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Authors: Alexander Aldoshin, Andrey Tabolin, Sema Ioffe, and Valentine G. Nenajdenko

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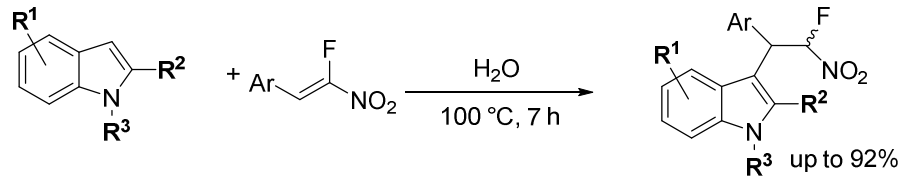
Grafical Abstract



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The alkylation of various indoles with 2-fluoro-2-nitrostyrenes resulted in highly regioselectively 3-(1-aryl-2-fluoro-2-nitroethyl)-1H-indoles in water in up to 92% isolated yield. As a result highly efficient green and catalyst-free synthesis of these compounds was elaborated. Subsequent reduction of nitro group with $NaBH_4$-$NiCl_2$ system leads to loss of fluorine to form non-fluorinated tryptamine derivatives.

Green, catalyst-free reaction of indoles with β-fluoro-β-nitrostyrenes in water

Alexander S. Aldoshin,[a] Andrey A. Tabolin,[b] Sema L. Ioffe[b]
and Valentine G. Nenajdenko*,[a]

[a] *Department of Chemistry, Lomonosov Moscow State University, Moscow, 11999, (Russian Federation)* Fax: (+)7-495-9328846, E-mail: nenajdenko@org.chem.msu.ru

[b] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences Leninsky prosp. 47, Moscow 119991 (Russian Federation)*

ABSTRACT: Reaction of 2-fluoro-2-nitrostyrenes with various indoles was investigated. It was found that the reaction proceeds as Michael addition to form highly regioselectively 3-(1-aryl-2-fluoro-2-nitroethyl)-1H-indoles. Green and catalyst-free synthesis of these compounds was elaborated using water as a reaction media. The high effectiveness of this approach was demonstrated to prepare target products in up to 92% isolated yield. Subsequent reduction of nitro group was investigated. It was found that due to instability of intermediate α-fluoro amines the reduction leads to non-fluorinated tryptamine derivatives.

KEYWORDS: Michael addition, fluorine, nitrostyrene, indole, regioselectivity.

INTRODUCTION

At the present time about 25% of drugs and more than 30% of agrochemicals includes at least one fluorine atom. Noteworthy the incorporation of a fluorine atom changes some important features of the target molecule - lipophilicity, solubility, binding to receptors, metabolism,

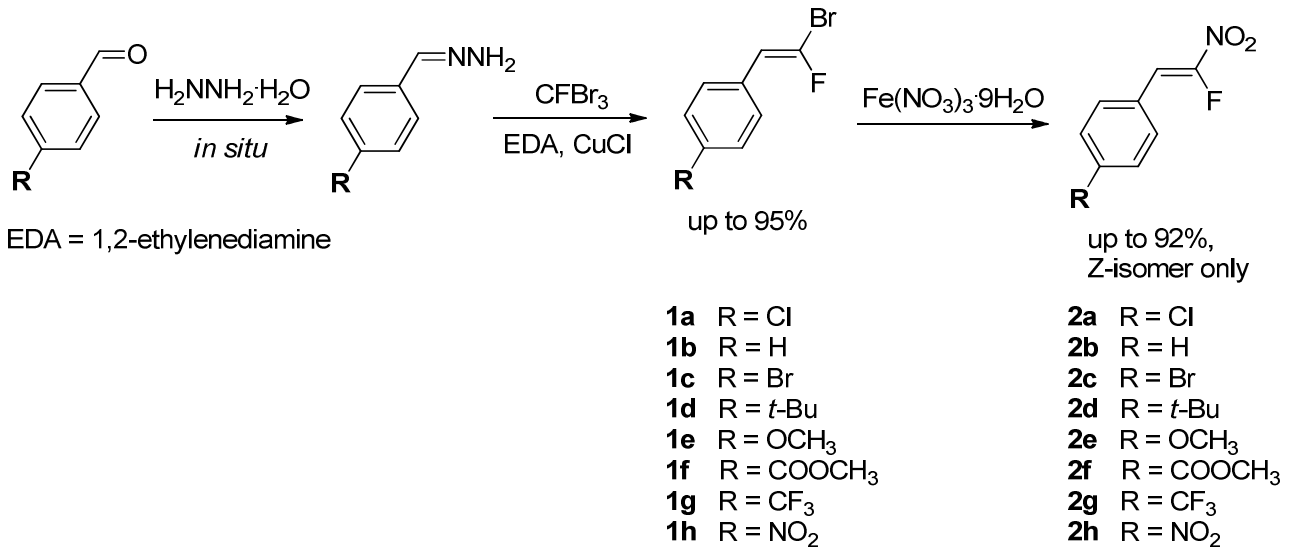
permeability of membranes, acid-base characteristics, and conformational properties of compounds. All these unique features are used as a working tool in the design of new drugs and materials.[1]

Indole ring is one of the most important and widely distributed structural subunits in the nature. Due to their biological and pharmacological activity the molecules containing indole nucleus have found wide application as antiasthmatic, antiallergic, antiviral, antiarrhythmic, anti-inflammatory, antidepressant, antipsychotic, anticancer, antihypertensive, antiemetic, analgesic, and anti-HIV drugs. A number of indole derivatives display antiulcer, antimycotic, antimalarial, antibacterial, antiplatelet, antileishmanial, antioxidant, antitubercular, and immunomodulator activities.[2,3] Therefore, nowadays the development of new pathways to indole derivatives is still actual and retains the high interest.[4]

One of the most important tools used for the synthesis of 3-substituted indole derivatives is a nucleophilic addition of 3-unsubstituted derivatives to Michael acceptors.[5] In turn, we have recently reported the effective and stereoselective method of preparation of β-fluoro-β-nitrostyrenes based on radical nitration of 2-bromo-2-fluorostyrenes. This process occurs with the simultaneous elimination of bromine giving the target structures solely as the *Z*-isomers in high yields (up to 92%).[6] Similarly to their nonfluorinated analogues, β-fluoro- β-nitrostyrenes have highly polar double C-C bond owing to the presence of a strong electron-withdrawing nitro group. These molecules are very attractive Michael acceptors to construct molecules having one fluorine atom in the structure.[7] This study is devoted to reaction of β-fluoro- β-nitrostyrenes with various indoles. Such approach opens straightforward way to valuable mono-fluorinated Michael adducts. In turn the latter can be employed as precursors to the further synthesis of diverse fluorine substituted indole derivatives. Herein we report for the first time a catalyst-free synthesis of novel 3-(1-aryl-2-fluoro-2-nitroethyl)-1H-indoles in water media.

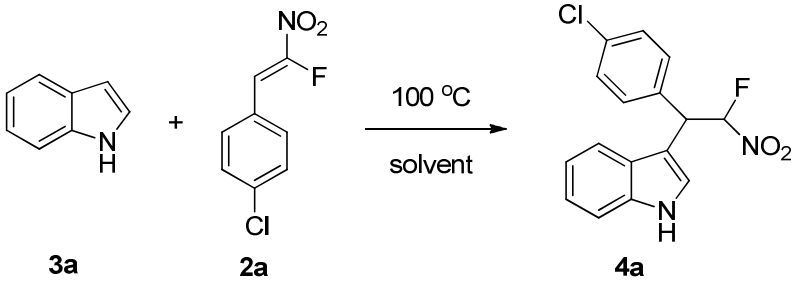
RESULTS AND DISCUSSION

Starting 2-fluoro-2-nitrostyrenes can be easily prepared using procedure elaborated by us recently (Scheme 1).[6] 2-Bromo-2-fluorostyrenes are available from the corresponding commercially available aldehydes and $CFBr_3$ using either catalytic olefination reaction or the Corey-Fuchs reaction.[8] Subsequent radical nitrative debromination of prepared 2-bromo-2-fluorostyrenes **1** with ferric nitrate nonahydrate opens straightforward route to the corresponding nitroalkenes **2**.[6]



Scheme 1. Preparation of 2-fluoro-2-nitrostyrenes

In order to find an optimal reaction conditions, parent indole **3a** was reacted with styrene **2a** as a model substrate. Different solvents in the absence of any additives or catalysts were studied. The reaction was performed at 100 °C (Scheme 2, Table 1). The reaction outcome (conversion and yield) was monitored by ^{19}F NMR using α,α,α-trifluorotoluene as an internal standard. When reaction was carried out in toluene and 1,4-dioxane, no conversion of styrene **2a** into the desired adduct **4a** was observed (Entries 1-2). Use of DMF and acetic acid as solvents showed the negligible conversion and products yield (Entries 3-4). Whereas the reactions in DMSO and 1-butanol resulted in the higher yields, 21 and 40 % respectively (Entries 5-6), the reaction rate was still low. To our delight, when the reaction was heated in water media, the full styrene conversion and high product yield **4a** (87 %) were achieved in 7 hours (Entry 7). The structure of compound **4a** was elucidated using combination of NMR spectra and confirmed by HRMS. It should be noted that the reaction is highly regioselective and styrene **2a** attacked indole **3a** in the position 3 only.



Scheme 2. Reaction of 1*H*-indole 3a with styrene 2a

Table 1. Reactions between indole and 2-fluoro-2-nitrostyrene **2a** in various solvents[a]

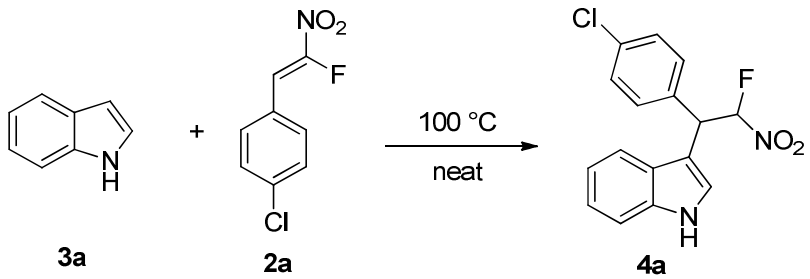
Entry	Solvent	Conversion of 2a,[b] %	Yield[b], %
1	Toluene	0	0

2	1,4-Dioxane	0	0
3	DMF	9	7
4	CH_3COOH	14	7
5	DMSO	26	21
6	1-BuOH	41	40
7	H_2O	100	87[c]

a –Reaction conditions: Styrene : Indole 1.0 : 1.2, 0.25 mmol of **2** in 1 ml of solvent, 7 h at 100 °C
b – calculated via ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard
c – isolated yield obtained by column chromatography.

Over the last few decades academia as well as industry urged by stringent environmental regulations has been giving more and more consideration to the development of cleaner, safer, and environmentally benign chemical processes. In this connection the use of water as a green media in organic synthesis has attracted the great interest and become an important research area. Many examples of synthesis of indole and its derivatives in water or water-containing media have been demonstrated.[2a, 5b]

Further, the additional reactions in neat were conducted to assess the role of water in this type of indole alkylation. Thus, mixture of indole and model styrene **2a** was heated at 100 °C in absence of water varying the molar ratio of the reagents (Scheme 3, Table 2). The data obtained demonstrate that water serves only as a reaction media and does not play any catalytic role. The reaction proceeds in neat also in high yield, but a larger excess of indole to achieve the full conversion of the reagents in comparison with the reaction in water was needed (Table 1, Entry 7; Table 2, Entry 2).



Scheme 3. Reaction of 1*H*-indole 3a with styrene 2a in neat

Table 2. Reactions between indole **3a** and 1-fluoro-1-nitrostyrene **2a** in neat[a]

Entry	Mol. ratio 2a:3a	Conversion of 2a,[b] %	Yield, %
1	1.0 : 1.0	87	67[c]
2	1.0 : 1.2	93	80[b] (78)[c]

3	1.0 : 1.5	100	87[b] (84)[c]

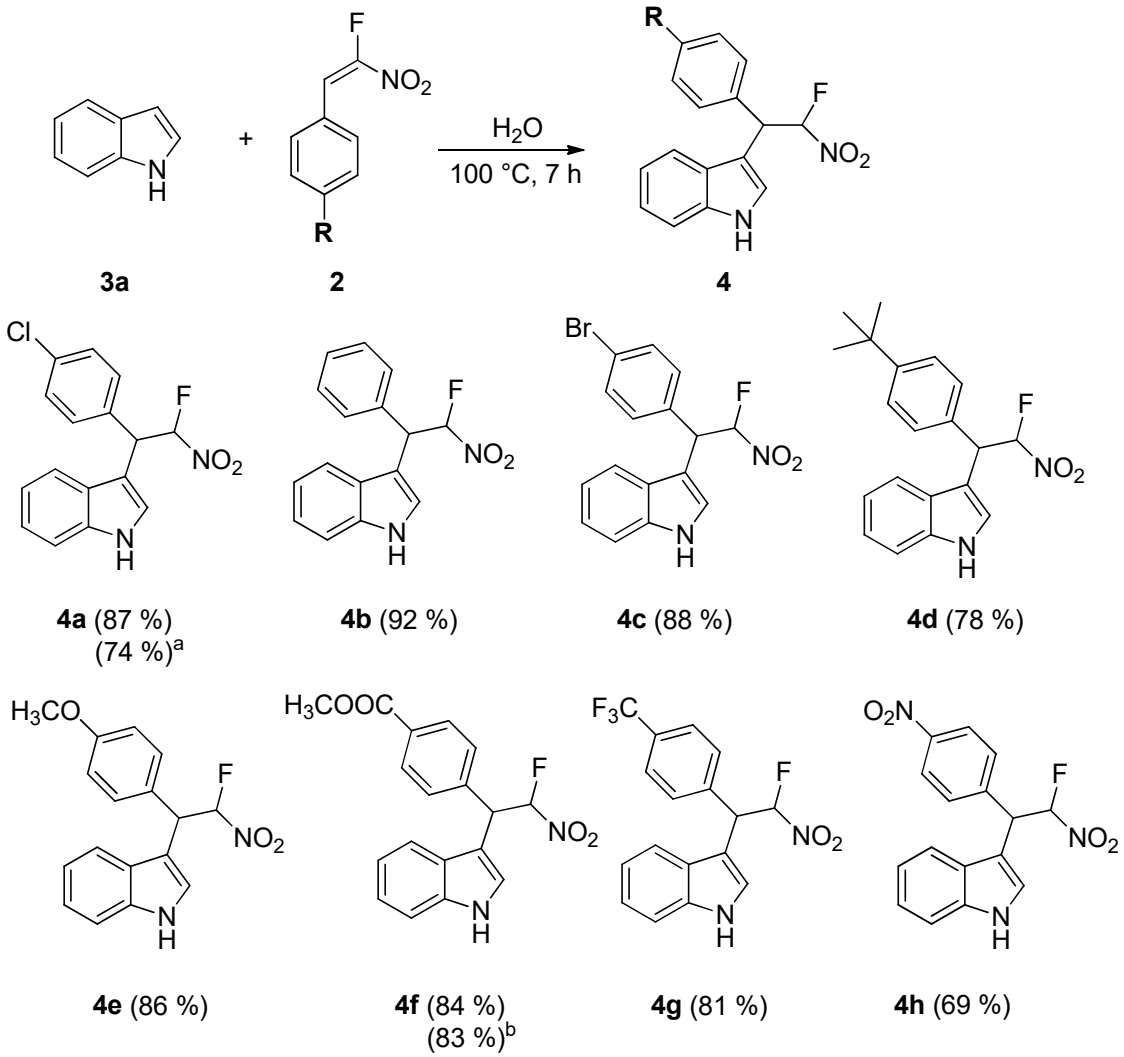
a – Reaction conditions: reaction time – 7 h, at 100 °C

b – calculated via ^{19}F NMR analysis using α,α,α-trifluorotoluene as an internal standard

c – isolated yield obtained by column chromatography

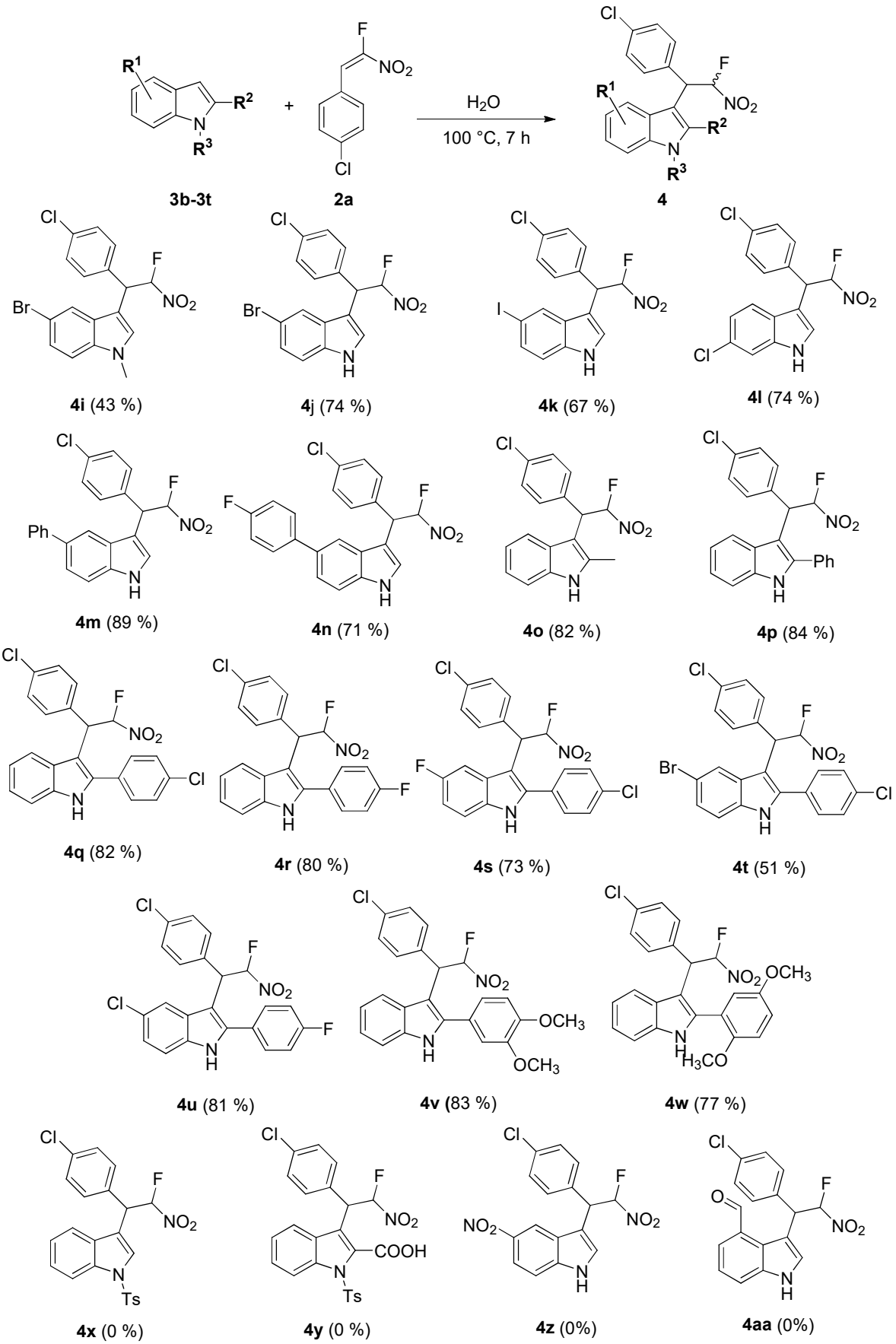
Noteworthy the use of water improve the technological effectiveness of the process probably due to the better reactants diffusion in a water emulsion compared to a viscous reaction mixture melt. Nevertheless, despite the more consumption of expensive indoles, neat conditions are also interesting in viewpoint of green chemistry, since enable to avoid some additional stages of purification (extraction or filtration and drying).

Having in hand these water-mediated conditions for alkylation of indole, the reaction of indole **3a** with various 2-fluoro-2-nitrostyrenes **2a-2h** was investigated (Scheme 4). Gratifyingly, the reaction has broad scope and led to the formation of desired adducts **4a**-**4h** in high yields. Various substituted nitrostyrenes **2a-2g** reacted smoothly as well. Somehow lower yield was observed in case of adduct **4h** deriving from styrene **2h** containing a strong electron-withdrawing nitro-group. In all cases regioselective reaction at the position 3 of indoles was observed.



Scheme 4. Reaction of indole 3a with styrenes 2 (0.5 mmol), [a] – **2** (2.5 mmol), [b] – **2** (5 mmol)

Next the scope of indoles was studied in the reaction with model styrene **2a**. It was found that the water-mediated conditions are applicable for a broad variety of substituted indoles. For this aim indole derivatives having substituents either in pyrrole ring (at the nitrogen or at the C-2 carbon) or in benzene ring of indole system were studied as substrates for the reaction (Scheme 5). Moreover, due to the considerable importance of 2-aryl-indole derivatives in pharmaceutical research,[9] the reaction of several 2-aryl-substituted indoles with **2a** was investigated under the above conditions. In all cases studied reasonably high isolated yields were observed. As a result a family of mono-fluorinated molecules having indole ring in the structure was prepared. We believe that these small molecules can be attractive for subsequent biological studies. In almost all cases examined NMR analysis showed the formation of a diastereoisomeric mixture of alkylated products **4** in ratio *ca* 1:1. Probably the formation of two diastereomers can be explained by high acidity of CH proton having fluorine and nitro group attached (estimated pKa of CH_2FNO_2 is around 9.5).[10]



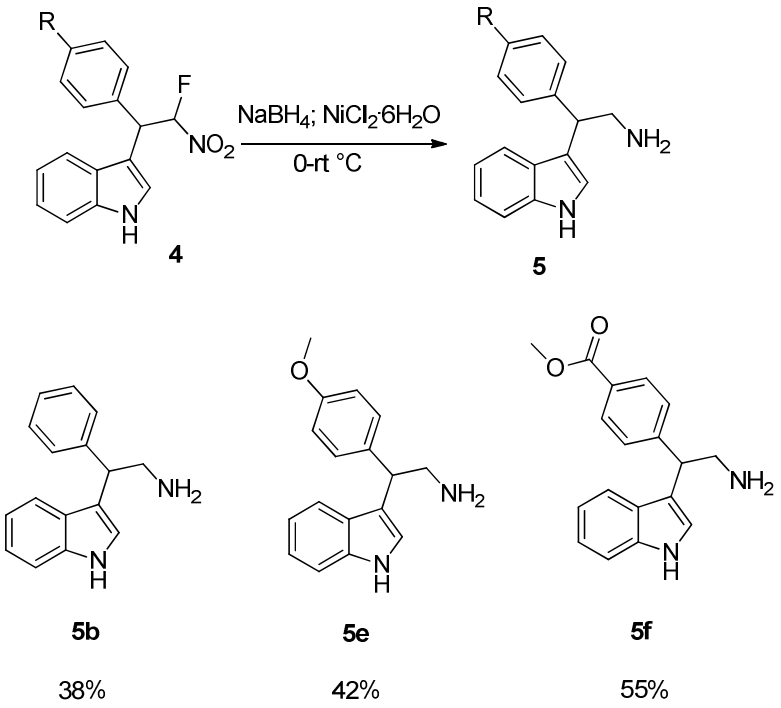
Scheme 5. Reaction of differently substituted indoles with styrene 2a

Gratifyingly, the reaction has only small restrictions in terms of indole structure. For example, we failed to involve into the reaction indoles having strong electron withdrawing groups

such as COOH, NO_2, CHO, Ts (Scheme 5) – either no reaction (**4x-z)** or decomposition (**4aa)** was observed. However, all other indoles were converted into target 3-substituted derivatives. The experimental data obtained for the product **4i** indicate appreciably lower reactivity of *N*-methylated indole compared to *N*-unsubstituted ones. Thus after conducting the reaction for 19 hours, 77% of styrene **2a** conversion was attained and adduct **4i** was isolated in moderate yield (43%). It should be noted that all other substituted 1H-indoles tested (Scheme 5, products **4j-s,4u-w**) exhibited a good reactivity resulting in high yields of the target adducts (67-89 %) except for 5-bromo-2-(4-chlorophenyl)-1H-indole **3m** giving moderate yield of adduct **4t**.

Finally in order to estimate an applicability of the developed method in larger scale, several scaled-up reactions were carried out. Thus the preparation of adducts **4a** expanded fivefold (2.5 mmol) and **4f** expanded tenfold (5 mmol) gave respectively 74% and 83% yields of isolated products (Scheme 2).

Tryptamines are of great interest compounds due to their pharmacological activity and their application in synthesis of carbolines and other biologically active molecules.[11] Many research works have been devoted to their preparation[12]. In this connection the possibility of reduction of the adducts **4** into the corresponding monofluorinated tryptamine derivatives was investigated. A lot of systems for reduction of nitro group in compounds **4** was investigated. The reduction of adducts **4** by $NaBH_4$ - $NiCl_2$·system resulted in formation of non-fluorinated tryptamines **5** in moderate yields (40-55%). This result can be explained by instability of intermideate α-fluorotryptamines, which are transfrormed into imines after HF elimination. Finally the formation of tryptamines **5** takes place (Scheme 5) yielding. Products **5** are the only identified products, however the reaction is complex and also a mixture of unidentified by-products was observed by NMR. Other reductive systems also resulted in formation of non-fluorinated tryptamines **5**, but with the appreciably lower selectivity (hydrogen or $HCOONH_4$ (Pd/C), $NH_2NH_2·H_2O$ – Ra-Ni, Zn in acetic acid). Thus searching of the suitable reaction conditions for reducing of 3-(2-fluoro-2-nitro-1-aryl)-1*H*-indoles into primary amines with preservation of a fluorine atom still remains important goal and in a case of success will be reported in our following works.



Scheme 5. Reduction of adducts **4** into tryptamines **5**.

CONCLUSIONS

In summary, a new synthetic route to 3-(1-aryl-2-fluoro-2-nitroethyl)-1H-indoles was elaborated. It was demonstrated that structurally diverse indoles and 1-fluoro-1-nitrostyrenes participated efficiently in this transformation. The Michael addition efficiently proceeds in catalyst-free and water-mediated conditions. Besides, a possibility of performing such processes in neat was also shown. According to the developed method a family of novel adducts of indoles was synthesized. The above synthetic approach represents a remarkable example of green, safe, environmentally benign chemical processes and opens the way to monofluorinated indole derivatives. An attempt to prepare fluorinated tryptamines by reduction of prepared adducts resulted in formation of the corresponding tryptamines with loss of fluorine atom.

EXPERIMENTAL SECTION

All reagents were purchased from commercial sources and used without any further purification. 1D NMR (^{1}H, ^{19}F, and ^{13}C) spectra were obtained with Bruker AV-400 and Agilent 400-MR spectrometers. Chemical shifts for 1H NMR spectroscopic data were referenced to internal tetramethylsilane (δ = 0.0 ppm) and the solvent resonance (7.26 ppm for $CDCl_3$ and 1.94 ppm for CD_3CN); chemical shifts for ^{13}C NMR spectroscopic data were referenced to $CDCl_3$ (δ = 77.16 ppm) or CD_3CN (δ = 1.32, 118.30 ppm); chemical shifts for ^{19}F NMR spectroscopic data were referenced to $PhCF_3$ (δ = –63.90 ppm). Data are reported as follows: chemical shift, integration

multiplicity (s = singlet, d = doublet, t = triplet, q = quadruplet, qui = quintet, sext = sextet, sept = septet, br = board, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets) and coupling constants (Hz).

Starting 2-fluoro-2-nitrostyrenes were prepared according to the described procedures.[6, 8f] **1a**[13], **1b**[11], **1e**[11], **1f**[11], **1g**[7], **1h** [11]are known compounds.

(Z)-1-Bromo-4-(2-fluoro-2-nitrovinyl)benzene (**2c**). The product was synthesized from 1-bromo-4-(2-bromo-2-fluorovinyl)benzene (**1c**) (3.634 g) according to method B[6]. The pure compound was obtained in 95% yield (3.044 g) as a pale yellow solid using hexane/dichloromethane (3:1) as elution mixture. M.p. = 123-126 °C. HRMS (ESI) *m/z* $[M+Na]^+$: Calcd for $C_8H_6{}^{79}BrFNO_2Na$ 245.9566; found 245.9560. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, $^3J_{CF}$ = 26.0 Hz, 1H), 7.52 (d, *J* = 8.6 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 2H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 108.93 (d, $^2J_{CF}$ = 6.3 Hz), 126.35 (d, J_{CF} = 3.8 Hz), 126.89 (d, J_{CF} = 6.3 Hz), 132.15 (d, J_{CF} = 7.8 Hz), 132.81. ^{19}F NMR (376 MHz, $CDCl_3$): δ -110.43 (d, *J* = 26.0 Hz, 1F).

(Z)-1-(Tert-butyl)-4-(2-fluoro-2-nitrovinyl)benzene (**2d**). The product was prepared from 4-(tert-butyl)benzaldehyde (3.250 g) via corresponding intermediate 1-(2-bromo-2-fluorovinyl)-4-(tert-butyl)benzene (**1d**) [8f]. Crude **1d** obtained was immediately subjected to radical nitrative debromination without isolation according to method B [6]. The pure **2d** was obtained in 50% yield (2.240 g) as a pale yellow solid using hexane/dichloromethane (6:1) as elution mixture. M.p. = 33-35 °C. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{12}H_{15}FNO_2$ 224.1087; found 224.1081.^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.36 (s, 9H), 7.41 (d, $^3J_{HF}$ = 26.8 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 31.12, 35.12, 110.16 (d, $^2J_{CF}$ = 6.4 Hz), 125.20 (d, $^4J_{CF}$ = 6.3 Hz), 126.52, 130.94 (d, $^3J_{CF}$ = 7.6 Hz), 152.69 (d, $^1J_{CF}$ = 292.6 Hz), 155.55 (d, $^6J_{CF}$ = 2.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.39 (d, *J* = 26.8 Hz, 1F).

Alkylation of indoles with α-fluoronitrostyrene. In a typical experiment, a mixture of indole **3** (0.6 mmol) and β-fluoro-β-nitrostyrene **2** (0.5 mmol) in water (2 mL) was heated at 100 °C while being stirred. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with ethyl acetate. The organic layer was separated, dried over anhydrous sodium sulfate and concentrated under vacuum. The desired adduct was isolated as a mixture of diasteroisomers by column chromatography. The relative configuration of the stereocenters was not determined.

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-1H-indole (**4a**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 87% yield (0.127 g) as a viscous pale brown oil by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{16}H_{13}{}^{35}ClFN_2O_2$ 319.0650; found 319.0644. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.22 (dd, *J* = 30.6 Hz, 2.9 Hz, 1H), 5.30 (dd, *J* = 31.3 Hz, 2.9 Hz, 1H), 6.25 (dd, *J* = 49.7 Hz,

3.1 Hz, 1H), 6.37 (dd, *J* = 49.9 Hz, 3.0 Hz, 1H), 7.05-7.46 (m, 18H), 8.60 (br s, 1H), 8.66 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.54 (d, $^2J_{CF}$ = 18.4 Hz), 45.58 (d, $^2J_{CF}$ = 18.8 Hz), 108.29, 110.93, 111.49, 111.64, 111.73 (d, $^1J_{CF}$ = 245.0 Hz), 112.56 (d, $^1J_{CF}$ = 246.1 Hz), 118.44, 118.62, 120.23, 120.34, 122.53 (d, $^4J_{CF}$ = 2.3 Hz), 122.81, 123.05, 123.35 (d, $^4J_{CF}$ = 3.1 Hz), 125.93, 126.53, 129.01, 129.22, 129.84, 130.54, 132.86, 134.06, 134.33, 135.10, 135.85, 136.06. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.27 (dd, *J* = 49.8 Hz, 31.4 Hz, 1F), -152.16 (dd, *J* = 49.9 Hz, 30.6 Hz, 1F).

3-(2-Fluoro-2-nitro-1-phenylethyl)-1H-indole (**4b**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 92% yield (0.145 g) as a viscous redish oil by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{16}H_{12}FN_2O_2$ 283.0888; found 283.0886.^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.27 (dd, *J* = 30.4 Hz, 3.3 Hz, 1H), 5.38 (dd, *J* = 31.4 Hz, 3.2 Hz, 1H), 6.31 (dd, *J* = 50.1 Hz, 3.2 Hz, 1H), 6.40 (dd, *J* =50.2 Hz, 3.4 Hz, 1H), 7.07-7.54 (m, 20H), 8.11 (br s, 1H), 8.14 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.21 (d, $^2J_{CF}$ = 18.5 Hz), 46.19 (d, $^2J_{CF}$ = 18.6 Hz), 108.72, 112.2 (d, $^1J_{CF}$ = 244.7 Hz), 111.28, 111.42, 111.58, 112.98 (d, $^1J_{CF}$ = 245.4 Hz), 118.54, 118.74, 120.09, 120.21, 122.63, 122.67 (d, $^4J_{CF}$ = 2.9 Hz), 122.87, 123.42 (d, $^4J_{CF}$ = 3.2 Hz), 126.13, 126.76, 128.13, 128.36, 128.48, 128.82, 129.07, 129.19, 134.44, 135.86, 136.06, 136.66. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -151.94 (dd, *J* = 50.0 Hz, 31.5 Hz, 1F), -151.56 (dd, *J* = 50.2 Hz, 30.5 Hz, 1F).

3-(1-(4-Bromophenyl)-2-fluoro-2-nitroethyl)-1H-indole (**4c**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 88% yield (0.157 g) as a red-orange solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. M.p. = 94 – 97 °C. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{16}H_{13}{}^{79}BrFN_2O_2$ 363.0144; found 363.0139. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.21 (dd, *J* = 30.6 Hz, 3.1 Hz, 1H), 5.30 (dd, *J* = 31.3 Hz, 3.1 Hz, 1H), 6.24 (dd, *J* = 50.0 Hz, 3.1 Hz, 1H), 6.37 (dd, *J* =50.1 Hz, 3.1 Hz, 1H), 7.07-7.52 (m, 18H), 8.18 (br s, 1H), 8.21 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.64 (d, $^2J_{CF}$ = 18.5 Hz), 45.70 (d, $^2J_{CF}$= 18.7 Hz), 108.30, 110.98, 111.48, 111.64, 111.67 (d, $^1J_{CF}$ = 245.1 Hz), 112.49 (d, $^1J_{CF}$ = 245.7 Hz), 118.47, 118.65, 120.29, 120.42, 122.29, 122.54 (d, $^4J_{CF}$ = 2.8 Hz), 122.62, 122.87, 123.13, 123.34 (d, $^4J_{CF}$ = 3.5 Hz), 125.96, 126.57, 130.21, 130.90, 132.02, 132.23, 133.40, 135.69, 135.89, 136.10. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.20 (dd, *J* = 49.9 Hz, 31.4 Hz, 1F), -152.05 (dd, *J* = 50.1 Hz, 30.5 Hz, 1F).

3-(1-(4-(Tert-butyl)phenyl)-2-fluoro-2-nitroethyl)-1H-indole (**4d**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 78% yield (0.130 g) as a pale yellow solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. M.p. = 103-108 °C. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{20}H_{22}FN_2O_2$ 341.1665; found 341.1660. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 (s, 9H), 1.33 (s, 9H), 5.23 (dd, *J* = 30.4, 3.2 Hz, 1H), 5.35 (dd, *J* = 32.2, 2.6 Hz, 1H), 6.29 (dd, *J* = 50.1 Hz, 2.9 Hz, 1H), 6.38 (dd, *J* = 50.3, 3.4 Hz, 1H), 7.05

– 7.58 (m, 18H), 8.19 (br s, 1H), 8.22 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 31.33, 34.56, 34.60, 45.74 (d, $^2J_{CF}$ = 18.5 Hz), 45.77 (d, $^2J_{CF}$ = 18.3 Hz), 109.00, 111.37, 111.55, 111.63, 112.3 (d, $^1J_{CF}$ = 244.4 Hz), 113.04 (d, $^1J_{CF}$ = 245.8 Hz), 118.62, 118.82, 120.07, 120.21, 122.63, 122.72 (d, $^4J_{CF}$ = 2.4 Hz), 122.89, 123.37 (d, $^4J_{CF}$ = 3.6 Hz), 125.78, 126.02, 126.22, 126.87, 128.82, 131.34, 131.34, 133.66, 135.87, 136.08, 151.08, 151.15. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.19 (dd, *J* = 50.1 Hz, 32.2 Hz, 1F), -151.31 (dd, *J* = 50.2 Hz, 30.4 Hz, 1F).

3-(2-Fluoro-1-(4-methoxyphenyl)-2-nitroethyl)-1H-indole (**4e**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 86 % yield (0.137 g) as a viscous yellowish oil by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. HRMS (ESI) *m/z* $[M–H^+]^–$: Calcd for $C_{17}H_{14}FN_2O_3$ 313.0994; found 313.0991. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 3H), 3.80 (s, 3H), 5.22 (dd, *J* = 31.2, 3.4 Hz, 1H), 5.30 (dd, *J* = 31.0, 3.8 Hz, 1H), 6.27 (dd, *J* = 50.0, 3.5 Hz, 1H), 6.37 (dd, J = 50.4, 3.2 Hz, 1H), 6.84-6.93 (m, 4H), 7.02-7.58 (m, 14H), 8.19 (br s, 1H), 8.22 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.51 (d, $^2J_{CF}$ = 18.6 Hz), 45.54 (d, $^2J_{CF}$ = 18.7 Hz), 55.20, 55.30, 110.43 (d, $^1J_{CF}$ = 249.1 Hz), 111.39, 111.55, 111.99, 112.15 (d, $^1J_{CF}$ = 244.2 Hz), 114.18, 114.41, 118.59, 118.80, 120.03, 120.15, 122.49 (d, $^4J_{CF}$ = 2.6 Hz), 122.60, 122.83, 123.15 (d, $^4J_{CF}$ = 3.3 Hz), 126.13, 126.32, 126.74, 128.57, 129.63, 130.33, 135.91, 136.11, 159.32, 159.48. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.24 (dd, *J* = 50.4 Hz, 31.0 Hz, 1F), -151.86 (dd, *J* = 50.0 Hz, 30.8 Hz, 1H).

Methyl 4-(2-fluoro-1-(1H-indol-3-yl)-2-nitroethyl)benzoate (**4f**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 84% yield (0.143 g) as a yellowish solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. M.p. = 68-72 °C. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{18}H_{16}FN_2O_4$ 343.1094; found 343.1089. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.91 (s, 3H), 3.94 (s, 3H), 5.30 (dd, *J* = 30.0, 3.2 Hz, 1H), 5.40 (dd, *J* = 31.3, 3.0 Hz, 1H), 6.31 (dd, *J* = 49.9, 3.1 Hz, 1H), 6.41 (dd, *J* = 49.9, 3.4 Hz, 1H), 7.05 - 7.53 (m, 14H), 7.98 - 8.06 (m, 4H), 8.55 (br s, 1H), 8.60 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 46.00 (d, $^2J_{CF}$ = 18.3 Hz), 46.05 (d, $^2J_{CF}$ = 18.8 Hz), 52.27, 52.31, 107.88, 110.49, 111.53, 111.68, 111.69 (d, $^1J_{CF}$ = 249.1 Hz), 112.34 (d, $^1J_{CF}$ = 245.7 Hz), 118.29, 118.52, 120.13, 120.23, 122.69, 122.77 (d, $^4J_{CF}$ = 2.5 Hz), 122.92, 123.63 (d, $^4J_{CF}$ = 3.0 Hz), 125.94, 126.56, 128.57, 129.31, 129.83, 129.99, 130.24, 135.91, 136.10, 139.69, 141.83, 166.81, 166.86. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.00 (dd, *J* = 49.9 Hz, 31.3 Hz, 1F), -151.62 (dd, *J* = 49.9 Hz, 30.1 Hz, 1F).

3-(2-Fluoro-2-nitro-1-(4-(trifluoromethyl)phenyl)ethyl)-1H-indole (**4g**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 81% yield (0.148 g) as a red solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. M.p. = 92-96 °C. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{17}H_{13}F_4N_2O_2$ 353.0913; found 353.0908. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.33 (dd, *J* = 30.1, 2.8 Hz, 1H), 5.44 (dd, *J* = 31.7, 1.8 Hz, 1H), 6.30

(dd, *J* = 49.8, 3.5 Hz, 1H), 6.41 (dd, *J* = 49.8, 3.5 Hz, 1H), 7.02-7.75 (m, 18H), 8.27 (br s, 1H), 8.32 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.95 (d, $^2J_{CF}$ = 19.0 Hz), 45.89 (d, $^2J_{CF}$ = 18.4 Hz), 107.88, 110.58, 111.58, 111.69 (d, $^1J_{CF}$ = 245.2 Hz), 111.72, 112.30 (d, $^1J_{CF}$ = 246.0 Hz), 118.35, 118.54, 120.35, 120.47, 122.73 (d, $^4J_{CF}$ = 2.5 Hz), 122.92, 123.16, 123.61 (d, $^4J_{CF}$ = 3.3 Hz), 125.38, 126.04 (d, $^3J_{CF}$ = 3.5 Hz), 125.93, 126.04 (d, $^3J_{CF}$ = 3.5 Hz), 126.54, 128.94, 129.65, 130.34 (q, $^2J_{CF}$ = 16.0 Hz), 135.92, 136.13, 138.53, 140.70. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.42 (dd, *J* = 49.9 Hz, 31.8 Hz, 1F), -151.85 (dd, *J* = 49.9 Hz, 30.2 Hz, 1F), -62.52 (s, 3F), -62.49 (s, 3F).

3-(2-Fluoro-2-nitro-1-(4-nitrophenyl)ethyl)-1H-indole (**4h**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 69% yield (0.109 g) as a pale brown solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. M.p. = 72-76 °C. HRMS (ESI) *m/z* $[M–H^+]^–$: Calcd for $C_{16}H_{11}FN_3O_4$ 328.0739, found 328.0737. ^{1}H NMR (400 MHz, CD_3CN): δ = 5.42 (dd, *J* = 28.6, 3.9 Hz, 1H), 5.54 (dd, *J* = 31.9, 3.2 Hz, 1H), 6.66 (dd, *J* = 49.4, 3.4 Hz, 1H), 6.76 (dd, *J* = 49.2, 4.0 Hz, 1H), 7.00-7.06 (m, 2H), 7.13-7.20 (m, 2H), 7.36-7.49 (m, 6H), 7.56 – 7.70 (m, 4H), 8.09-8.19 (m, 4H), 9.52 (br s, 2H). ^{13}C NMR (100 MHz, CD_3CN): δ = 46.18 (d, $^2J_{CF}$ = 18.3 Hz), 46.37 (d, $^2J_{CF}$ = 18.3 Hz), 112.51, 112.72, 112.78, 112.99 (d, $^1J_{CF}$ = 242.9 Hz), 113.17 (d, $^1J_{CF}$ = 242.8 Hz), 119.24, 119.95, 120.06, 120.75, 120.77, 122.72, 123.32, 123.43, 124.36, 124.54 (d, $^4J_{CF}$ = 2.7 Hz), 124.62, 124.72, 124.81, 125.42 (d, $^4J_{CF}$ = 2.2 Hz), 130.34, 130.62, 131.19, 137.05, 137.21, 144.00, 145.54. ^{19}F NMR (376 MHz, CD_3CN): δ = -153.31 (dd, *J* = 49.3 Hz, 31.8 Hz, 1F), -152.01 (dd, *J* = 49.1 Hz, 28.5 Hz, 1F).

5-Bromo-3-(1-(4-chlorophenyl)-2-fluoro-2-nitroethyl)-1-methyl-1H-indole (**4i**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 43% yield (0.089 g) as a viscous pale yellow oil by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. HRMS (ESI) *m/z* $[M–H^+]^–$: Calcd for $C_{17}H_{12}{}^{79}Br^{35}ClFN_2O_2$ 408.9760, found 408.9757; *m/z* $[M+H]^+$: Calcd for $C_{17}H_{14}{}^{79}Br^{35}ClFN_2O_2$ 410.9911, found 410.9910. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 1H), 3.78 (s, 1H), 5.12 (dd, *J* = 30.5, 3.1 Hz, 1H), 5.22 (dd, *J* = 31.7, 3.0 Hz, 1H), 6.20 (dd, *J* = 50.0, 3.0 Hz, 1H), 6.30 (dd, *J* = 50.1, 3.2 Hz, 1H), 7.11–7.37 (m, 14H), 7.47 (d, *J* = 1.4 Hz, 1H), 7.54 (d, *J* = 1.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ =32.25, 33.24 45.34 (d, $^2J_{CF}$ = 18.6 Hz), 45.42 (d, $^2J_{CF}$ = 18.8 Hz), 106.41, 109.10, 111.16, 111.34, 111.57 (d, $^1J_{CF}$ = 244.9 Hz), 112.34 (d, $^1J_{CF}$ = 245.4 Hz), 113.35, 113.42, 121.07, 121.24, 125.35, 125.61, 128.14, 128.38 (d, $^4J_{CF}$ = 2.8 Hz), 128.81, 129.05 (d, $^4J_{CF}$ = 3.7 Hz), 129.17, 129.39, 129.79, 130.47, 132.71, 134.31, 134.56, 135.01, 135.5, 135.70. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.81 (dd, *J* = 49.9 Hz, 31.8 Hz, 1F), -152.29 (dd, *J* = 50.1 Hz, 30.5 Hz, 1F).

5-Bromo-3-(1-(4-chlorophenyl)-2-fluoro-2-nitroethyl)-1H-indole (**4j**). The mixture of diastereoisomers (d.r. = 1.0:1.2) was obtained in 74 % yield (0.146 g) as a red-orange solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. M.p.

= 115-121 °C. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{16}H_{10}{}^{79}Br^{35}ClFN_2O_2$ 394.9604; found 394.9603. ^{1}H NMR (400 MHz, $CDCl_3$) : δ = 5.13 (dd, *J* = 30.5, 2.7 Hz, 1H), 5.24 (dd, *J* = 31.8, 2.5 Hz, 1H), 6.23 (dd, *J* = 49.9, 2.8 Hz, 1H), 6.33 (dd, *J* = 50.0, 2.9 Hz, 1H), 7.14–7.40 (m, 14H), 7.48 (s, 1H), 7.53 (s, 1H), 8.29 (br s, 1H), 8.33 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.34 (d, $^2J_{CF}$ = 18.5 Hz), 45.44 (d, $^2J_{CF}$ = 18.7 Hz), 108.05, 110.07, 110.76, 111.55 (d, $^1J_{CF}$ = 245.2 Hz), 112.4 (d, $^1J_{CF}$ = 247.6 Hz), 113.0, 113.15, 113.71, 121.04, 121.19, 123.75 (d, $^4J_{CF}$ = 3.0 Hz), 124.58 (d, $^4J_{CF}$ = 3.7 Hz), 125.86, 126.10, 127.75, 128.34, 129.20, 129.43, 129.80, 130.49, 132.42, 134.38, 134.56, 134.64, 134.67, 134.77. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.81 (dd, *J* = 49.9 Hz, 31.8 Hz, 1F), -152.29 (dd, *J* = 50.1 Hz, 30.5 Hz, 1F).

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-5-iodo-1H-indole (**4k**). The mixture of diastereoisomers (d.r. = 1.3:1.0) was obtained in 67 % yield (0.126 g) as a red solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. M.p. = 59-62 °C. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{16}H_{10}{}^{35}ClFIN_2O_2$ 442.9465; found 442.9460. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.13 (dd, *J* = 30.5, 3.0 Hz, 1H), 5.23 (dd, *J* = 31.7, 2.9 Hz, 1H), 6.22 (dd, *J* = 49.9, 3.0 Hz, 1H), 6.32 (dd, *J* =50.1, 3.2 Hz, 1H), 7.08 –7.17 (m, 2H)., 7.19–7.36 (m, 14H), 7.40–7.50 (m, 2H), 7.68 (s, 1H), 7.74 (s, 1H), 8.33 (br s, 1H), 8.38 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.27 (d, $^2J_{CF}$ = 18.6 Hz), 45.36 (d, $^2J_{CF}$ = 18.8 Hz), 83.88, 83.91, 107.70, 110.39, 111.55 (d, $^1J_{CF}$ = 244.9 Hz), 112.38 (d, $^1J_{CF}$ = 246.8 Hz), 112.76, 113.46, 113.61, 123.4 (d, $^4J_{CF}$ = 3.0 Hz), 124.17 (d, $^4J_{CF}$ = 3.8 Hz), 127.23, 127.37, 128.52, 129.16, 129.39, 129.79, 130.47, 131.28, 131.52, 132.42, 134.35, 134.59, 134.65, 134.97, 135.19. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.77 (dd, *J* = 49.8 Hz, 31.8 Hz, 1F), -152.3 (dd, *J* = 50.1 Hz, 30.6 Hz, 1F).

6-Chloro-3-(1-(4-chlorophenyl)-2-fluoro-2-nitroethyl)-1H-indole (**4l**). The mixture of diastereoisomers (d.r. = 1:1) was obtained in 74 % yield (0.131 g) as a viscous pale brown oil by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{16}H_{10}{}^{35}Cl_2FN_2O_2$ 351.0109; found 351.0109. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.16 (dd, *J* = 30.2, 3.0 Hz, 1H), 5.26 (dd, *J* = 31.3, 2.8 Hz, 1H), 6.26 (dd, *J* = 49.9, 3.1 Hz, 1H), 6.36 (dd, *J* = 50.1, 3.2 Hz, 1H), 7.00–7.10 (m, 2H), 7.21–7.37 (m, 14H), 8.25 (br s, 1H), 8.28 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.46 (d, $^2J_{CF}$ = 18.7 Hz), 45.52 (d, $^2J_{CF}$ = 18.7 Hz), 108.58, 111.24, 111.42, 111.56, 111.61 (d, $^1J_{CF}$ = 245.1 Hz), 112.41 (d, $^1J_{CF}$ = 246.0 Hz), 119.43, 119.61, 121.03, 121.12, 123.14 (d, $^4J_{CF}$ = 3.0 Hz), 124.10 (d, $^4J_{CF}$ = 3.3 Hz), 124.61, 125.15, 128.75, 129.00, 129.12, 129.34, 129.76, 130.48, 132.58, 134.27, 134.55, 134.81, 136.28, 136.49. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.51 (dd, *J* = 49.9 Hz, 31.3 Hz, 1F), -152.21 (dd, *J* = 50.0 Hz, 30.2 Hz, 1F).

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-5-phenyl-1H-indole (**4m**). The mixture of diastereoisomers (d.r. = 1: 1) was obtained in 89 % yield (0.177 g) as a viscous pale brown oil by

column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{22}H_{15}{}^{35}ClFN_2O_2$ 393.0812; found 393.0809. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.30 (dd, *J* = 30.5, 3.1 Hz, 1H), 5.40 (dd, *J* = 31.5, 3.0 Hz, 1H), 6.25 (dd, *J* = 49.8, 3.1 Hz, 1H), 6.37 (dd, *J* = 49.9, 3.2 Hz, 1H), 7.20 – 7.73 (m, 26H), 8.22 (br s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.47 (d, $^2J_{CF}$ = 18.5 Hz), 45.52 (d, $^2J_{CF}$ = 18.7 Hz), 108.66, 111.75 (d, $^1J_{CF}$ = 245.0 Hz), 111.76, 111.91, 112.52 (d, $^1J_{CF}$ = 246.4 Hz), 116.78, 116.98, 122.74, 122.97, 123.29 (d, $^4J_{CF}$ = 2.6 Hz), 124.09 (d, $^4J_{CF}$ = 3.3 Hz), 126.50, 126.69, 126.81, 127.11, 127.47, 128.81, 128.88, 129.08, 129.28, 129.85, 130.54, 132.81, 133.87, 134.02, 134.14, 134.41, 135.04, 135.38, 135.56, 142.04, 142.16. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.29 (dd, *J* = 49.8 Hz, 31.5 Hz, 1F), -152.01 (dd, *J* = 49.9 Hz, 30.5 Hz, 1F).

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-5-(4-fluorophenyl)-1H-indole (**4n**). The mixture of diasteroisomers (d.r. = 1.3:1.0) was obtained in 71 % yield (0.147 g) as a pale brown solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. Mp = 77-80 °C. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{22}H_{14}{}^{35}ClF_2N_2O_2$ 411.0717; found 411.0713. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.28 (dd, *J* = 30.4, 2.8 Hz, 1H), 5.38 (dd, *J* = 31.5, 2.2 Hz, 1H), 6.26 (dd, *J* = 49.8 Hz, 2.4 Hz, 1H), 6.39 (dd, *J* = 49.9 Hz, 2.5 Hz, 1H), 7.00–7.08 (m, 2H), 7.20–7.66 (m, 24H), 8.29 (br s, 1H), 8.32 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.47 (d, $^2J_{CF}$ = 18.6 Hz), 45.53 (d, $^2J_{CF}$ = 18.8 Hz), 108.84, 111.52, 111.75 (d, $^1J_{CF}$ = 245.1 Hz), 111.88, 112.05, 112.50 (d, $^1J_{CF}$ = 245.9 Hz), 113.39 (d, $^2J_{CF}$ = 21.0 Hz), 113.52 (d, $^2J_{CF}$ = 21.1 Hz), 114.12 (d, J_{CF} = 1.8Hz), 114.34 (d, J_{CF} = 1.5 Hz), 116.89, 117.09, 122.61, 122.86, 123.07 (d, J_{CF} = 2.2 Hz), 123.46 (d, J_{CF} = 2.7 Hz), 124.30 (d, J_{CF} = 3.6 Hz), 126.54, 127.15, 129.15, 129.37, 129.87, 130.22 (d, J_{CF} = 8.1 Hz), 130.30 (d, J_{CF} = 8.1 Hz), 130.55, 132.66 (d, J_{CF} = 1.7 Hz), 132.76, 132.82 (d, J_{CF} = 1.7 Hz), 134.27, 134.53, 135.00, 135.66, 135.86, 144.37 (d, J_{CF} = 7.9 Hz), 144.49 (d, J_{CF} = 7.5 Hz), 163.26 (d, $^1J_{CF}$ = 245.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = -152.52 (dd, *J* = 49.8 Hz, 31.6 Hz), -152.05 (dd, *J* = 50.0 Hz, 30.6 Hz), -113.25 (td, *J* = 9.3 Hz, 6.2 Hz,1F), -113.12 (td, *J* = 9.3, 6.1 Hz).

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-2-methyl-1H-indole (**4o**). The mixture of diasteroisomers (d.r. = 1:1) was obtained in 82% yield (0.136 g) as a redish solid by column chromatography on silica gel using hexane/dichloromethane (1:1) as elution mixture. M.p. = 134-138 °C. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{17}H_{15}{}^{35}ClFN_2O_2$ 333.0806; found 333.0806. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.27 (s, 3H), 2.31 (s, 3H), 5.11 (dd, *J* = 22.2, 4.6 Hz, 1H), 5.26 (d, *J* = 32.6 Hz, 1H), 6.50 (dd, 50.5 Hz, 5.1 Hz, 1H), 6.60 (d, 50.0 Hz, 1H), 6.99–7.56 (m, 16H), 7.95 (br s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.03, 12.06, 44.65 (d, $^2J_{CF}$ = 20.0 Hz), 45.07 (d, $^2J_{CF}$ = 19.9 Hz), 104.20, 105.72, 110.64, 110.97, 112.10 (d, $^1J_{CF}$ = 245.8 Hz), 112.94 (d, $^1J_{CF}$ = 244.4 Hz), 118.57 (d, $^4J_{CF}$ = 2.2 Hz), 119.49 (d, $^4J_{CF}$ = 5.3 Hz), 120.17, 120.36, 121.72, 121.89, 126.81, 127.53, 128.96, 129.07, 129.17, 129.98, 133.51, 133.71, 133.86, 134.47, 134.56,

135.33, 135.38. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -149.07 (dd, *J* = 50.5 Hz, 32.6 Hz, 1F), -143.56 (dd, *J* = 50.1 Hz, 22.3 Hz, 1F).

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-2-phenyl-1H-indole (**4p**). The mixture of diastereoisomers (d.r. = 1.9 : 1.0) was obtained in 84% yield (0.168 g) as a pale yellow solid by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. M.p. = 158-161 °C. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{22}H_{17}{}^{35}ClFN_2O_2$ 395.0963; found 395.0957.^{1}H NMR (400 MHz, CD_3CN): δ = 5.20 (dd, *J* = 21.4, 6.9 Hz, 1H), 5.41 (dd, *J* = 33.0, 3.6 Hz, 1H), 6.79 (dd, *J* = 49.9, 3.7 Hz, 1H), 6.85 (dd, *J* = 49.3, 6.9 Hz, 1H), 7.04 –7.27 (m, 4H), 7.29-7.61 (m, 20H), 7.70 (d, *J* = 8.1 Hz, 2H), 9.69 (br s, 1H), 9.72 (br s, 1H). ^{13}C NMR (100 MHz, CD_3CN): δ = 45.56 (d, $^2J_{CF}$ = 19.8 Hz), 46.50 (d, $^2J_{CF}$ = 20.4 Hz), 105.38, 106.88, 106.94, 112.43, 112.7, 113.51 (d, $^1J_{CF}$ = 244.6 Hz), 113.86 (d, $^1J_{CF}$ = 241.9 Hz), 120.92 (d, $^4J_{CF}$ = 3.3 Hz), 120.99, 121.22, 121.97, 122.06, 123.30, 123.45, 127.39, 127.87, 129.70, 129.78, 129.87, 129.91, 129.98, 130.68, 131.19, 132.58, 132.73, 133.93, 134.09, 136.60, 137.09, 137.31, 137.37, 139.03, 139.94. ^{19}F NMR (376 MHz, CD_3CN): δ = -149.47 (ddd, *J* = 49.9 Hz, 33.1 Hz, 3.2 Hz, 1F), -144.24 (dd, *J* = 49.3 Hz, 21.4 Hz, 1F).

2-(4-Chlorophenyl)-3-(1-(4-chlorophenyl)-2-fluoro-2-nitroethyl)-1H-indole (**4q**). The mixture of diastereoisomers (d.r. = 1.6:1.0) was obtained in 82% yield (0.177 g) as a pale yellow solid by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. Mp = 191-194 °C. HRMS (ESI) *m/z* $[M+H]^+$: Calcd for $C_{22}H_{15}{}^{35}Cl_2FN_2O_2$ 429.0573; found 429.0567.^{1}H NMR (400 MHz, CD_3CN): δ = 5.13 (dd, *J* = 21.1, 6.9 Hz, 1H), 5.36 (dd, *J* = 33.0, 3.6 Hz, 1H), 6.79 (dd, *J* = 49.8, 3.7 Hz, 1H), 6.83 (dd, *J* = 49.3, 6.9 Hz, 1H), 7.01–7.59 (m, 22H), 7.64–7.70 (m, 2H), 9.71 (br s, 1H), 9.72 (br s, 1H). ^{13}C NMR (100 MHz, CD_3CN): δ = 45.42 (d, $^2J_{CF}$ = 19.8 Hz), 46.39 (d, $^2J_{CF}$ = 20.5 Hz), 112.48, 112.75, 113.39 (d, $^1J_{CF}$ = 245.1 Hz), 113.75 (d, $^1J_{CF}$ = 241.9 Hz), 120.94 (d, $^4J_{CF}$ = 3.2 Hz), 121.08, 121.31, 122.00, 122.08, 123.52, 123.67, 127.30, 129.70, 129.77, 129.91, 130.03, 130.68, 131.19, 131.34, 131.53, 131.56, 133.96, 134.13, 135.16, 135.28, 136.45, 136.94, 137.36, 137.43, 137.70. ^{19}F NMR (376 MHz, CD_3CN): δ = -149.98 -149.61 (m, 1F), -144.3 (ddd, *J* = 49.1, 21.0, 6.3 Hz, 1F).

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-2-(4-fluorophenyl)-1H-indole (**4r**). The mixture of diastereoisomers (d.r. = 1.8:1.0) was obtained in 80% yield (0.164 g) as a colorless solid by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. Mp = 172–175 °C. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{22}H_{14}{}^{35}ClF_2N_2O_2$ 411.0717; found 411.0713.^{1}H NMR (400 MHz, CD_3CN) δ = 5.15 (dd, *J* = 21.2, 6.9 Hz, 1H), 5.36 (dd, *J* = 33.0, 3.6 Hz, 1H), 6.79 (dd, *J* = 49.8, 3.7 Hz, 1H), 6.85 (dd, *J* = 49.3, 6.9 Hz, 1H), 7.02 – 7.57 (m, 22H), 7.67 – 7.73 (m, 2H), 9.69 (br s, 1H), 9.67 (br s, 1H). ^{13}C NMR (100 MHz, CD_3CN): δ = 45.49 (d, $^2J_{CF}$ = 20.5 Hz), 46.44 (d, $^2J_{CF}$ = 19.8 Hz), 105.65, 107.17 (d, J_{CF} = 6.3 Hz), 112.44, 112.71, 113.43 (d, $^1J_{CF}$ = 244.9

Hz), 113.8 (d, $^{1}J_{CF}$ = 241.9 Hz), 116.69 (d, $^{2}J_{CF}$ = 21.8 Hz), 116.82 (d, $^{2}J_{CF}$ = 21.9 Hz), 120.87 (d, J_{CF} = 3.0 Hz), 121.05, 121.28, 121.97 (d, J_{CF} = 8.7 Hz), 123.39, 123.53, 127.30, 127.80, 128.93 (d, J_{CF} = 2.9 Hz), 129.05 (d, J_{CF} = 3.2 Hz), 129.69, 129.76, 130.65, 131.17, 132.06 (d, J_{CF} = 8.0 Hz), 132.16 (d, J_{CF} = 8.3 Hz), 133.95, 134.11, 136.49, 136.98, 137.25, 137.31, 138.02, 138.90, 163.83 (d, $^{1}J_{CF}$= 246.6 Hz), 163.87 (d, $^{1}J_{CF}$ = 246.7 Hz). ^{19}F NMR (376MHz, CD_3CN): δ = -149.60 (dd, *J* = 49.8, 33.0 Hz, 1F), -144.22 (dd, *J* = 49.3 Hz, 21.2 Hz, 1F), -114.12 (tt, *J* = 8.9 Hz, 5.4 Hz, 1F), -113.91 (tt, *J* = 8.9 Hz, 5.3 Hz 1F).

2-(4-Chlorophenyl)-3-(1-(4-chlorophenyl)-2-fluoro-2-nitroethyl)-5-fluoro-1H-indole (**4s**). The mixture of diastereoisomers (d.r. = 2:1) was obtained in 73 % yield (0.166 g) as a yellowish solid by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. M.p. = 198-204 °C. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{22}H_{13}{}^{35}Cl_2F_2N_2O_2$ 445.0328; found 445.0325.^{1}H NMR (400 MHz, CD_3CN): δ = 5.11 (dd, *J* = 21.8, 6.7 Hz, 1H), 5.35 (dd, *J* = 33.6, 3.4 Hz, 1H), 6.78 (dd, *J* = 49.7, 3.5 Hz, 1H),), 6.79 (dd, *J* = 49.2, 6.8 Hz, 1H), 6.96-7.06 (m, 2H), 7.12-7.18 (m, 1H), 7.29–7.61 (m, 19H), 9.77 (br s, 1H), 9.79 (br s, 1H). ^{13}C NMR (100 MHz, CD_3CN): δ = 45.20 (d, $^{2}J_{CF}$ = 19.6 Hz), 46.20 (d, $^{2}J_{CF}$ = 20.6 Hz), 105.55 (d, $^{3}J_{CF}$ = 3.7 Hz), 105.80 (d, $^{3}J_{CF}$ = 3.6 Hz), 106.52 (d, J_{CF} = 10.1 Hz), 106.76 (d, J_{CF} = 9.4 Hz), 111.74 (d, $^{2}J_{CF}$ = 26.5 Hz), 111.85 (d, $^{2}J_{CF}$ = 26.4 Hz), 111.98, 113.35 (d, $^{1}J_{CF}$= 244.2 Hz), 113.56 (d, J_{CF} = 9.8 Hz), 113.56 (d, $^{1}J_{CF}$ = 242.2 Hz), 113.84 (d, J_{CF} = 9.9 Hz), 127.56, 127.65, 129.79, 129.87, 128.6, 129.96, 130.08, 130.66, 131.01, 131.16, 131.51, 131.57, 133.94, 134.02, 134.08, 134.25, 135.42, 135.55, 136.11, 136.59, 139.65, 158.75 (d, $^{1}J_{CF}$ = 233.0 Hz), 158.88 (d, $^{1}J_{CF}$ = 233.3 Hz). ^{19}F NMR (376 MHz, CD_3CN): δ = -150.1 (ddd, *J* = 49.7 Hz, 33.7 Hz, 2.6 Hz, 1F), -144.90 (dd, *J* = 49.1, 21.8 Hz), -124.75 (ddd, *J* = 10.4 Hz, 9.5 Hz, 4.7 Hz, 1F), -124.31 (ddd, *J* = 10.2 Hz, 9.6 Hz, 4.7 Hz, 1F).

5-Bromo-2-(4-chlorophenyl)-3-(1-(4-chlorophenyl)-2-fluoro-2-nitroethyl)-1H-indole (**4t**). The mixture of diastereoisomers (d.r. = 1.3:1.0) was obtained in 51 % yield (0.133 g) as a colorless solid by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. Mp = 228 - 232 °C. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{22}H_{13}{}^{79}Br^{35}Cl_2FN_2O_2$ 504.9527; found 504.9528. ^{1}H NMR (400 MHz, CD_3CN): δ = 5.10 (dd, *J* = 21.4, 6.9 Hz, 1H), 5.35 (dd, *J* = 33.7, 3.4 Hz, 1H), 6.79 (dd, *J* = 49.8, 3.4 Hz, 1H), 6.82 (dd, *J* = 49.0, 6.9 Hz, 1H), 7.26–7.61 (m, 21H), 7.80 (br s, 1H), 9.87 (br s, 2H). ^{13}C NMR (100 MHz, CD_3CN) δ = 45.07 (d, $^{2}J_{CF}$ = 19.4 Hz), 46.10 (d, $^{2}J_{CF}$ = 20.6 Hz), 113.19 (d, $^{1}J_{CF}$ = 244.2 Hz), 113.49 (d, $^{1}J_{CF}$ = 242.0 Hz), 113.85, 114.08, 114.34, 114.54, 123.05 (d, ^{4}J = 3.2 Hz), 124.05, 124.15, 126.19, 126.36, 129.06, 129.57, 129.70, 129.78, 129.88, 130.09, 130.58, 130.68, 130.77, 130.87, 131.11, 131.52, 131.59, 131.91, 132.23, 134.11, 134.26, 135.51, 135.63, 136.0, 136.04, 136.09, 136.46. ^{19}F NMR (376 MHz, CD_3CN): δ = -150.18 (dd, J = 49.8, 33.8 Hz, 1F), -144.61 (dd, J = 49.0, 21.4 Hz, 1F).

5-Chloro-3-(1-(4-chlorophenyl)-2-fluoro-2-nitroethyl)-2-(4-fluorophenyl)-1H-indole (**4u**). The mixture of diasteroisomers (d.r. = 1.2:1.0) was obtained in 81 % yield (0.186 g) as a colorless solid by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. M.p. = 197-202 °C, HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{22}H_{13}{}^{35}Cl_2F_2N_2O_2$ 445.0328; found 445.0330. ^{1}H NMR (400 MHz, CD_3CN): δ = 5.09 (dd, *J* = 21.5, 6.9 Hz, 1H), 5.33 (dd, *J* = 33.7, 3.3 Hz, 1H), 6.79 (dd, *J* = 49.8, 3.4 Hz, 2H), 6.81 (dd, *J* = 49.1, 6.9 Hz, 2H), 7.10 –7.50 (m, 21H), 7.57 – 7.67 (m, 1H), 9.84 (br s, 2H). ^{13}C NMR (100 MHz, CD_3CN): δ = 45.13 (d, $^2J_{CF}$ = 19.7 Hz), 46.14 (d, $^2J_{CF}$ = 20.7 Hz), 105.43, 107.05 (d, J_{CF} = 8.0 Hz), 113.25 (d, $^1J_{CF}$ = 244.4 Hz), 113.54 (d, $^1J_{CF}$ = 241.8 Hz), 113.87, 114.09, 116.77 (d, $^2J_{CF}$ = 21.9 Hz), 116.89 (d, $^2J_{CF}$ = 22.0 Hz), 119.94 (d, $^4J_{CF}$ = 3.4 Hz), 120.92, 121.01, 123.44, 123.59, 126.20, 126.45, 128.39, 128.5 (d, J_{CF} = 3.0 Hz), 128.91, 129.77, 129.87, 130.59, 131.10, 132.09 (d, $^4J_{CF}$ = 8.9 Hz), 132.18 (d, $^4J_{CF}$ = 8.8 Hz), 134.08, 134.23, 135.64, 135.73, 136.13, 136.57, 139.70, 140.06, 163.65 (d, $^1J_{CF}$ = 245.1 Hz), 164.04 (d, $^1J_{CF}$ = 247.4 Hz). ^{19}F NMR (376 MHz, CD_3CN): δ = -150.10 (ddd, *J* = 49.8 Hz, 33.8 Hz, 2.7 Hz, 1F), -144.7 (dd, *J* = 49.1 Hz, 21.5 Hz), -113.80 (tt, *J* = 8.8 Hz, 5.4 Hz, 1F), -113.61 (tt, *J* = 8.9 Hz, 5.4 Hz, 1F)

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-2-(3,4-dimethoxyphenyl)-1H-indole (**4v**). The mixture of diasteroisomers (d.r. = 2.2:1.0) was obtained in 83 % yield (0.196 g) as a pale yellow solid by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. M.p. = 86-89 °C. HRMS (ESI) *m/z* $[M-H^+]^-$: Calcd for $C_{24}H_{19}{}^{35}ClFN_2O_4$ 453.1023; found 453.1019. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 3.77 (s, 6H), 3.90 (s, 6H), 5.22 (dd, *J* = 21.2, 6.3 Hz, 1H), 5.24 (dd, *J* = 29.8, 5.4 Hz, 1H), 6.52 (dd, *J* = 50.6, 6.5 Hz, 1H), 6.53 (dd, *J* = 49.5, 4.8 Hz, 1H), 6.78-6.95 (m, 6H), 7.09–7.45 (m, 14H), 7.64-7.74 (m, 2H), 8.51 (br s, 1H), 8.55 (br s, 1H). ^{13}C NMR (100 MHz, CD_3Cl): δ = 45.50 (d, $^2J_{CF}$ = 17.4 Hz), 45.69 (d, $^2J_{CF}$ = 20.0 Hz), 55.74, 55.86, 104.70, 105.98 (d, $^3J_{CF}$ = 5.5 Hz), 111.32 (d, $^3J_{CF}$ = 4.1 Hz), 111.46, 111.54, 111.85, 112.06, 112.57 (d, $^1J_{CF}$ = 249.0 Hz), 112.84 (d, $^1J_{CF}$ = 244.5 Hz), 119.84 (d, $^4J_{CF}$ = 4.0 Hz), 120.53, 120.67, 120.79, 121.50, 121.63, 122.46, 122.56, 124.08, 124.22, 126.68, 126.83, 128.86, 129.07, 129.39, 130.13, 133.64, 133.74, 134.79, 135.36, 135.85, 137.95, 138.76, 148.96, 149.05, 149.44, 149.48. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -145.95 (dd, *J* = 50.7 Hz, 29.7 Hz, 1F), -142.84 (dd, *J* = 49.4 Hz, 21.1 Hz, 1F).

3-(1-(4-Chlorophenyl)-2-fluoro-2-nitroethyl)-2-(2,5-dimethoxyphenyl)-1H-indole (**4w**). The mixture of diasteroisomers (d.r. = 2.1:1.0) was obtained in 77 % yield (0.179 g) as a pale yellow solid by column chromatography on silica gel using hexane/dichloromethane (2:1) as elution mixture. M.p. = 68-72 °C. HRMS (ESI) *m/z* $[M]^-$: Calcd for $C_{24}H_{19}{}^{35}ClFN_2O_4$ 453.1023; found 453.1020. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.61 (br s, 2H), 3.67 (br s, 4H), 3.77 (br s, 6H), 5.16 (dd, *J* = 25.8, 5.2 Hz, 1H), 5.19 (dd, *J* = 30.0, 4.0 Hz, 1H), 6.49 (dd, *J* = 50.2, 5.3 Hz, 1H), 6.52 (dd,

J = 50.5, 4.3 Hz, 1H), 6.80-6.84 (m, 2H), 6.91–7.04 (m, 4H), 7.10–7.41 (m, 14H), 7.56-7.70 (m, 2H), 8.52 (br s, 1H), 8.54 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.53 (d, $^2J_{CF}$ = 23.2 Hz), 45.76 (d, $^2J_{CF}$ = 19.4 Hz), 55.76, 56.05, 106.23, 108.10 (d, $^3J_{CF}$ = 3.9 Hz), 111.28, 111.47, 112.42 (d, $^1J_{CF}$ = 245.4 Hz), 112.79, 112.85, 112.91 (d, $^1J_{CF}$ = 245.4 Hz), 115.61, 115.67, 116.88, 120.07 (d, $^4J_{CF}$= 5.0 Hz), 120.27, 120.44, 120.77, 120.86 (d, $^4J_{CF}$ = 7.3 Hz), 122.43, 122.56, 126.39, 126.72, 128.71, 128.92, 129.41, 130.2, 133.41, 133.49, 134.06, 134.59, 134.98, 135.45, 136.06, 151.37, 151.57, 153.52, 153.60. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -146.84 (dd, *J* = 50.5 Hz, 30.1 Hz, 1F),-144.95 (dd, *J* = 50.2 Hz, 25.8 Hz, 1F).

Reduction of adducts of indole. To a solution of selected 3-(2-fluoro-2-nitro-1-aryl)-1*H*-indole **4** (100-150 mg, 1 mol. equiv.) and $NiCl_2{\cdot}6H_2O$ (1 mol. equiv.) in methanol (2-3 mL) was added $NaBH_4$ (5 mol. equiv.) at 0 °C and the reaction mixture was stirred until completion of the reaction. The progress of reaction was monitored by TLC. After completion the reaction mixture was poured into water and extracted with ethyl acetate. The organic layer was separated, dried over anhydrous sodium sulfate and concentrated under vacuum. The product was isolated by column chromatography on silica using DCM/CH_3OH (20:1-10:1-5:1) as elution mixture.

2-(1H-indol-3-yl)-2-phenylethanamine (**5b**). The product was obtained in 38% yield (42.04 mg) as a viscous pale yellow oil. ^{1}H NMR (400MHz, $CDCl_3$): 3.00 (br s, 2H), 3.14 – 3.27 (m, 1H), 3.28 – 3.42 (m, 1H), 4.26 (t, *J* = 7.1 Hz, 1H), 6.94 – 7.05 (m, 2H), 7.10 – 7.28 (m, 6H), 7.33 (d, *J* = 8.1 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 8.74 (br s, 1H). Analysis of the sample was consistent with the data reported in the literature.[14]

*2-(1H-Indol-3-yl)-2-(4-methoxyphenyl)ethanamine (***5e**). The product was obtained in 42% yield (45.52 mg) as a viscous pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.78 (br s, 2H), 3.32 – 3.45 (m, 1H), 3.12 – 3.27 (m, 1H), 3.75 (s, 3H), 4.22 (t, *J* = 8.0 Hz, 1H), 6.75 – 6.85 (m, 2H), 6.95 – 7.08 (m, 2H), 7.09 – 7.23 (m, 3H), 7.32 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 7.7 Hz, 1H), 8.61 (br s, H). Analysis of the sample was consistent with the data reported in the literature.[15]

Methyl 4-(2-amino-1-(1H-indol-3-yl)ethyl)benzoate (**5f**). The product was obtained in 55% yield (36.48 mg) as a viscous pale yellow oil. HRMS (ESI) m/z $[M+H]^+$: Calcd for $C_{18}H_{19}N_2O_2$ 295.1441; found 295.1441. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 2.03 (br s, 2H), 3.28 (dd, *J* = 12.7, 7.5 Hz, 1H), 3.42 (dd, *J* = 12.6, 7.4 Hz, 2H), 4.32 (t, *J* = 7.3 Hz, 1H), 6.94 – 7.10 (m, 2H), 7.13 – 7.19 (m, 1H), 7.28 – 7.46 (m, 4H), 7.95 (d, *J* = 8.3 Hz, 2H), 8.71 (br s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ = 46.52, 46.73, 52.15, 111.42, 116.28, 119.23, 119.56, 121.67, 122.33, 126.86, 128.24, 128.47, 129.95, 136.62, 148.52, 167.17.

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