reaction (Table 2) showed that 1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-ones **3** bearing a variety of useful functional groups can be prepared in moderate-to-good yields.

Table 2. Synthesis of 2-substituted 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one 3 from indol-2-ylmethyl acetates 1 and Meldrum's acid derivatives 2. [a]



1 **2** **3**

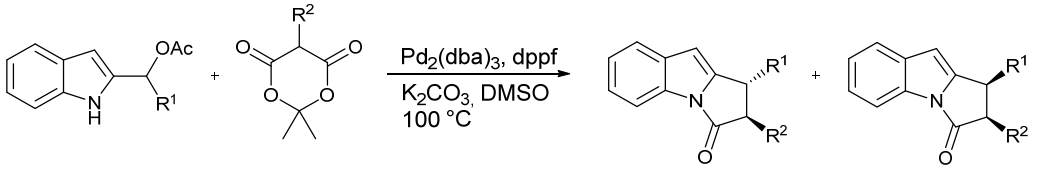
Table 2. *Cont.*

Entry	1	R^1	R^2	2	R^3	t (h)	Yield 3 (%) [b]
1	**1a**	H	H	**2b**	-CH_2(4-OMe-C_6H_4)	1	**3b** (78)
2	**1a**	H	H	**2c**	-CH_2(furyl)	4	**3c** (63)
3	**1a**	H	H	**2d**	-Ph	24	(/)
4	**1a**	H	H	**2e**	-$CH_2CH_2CO_2Me$	3	**3d** (74)
5	**1c**	5-Me	H	**2a**	-Me	3	**3e** (70)
6	**1d**	5-Br	H	**2a**	-Me	5	**3f** (50)
7	**1e**	5-(4-Me-C_6H_4)	H	**2a**	-Me	4.5	**3g** (70)
8	**1f**	5-(4-F,3-Me-C_6H_3)	H	**2a**	-Me	5	**3h** (70)
9	**1g**	H	Ph	**2a**	-Me	3	**3i** (58)
10	**1g**	H	-Ph	**2b**	-CH_2(4-OMe-C_6H_4)	2	**3j** (64)
11	**1g**	H	-Ph	**2c**	-CH_2(2-furyl)	2	**3k** (54)
12	**1g**	H	-Ph	**2e**	-$CH_2CH_2CO_2Me$	2.5	**3l** (66)
13	**1h**	H	4-CF_3-C_6H_4	**2a**	-Me	1	**3m** (71)
14		H	H	**2a**	-Me	3	**3a** (72) [c]

[a] Unless otherwise stated, reactions were carried out on a 0.35 mmol scale under an argon atmosphere using 0.02 equiv. of $Pd_2(dba)_3$, 0.04 equiv. of dppf, 1.5 equiv. of **2**, 1.5 equiv. of K_2CO_3 in 1.5 mL of DMSO at 100 °C. [b] Yields are given for isolated products. [c] The reaction was carried out on a 5.28 mmol scale.

Several substituents, including methyl, nitro, fluoro, bromo, and tolyl, on the indole moiety of **3** were tolerated. A gram-scale experiment was also performed and showed the practicability of this methodology (Table 2, entry 14) Moreover, we tested the reactivity of the (1H-indol-2-yl)(phenyl)methyl acetate **4a** and the 1-(1H-indol-2-yl)ethyl acetate **4b** with some 5-substituted Meldrum's acid derivatives (Table 3).

Table 3. Synthesis of 1,2-disubstituted 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one 5/5′ from indol-2-ylmethyl acetates 4 and Meldrum's acid derivatives 2. [a]



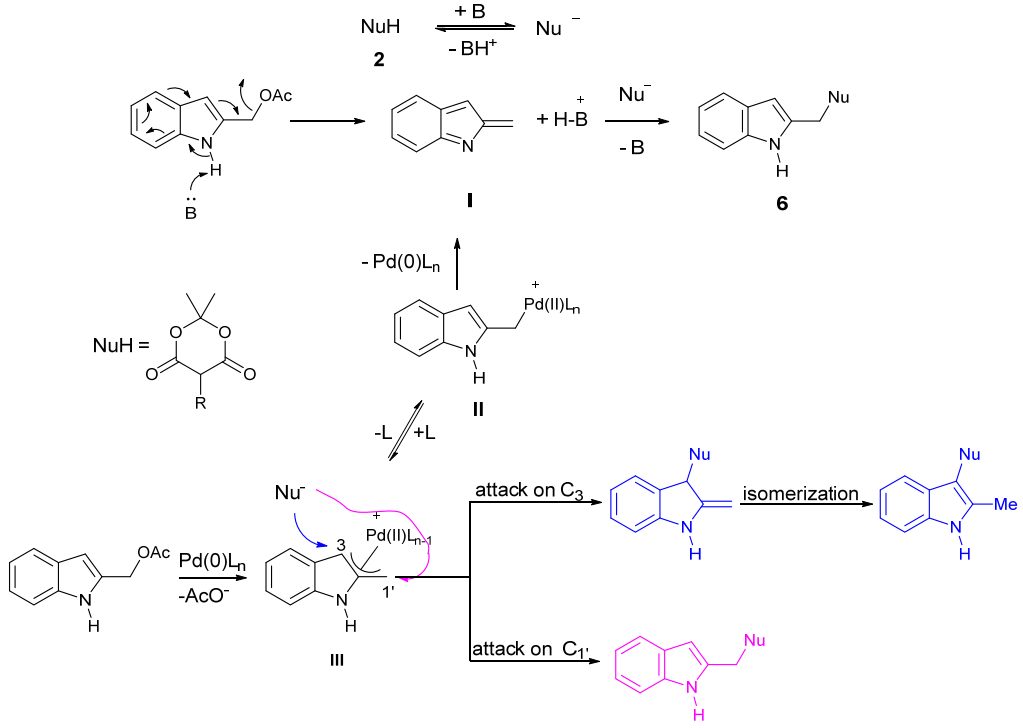
4 **2** **5** **5'**

Entry	4	R^1	2	R^2	t (h)	Ratio 5/5′ [b]	Yield 5 + 5′ (%) [c]
1	**4a**	-Ph	**2a**	-Me	2	84/16	**5a + 5′a** (74)
2	**4a**	-Ph	**2b**	-CH_2(4-OMe-C_6H_4)	3	94/6	**5b + 5′b** (50)
3	**4a**	-Ph	**2c**	-CH_2(furyl)	2	74/26	**5c + 5′c** (52)
4	**4b**	-Me	**2a**	-Me	24	84/16	**5d + 5′d** (76)

[a] Unless otherwise stated, reactions were carried out on a 0.35 mmol scale under an argon atmosphere at 100 °C using 0.02 equiv. of $Pd_2(dba)_3$, 0.04 equiv. of dppf, 1.5 equiv. of **2**, 1.5 equiv. of K_2CO_3 in 1.5 mL of DMSO. [b] Diastereomeric ratios were calculated from the ^{1}H NMR analyses. [c] Yields are given for isolated products.

In all the tested cases, the reaction led to the formation of the corresponding 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one with good-to-excellent diastereoselectivity. Control experiments have shown that the observed diastereoselectivity depends on the relative stability of the *trans* **5** compared to the *cis*- diastereomer **5′**. In fact, by heating the pure diastereomer **5a** or **5a′** (R^1 = Ph, R^2 = Me) at 100 °C in DMSO for 1h in the presence of K_2CO_3, a rapid equilibrium occurred, leading to the formation of the mixture of the two diastereomers in equal ratio to that observed in the synthetic run (Table 3, entry 1). These data match with ΔG°calculated with Gaussian (HF, 3–21G*) (the *trans* stereoisomer is more stable than *cis* by 1.23 Kcal/mol, corresponding to the 88/12 **5a**/**5a′** ratio) [39].

Regarding the reaction mechanism for the one-pot synthesis of 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one **3** from indol-2-ylmethyl acetates and Meldrum's acid derivatives, we believe that the in situ generation of the indolyl methide intermediate **I** could be a common intermediate both for the base promoted and the palladium-catalyzed process (Scheme 2). Experiments to detect the key intermediate **I** under basic conditions have been previously described. [31] Regarding the palladium-catalyzed procedure, it is well known that the oxidative addition of the Pd(0) to the indol-2-ylmethyl acetate generates the η^3 palladium complex **III** in equilibrium with the η^1 palladium complex **II**. It may be supposed that an unusual 1,4- elimination from this later intermediate, involving cleavage of the N-H bond, [40] may afford the indolyl methide **I** with the regeneration of the Pd(0) catalyst. Although the formation of the intermediate derivative **6** via the palladium-catalyzed Tsuji–Trost-type reaction could not be ruled out, we failed to isolate any C3 functionalized indole derivative.

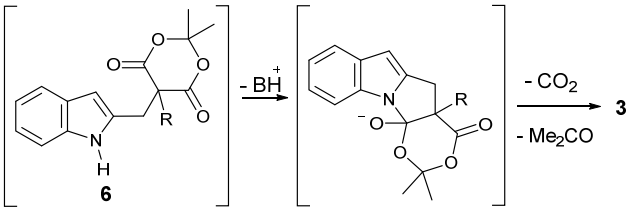


Scheme 2. The reaction of **1a** with Meldrum's acid **2**.

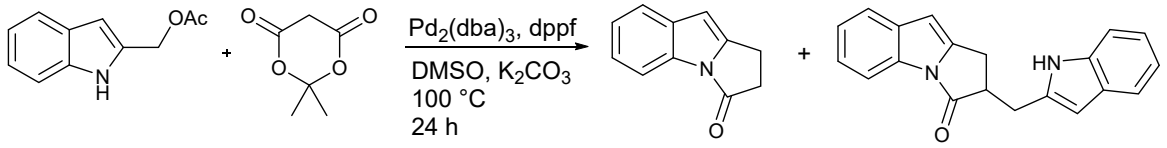
The subsequent sequential cyclization of **6**, followed by the elimination of acetone and CO_2, affords the target products (Scheme 3).

Accordingly, we continued our studies to address product selectivity control. For this purpose, we analyzed the reaction outcome when the indol-2-ylmethyl acetate **1a** was reacted with unsubstituted Meldrum's acid **7** in different stoichiometric ratios. Our result suggested that the competitive deprotonation of the Michael adduct **6a** under the basic reaction conditions generates a new enolate species which is prone to undergo a second Michael addition over the indolyl methide intermediate to afford the 2-((1*H*-indol-

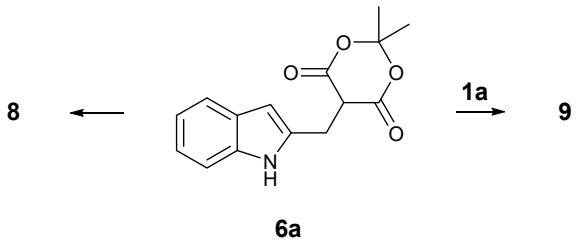
2-yl)methyl)-1,2-dihydro-3*H*-pyrrolo[1,2-a]indol-3-one **9** after cyclization. Conversely, the prevalence of the cyclization of **6a** allowed the isolation of the 1,2-dihydro-3*H*-pyrrolo[1,2-a]indol-3-one **8** when the reaction was carried out in the presence of a large excess of Meldrum's acid (Scheme 4).



Scheme 3. Cyclization of **6**.

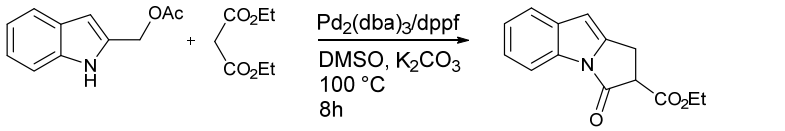


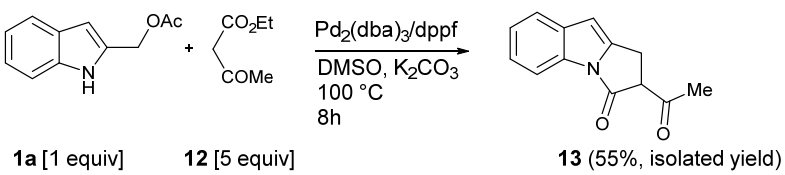
1a [1.0 equiv]	**7** [1.5 equiv.]	**8** (/)	**9** (54 %, isolated yield)
1a [2.5 equiv]	**7** [1.0 equiv.]	**8** (/)	**9** (42 %, isolated yield)
1a [1.0 equiv]	**7** [5.0 equiv.]	**8** (52%, isolated yield)	**9** (/)



Scheme 4. The reaction of **1a** with Meldrum's acid **7**.

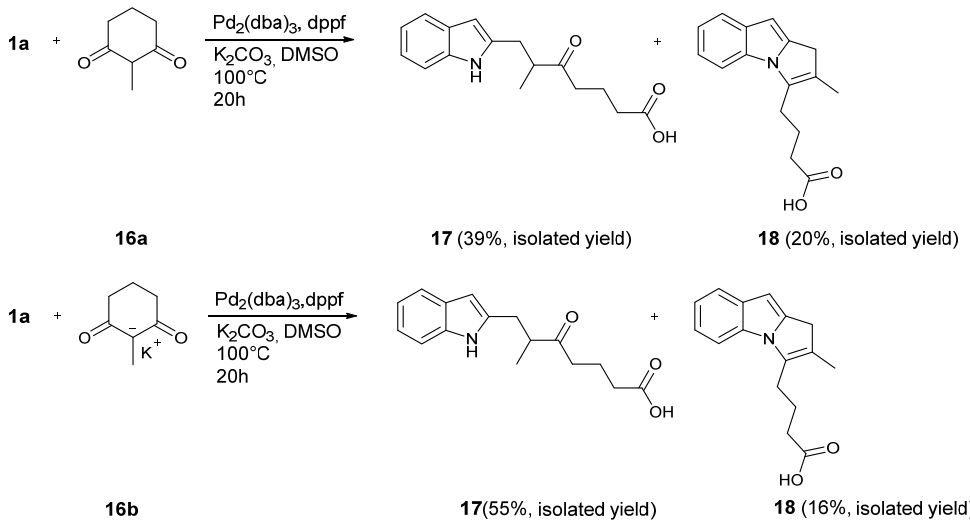
Next, we explored the reactivity of the building block **1a** with other methylene active compounds. Both the ethyl malonate **10** and the ethyl-3-oxobutanoate **12** were compatible with the procedure, allowing to obtain, respectively, the title products **11** and **13** in moderate yields in the presence of 5 equiv. excess of the starting dicarbonyl (Scheme 5).





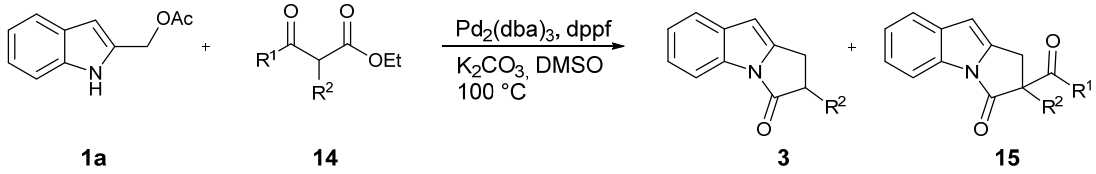
Scheme 5. Reaction of **1a** with ethyl malonate **10** and the ethyl-3-oxobutanoate **12**.

More intriguing results were observed when **1a** was reacted with the ethyl 2-methyl-3-oxobutanoate **14a** or the diethyl 2-methylmalonate **14b** (Scheme 6). Surprisingly, both the palladium reaction of the ethyl 2-methyl-3-oxobutanoate **14a** and its base-promoted one occurred with poor results, while a good yield of the corresponding product **3** was observed in the reaction of **1a** with the ethyl 2-acetylpent-4-enoate **14c** (Table 4, entries 3). Moreover, we isolated in satisfactory yield the ethyl 2-methyl-3-oxo-2,3-dihydro-1*H*-pirrolo[1,2-a]indole-2-carboxylate **15** in the palladium-catalyzed reaction of **1a** with **14b**.



Scheme 6. Reaction of indol-2-ylmethyl acetate **1a** with 2-methylciclohexan-1,3-dione **16a** and its potassium salt **16b**.

Table 4. Synthesis of 2-substituted 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one **3/15** from indol-2-ylmethyl acetates **1a** and substituted methylene active compound **14**. [a]



a: R^1 = Me; R^2= Me
b: R^1 = OEt; R^2= Me
c: R^1 = Me; R^2= -CH2CH=CH

Entry	14	R^1	R^2	t (h)	Yield 3 (%)	Yield 15 (%) [b]
1	**14a**	-Me	-Me	1	**3a** (45)	**15a** (18) [c]
2	**14a**	-Me	-Me	3	**3a** (46)	traces
3	**14b**	-OEt	-Me	24	/	**15b** (60)
4	**14c**	-Me	$-CH_2CH = CH$	4	**3n** (71)	/

[a] Unless otherwise stated, reactions were carried out on a 0.35 mmol scale under an argon atmosphere at 100 °C using 0.02 equiv. of $Pd_2(dba)_3$, 0.04 equiv. of dppf, 1.5 equiv. of **14**, 1.5 equiv. of K_2CO_3 in 1.5 mL of DMSO. [b] Yields are given for isolated products. [c] The reaction was carried out without a catalyst.

Finally, we examined the reaction of **1a** with the 2-methylcyclohexan-1,3-dione **16a** or its potassium salt **16b**. In both cases, the product of sequential Michael addition/retro Dieckmann reaction 7-(1*H*-indol-2-yl)-6-methyl-5-oxoheptanoic acid **17,** together with its cyclized derivative 4-(2-methyl-1*H*-pyrrolo[1,2-*a*]indol-3-yl)butanoic acid **18** (16% yield), was isolated (Scheme 6).

3. Materials and Methods

3.1. General Information

All the commercially available reagents, catalysts, bases, and solvents were used as purchased, without further purification. Starting materials and reaction products were purified by flash chromatography using SiO_2 as the stationary phase, eluting with *n*-hexane/ethyl acetate mixture. ^{1}H NMR (400.13 MHz), ^{13}C NMR (100.6 MHz), and ^{19}F spectra (376.5 MHz) were recorded with an Avance 400 spectrometer (Bruker, Milan, Italy). Splitting patterns were designed as s (singlet), d (doublet), t (triplet), dt (doublets of triplets), td (triplet of doublets), triplets of triplets (tt), q (quartet), m (multiplet), or br s (broad singlet). IR spectra were recorded with a FT/IR-430 spectrometer (Jasco Europe, Milan, Italy) (compounds **1e-f**, **2e**, **3a-h**, **3j-n**, **5a-d, 5′a-d, 15a-b, 18**) and FT/IR 6800, ATR (Jasco Europe, Milan, Italy) (compounds **1a**, **1c-d**, **1g-h**, **2b-c**, **3i**, **4a-b**, **8**, **9**, **11**, **13**, **17**). HRMS were recorded on Orbitrap Elite Mass Spectrometer (Thermo Fisher, Monza, Italy) (**3a-h**, **3j-n**, **5a-d**, **11**, **13**, and **17**), or on Orbitrap Exactive Mass Spectrometer (Thermo Fisher, Monza Italy) (**1a, c-h**, **2b-e, 3i, 4a-b**, **8**, **9**, **15**, **18**). Melting points were determined with a Büchi B-545 apparatus (Büchi, Milan, Italy) and were uncorrected. To obtain suitable NMR spectra of diastereoisomers **5** and **5′**, the isomeric mixtures were further purified by semi-preparative HPLC (Waters, Milan, Italy) under normal phase conditions using a Nucleodur 100-5 column (762007.100) and eluting with *n*-hexane/AcOEt mixtures (Merck Science Life, Milan, Italy).

3.2. Synthetic Procedures and Characterization Data

3.2.1. General Procedure for the Preparation of (1H-indol-2-yl)methyl Acetates

The (1*H*-indol-2-yl)methyl acetates (**1a**, **1c-h**; **4a-b**) were synthesized according to the procedures reported in the Supplementary Materials.

3.2.2. Characterization Data of (1H-indol-2-yl)methyl Acetates (**1a**, **c-h**; **4a-b**)

(1H-indol-2-yl)methyl acetate (**1a**): known compound; 95% yield (7.47 mmol scale, 1.34 g); yellow solid; lit. [35] mp: 111–112 °C;. mp: 111–112 °C; R_f = 0.27 (*n*-hexane-EtOAc, 80:20); IR (neat): 3303, 1726, 1045, 1454, 1274, 805 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ = 8.51 (br s, 1 H), 7.52 (d, *J* = 8.0 Hz, 1 H), 7.27 (d, *J* = 8.0 Hz, 1 H), 7.13 (t, *J* = 7.6 Hz, 1 H), 7.00 (t, J_1 = 7.6 Hz, 1 H), 6.46 (s, 1 H), 5.15 (s, 2 H), 2.03 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.3 (C), 136.6 (C), 133.0 (C), 127.5 (C), 122.8 (CH), 120.9 (CH), 120.1 (CH), 111.1 (CH), 103.9 (CH), 59.8 (CH_2), 21.0 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{11}H_{12}NO_2$: 188.0717; found: 188.0705.

(5-methyl-1H-indol-2-yl)methyl acetate (**1c**): known compound; 98% yield (7.47 mmol scale, 1.49 g); brown solid; lit. [35] mp: 84–86 °C; mp: 84–86 °C; R_f = 0.24 (*n*-hexane-EtOAc, 75:25); IR (neat): 3427, 1718, 1361, 806 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.42 (br s, 1 H), 7.31 (q, *J* = 0.80 Hz, 1 H), 7.16 (d, *J* = 8.2 Hz, 1 H), 6.96 (dd, J_1 = 8.2 Hz, J_2 = 1.6 Hz, 1 H), 6.38 (d, *J* = 1.6 Hz, 1 H), 5.14 (s, 2 H), 2.36 (s, 3 H), 2.03 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.3 (C), 134.9 (C), 133.1 (C), 129.2 (C), 127.8 (C), 124.5 (CH), 120.5 (CH), 110.8 (CH), 103.4 (CH), 59.8 (CH_2), 21.5 (CH_3), 21.0 (CH_3); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{12}H_{15}NO_2Na$: 226.0838; found: 226.0838.

(5-bromo-1H-indol-2-yl)methyl acetate (**1d**): 98% yield (7.47 mmol scale, 1.96 g); brown solid; mp: 69–71 °C; R_f = 0.21 (*n*-hexane-EtOAc, 87:13); IR (neat): 3323, 2916, 1714, 1383, 1211, 1133 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.87 (br s, 1 H), 7.71 (d, *J* = 1.2 Hz, 1 H), 7.28 (dd, J_1 = 8.5 Hz, J_2 = 1.7 Hz, 1 H), 7.21 (d, *J* = 8.5 Hz, 1 H), 6.47 (d, *J* = 1.2 Hz, 1 H), 5.20 (s, 2 H), 2.11 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.5 (C), 135.2 (C), 134.4 (C), 129.4 (C), 125.8 (CH), 123.5 (CH), 113.2 (C), 112.7 (CH), 103.5(CH), 59.6 (CH_2), 21.1 (CH_3); HRMS: *m/z* $[M - H]^-$ calcd. for $C_{11}H_9BrNO_2$: 265.9822; found: 265.9818.

(5-(p-tolyl)-1H-indol-2-yl)methyl acetate (**1e**): 98% yield (4.35 mmol scale, 1.19 g); yellow solid; mp: 178–180 °C; R_f = 0.23 (*n*-hexane-EtOAc, 75:25); IR (KBr): 3399, 2919, 1728, 1385, 1235; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ = 8.62 (br s, 1 H), 7.79 (s, 1 H), 7.55–7.53 (m, 2 H), 7.45 (dd, J_1 = 8.50 Hz, J_2 = 1.62, 1 H), 7.39 (d, *J* = 8.50 Hz, 1 H), 7.25 (m,

2 H), 6.58 (d, *J* = 1.17 Hz, 1 H), 5.24 (s, 2 H), 2.40 (s, 3 H), 2.11 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ = 172.5 (C), 139.6 (C), 136.1 (C), 136.0 (C), 133.8 (C), 133.7 (C), 129.5 (CH), 128.2 (C), 127.3 (CH), 122.8 (CH), 119.2 (CH), 111.4 (CH), 104.3 (CH), 59.9 (CH_2), 21.2 (CH_3), 21.1 (CH_3); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{18}H_{17}NO_2Na$: 302.1152; found: 302.1153.

(5-(4-fluoro-3-methylphenyl)-1H-indol-2-yl)methyl acetate (**1f**): 97% yield (3.14 mmol scale, 0.90 g); yellow solid; mp: 98–100 °C; R_f = 0.26 (*n*-hexane-EtOAc, 80:20); IR (KBr): 3366, 2919, 1712, 1472, 1385, 1265; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ = 8.55 (s, 1 H), 7.73 (s, 1 H), 7.543–7.37 (m, 4 H), 7.51–7.34 (m, 3 H), 7.05 (t, *J* = 8.9 Hz, 1 H), 6.57 (d, *J* = 1.4 Hz, 1 H), 5.24 (s, 2 H), 2.34 (s, 3 H), 2.11 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ = 172.5 (C), 161.0 (d, *J* = 241.5 Hz) (C), 138.3 (d, *J* = 3.2 Hz) (C), 136.1 (C), 134.0 (C), 133.0 (C), 130.3 (d, *J* = 5.0 Hz), 128.2 (C), 126.2 (d, *J* = 7.0 Hz) (CH), 125.0 (d, *J* = 15.5 Hz) (C), 122.7 (CH), 119.3 (CH), 121.4, 118.6, 115.16 (d, *J* = 15.5 Hz) (C), 111.5 (CH), 104.3 (CH), 59.86 (CH_2), 21.2 (CH_3), 14.9 (d, *J* = 3.5 Hz); ^{1}H-coupled ^{19}F (376.5 MHz) ($CDCl_3$): δ −121.6 (hept, *J* = 3.0 Hz); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{18}H_{16}FNO_2Na$: 320.1057; found: 320.1051.

(3-phenyl-1H-indol-2-yl)methyl acetate (**1g**): yield quantitative (5.15 mmol scale, 1.37 g); yellow solid; mp: 133–135 °C; R_f = 0.25 (*n*-hexane-EtOAc, 80:20); IR (neat): 3391, 2917, 1730, 1456, 1384, 1231 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.71 (br s, 1 H), 7.65 (d, *J* = 8.0 Hz, 1 H), 7.47 (d, *J* = 7.5 Hz, 2 H), 7.41 (t, *J* = 7.5 Hz, 2 H), 7.30 (t, *J* = 8.3 Hz, 2 H), 7.17 (d, *J* = 7.0 Hz, 1 H), 7.06 (t, *J* = 7.5 Hz, 1 H), 5.19 (s, 2 H), 2.06 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.8 (C), 135.8 (C), 134.2 (C), 129.8 (CH), 129.4 (C), 128.8 (CH), 126.8 (CH), 126.7 (C) 123.5 (CH), 120.4 (CH), 120.2(CH), 118.8 (C), 111.4(CH), 58.5 (CH_2), 21.2 (CH_3); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{17}H_{15}NO_2Na$: 288.0995; found: 288.0997.

(3-(4-(trifluoromethyl)phenyl)-1H-indol-2-yl)methyl acetate (**1h**): 95% yield (5.39 mmol scale, 1.71 g); red solid; mp: 120–122 °C; R_f = 0.30 (*n*-hexane-EtOAc, 75:25); IR (neat): 3388, 3287, 2941, 1730, 1616, 1384, 1326 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.81 (br s, 1 H), 7.67 (d, *J* = 8.2 Hz, 2 H), 7.62–7.57 (m, 3 H), 7.33 (d, *J* = 8.1 Hz, 1 H), 7.21 (t, *J* = 7.4 Hz, 1 H), 7.09 (t, *J* = 7.4 Hz, 1 H), 5.17 (s, 2 H), 2.07 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.6 (C), 138.0 (C), 135.7 (C), 129.9 (C), 129.8 (CH), 128.7 (q, J_{CF} = 33.2 Hz, C), 126.2 (C), 125.7 (q, J_{CF} = 3.6 Hz, CH), 124.3 (q, J_{CF} = 273.4 Hz, C), 123.7 (CH), 120.7 (CH), 119.6 (CH), 117.3 (C), 111.5 (CH), 58.1 (CH_2), 21.0 (CH_3); ^{19}F NMR (376.5 MHz) ($CDCl_3$): δ = −62.3; HRMS: *m/z* $[M - H]^-$ calcd. for $C_{18}H_{13}F_3NO_2$: 332.0904; found: 332.0894.

(1H-indol-2-yl)(phenyl)methyl acetate (**4a**): 95% yield (6.20 mmol scale, 1.56 g); yellow solid; mp: 93–95 °C; R_f = 0.25 (*n*-hexane-EtOAc, 85:15); IR (neat): 3362, 2919, 1445, 1383, 1238 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.45 (br s, 1 H), 7.53 (d, *J* = 8.3 Hz, 1 H), 7.50–7.48 (m, 2 H), 7.45–7.39 (m, 3 H), 7.34–7.32 (m, 1 H), 7.19 (td, J_1 = 7.7 Hz, J_2 = 1.1 Hz, 1 H), 7.01 (td, J_1 = 7.7 Hz, J_2 = 1.1 Hz, 1 H), 7.05 (s, 1 H), 6.22–6.21 (m, 1 H), 2.18 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ = 171.2 (C), 137.6 (C), 136.9 (C), 136.4 (C), 128.6 (CH), 128.5 (CH), 127.5 (C), 127.2 (CH), 122.7 (CH), 120.9 (CH), 120.0 (CH), 111.1 (CH), 103.4 (CH), 71.8 (CH), 21.3 (CH_3);); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{17}H_{15}NO_2Na$: 288.0995; found: 288.0989.

1-(1H-indol-2-yl)ethyl acetate (**4b**): 96% yield (6.20 mmol scale, 1.18 g); brown solid; mp: 209–211 °C; R_f = 0.23 (*n*-hexane-EtOAc, 80:20); IR (neat): 3330, 2918, 1713, 1455, 1384 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.60 (br s, 1 H), 7.60 (d, *J* = 8.0 Hz, 1 H), 7.35 (dd, J_1 = 8.2 Hz, J_2 = 0.7 Hz, 1 H), 7.19 (td, J_1 = 7.2 Hz, J_2 = 1.1 Hz, 1 H), 7.10 (td, J_1 = 7.2 Hz, J_2 = 1.1 Hz, 1 H), 6.53–6.53 (m, 1 H), 6.07 (q, *J* = 6.4 Hz, 1 H), 2.09 (s, 3 H), 1.74 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.1 (C), 138.0 (C), 136.1 (C), 127.5 (CH), 122.7 (CH), 121.0 (CH), 120.1, 111.2 (CH), 100.7, 66.5 (CH), 21.4 (CH_3), 18.7 (CH_3); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{12}H_{13}NO_2Na$: 266.0838; found: 266.0838.

3.2.3. General Procedure for the Preparation of 5-(aryl-2-ylmethyl)-2,2-dimethyl-1,3-dioxane-4,6-diones (**2**)

The 5-(aryl-2-ylmethyl)-2,2-dimethyl-1,3-dioxane-4,6-diones (**2a-c**) were synthesized according to the *one-pot* procedure reported by Shibasaki et al.; [41] (**2e**) was synthesized according to the procedure reported by Chande et al. [42].

3.2.4. Characterization Data of 5-(aryl-2-ylmethyl)-2,2-dimethyl-1,3-dioxane-4,6-diones (**2**)

5-(4-Methoxybenzyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (**2b**): known compound; 98% yield (4.50 mmol scale, 1.17 g); yellow solid; lit. [41] mp: 82–85 °C; mp: 83–85 °C; R_f 0.24 (*n*-hexane-EtOAc, 75:25); IR (neat): 3036, 2920, 1784, 1743, 1514, 1243 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ 7.25 (d, *J* = 8.8 Hz, 2 H), 6.82 (d, *J* = 8.8 Hz, 2 H), 3.77 (s, 3 H), 3.72 (t, *J* = 4.9 Hz, 1 H), 3.44 (d, *J* = 4.9 Hz, 2 H), 1.72 (s, 3 H), 1.48 (d, 3 H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 165.6 (C), 158.9 (C), 131.1 (CH), 129.2 (C), 114.1 (CH), 105.3 (C), 55.4 (CH_3), 48.5 (CH), 31.7 (CH_2), 28.6 (CH_3), 27.5 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{14}H_{15}O_5$: 263.0925; found: 263.0922.

5-(Furan-2-ylmethyl)-2,2-dimethyl-1,3-dioxane-4,6-dione (**2c**): known compound; 98% yield (4.50 mmol scale, 988.8 mg); grey solid; lit. [41] mp: 92–93 °C; mp: 92–93 °C; R_f 0.30 (R_f = 0.24 (*n*-hexane-EtOAc, 85:15); IR (neat): 3123, 2896, 1783, 1740, 1067, 907 cm^{-1}; ^1H NMR (400.13 MHz, $CDCl_3$): δ 7.30 (dd, J_1 = 1.8 Hz, J_2 = 0.7 Hz, 1 H), 6.29 (dd, J_1 = 3.2 Hz, J_2 = 1.8 Hz, 1 H), 6.18 (dd, J_1 = 3.2 Hz, J_2 = 0.7 Hz, 1 H), 3.83 (t, *J* = 5.0 Hz, 1 H), 3.51 (d, *J* = 5.0 Hz, 2 H), 1.79 (s, 3 H), 1.67 (s, 3 H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 164.9 (C), 150.7 (C), 141.7 (CH), 110.8 (CH), 107.9 (CH), 105.4 (C), 45.6 (CH), 28.5 (CH_3), 27.2 (CH_3), 25.1 (CH_2); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{11}H_{12}O_5Na$: 247.0577; found: 247.0581.

Methyl 3-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)propanoate (**2e**): known compound; 78% yield (4.50 mmol scale, 1.10 g); white solid; lit. [42] mp: 75–76 °C; mp: 78–80 °C; R_f 0.21 (R_f = 0.24 (*n*-hexane-EtOAc, 75:25); IR (KBr): 2995, 2952, 2893, 1749 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ = 3.92 (t, *J* = 5.5 Hz, 1 H), 3.67 (s, 3 H), 2.64 (t, *J* = 7.2 Hz, 2 H), 2.40–2.35 (m, 2 H), 1.82 (s, 3 H), 1.77 (s, 3 H), ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ = 173.4 (C), 165.2 (C), 105.2 (C), 51.8 (CH_3), 44.8 (CH), 30.1 (CH_2), 28.6 (CH_3), 26.5 (CH_3), 21.2 (CH_2); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{19}H_{18}NO_2$: 292.1332; found: 292.1321.

3.2.5. Typical Procedure for the Preparation of 1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-ones (**3a-m**; **5a-d**): Synthesis of 2-methyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3a**)

In a 50 mL Carousel Tube Reactor (Radely Discovery Technology) containing a magnetic stirring bar, Pd_2dba_3 (6.4 mg, 0.007 mmol, 0.025 equiv.) and dppf (7.8 mg, 0.014 mmol, 0.04 equiv.) were dissolved with 1.5 mL of anhydrous DMSO, at room temperature under Ar. Then, (1*H*-indol-2-il)methyl acetate (**1a**) (66.15 mg, 0.35 mmol, 1.0 equiv.), 2,2,5-trimethyl-1,3-dioxane-4,6-dione (**5a**) (138.6, 0.525 mmol, 1.5 equiv.) and K_2CO_3 (72.5 mg, 0.525 mmol, 1.5 equiv.) were added and the mixture reaction was stirred for 1h at 100 °C. After this time, the reaction mixture was cooled to room temperature, diluted with Et_2O, and washed with a solution of $KHSO_4$ (10% w/w) and with brine. The organic extract was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by chromatography on SiO_2 (25–40 μm), eluting with a 80/20 (v/v) *n*-hexane/EtOAc mixture (R_f = 0.22) to obtain 102.4 mg (85% yield) of 2-methyl-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one (**3a**): known compound [7]; 85% yield (0.35 mmol scale, 102.4 mg); yellow solid; mp: 73–76 °C; R_f = 0.22 (*n*-hexane-EtOAc, 80:20); IR (KBr): 3052, 2969, 1729, 1589, 1384 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ = 8.00–7.97 (m, 1 H), 7.42–7.40 (m, 1 H), 7.20–7.15 (m, 2 H), 6.17 (s, 1 H), 3.31 (m, 1 H), 3.19–3.10 (m, 1 H), 2.68 (m, 1 H), 1.37 (d, *J* = 7.5 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ = 174.7 (C), 142.0 (C), 135.3 (C), 130.5 (C), 124.0 (C), 123.2 (CH), 120.5 (CH), 113.6 (CH), 100.3 (CH), 41.6 (CH), 28.4 (CH2), 17.0 (CH3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{12}H_{12}NO$: 186.0913; found: 186.0902.

3.2.6. Characterization Data of of 1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-ones (**3b-3m**; **5a-d**)

2-(4-methoxybenzyl)-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3b**): known compound; [43] 78% yield (0.35 mmol scale, 79mg); yellow solid; mp: 109–110 °C; R_f = 0.23 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3098, 2924, 1744, 1384 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ = 8.09–8.07 (m, 1 H), 7.48–7.45 (m, 1 H), 7.27–7.25 (m, 2 H), 7.16 (d, *J* = 8.6 Hz, 2 H), 6.83 (d, *J* = 8.6 Hz, 2 H), 6.20 (br s, 1 H), 3.77 (s, 3 H), 3.48–3.41 (m, 1 H), 3.32 (dd, J_1 = 14.1 Hz, J_2 = 4.5 Hz, 1 H), 3.17–3.10 (m, 1 H), 2.91–2.84 (m, 2 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 173.4 (C), 158.6 (C), 142.2 (C), 135.4 (C), 130.5 (C), 130.2 (C), 130.1 (CH), 124.2 (CH),

123.4 (CH), 120.6 (CH), 114.2 (CH), 113.8 (CH), 100.5 (CH), 55.4 (CH_3), 48.5 (CH), 36.3 (CH_2), 25.4 (CH_2); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{19}H_{18}NO_2$: 292.1332; found: 292.1321.

2-(furan-2-ylmethyl)-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3c**): 63% yield (0.35 mmol scale, 55 mg); brown solid; mp: 95–97 °C; R_f = 0.25 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3092, 2917, 1737, 1454, 1384 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.03–7.97 (m, 2 H), 7.42–7.38 (m, 2 H), 7.22–7.15 (m, 3 H), 6.19 (dd, J_1 = 3.3 Hz, J_2 = 1.9 Hz, 1 H), 6.15 (br s, 1 H), 6.02 (dd, J_1 = 3.14 Hz, J_2 = 0.6 Hz, 1 H), 3.46–3.39 (m, 1 H), 3.27 (dd, J_1 = 15.3 Hz, J_2 = 4.4 Hz 1 H), 3.23–3.17 (m, 1 H), 2.95 (dd, J_1 = 15.3 Hz, J_2 = 9.2 Hz 1 H), 2.90–2.85 (m, 1 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.3 (C), 152.2 (C), 142.0 (C), 141.9 (CH), 135.3 (C), 130.5 (C), 124.1 (CH), 123.3 (CH), 120.6 (CH), 113.7 (CH), 110.3 (CH), 107.0 (CH), 100.5 (CH), 46.0 (CH), 29.6 (CH_2), 25.8 (CH_2); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{16}H_{14}NO_2$: 252.1019; found: 252.1009.

methyl 3-(3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-2-yl)propanoate (**3d**): 74% yield (0.35 mmol scale, 67 mg); brown solid; mp: 41–43 °C; R_f = 0.25 (*n*-hexane-EtOAc, 80:20); IR (KBr): 3007, 2916, 1754, 1455, 1385 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ = 8.06–8.03 (m, 1 H), 7.50–7.48 (m, 1 H), 7.27–7.25 (m, 2 H), 6.27 (br s, 1 H), 3.70 (s, 3 H), 3.39–3.32 (m, 1 H), 3.26–3.19 (m, 1 H), 2.82 (dd, J_1 = 15.3 Hz, J_2 = 4.4 Hz, 1 H), 2.58 (m, 1 H), 2.34–2.26 (m, 1 H), 2.08–2.00 (m, 1 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ = 173.3 (C), 173.2 (C), 141.7 (C), 135.4 (C), 130.5 (C), 124.2 (CH), 123.4 (CH), 120.7 (CH), 113.8 (CH), 100.6 (CH), 52.0 (CH_3), 45.8 (CH), 31.4 (CH_2), 27.1 (CH_2), 26.4 (CH_2); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{15}H_{16}NO_3$: 258.1114; found: 258.1124.

2,7-dimethyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3e**): 70% yield (0.35 mmol scale, 49 mg); brown wax; R_f = 0.20 (*n*-hexane-EtOAc, 90:10); IR (KBr): 3004, 2918, 1717, 1475, 1352 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ = 7.93 (d, *J* = 8.2 Hz, 1 H), 7.29 (br s, 1 H), 7.09 (dd, J_1 = 1.1 Hz, J_2 = 8.2 Hz, 1 H), 6.19–6.18 (m, 1 H), 3.42–3.34 (m, 1 H), 3.26–3.20 (m, 1 H), 2.78–2.72 (m, 1 H), 2.44 (br s, 3 H), 1.45 (d, *J* = 7.4 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ = 174.7 (C), 142.2 (C), 135.8 (C), 133.8 (C), 128.8 (CH), 124.6 (CH),120.6 (CH), 113.3 (CH), 100.2 (CH), 41.7 (CH_3), 28.5 (CH_3), 21.8 (CH_2), 17.7 (CH); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{13}H_{14}NO$: 200.1070; found: 200.1062.

7-bromo-2-methyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3f**): 50% yield (0.35 mmol scale, 46 mg); yellow solid; mp: 96–99 °C; R_f = 0.21 (*n*-hexane-EtOAc, 90:10; IR (KBr): 3091.0, 2918.7, 1731.8, 1590.0, 1447.5, 1384.6 cm^{-1}; ^1H NMR (400.13 MHz) (DMSO-d_6): δ = 7.85 (d, *J* = 8.3 Hz, 1 H), 7.79 (d, *J* = 1.6 Hz, 1 H), 7.40 (dd, J_1 = 8.5 Hz, J_2 = 1.9 Hz, 1 H), 6.39 (s, 1 H), 3.45–3.30 (m, 2 H), 2.82–2.77 (m, 1 H), 1.34 (d, *J* = 7.3 Hz, 3 H); ^{13}C NMR (100.6 MHz) (DMSO-d_6): δ 175.3 (C), 145.3 (C), 137.5 (C), 128.9 (C), 125.9 (CH) (CH), 123.6 (CH), 116.6 (C), 114.8 (CH), 99.5 (CH), 41.4 (CH), 28.4 (CH_2), 16.9 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{12}H_{11}BrNO$: 264.0019; found: 264.0008.

2-methyl-7-(p-tolyl)-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3g**): 70% yield (0.35 mmol scale, 67 mg); yellow solid; mp: 140–143 °C; R_f = 0.18 R_f = 0.24 (*n*-hexane-EtOAc, 75:25); IR (KBr): 3071, 2917, 1728, 1585, 1470, 1384 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.09 (d, *J* = 8.5 Hz, 1 H), 7.68 (d, *J* = 1.3 Hz, 1 H), 7.55–7.52 (m, 3 H), 7.50 (dd, J_1 = 8.4 Hz; J_2 = 1.7Hz, 1 H), 7.26 (d, *J* = 7.8 Hz, 2 H), 6.31 (s, 1 H), 3.46–3.39 (m, 1 H), 3.30–3.21 (m, 1 H), 2.82–2.77 (m, 1 H), 3.10 (s, 3 H); 1.48 (d, *J* = 7.4 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 174.7 (C), 142.7 (C), 139.0 (C), 137.5 (C), 136.8 (C), 136.0 (C), 129.8 (CH), 129.6 (CH), 127.4 (CH), 122.8 (CH), 118.9 (CH), 113.8 (CH), 100.7 (CH), 41.7 (CH), 28.5 (CH_2), 21.1 (CH_3), 17.1 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{19}H_{18}NO$: 276.1383; found: 276.1372.

7-(4-fluoro-3-methylphenyl)-2-methyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3h**): 70% yield (0.35 mmol scale, 72 mg); pink solid; mp: 136–139 °C; R_f = 0.23 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3102, 2972, 1743, 1586, 1467, 1384 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.09 (d, *J* = 8.5 Hz, 1 H), 7.68 (d, *J* = 1.3 Hz, 1 H), 7.46–7.37 (m, 3 H), 7.07 (t, J_1 = 8.4 Hz, 1 H), 6.31 (s, 1 H), 3.46–3.39 (m, 1 H), 3.30–3.21 (m, 1 H), 2.82–2.77 (m, 1 H), 2.34 (s, 3 H); 1.48 (d, *J* = 7.4 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 174.7 (C), 161.0 (d, *J* = 249.3 Hz) (C), 142.8 (C), 137.8 (d, *J* = 3.5 Hz) (C), 136.8 (C), 136.0 (C), 130.6 (d, *J* = 5.12 Hz) (CH), 129.8 (C), 126.3 (d, *J* = 7.9 Hz) (CH), 125.2 (C)., 125.0 (C), 120.9 (d, *J* = 380.8 Hz) (CH),

115.4 (CH), 115.2 (CH), 107.2 (d, J = 1337.1 Hz), 41.8 (CH), 28.6 (CH_2), 17.2 (CH_3), 14.8 (d, J = 3.4 Hz) (CH_3); ^{1}H-coupled ^{19}F (376.5 MHz) ($CDCl_3$): δ −120.6 (hept, J = 2.9 Hz); HRMS: m/z $[M + H]^+$ calcd. for $C_{19}H_{17}FNO$: 294.1289; found: 294.1275.

2-methyl-9-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3i**): 58% yield (0.35 mmol scale, 53 mg); white solid; mp: 148–149 °C; R_f = 0.24(*n*-hexane-EtOAc, 85:15); IR (neat): 2973, 2924, 1720, 1603, 1079 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.16–8.13 (m, 1 H), 7.80–7.77(m, 1 H), 7.61 (d, J = 7.9 Hz 2 H), 7.49 (d, J = 7.9 Hz 2 H), 7.36–7.33 (m, 3 H), 3.60–3.54 (m, 1 H), 3.34–3.25 (m, 1 H), 2.97–2.92 (m, 1 H), 1.50 (d, J = 7.5 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 174.7 (C), 138.4 (C), 133.8 (C), 133.7 (C), 130.9 (C), 129.0 (CH), 128.5 (CH), 127.9 (CH), 126.8(CH), 124.4 (CH), 123.8 (CH), 119.8 (CH), 114.8 (C), 114.0 (CH), 41.5 (CH), 28.8 (CH_2), 17.2 (CH_3); HRMS: m/z $[M + Na]^+$ calcd. for $C_{18}H_{15}NONa$: 284.1046; found: 284.1046.

2-(4-methoxybenzyl)-9-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3j**): 64% yield (0.35 mmol scale, 82 mg); white solid; mp: 156–159 °C; R_f = 0.21 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3093, 2917, 1742, 1582 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.09–8.04 (m, 1 H), 7.68–7.63 (m, 1 H), 7.46–7.43 (m, 2 H), 7.37–7.33 (m, 2 H), 7.27–7.20 (m, 3 H), 7.09–7.06 (m, 2 H), 6.77–6.73 (m, 2 H), 3.68 (s, 3 H), 3.44–3.37 (m, 1 H), 3.28 (dd, J_1 = 14.2 Hz, J_2 = 4.6 Hz, 1 H), 3.20 (dd, J_1 = 17.8 Hz, J_2 = 8.7 Hz, 1 H), 2.90 (dd, J_1 = 17.5 Hz, J_2 = 5.0 Hz, 1 H), 2.81 (dd, J_1 = 14.2 Hz, J_2 = 9.8 Hz, 1 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 173.2 (C), 158.6 (C), 138.4 (C), 133.9 (C), 133.6 (C), 130.9 (C), 130.2 (C), 130.0 (CH), 129.0 (CH), 127.9 (CH), 126.9 (CH), 124.5 (CH), 123.9 (CH), 119.8 (CH), 114.9 (C), 114.3 (CH), 114.0 (CH), 55.4 (CH_3), 48.3 (CH), 36.3 (CH_2), 25.7 (CH_2).); HRMS: m/z $[M + H]^+$ calcd. for $C_{25}H_{22}NO_2$: 368.1645; found: 368.1629.

2-(furan-2-ylmethyl)-9-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3k**): 54% yield (0.35 mmol scale, 62 mg); white solid; mp: 162–165 °C; R_f = 0.23 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3002, 2917, 1733, 1576, 1455 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.18–8.12 (m, 1 H), 7.79–7.76 (m, 1 H), 7.58–7.56 (m, 2 H), 7.49–7.45 (m, 2 H), 7.35–7.33 (m, 2 H), 7.31–7.30 (m, 1 H), 6.29 (dd, J_1 = 3.3 Hz, J_2 = 1.9 Hz, 1 H), 6.13 (dd, J_1 = 3.3 Hz, J_2 = 0.5 Hz, 1 H), 3.61–3.55 (m, 1 H), 3.49–3.38 (m, 2 H), 3.15–3.13 (m, 2 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.7 (C), 152.2 (C), 142.0 (CH), 138.2 (C), 133.9 (C), 133.5 (C), 130.9 (C), 129.0 (CH), 128.0(CH), 126.9 (CH), 124.5 (CH), 123.9 (CH), 119.9 (CH), 115.0 (C), 114.1 (CH), 110.5 (CH), 107.2 (CH), 46.0 (CH), 29.8 (CH_2), 26.2 (CH_2); HRMS: m/z $[M + H]^+$ calcd. for $C_{22}H_{18}NO_2$: 328.1332; found: 328.1317.

methyl 3-(3-oxo-9-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]indol-2-yl)propanoate (**3l**): 66% yield (0.35 mmol scale, 77 mg); brown solid; mp: 126–129 °C; R_f = 0.19 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3004, 2918, 1737, 1454, 1383 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.15–8.10 (m, 1 H), 7.80–7.76 (m, 1 H), 7.61–7.59 (m, 2 H), 7.51–7.47 (m, 2 H), 7.37–7.32 (m, 3 H), 3.70 (s, 3 H), 3.53 (dd, J_1 = 17.3 Hz, J_2 = 8.8 Hz, 1 H), 3.33–3.26 (m, 1 H), 2.99 (dd, J_1 = 17.3 Hz, J_2 = 4.9 Hz, 1 H), 2.67–2.54 (m, 2 H), 2.40–2.31 (m, 1 H), 2.11–2.02 (m, 1 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 173.2 (C), 173.1 (C), 138.0 (C), 133.9 (C), 133.5 (C), 130.8 (C), 129.1 (CH), 127.9 (CH), 127.0 (CH), 124.5 (CH), 124.0 (CH), 119.9 (CH), 115.0 (C), 114.1 (CH), 51.9 (CH_3), 45.6 (CH), 31.4 (CH_2), 27.2 (CH_2), 26.8 (CH_2); HRMS: m/z $[M + H]^+$ calcd. for $C_{21}H_{20}NO_3$: 334.1438; found: 334.1421.

2-methyl-9-(4-(trifluoromethyl)phenyl)-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3m**): 71% yield (0.35 mmol scale, 82 mg); white solid; mp: 128–130 °C; R_f = 0.19 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3103, 2972, 1753, 1323, 1132 cm^{-1}; ^{1}H NMR (400.13 MHz) ($CDCl_3$): δ 8.17–8.14 (m, 1 H), 7.76–7.69 (m, 5 H), 7.38–7.33 (m, 2 H), 3.56 (dd, J_1 = 8.8 Hz, J_2 = 8.7 Hz, 1 H), 3.35–3.27 (m, 1 H), 2.95 (dd, J_1 = 17.4 Hz, J_2 = 4.7 Hz, 1 H), 1.51 (d, J = 7.5 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 174.5 (C), 139.5 (C), 137.5 (C), 133.3 (C), 130.9 (C), 128.9 (q, J = 32.4 Hz) (CH), 128.0 (CH), 126.0 (q, J = 3.7 Hz) (CH), 124.8 (CH), 124.5 (q, J = 272.1 Hz) (CH), 124.2 (CH), 119.5 (CH), 114.2 (CH), 113.6 (C), 41.6 (CH), 29.09 (CH_2), 17.0 (CH_3); ^{19}F (376.5 MHz) ($CDCl_3$): δ −62.4; HRMS: m/z $[M + H]^+$ calcd. for $C_{19}H_{15}F_3NO$: 330.1100; found: 330.1084.

(trans)- 2-methyl-1-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**5a**): 62% yield (0.35 mmol scale, 57 mg); yellow wax; R_f = 0.24 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3021, 2919, 1736, 1587, 1452, 1385 cm^{-1}; ^1H NMR (400.13 MHz) (DMSO-d_6): δ = 7.98 (d, *J* = 7.42 Hz, 1 H), 7.58–7.56 (m, 1 H), 7.43–7.37 (m, 4 H), 7.35–7.26 (m, 3 H), 6.27 (s, 1 H), 4.37 (d, *J* = 6.5 Hz, 1 H), 3.28–3.21 (m, 1 H), 3.15 (d, *J* = 7.2, 3 H); ^{13}C NMR (100.6 MHz) (DMSO-d_6): δ 173.4, 146.4, 140.6, 135.3, 130.3, 129.3 (CH), 128.3 (CH), 127.8 (CH), 124.3 (CH), 123.8 (CH), 121.5 (CH), 113.4 (CH), 100.5 (CH), 51.5 (CH), 47.3 (CH), 14.5 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{18}H_{16}NO$: 262.1226; found: 262.1215.

(cis)- 2-methyl-1-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one+ (**5′a**): 12% yield (0.35 mmol scale, 11 mg); yellow wax; R_f = 0.24 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3060, 2919, 1736, 1452, 1386 cm^{-1}; ^1H NMR (400.13 MHz) (DMSO-d_6): δ 8.01–7.97 (m, 1 H), 7.61–7.56 (m, 1 H), 7.36–7.26 (m, 5 H), 7.13–7.10 (m, 2 H), 6.41 (m, 1 H), 4.94 (dd, J_1 = 8.7 Hz, J_2 = 0.83 Hz, 1 H), 3.78–3.70 (m, 1 H), 0.80 (d, *J* = 7.7, 3 H).

(trans)-2-(4-methoxybenzyl)-1-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**5b**): 48% yield (0.35 mmol scale, 62 mg); orange solid; mp: 111–113 °C; R_f = 0.19 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3074, 2918, 1738, 1451, 1384 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.14 (d, *J* = 7.9 Hz, 1 H), 7.48 (d, *J* = 7.3 Hz, 1 H), 7.34–7.21 (m, 5 H), 7.19 (d, *J* = 8.6 Hz, 2 H), 7.02–6.99 (m, 2 H), 6.84–6.80 (m, 2 H), 6.13 (d, *J* = 0.9 Hz, 1 H), 4.30 (dd, J_1 = 5.2 Hz, J_2 = 1.1 Hz, 1 H), 3.78 (s, 3 H), 3.42–3.37 (m, 1 H), 3.25–3.15 (m, 2 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 172.2 (C), 158.7 (C), 145.6 (C), 141.1 (C), 135.3 (C), 130.7 (CH), 130.5 (C), 129.5 (C), 128.9 (CH), 127.7 (CH), 127.4 (CH), 124.3 (CH), 123.8 (CH), 121.0 (CH), 114.3 (CH), 114.1 (CH), 101.5 (CH), 58.8 (CH_3), 55.4 (CH), 43.6 (CH), 34.9 (CH_2); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{25}H_{22}NO_2$: 368.1645; found: 368.1627.

(cis)-2-(4-methoxybenzyl)-1-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**5′b**): 2% yield (0.35 mmol scale, 3 mg); yellow solid; mp: 135–138 °C; R_f = 0.19 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3074, 2919, 1737, 1512, 1452, 1385 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.15 (d, *J* = 7.9 Hz, 1 H), 7.51 (d, *J* = 7.2 Hz, 1 H), 7.36–7.22 (m, 5 H), 6.91–6.89 (m, 2 H), 6.75–6.71 (m, 4 H), 6.24 (s, 1 H), 4.70 (d, *J* = 8.4 Hz, 1 H), 3.88–3.82 (m, 1 H), 3.78 (s, 3 H), 3.17 (dd, J_1 = 15.0 Hz, J_2 = 4.9 Hz, 1 H), 2.43 (dd, J_1 = 15.0 Hz, J_2 = 10.1 Hz, 1 H).

(trans)-2-(furan-2-ylmethyl)-1-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**5c**): 39% yield (0.35 mmol scale, 44.2 mg); red solid; mp: 101–103 °C; R_f = 0.19 (*n*-hexane-EtOAc, 90:10); IR (KBr): 3053, 2197, 1739, 1586, 1453 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.14 (d, *J* = 7.8 Hz, 1 H), 7.49 (d, *J* = 7.2 Hz, 1 H), 7.35–7.24 (m, 6 H), 7.12–7.10 (m, 2 H), 6.28–6.27 (m, 1 H), 6.18 (d, *J* = 0.9 Hz, 1 H), 6.16 (d, *J* = 2.8 Hz, 1 H), 4.35 (dd, J_1 = 5.4 Hz, J_2 = 1.3 Hz, 1 H), 3.43–3.39 (m, 1H), 3.33–3.22 (m, 2 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 171.6 (C), 151.7 (C), 145.3 (C), 142.0 (CH), 140.8 (C), 135.3 (C), 130.6 (C), 129.0 (CH), 127.7 (CH), 127.6 (CH), 124.4 (CH), 123.8 (CH), 121.0 (CH), 114.1 (CH), 110.5 (CH), 108.0 (CH), 101.6 (CH), 56.7 (CH), 44.3 (CH), 28.3 (CH_2); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{22}H_{18}NO_2$: 328.1332; found: 328.1316.

(cis)-2-(furan-2-ylmethyl)-1-phenyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**5′c**): 13% yield (0.35 mmol scale, 15.5 mg); a suitable characterization is not available.

(trans)- 1,2-dimethyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**5d**): 64% yield (0.35 mmol scale, 45 mg); yellow solid; mp: 46–49 °C; R_f = 0.23 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3058, 2918, 1741, 1453, 1384 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.05–8.03 (m, 1 H), 7.51–7.49 (m, 1 H), 7.29–7.23 (m, 2 H), 6.27 (d, *J* = 0.9 Hz, 1 H), 3.08–3.04 (m, 1 H), 2.78–2.71 (m, 1 H), 1.47 (d, *J* = 7.1 Hz, 3 H), 1.45 (d, *J* = 7.5 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 174.0 (C), 147.6 (C), 135.3 (C), 130.5 (C), 124.1 (CH), 123.5 (CH), 120.7 (CH), 113.9 (CH), 99.4 (CH), 50.4 (CH), 36.6 (CH), 18.7 (CH_3), 15.2 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{13}H_{14}NO$: 200.1070; found: 200.1061.

(cis)-1,2-dmethyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**5′d**): 12% yield (0.35 mmol scale, 8 mg); yellow solid; mp: 58–61 °C; R_f = 0.23 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3060, 2917, 1735, 1584, 1453 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.06–8.04 (m, 1 H), 7.52–7.50(m, 1 H), 7.30–7.24 (m, 2 H), 6.29 (s, 1 H), 3.63–3.55 (m, 1 H), 3.31 (quint, *J* = 7.8 Hz, 1 H), 1.34 (d, *J* = 5.7 Hz, 3 H), 1.32 (d, *J* = 5.4 Hz, 3 H).

3.2.7. Typical Procedure for the Preparation of 1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**8**), ethyl 3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indole-2-carboxylate (**11**) and 2-acetyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**13**)

The products 10 and 12 were synthesized according to the typical procedure described for the preparation of 1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-ones using 5 equiv. of 9 and 11, respectively, as a nucleophile instead of 5.

1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**8**): known compound of 52% yield (0.35 mmol scale, 31 mg); grey solid; lit. [44] mp: 150–151 °C, mp: 153–154; R_f = 0.20 (*n*-hexane-EtOAc, 85:15); IR (neat): 2973, 2937, 1722, 1387, 1168 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ = 8.11–8.08 (m, 1 H), 7.53–7.51 (m, 1 H), 7.30–7.28 (m, 2 H), 6.32 (s, 1 H), 3.20–3.17 (m, 2 H), 3.13–3.09 (m, 2 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ = 171.8 (C), 143.7 (C), 135.4 (C), 124.2 (CH), 123.4 (CH), 120.6 (CH), 113.7 (CH), 100.5 (CH), 35.0 (CH_2), 19.7 (CH_2); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{11}H_9NONa$: 194.0576; found: 194.0578.

2-((1H-indol-2-yl)methyl)-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**9**): 54% yield (0.35 mmol scale, 57 mg); purple solid; mp: 164–165 R_f = 0.24 (*n*-hexane-EtOAc, 85:15); IR (neat): 3404, 1715, 1593, 1544, 1173, 667 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.64 (br s, 1 H), 8.02–8.00 (m, 1 H), 7.45 (d, *J* = 7.8 Hz, 1 H), 7.41–7.39 (m, 1 H), 7.25 (d, *J* = 7.8 Hz, 2 H), 7.22–7.17 (m, 2 H), 7.05 (dd, J_1 = 7.3 Hz, J_2 = 1.1 Hz, 1 H), 6.99 (dd, J_1 = 7.3 Hz, J_2 = 1.1 Hz, 1 H), 6.24 (s, 1 H), 6.17 (s, 1 H), 3.52–3.48 (m, 1 H), 3.32–3.28 (m, 1 H), 3.25–3.22 (m, 2 H), 2.92 (dd, J_1 = 16.9 Hz, J_2 = 1.3 Hz, 1 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 174.1, 141.7, 136.6, 135.5, 135.3, 130.5, 128.4, 124.5, 123.6, 121.7, 120.8, 120.1, 119.9, 113.8, 110.9, 101.8, 101.2, 47.1, 29.6, 26.1; HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{20}H_{16}N_2ONa$: 323.1155; found: 323.1154.

ethyl 3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indole-2-carboxylate (**11**): 58% yield (0.35 mmol scale, 49 mg); white solid; mp: 99–100; R_f = 0.23 (*n*-hexane-EtOAc, 80:20); IR (neat): 2991, 2919, 1726, 1596, 1187, 743 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.10–8.08 (m, 1 H), 7.55–7.53 (m, 1 H), 7.33–7.31 (m, 2 H), 6.34 (s, 1 H), 4.25 (dd, J_1 = 7.3 Hz, J_2 = 0.8 Hz, 1 H), 4.22 (dd, J_1 = 7.3 Hz, J_2 = 0.8 Hz, 1 H), 3.68 (dd, J_1 = 17.4 Hz, J_2 = 1.5 Hz, 1 H), 3.07 (dd, J_1 = 17.4 Hz, J_2 = 1.5 Hz, 1 H), 1.72 (s, 3 H), 1.26 (t, *J* = 7.3 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 168.2 (C), 166.1 (C), 141.1 (C), 135.6 (C), 130.6 (C), 124.6 (CH), 123.7 (CH), 120.8 (CH), 113.8 (CH), 101.2 (CH), 62.4 (CH_2), 52.7 (CH), 24.3 (CH_2), 14.2 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{14}H_{14}NO_3$: 244.0868; found: 244.0857.

2-acetyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**13**): 55% yield (0.35 mmol scale, 40 mg); brown solid; mp: 96–97; R_f = 0.21 (*n*-hexane-EtOAc, 85:15); IR (neat): 2916, 2849, 1641, 1454, 1190, 772 cm^{-1}. In a chloroform solution, this compound has as an equilibrium mixture of ketone and enol forms; both tautomers were observed by ^1H NMR, and the peaks of enol form were reported as marked with an asterisk*; ^1H NMR (400.13 MHz) ($CDCl_3$) (ketone: enol = 75/25): δ 11.41* (br s, 1 H) 8.04–7.98 (m, 2 H, aromatic protons of both tautomers), 7.53–7.47 (m, 2 H, aromatic protons of both tautomers), 7.29–7.25 (m, 4 H aromatic protons of both tautomers), 6.32* (br s, 1 H), 6.30 (br s, 1 H), 4.26 (dd, J_1 = 8.7 Hz, J_2 = 4.3 Hz, 1 H), 3.76* (m, 1 H), 3.64* (s, 2 H), 3.17–3.10 (m, 1 H), 2.56 (s, 3 H), 2.06* (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$) (unselected signals): δ 200.2 (C), 169.5 (C), 167.7 (C), 166.5 (C), 141.4 (C), 139.7 (C), 135.6 (C), 134.6 (C), 130.6 (C), 124.7 (CH), 123.8 (CH), 123.7 (CH), 123.2 (CH), 120.9 (CH), 120.8 (CH), 113.7 (CH), 113.5 (CH), 102.7 (C), 101.3 (CH), 100.2 (CH), 60.5 (CH), 29.8 (CH_2), 29.7 (CH_3), 23.6 (CH_2), 21.5 (CH_2), 19.1 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{13}H_{12}NO_2$: 214.0862; found: 214.0887.

2-allyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**3n**): 71% yield (0.35 mmol scale, 52 mg); brown oil; R_f = 0.25 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3081, 2918, 1714, 1454, 1385 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.11–8.09 (m, 1 H), 7.53–7.50 (m, 1 H), 7.32–7.27 (m, 2 H), 6.29 (s, 1 H), 5.89–5.78 (m, 1 H), 5.23–5.11 (m, 2 H), 3.34–3.26 (m, 2 H), 2.96–2.88 (m, 1 H), 2.81–2.75 (m, 1 H), 2.53–2.46 (m, 1 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 173.5 (C), 142.3 (C), 135.5 (C), 134.2 (CH), 130.5 (C), 124.2 (CH), 123.4 (CH), 120.6 (CH), 118.2 (CH_2), 113.8 (CH), 100.5 (CH), 46.2 (CH), 35.8 (CH_2), 25.5 (CH_2); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{14}H_{14}NO$: 212.1070; found: 212.1057.

2-acetyl-2-methyl-1,2-dihydro-3H-pyrrolo[1,2-a]indol-3-one (**15a**): 18% yield (0.35 mmol scale, 14 mg); brown oil; R_f = 0.23 (*n*-hexane-EtOAc, 85:15); IR (KBr): 3073, 2919, 1736, 1714, 1455, 1386 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.05–8.02 (m, 1 H), 7.52–7.50 (m, 1 H), 7.30–7.28 (m, 2 H), 6.32 (s, 1 H), 3.84 (dd, J_1 = 17.6 Hz, J_2 = 1.3 Hz, 1 H), 2.88 (dd, J_1 = 17.6 Hz, J_2 = 1.5 Hz, 1 H), 2.37 (s, 3 H), 1.70 (s, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 203.5 (C), 170.8 (C), 140.0 (C), 135.5 (C), 130.6 (C), 124.6 (CH), 123.7 (CH), 120.8 (CH), 113.8 (CH), 101.4 (CH), 63.9 (C), 30.9 (CH_2), 25.8 (CH_3), 21.9 (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{13}H_{11}NO_2$: 214.0862; found: 214.0887.

ethyl 2-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indole-2-carboxylate (**15b**): 60% yield (0.35 mmol scale, 54 mg); yellow oil; R_f = 0.23 (*n*-hexane-EtOAc, 80:20); IR (KBr): 2984, 2934, 1710, 1602, 1127 cm^{-1}; ^1H NMR (400.13 MHz) ($CDCl_3$): δ 8.10–8.08 (m, 1 H), 7.55–7.53 (m, 1 H), 7.33–7.31 (m, 2 H), 6.34 (s, 1 H), 4.25 (dd, J_1 = 7.3 Hz, J_2 = 0.8 Hz, 1 H), 4.22 (dd, J_1 = 7.3 Hz, J_2 = 0.8 Hz, 1 H), 3.68 (dd, J_1 = 17.4 Hz, J_2 = 1.5 Hz, 1 H), 3.07 (dd, J_1 = 17.4 Hz, J_2 = 1.5 Hz, 1 H), 1.72 (s, 3 H), 1.26 (t, J = 7.3 Hz, 3 H); ^{13}C NMR (100.6 MHz) ($CDCl_3$): δ 168.2 (C), 166.1 (C), 141.1 (C), 135.6 (C), 130.6 (C), 124.6 (CH), 123.7 (CH), 120.8 (CH), 113.8 (CH), 101.2 (CH), 62.4 (CH_2), 52.7 (CH), 24.3 (CH_2), 14.2 (CH_3); HRMS: *m/z* $[M + Na]^+$ calcd. for $C_{15}H_{15}NO_3Na$: 280.0944; found: 280.0943.

7-(1H-indol-2-yl)-6-methyl-5-oxoheptanoic acid (**17**): 47% yield (0.35 mmol scale, 45 mg); red solid; mp: 112–115 °C; R_f = 0.18 (*n*-hexane-EtOAc, 70:30, 10% $MeCO_2H$); IR (neat): 3055, 2951, 1735, 1713, 1456 cm^{-1}; ^1H NMR (400.13 MHz) (DMSO-d_6): δ 12.08 (br s, 1 H), 10.90 (s, 1 H), 7.40 (d, J = 7.8 Hz, 1 H), 7.28 (d, J = 7.9 Hz, 1 H), 7.00 (td, J_1 = 7.1 Hz, J_2 = 1.1 Hz, 1 H), 6.92 (td, J_1 = 7.1 Hz, J_2 = 1.0 Hz, 1 H), 6.11 (d, J = 1.1 Hz, 1 H), 3.04–2.98 (m, 2 H), 2.68–2.56 (m, 2 H), 2.49–2.45 (m, 1 H), 2.17 (t, J = 7.3 Hz, 2 H), 1.66 (quint, J = 7.3 Hz, 2 H), 1.03 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (100.6 MHz) (DMSO-d_6): δ 213.2 (C), 174.7 (C), 138.2 (C), 136.4 (C), 128.7 (C), 120.6 (CH), 119.6 (CH), 119.1 (CH), 111.1 (CH), 99.7 (CH), 45.8 (CH), 39.9 (CH_2), 33.2 (CH_2), 31.2 (CH_2), 19.1 (CH_2), 16.6. (CH_3); HRMS: *m/z* $[M + H]^+$ calcd. for $C_{16}H_{20}NO_3$: 274.1438; found: 274.1425.

4-(2-methyl-1H-pyrrolo[1,2-a]indol-3-yl)butanoic acid (**18**): 22% yield (0.35 mmol scale, 20 mg); red solid; mp: 130–133 °C; R_f = 0.25 (*n*-hexane-EtOAc, 70:30, 10% $MeCO_2H$); IR (KBr): 3102, 2918, 1699, 1485, 1452, 1384 cm^{-1}; ^1H NMR (400.13 MHz) (DMSO-d_6): δ 12.18 (br s, 1 H), 7.48 (d, J = 7.5 Hz, 1 H), 7.43 (d, J = 7.5 Hz, 1 H), 7.30 (t, J = 7.5 Hz, 1 H), 7.06 (t, J = 7.5 Hz, 1 H), 5.83 (s, 1 H), 3.77 (s, 2 H), 2.85 (t, J = 7.5 Hz, 2 H), 2.30 (t, J = 6.9 Hz, 2 H), 2.02 (s, 3 H), 1.76 (quint., J = 7.5 Hz, 2 H); ^{13}C NMR (100.6 MHz) (DMSO-d_6): δ 179.1 (C), 142.0 (C), 135.2 (C), 134.0 (C), 127.5 (CH), 125.9 (CH), 122.3 (CH), 122.2 (C), 120.8 (C), 110.3 (CH), 102.8 (CH), 32.8 (CH_2), 28.7 (CH_2), 24.9 (CH_2), 23.9 (CH_2), 11.6 (CH3); HRMS: *m/z* $[M - H]^-$ calcd. for $C_{16}H_{16}NO_2$: 254.1187; found: 254.1179.

4. Conclusions

In summary, a viable approach to polysubstituted 1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones through a domino palladium-catalyzed reaction of the readily available indol-2-ylmethyl acetates with 1,3-dicarbonyl derivatives has been developed. The employment of 5-substituted Meldrum's as the dicarbonyl source in the palladium-catalyzed reaction with indol-2-ylmethyl acetates method allowed the synthesis of the 2-substituted-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-one derivatives in moderate-to-high yields and tolerates a variety of useful functional groups both in the indole and in Meldrum's acids, including bromo, fluoro, nitro, aryl, heteroaryl ether, and ester groups. The extension of the procedure to the highly diastereoselective synthesis of the *trans*- 1,2-disubstituted-1,2-dihydro-3*H*-pyrrolo[1,2-*a*]indol-3-ones from the (1*H*-indol-2-yl)phenyl acetate under the same reaction conditions has been explored. The product selectivity control of the outcome of the reaction of indol-2-ylmethyl acetate with various alicyclic 1,3-dicarbonyls was addressed by a suitable choice of the reagent ratio. A different cascade reaction of the indol-2-ylmethyl acetate with 2-methylcyclohexan-1,3-dione and the corresponding potassium salt involving Michael addition/retro Dieckmann or/and Michael addition/retro Dieckmann/cyclization

sequences provides promise for further challenging the elaboration of the indole nucleus, and is under investigation in our laboratories.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/catal12121516/s1 [35,45–48].

Author Contributions: Conceptualization: G.F.; Data curation: A.I. and A.G.; Formal analysis: A.S. (Alessio Sferrazza); Funding acquisition: G.F.; Investigation: A.I., S.D., F.M., A.S. (Andrea Serraiocco) and K.U.; Methodology: A.I. and A.S. (Alessio Sferrazza); Project administration: G.F.; Supervision: A.G.; Writing—original draft: A.A.; Writing—review and editing: A.I., A.G. and A.S. (Alessio Sferrazza). All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Data Availability Statement: Not applicable.

Acknowledgments: We gratefully acknowledge "Sapienza", University of Rome, University of L' Aquila, the Catholic University of Sacred Heart, and PRIN project 2017 "Targeting Hedgehog pathway: virtual screening identification and sustainable synthesis of novel Smo and Gli inhibitors and their pharmacological drug delivery strategies for improved therapeutic effects in tumors" (2017SXBSX4), for financial support.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Dethe, D.H.; Erande, R.D.; Ranjan, A. Biomimetic Total Syntheses of Borreverine and Flinderole Alkaloids. *J. Org. Chem.* **2013**, *78*, 10106–10120. [CrossRef] [PubMed]
2. Vallakati, R.; May, J.A. Biomimetic Synthesis of the Antimalarial Flindersial Alkaloids. *J. Am. Chem. Soc.* **2012**, *134*, 6936–6939. [CrossRef] [PubMed]
3. Lucas, S.; Negri, M.; Heim, R.; Zimmer, C.; Hartmann, R.W. Fine-tuning the selectivity of aldosterone synthase inhibitors: Structure-activity and structure-selectivity insights from studies of heteroaryl substituted 1,2,5,6-tetrahydropyrrolo[3,2,1-ij]quinolin-4-one derivatives. *J. Med. Chem.* **2011**, *54*, 2307–2319. [CrossRef]
4. Dethe, D.H.; Erande, R.D.; Ranjan, A. Biomimetic total syntheses of flinderoles B and C. *J. Am. Chem. Soc.* **2011**, *133*, 2864–2867. [CrossRef]
5. Zeldin, R.M.; Toste, F.D. Synthesis of flinderoles B and C by a gold-catalyzed allene hydroarylation. *Chem. Sci.* **2011**, *2*, 1706–1709. [CrossRef]
6. Fernandez, L.S.; Buchanan, M.S.; Carroll, A.R.; Feng, Y.J.; Quinn, R.J.; Avery, V.M. Flinderoles A-C: Antimalarial bis-indole alkaloids from Flindersia species. *Org. Lett.* **2009**, *11*, 329–332. [CrossRef]
7. Galm, U.; Hager, M.H.; Van Lanen, S.G.; Ju, J.; Thorson, J.S.; Shen, B. Antitumor antibiotics: Bleomycin, enediynes, and mitomycin. *Chem. Rev.* **2005**, *105*, 739–758.
8. Wolkenberg, S.E.; Boger, D.L. Mechanisms of in Situ Activation for DNA-Targeting Antitumor Agents. *Chem. Rev.* **2002**, *102*, 2477–2496. [CrossRef]
9. Liu, J.-F.; Jiang, Z.-Y.; Wang, R.-R.; Zheng, Y.-T.; Chen, J.-J.; Zhang, X.-M.; Ma, Y.-B. Isatisine A, a Novel Alkaloid with an Unprecedented Skeleton from Leaves of Isatis indigotica. *Org. Lett.* **2007**, *9*, 4127–4129. [PubMed]
10. Dorow, R.L.; Herrington, P.M.; Hohler, R.A.; Maloney, M.T.; Mauragis, M.A.; McGhee, W.E.; Moeslein, J.A.; Strohbach, J.W.; Veley, M.F. Development of an Efficient Synthesis of the Pyrrolquinolone PHA-529311. *Org. Process. Res. Dev.* **2006**, *10*, 493–499. [CrossRef]
11. Elmegeed, G.A.; Baiuomy, A.R.; Abdel-Salam, O.M. Evaluation of the anti-inflammatory and anti-nociceptive activities of novel synthesized melatonin analogues. *Eur. J. Med. Chem.* **2007**, *42*, 1285–1292. [CrossRef] [PubMed]
12. Protter, A.A.; Chakravarty, S. Compounds and Methods of Treating Hypertension. U.S. Patent WO2012/112961A1, 23 August 2012.
13. Danishefsky, S.; Taniyama, E. Cyclizations of mercury and palladium substituted acyrylanilides. *Tetrahedron Lett.* **1983**, *24*, 15–18. [CrossRef]
14. Duan, X.-Y.; Tian, Z.; Liu, B.; He, T.; Zhao, L.-L.; Dong, M.; Zhang, P.; Qi, J. Highly Enantioselective Synthesis of Pyrroloindolones and Pyrroloquinolinones via an N-Heterocyclic Carbene-Catalyzed Cascade Reaction. *Org. Lett.* **2021**, *23*, 3777–3781. [CrossRef]
15. Yang, W.-L.; Sun, Z.-T.; Sun, H.; Deng, W.-P. Nickel(II)-Catalyzed Diastereo- and Enantioselective [3 + 2] Cycloaddition of α-Ketoesters with 2-Nitrovinylindoles and 2-Nitrovinylpyrroles. *Chin. J. Chem.* **2019**, *37*, 216–220. [CrossRef]
16. Yang, Y.-J.; Ji, Y.; Qi, L.; Wang, G.; Hui, X.-P. Asymmetric Synthesis of Cyclopenta[3,4]pyrroloindolones via N-Heterocyclic Carbene-Catalyzed Michael/Aldol/Lactamization Cascade Reaction. *Org. Lett.* **2017**, *19*, 3271–3274. [CrossRef]
17. Wang, C.; Wang, A.; Rueping, M. Manganese-Catalyzed C−H Functionalizations: Hydroarylations and Alkenylations Involving an Unexpected Heteroaryl Shift. *Angew. Chem. Int. Ed.* **2017**, *56*, 9935–9938. [CrossRef]

18. Ghosh, A.; Bainbridge, D.T.; Stanley, L.M. Enantioselective Model Synthesis and Progress toward the Putative Structure of Yuremamine. *J. Org. Chem.* **2016**, *81*, 7945–7951. [CrossRef]
19. Lu, H.; Lin, J.-B.; Liu, J.-Y.; Xu, P.-F. One-Pot Asymmetric Synthesis of Quaternary Pyrroloindolones through a Multicatalytic N-Allylation/Hydroacylation Sequence. *Chem. Eur. J.* **2014**, *20*, 11659–11663. [CrossRef]
20. Ikemoto, H.; Yoshino, T.; Sakata, K.; Matsunaga, S.; Kanai, M. Pyrroloindolone Synthesis via a Cp*CoIII-Catalyzed Redox-Neutral Directed C–H Alkenylation/Annulation Sequence. *J. Am. Chem. Soc.* **2014**, *136*, 5424–5431. [CrossRef] [PubMed]
21. Ni, Q.; Zhang, H.; Grossmann, A.; Loh, C.C.J.; Merkens, C.; Enders, D. Asymmetric Synthesis of Pyrroloindolones by N-Heterocyclic Carbene Catalyzed [2+3] Annulation of α-Chloroaldehydes with Nitrovinylindoles. *Angew. Chem. Int. Ed.* **2013**, *52*, 13562–13566. [CrossRef]
22. Wang, Y.; Lu, H.; Xu, P.-F. Asymmetric Catalytic Cascade Reactions for Constructing Diverse Scaffolds and Complex Molecules. *Acc. Chem. Res.* **2015**, *48*, 1832–1844. [CrossRef]
23. Arcadi, A.; Cacchi, S.; Fabrizi, G.; Ghirga, F.; Goggiamani, A.; Iazzetti, A.; Marinelli, F. Synthesis of indolo[1,2-*c*]quinazolines from 2-alkynylaniline derivatives through Pd-catalyzed indole formation/cyclization with *N*,*N*-dimethylformamide dimethyl acetal. *Beilstein J. Org. Chem.* **2018**, *14*, 2411–2417. [CrossRef] [PubMed]
24. Arcadi, A.; Blesi, F.; Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Marinelli, F. Multisubstituted benzo[b]furans through a copper- and/or palladium-catalyzed assembly and functionalization process. *Tetrahedron* **2013**, *69*, 1857–1871. [CrossRef]
25. Arcadi, A.; Blesi, F.; Cacchi, S.; Fabrizi, G.; Goggiamani, A.; Marinelli, F. Palladium-Catalyzed Cascade Reactions of 1-(3-Arylprop-2-ynyloxy)-2-bromo Benzene Derivatives with Organoboron Compounds. *J. Org. Chem.* **2013**, *78*, 4490–4498. [CrossRef] [PubMed]
26. Cera, G.; Piscitelli, S.; Chiarucci, M.; Fabrizi, G.; Goggiamani, A.; Ramón, R.S.; Nolan, S.P.; Bandini, M. One-Pot Gold-Catalyzed Synthesis of Azepino[1,2-a]indoles. *Angew. Chem. Int. Ed.* **2012**, *51*, 9891–9895. [CrossRef]
27. Caruana, L.; Mondatori, M.; Corti, V.; Morales, S.; Mazzanti, A.; Fochi, M.; Bernardi, L. Catalytic Asymmetric Addition of Meldrum's Acid, Malononitrile, and 1,3-Dicarbonyls to ortho-Quinone Methides Generated In Situ Under Basic Conditions. *Chem. Eur. J.* **2015**, *21*, 6037–6041. [CrossRef] [PubMed]
28. Arcadi, A.; Calcaterra, A.; Fabrizi, G.; Fochetti, A.; Goggiamani, A.; Iazzetti, A.; Marrone, F.; Mazzoccanti, G.; Serraiocco, A. One-pot synthesis of dihydroquinolones by sequential reactions of o-aminobenzyl alcohol derivatives with Meldrum's acids. *Org. Biomol. Chem.* **2022**, *20*, 3160–3173. [CrossRef]
29. Ouyang, J.; Maji, R.; Leutzsch, M.; Mitschke, B.; List, B. Design of an Organocatalytic Asymmetric (4 + 3) Cycloaddition of 2-Indolylalcohols with Dienolsilanes. *J. Am. Chem. Soc.* **2022**, *144*, 8460–8466. [CrossRef] [PubMed]
30. Tan, W.; Shi, F. A breakthrough in 2-indolylmethanol-involved organocatalytic asymmetric reactions. *Chem. Synth.* **2022**, *2*, 11. [CrossRef]
31. Bera, K.; Schneider, C. Brønsted Acid Catalyzed [3 + 2]-Cycloaddition of Cyclic Enamides with in Situ Generated 2-Methide-2H-indoles: Enantioselective Synthesis of Indolo[1,2-a]indoles. *Org. Lett.* **2016**, *18*, 5660–5663. [CrossRef] [PubMed]
32. Bera, K.; Schneider, C. Brønsted Acid Catalyzed [3 + 2]-Cycloaddition of 2-Vinylindoles with In Situ Generated 2-Methide-2H-indoles: Highly Enantioselective Synthesis of Pyrrolo[1,2-a]indoles. *Chem. Eur. J.* **2016**, *22*, 7074–7078. [CrossRef]
33. Arcadi, A.; Berden, G.; Ciogli, A.; Corinti, D.; Crestoni, M.E.; De Angelis, M.; Fabrizi, G.; Goggiamani, A.; Iazzetti, A.; Marrone, F.; et al. Reactivity of Indolylmethylacetates with N, O, and S Soft Nucleophiles: Evidence of 2-Alkylideneindolenines and 3-Alkylideneindoleninium Generation by ESI-MS and IRMPD Spectroscopy. *Eur. J. Org. Chem.* **2022**, *2022*, e202201166. [CrossRef]
34. Arcadi, A.; Fabrizi, G.; Fochetti, A.; Ghirga, F.; Goggiamani, A.; Iazzetti, A.; Marrone, F.; Mazzoccanti, G.; Serraiocco, A. Palladium-catalyzed Tsuji–Trost-type reaction of benzofuran-2-ylmethyl acetates with nucleophiles. *Rsc. Adv.* **2021**, *11*, 909–917. [CrossRef] [PubMed]
35. Arcadi, A.; Calcaterra, A.; Chiarini, M.; Fabrizi, G.; Fochetti, A.; Goggiamani, A.; Iazzetti, A.; Marrone, F.; Marsicano, V.; Serraiocco, A. Synthesis of Indole/Benzofuran-Containing Diarylmethanes through Palladium-Catalyzed Reaction of Indolylmethyl or Benzofuranylmethyl Acetates with Boronic Acids. *Synthesis* **2022**, *54*, 741–753.
36. Kuwano, R.; Kondo, Y.; Shirahama, T. Transformation of Carbonates into Sulfones at the Benzylic Position via Palladium-Catalyzed Benzylic Substitution. *Org. Lett.* **2005**, *7*, 2973–2975. [CrossRef] [PubMed]
37. Kuwano, R.; Kondo, Y. Palladium-catalyzed benzylation of active methine compounds without additional base: Remarkable effect of 1,5-cyclooctadiene. *Org. Lett.* **2004**, *6*, 3545–3547. [CrossRef]
38. Kuwano, R.; Kondo, Y.; Matsuyama, Y. Palladium-Catalyzed Nucleophilic Benzylic Substitutions of Benzylic Esters. *J. Am. Chem. Soc.* **2003**, *125*, 12104–12105. [CrossRef] [PubMed]
39. *Calculated by HF, 3-21G* in Titan 1.0.1 2000*; Wavefunction Inc.: Irvine, CA, USA, 2000.
40. Rossi, E.; Arcadi, A.; Abbiati, G.; Attanasi, O.A.; De Crescentini, L. Sequential base-promoted annulation/ palladium-catalyzed domino 1,5-enyne arylation and vinylation of alpha-propargylaminohydrazones. *Angew. Chem. Int. Ed.* **2002**, *41*, 1400–1402. [CrossRef]
41. Yu, J.-S.; Espinosa, M.; Noda, H.; Shibasaki, M. Traceless Electrophilic Amination for the Synthesis of Unprotected Cyclic β-Amino Acids. *J. Am. Chem. Soc.* **2019**, *141*, 10530–10537. [CrossRef] [PubMed]
42. Chande, M.S.; Khanwelkar, R.R. Michael addition approach for the synthesis of novel spiro compounds and 2-substituted malonic acid derivatives from Meldrum's acid. *Tetrahedron Lett.* **2005**, *46*, 7787–7792. [CrossRef]
43. Chen, J.-P.; Xu, M.-H. Chiral diene-promoted room temperature conjugate arylation: Highly enantioselective synthesis of substituted chiral phenylalanine derivatives and α,α-di(arylmethyl)acetates. *Org. Biomol. Chem.* **2020**, *18*, 4569–4574. [CrossRef]

44. Saget, T.; König, B. Photocatalytic Synthesis of Polycyclic Indolones. *Chem. Eur. J.* **2020**, *26*, 7004–7007. [CrossRef] [PubMed]
45. Hammoud, S.; Anselmi, E.; Cherry, K.; Kizirian, J.-C.; Thibonnet, J. Synthesis and Reactivity of Oxazinoindolones via Regioselective 6-*exo-dig* Iodolactonization. *Eur. J. Org. Chem.* **2018**, *45*, 6314–6327. [CrossRef]
46. Goriya, Y.; Ramana, C.V. 2-Aroylindoles from o-bromochalcones via Cu (i)-catalyzed SN Ar with an azide and intramolecular nitrene C–H insertion. *Chem. Comm.* **2014**, *50*, 7790–7792. [CrossRef]
47. Collot, V.; Schmitt, M.; Marwah, P. Regiospecific functionalization of indole-2-carboxylates and diastereoselective preparation of the corresponding indolines. *Heterocycles* **1999**, *51*, 2823–2847. [CrossRef]
48. Akunuri, R.; Veerareddy, V.; Kaul, G.; Akhir, A.; Unnissa, T.; Parupalli, R.; Nanduri, S. Synthesis and antibacterial evaluation of (E)-1-(1H-indol-3-yl) ethanone O-benzyl oxime derivatives against MRSA and VRSA strains. *Bioorg. Chem.* **2021**, *116*, 105288. [CrossRef]