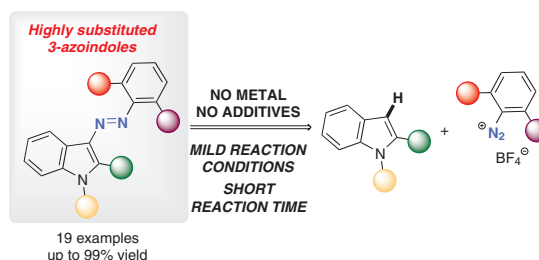


Highly Efficient Synthesis of Hindered 3-Azoindoles via Metal-Free C–H Functionalization of Indoles

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Abstract Although 3-azoindoles have recently emerged as an appealing family of photoswitch molecules, the synthesis of such compounds has been poorly covered in the literature. Herein a high-yielding and operationally simple protocol is reported allowing the synthesis of 3-azoindoles, featuring important steric hindrance around the azo motif. Remarkably, this C–H coupling is characterized by excellent atom economy and occurs under metal-free conditions, at room temperature, and within few minutes, delivering the expected products in excellent yields (quantitatively in most of the cases). Accordingly, a library of new molecules, with potential applications as photochromic compounds, is prepared.

Key words azoindole, C–H functionalization of indoles, azoswitches, diazenylation

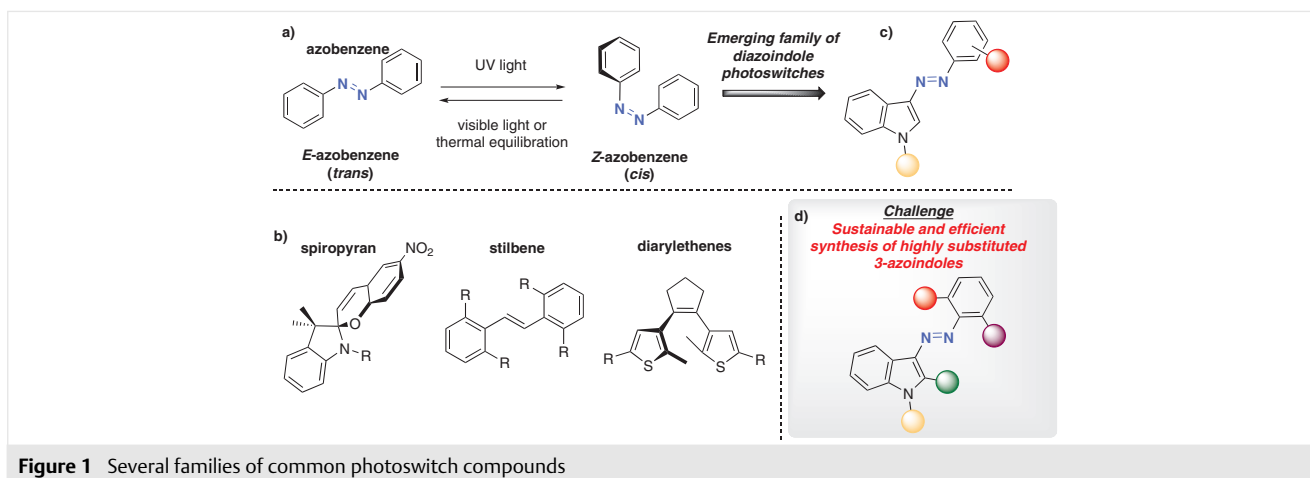
Reversible modification of the key properties of a molecule, such as geometry, rigidity, dielectric constant, or refractive index under light irradiation is an intriguing feature of photochromic compounds with great potential applications in different fields.¹ Thus, not surprisingly, molecular photoswitches have been attracting, over the last few decades, a growing attention and consequently these molecules have found numerous applications in light-triggered materials and machines,² 3D data storage systems,³ light driven molecular motors,⁴ polymers,⁵ drug delivery,⁶ and control of cell death.⁷ Such a large range of applications can be reached, because the physical properties of photoswitches, and in particular the thermal lifetime of the metastable *Z*-isomer (varying from nanosecond scale range to days), can be controlled by carefully selecting the appropriate photochromic scaffolds (Figure 1a). For example, if molecular storage,⁸ or biological applications in photomodulation of protein expression systems or oligonucleotide recognition applications are targeted,⁹ stable photoswitch-

es will be selected (long thermal lifetime) while compounds characterized by short thermal lifetime are used in real-time optical information transmitting materials,¹⁰ in medicinal chemistry for neurons or ion channel stimulation purposes.¹¹ Accordingly, several families of molecular photoswitches have been designed (Figure 1b) including spiro-pyrans,¹² stilbenes¹³ and diarylethenes,¹⁴ but the azobenzenes¹⁵ are, by far, the most commonly applied ones (Figure 1a). More recently, indigoids¹⁶ or Stenhouse adducts¹⁷ have been disclosed. Considerable attention has also been focused on heteroazoswitches,¹⁸ including compounds featuring pyridine, imidazole, pyrazole, and purine motifs.

In clear contrast, 3-arylaazoindoles are relatively underexplored molecules.¹⁹ Surprisingly, only few literature reports disclose synthesis of indoles bearing a diazo moiety in C3 position²⁰ and the recent methodologies request use of sophisticated coupling partners such as aryltriazenes²¹ in ionic liquid medium or arylhydrazine hydrochlorides²² under visible-light irradiation or heating at 90 °C.

Very recently, a unique potential of 3-arylaazoindole photoswitches has been demonstrated by König (Figure 1c)²³ and thus development of truly efficient, sustainable and straightforward protocols delivering such compounds is timely. In particular, as the properties of azoswitches, and especially their thermal lifetime, are impacted by the substitution pattern around the azo moiety, synthesis of a library of 3-arylaazoindoles bearing various substituents in proximity of N=N motif, on both C2 position of the indole and *ortho*-, *ortho'*-positions of the aromatic ring, seems very appealing (Figure 1d).²⁴ Accordingly, we report herein an extremely simple but highly efficient strategy to prepare sterically hindered 2-substituted 3-arylaazoindoles, the molecules with promising photochromic properties.

Our investigations began by exploring the coupling between 2-(*tert*-butyl)-1*H*-indole (**1a**) and electron-rich *para*-methoxyphenyldiazonium salt **2a**. The reaction occurred



smoothly in methanol medium and at room temperature, delivering the expected (*E*)-2-(*tert*-butyl)-3-[(4-methoxyphenyl)diazenyl]-1*H*-indole (**3a**) in quantitative yield (Table 1, entry 1). Comparable results were obtained when using 2-(methyl)-1*H*-indole (**1b**) as substrate (entry 2). Besides, the reaction is extremely fast as full conversion of **1b** could be achieved in less than 10 minutes (entry 3), even in the presence of equimolar amounts of both coupling partners (entry 4). Electron-poor Ac-substituted aryldiazonium salts may also be converted into 3-arylaazoindoles, but the reaction generally requires a slight excess of the diazonium salts coupling partners (entry 5). Accordingly, the general reaction conditions have been determined, that is, use of 1.3 equivalents of diazonium salt in MeOH medium and 30 minutes as standard reaction time (entry 6). Of note is that the desired products are isolated *via* simple filtration of the crude mixture through silica gel pad, further demonstrating the experimental simplicity and efficiency of this protocol. This transformation hence perfectly follows the requirements of sustainable and green chemistry, as neither a catalysts nor sophisticated additives or strong oxidants are required and this coupling is characterized by excellent atom economy. Finally, the reaction performed in water is sluggish and the desired product **4a** was formed in only 68% NMR conversion after 4 days (entry 7).

The generality of this new protocol was subsequently explored (Scheme 1). Rewardingly, indole **1a** bearing a highly hindering *tert*-butyl motif in C2 position could be coupled very smoothly with diverse diazo coupling partners, both electron-rich and electron-poor, affording the expected products in excellent yields and in short reaction time. Importantly, the presence of a substituent in the *ortho*-position of **2** is tolerated well, as **3b**, **3c**, and **3e** could be isolated in almost quantitative yields. In addition, very congested azoindole **3g** could also be synthesized following the standard procedure in 93% yield. Interestingly, our protocol also tolerates relatively well a halogen atom on the indole scaffold, as **3h** could be isolated in 70% yield, albeit excess of

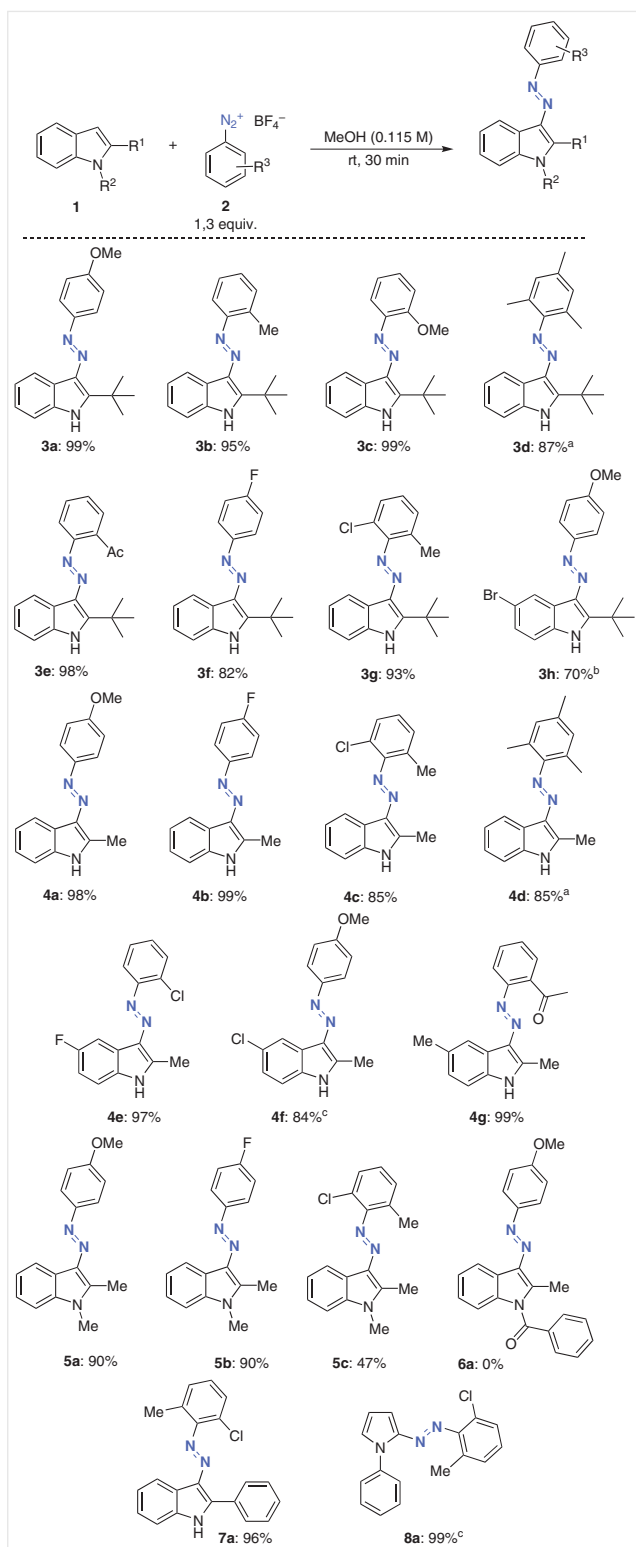
Table 1 Optimization Study^a

| Entry | R ¹ | R ² | 3 | x (equiv.) | Time | Yield (%) |
|----------------|----------------|----------------|-----------|------------|--------|-----------|
| 1 | <i>t</i> -Bu | 4-OMe | 3a | 1.5 | 16 h | 99 |
| 2 | Me | 4-OMe | 4a | 1.5 | 16 h | 99 |
| 3 | Me | 4-OMe | 4a | 1.5 | 10 min | 99 |
| 4 | Me | 4-OMe | 4a | 1.0 | 10 min | 99 |
| 5 | <i>t</i> -Bu | 2-Ac | 3e | 1.5 | 16 h | 99 |
| 6 | <i>t</i> -Bu | 2-Ac | 3e | 1.3 | 30 min | 99 |
| 7 ^b | Me | 4-OMe | 4a | 1.3 | 96 h | 68 |

^a Standard reaction conditions: **1** (0.115 mmol, 1 equiv.), **2** (0.150 mmol, 1.3 equiv.), MeOH (1 mL), rt, under air, approx. 30 min; isolated yield.

^b Reaction performed in H₂O, conversion determined by ¹H NMR analysis.

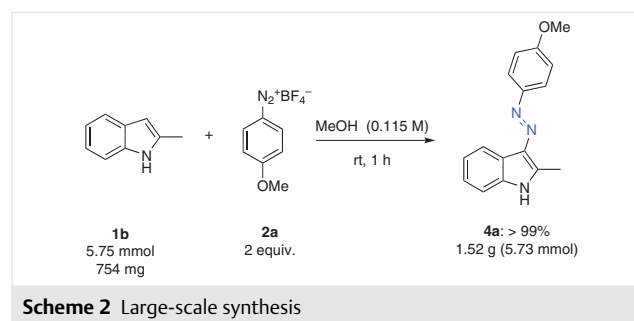
2 and prolonged reaction time were required in this case. Also, the coupling using mesityldiazonium salt was more sluggish; additional portion of the diazonium salt and longer reaction time (2 h) were needed to reach full conversion but, rewardingly, under such a modified protocol **3d** was afforded in high 87% yield. The reaction occurs with a comparable outcome when using the less hindered 2-(methyl)-1*H*-indole (**1b**), furnishing the coupling products **4a–c** in very high yields. The mesityl-derived azoindole **4d** was obtained in 85% yield using 2 equivalents of the diazo salt partner. Functionalized indole substrates bearing F, Cl, and Me motifs could also be converted into the expected products **4e–g** in excellent yields. Of note is that this reaction is not specific to 1*H*-indoles, and diazo-(*N*-methyl)indoles **5a–c** were also synthesized successfully. In contrast, acyl-



Scheme 1 Scope of C3-diazenylation of indoles. Isolated yields are shown. a) an additional portion of 0.7 equiv. of **2** was added after 30 min, and stirred for 2 h; b) an additional portion of 0.7 equiv. of **2** was added twice after 30 min, and stirred for 1 h; c) an additional portion of 0.7 equiv. of **2** was added after 30 min, and stirred for 30 min.

protected indole turned out to be ineffective. Finally, under the standard reaction conditions, 2-phenylindole was converted into the corresponding diazo compound **7a** in 96% yield and pyrrole-derived substrate undergoes selective C2-functionalization delivering **8a** in quantitative yield.

Importantly, the reaction is also efficient even at 50 times larger scale (5.75 mmol, 754 mg of **1b**) and appealing product **4a** could hence be isolated in quantitative yield (Scheme 2). However, larger excess of **2a** (2 equiv.) and slightly longer reaction time (1 h) were critical to reach full conversion.



Scheme 2 Large-scale synthesis

Subsequently, in order to gather additional information about the newly synthesized compounds, their UV/Vis absorption spectra were recorded (Figure 2). Interestingly, all compounds present rather similar absorption patterns, ranging from 353 nm (for 3-azaindoles bearing mesityl

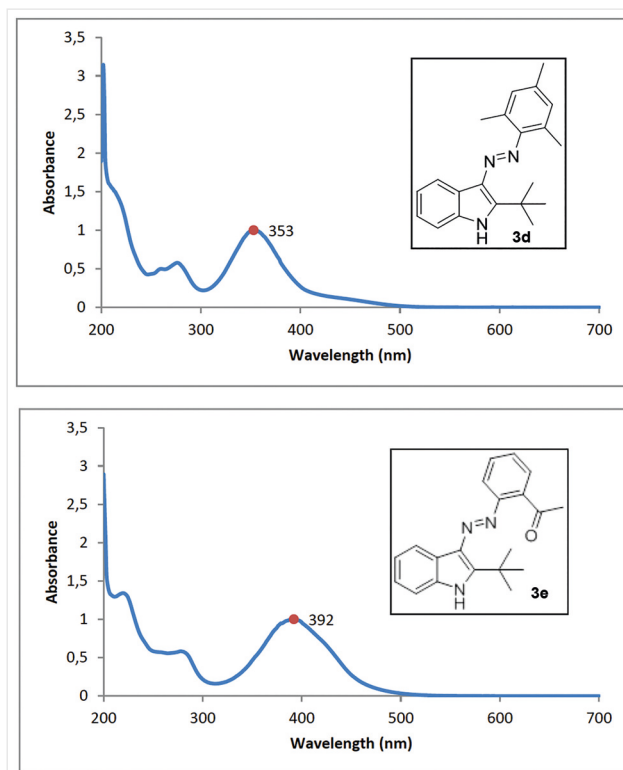


Figure 2 Examples of UV/Vis absorption spectra of the selected products

motif such as **3d** and **4d**) to 393 nm (for 3-azaindole featuring 2-Ac phenyl motif such as **3e**). Besides, the initial testes of *cis*–*trans* photoisomerization indicate that this process is relatively fast, inferior to the minute scale.

In conclusion, we have described herein a very efficient synthesis of original, highly substituted 3-azaindoles. The coupling occurs *via* metal-free C–H diazenylation of indoles, using aryldiazonium salts as coupling partners. Remarkably, the reaction does not require addition of a catalyst and performs smoothly at room temperature within few minutes delivering the expected products in quantitative yields in most of the cases. This sustainable, particularly mild and atom-economical protocol is highly tolerant towards various functionalities, furnishing a library of interesting scaffolds. These unprecedented molecules appear as privileged candidates for original photoswitch design. Besides, the simplicity of this protocol renders it perfectly suitable to be used in late-modification of sophisticated indole-containing drugs.

All the reactions were performed under air atmosphere, using tube reactors (10 mL). Chemicals and solvents (suppliers: Aldrich, Alfa Aesar, Fluorochem, TCI) were directly used without further purification. Technical grade solvents for purification were used without further purification or distillation. ^1H , ^{13}C , and ^{19}F NMR spectra were recorded in CDCl_3 or acetone- d_6 at rt on Bruker, Avance 400 (400 MHz) or Avance III-HD (500 MHz) spectrometers and FID was processed in MestreNova software. Chemical shifts were referenced to residual solvent peaks and reported in ppm (i.e., CDCl_3 referenced at 7.26 and 77.16 ppm respectively and acetone- d_6 referenced at 2.05 ppm). Standard abbreviations were used for NMR spectra to represent the signal multiplicity. The coupling constants were reported in hertz (Hz). Thin-layer chromatography (TLC) were carried out on precoated aluminum sheets (Merck 60-F $_{254}$ plates) and the components were visualized by observation under UV light at 254 nm. Products were purified by column chromatography on 40–63 mesh silica gel, SiO_2 . HRMS measurements were carried out by Service de Spectrométrie de Masse de l'Institut de Chimie at the University of Strasbourg.

The preparation of starting aryldiazonium tetrafluoroborates **2** and indoles **1** are provided in the Supporting Information.

3-Azaindoles; General Procedure

A 10 mL reaction tube equipped with magnetic stir bar was filled with indole derivative **1** (0.115 mmol, 1 equiv.) and diazonium tetrafluoroborate salt **2** (0.150 mmol, 1.3 equiv.) under air. Then, anhydrous MeOH (1 mL) was added, the reaction mixture turned immediately to a deep dark red color. The resulting mixture was stirred at rt for 30 min. Afterwards, the reaction mixture was filtered through a short pad of silica gel. The reaction tube and the pad of silica gel were washed with DCM until the disappearance of color of the filtrate (~100 mL). The solvent was removed under reduced pressure and the resulting highly colored solid was dried under vacuum to give the expected pure product.

(E)-2-(tert-Butyl)-3-[(4-methoxyphenyl)diazonyl]-1H-indole (**3a**)

Deep orange solid; yield: 35 mg (99%, 0.114 mmol).

^1H NMR (CDCl_3 , 400 MHz): δ = 8.61–8.54 (m, 1 H), 8.28 (br s, 1 H), 7.86 (d, J = 8.9 Hz, 2 H), 7.37–7.30 (m, 1 H), 7.30–7.18 (m, 2 H), 7.01 (d, J = 9.0 Hz, 2 H), 3.89 (s, 3 H), 1.69 (s, 9 H).

^{13}C NMR (CDCl_3 , 101 MHz): δ = 160.21, 151.70, 148.76, 133.68, 123.33, 123.32, 123.31, 123.25, 122.96, 120.49, 114.20, 110.69, 55.67, 34.11, 31.01.

HRMS (ESI): m/z [$M + H$] $^+$ calcd for $\text{C}_{19}\text{H}_{22}\text{N}_3\text{O}$: 308.1757; found: 308.1754.

(E)-2-(tert-Butyl)-3-(o-tolyldiazonyl)-1H-indole (**3b**)

Deep orange solid; yield: 32 mg (95%, 0.110 mmol).

^1H NMR (CDCl_3 , 400 MHz): δ = 8.51 (dd, J = 7.4, 1.8 Hz, 1 H), 8.33 (br s, 1 H), 7.70–7.63 (m, 1 H), 7.38–7.32 (m, 2 H), 7.31–7.26 (m, 3 H), 7.26–7.22 (m, 1 H), 2.81 (s, 3 H), 1.71 (s, 9 H).

^{13}C NMR (CDCl_3 , 101 MHz): δ = 152.81, 152.34, 136.60, 133.71, 132.50, 131.13, 128.57, 126.41, 123.50, 123.33, 123.13, 120.25, 114.96, 110.78, 34.21, 31.05, 18.49.

HRMS (ESI): m/z [$M + H$] $^+$ calcd for $\text{C}_{19}\text{H}_{22}\text{N}_3$: 292.1808; found: 292.1801.

(E)-2-(tert-Butyl)-3-[(2-methoxyphenyl)diazonyl]-1H-indole (**3c**)

Deep red solid; yield: 35 mg (99%, 0.114 mmol).

^1H NMR (CDCl_3 , 400 MHz, 333 K): δ = 8.59 (br s, 1 H), 8.50 (d, J = 7.4 Hz, 1 H), 7.68 (dd, J = 7.9, 1.7 Hz, 1 H), 7.38 (d, J = 7.6 Hz, 1 H), 7.29–7.23 (m, 3 H), 7.08 (dd, J = 8.2, 1.2 Hz, 1 H), 7.03 (td, J = 7.6, 1.2 Hz, 1 H), 4.07 (s, 3 H), 1.69 (s, 9 H).

^{13}C NMR (CDCl_3 , 101 MHz, 333 K): δ = 155.66, 153.34, 143.87, 133.79, 132.55, 129.10, 124.36, 123.81, 123.34, 121.30, 120.79, 116.30, 113.38, 111.85, 56.99, 34.56, 31.01.

HRMS (ESI): m/z [$M + H$] $^+$ calcd for $\text{C}_{19}\text{H}_{22}\text{N}_3\text{O}$: 308.1757; found: 308.1748.

(E)-2-(tert-Butyl)-3-(mesityldiazonyl)-1H-indole (**3d**)

Prepared according to the general procedure, with a following modification: an additional portion of 0.7 equiv of mesityldiazonium tetrafluoroborate was added after 30 min; stirred for 2 h; deep orange solid; yield: 32 mg (87%, 0.100 mmol).

^1H NMR (CDCl_3 , 400 MHz): δ = 8.57–8.48 (m, 1 H), 8.29 (br s, 1 H), 7.40–7.33 (m, 1 H), 7.31–7.21 (m, 2 H), 6.96 (s, 2 H), 2.42 (s, 6 H), 2.35 (s, 3 H), 1.65 (s, 9 H).

^{13}C NMR (CDCl_3 , 101 MHz): δ = 152.00, 150.67, 136.14, 133.45, 132.31, 130.35, 129.69, 123.35, 123.25, 123.19, 120.32, 110.63, 34.07, 30.90, 21.11, 19.60.

HRMS (ESI): m/z [$M + H$] $^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{N}_3$: 320.2121; found: 320.2122.

(E)-1-(2-[(2-(tert-Butyl)-1H-indol-3-yl]diazonyl]phenyl)ethan-1-one (**3e**)

Deep orange solid; yield: 36 mg (98%, 0.113 mmol).

^1H NMR (CDCl_3 , 400 MHz): δ = 12.87 (br s, 1 H), 8.35 (d, J = 6.9 Hz, 1 H), 7.97 (d, J = 8.5 Hz, 1 H), 7.93 (d, J = 7.9 Hz, 1 H), 7.64 (t, J = 7.8 Hz, 1 H), 7.59 (d, J = 6.5 Hz, 1 H), 7.45–7.38 (m, 2 H), 7.11 (t, J = 7.5 Hz, 1 H), 2.75 (s, 3 H), 1.60 (s, 9 H).

^{13}C NMR (CDCl_3 , 101 MHz): δ = 202.25, 179.13, 145.95, 141.96, 135.64, 132.13, 130.49, 126.41, 122.52, 121.72, 121.47, 120.90, 119.83, 114.96, 36.53, 30.53, 28.27 (1 C undetected due to overlapping).

HRMS (ESI): m/z [M + H]⁺ calcd for C₂₀H₂₂N₃O: 320.1757; found: 320.1744.

(E)-2-(tert-Butyl)-3-[(4-fluorophenyl)diazenyl]-1H-indole (3f)

Deep yellow solid; yield: 28 mg (82%, 0.095 mmol).

¹H NMR (CDCl₃, 400 MHz): δ = 8.59–8.52 (m, 1 H), 8.34 (br s, 1 H), 7.88–7.83 (m, 2 H), 7.38–7.33 (m, 1 H), 7.31–7.22 (m, 2 H), 7.20–7.12 (m, 2 H), 1.69 (s, 9 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 162.97 (d, *J* = 248.0 Hz), 152.87, 150.89 (d, *J* = 3.0 Hz), 133.70, 131.57, 123.59, 123.46 (d, *J* = 8.5 Hz), 123.27, 123.23, 120.33, 115.82 (d, *J* = 22.5 Hz), 110.80, 34.19, 31.03.

¹⁹F NMR (CDCl₃, 376 MHz): δ = –113.73 (s, 1 F).

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₈H₁₉FN₃: 296.1557; found: 296.1544.

(E)-2-(tert-Butyl)-3-[(2-chloro-6-methylphenyl)diazenyl]-1H-indole (3g)

Deep orange solid; yield: 35 mg (93%, 0.107 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 8.56 (dd, *J* = 6.5, 2.1 Hz, 1 H), 8.39 (br s, 1 H), 7.38–7.34 (m, 2 H), 7.30–7.24 (m, 2 H), 7.17 (ddd, *J* = 7.6, 1.5, 0.7 Hz, 1 H), 7.09 (t, *J* = 7.8 Hz, 1 H), 2.39 (s, 3 H), 1.65 (s, 9 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 153.84, 150.84, 133.59, 132.55, 131.56, 129.71, 128.11, 127.33, 126.78, 123.75, 123.72, 123.40, 120.17, 110.73, 34.26, 30.92, 19.47.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₉H₂₁ClN₃: 326.1419; found: 326.1408.

(E)-5-Bromo-2-(tert-butyl)-3-[(4-methoxyphenyl)diazenyl]-1H-indole (3h)

Prepared according to the general procedure, with a following modification: two additional portions of 0.7 equiv of mesityldiazonium tetrafluoroborate were added after 30 min and 1 h; stirred for 1 h; deep orange solid; yield: 31 mg (70%, 0.0803 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 8.72 (d, *J* = 1.9 Hz, 1 H), 8.30 (br s, 1 H), 7.86 (d, *J* = 9.0 Hz, 2 H), 7.31 (dd, *J* = 8.5, 2.0 Hz, 1 H), 7.20 (d, *J* = 8.5 Hz, 1 H), 7.01 (d, *J* = 8.9 Hz, 2 H), 3.89 (s, 3 H), 1.67 (s, 9 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.48, 152.42, 148.49, 132.29, 130.63, 126.07, 125.73, 123.49, 121.91, 116.10, 114.23, 112.13, 55.68, 34.15, 30.89.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₉H₂₁BrN₃O: 386.0863; found: 386.0847.

(E)-3-[(4-Methoxyphenyl)diazenyl]-2-methyl-1H-indole (4a)

Deep red solid; yield: 30 mg (98%, 0.113 mmol).

¹H NMR (CDCl₃, 400 MHz): δ = 8.57–8.50 (m, 1 H), 8.18 (br s, 1 H), 7.89 (d, *J* = 8.9 Hz, 2 H), 7.30–7.26 (m, 1 H), 7.26–7.20 (m, 2 H), 7.01 (d, *J* = 9.0 Hz, 2 H), 3.88 (s, 3 H), 2.80 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.33, 148.61, 141.70, 135.10, 132.66, 123.45, 123.26, 122.71, 122.57, 119.88, 114.18, 110.55, 55.66, 11.67.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₆H₁₆N₃O: 266.1285; found: 266.1288.

(E)-3-[(4-Fluorophenyl)diazenyl]-2-methyl-1H-indole (4b)

Deep yellow solid; yield: 29 mg (99%, 0.115 mmol).

¹H NMR (CDCl₃, 400 MHz): δ = 8.54–8.48 (m, 1 H), 8.28 (br s, 1 H), 7.91–7.86 (m, 2 H), 7.33–7.24 (m, 3 H), 7.20–7.12 (m, 2 H), 2.82 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 163.08 (d, *J* = 248.2 Hz), 150.75 (d, *J* = 1.8 Hz), 142.92, 135.14, 132.81, 123.75, 123.41 (d, *J* = 8.4 Hz), 123.03, 122.57, 119.70, 115.80 (d, *J* = 22.7 Hz), 110.65, 11.72.

¹⁹F NMR (CDCl₃, 376 MHz): δ = –113.55 (s, 1 F).

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₅H₁₃FN₃: 254.1088; found: 254.1076.

(E)-3-[(2-Chloro-6-methylphenyl)diazenyl]-2-methyl-1H-indole (4c)

Deep orange solid; yield: 28 mg (85%, 0.099 mmol).

¹H NMR (CDCl₃, 400 MHz): δ = 8.50 (d, *J* = 7.4 Hz, 1 H), 8.31 (br s, 1 H), 7.35 (dd, *J* = 8.0, 0.7 Hz, 1 H), 7.33–7.24 (m, 3 H), 7.16 (d, *J* = 7.6 Hz, 1 H), 7.09 (t, *J* = 7.7 Hz, 1 H), 2.79 (s, 3 H), 2.42 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 150.46, 143.72, 135.11, 133.74, 131.57, 130.05, 128.20, 127.05, 123.90, 123.89, 123.44, 122.62, 119.42, 110.61, 19.61, 11.64.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₆H₁₅ClN₃: 284.0949; found: 284.0946.

(E)-3-(Mesityldiazenyl)-2-methyl-1H-indole (4d)

Prepared according to the general procedure, with a following modification: an additional portion of 0.7 equiv of mesityldiazonium tetrafluoroborate was added after 30 min; stirred for 2 h.

Deep yellow solid; yield: 27 mg (85%, 0.097 mmol).

¹H NMR (CDCl₃, 400 MHz): δ = 8.47–8.41 (m, 1 H), 8.20 (br s, 1 H), 7.33–7.23 (m, 3 H), 6.95 (s, 2 H), 2.77 (s, 3 H), 2.45 (s, 6 H), 2.33 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 150.24, 142.10, 136.47, 135.06, 133.41, 130.79, 129.94, 123.47, 122.92, 122.37, 119.50, 110.56, 21.15, 19.68, 11.58.

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₈H₂₀N₃: 278.1652; found: 278.1648.

(E)-3-[(2-Chlorophenyl)diazenyl]-5-fluoro-2-methyl-1H-indole (4e)

Deep yellow solid; yield: 32 mg (97%, 0.111 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 8.32 (dd, *J* = 9.7, 2.7 Hz, 1 H), 8.29 (br s, 1 H), 7.80 (dd, *J* = 7.9, 1.8 Hz, 1 H), 7.55 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.34–7.30 (m, 1 H), 7.28 (dd, *J* = 7.7, 1.8 Hz, 1 H), 7.19 (dd, *J* = 8.7, 4.3 Hz, 1 H), 6.98 (td, *J* = 8.9, 2.6 Hz, 1 H), 2.82 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.30 (d, *J* = 237.9 Hz), 149.83, 145.08, 134.19 (d, *J* = 3.9 Hz), 134.10, 131.48, 130.56, 129.58, 127.19, 120.02 (d, *J* = 11.3 Hz), 116.95, 111.81 (d, *J* = 26.3 Hz), 111.23 (d, *J* = 9.5 Hz), 108.63 (d, *J* = 25.6 Hz), 11.81.

¹⁹F NMR (CDCl₃, 376 MHz): δ = –120.04 (s, 1 F).

HRMS (ESI): m/z [M + H]⁺ calcd for C₁₅H₁₂ClFN₃: 288.0698; found: 288.0686.

(E)-5-Chloro-3-[(4-methoxyphenyl)diazenyl]-2-methyl-1H-indole (4f)

Prepared according to the general procedure, but by using another 0.7 equiv of the corresponding aryldiazonium tetrafluoroborate after 30 min; stirred for 30 min.

Deep orange solid; yield: 29 mg (84%, 0.097 mmol).

¹H NMR (CDCl₃, 400 MHz): δ = 8.51 (dd, *J* = 1.9, 0.8 Hz, 1 H), 8.26 (br s, 1 H), 7.88 (d, *J* = 9.0 Hz, 2 H), 7.19 (d, *J* = 0.8 Hz, 1 H), 7.18 (d, *J* = 1.9 Hz, 1 H), 7.00 (d, *J* = 9.0 Hz, 2 H), 3.89 (s, 3 H), 2.80 (s, 3 H).

¹³C NMR (CDCl₃, 101 MHz): δ = 160.60, 148.22, 142.74, 133.42, 132.03, 128.28, 123.62, 123.38, 122.14, 120.74, 114.23, 111.54, 55.68, 11.73.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₆H₁₅ClN₃O: 300.0898; found: 300.0888.

(E)-1-2-[(2,5-Dimethyl-1H-indol-3-yl)diazenyl]phenyl]ethan-1-one (4g)

Deep orange solid; yield: 33 mg (quant, 0.115 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 8.15 (s, 1 H), 8.03 (d, *J* = 8.3 Hz, 1 H), 7.88 (d, *J* = 7.8 Hz, 1 H), 7.63 (ddd, *J* = 8.5, 7.2, 1.5 Hz, 1 H), 7.39 (d, *J* = 7.9 Hz, 1 H), 7.22–7.18 (m, 2 H), 2.72 (s, 3 H), 2.65 (s, 3 H), 2.53 (s, 3 H) (NH proton not detected).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₈H₁₉N₃O: 292.1444; found: 292.1439.

(E)-3-[(4-Methoxyphenyl)diazenyl]-1,2-dimethyl-1H-indole (5a)

Deep orange solid; yield: 29 mg (90%, 0.104 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 8.59–8.54 (m, 1 H), 7.87 (d, *J* = 9.0 Hz, 2 H), 7.34–7.26 (m, 3 H), 7.00 (d, *J* = 8.9 Hz, 2 H), 3.88 (s, 3 H), 3.76 (s, 3 H), 2.82 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 160.10, 148.72, 143.88, 136.96, 132.30, 123.11, 122.69, 122.66, 119.27, 114.16, 108.85, 55.66, 29.98, 10.30 (1 C undetected due to overlapping).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₇H₁₈N₃O: 280.1444; found: 280.1433.

(E)-3-[(4-Fluorophenyl)diazenyl]-1,2-dimethyl-1H-indole (5b)

Deep orange solid; yield: 33.5 mg (90%, 0.112 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 8.58–8.52 (m, 1 H), 7.90–7.85 (m, 2 H), 7.34–7.27 (m, 3 H), 7.15 (t, *J* = 8.7 Hz, 2 H), 3.76 (s, 3 H), 2.82 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 162.88 (d, *J* = 247.5 Hz), 150.81 (d, *J* = 2.4 Hz), 145.19, 137.08, 132.42, 123.43, 123.24 (d, *J* = 8.4 Hz), 123.07, 122.66, 119.11, 115.76 (d, *J* = 22.6 Hz), 109.00, 30.08, 10.34.

¹⁹F NMR (CDCl₃, 376 MHz): δ = –113.97 (s, 1 F).

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₆H₁₅FN₃: 268.1244; found: 268.1230.

(E)-3-[(2-Chloro-6-methylphenyl)diazenyl]-1,2-dimethyl-1H-indole (5c)

Deep orange solid; yield: 16 mg (47%, 0.054 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 8.56–8.50 (m, 1 H), 7.37–7.27 (m, 4 H), 7.16 (ddd, *J* = 7.6, 1.5, 0.8 Hz, 1 H), 7.07 (t, *J* = 7.7 Hz, 1 H), 3.77 (s, 3 H), 2.79 (s, 3 H), 2.42 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 150.60, 145.74, 137.05, 133.36, 131.65, 129.98, 128.19, 128.16, 126.81, 123.51, 123.41, 122.69, 118.84, 108.93, 30.04, 19.63, 10.19.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₇H₁₇ClN₃: 298.1106; found: 298.1090.

(E)-3-[(2-Chloro-6-methylphenyl)diazenyl]-2-phenyl-1H-indole (7a)

Deep orange solid; yield: 38 mg (96%, 0.110 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 8.67–8.63 (m, 1 H), 8.61 (br s, 1 H), 8.03–7.98 (m, 2 H), 7.53–7.47 (m, 2 H), 7.46–7.42 (m, 2 H), 7.39–7.30 (m, 3 H), 7.15 (ddd, *J* = 7.6, 1.5, 0.8 Hz, 1 H), 7.10 (t, *J* = 7.7 Hz, 1 H), 2.39 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 150.58, 142.92, 135.46, 133.22, 131.66, 130.64, 129.94, 129.57, 129.18, 128.96, 128.24, 127.70, 127.33, 124.88, 123.99, 123.87, 119.87, 111.01, 19.66.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₂₁H₁₇ClN₃: 346.1106; found: 346.1091.

(E)-N-(2-Chloro-6-methylphenyl)-1-(1-phenyl-1H-pyrrol-2-yl)methanimine (8a)

Prepared according to the general procedure, but by using another 0.7 equiv. of the corresponding aryldiazonium tetrafluoroborate after 30 min; stirred for 30 min; deep orange solid; yield: 34 mg (99%, 0.115 mmol).

¹H NMR (CDCl₃, 500 MHz): δ = 7.53–7.48 (m, 2 H), 7.46–7.41 (m, 2 H), 7.38–7.34 (m, 1 H), 7.29–7.26 (m, 1 H), 7.23 (dd, *J* = 2.8, 1.6 Hz, 1 H), 7.08–7.03 (m, 2 H), 6.93 (dd, *J* = 4.2, 1.7 Hz, 1 H), 6.48 (dd, *J* = 4.1, 2.8 Hz, 1 H), 2.16 (s, 3 H).

¹³C NMR (CDCl₃, 126 MHz): δ = 149.50, 147.43, 138.66, 131.93, 129.93, 128.94, 128.22, 128.19, 127.81, 127.68, 127.27, 126.55, 111.24, 100.20, 19.43.

HRMS (ESI): *m/z* [M + H]⁺ calcd for C₁₇H₁₅ClN₃: 296.0949; found: 296.0940.

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Supporting Information

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