JOC The Journal of Organic Chemistry

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J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.7b03017 • Publication Date (Web): 22 Jan 2018

Just Accepted

ACS Publications

The Journal of Organic Chemistry is published by the American Chemical Society.
1155 Sixteenth Street N.W., Washington, DC 20036

Sustainable Radical Cascades to Synthesize Difluoroalkylated Pyrrolo[1,2-*a*]indoles

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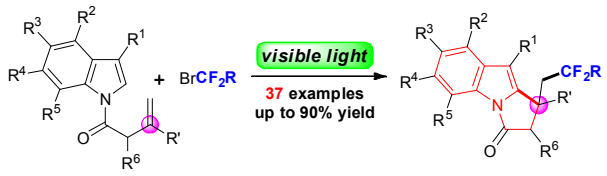


Abstract. We disclosed herein a photocatalytic difluoroalkylation and cyclization cascade reaction of *N*-(but-2-enoyl)indoles with broad substrate scopes in up to 90% isolated yield. This method provides a sustainable and efficient access to synthesize difluoroalkylated pyrrolo[1,2-*a*]indoles with a quaternary carbon center under mild conditions.

Keywords: photoredox; difluoroalkylation; radical cascade; N-(but-2-enoyl)indole; polycycles

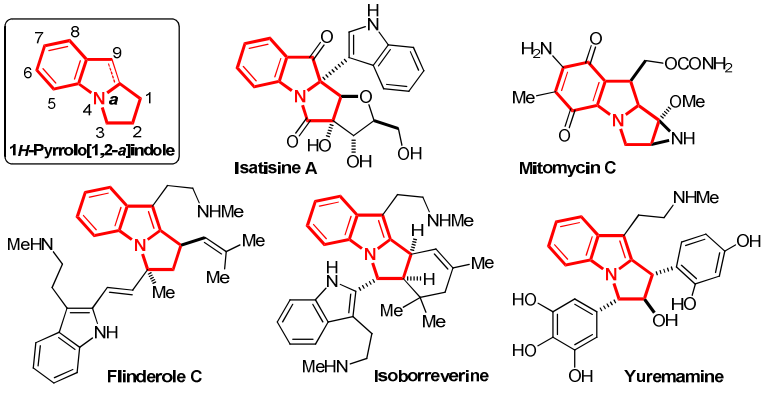
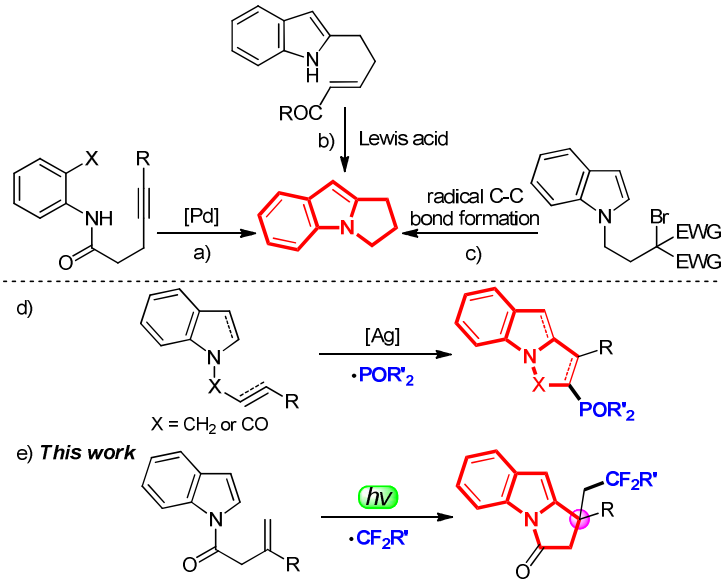


Figure 1 Representative biologically active compounds containing pyrrolo[1,2-*a*]indole motifs.

Pyrrolo[1,2-*a*]indoles are important key structural components that are widely found in a number of natural products and pharmacologically important agents (Figure 1).[1] In this respect, great effort has been devoted to the development of efficient methods toward these unique skeletons.[2] For example, Lu and coworkers reported in 2006 an intresting pallidium-catalyzed intramolecular alkyne insertion protocol to rapidly establish pyrrolo[1,2-*a*]indole skeletons (Scheme 1a).[3] Remarkably, You group accomplished an asymmetric version of pyrrolo[1,2-*a*]indole formation through intramolecular conjugated addition of C2-substituted indoles in the presence of chiral phosphoric acids (Scheme 1b).[4] Meanwhile, radical cascade cyclization has been recognized as an useful organic reaction to convert simple starting materials to complex polycyclic molecules in a single synthetic operation. In 2010, Stephenson et.al. disclosed visible light promoted intramolecular radical C-C bond formation of substituted indoles for accessing a variety of biologically active molecules (Scheme 1c).[5] Notably, Tang group and Song group reported separately silver-mediated oxidative phosphinoylation of substituted indoles to construct a variety of 2-phosphinoyl-pyrrolo[1,2-*a*]indoles under mild conditions (Scheme 1d).[6] While a number of new synthetic methods for pyrroles have been developed in the last decades, the demand for sustainable, simple and robust methods remains high, espacially in terms of formation for multifunctional compounds with general diversity, applicability, and practicality.

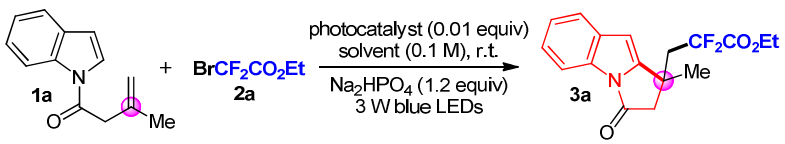


Scheme 1 Examples to construct pyrrolo[1,2-*a*]indole motifs.

Difluoroalkylation reaction is particularly of high significance, through which CF_2 motif could be introduced to molecules and improve molecules' properties dramatically, such as electronegativity, hydrophobicity, metabolic stability, and bioavailability.[7] In addition, the alkyl groups (e.g. CF_2CO_2Et moiety) offered further possibility of postfunctionalization. Recently, visible light-induced photoredox alkylation turns out to be an efficient, sustainable method for introducing the difluoroacetyl functionality.[8] Herein, we envisioned a photoredox difluoroalkylation/cyclization of *N*-(but-2-enoyl)indoles to generate difluoroalkylated pyrrolo[1,2-*a*]indoles notably with one quaternary carbon center (Scheme 1e).

We began our studies by using *N*-(but-2-enoyl)indole **1a** and $BrCF_2CO_2Et$ as model substrates (details for optimizations can be found in Supporting Information). At the beginning, the varies of organophotocatalysts were tested; however all of them failed to launch this transformation (Table 1, entries 1-4). To our great delight, careful optimizations with transtion-metal photocatalysts revealed that *fac*-Ir(ppy)$_3$ was the best catalyst under irradiation of 3 W blue LEDs in the presence of Na_2HPO_4 for 12 hours (Table 1, entry 6). The expected product **3a** was isolated in 71% yield. Other iridium complexes were also tested; however, no better results were achieved (entries 7 and 8). The solvent also affected this transformation significantly. Solvents, such as DMF, DMSO, dioxane or CH_3CN, were examined but did not lead to any improvement (entries 9-12). It is to our surprise that reaction in toluene underwent smoothly with a yield of 33%, as toluene are generally considered to be inactive solvent for photochemistry (entry 13). Gratefully, DCM turned out to be the best solvent for this transformation with a full conversion and 85% isolated yield (entry 14). Therefore, the best reaction conditions were revealed in entry 14 as follows: **1a**, **2a** (2.5 equiv.), *fac*-Ir(ppy)$_3$ (0.01 equiv.) as photocatalyst, Na_2HPO_4 (1.2 equiv.) as the base in DCM (0.1 M) irradiated by 3W blue LEDs for 12 hours.

Table 1 Screening of optimal reaction conditions.

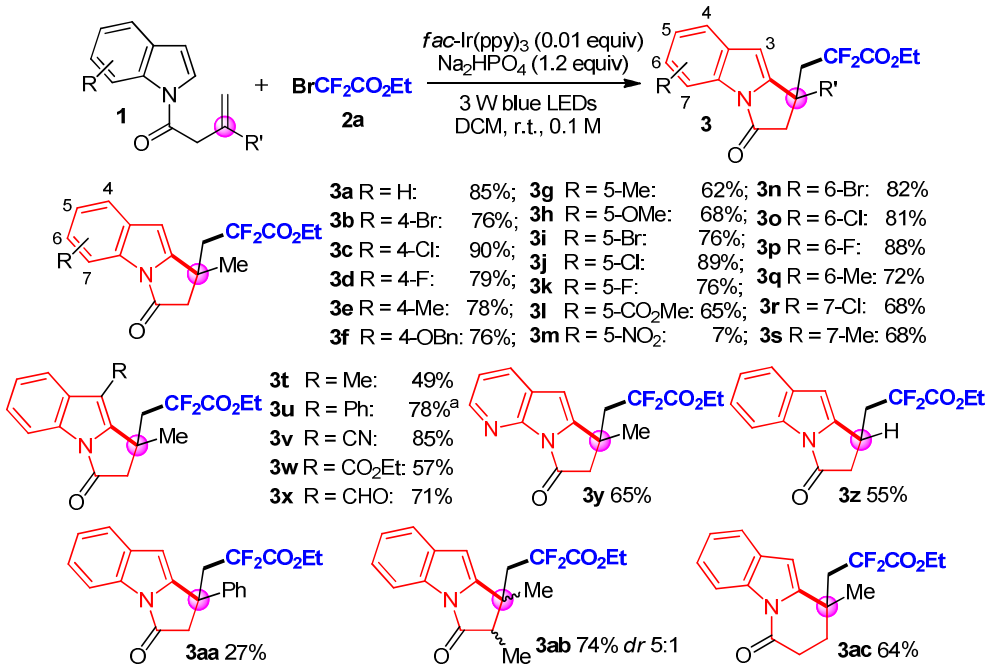


entry[a]	photocatalyst	solvent	**3a**[b]
1	9-fluorenone	THF	n.r.
2	Mehtyl Blue	THF	n.r.
3	Eosin Y	THF	n.r.
4	Eosin B	THF	n.r.
5	$Ru(bpy)_3Cl_2$	THF	n.r.
6	*fac*-$Ir(ppy)_3$	THF	81% (71%)
7	$Ir(dF(CF_3)ppy)_2(bpy)(PF_6)$	THF	25%
8	$Ir(ppy)_2(dtppy)$	THF	n.r.
9	*fac*-$Ir(ppy)_3$	DMF	11%
10	*fac*-$Ir(ppy)_3$	DMSO	48%
11	*fac*-$Ir(ppy)_3$	1,4-dioxane	57%
12	*fac*-$Ir(ppy)_3$	CH_3CN	n.r.
13	*fac*-$Ir(ppy)_3$	toluene	33%
14	***fac*-$Ir(ppy)_3$**	**DCM**	**99% (85%)**

[a]*Reaction conditions*: **1a** (0.2 mmol), $BrCF_2CO_2Et$ **2a** (0.5 mmol), Na_2HPO_4 (0.24 mmol) and photocatalyst (0.002 mmol) in solvent (2 mL) irradiated by 3 W blue LEDs at room temperature for 12 h. [b]Determined by crude ^{19}F NMR with α,α,α-trifluoromethyl benzene as the internal standard. Isolated yields were given in parentheses.

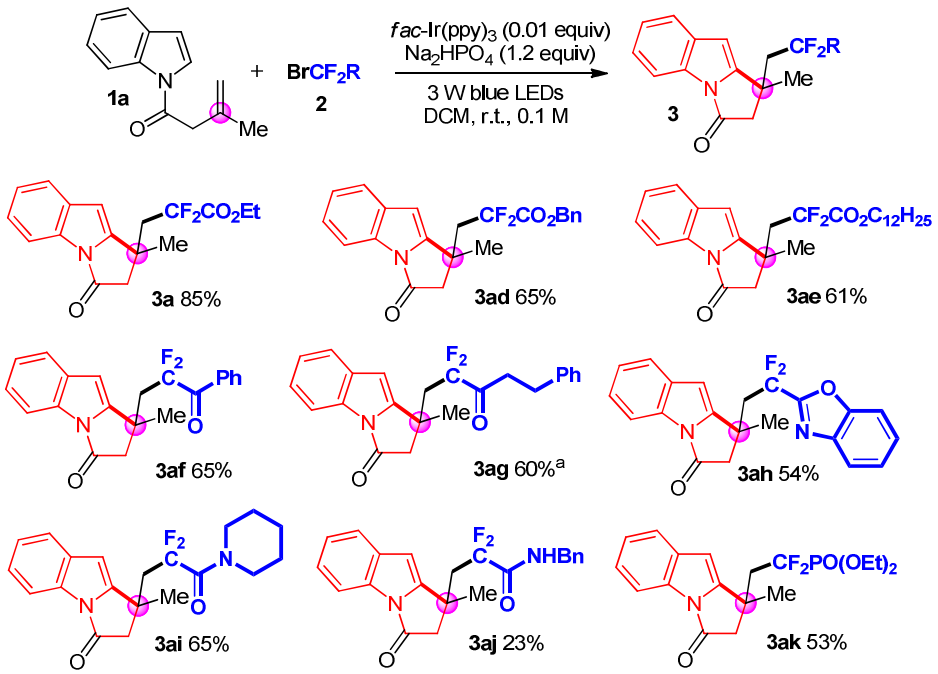
With the optimized conditions in hand, we explore the scope and limitations to this cascade protocol (Scheme 2). Firstly, the substitution patterns on the aromatic ring were studied. Either electron-donating or electron-withdrawing groups were well tolerated on the different positions of the aromatic ring and the desired products were generated in good yields (**3b**-**3q**). Generally, substrates with electron-donating groups showed higher reactivity than those with electron-withdrawing groups (**3b**, **3c** and **3d** *vs* **3e** and **3f**; **3i-3l** *vs* **3g** and **3h**; **3n-3p** *vs* **3q**). However, **3m** with 5-nitro substituent was obtained in a yield of 7% probably because the substrate **1m** was not stable when applied to the

standard conditions. We then examine the substituents on the hetero-aromatic ring. To our delight, phenyl substitute, methyl substitute, cyano substitute, ester substitute and formyl substitute on the 3-position of the hetero-aromatic ring were also compatible (**3t-3x**, 49%-85% yields). The partially decreased yield of **3r** (49%) might be due to the steric hinder effect of the methyl group. Moreover, our attempt to apply substrate with 7-azoindole motif instead of indole was successes and the desired product **3y** was obtained in a yield of 65%. Our further attempts to modify the terminal olefin motif were carried out. Applying hydrogen and phenyl group instead of methyl group on the olefin motif, the corresponding products **3z** and **3aa** were also generated smoothly, albeit with decreased yields of 55% and 27%. We reasoned that the decreased yield of **3z** might due to that hydrogen group are weak substituent to stablize intermediate **I** (as proposed in Scheme 6). Phenyl group, on the other side, was too steric hinder to fulfil the step from intermediate **I** to **II**. 1-(1*H*-Indol-1-yl)-2,3-dimethylbut-3-en-1-one (**1ab**), with a methyl substituent attached on the α-carbon of the carbonyl unit, was conducted also and transformed to the desired product **3ab** in a good yield of 74% with a *dr* ratio of 5 to 1. Notably, when we conducted substrate **1ac** with longer chain number olefin, the difluoroalkylated product **3ac**, with an interesting tetrahydropyrido[1,2-*a*]indole skeleton, was generated in a reasonable yield of 64%.



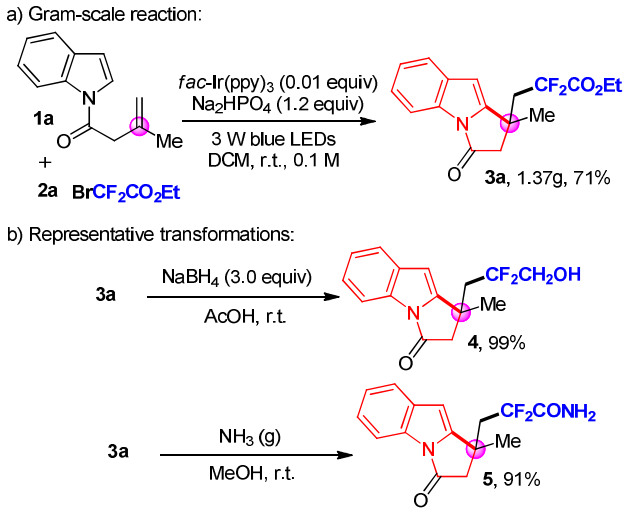
Scheme 2 *Reaction conditions*: **1** (0.2 mmol), $BrCF_2CO_2Et$ **2a** (0.5 mmol), Na_2HPO_4 (0.24 mmol) and *fac*-Ir(ppy)$_3$ (0.002 mmol) in DCM (2 mL) irradiated by 3 W blue LEDs at room temperature for 12 h. Isolated yields were reported. [a]$CHCl_3$ as the solvent.

Subsequently, we evaluated the scope of difluoroalkyl bromides (Scheme 3). An array of bromodifluoroacetates (**3a**, **3ad** and **3ae**), bromodifluoromethyl ketones (**3af**, **3ag** and **3ah**), bromodifluoroacetamides (**3ai** and **3aj**) and bromodifluoromethyl phosphonate (**3ak**) were found to be compatible substrates, therefore yielding the corresponding products in moderate to good yields. As **3ag** was provided in a yield of 41% when CH_2Cl_2 was used as the solvent, we then switched the solvent to chloroform, which can afford almost equivalent result to CH_2Cl_2 during the optimizations (details in SI). Gratefully, **3ag** was generated in 60% yield with chloroform as solvent. Notably, reaction of **1a** with **2h** gave **3aj** in a relatively low yield of 23%, and we reasoned that the free *N*-hydrogen might quench the excited state photocatalyst.

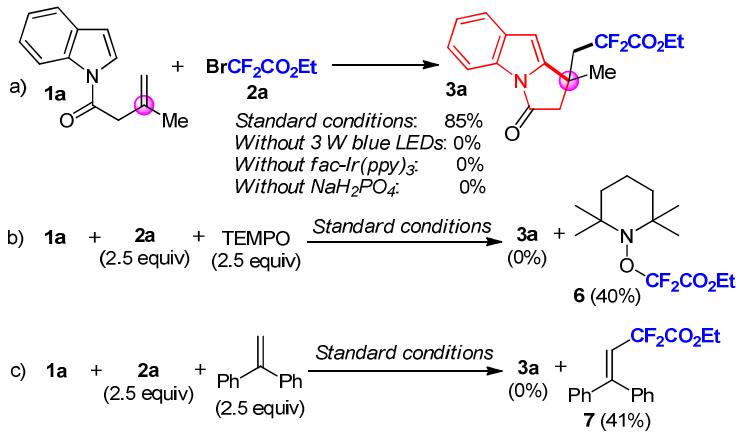


Scheme 3 *Reaction conditions*: **1a** (0.2 mmol), **2** (0.5 mmol), Na_2HPO_4 (0.24 mmol) and *fac*-Ir(ppy)$_3$ (0.002 mmol) in DCM (2 mL) irradiated by 3 W blue LEDs at room temperature for 12 h. Isolated yields were reported. [a]$CHCl_3$ as the solvent.

In order to demonstrate the potential synthetic utility of this method, a gram-scale experiment with **1a** was conducted which yielded **3a** in a reasonable isolated yield of 71% (1.37 g, Scheme 4a). Further transformations of the difluoroalkylation product **3a** were explored to realize postfunctionalizations of the CO_2Et group (Scheme 4b). **3a** can be easily reduced to the difluoroalkyl alcohol **4** in a quantitative yield after simple reduction. Furthermore, the corresponding difluoroalkyl amide **5** could be obtained in a suitable yield of 91%.



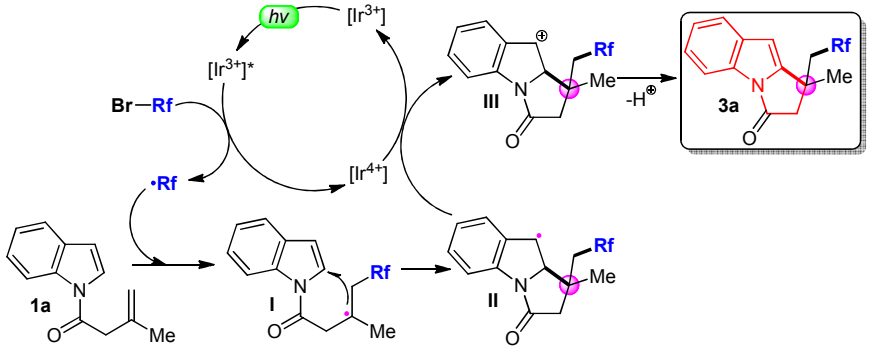
Scheme 4 Synthetic utility of **3a**.



Scheme 5 Mechanistic studies.

To gain insight into the mechanism of this cascade cyclization, control experiments were carried out. Irradiated by visible light, the addition of both photocatalyst and base are crucial for this

transformation (Scheme 5a). We then conducted radical trapping experiments to investigate the possibility of a radical pathway. Experiments were performed with the addition of radical scavenger (2,2,6,6-tetramethyl-1-piperidinoxyl (TEMPO, 2.5 equiv.) or 1,1-diphenylethylene (2.5 equiv)) to the standard reaction of **1a** (Scheme 5b and 5c). The formation of **3a** was totally inhibited with the observations of difluoroalkyl radical trapping compounds. These results confirmed the involvement of a free radical pathway in this transformation. We also calculated the apparent quantum yield of the model transformation with **1a** (details found in the SI). A value of (1.53×10^{-3}) unambiguously indicates that this protocol proceeds *via* a photocatalytic pathway rather than radical propagation.



Scheme 6 Proposed mechanism.

Based on these preliminary studies, we proposed a reaction mechanisum as following (Scheme 6, take the formation of **3a** for example). Irradiated by visible light, the photocatalyst [Ir^{3+}] transfer to an excited state which is subsequently oxidized by RfBr to give [Ir^{4+}] complex and Rf radical. The addition of Rf radical to **1a** produce intermediate **I**. Intromelacular radical cyclizition on C2 of the indole ring deliver intermediate **II** which is subsequently oxidized by [Ir^{4+}] complex to form the intermediate **III** and regenerate the [Ir^{3+}] catalyst. Finally, deprotonation of this cationic intermediate **III** by base eventually yields the terminal product **3a**.

In conclusion, we have developed an efficient procedure to generate a wide range of difluoroalkylated pyrrolo[1,2-*a*]indoles with one quaternary carbon center through visible-light-mediated radical difluoroalkylation/cyclization. This sustainable strategy has attracted special attention due to its commendable functional group tolerance, operational simplicity, and good to high yields under mild conditions. Moreover, these products, difluoroalkylated pyrrolo[1,2-*a*]indoles, could be of importance in medicinal and synthetic chemistry.

Experimental Section

General Information: Unless otherwise stated, all reactions utilizing air-sensitive reagents were carried out in flame-dried glassware under nitrogen. All solvents were purified and dried according to standard methods prior to use. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded on a BRUKER 400 MHz spectrometer in deuterated solvent. ^{1}H NMR chemical shifts are reported in ppm with internal TMS signal at 0.0 ppm as a standard. The data is reported as (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or unresolved, brs = broad singlet, coupling constant(s) in Hz, integration). ^{13}C NMR spectra were recorded in deuterated solvent. Chemical shifts are reported in ppm with internal solvent signal as standard. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as the external standard. ^{31}P NMR chemical shifts were determined relative to H_3PO_4 (85%) as the external standard. HRMS were obtained on Bruker Compact Q-TOF and Waters GCT-TOF. IR measurements were conducted on Nicolet is 50 KBr pelleting method. Known substrates **2b-2e**[9], **2f**[10], **2g-2h**[11] were prepared according to literature procedures.

General Procedure A for the Synthesis of 1a-1k, 1n-1u, 1y-1ac: To a solution of indole (2 mmol) in AcOH (5 mL) at room temperature was added $NaBH_3CN$ (6 mmol, 377 mg). The reaction was stirred at the room temperature for 2-4 h until the disappearance of indole confirmed by TLC, then H_2O was added to reaction mixture and pH value of the reaction was adjusted to 9-10 by adding saturated aqueous NaOH. Then reaction mixture was diluted with EtOAc, washed with brine and H_2O; and dried over anhydrous Na_2SO_4. Removal of the solvent provided intermediate indoline, which was used without further purification. 3-Methylbut-3-enoyl chloride (4 mmol, 474 mg) was added to a stirred suspension of K_2CO_3 (4 mmol, 553 mg) in distilled water (5 mL) and acetone (20 mL) at 0 °C, and intermediate indoline was added dropwise into the mixture. The suspension was stirred at 0 °C, until the disappearance of intermediate indoline confirmed by TLC. The mixture was concentrated under reduced pressure and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, concentrated under reduced pressure to give intermediate 1-(indolin-1-yl)-3-methylbut-3-en-1-one. Then 1-(indolin-1-yl)-3-methylbut-3-en-1-one was dissolved in dry toluene (15 mL) in a round bottomed flask equipped with a reflux condenser and DDQ (5 mmol, 1.13 g) was added. The reaction mixture was refluxed for 12 hours. The reaction was then cooled to room temperature, diluted with

EtOAc, washed with water and brine, dried over anhydrous Mg_2SO_4. The solvent was removed in vacuo and the crude reaction mixture was purified by flash column chromatography on silica gel to give **1a-1k, 1n-1u, 1y-1ac (**three steps).

General Procedure B for the Synthesis of 1l, 1m, 1w-1x: 3-Methylbut-3-enoyl chloride (4 mmol, 474 mg) was added to a stirred suspension of K_2CO_3 (4 mmol, 553 mg) in distilled water (5 mL) and acetone (20 mL) at 0 °C, and indole (2 mmol) was added dropwise into the mixture. The suspension was stirred at 0 °C, until the disappearance of indole confirmed by TLC. The mixture was concentrated under reduced pressure and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, The solvent was removed in vacuo and the crude reaction mixture was purified by flash column chromatography on silica gel to give **1l**, **1m**, **1w-1x**.

Characterization of New Substrates. *1-(Indol-1-yl)-3-methylbut-3-en-1-one* **(1a)**. According to general procedure A with indole and 3-methylbut-3-enoyl chloride, **1a** was obtained in 72% yield (287 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, *J* = 8.3 Hz, 1H, Ar-*H*), 7.61 (d, *J* = 7.7 Hz, 1H, Ar-*H*), 7.48 (t, *J* = 2.9 Hz, 1H, Ar-*H*), 7.41 (t, *J* = 7.9 Hz, 1H, Ar-*H*), 7.33 (td, *J* = 7.5, 1.9 Hz, 1H, Ar-*H*), 6.66 (t, *J* = 2.9 Hz, 1H, Ar-*H*), 5.09 (s, 1H, C=C*H*H), 4.96 (s, 1H, C=CH*H*), 3.66 (s, 2H, COCH_2), 1.94 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 138.6, 135.7, 130.4, 125.2, 125.1, 123.8, 120.8, 116.8, 115.4, 109.2, 45.4, 22.7; HRMS (ESI) exact mass calculated for $C_{13}H_{14}NO^+$ [M+H$^+$]: 200.1070, found: 200.1071; IR (neat): ν_{max} (cm^{-1}) = 1701, 1654, 1554, 1449, 1362, 1122, 924, 754; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(4-Bromo-indol-1-yl)-3-methylbut-3-en-1-one (**1b**). According to general procedure A with 4-bromo-indole and 3-methylbut-3-enoyl chloride, **1b** was obtained in 30% yield (138 mg, white solid, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 8.3 Hz, 1H, Ar-*H*), 7.55 (d, *J* = 3.9 Hz, 1H, Ar-*H*), 7.47 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.25 (t, *J* = 8.1 Hz, 1H, Ar-*H*), 6.74 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.09 (s, 1H, C=C*H*H), 4.95 (s, 1H, C=CH*H*), 3.67 (s, 2H, COCH_2), 1.92 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 138.3, 136.0, 131.0, 126.7, 126.2, 125.6, 115.8, 115.6, 114.6, 109.0, 45.4, 22.6; HRMS (ESI) exact mass calculated for $C_{13}H_{13}BrNO^+$ [M+H$^+$]: 278.0175, found: 278.0178; IR (neat): ν_{max} (cm^{-1}) = 1709, 1623, 1533, 1470, 1420, 1246, 822, 750; m.p. = 50-52 ^{o}C; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(4-Chloro-indol-1-yl)-3-methylbut-3-en-1-one (**1c**). According to general procedure A with 4-chloro-indole and 3-methylbut-3-enoyl chloride, **1c** was obtained in 49% yield (343 mg, white solid, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (s, 1H, Ar-*H*), 7.49 (d, *J* = 3.9 Hz, 1H, Ar-*H*), 7.33-7.25 (m, 2H, 2(Ar-*H*)), 6.75 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.08 (s, 1H, C=CH*H*), 4.95 (s, 1H, C=C*H*H), 3.64 (s, 2H, COCH_2), 1.92 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 138.3, 136.3, 129.1, 126.0, 125.9, 125.6, 123.6, 115.6, 115.2, 107.1, 45.3, 22.6; HRMS (ESI) exact mass calculated for $C_{13}H_{13}ClNO^+$ [M+H$^+$]: 234.0680, found: 234.0683; IR (neat): ν_{max} (cm^{-1}) = 1712, 1611, 1550, 1423, 1340, 1246, 895, 750; m.p. = 60-61 ^{o}C; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(4-Fluoro-indol-1-yl)-3-methylbut-3-en-1-one (**1d**). According to general procedure A with 4-fluoro-indole and 3-methylbut-3-enoyl chloride, **1d** was obtained in 35% yield (153 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (d, *J* = 8.3 Hz, 1H, Ar-*H*), 7.46 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.31 (td, *J* = 8.2, 5.5 Hz, 1H, Ar-*H*), 6.99 (dd, *J* = 9.6, 8.1 Hz, 1H, Ar-*H*), 6.75 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.09 (s, 1H, C=C*H*H), 4.95 (s, 1H, C=CH*H*), 3.66 (s, 2H, COCH_2), 1.92 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 155.6 (d, *J* = 248.0 Hz), 138.3, 137.7 (d, *J* = 9.2 Hz), 126.0 (d, *J* = 7.3 Hz), 125.0, 119.1 (d, *J* = 21.9 Hz), 115.5, 112.8 (d, *J* = 3.9 Hz), 109.1 (d, *J* = 18.4 Hz), 104.6, 45.4, 22.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -(121.94-121.98) (m); HRMS (ESI) exact mass calculated for $C_{13}H_{13}FNO^+$ [M+H$^+$]: 218.0976, found: 218.0978; IR (neat): ν_{max} (cm^{-1}) = 1708, 1599, 1543, 1485, 1432, 1214, 789, 744; R_f = 0.3 (petroleum ether/EtOAc 30:1).

3-Methyl-1-(4-methyl-indol-1-yl)but-3-en-1-one (**1e**). According to general procedure A with 4-methyl-indole and 3-methylbut-3-enoyl chloride, **1e** was obtained in 58% yield (245 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.2 Hz, 1H, Ar-*H*), 7.49 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.35-7.23 (m, 1H, Ar-*H*), 7.12 (d, *J* = 7.3 Hz, 1H, Ar-*H*), 6.70 (d, *J* = 3.7 Hz, 1H, Ar-*H*), 5.20-5.04 (m, 1H, C=C*H*H), 4.96 (s, 1H, C=CH*H*), 3.67 (s, 2H, COCH_2), 2.56 (s, 3H, Ar-CH_3), 1.93 (s, 3H, CH_2=CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 138.7, 135.5, 130.2, 130.0, 125.3, 124.6, 124.3, 115.3, 114.3, 107.5, 45.3, 22.7, 18.5; HRMS (ESI) exact mass calculated for $C_{14}H_{16}NO^+$ [M+H$^+$]: 214.1226, found: 214.1228; IR (neat): ν_{max} (cm^{-1}) = 1703, 1643, 1540, 1486, 1420, 1264, 735, 704; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(4-(Benzyloxy)-indol-1-yl)-3-methylbut-3-en-1-one (**1f**). According to general procedure A with 4-benzyloxy-indole and 3-methylbut-3-enoyl chloride, **1f** was obtained in 37% yield (282 mg, white solid, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.3 Hz, 1H, Ar-*H*), 7.52 (d, *J* = 6.9 Hz, 2H, 2(Ar-*H*)), 7.47-7.35 (m, 4H, 4(Ar-*H*)), 7.31 (t, *J* = 8.1 Hz, 1H, Ar-*H*), 6.89-6.79 (m, 2H, 2(Ar-*H*)), 5.24 (s, 2H, Ar-CH_2), 5.15-5.04 (m, 1H, C=C*H*H), 4.96 (s, 1H, C=CH*H*), 3.66 (s, 2H, COCH_2), 1.93 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 151.9, 138.5, 137.1, 137.0, 128.6, 127.9, 127.4, 126.1, 123.5, 120.9, 115.4, 110.1, 106.4, 105.8, 70.1, 45.5, 31.0, 22.6; HRMS (ESI) exact mass calculated for $C_{20}H_{20}NO_2^+$ [M+H$^+$]: 306.1489, found: 306.1491; IR (neat): ν_{max} (cm^{-1}) = 1706, 1629, 1554, 1488, 1432, 1242, 744, 695; m.p. = 38-40 ^{o}C; R_f = 0.3 (petroleum ether/EtOAc 20:1).

3-Methyl-1-(5-methyl-indol-1-yl)but-3-en-1-one (**1g**). According to general procedure A with 5-methyl-indole and 3-methylbut-3-enoyl chloride, **1g** was obtained in 37% yield (156 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.44 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.39 (s, 1H, Ar-*H*), 7.22 (dd, *J* = 8.4, 1.7 Hz, 1H, Ar-*H*), 6.59 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.08 (s, 1H, C=C*H*H), 4.95 (s, 1H, C=CH*H*), 3.64 (s, 2H, COCH_2), 2.49 (s, 3H, Ar-CH_3), 1.93 (s, 3H, CH_2=CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 138.7, 133.9, 133.4, 130.6, 126.5, 125.1, 120.8, 116.3, 115.2, 109.0, 45.3, 22.6, 21.4; HRMS (ESI) exact mass calculated for $C_{14}H_{16}NO^+$ [M+H$^+$]: 214.1226, found: 214.1228; IR (neat): ν_{max} (cm^{-1}) = 1697, 1552, 1497, 1466, 1372, 1203, 809, 716; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(5-Methoxy-indol-1-yl)-3-methylbut-3-en-1-one (**1h**). According to general procedure A with 5-methoxy-indole and 3-methylbut-3-enoyl chloride, **1h** was obtained in 52% yield (237 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, *J* = 9.0 Hz, 1H, Ar-*H*), 7.44 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.05 (d, *J* = 2.6 Hz, 1H, Ar-*H*), 6.99 (dd, *J* = 9.0, 2.5 Hz, 1H, Ar-*H*), 6.57 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.06 (s, 1H, C=C*H*H), 4.99-4.81 (m, 1H, C=CH*H*), 3.87 (s, 3H, Ar-OCH_3), 3.61 (s, 2H, COCH_2), 1.88 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 156.6, 138.7, 131.4, 130.4, 125.7, 117.5, 115.2, 113.5, 109.0, 103.6, 55.6, 45.1, 22.6; HRMS (ESI) exact mass calculated for $C_{14}H_{16}NO_2^+$ [M+H$^+$]: 230.1176, found: 230.1178; IR (neat): ν_{max} (cm^{-1}) = 1698, 1611, 1559, 1473, 1339, 1147, 811, 715; R_f = 0.3 (petroleum ether/EtOAc 25:1).

1-(5-Bromo-indol-1-yl)-3-methylbut-3-en-1-one (**1i**). According to general procedure A with 5- bromo -indole and 3-methylbut-3-enoyl chloride, **1i** was obtained in 65% yield (261 mg, white solid, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (d, *J* = 8.7 Hz, 1H, Ar-*H*), 7.69 (d, *J* = 2.0 Hz, 1H, Ar-*H*), 7.53-7.38 (m, 2H, 2(Ar-*H*)), 6.57 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.08 (s, 1H, C=C*H*H), 4.94 (s, 1H, C=CH*H*), 3.63 (s, 2H, COCH_2), 1.91 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 138.3, 134.3, 132.0, 128.0, 126.1, 123.5, 118.1, 117.1, 115.5, 108.3, 45.3, 22.6; HRMS (ESI) exact mass calculated for $C_{13}H_{13}BrNO^+$ [M+H$^+$]: 278.0175, found: 278.0177; IR (neat): ν_{max} (cm^{-1}) = 1705, 1623, 1559, 1433, 1336, 1197, 794, 715; m.p. = 44-45 ^{o}C; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(5-Chloro-indol-1-yl)-3-methylbut-3-en-1-one (**1j**). According to general procedure A with 5-chloro-indole and 3-methylbut-3-enoyl chloride, **1j** was obtained in 75% yield (440 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.9 Hz, 1H, Ar-*H*), 7.55 (d, *J* = 2.1 Hz, 1H, Ar-*H*), 7.51 (d, *J* = 3.7 Hz, 1H, Ar-*H*), 7.33 (dd, *J* = 8.9, 2.1 Hz, 1H, Ar-*H*), 6.60 (d, *J* = 3.7 Hz, 1H, Ar-*H*), 5.08 (d, *J* = 2.3 Hz, 1H, C=C*H*H), 5.01-4.87 (m, 1H, C=CH*H*), 3.65 (s, 2H, COCH_2), 1.92 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 138.3, 134.0, 131.5, 129.4, 126.3, 125.3, 120.4, 117.7, 115.5, 108.5, 45.3, 22.6; HRMS (ESI) exact mass calculated for $C_{13}H_{13}ClNO^+$ [M+H$^+$]: 234.0680, found: 234.0682; IR (neat): ν_{max} (cm^{-1}) = 1702, 1624, 1557, 1445, 1370, 1182, 797, 715; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(5-Fluoro-indol-1-yl)-3-methylbut-3-en-1-one (**1k**). According to general procedure A with 5-fluoro-indole and 3-methylbut-3-enoyl chloride, **1k** was obtained in 32% yield (138 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (dd, *J* = 9.0, 4.8 Hz, 1H, Ar-*H*), 7.53 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.24 (dd, *J* = 8.7, 2.6 Hz, 1H, Ar-*H*), 7.17-7.05 (m, 1H, Ar-*H*), 6.62 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.08 (s, 1H, C=C*H*H), 5.00-4.89 (m, 1H, C=CH*H*), 3.66 (s, 2H, COCH_2), 1.91 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 159.7 (d, *J* = 240.2 Hz), 138.5, 132.1, 131.3 (d, *J* = 10.0 Hz), 126.6, 117.7 (d, *J* = 9.0 Hz), 115.4, 112.8 (d, *J* = 24.7 Hz), 108.8 (d, *J* = 4.0 Hz), 106.4 (d, *J* = 23.8 Hz), 45.2, 22.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -(115.51-116.58) (d, *J* = 5.9 Hz); HRMS (ESI) exact mass calculated for $C_{13}H_{13}FNO^+$ [M+H$^+$]: 218.0976, found: 218.0980; IR (neat): ν_{max} (cm^{-1}) = 1701, 1465, 1445, 1378, 1346, 1243, 814, 718; R_f = 0.3 (petroleum ether/EtOAc 30:1).

Methyl 1-(3-methylbut-3-enoyl)-indole-5-carboxylate **(1l)**. According to general procedure B with methyl indol-5-carboxylate and 3-methylbut-3-enoyl chloride, **1l** was obtained in 19% yield (103 mg, white solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.8 Hz, 1H, Ar-*H*), 8.30 (t, *J* = 1.7 Hz, 1H, Ar-*H*), 8.06 (dd, *J* = 8.8, 1.5 Hz, 1H, Ar-*H*), 7.54 (dd, *J* = 3.8, 1.7 Hz, 1H, Ar-*H*), 6.70 (dd, *J* = 4.0, 2.1 Hz, 1H, Ar-*H*), 5.08 (s, 1H, C=C*H*H), 4.95 (s, 1H, C=CH*H*), 3.96 (s, 3H, CO_2CH_3), 3.66 (s, 2H, $COCH_2$), 1.91 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 167.3, 138.2, 130.1, 126.5, 126.3, 125.7, 123.0, 116.3, 115.6, 109.5, 100.0, 52.1, 45.4, 22.6; HRMS (EI) exact mass calculated for $C_{15}H_{15}NO_3^+$ [M^+]: 257.1046, found: 257.1046; IR (neat): ν_{max} (cm^{-1}) = 1710, 1612, 1540, 1436, 1374, 1204, 777, 756; m.p. = 68-70 °C; R_f = 0.3 (petroleum ether/EtOAc 15:1).

3-Methyl-1-(5-nitro-indol-1-yl)but-3-en-1-one **(1m)**. According to general procedure B with *5-nitro*-indole and 3-methylbut-3-enoyl chloride, **1m** was obtained in 65% yield (318 mg, yellow solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, *J* = 9.1 Hz, 1H, Ar-*H*), 8.51 (d, *J* = 2.2 Hz, 1H, Ar-*H*), 8.27 (dd, *J* = 9.1, 2.3 Hz, 1H, Ar-*H*), 7.67 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 6.81 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.12 (s, 1H, C=C*H*H), 4.97 (s, 1H, C=CH*H*), 3.70 (s, 2H, $COCH_2$), 1.94 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 144.4, 138.6, 137.9, 130.2, 127.9, 120.4, 117.0, 116.9, 115.9, 109.5, 45.4, 22.6; HRMS (EI) exact mass calculated for $C_{13}H_{12}N_2O_3^+$ [M^+]: 244.0845, found: 244.0845; IR (neat): ν_{max} (cm^{-1}) = 1718, 1515, 1443, 1333, 1308, 1192, 790, 743; m.p. = 39-40 °C; R_f = 0.3 (petroleum ether/EtOAc 15:1).

1-(6-Bromo-indol-1-yl)-3-methylbut-3-en-1-one (**1n**). According to general procedure with 6-bromo-indole and 3-methylbut-3-enoyl chloride, **1n** was obtained in 50% yield (414 mg, colorless oil, three steps) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 1.3 Hz, 1H, Ar-*H*), 7.42 (d, *J* = 3.9 Hz, 1H, Ar-*H*), 7.39 (d, *J* = 1.5 Hz, 2H, 2(Ar-*H*)), 6.58 (dd, *J* = 3.8, 0.8 Hz, 1H, Ar-*H*), 5.12-5.02 (m, 1H, C=C*H*H), 4.93 (t, *J* = 1.2 Hz, 1H, C=CH*H*), 3.61 (s, 2H, $COCH_2$), 1.90 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 138.3, 136.2, 129.1, 127.0, 125.6, 121.8, 120.0, 118.8, 115.5, 108.9, 45.2, 22.6; HRMS (ESI) exact mass calculated for $C_{13}H_{13}BrNO^+$ [$M+H^+$]: 278.0175, found: 278.0179; IR (neat): ν_{max} (cm^{-1}) = 1705, 1612, 1578, 1448, 1424, 1339, 885, 809; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(6-Chloro-1-indol-yl)-3-methylbut-3-en-1-one (**1o**). According to general procedure A with 6-chloro-indole and 3-methylbut-3-enoyl chloride, **1o** was obtained in 73% yield (344 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 (s, 1H, Ar-*H*), 7.49 (d, *J* = 8.0 Hz, 2H, 2(Ar-*H*)),

7.42-7.18 (m, 1H, Ar-*H*), 6.62 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.08 (s, 1H, C=C*H*H), 4.95 (s, 1H, C=CH*H*), 3.65 (s, 2H, COCH_2), 1.92 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 138.3, 135.9, 131.1, 128.7, 125.6, 124.4, 121.4, 117.0, 115.5, 108.9, 45.3, 22.6; HRMS (ESI) exact mass calculated for $C_{13}H_{13}ClNO^+$ [M+H$^+$]: 234.0680, found: 234.0683; IR (neat): ν_{max} (cm^{-1}) = 1707, 1621, 1567, 1427, 1343, 895, 812, 782; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(6-Fluoro-indol-1-yl)-3-methylbut-3-en-1-one (**1p**). According to general procedure A with 6-fluoro-indole and 3-methylbut-3-enoyl chloride, **1p** was obtained in 63% yield (407 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 10.3, 2.4 Hz, 1H, Ar-*H*), 7.54-7.39 (m, 2H, 2(Ar-*H*)), 7.04 (td, *J* = 8.9, 2.4 Hz, 1H, Ar-*H*), 6.60 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.07 (t, *J* = 1.5 Hz, 1H, C=C*H*H), 5.00-4.85 (m, 1H, C=CH*H*), 3.62 (s, 2H, COCH_2), 1.91 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 161.3 (d, *J* = 240.6 Hz), 138.3, 135.7 (d, *J* = 13.0 Hz), 126.6 (d, *J* = 1.7 Hz), 125.4 (d, *J* = 4.0 Hz), 121.3 (d, *J* = 9.9 Hz), 115.5, 111.9 (d, *J* = 24.2 Hz), 108.9, 104.1 (d, *J* = 28.6 Hz), 45.2, 22.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -(116.47-116.60) (m); HRMS (ESI) exact mass calculated for $C_{13}H_{13}FNO^+$ [M+H$^+$]: 218.0976, found: 218.0979; IR (neat): ν_{max} (cm^{-1}) = 1702, 1612, 1579, 1476, 1436, 1344, 918, 811; R_f = 0.3 (petroleum ether/EtOAc 30:1).

3-Methyl-1-(6-methyl-indol-1-yl)but-3-en-1-one (**1q**). According to general procedure A with 6-methyl-indole and 3-methylbut-3-enoyl chloride, **1q** was obtained in 36% yield (198 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H, Ar-*H*), 7.47 (d, *J* = 7.9 Hz, 1H, Ar-*H*), 7.41 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.15 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 6.61 (d, *J* = 3.7 Hz, 1H, Ar-*H*), 5.08 (s, 1H, C=C*H*H), 4.95 (s, 1H, C=CH*H*), 3.65 (s, 2H, COCH_2), 2.53 (s, 3H, Ar-CH_3), 1.93 (s, 3H, CH_2=CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 138.7, 136.1, 135.3, 128.0, 125.2, 124.5, 120.3, 117.0, 115.2, 109.1, 45.4, 22.6, 22.0; HRMS (ESI) exact mass calculated for $C_{14}H_{16}NO^+$ [M+H$^+$]: 214.1226, found: 214.1229; IR (neat): ν_{max} (cm^{-1}) = 1702, 1613, 1580, 1429, 1383, 810, 783, 715; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(7-Chloro-indol-1-yl)-3-methylbut-3-en-1-one (**1r**). According to general procedure A with 7-chloro-indole and 3-methylbut-3-enoyl chloride, **1r** was obtained in 49% yield (343 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.47 (m, 2H, 2(Ar-*H*)), 7.38 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.24 (t, *J* = 7.8 Hz, 1H, Ar-*H*), 6.64 (dd, *J* = 3.7, 1.2 Hz, 1H, Ar-*H*), 5.06 (s, 1H, C=C*H*H), 5.00 (s, 1H,

C=CH*H*), 3.69 (s, 2H, COCH_2), 1.93 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 138.5, 134.2, 132.7, 127.3, 126.9, 124.6, 121.5, 119.6, 115.8, 108.2, 46.3, 22.4; HRMS (ESI) exact mass calculated for $C_{13}H_{13}ClNO^+$ [M+H$^+$]: 234.0680, found: 234.0683; IR (neat): ν_{max} (cm^{-1}) = 1712, 1611, 1579, 1454, 1363, 899, 754, 705; R_f = 0.3 (petroleum ether/EtOAc 30:1).

3-Methyl-1-(7-methyl-indol-1-yl)but-3-en-1-one (**1s**). According to general procedure A with 7-methyl-indole and 3-methylbut-3-enoyl chloride, **1s** was obtained in 62% yield (520 mg, light yellow oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 9.0, 5.6 Hz, 2H, 2(Ar-*H*)), 7.33-7.09 (m, 2H, 2(Ar-*H*)), 6.65 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.10 (s, 1H, C=C*H*H), 5.01 (s, 1H, C=CH*H*), 3.69 (s, 2H, COCH_2), 2.62 (s, 3H, Ar-CH_3), 1.95 (s, 3H, CH_2=CCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 138.9, 135.3, 132.1, 128.3, 126.7, 126.5, 124.3, 118.7, 115.6, 109.0, 45.9, 22.9, 22.6; HRMS (ESI) exact mass calculated for $C_{14}H_{16}NO^+$ [M+H$^+$]: 214.1226, found: 214.1229; IR (neat): ν_{max} (cm^{-1}) = 1712, 1613, 1576, 1456, 1336, 899, 786, 753; R_f = 0.3 (petroleum ether/EtOAc 30:1).

3-Methyl-1-(3-methyl-indol-1-yl)but-3-en-1-one (**1t**). According to general procedure A with 3-methyl-indole and 3-methylbut-3-enoyl chloride, **1t** was obtained in 23% yield (124 mg, yellow oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.2 Hz, 1H, Ar-*H*), 7.59-7.47 (m, 1H, Ar-*H*), 7.46-7.38 (m, 1H, Ar-*H*), 7.35 (dd, *J* = 7.5, 1.2 Hz, 1H, Ar-*H*), 7.24 (s, 1H, Ar-*H*), 5.08 (s, 1H, C=C*H*H), 4.96 (s, 1H, C=CH*H*), 3.62 (s, 2H, COCH_2), 2.32 (s, 3H, Ar-CH_3), 1.94 (s, 3H, CH_2=CCH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 138.8, 136.0, 131.4, 125.2, 123.5, 122.0, 118.8, 118.5, 116.8, 115.1, 45.4, 22.7, 10.0; HRMS (ESI) exact mass calculated for $C_{14}H_{16}NO^+$ [M+H$^+$]: 214.1226, found: 214.1229; IR (neat): ν_{max} (cm^{-1}) = 1756, 1701, 1669, 1524, 1450, 1351, 1132, 752; R_f = 0.3 (petroleum ether/EtOAc 30:1).

3-Methyl-1-(3-phenyl-indol-1-yl)but-3-en-1-one (**1u**). According to general procedure A with 3-phenyl-indole and 3-methylbut-3-enoyl chloride, **1u** was obtained in 47% yield (324 mg, white solid, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 8.2 Hz, 1H, Ar-*H*), 7.85 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.72-7.64 (m, 2H, 2(Ar-*H*)), 7.60 (s, 1H, Ar-*H*), 7.53 (t, *J* = 7.5 Hz, 2H, 2(Ar-*H*)), 7.50-7.35 (m, 3H, 3(Ar-*H*)), 5.11 (s, 1H, C=C*H*H), 5.00 (s, 1H, C=CH*H*), 3.72 (s, 2H, COCH_2), 1.96 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 138.5, 136.4, 133.3, 128.9, 127.9, 127.5, 125.5, 124.0, 123.8, 121.8, 120.0, 116.9, 115.3, 45.2, 22.6; HRMS (ESI) exact mass calculated for $C_{19}H_{18}NO^+$ [M+H$^+$]:

276.1383, found: 276.1384; IR (neat): ν_{max} (cm^{-1}) = 1705, 1634, 1587, 1451, 1372, 1206, 1190, 1144 747, 699; m.p. = 45-47 °C; R_f = 0.3 (petroleum ether/EtOAc 25:1).

1-(3-Methylbut-3-enoyl)-indole-3-carbonitrile **(1v)**. According to general procedure B with indol-3-carbonitrile and 3-methylbut-3-enoyl chloride, **1v** was obtained in 71% yield (320 mg, white solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (dd, *J* = 8.2, 3.1 Hz, 1H, Ar-*H*), 8.05 (d, *J* = 3.3 Hz, 1H, Ar-*H*), 7.84-7.60 (m, 1H, Ar-*H*), 7.55-7.36 (m, 2H, 2(Ar-*H*)), 5.12 (s, 1H, C=C*H*H), 4.98 (s, 1H, C=CH*H*), 3.69 (s, 2H, COCH_2), 1.92 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 137.7, 134.7, 132.5, 127.7, 127.1, 125.3, 119.6, 117.0, 116.2, 113.9, 93.9, 45.2, 22.5; HRMS (EI) exact mass calculated for $C_{14}H_{12}N_2O^+$ [M^+]: 224.0944, found: 224.0951; IR (neat): ν_{max} (cm^{-1}) = 2225, 1720, 1549, 1454, 1363, 1198, 902, 748; m.p. = 54-55 °C; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Methyl 1-(3-methylbut-3-enoyl) -indole-3-carboxylate **(1w)**. According to general procedure B with methyl indol-3-carboxylate and 3-methylbut-3-enoyl chloride, **1w** was obtained in 39% yield (199 mg, white solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52-8.43 (m, 1H, Ar-*H*), 8.18-8.09 (m, 2H, 2(Ar-*H*)), 7.48-7.33 (m, 2H, 2(Ar-*H*)), 5.09 (s, 1H, C=C*H*H), 4.96 (s, 1H, C=CH*H*), 3.95 (s, 3H, CO_2CH_3), 3.68 (s, 2H, COCH_2), 1.92 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 164.3, 138.0, 136.0, 131.0, 127.2, 126.0, 124.9, 121.5, 116.6, 115.9, 113.7, 51.6, 45.1, 22.6; HRMS (EI) exact mass calculated for $C_{15}H_{15}NO_3$ [M]: 257.1052, found: 257.1056; IR (neat): ν_{max} (cm^{-1}) = 1710, 1559, 1449, 1366, 1198, 1150, 773, 753; m.p. = 50-51 °C; R_f = 0.3 (petroleum ether/EtOAc 15:1).

1-(3-Methylbut-3-enoyl)-indole-3-carbaldehyde **(1x)**. According to general procedure B with indol-3-carbaldehyde and 3-methylbut-3-enoyl chloride, **1x** was obtained in 42% yield (190 mg, white solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.15 (s, 1H, C*H*O), 8.48 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 8.42-8.21 (m, 1H, Ar-*H*), 8.13 (s, 1H, Ar-*H*), 7.61-7.34 (m, 2H, 2(Ar-*H*)), 5.14 (s, 1H, C=C*H*H), 5.00 (s, 1H, C=CH*H*), 3.75 (s, 2H, COCH_2), 1.95 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.6, 169.3, 137.9, 136.4, 135.2, 126.9, 125.9, 125.5, 122.6, 121.8 116.5, 116.0, 45.2, 22.6; HRMS (EI) exact mass calculated for $C_{14}H_{13}NO_2$ [M]: 227.0946, found: 227.0955; IR (neat): ν_{max} (cm^{-1}) = 1722, 1673, 1551, 1448, 1350, 1185, 782, 574; m.p. = 56-58 °C; R_f = 0.3 (petroleum ether/EtOAc 15:1).

3-Methyl-1-(1-pyrrolo[2,3-b]pyridin-1-yl)but-3-en-1-one (**1y**). According to general procedure with 1-pyrrolo[2,3-b]pyridine and 3-methylbut-3-enoyl chloride, **1y** was obtained in 36% yield (217 mg,

yellow oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 4.8, 1.7 Hz, 1H, Ar-*H*), 8.03 (d, *J* = 4.2 Hz, 1H, Ar-*H*), 7.89 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar-*H*), 7.21 (dd, *J* = 7.8, 4.8 Hz, 1H, Ar-*H*), 6.62 (d, *J* = 4.1 Hz, 1H, Ar-*H*), 5.00 (t, *J* = 1.6 Hz, 1H, C=C*H*H), 4.95 (s, 1H, C=CH*H*), 4.36 (d, *J* = 1.0 Hz, 2H, COCH_2), 1.95 (d, *J* = 1.1 Hz, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 147.6, 143.7, 139.2, 129.3, 125.6, 123.8, 118.7, 114.6, 105.9, 45.9, 23.0; HRMS (ESI) exact mass calculated for $C_{12}H_{13}N_2O^+$ [M+H$^+$]: 201.1022, found: 201.1024; IR (neat): ν_{max} (cm^{-1}) = 1765, 1654, 1584, 1503, 1422, 799, 772, 730; R_f = 0.3 (petroleum ether/EtOAc 20:1).

1-(Indol-1-yl)but-3-en-1-one (**1z**). According to general procedure with indole and but-3-enoyl chloride, **1z** was obtained in 55% yield (205 mg, yellow oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 8.3 Hz, 1H, Ar-*H*), 7.60 (d, *J* = 7.7 Hz, 1H, Ar-*H*), 7.48 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.39 (t, *J* = 7.7 Hz, 1H, Ar-*H*), 7.35-7.25 (m, 1H, Ar-*H*), 6.68 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 6.28-6.03 (m, 1H, C*H*=CH_2), 5.36-5.18 (m, 2H, CH=CH_2), 3.74 (d, *J* = 6.6 Hz, 2H, COCH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 135.7, 130.3, 129.8, 125.2, 124.6, 123.8, 120.8, 119.5, 116.7, 109.4, 40.8; HRMS (ESI) exact mass calculated for $C_{12}H_{12}NO^+$ [M+H$^+$]: 186.0913, found: 186.0915; IR (neat): ν_{max} (cm^{-1}) = 1742, 1625, 1581, 1454, 1389, 1157, 1094, 753; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(Indol-1-yl)-3-phenylbut-3-en-1-one (**1aa**). According to general procedure with indole and 3-phenylbut-3-enoyl chloride, **1aa** was obtained in in 28% yield (146 mg, yellow oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.52 (d, *J* = 8.2 Hz, 1H, Ar-*H*), 7.61 (d, *J* = 7.7 Hz, 1H, Ar-*H*), 7.57-7.50 (m, 3H, 3(Ar-*H*)), 7.45-7.27 (m, 5H, 5(Ar-*H*)), 6.68 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 5.70 (s, 1H, C=C*H*H), 5.31 (s, 1H, C=CH*H*), 4.15 (s, 2H, COCH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 140.9, 139.7, 135.7, 130.4, 128.7, 128.2, 125.8, 125.3, 125.0, 123.9, 120.9, 116.8, 116.7, 109.5, 42.9; HRMS (ESI) exact mass calculated for $C_{18}H_{16}NO^+$ [M+H$^+$]: 262.1226, found: 262.1228; IR (neat): ν_{max} (cm^{-1}) = 1736, 1641, 1554, 1489, 1357, 1101, 753, 689; R_f = 0.3 (petroleum ether/EtOAc 30:1).

1-(Indol-1-yl)-2,3-dimethylbut-3-en-1-one **(1ab)**. According to general procedure with indole and 2,3-dimethylbut-3-enoyl chloride, **1ab** was obtained in 39% yield (168 mg, colorless oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, *J* = 8.3 Hz, 1H, Ar-*H*), 7.61 (d, *J* = 7.7 Hz, 1H, Ar-*H*), 7.56 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.47-7.38 (m, 1H, Ar-*H*), 7.33 (t, *J* = 7.5 Hz, 1H, Ar-*H*), 6.65 (d, *J* = 3.9 Hz, 1H, Ar-*H*), δ 5.02 (s, 2H, C=CH_2), 3.92 (q, *J* = 6.8 Hz, 1H, C*H*CH_3), 1.86 (s, 3H, CCH_3), 1.52 (d, *J* = 6.7

Hz, 3H, CHCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 144.6, 135.9, 130.3, 125.1, 125.1, 123.8, 120.8, 116.9, 113.7, 108.9, 47.6, 20.1, 16.7; HRMS (EI) exact mass calculated for $C_{14}H_{15}NO$ [M]: 213.1154, found: 213.1157; IR (neat): ν_{max} (cm^{-1}) = 1702, 1538, 1450, 1348, 1299, 907, 750, 715; R_f = 0.4 (petroleum ether/EtOAc 30:1).

1-(Indol-1-yl)-4-methylpent-4-en-1-one (**1ac**). According to general procedure with indole and 4-methylpent-4-enoyl chloride, **1ac** was obtained in 48% yield (204 mg, yellow oil, three steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, *J* = 8.3 Hz, 1H, Ar-*H*), 7.61 (d, *J* = 7.7 Hz, 1H, Ar-*H*), 7.49 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 7.44-7.35 (m, 1H, Ar-*H*), 7.32 (t, *J* = 7.4 Hz, 1H, Ar-*H*), 6.67 (d, *J* = 3.8 Hz, 1H, Ar-*H*), 4.87 (s, 1H, C=C*H*H), 4.81 (s, 1H, C=CH*H*), 3.08 (t, 2H, *J* = 7.2 Hz, COCH_2CH_2), 2.58 (t, 2H, *J* = 7.4 Hz, COCH_2CH_2), 1.87 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.0, 144.0, 135.7, 130.4, 125.1, 124.5, 123.6, 120.8, 116.6, 110.7, 109.2, 34.2, 32.1, 22.8; HRMS (ESI) exact mass calculated for $C_{15}H_{18}NO^+$ [M+H$^+$]: 228.1383, found: 228.1388; IR (neat): ν_{max} (cm^{-1}) = 1702, 1635, 1559, 1450, 1323, 765, 745, 715; R_f = 0.3 (petroleum ether/EtOAc 30:1).

General Procedure for the Synthesis of 3a-3ak: To a 10 mL sealed tube equipped with a rubber septum and magnetic stir bar, **1** (0.2 mmol), *fac*-Ir(ppy)$_3$ (0.002 mmol, 1.3 mg) and Na_2HPO_4 (0.24 mmol, 32.4 mg) were added. The tube was evacuated and backfilled with nitrogen for 3 times. **2** (0.5 mmol) and DCM (2.0 mL) were added; then the mixture was stirred and irradiated by 3 W blue LEDs for 12 hours at room temperature. After the reaction was completed (detected by TLC), the crude mixture was purified directly by flash column chromatography on silica gel to give **3**.

Ethyl 2,2-difluoro-3-(1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3a**). According to general procedure with **1a** and **2a**, **3a** was obtained in 85% yield (55 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-7.99 (m, 1H, Ar-*H*), 7.69-7.45 (m, 1H, Ar-*H*), 7.31 (td, *J* = 7.1, 1.6 Hz, 2H, 2(Ar-*H*)), 6.32 (s, 1H, Ar-*H*), 4.16-4.08 (m, 1H, CF_2C*H*H), 3.96 (dd, *J* = 10.8, 7.1 Hz, 1H, CF_2CH*H*), 3.36 (d, *J* = 18.2 Hz, 1H, COC*H*H), 3.11-2.80 (m, 1H, COCH*H*), 2.67 (dd, *J* = 17.6, 15.9 Hz, 2H, CO_2CH_2), 1.61 (s, 3H, CCH_3), 1.18 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 163.8 (t, *J* = 32.0 Hz), 149.5, 134.7, 130.1, 124.3, 124.0, 120.9, 115.5 (dd, *J* = 253.7, 251.2 Hz), 114.0, 99.9, 63.3, 49.0 (d, *J* = 3.5 Hz), 44.0 (t, *J* = 22.3 Hz), 35.5 (dd, *J* = 3.7, 1.4 Hz), 28.8 (d, *J* = 2.0 Hz), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.47 (dt, *J* = 266.4, 15.9 Hz), -104.54 (dt, *J* = 266.4,

17.5 Hz); HRMS (ESI) exact mass calculated for $C_{17}H_{18}F_2NO_3^+$ [M+H$^+$]: 322.1249, found: 322.1251; IR (neat): ν_{max} (cm^{-1}) = 1700, 1612, 1588, 1475, 1438, 1362, 811 755; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(8-bromo-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3b**). According to general procedure with **1b** and **2a**, **3b** were obtained in 76% yield (61 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.1 Hz, 1H, Ar-*H*), 7.46 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.19 (t, *J* = 7.9 Hz, 1H, Ar-*H*), 6.41 (s, 1H, Ar-*H*), 4.19-4.10 (m, 1H, CF_2CHH), 4.09-4.00 (m, 1H, CF_2CHH), 3.39 (d, *J* = 18.4 Hz, 1H, COC*H*H), 2.97 (d, *J* = 18.4 Hz, 1H, COCH*H*), 2.69 (t, *J* = 16.5 Hz, 2H, CO_2CH_2), 1.63 (s, 3H, CCH_3), 1.22 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 163.6 (t, *J* = 32.0 Hz), 150.0, 135.2, 130.4, 127.1, 125.1, 115.4 (dd, *J* = 253.3, 251.7 Hz), 114.2, 113.0, 99.8, 63.4, 48.8 (d, *J* = 3.7 Hz), 43.9 (t, *J* = 22.4 Hz), 35.6 (d, *J* = 3.4 Hz), 28.9 (d, *J* = 1.9 Hz), 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.33 (dt, *J* = 267.1, 15.7 Hz), -104.85 (dt, *J* = 267.1, 17.4 Hz); HRMS (ESI) exact mass calculated for $C_{17}H_{17}BrF_2NO_3^+$ [M+H$^+$]: 400.0354, found: 400.0357; IR (neat): ν_{max} (cm^{-1}) = 1749, 1645, 1594, 1420, 1265, 1177, 732, 703; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(8-chloro-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3c**). According to general procedure with **1c** and **2a**, **3c** were obtained in 90% yield (64 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.38-7.13 (m, 2H, 2(Ar-*H*)), 6.45 (s, 1H, Ar-*H*), 4.19-4.09 (m, 1H, CF_2CHH), 4.09-3.99 (m, 1H, CF_2CHH), 3.39 (d, *J* = 18.4 Hz, 1H, COC*H*H), 2.97 (d, *J* = 18.4 Hz, 1H, COCH*H*), 2.69 (t, *J* = 16.6 Hz, 2H, CO_2CH_2), 1.63 (s, 3H, CCH_3), 1.22 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 163.6 (t, *J* = 32.0 Hz), 150.0, 133.3, 130.7, 125.7, 124.8, 124.0, 115.4 (dd, *J* = 253.4, 251.6 Hz), 112.4, 98.1, 63.3, 48.8 (d, *J* = 3.6 Hz), 43.9 (t, *J* = 22.5 Hz), 35.6 (d, *J* = 3.6 Hz), 28.9 (d, *J* = 1.8 Hz), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.46 (dt, *J* = 267.1, 15.8 Hz), -104.82 (dt, *J* = 267.1, 17.4 Hz); HRMS (ESI) exact mass calculated for $C_{17}H_{17}ClF_2NO_3^+$ [M+H$^+$]: 356.0680, found: 356.0683; IR (neat): ν_{max} (cm^{-1}) = 1721, 1645, 1589, 1425, 1381, 1383, 1063, 776; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 2,2-difluoro-3-(8-fluoro-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3d**). According to general procedure with **1d** and **2a**, **3d** was obtained in 79% yield (54 mg, yellow

oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 7.44-7.20 (m, 1H, Ar-*H*), 7.00 (dd, *J* = 10.0, 8.1 Hz, 1H, Ar-*H*), 6.43 (s, 1H, Ar-*H*), 4.20-4.12 (m, 1H, CF_2CHH), 4.10-4.02 (m, 1H, CF_2CHH), 3.39 (d, *J* = 18.4 Hz, 1H, COC*H*H), 2.99 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.77-2.53 (m, 2H, CO_2CH_2), 1.63 (s, 3H, CCH_3), 1.23 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 163.7 (t, *J* = 32.0 Hz), 155.3 (d, *J* = 248.5 Hz), 149.6, 132.0 (d, *J* = 9.9 Hz), 125.0 (d, *J* = 7.3 Hz), 123.1 (d, *J* = 21.2 Hz), 115..4 (dd, *J* = 254.4, 252.7 Hz), 110.1 (d, *J* = 3.9 Hz), 109.7 (d, *J* = 18.7 Hz), 95.7, 63.3, 49.0 (d, *J* = 3.5 Hz), 43.9 (t, *J* = 22.3 Hz), 35.5 (d, *J* = 3.5 Hz), 28.8 (d, *J* = 1.8 Hz), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.78 (dt, *J* = 266.9, 16.1 Hz), -104.64 (dt, *J* = 266.9, 17.4 Hz), -(121.43-121.47) (m); HRMS (ESI) exact mass calculated for $C_{17}H_{17}F_3NO_3^+$ [M+H$^+$]: 340.1155, found: 340.1158; IR (neat): ν_{max} (cm^{-1}) = 1715, 1644, 1588, 1492, 1437, 1383, 903, 779; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(1,8-dimethyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3e**). According to general procedure with **1e** and **2a**, **3e** was obtained 78% yield (52 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 7.24 (t, *J* = 7.7 Hz, 1H, Ar-*H*), 7.11 (d, *J* = 7.4 Hz, 1H, Ar-*H*), 6.36 (s, 1H, Ar-*H*), 4.17-4.19 (m, 1H, CF_2CHH), 4.02-4.39 (m, 1H, CF_2CHH), 3.36 (d, *J* = 18.2 Hz, 1H, COC*H*H), 2.96 (d, *J* = 18.2 Hz, 1H, COCH*H*), 2.68 (t, *J* = 16.6 Hz, 2H, CO_2CH_2), 2.52 (s, 3H, Ar-CH_3), 1.62 (s, 3H, CCH_3), 1.19 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 163.8 (t, *J* = 32.0 Hz), 148.9, 134.3, 130.3, 129.8, 124.7, 124.1, 115.5 (dd, *J* = 253.6, 251.0 Hz), 111.5, 98.4, 63.3, 49.1(d, *J* = 3.7 Hz), 44.1 (t, *J* = 22.3 Hz), 35.5 (d, *J* = 3.7 Hz), 28.8 (d, *J* = 2.0 Hz), 18.5, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.57 (dt, *J* = 266.4, 15.9 Hz), -104.52 (dt, *J* = 266.6, 17.5 Hz); HRMS (ESI) exact mass calculated for $C_{18}H_{20}F_2NO_3^+$ [M+H$^+$]: 336.1406, found: 336.1409; IR (neat): ν_{max} (cm^{-1}) = 1710, 1653, 1589, 1470, 1380, 1202, 777, 736; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(8-(benzyloxy)-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropano ate (**3f**). According to general procedure with **1f** and **2a**, **3f** was obtained in 76% yield (65 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 7.50 (d, *J* = 7.1 Hz, 2H, 2(Ar-*H*)), 7.43 (t, *J* = 7.2 Hz, 2H, 2(Ar-*H*)), 7.41-7.34 (m, 1H, Ar-*H*), 7.25 (t, *J* = 8.1 Hz, 1H, Ar-*H*), 6.82 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 6.50 (s, 1H, Ar-*H*), 5.22 (s, 2H, Ar-CH_2), 4.18-4.10 (m, 1H, CF_2CHH), 4.06-4.98

(m, 1H, CF_2CHH), 3.38 (d, J = 18.3 Hz, 1H, $COCHH$), 2.96 (d, J = 18.3 Hz, 1H, $COCHH$), 2.67 (t, J = 16.7 Hz, 2H, CO_2CH_2), 1.61 (s, 3H, CCH_3), 1.19 (t, J = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.7, 163.8 (t, J = 29.7 Hz), 151.8, 148.0, 137.0, 131.2, 128.6, 128.0, 127.4, 125.1, 125.0, 115.5 (t, J = 250.8 Hz), 107.3, 106.1, 97.3, 70.1, 63.3, 49.1 (d, J = 3.6 Hz), 44.1 (t, J = 22.4 Hz), 35.4, 28.9, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.55 (dt, J = 266.3, 16.0 Hz), -104.70 (dt, J = 266.3, 17.5 Hz); HRMS (ESI) exact mass calculated for $C_{24}H_{24}F_2NO_4^+$ [M+H$^+$]: 428.1668, found: 428.1670; IR (neat): ν_{max} (cm^{-1}) = 1744, 1661, 1567, 1495, 1434, 1382, 972, 774; R_f = 0.3 (petroleum ether/EtOAc 10:1).

Ethyl (1,7-dimethyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3g**). According to general procedure with **1g** and **2a**, **3g** was obtained in 62% yield (42 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.2 Hz, 1H, Ar-H), 7.31 (s, 1H, Ar-H), 7.14 (d, J = 8.2 Hz, 1H, Ar-H), 6.24 (s, 1H, Ar-H), 4.18-4.07 (m, 1H, CF_2CHH), 4.06-3.91 (m, 1H, CF_2CHH), 3.34 (d, J = 18.2 Hz, 1H, $COCHH$), 2.94 (d, J = 18.2 Hz, 1H, $COCHH$), 2.65 (t, J = 16.7 Hz, 2H, CO_2CH_2), 2.46 (s, 3H, Ar-CH_3), 1.60 (s, 3H, CCH_3), 1.19 (t, J = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 163.8 (t, J = 32.0 Hz), 149.6, 135.0, 134.0, 128.3, 125.3, 120.8, 115.5 (dd, J = 252.2, 254.5 Hz), 113.5, 99.7, 63.3, 49.0 (d, J = 3.4 Hz), 44.0 (t, J = 22.3 Hz), 35.4 (dd, J = 3.5, 1.5 Hz), 28.8 (d, J = 2.0 Hz), 21.6, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.57 (dt, J = 266.3, 16.0 Hz), -104.43 (dt, J = 266.2, 17.5 Hz); HRMS (ESI) exact mass calculated for $C_{18}H_{20}F_2NO_3^+$ [M+H$^+$]: 336.1406, found: 336.1410; IR (neat): ν_{max} (cm^{-1}) = 1698, 1638, 1423, 1392, 1264, 1194, 731, 703; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 2,2-difluoro-3-(7-methoxy-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3h**). According to general procedure with **1h** and **2a**, **3h** was obtained in 68% yield (48 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.8 Hz, 1H, Ar-H), 6.99 (d, J = 2.4 Hz, 1H, Ar-H), 6.93 (dd, J = 8.8, 2.4 Hz, 1H, Ar-H), 6.26 (s, 1H, Ar-H), 4.18-4.10 (m, 1H, CF_2CHH), 4.03-3.95 (m, 1H, CF_2CHH), 3.87 (s, 3H, Ar-OCH_3), 3.34 (d, J = 18.2 Hz, 1H, $COCHH$), 2.94 (d, J = 18.3 Hz, 1H, $COCHH$), 2.65 (t, J = 16.4 Hz, 2H, CO_2CH_2), 1.60 (s, 3H, CCH_3), 1.20 (t, J = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 163.8 (t, J = 28.2 Hz), 157.0, 150.4, 135.8, 124.9, 115.5 (dd, J = 252.8,247.2 Hz), 114.6, 112.4, 103.9, 99.9, 63.4, 55.7, 48.9 (d, J = 3.4 Hz), 44.0 (t, J = 22.3 Hz), 35.5

(d, J = 3.7 Hz), 28.8, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.59 (dt, J = 266.3, 16.0 Hz), -104.44 (dt, J = 266.4, 17.5 Hz); HRMS (ESI) exact mass calculated for $C_{18}H_{20}F_2NO_4^+$ [M+H$^+$]: 352.1355, found: 352.1358; IR (neat): ν_{max} (cm^{-1}) = 1717, 1590, 1511, 1444, 1477, 1199, 862, 737; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(7-bromo-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanote (**3i**). According to general procedure with **1i** and **2a**, **3i** was obtained in 76% yield (61 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 8.5 Hz, 1H, Ar-*H*), 7.66 (s, 1H, Ar-*H*), 7.42 (d, J = 8.3 Hz, 1H, Ar-*H*), 6.27 (s, 1H, Ar-*H*), 4.15 (dt, J = 14.3, 7.2 Hz, 1H, CF_2CHH), 4.09-3.96 (m, 1H, CF_2CHH), 3.36 (d, J = 18.3 Hz, 1H, COC*H*H), 2.95 (d, J = 18.3 Hz, 1H, COCH*H*), 2.66 (t, J = 16.8 Hz, 2H, CO_2CH_2), 1.61 (s, 3H, CCH_3), 1.22 (t, J = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 163.7 (t, J = 32.0 Hz), 150.8, 136.4, 128.7, 126.9, 123.6, 117.5, 115.4 (dd, J = 252.6, 254.5 Hz), 115.2, 99.2, 63.3, 48.8 (d, J = 3.4 Hz), 43.8 (t, J = 22.3 Hz), 35.6 (d, J = 3.3 Hz), 28.8 (d, J = 1.9 Hz), 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.88 (dt, J = 266.7, 16.3 Hz), -104.47 (dt, J = 266.9, 17.5 Hz); HRMS (ESI) exact mass calculated for $C_{17}H_{17}BrF_2NO_3^+$ [M+H$^+$]: 400.0354, found: 400.0357; IR (neat): ν_{max} (cm^{-1}) = 1720, 1665, 1583, 1447, 1360, 1193, 807, 751; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(7-chloro-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanote (**3j**). According to general procedure with **1j** and **2a**, **3j** was obtained in 89% yield (63 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.7 Hz, 1H, Ar-*H*), 7.49 (s, 1H, Ar-*H*), 7.28 (d, J = 8.8 Hz, 1H, Ar-*H*), 6.27 (s, 1H, Ar-*H*), 4.19-4.11 (m, 1H, CF_2CHH), 4.01 (d, J = 10.6 Hz, 1H, CF_2CHH), 3.36 (d, J = 18.3 Hz, 1H, COC*H*H), 2.95 (d, J = 18.3 Hz, 1H, COCH*H*), 2.66 (t, J = 16.8 Hz, 2H, CO_2CH_2), 1.61 (s, 3H, CCH_3), 1.21 (t, J = 7.3 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 163.7 (t, J = 32.1 Hz), 151.0, 135.9, 129.8, 128.4, 124.2, 120.6, 115.4 (dd, J = 253.4, 251.7 Hz), 114.8, 99.3, 63.3, 48.8 (d, J = 3.5 Hz), 43.8 (t, J = 22.3 Hz), 35.6 (dd, J = 3.3, 1.4 Hz), 28.7 (d, J = 2.1 Hz), 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.83 (dt, J = 266.6, 16.2 Hz), -104.49 (dt, J = 266.6, 17.4 Hz); HRMS (ESI) exact mass calculated for $C_{17}H_{17}ClF_2NO_3^+$ [M+H$^+$]: 356.0860, found: 356.0864; IR (neat): ν_{max} (cm^{-1}) = 1721, 1652, 1585, 1450, 1265, 1065, 808, 740.; R_f = 0.3 (petroleum ether/EtOAc 15:1). *Ethyl 2,2-difluoro-3-(7-fluoro-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate* (**3k**).

According to general procedure with **1k** and **2a**, **3k** was obtained in 76% yield (51 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 8.7, 4.7 Hz, 1H, Ar-*H*), 7.30-7.13 (m, 1H, Ar-*H*), 7.05 (t, *J* = 9.1 Hz, 1H, Ar-*H*), 6.30 (s, 1H, Ar-*H*), 4.15 (t, *J* = 8.9 Hz, 1H, CF_2CHH), 4.06-3.98 (m, 1H, CF_2CHH), 3.36 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.96 (d, *J* = 18.2 Hz, 1H, COC*H*H), 2.66 (t, *J* = 16.8 Hz, 2H, CO_2CH_2), 1.62 (s, 3H, CCH_3), 1.22 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.1, 163.7 (t, *J* = 31.9 Hz), 160.1 (d, *J* = 240.6 Hz), 151.3, 135.7 (d, *J* = 10.3 Hz), 126.5 (d, *J* = 1.4 Hz), 115.4 (t, *J* = 268.4 Hz), 114.8 (d, *J* = 9.8 Hz), 111.9 (d, *J* = 25.6 Hz), 106.7 (d, *J* = 24.2 Hz), 99.8 (d, *J* = 4.0 Hz), 63.3, 48.8 (dd, *J* = 3.5, 1.0 Hz), 43.9 (dd, *J* = 22.9, 21.8 Hz), 35.5 (dd, *J* = 3.3, 1.5 Hz), 28.7 (d, *J* = 2.0 Hz), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.78 (dt, *J* = 267.0, 16.3 Hz), -104.52 (dt, *J* = 266.6, 17.5 Hz), -(117.60-117.79) (m); HRMS (ESI) exact mass calculated for $C_{17}H_{17}F_3NO_3^+$ [M+H$^+$]: 340.1155, found: 340.1157; IR (neat): ν_{max} (cm^{-1}) = 1716, 1612, 1590, 1472, 1444, 1365, 1065, 737; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Methyl 1-(3-ethoxy-2,2-difluoro-3-oxopropyl)-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indole-7-carboxylate **(3l)**. According to general procedure with **1l** and **2a**, **3l** was obtained in 65% yield (50 mg, white solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 1.6 Hz, 1H, Ar-*H*), 8.13-7.94 (m, 2H, 2(Ar-*H*)), 6.39 (s, 1H, Ar-*H*), 4.17-4.09 (m, 1H, CF_2CHH), 4.03-3.96 (m, 4H, CF_2CHH and CO_2CH_3), 3.38 (d, *J* = 18.4 Hz, 1H, COC*H*H), 2.98 (d, *J* = 18.4 Hz, 1H, COCH*H*), 2.68 (t, *J* = 16.7 Hz, 2H, CO_2CH_2), 1.63 (s, 3H, CCH_3), 1.19 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 167.2, 163.7 (t, *J* = 32.0 Hz), 150.6, 134.5, 132.6, 126.1, 125.4, 123.1, 115.4 (dd, *J* = 254.2, 252.6 Hz), 113.5, 100.3, 63.3, 52.2, 48.9 (d, *J* = 3.4 Hz), 43.9 (t, *J* = 22.3 Hz), 35.6 (d, *J* = 3.9 Hz), 28.8 (d, *J* = 2.0 Hz), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.73 (dt, *J* = 266.8, 16.0 Hz), -104.52 (dt, *J* = 266.9, 17.5 Hz); HRMS (EI) exact mass calculated for $C_{19}H_{19}F_2NO_5$ [M]: 379.1231, found: 379.1232; IR (neat): ν_{max} (cm^{-1}) = 1749, 1712, 1437, 1388, 1299, 1191, 1086, 769; m.p. = 61-63°C; R_f = 0.3 (petroleum ether/EtOAc 10:1).

Ethyl 2,2-difluoro-3-(1-methyl-7-nitro-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3m**). According to general procedure with **1m** and **2a**, **3m** was obtained in 7% yield (5 mg, colorless oil); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 2.1 Hz, 1H, Ar-*H*), 8.25 (dd, *J* = 9.0, 2.1 Hz, 1H, Ar-*H*), 8.17 (d, *J* = 8.9 Hz, 1H, Ar-*H*), 6.50 (s, 1H, Ar-*H*), 4.26-4.13 (m, 1H, CF_2CHH), 4.17-4.04 (m,

1H, CF_2CHH), 3.43 (d, *J* = 18.5 Hz, 1H, COC*H*H), 3.03 (d, *J* = 18.5 Hz, 1H, COCH*H*), 2.70 (t, *J* = 17.6 Hz, 2H, CH_2CH_3), 1.59 (s, 3H, CCH_3), 1.26 (t, *J* = 6.8 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 163.6 (t, *J* =28.8 Hz), 152.5, 144.8, 134.6, 115.3 (t, *J* = 263.2 Hz), 128.9, 119.5, 117.3, 114.0, 100.4, 63.4, 52.7, 48.7, 43.7 (t, *J* = 22.3 Hz), 35.9, 13.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.46 (dt, *J* = 267.1, 16.0 Hz), -104.46 (dt, *J* = 267.4, 17.5 Hz); HRMS (EI) exact mass calculated for $C_{17}H_{16}F_2N_2O_5$ [M]: 366.1027, found: 366.1031; IR (neat): ν_{max} (cm^{-1}) = 1753, 1523, 1460, 1341, 1191, 1066, 817, 733; m.p. = 56-59 °C; R_f = 0.3 (petroleum ether/EtOAc 8:1).

Ethyl 3-(6-bromo-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3n**). According to general procedure with **1n** and **2a**, **3n** was obtained in 82% yield (65 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (s, 1H, Ar-*H*), 7.39 (d, *J* = 3.1 Hz, 2H, 2(Ar-*H*)), 6.29 (s, 1H, Ar-*H*), 4.22-4.09 (m, 1H, CF_2CHH), 4.03 (d, *J* = 7.1 Hz, 1H, CF_2CHH), 3.36 (d, *J* = 18.4 Hz, 1H, COC*H*H), 2.96 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.66 (t, *J* = 16.8 Hz, 2H, CO_2CH_2), 1.61 (s, 3H, CCH_3), 1.22 (t, *J* = 7.2, Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.3, 163.7 (t, *J* = 32.0 Hz), 149.9, 133.5, 130.6, 127.5, 122.0, 117.4, 117.0, 115.4 (dd, *J* = 252.5, 254.5 Hz), 99.7, 63.3, 48.9 (d, *J* = 3.2 Hz), 43.9 (t, *J* = 22.3 Hz), 35.6 , 28.7 (d, *J* = 1.9 Hz), 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.85 (dt, *J* = 266.9, 16.2 Hz), -104.47 (dt, *J* = 266.8, 17.4 Hz); HRMS (ESI) exact mass calculated for $C_{17}H_{17}BrF_2NO_3^+$ [M+H$^+$]: 400.0354, found: 400.0357; IR (neat): ν_{max} (cm^{-1}) = 1719, 1615, 1583, 1440, 1357, 823, 737, 592; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(6-chloro-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3o**). According to general procedure with **1o** and **2a**, **3o** was obtained in 81% yield (65 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H, Ar-*H*), 7.43 (d, *J* = 8.4 Hz, 1H, Ar-*H*), 7.34-7.16 (m, 1H, Ar-*H*), 6.30 (s, 1H, Ar-*H*), 4.14 (dt, *J* = 14.1, 7.2 Hz, 1H, CF_2CHH), 4.02 (dt,*J* = 14.5, 7.2 Hz, 1H, CF_2CHH), 3.36 (d, *J* = 18.3 Hz, 1H, COC*H*H), 2.96 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.66 (t, *J* = 16.8 Hz, 2H, CO_2CH_2), 1.62 (s, 3H, CCH_3), 1.22 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 163.7 (t, *J*= 32.0 Hz), 150.0, 133.1, 130.3, 129.9, 124.9, 121.6, 115.4 (dd, *J* = 253.5, 251.6 Hz), 114.2, 99.7, 63.3, 48.9 (d, *J* = 3.5 Hz), 43.9 (t, *J* = 22.3 Hz), 35.6 (d, *J* = 3.3 Hz), 28.8 (d, *J* = 1.8 Hz), 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.84 (dt, *J* = 266.7, 16.1 Hz), -104.47 (dt, *J* = 266.9, 17.5

Hz); HRMS (ESI) exact mass calculated for $C_{17}H_{17}ClF_2NO_3^+$ [M+H$^+$]: 356.0860, found: 356.0865; IR (neat): ν_{max} (cm^{-1}) = 1717, 1654, 1597, 1444, 1370, 825, 736; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 2,2-difluoro-3-(6-fluoro-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3p**). According to general procedure with **1p** and **2a**, **3p** was obtained in 88% yield (60 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (dd, *J* = 8.8, 2.4 Hz, 1H, Ar-*H*), 7.44 (dd, *J* = 8.7, 5.0 Hz, 1H, Ar-*H*), 7.04 (td, *J* = 9.1, 2.4 Hz, 1H, Ar-*H*), 6.29 (s, 1H, Ar-*H*), 4.17-4.09 (m, 1H, CF_2CHH), 4.04-3.96 (m, 1H, CF_2CHH), 3.35 (d, *J* = 18.3 Hz, 1H, COC*H*H), 2.96 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.66 (dd, *J* = 17.5, 16.0 Hz, 2H, CO_2CH_2), 1.61 (s, 3H, CCH_3), 1.20 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 163.7 (t, *J* = 32.0 Hz), 160.4 (d, *J* = 241.8 Hz), 149.6 (d, *J* = 4.0 Hz), 130.9 (d, *J* = 1.8 Hz), 129.9 (d, *J* = 12.8 Hz), 121.5 (d, *J* = 9.6 Hz), 115.4 (dd, *J* = 253.5, 251.3 Hz), 112.5 (d, *J* = 24.2 Hz), 101.4, 101.1, 99.6, 63.3, 48.9 (dd, *J* = 3.5, 1.2 Hz), 44.0 (dd, *J* = 22.9, 21.7 Hz), 35.5 (dd, *J* = 3.6, 1.4 Hz), 28.8 (d, *J* = 2.5 Hz), 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.72 (dt, *J* = 266.9, 16.1 Hz), -104.52 (dt, *J* = 266.9, 17.5 Hz), -(117.31-117.37) (m); HRMS (ESI) exact mass calculated for $C_{17}H_{17}F_3NO_3^+$ [M+H$^+$]: 340.1155, found: 340.1159; IR (neat): ν_{max} (cm^{-1}) = 1713, 1607, 1578, 1447, 1375, 865, 822; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(1,6-dimethyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3q**). According to general procedure with **1q** and **2a**, **3q** was obtained in 72% yield (48 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (s, 1H, Ar-*H*), 8.01 (dd, *J* = 8.4, 1.7 Hz, 1H, Ar-*H*), 7.56 (dd, *J* = 8.3, 1.4 Hz, 1H, Ar-*H*), 6.38 (s, 1H, Ar-*H*), 4.18-4.09 (m, 1H, CF_2CHH), 4.08-3.99 (m, 1H, CF_2CHH), 3.97 (s, 3H, Ar-CH_3), 3.40 (d, *J* = 18.3 Hz, 1H, COC*H*H), 3.00 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.69 (t, *J* = 16.8 Hz, 2H, CO_2CH_2), 1.64 (s, 3H, CCH_3), 1.21 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.2, 167.2, 163.7 (t, *J* = 32.0 Hz), 152.8, 138.4, 129.6, 125.9, 125.6, 120.5, 115.6, 99.9, 63.3, 52.1, 48.8 (d, *J* = 3.3 Hz), 43.8 (t, *J* = 22.3 Hz), 35.7 (d, *J* = 3.2 Hz), 28.7, 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.88 (dt, *J* = 267.0, 16.3 Hz), -104.45 (dt, *J* = 267.0, 17.4 Hz); HRMS (ESI) exact mass calculated for $C_{18}H_{20}F_2NO_3^+$ [M+H$^+$]: 336.1406, found: 336.1408; IR (neat): ν_{max} (cm^{-1}) = 1698, 1567, 1445, 1312, 1211, 1104, 801, 754; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(5-chloro-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3r**). According to general procedure with **1r** and **2a**, **3r** was obtained in 68% yield (48 mg, yellow oil).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 7.7 Hz, 1H, Ar-*H*), 7.30 (t, *J* = 6.5 Hz, 1H, Ar-*H*), 7.20 (t, *J* = 7.8 Hz, 1H, Ar-*H*), 6.37 (s, 1H, Ar-*H*), 4.17 (dd, *J* = 10.7, 7.2 Hz, 1H, CF_2CHH), 4.03 (dd, *J* = 10.8, 7.2 Hz, 1H, CF_2CHH), 3.37 (d, *J* = 18.1 Hz, 1H, COC*H*H), 2.98 (d, *J* = 18.1 Hz, 1H, COCH*H*), 2.72-2.57 (m, 2H, CO_2CH_2), 1.61 (s, 3H, CCH_3), 1.23 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 163.7 (t, *J* = 32.0 Hz), 152.1, 137.6, 128.9, 126.0, 125.1, 120.1, 119.2, 115.4 (dd, *J* = 253.4, 251.8 Hz), 100.1, 63.3, 48.9 (dd, *J* = 3.4, 1.2 Hz), 43.9 (t, *J* = 22.4 Hz), 34.5 (dd, *J* = 3.1, 1.7 Hz), 28.7 (d, *J* = 2.1 Hz), 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.16 (ddd, *J* = 266.6, 18.6, 14.7 Hz), -104.10 (dt, *J* = 266.7, 17.2 Hz); HRMS (ESI) exact mass calculated for $C_{17}H_{17}ClF_2NO_3^+$ [M+H$^+$]: 356.0860, found: 356.0864; IR (neat): ν_{max} (cm^{-1}) = 1756, 1603, 1557, 1412, 1321, 1267, 1189, 865, 733; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(1,5-dimethyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3s**). According to general procedure with **1s** and **2a**, **3s** was obtained in 68% yield (45 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 7.7 Hz, 1H, Ar-*H*), 7.18 (t, *J* = 7.6 Hz, 1H, Ar-*H*), 7.08 (d, *J* = 7.3 Hz, 1H, Ar-*H*), 6.32 (s, 1H, Ar-*H*), 4.13 (dd, *J* = 10.7, 7.2 Hz, 1H, CF_2CHH), 3.98 (dd, *J* = 10.8, 7.2 Hz, 1H, CF_2CHH), 3.35 (d, *J* = 18.1 Hz, 1H, COC*H*H), 2.95 (d, *J* = 18.2 Hz, 1H, COCH*H*), 2.90 (s, 3H, Ar-CH_3), 2.75-2.51 (m, 2H, CO_2CH_2), 1.60 (s, 3H, CCH_3), 1.20 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 179.9, 174.6, 169.1 (d, *J* = 1.1 Hz), 163.8, 151.0, 138.6, 136.3, 135.6, 130.9, 130.3, 129.4, 126.7, 125.7, 124.6, 118.1, 115.1 (dd, *J* = 252.5, 254.6 Hz), 100.4, 49.0 (d, *J* = 2.6 Hz), 44.1 (dd, *J* = 21.9, 22.6 Hz), 34.5 (dd, *J* = 3.5, 1.7 Hz), 28.8, 21.6, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.71 (dt, *J* = 266.3, 16.1 Hz), -104.35 (dt, *J* = 266.4, 17.4 Hz); HRMS (ESI) exact mass calculated for $C_{18}H_{20}F_2NO_3^+$ [M+H$^+$]: 336.1406, found: 336.1408; IR (neat): ν_{max} (cm^{-1}) = 1709, 1605, 1589, 1403, 1367, 1271, 1190, 769, 745; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(1,9-dimethyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3t**). According to general procedure with **1t** and **2a**, **3t** were obtained in 49% yield (35 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21-7.96 (m, 1H, Ar-*H*), 7.46 (dd, *J* = 7.3, 1.9 Hz, 1H, Ar-*H*), 7.40-7.22 (m, 2H, 2(Ar-*H*)), 4.00 (dd, *J* = 10.8, 7.1 Hz, 1H, CF_2CHH), 3.71 (dd, *J* = 10.8, 7.1 Hz, 1H, CF_2CHH), 3.40 (d, *J* = 18.3 Hz, 1H, COC*H*H), 2.93 (dd, *J* = 18.2, 1.7 Hz, 1H, COCH*H*), 2.87-2.52 (m, 2H, CO_2CH_2), 2.27 (s, 3H, Ar-CH_3), 1.64 (s, 3H, CCH_3), 1.07 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101

MHz, $CDCl_3$) δ 169.2, 163.6 (t, *J* = 31.9 Hz), 142.7, 135.9, 129.7, 124.1, 124.0, 118.9, 115.6 (dd, *J* = 255.4, 249.8 Hz), 113.8, 109.3, 63.3, 49.1 (d, *J* = 4.4 Hz), 43.3 (dd, *J* = 23.1, 21.6 Hz), 35.4 (d, *J* = 4.9 Hz), 27.6 (d, *J* = 1.5 Hz), 13.4, 8.53; ^{19}F NMR (376 MHz, $CDCl_3$) δ -97.80 (dt, *J* = 265.7, 14.7 Hz), -105.61 (ddd, *J* = 265.7, 19.5, 16.5 Hz); HRMS (ESI) exact mass calculated for $C_{18}H_{20}F_2NO_3^+$ [M+H$^+$]: 336.1406, found: 336.1409; IR (neat): ν_{max} (cm^{-1}) = 1736, 1597, 1551, 1457, 1376, 1363, 779, 758; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 2,2-difluoro-3-(1-methyl-3-oxo-9-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3u**). According to general procedure with **1u** and **2a**, **3u** was obtained in 78% yield (62 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.9 Hz, 1H, Ar-*H*), 7.48 (td, *J* = 10.2, 9.6, 6.8 Hz, 5H, 5(Ar-*H*)), 7.54-7.47 (m, 2H, 2(Ar-*H*)), 7.34-7.26 (m, 1H, Ar-*H*), 4.18-4.11 (m, 1H, CF_2CHH), 4.05-3.97 (m, 1H, CF_2CHH), 3.46 (d, *J* = 18.2 Hz, 1H, COC*H*H), 2.99 (d, *J* = 18.2 Hz, 1H, COCH*H*), 2.57 (t, *J* = 17.3 Hz, 2H, CO_2CH_2), 1.60 (s, 3H, CCH_3), 1.22 (t, *J* = 7.2, Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6, 163.7 (t, *J* = 32.2 Hz), 144.2, 135.4, 132.4, 129.9, 129.6, 128.7, 127.8, 124.5, 124.4, 119.8, 116.2, 115.5 (dd, *J* = 3.0, 1.4 Hz), 113.8, 63.3, 49.1 (d, *J* = 3.0 Hz), 43.2 (t, *J* = 22.0 Hz), 36.4, 28.7, 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.32 (dt, *J* = 264.8, 17.2 Hz), -103.87 (dt, *J* = 264.6, 17.1 Hz); HRMS (ESI) exact mass calculated for $C_{23}H_{22}F_2NO_3^+$ [M+H$^+$]: 398.1562, found: 398.1565; IR (neat): ν_{max} (cm^{-1}) = 1740, 1633, 1598, 1451, 1380, 1264, 735, 702; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(9-cyano-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate **(3v)**. According to general procedure with **1v** and **2a**, **3v** was obtained in 85% yield (59 mg, white solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-8.03 (m, 1H, Ar-*H*), 7.77-7.62 (m, 1H, Ar-*H*), 7.54-7.36 (m, 2H, Ar-*H*), 4.32-3.99 (m, 2H, CF_2CH_2), 3.51 (d, *J* = 18.6 Hz, 1H, COC*H*H), 3.02 (d, *J* = 18.7 Hz, 1H, COCH*H*), 2.94-2.68 (m, 2H, CO_2CH_2), 1.76 (s, 3H, CCH_3), 1.30 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.0, 163.1 (t, *J* = 32.0 Hz), 157.6, 132.1, 129.1, 126.0, 125.8, 119.8, 115.1 (t, *J* = 253.9 Hz), 114.3, 113.2, 84.8, 63.6, 47.5 (t, *J* = 3.0 Hz), 42.3 (t, *J* = 22.1 Hz), 36.6 (t, *J* = 1.8 Hz), 27.6 (d, *J* = 1.7 Hz), 13.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -(100.16-101.13) (m), -(103.90-105.41) (m); HRMS (EI) exact mass calculated for $C_{18}H_{16}F_2N_2O_3^+$ [M$^+$]: 346.1124, found:

346.1122; IR (neat): ν_{max} (cm^{-1}) = 2225, 1762, 1577, 1452, 1344, 1182, 760, 689; m.p. = 59-62 °C, R_f = 0.3 (petroleum ether/EtOAc 15:1).

Methyl 1-(3-ethoxy-2,2-difluoro-3-oxopropyl)-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indole-9-carboxylate **(3w)**. According to general procedure with **1w** and **2a**, **3w** was obtained in 57% yield (43 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21-8.05 (m, 2H, 2(Ar-*H*)), 7.48-7.36 (m, 2H, 2(Ar-*H*)), 4.13-4.04 (m, 1H, CF_2CHH), 4.02-3.94 (m, 4H, CF_2CHH and CO_2CH_3), 3.55 (d, *J* = 18.8 Hz, 1H, COC*H*H), 3.74-3.14 (m, 1H, CO_2CHH), 3.04-2.85 (m, 2H, COCH*H* and CO_2CHH), 1.76 (s, 3H, CCH_3), 1.18 (t, *J* = 7.1 Hz, 3H, CH_2CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 164.3, 163.7 (t, *J* = 32.1 Hz), 155.6, 131.7, 129.6, 125.4, 125.0, 122.2, 115.7 (dd, *J* = 254.6, 252.3 Hz), 113.8, 106.4, 63.3, 51.6, 47.8 (t, *J* = 2.4 Hz), 40.8 (dd, *J* = 22.7, 20.9 Hz), 37.2 (d, *J* = 3.5 Hz), 26.8, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.29 (ddd, *J* = 263.0, 20.7, 12.0 Hz), -104.50 (ddd, *J* = 263.1, 20.2, 16.3 Hz); HRMS (EI) exact mass calculated for $C_{19}H_{19}F_2NO_5$ [M]: 379.1231, found: 379.1236; IR (neat): ν_{max} (cm^{-1}) = 1756, 1706, 1564, 1454, 1179, 1147, 795, 756; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 2,2-difluoro-3-(9-formyl-1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate **(3x)**. According to general procedure with **1x** and **2a**, **3x** was obtained in 76% yield (53 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.34 (s, 1H, C*H*O), 8.22-8.02 (m, 2H, 2(Ar-*H*)), 7.53-7.35 (m, 2H, 2(Ar-*H*)), 4.18-3.96 (m, 2H, CO_2CH_2), 3.56 (d, *J* = 18.7 Hz, 1H, COC*H*H), 3.14-2.98 (m, 2H, CF_2CHH and COCH*H*), 2.97-2.79 (m, 1H, CF_2CH*H*), 1.77 (s, 3H, CCH_3), 1.21 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 184.1, 170.3, 163.4 (t, *J* = 32.0 Hz), 156.8, 131.6, 129.8, 125.9, 125.5, 120.4, 115.4 (dd, *J* = 255.4, 252.9 Hz), 114.0, 113.9, 63.4, 47.6 (t, *J* = 2.9 Hz), 42.4 (dd, *J* = 22.7, 21.2 Hz), 37.2 (d, *J* = 2.9 Hz), 28.0 (d, *J* = 1.5 Hz), 13.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.83 (ddd, *J* = 264.7, 21.2, 11.9 Hz), -104.72 (ddd, *J* = 264.5, 20.2, 14.7 Hz); HRMS (EI) exact mass calculated for $C_{18}H_{17}F_2NO_4$ [M]: 349.1126, found: 349.1132; IR (neat): ν_{max} (cm^{-1}) = 1758, 1668, 1552, 1455, 1338, 1178, 1062, 759; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 2,2-difluoro-3-(6-methyl-8-oxo-7,8-dihydro-6H-pyrido[3,2-b]pyrrolizin-6-yl)propanoate (**3y**). According to general procedure with **1y** and **2a**, **3y** was obtained in 65% yield (42 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 (s, 1H, Ar-*H*), 7.86 (d, *J* = 7.9 Hz, 1H, Ar-*H*), 7.26 (s, 1H, Ar-*H*), 6.32 (s, 1H, Ar-*H*), 4.19 (s, 1H, CF_2CH*H*), 4.08 (s, 1H, CF_2CHH), 3.41 (d, *J* = 18.4 Hz, 1H, COC*H*H), 3.03

(d, *J* = 18.3 Hz, 1H, COCH*H*), 2.68 (t, *J* = 16.9 Hz, 2H, CO_2CH_2), 1.64 (s, 3H, CCH_3), 1.24 (t, *J* = 7.2 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 163.7 (t, *J* = 32.1 Hz), 150.1, 144.9, 143.7, 129.2, 127.5, 119.8, 115.3 (dd, *J* = 252.6, 254.7 Hz), 97.6, 63.4, 49.2 (dd, *J* = 3.2, 1.0 Hz), 43.7 (t, *J* = 22.6 Hz), 35.4 (dd, *J* = 2.7, 1.5 Hz), 28.7 (d, *J* = 1.3 Hz), 13.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.40 (dt, *J* = 266.9, 16.0 Hz), -104.09 (dt, *J* = 267.2, 17.3 Hz); HRMS (ESI) exact mass calculated for $C_{16}H_{17}F_2N_2O_3^+$ [M+H$^+$]: 323.1202, found: 323.1205; IR (neat): ν_{max} (cm^{-1}) = 1728, 1624, 1559, 1409, 1370, 1282, 819, 712; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 2,2-difluoro-3-(3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3z**). According to general procedure with **1z** and **2a**, **3z** obtained in 55% yield (34 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.5 Hz, 1H, Ar-*H*), 7.55 (d, *J* = 7.1 Hz, 1H, Ar-*H*), 7.34-7.30 (m, 2H, 2(Ar-*H*)), 6.41 (s, 1H, Ar-*H*), 4.38 (q, *J* = 7.2 Hz, 2H, CO_2CH_2), 3.97-3.72 (m, 1H, CH_2CH), 3.39 (dd, *J* = 18.4, 8.7 Hz, 1H, COC*H*H), 2.96 (dd, *J* = 18.4, 4.8 Hz, 1H, COCH*H*), 2.82-2.62 (m, 1H, CF_2CHH), 2.58-2.35 (m, 1H, CF_2CHH), 1.40 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 163.7 (t, *J* = 32.2 Hz), 145.2, 134.9, 130.4, 124.3, 123.9, 120.9, 116.4 (t, *J* = 252.8 Hz), 113.8, 101.1, 63.4, 42.0, 39.5 (t, *J* = 22.7 Hz), 26.9 (t, *J* = 4.1 Hz), 13.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.13 (dd, *J* = 21.0, 13.1 Hz), -105.32 (dd, *J* = 20.2, 14.1 Hz); HRMS (ESI) exact mass calculated for $C_{16}H_{16}F_2NO_3^+$ [M+H$^+$]: 308.1093, found: 308.1096; IR (neat): ν_{max} (cm^{-1}) = 1742, 1632, 1598, 1454, 1389, 1357, 1310, 865, 753; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 2,2-difluoro-3-(3-oxo-1-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3aa**). According to general procedure with **1aa** and **2a**, **3aa** obtained in 27% yield (21 mg, yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 7.6 Hz, 1H, Ar-*H*), 7.69-7.57 (m, 1H, Ar-*H*), 7.46 (d, *J* = 8.1 Hz, 2H, 2(Ar-*H*)), 7.42-7.27 (m, 5H, 5(Ar-*H*)), 6.60 (s, 1H, Ar-*H*), 3.87 (dt, *J* = 14.2, 7.1 Hz, 1H, CF_2CHH), 3.77-3.63 (m, 2H, CF_2CH*H* and COC*H*H), 3.51 (d, *J* = 18.1 Hz, 1H, COCH*H*), 3.20-3.02 (m, 2H, CO_2CH_2), 1.06 (td, *J* = 7.2, 1.3 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.8, 163.4 (t, *J* = 31.8 Hz), 145.3, 142.8, 134.4, 130.3, 128.9, 127.7, 126.2, 124.4, 124.4, 121.0, 114.1, 103.9 (d, *J* = 2.1 Hz), 63.2, 50.2 (d, *J* = 2.9 Hz), 45.4 (dd, *J* = 23.9, 21.7 Hz), 43.5 (d, *J* = 5.3 Hz), 13.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -96.68 (dt, *J* = 269.2, 13.6 Hz), -103.34 (dt, *J* = 269.3, 17.0 Hz); HRMS (ESI)

exact mass calculated for $C_{22}H_{20}F_2NO_3^+$ [M+H$^+$]: 384.1406, found: 384.1410; IR (neat): ν_{max} (cm^{-1}) = 1722, 1598, 1467, 1354, 1289, 754, 690, 553; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Ethyl 3-(1,2-dimethyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)-2,2-difluoropropanoate (**3ab**). According to general procedure with **1ab** and **2a**, **3ab** was obtained in 74% yield (50 mg, colorless oil, unseparated mixture with *dr* ratio of 5 to 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18-7.92 (m, 1H), 7.60-7.45 (m, 1H), 7.40-7.17 (m, 2H), 6.35 (s, 1H, major) (6.37 (s, 1H, minor)), 4.25-4.14 (m, 1H, major) (4.00-3.90 (m, 1H, minor)), 4.13-4.02 (m, 1H, major) (3.73-3.61 (m, 1H, minor)), 3.35 (q, *J* = 7.4 Hz, 1H, major) (3.03 (q, *J* = 7.3 Hz, 1H, minor)), 2.80-2.42 (m, 2H), 1.50-1.33 (m, 6H), 1.25 (t, *J* = 7.1 Hz, 3H, major) (1.00 (t, *J* = 7.1 Hz, 3H, minor)); ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.7 (172.1) , 163.9 (t, *J* = 32.2 Hz) (163.5 (t, *J* = 30.00 Hz)), 149.4 (146.8), 134.6 (134.1), 130.1 (130.5), 124.2 (124.1), 123.9, 120.9, 115.5 (t, *J* = 253.6 Hz) (115.7 (t, *J* = 253.2 Hz)), 114.0 (113.9), 99.7 (101.74), 63.3 (63.1), 50.8 (55.0), 43.7 (t, *J* = 22.4 Hz) (40.0 (t, *J* = 22.7 Hz)), 38.6 (d, *J* = 2.2 Hz) (38.7 (d, *J* = 1.3 Hz)), 24.2 (26.3), 13.7 (13.4), 10.7 (10.0); ^{19}F NMR (376 MHz, $CDCl_3$) -103.34 (ddd, *J* = 264.1, 26.5, 13.5 Hz) (δ -99.75 (ddd, *J* = 273.9, 17.9, 13.2 Hz)), -103.02 (ddd, *J* = 264.7, 20.4, 16.3 Hz) (δ -102.05 (ddd, *J* = 274.3, 19.8, 13.7 Hz)); HRMS (EI) exact mass calculated for $C_{18}H_{19}F_2NO_3^+$ [M$^+$]: 335.1328, found: 335.1325; IR (neat): ν_{max} (cm^{-1}) = 1740, 1585, 1453, 1383, 1194, 1082, 807, 754; R_f = 0.3 (petroleum ether/EtOAc 20:1).

Ethyl 2,2-difluoro-3-(9-methyl-6-oxo-6,7,8,9-tetrahydropyrido[1,2-a]indol-9-yl)propanoate (**3ac**). According to general procedure with **1ac** and **2a**, **3ac** was obtained in 64% yield (43 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (d, *J* = 8.1 Hz, 1H, Ar-*H*), 7.50 (d, *J* = 7.6 Hz, 1H, Ar-*H*), 7.39-7.32 (m, 1H, Ar-*H*), 7.31-7.28 (m, 2H, 2(Ar-*H*)), 6.43 (s, 1H, Ar-*H*), 3.98-3.86 (m, 1H, CF_2CHH), 3.83-3.73 (m, 1H, CF_2CHH), 3.03-2.82 (m, 2H, CO_2CH_2), 2.78-2.61 (m, 1H, COC*H*HCHH), 2.57-2.36 (m, 1H, COCH*H*CHH), 2.27-2.15 (m, 1H, COCHHC*H*H), 2.16-2.02 (m, 1H, COCHHC*H*H), 1.64 (s, 3H, CCH_3), 1.14 (t, *J* = 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 163.3 (t, *J* = 31.8 Hz), 143.2, 135.1, 129.0, 124.9, 124.2, 120.1, 116.5, 115.8 (dd, *J* = 254.8, 248.2 Hz), 105.7, 63.1, 42.3 (t, *J* = 22.3 Hz), 33.5 (d, *J* = 2.1 Hz), 32.9 (d, *J* = 4.7 Hz), 30.5, 27.3 (d, *J* = 3.9 Hz), 26.9, 13.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -96.66 (dt, *J* = 268.5, 14.9 Hz), -104.17 (dt, *J* = 268.7, 18.9 Hz); HRMS

(ESI) exact mass calculated for $C_{18}H_{20}F_2NO_3^+$ [M+H$^+$]: 336.1406, found: 336.1410; IR (neat): ν_{max} (cm^{-1}) = 1764, 1705, 1668, 1454, 1350, 1189, 1148, 855, 755; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Benzyl 2,2-difluoro-3-(1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3ad**). According to general procedure with **1a** and **2b**, **3ad** was obtained in 65% yield (50 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 7.5 Hz, 1H, Ar-*H*), 7.53 (d, *J* = 7.3 Hz, 1H, Ar-*H*), 7.43-7.17 (m, 7H, 7(Ar-*H*)), 6.32 (s, 1H, Ar-*H*), 5.12 (d, *J* = 12.1 Hz, 1H, CF_2CHH), 4.95 (d, *J* = 12.1 Hz, 1H, CF_2CHH), 3.34 (d, *J* = 18.3 Hz, 1H, COC*H*H), 2.94 (d, *J* = 18.2 Hz, 1H, COC*H*H), 2.68 (t, *J* = 16.8 Hz, 2H, Ar-CH_2), 1.59 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 163.6 (t, *J* = 31.5), 149.5, 134.7, 133.8, 130.1, 128.9, 128.8 (d, *J* = 2.2 Hz), 128.7, 128.5, 124.3, 124.1, 120.9, 115.5 (dd, *J* = 253.5, 251.8 Hz), 114.0, 99.9, 68.7, 49.1, 44.0 (t, *J* = 22.2 Hz), 35.5, 28.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.70 (dt, *J* = 267.3, 16.4 Hz), -104.06 (dt, *J* = 267.2, 17.5 Hz); HRMS (ESI) exact mass calculated for $C_{22}H_{20}F_2NO_3^+$ [M+H$^+$]: 384.1406, found: 384.1409; IR (neat): ν_{max} (cm^{-1}) = 1713, 1644, 1455, 1360, 1301, 1196, 754, 699; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Dodecyl 2,2-difluoro-3-(1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanoate (**3ae**). According to general procedure with **1a** and **2c**, **3ae** was obtained in 61% yield (57 mg, light yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.6 Hz, 1H, Ar-*H*), 7.53 (d, *J* = 7.5 Hz, 1H, Ar-*H*), 7.31 (dd, *J* = 12.3, 5.3 Hz, 2H, 2(Ar-*H*)), 6.32 (s, 1H, Ar-*H*), 4.09-4.03 (m, 1H, CF_2CHH), 3.92-3.86 (m, 1H, CF_2CHH), 3.37 (d, *J* = 18.3 Hz, 1H, COC*H*H), 2.96 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.67 (t, *J* = 16.7 Hz, 2H, CO_2CH_2), 1.62 (s, 3H, CCH_3), 1.59-1.49 (m, 2H), 1.35-1.26 (m, *J* = 8.7 Hz, 16H), 0.91 (t, *J* = 6.7 Hz, 3H, CH_2CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.5, 163.9 (t, *J* = 32.0 Hz), 149.4, 134.7, 130.1, 124.3, 124.0, 120.9, 115.5 (dd, *J* = 253.6, 251.3 Hz), 114.0, 99.9, 67.3, 63.0, 49.0 (d, *J* = 3.5 Hz), 44.0 (t, *J* = 22.3 Hz), 33.3 (dd, *J* = 3.3, 1.5 Hz), 32.8, 31.9, 29.7, 29.6 (d, *J* = 2.7 Hz), 29.5, 29.5, 29.4, 29.4, 29.1, 28.8, 28.0, 25.8, 25.5, 22.7, 14.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.48 (dt, *J* = 266.7, 16.2 Hz), -104.32 (dt, *J* = 266.8, 17.6 Hz); HRMS (ESI) exact mass calculated for $C_{27}H_{38}F_2NO_3^+$ [M+H$^+$]: 462.2814, found: 462.2818; IR (neat): ν_{max} (cm^{-1}) = 1716, 1662, 1593, 1456, 1396, 1300, 866, 756; R_f = 0.3 (petroleum ether/EtOAc 15:1).

Dodecyl 1-(2,2-difluoro-3-oxo-3-phenylpropyl)-1-methyl-1H-pyrrolo[1,2-a]indol-3(2H)-one (**3af**). According to general procedure with **1a** and **2d**, **3af** was obtained in 65% yield (46 mg, yellow oil). ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.06 (dd, *J* = 16.1, 7.7 Hz, 3H, 3(Ar-*H*)), 7.64 (t, *J* = 7.5 Hz, 1H, Ar-*H*), 7.49 (q, *J* = 7.9, 7.0 Hz, 3H, 3(Ar-*H*)), 7.35-7.18 (m, 2H, 2(Ar-*H*)), 6.32 (s, 1H, Ar-*H*), 3.41 (d, *J* = 18.3 Hz, 1H, CF_2CHH), 3.02 (d, *J* = 18.2 Hz, 1H, CF_2CHH), 2.84 (ddd, *J* = 22.5, 14.4, 5.6 Hz, 2H, $COCH_2$), 1.67 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 188.6 (t, *J* = 31.0 Hz), 169.7, 150.5, 134.9, 134.5, 131.4 (t, *J* = 2.4 Hz), 130.2 (t, *J* = 3.4 Hz), 130.1, 128.7, 124.2, 123.9, 120.9, 119.4 (t, *J* = 255.5 Hz), 113.9, 99.8, 49.5 (t, *J* = 2.4 Hz), 42.9 (t, *J* = 21.3 Hz), 35.7 (d, *J* = 1.7 Hz), 29.0 (d, *J* = 2.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -95.84 (dt, *J* = 293.7, 20.5 Hz), -98.13 (dt, *J* = 293.4, 15.4 Hz); HRMS (ESI) exact mass calculated for $C_{21}H_{18}F_2NO_2^+$ [M+H$^+$]: 354.1300, found: 354.1305; IR (neat): ν_{max} (cm^{-1}) = 1712, 1556, 1475, 1411, 1389, 1245, 803, 735; R_f = 0.3 (petroleum ether/EtOAc 15:1).

1-(2,2-Difluoro-3-oxo-5-phenylpentyl)-1-methyl-1H-pyrrolo[1,2-a]indol-3(2H)-one (**3ag**). According to general procedure with **1a** and **2e**, **3ag** was obtained in 60% yield (46 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.7 Hz, 1H, Ar-*H*), 7.56 (d, *J* = 7.5 Hz, 1H, Ar-*H*), 7.35 (q, *J* = 7.5 Hz, 2H, 2(Ar-*H*)), 7.27 (t, *J* = 7.7 Hz, 2H, 2(Ar-*H*)), 7.21 (d, *J* = 7.1 Hz, 1H, Ar-*H*), 7.01 (d, *J* = 7.4 Hz, 2H, 2(Ar-*H*)), 6.28 (s, 1H, Ar-*H*), 3.33 (d, *J* = 18.2 Hz, 1H, CF_2CHH), 2.96 (d, *J* = 18.5 Hz, 1H, CF_2CHH), 2.92-2.49 (m, 6H, $COCH_2$ and COC_2H_4Ph), 1.59 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.7 (dd, *J* = 32.7, 29.8 Hz), 169.6 (d, *J* = 1.1 Hz), 149.7, 139.9, 134.8, 130.0, 128.5, 128.2, 126.4, 124.4, 124.1, 121.0, 117.7 (dd, *J* = 255.0, 253.1 Hz), 114.0, 100.3, 49.4 (dd, *J* = 3.5, 1.2 Hz), 42.0 (dd, *J* = 22.2, 20.8 Hz), 37.8, 35.4 (dd, *J* = 3.0, 1.3 Hz), 29.1 (d, *J* = 1.8 Hz), 28.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -99.72 (ddd, *J* = 285.4, 20.3, 13.9 Hz), -107.66 (dt, *J* = 285.4, 17.9 Hz); HRMS (ESI) exact mass calculated for $C_{23}H_{22}F_2NO_2^+$ [M+H$^+$]: 382.1613, found: 382.1615; IR (neat): ν_{max} (cm^{-1}) = 1719, 1669, 1455, 1394, 1264, 1212, 731, 703; R_f = 0.3 (petroleum ether/EtOAc 10:1).

1-(2-(Benzo[d]oxazol-2-yl)-2,2-difluoroethyl)-1-methyl-1H-pyrrolo[1,2-a]indol-3(2H)-one (**3ah**). According to general procedure with **1a** and **2f**, **3ah** was obtained in 54% yield (40 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.0 Hz, 1H, Ar-*H*), 7.64 (d, *J* = 7.8 Hz, 1H, Ar-*H*), 7.45 (d, *J* = 8.1 Hz, 1H, Ar-*H*), 7.36 (dt, *J* = 21.0, 7.4 Hz, 2H, 2(Ar-*H*)), 7.30-7.20 (m, 2H, 2(Ar-*H*)), 7.17 (t, *J* = 7.5 Hz, 1H, Ar-*H*), 6.13 (s, 1H, Ar-*H*), 3.46 (d, *J* = 18.2 Hz, 1H, CF_2CHH), 3.22-2.85 (m, 3H, $COCH_2$ and CF_2CHH), 1.64 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.4, 157.3, 150.4, 149.4, 139.7, 134.7, 130.0, 126.9, 125.3, 124.1, 123.8, 121.0, 120.6, 117.5 (dd, *J* = 421.2, 175.2 Hz), 113.9,

113.8, 111.1, 99.5, 48.9 (dd, *J* = 3.6, 1.1 Hz), 45.7 (dd, *J* = 23.6, 22.1 Hz), 35.7 (d, *J* = 2.8 Hz), 29.0 (d, *J* = 1.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -91.91 (dt, *J* = 278.9, 15.4 Hz), -97.90 (dt, *J* = 279.2, 17.7 Hz); HRMS (ESI) exact mass calculated for $C_{22}H_{17}F_2N_2O_3^+$ [M+H$^+$]: 395.1202, found: 395.1206; IR (neat): ν_{max} (cm^{-1}) = 1739, 1623, 1452, 1359, 1382, 1391, 748, 705; R_f = 0.3 (petroleum ether/EtOAc 10:1).

1-(2,2-Difluoro-3-oxo-3-(piperidin-1-yl)propyl)-1-methyl-1H-pyrrolo[1,2-a]indol-3(2H)-one (**3ai**). According to general procedure with **1a** and **2g**, **3ai** was obtained in 65% yield (47 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13-8.04 (m, 1H, Ar-*H*), 7.59-7.49 (m, 1H, Ar-*H*), 7.30 (tt, *J* = 7.2, 5.7 Hz, 2H, 2(Ar-*H*)), 6.34 (s, 1H, Ar-*H*), 3.60 (t, *J* = 5.3 Hz, 2H, CF_2CH_2), 3.54 (t, *J* = 5.4 Hz, 2H), 3.37 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.96 (d, *J* = 18.3 Hz, 1H, COC*H*H), 2.88-2.75 (m, 2H), 1.69-1.51 (m, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.0, 161.3 (t, *J* = 28.5 Hz), 151.1, 135.0, 130.1, 102.4, 123.6, 120.9, 119.4 (t, *J* = 257.1 Hz), 113.9, 99.3, 49.3 (t, *J* = 2.5 Hz), 46.9 (t, *J* = 6.8 Hz), 44.7, 43.5 (t, *J* = 21.4 Hz), 35.7 (d, *J* = 1.5 Hz), 29.1 (d, *J* = 2.2 Hz), 26.5, 25.6, 24.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -96.12 (dt, *J* = 281.9, 19.2 Hz), -97.91 (dt, *J* = 282.1, 18.9 Hz); HRMS (ESI) exact mass calculated for $C_{20}H_{23}F_2N_2O_2^+$ [M+H$^+$]: 361.1722, found: 361,1726; IR (neat): ν_{max} (cm^{-1}) = 1736, 1659, 1452, 1361, 1190, 750, 734, 702; R_f = 0.3 (petroleum ether/EtOAc 10:1).

N-Benzyl-2,2-difluoro-3-(1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)propanamide (**3aj**). According to general procedure with **1a** and **2h**, **3aj** was obtained in 23% yield (18 mg, white solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.4 Hz, 1H, Ar-*H*), 7.55 (d, *J* = 7.3 Hz, 1H, Ar-*H*), 7.42-.23 (m, 5H, 5(Ar-*H*)), 7.13-7.01 (m, 2H, 2(Ar-*H*)), 6.62 (s, 1H, N*H*), 6.36 (s, 1H, Ar-*H*), 4.36 (dd, *J* = 14.6, 6.2 Hz, 1H, CF_2CH*H*), 3.98 (dd, *J* = 14.6, 5.2 Hz, 1H, CF_2CH*H*), 3.32 (d, *J* = 18.2 Hz, 1H, COCH*H*), 2.92 (d, *J* = 18.3 Hz, 1H, COC*H*H), 2.86-2.59 (m, 2H, Ar-CH_2), 1.60 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 163.6 (t, *J* = 28.4 Hz), 149.4, 136.3, 135.0, 130.0, 128.8, 127.9 (d, *J* = 6.9 Hz), 124.3, 123.9, 121.1, 117.6 (dd, *J* = 255.6, 253.2 Hz), 113.9, 100.3, 49.2 (d, *J* = 3.2 Hz), 43.6, 43.1 (t, *J* = 22.1 Hz), 35.4 (d, *J* = 3.4 Hz), 29.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -98.35 (dt, *J* = 263.1, 16.4 Hz), -106.69 (dt, *J* = 263.2, 17.9 Hz); HRMS (EI) exact mass calculated for $C_{22}H_{20}F_2N_2O_2$ [M]: 383.1493, found: 382.1490; IR (neat): ν_{max} (cm^{-1}) = 3332, 1691, 1541, 1454, 1380, 1361, 1191, 733, 698; m.p. = 79-81 ^{o}C; R_f = 0.3 (petroleum ether/EtOAc 8:1).

Diethyl (1,1-difluoro-2-(1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-1-yl)ethyl) phosphonate (**3ak**). According to general procedure with **1a** and diethyl (bromodifluoromethyl)phosphonate, **3ak** was obtained in 53% yield (43 mg, white solid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21-8.3 (m, 1H, Ar-*H*), 7.67-7.39 (m, 1H, Ar-*H*), 7.28 (tt, *J* = 7.4, 5.7 Hz, 2H, 2(Ar-*H*)), 6.32 (s, 1H, Ar-*H*), 4.32-4.13 (m, 4H, $PO(OCH_2CH_3)_2$), 3.35 (d, *J* = 18.3 Hz, 1H, COC*H*H), 2.97 (d, *J* = 18.3 Hz, 1H, COCH*H*), 2.82-2.48 (m, 2H, CF_2CH_2), 1.62 (d, *J* = 1.3 Hz, 3H, CCH_3), 1.36 (td, *J* = 7.0, 5.8 Hz, 6H, $PO(OCH_2CH_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 150.9, 134.9, 130.1, 124.2, 123.8, 120.9, 113.9, 99.4, 64.8 (dd, *J* = 9.4, 7.0 Hz), 49.3, 42.6 (dd, *J* = 35.1, 22.4, Hz), 36.0 (d, *J* = 1.4 Hz), 35.9 (d, *J* = 1.6 Hz), 28.7, 16.4 (d, *J* = 5.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -(108.03-109.74) (m), -(111.63-113.25) (m); ^{31}P NMR (162 MHz, $CDCl_3$) δ 6.11 (t, *J* = 105.7 Hz); HRMS (ESI) exact mass calculated for $C_{18}H_{23}F_2NO_4P^+$ [M+H$^+$]: 386.1327, found: 386.1331; IR (neat): ν_{max} (cm^{-1}) = 1719, 1654, 1394, 1264, 1212, 1078, 731, 703; m.p. = 84-85 ^{o}C; R_f = 0.3 (petroleum ether/EtOAc 5:1).

1-(2,2-Difluoro-3-hydroxypropyl)-1-methyl-1H-pyrrolo[1,2-a]indol-3(2H)-one (**4**).To a stirred solution of **3a** (0.2 mmol, 64.3 mg) in methanol (2.0 mL) at room temperature was added $NaBH_4$ (0.6 mmol, 22.7 mg). Until **3a** was consumed (monitored by TLC), the reaction mixture was quenched with water. The aqueous layer was extracted with ethyl acetate (10 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude residue was purified by flash column chromatography on silica gel to afford **4** in 99% yield (58 mg, light yellow oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 7.2 Hz, 1H, Ar-*H*), 7.52 (d, *J* = 7.1 Hz, 1H, Ar-*H*), 7.30 (t, *J* = 5.5 Hz, 2H, 2(Ar-*H*)), 6.33 (s, 1H, Ar-*H*), 3.67 (t, *J* = 13.0 Hz, 2H, CF_2CH_2), 3.36 (d, *J* = 18.4 Hz, 1H, COC*H*H), 2.95 (d, *J* = 18.4 Hz, 1H, COCH*H*), 2.64 (s, 1H, CH_2OH), 2.54-2.40 (m, 2H, CH_2OH), 1.61 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.4 (d, *J* = 1.3 Hz), 151.3, 135.0, 130.1, 122.9 (t, *J* = 254.1 Hz), 124.3, 123.8, 120.9, 113.9, 99.2 (d, *J* = 1.3 Hz), 64.9 (t, *J* = 32.1 Hz), 51.5-46.8 (m), 42.7 (t, *J* = 22.3 Hz), 35.8 (d, *J* = 1.1 Hz), 28.8 (dd, *J* = 2.5, 1.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -(102.18-103.62) (m), -(107.25-108.29) (m); HRMS (ESI) exact mass calculated for $C_{15}H_{16}F_2NO_2^+$ [M+H$^+$]: 280.1144, found: 280.1147; IR (neat): ν_{max} (cm^{-1}) = 1714, 1661, 1524, 1454, 1383, 1276, 753, 698; R_f = 0.3 (petroleum ether/EtOAc 5:1).

2,2-Difluoro-3-(1-methyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-a]indol-yl)propanamide (**5**). To a stirred solution of **3a** (0.2 mmol, 64.3 mg) in methanol (2.0 mL) at room temperature, NH_3 (gas, generated through heating $NH_3 \cdot H_2O$) was bubbled. Until **3a** was consumed (monitored by TLC), the reaction mixture was diluted with water. The aqueous layer was extracted with ethyl acetate (10 mL×3). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude residue was purified by flash column chromatography on silica gel to afford **5** in 91% yield (48 mg, colorless oil). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.5 Hz, 1H, Ar-*H*), 7.64-7.42 (m, 1H, Ar-*H*), 7.39-7.21 (m, 2H, 2(Ar-*H*)), 6.34 (s, 1H, Ar-*H*), 6.30 (s, 1H, CON*H*H), 6.22 (s, 1H, CONH*H*), 3.35 (d, *J* = 18.2 Hz, 1H, COCH*H*), 2.96 (d, *J* = 18.2 Hz, 1H, COC*H*H), 2.70 (t, *J* = 17.7 Hz, 2H, CF_2CH_2), 1.61 (s, 3H, CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.8, 166.1 (t, *J* = 29.2 Hz), 149.9, 134.9, 130.0, 124.3, 123.9, 121.0, 117.2 (t, *J* = 255.5 Hz); 113.9, 100.0, 49.1 (d, *J* = 2.2 Hz), 42.9 (t, *J* = 21.8 Hz), 35.5 (t, *J* = 2.0 Hz), 28.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.55 (dt, *J* = 263.1, 17.7 Hz), -104.83 (dt, *J* = 263.4, 17.7 Hz); HRMS (ESI) exact mass calculated for $C_{15}H_{15}F_2N_2O_2^+$ [M+H$^+$]: 293.1096, found: 293.1100; IR (neat): ν_{max} (cm^{-1}) = 1706, 1599, 1524, 1453, 1362, 1192, 750, 575; R_f = 0.3 (petroleum ether/EtOAc 4:1).

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Notes

The authors declare no competing financial interest.

Acknowledgements

Financial support from National Natural Science Foundation of China (21402028) and the Open Project Program of the State Key Laboratory of Photocatalysis on Energy and Environment (52003426), Fuzhou University are gratefully acknowledged.

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.xxxxxxx.

Detailed experimental procedures and spectral data for **1a-1ac**, **2b-2h**, **3a-3ak**, **4**, **5, 6, 7**. (PDF)

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