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# Rhodium-Catalyzed Selective C−H Trideuteromethylation of Indole at C7 Position Using Acetic-$d_6$ Anhydride

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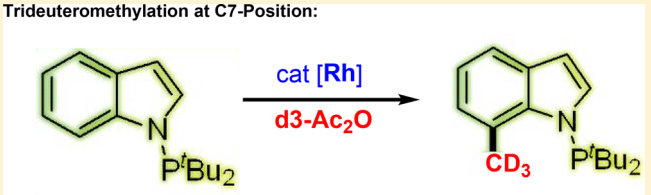
Supporting Information

**ABSTRACT:** Rhodium-catalyzed C7-selective decarbonylative trideuteromethylation of indoles with commercially available $Ac_2O$-$d_6$ via C−H and C−C bond activation has been developed. The key to the high reactivity and regioselectivity of this transformation is the appropriate choice of an indole N−P$^t$Bu$_2$ chelation-assisting group. This method has many advantages, including easy access and removal of the directing group, the use of cheap and widely available deuterium methylating source, no requirement of an external ligand or oxidant, a broader substrate scope, high efficiency, and the sole regioisomer.






## INTRODUCTION

Indoles and their derivatives belong to an important substance class which is often found in natural products and drug molecules.[1] Considerable attention has been turned to the synthesis and selective functionalization of these important molecules over the years. Due to the principles of atom and step economy, there is continuing interest in the C−H functionalization of indoles.[2] In an indole scaffold, there are six C−H bonds, including C2−C3 and C4−C7 positions, that can be functionalized. The usual reactivity of indoles suggested that C−H functionalization would take place preferentially at the C3-position.[3] To override this intrinsic selectivity, the introduction of directing groups on the N atom has been used as a powerful strategy to ensure C2-selectivity.[4] However, general methods to access selectivity at the benzene core of indole directly, especially the C7-position, continue to be scarce.[5] In 2010, Hartwig et al. developed the first iridium-catalyzed C−H borylation of indoles at the C7-position, in which the regioselectivity was controlled by a N-silyl-directing group.[6] In 2016, our group developed the first Pd(II)-catalyzed direct C7-arylation of indoles with arylboronic acids using a sterically hindered N−P(O)$^t$Bu$_2$ (TBPO) directing group by O atom chelation.[7] Later, our group further developed the rational design of a P(III) directing group (N−P$^t$Bu$_2$) for C−H hydroarylation of activated olefins,[8] C−H arylation of aryl halides[9] and carboxylic anhydrides[10] at indole C7-position. These results led us to explore whether this C7-functionalization strategy can be applied for other related transformations.

The installation of a methyl group to a drug lead may cause a dramatic improvement of its biological and physical properties.[11] This so-called magic methyl effect calls for the development of efficient catalytic methods for the methylation of organic compounds.[12] Deuterium atoms can be used as tracer atoms to elucidate metabolic pathways in medicinal chemistry. Owing to the higher pyrolysis energy than the H atom, the incorporation of deuterium can impart dramatic improvements to drug candidates, related to absorption, distribution, and metabolism in organisms. A significant number of deuterium-labeled drug candidates have been synthesized and submitted to clinical trials in the past few decades. Austedo (deutetrabenazine), a treatment for symptoms of Huntington's disease, was finally approved by the FDA in 2017 as the first deuterated drug (Figure 1a).[13] In general, the $d_3$-methylated group has extraordinary significance, being one of the most common fragments in biologically active molecules. From the viewpoint of synthetic chemistry, $d_3$-methylation is the most ideal approach because it has the capability to directly introduce the D-labeled methyl group into structurally diverse molecules.

Methylated indoles are key building blocks in several biologically active compounds. Remarkable progress has been made in C−H trideuteromethylation of indoles during the past five years (Figure 1b). C3-Trideuteromethylation has been developed using methanol-$d_3$ as a C1 building block by transition-metal-catalyzed hydrogen-borrowing approach.[14] Very recently, Yoshikai and co-worker reported a cobalt-catalyzed directed C2 selective C−H trideuteromethylation of indole using readily available methyl tosylate as a $d_3$-methylating agent.[15] Inspired by our recent results on P$^{III}$-chelation-assisted C−H functionalization of indoles, here, we reported selective C−H trideuteromethylation of indole at C7

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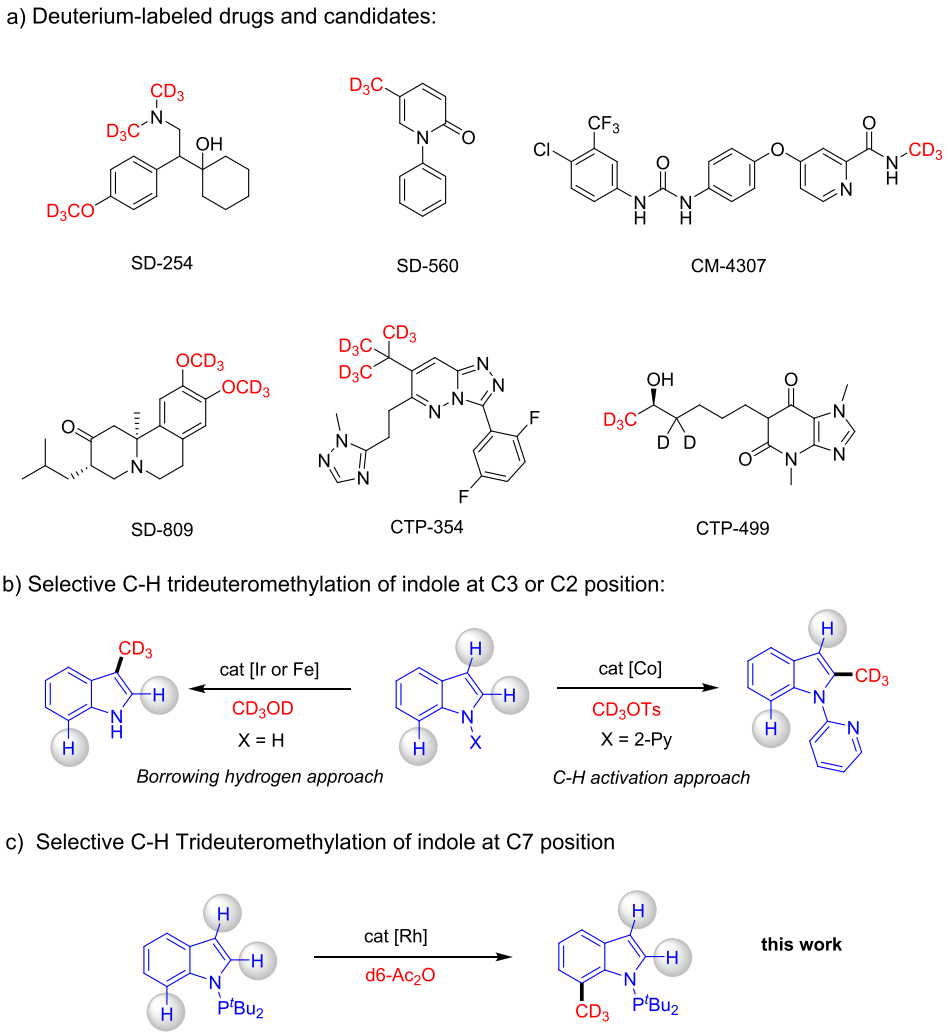


**Figure 1.** Development of a protocol for the selective C−H trideuteromethylation of indoles at C7 position.

position by Rh-catalyzed C−H trideuteromethylation using inexpensive and readily available acetic-$d_6$ anhydride as the deuterated methyl source (Figure 1c).

## RESULTS AND DISCUSSION

We studied the selective deuteration methylation process of indole with indole **1a** as the initial substrate (Table 1). The experiments were performed with 3.0 equiv of $Ac_2O$-$d_6$ in the presence of 2.5 mol % $[Rh(cod)Cl]_2$, 3.0 equiv $NaHCO_3$, at 150 °C under an Ar atmosphere in dry DMA. To our delight, the desired target product **2a** was observed in 10% yield after 18 h in GC−MS and 93% deuterated incorporation in $^1H$ NMR (Table 1, entry 1). Among various solvents (Table 1, entry 1−5), we found that the effect of dry toluene is the most significant, increasing the yield to 52% and deuterium ratio to 94% (Table 1, entry 5); no product was observed using HMPT as the solvent (Table 1, entry 4). Under the conditions, we tested different bases, such as $Cs_2CO_3$ (Table 1, entry 6), NaOAc (Table 1, entry 7), $Na_2CO_3$ (Table 1, entry 8), NaOH (Table 1, entry 9), NaOMe (Table 1, entry 10), $Et_3N$ (Table 1, entry 11), and $KH_2PO_4$ (Table 1, entry 12). Among these bases, we found the best efficiency by using $KH_2PO_4$, observed with 71% yield of **2a** (78% isolated yield) and deuterium ratio of 95%; when $Cs_2CO_3$ (Table 1, entry 6) was used as a base, no generation of **2a** was detected. Traditionally, $CD_3I$ and $(CD_3)_2SO_4$ have been widely used as deuterium methylating reagents, albeit with volatility, corrosion, toxicity, and carcinogenicity concerns. However, these reagents did not show any reactivity in this reaction (Table 1, entries 13−14). Finally, with control experiments performed in the absence of a $[Rh(cod)Cl]_2$ catalyst, no product is observed (Table 1, entry 15).

To evaluate the utility of the $P^{III}$-chelation-assisted indole C7-deuterated methylation by rhodium catalysis, a series of substituents at different positions of indole were tested in Table 2. Gratifyingly, the benzene core of the indole that incorporates electron-donating substituents C4−C6 positions was readily tolerated. Due to the acidity of hydrogen at the C3 position, different level H/D exchange occurs under the base in the presence of rhodium species. Such as methyl (**2b−2c**), methoxy (**2d−2f**), ether (**2g**), all the corresponding deuterated methylation products are obtained in high deuterium ratio and high yield. The substrates containing halogens like F (**2h−2i**), Cl (**2j**), Br (**2k−2i**) were well converted into deuterated methylation products, reflecting the potential application value of the strategy that can be cross-coupled with other groups. The electron-deficient substituents like cyano (**3ja**) group showed that the corresponding deuterated methylation products can also be obtained in higher yields and deuteration rate. Surprisingly, in the presence of phenyl (**2n**) and some


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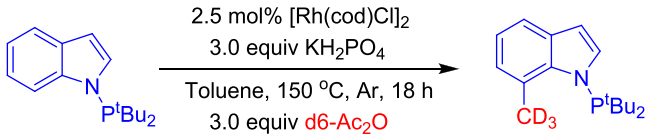
**Table 1. Reaction Development**[a]




1a 2a

| entry | cat [M] | base | solvent | [D] (%)[b] | yield (%)[c] |
|---|---|---|---|---|---|
| 1 | $[Rh(cod)Cl]_2$ | $NaHCO_3$ | DMA | 93 | 10 |
| 2 | $[Rh(cod)Cl]_2$ | $NaHCO_3$ | NMP | 92 | 5 |
| 3 | $[Rh(cod)Cl]_2$ | $NaHCO_3$ | DMSO | 93 | 24 |
| 4 | $[Rh(cod)Cl]_2$ | $NaHCO_3$ | HMPT | – | 0 |
| 5 | $[Rh(cod)Cl]_2$ | $NaHCO_3$ | Toluene | 94 | 52 |
| 6 | $[Rh(cod)Cl]_2$ | $Cs_2CO_3$ | Toluene | – | 0 |
| 7 | $[Rh(cod)Cl]_2$ | NaOAc | Toluene | 94 | 31 |
| 8 | $[Rh(cod)Cl]_2$ | $Na_2CO_3$ | Toluene | 95 | 55 |
| 9 | $[Rh(cod)Cl]_2$ | NaOH | Toluene | 92 | 57 |
| 10 | $[Rh(cod)Cl]_2$ | NaOMe | Toluene | 92 | 65 |
| 11 | $[Rh(cod)Cl]_2$ | $Et_3N$ | Toluene | 93 | 60 |
| **12** | **$[Rh(cod)Cl]_2$** | **$KH_2PO_4$** | **Toluene** | **95** | **71(78)**[d] |
| 13[e] | $[Rh(cod)Cl]_2$ | $KH_2PO_4$ | Toluene | – | 0 |
| 14[f] | $[Rh(cod)Cl]_2$ | $KH_2PO_4$ | Toluene | – | 0 |
| 15 | – | $KH_2PO_4$ | Toluene | – | 0 |

[a]Reaction conditions: **1a** (0.20 mmol), $Ac_2O$-$d_6$ (0.60 mmol), 2.5 mol % of catalyst, 3.0 equiv of base in solvent (1.0 mL) at 150 °C, 18 h, under Ar. [b]Determined by $^1H$ NMR. [c]Determined by GC analysis. [d]Isolated yield. [e]Using $CD_3I$ instead of $Ac_2O$-$d_6$. [f]Using DMSO-$d_6$ instead of $Ac_2O$-$d_6$.

chelating groups at C3 position of indole like acetyl (**2o**), methyl ester (**2p**), cyanomethyl (**2q**), and amide (**2r**) with a single selectivity, deuterated methylation at the C7 position could be obtained in high deuterium ratio and yield. Noteworthy, when the acidic hydrogen atoms are $\alpha$ to the functional group, like acetyl (**2o**), in the presence of a base, 60% H/D exchange with these hydrogen atoms was observed. Meanwhile, N–P$^t$Bu$_2$ protected carbazole (**2s**) has also been proven to be convertible to the desired product with excellent deuterium incorporation and good yield. It can also install two deuterated methyl groups in the 3,3′-dimercaptomethane derivative (**2t**) by this method.

The N–P$^t$Bu$_2$ directing group can be easily removed by treatment with TBAF. As shown in Scheme 1, the removal of the N–P$^t$Bu$_2$ directing group in products **2d** and **2n** formed the desired N-free indole in good yields under mild reaction conditions.

Although the detailed mechanism of the reaction remains unclear, we propose a possible catalytic cycle as shown in Figure 2. The rhodium species **A** first coordinates with the indole **1** to form a complex **B**. Then the deprotonation of the C–H bond at C7 position of indole generates the rhodacycle **D**[16] through the assistance of the anion to transition state **C**. The formed rhodacycle **D** can induce oxidative addition of acetic-$d_6$ anhydride to generate the Rh$^{III}$ species **E**.[17] Subsequent decarboxylation can further yield the rhodium species **F**. Finally, the reductive elimination of **F** produces the final products **2** and regenerates the active catalyst **A**.

In summary, we have reported an efficient C7-selective direct trideuteromethylation of indoles with the aid of the P(III)-directed group by rhodium catalysis. The reaction employed commercially available acetic-$d_6$ anhydride, does not require the addition of an exogenous ligand, and is applicable to the coupling of a variety of indoles. These present results represent an important discovery that is expected to be substantially extended to other new transformations.

## EXPERIMENTAL SECTION

All new compounds were fully characterized. NMR spectra were recorded on Bruker AV-300, ARX-400 MHz, or a ARX-600 Associated. Mass spectra were conducted at Micromass Q-ToF instrument (ESI) and Agilent Technologies 5973N (EI). All reactions were carried out in flame-dried reaction vessels with Teflon screw caps under argon. Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. $[Rh(cod)Cl]_2$, $KH_2PO_4$ were purchased from were purchased from Acros, $Ac_2O$-$d_6$ was purchased from Sigma-Aldrich. In Table 2, **1la–1t** are known compounds.[7−10]

**General Procedure A: P$^{III}$-Directed Indole C7-Methylation.** To a 25 mL Schlenk tube was added indole substrates **1a** (52.2 mg, 0.20 mmol), $[Rh(cod)Cl]_2$ (4.9 mg, 0.01 mmol) and $KH_2PO_4$ (81.6 mg, 0.60 mmol). The tube was purged with Ar three times, followed by addition of anhydrous toluene (1.0 mL) then addition of acetic anhydride (61.2 mg, 0.60 mmol). The mixture was stirred at 150 °C with the heating mantle for 18 h. The solution was then cooled to room temperature, and the solvent was removed under a vacuum directly. The crude product was purified by column chromatography on silica gel.

**General Procedure B: P$^{III}$-Directed Indole C7-Deuterated Methylation.** To a 25 mL Schlenk tube was added indole substrates **1a** (52.2 mg, 0.20 mmol), $[Rh(cod)Cl]_2$ (4.9 mg, 0.01 mmol) and $KH_2PO_4$ (81.6 mg, 0.60 mmol). The tube was purged with Ar three times, followed by addition of anhydrous toluene (1.0 mL) and then addition of $Ac_2O$-$d_6$ (64.8 mg, 0.60 mmol). The mixture was stirred at 150 °C with the heating mantle for 18 h. The solution was then cooled to room temperature, and the solvent was removed under a vacuum directly. The crude product was purified by column chromatography on silica gel.

**General Procedure C: Removal of the P$^{III}$ Directing Group.** To the product **2d′** (30.5 mg, 0.1 mmol) or product **2d** (30.8 mg, 0.1 mmol) in 25 mL Schlenk tube was added anhydrous THF (1.0 mL), and then TBAF (0.8 mL, 0.8 mmol, 1 M in THF) was added. The mixture was stirred under 60 °C until was consumed as determined by TLC. The reaction was cooled to room temperature and 5 mL $H_2O$ was added, and then the mixture was extracted by ethyl acetate and the organic phase was combined and dried with anhydrous $Na_2SO_4$. The solvent was evaporated under reduced pressure, and the crude was purified by column chromatography on silica gel to provide **3d′** as white solid (11.4 mg, 71%) or **3d** as white solid (11.8 mg, 72%).

**1-(Di-*tert*-butylphosphanyl)-7-methyl-1*H*-indole (2a′) and 1-(Di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indole (2a).** Following the general procedure A, **2a′** was prepared from **1a** as colorless oil (43.5 mg, 79%): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.50–7.48 (m, 2H), 7.06 (t, $J$ = 7.4 Hz, 1H), 6.99 (d, $J$ = 7.1 Hz, 1H), 6.66 (dd, $J$ = 3.3, 1.4 Hz, 1H), 2.90 (d, $J$ = 4.4 Hz, 3H), 1.25 (d, $J$ = 12.6 Hz, 18H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 141.1 (d, $J$ = 15.2 Hz), 132.1 (d, $J$ = 6.1 Hz), 129.8 (d, $J$ = 2.8 Hz), 125.9, 123.7, 120.3, 118.5, 105.6 (d, $J$ = 2.3 Hz), 35.8 (d, $J$ = 29.8 Hz), 29.4 (d, $J$ = 17.3 Hz), 24.5 (d, $J$ = 28.3 Hz). $^{31}P$ NMR (162 MHz, $CDCl_3$) $\delta$ 79.1. Following the general procedure B, **2a** was prepared from **1a** as colorless oil (43.4 mg, 78%): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.49–7.44 (m, 2H), 7.03 (t, $J$ = 7.4 Hz, 1H), 6.96 (dd, $J$ = 7.1, 1.3 Hz, 1H), 6.63 (dd, $J$ = 3.3, 1.5 Hz, 0.65H), 2.84 (m, 0.15H), 1.22 (d, $J$ = 12.6 Hz, 18H). IR (film) 2941, 1698, 1684, 1653, 1558, 1541, 1473, 1364, 1136, 805, 765, 521 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{17}H_{24}D_3NP$ $(M + H)^+$: 279.2064, found 279.2065. According to $^1H$ NMR, 35% deuterium incorporation C3 position and 95% deuterium incorporation at C7 position was generated in product **2a**.

**1-(Di-*tert*-butylphosphanyl)-4,7-dimethyl-1*H*-indole (2b′) and 1-(Di-*tert*-butylphosphanyl)-4-methyl-7-(methyl-$d_3$)-1*H*-indole (2b).** Following the general procedure A, **2b′** was prepared from **1b** as white solid (37.6 mg, 65%): $^1H$ NMR (400 MHz, $CDCl_3$)


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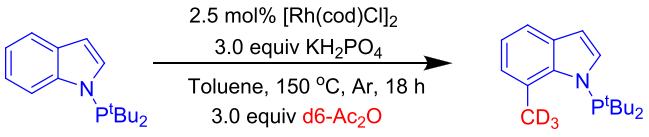
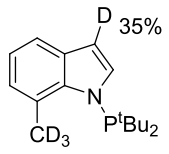
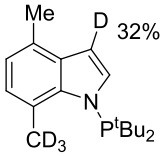
**Table 2. Substrate Scope**[a]

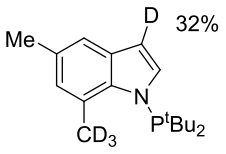


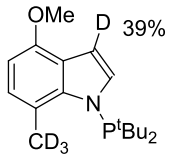

**2a,** 78%, 95% D



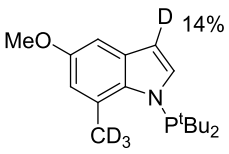

**2b**, 60%, 91% D



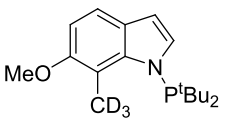

**2c**, 68%, 91% D



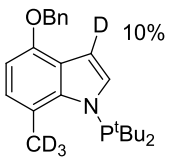

**2d**, 81%, 94% D



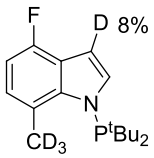

**2e**, 72%, 94% D



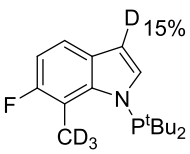

**2f**, 73%, 99% D



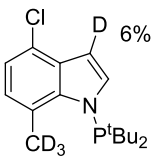

**2g**, 67%, 95% D



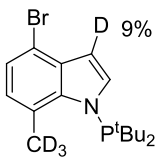

**2h**, 79%, 93% D



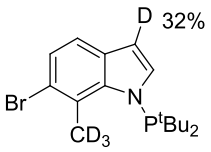

**2i**, 63%, 95% D



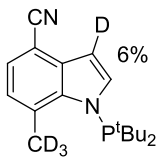

**2j**, 84%, 95% D



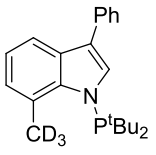

**2k**, 80%, 96% D



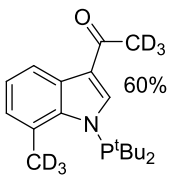

**2l**, 74%, 97% D



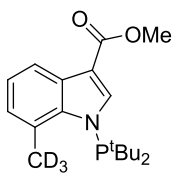

**2m**, 63%, 92% D



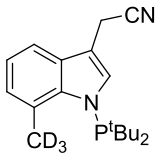

**2n**, 76%, 91% D



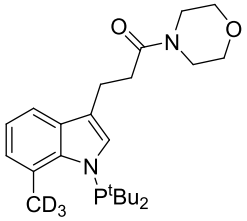

**2o**, 74%, 97% D



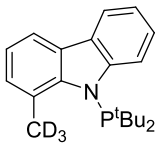

**2p**, 75%, 94% D



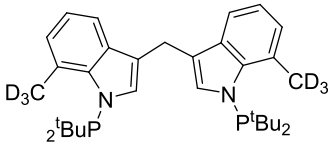

**2q**, 83%, 95% D




**2r**, 60%, 94% D




**2s**, 82%, 93% D




**2t**, 50% 90% D

[a]Reaction conditions: **1a** (0.20 mmol), $Ac_2O$-$d_6$ (0.60 mmol), 2.5 mol % of $[Rh(cod)Cl]_2$, $KH_2PO_4$ (0.6 mmol) in 1.0 mL dry toluene at 150 °C, 18 h, under Ar.

$\delta$ 7.46 (d, $J$ = 3.4 Hz, 1H), 6.86 (q, $J$ = 7.3 Hz, 2H), 6.66 (dd, $J$ = 3.4, 1.4 Hz, 1H), 2.85 (d, $J$ = 4.5 Hz, 3H), 2.52 (s, 3H), 1.23 (d, $J$ = 12.6 Hz, 18H). $^{13}C\{1H\}$ NMR (101 MHz, $CDCl_3$) $\delta$ 140.7 (d, $J$ = 15.3 Hz), 131.6 (d, $J$ = 6.1 Hz), 129.5 (d, $J$ = 2.9 Hz), 127.4, 125.9, 121.2, 120.6, 103.9 (d, $J$ = 2.3 Hz), 35.8 (d, $J$ = 29.9 Hz), 29.4 (d, $J$ = 17.4 Hz), 24.4 (d, $J$ = 28.4 Hz), 18.5. $^{31}P$ NMR (162 MHz, $CDCl_3$) $\delta$ 78.7. Following the general procedure B, **2b** was prepared from **1b** as white solid (35.0 mg, 60%): $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.47 (d, $J$ = 3.0 Hz, 1H), 6.87 (q, $J$ = 7.2 Hz, 2H), 6.67 (dd, $J$ = 3.3, 1.3 Hz, 0.68H), 2.83 (s, 0.27H), 2.54 (s, 3H), 1.24 (d, $J$ = 12.6 Hz, 18H). IR (film) 2940, 1495, 1463, 1360, 1560, 1275, 1145, 1123, 806, 764, 637, 498 $cm^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{18}H_{26}D_3NP$ $(M + H)^+$: 293.2220, found 293.2226. According to $^1H$ NMR, According to $^1H$ NMR, 32%



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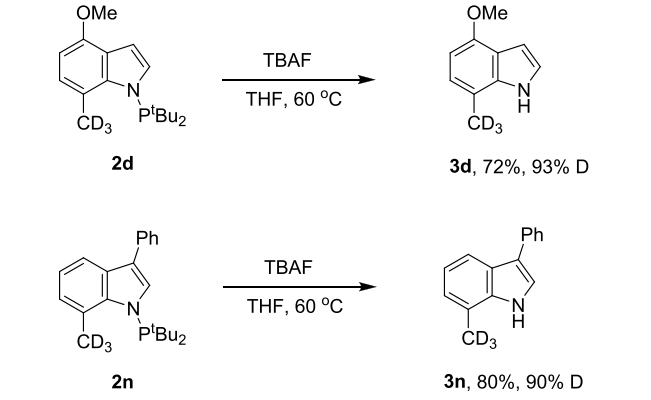
**Scheme 1. Removal of the Directing Group**



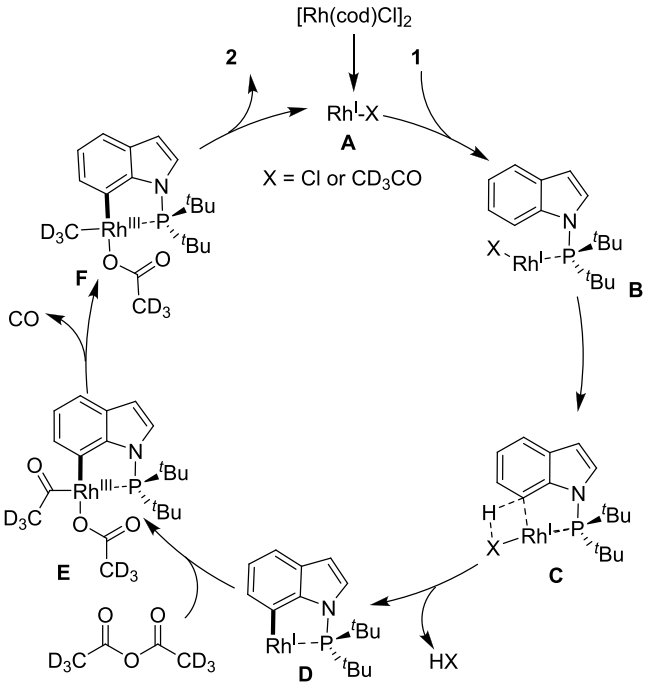




**Figure 2.** Proposed catalytic cycle.

deuterium incorporation C3 position and 91% deuterium incorporation at C7 position was generated in product **2b**.

**1-(Di-*tert*-butylphosphanyl)-5,7-dimethyl-1*H*-indole (2c′) and 1-(Di-*tert*-butylphosphanyl)-5-methyl-7-(methyl-$d_3$)-1*H*-indole (2c).** Following the general procedure A, **2c′** was prepared from **1c** as white solid (39.3 mg, 68%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44 (d, $J$ = 3.3 Hz, 1H), 7.28 (s, 1H), 6.84 (s, 1H), 6.58 (dd, $J$ = 3.3, 1.5 Hz, 1H), 2.86 (d, $J$ = 4.3 Hz, 3H), 2.43 (s, 3H), 1.25 (d, $J$ = 12.6 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 139.3 (d, $J$ = 15.5 Hz), 132.2 (d, $J$ = 6.1 Hz), 130.2 (d, $J$ = 2.5 Hz), 129.5, 127.6, 123.3, 118.2, 105.2 (d, $J$ = 1.3 Hz), 35.8 (d, $J$ = 29.6 Hz), 29.4 (d, $J$ = 17.3 Hz), 24.3 (d, $J$ = 27.9 Hz), 20.9. $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 78.6. Following the general procedure B, **2c** was prepared from **1c** as white solid (39.7 mg, 68%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.40 (d, $J$ = 1.9 Hz, 1H), 7.24 (d, $J$ = 2.3 Hz, 1H), 6.80 (d, $J$ = 0.9 Hz, 1H), 6.54 (dd, $J$ = 3.0, 1.1 Hz, 0.68 H), 2.79 (d, $J$ = 2.1 Hz, 0.27 H), 2.39 (s, 3H), 1.21 (d, $J$ = 12.6 Hz, 18H). IR (film) 2941, 1494, 1472, 1363, 1558, 1275, 1145, 1120, 806, 764, 637, 498 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{18}H_{26}D_3NP$ (M + H)$^+$: 293.2220, found 293.2228. According to $^1$H NMR, According to $^1$H NMR, 32% deuterium incorporation C3 position and 91% deuterium incorporation at C7 position was generated in product **2c**.

**1-(Di-*tert*-butylphosphanyl)-4-methoxy-7-methyl-1*H*-indole (2d′) and 1-(Di-*tert*-butylphosphanyl)-4-methoxy-7-(methyl-$d_3$)-1*H*-indole (2d).** Following the general procedure A, **2d′** was prepared from **1d** as white solid (48.8 mg, 80%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.39 (d, $J$ = 3.4 Hz, 1H), 6.89 (d, $J$ = 7.9 Hz, 1H), 6.78 (dd, $J$ = 3.3, 1.5 Hz, 1H), 6.49 (d, $J$ = 7.9 Hz, 1H), 3.94 (s, 3H), 2.81 (d, $J$ = 4.6 Hz, 3H), 1.24 (d, $J$ = 12.6 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 151.5 (d, $J$ = 1.4 Hz), 142.0 (d, $J$ = 16.2 Hz), 130.8 (d, $J$ = 6.1 Hz), 125.8, 120.3 (d, $J$ = 3.3 Hz), 116.7, 102.4 (d, $J$ = 2.3 Hz), 100.0, 55.2, 35.7 (d, $J$ = 29.7 Hz), 29.3 (d, $J$ = 17.4 Hz), 24.0 (d, $J$ = 28.4 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 78.5. Following the general procedure B, **2d** was prepared from **1d** as white solid (49.8 mg, 81%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41−7.35 (m, 1H), 6.87 (d, $J$ = 7.9 Hz, 1H), 6.76 (dd, $J$ = 3.3, 1.5 Hz, 0.61H), 6.47 (d, $J$ = 7.9 Hz, 1H), 3.93 (s, 3H), 2.76 (d, $J$ = 2.3 Hz, 0.18 H), 1.22 (d, $J$ = 12.6 Hz, 18H). IR (film) 2940, 2360, 1579, 1495, 1473, 1267, 1172, 1123, 1106, 806, 752, 603 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{18}H_{26}D_3NOP$ (M + H)$^+$: 309.2170, found 309.2175. According to $^1$H NMR, According to $^1$H NMR, 39% deuterium incorporation C3 position and 94% deuterium incorporation at C7 position was generated in product **2d**.

**1-(Di-*tert*-butylphosphanyl)-5-methoxy-7-methyl-1*H*-indole (2e′) and 1-(Di-*tert*-butylphosphanyl)-5-methoxy-7-(methyl-$d_3$)-1*H*-indole (2e).** Following the general procedure A, **2e′** was prepared from **1e** as white solid (45.7 mg, 75%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43 (d, $J$ = 3.3 Hz, 1H), 6.93 (s, 1H), 6.65 (d, $J$ = 2.4 Hz, 1H), 6.57 (dd, $J$ = 3.3, 1.4 Hz, 1H), 3.84 (s, 3H), 2.84 (d, $J$ = 4.2 Hz, 3H), 1.23 (d, $J$ = 12.6 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 154.1, 136.1 (d, $J$ = 15.5 Hz), 132.8 (d, $J$ = 6.1 Hz), 130.3 (d, $J$ = 3.1 Hz), 124.9, 115.6, 105.5 (d, $J$ = 2.3 Hz), 99.8, 55.5, 35.8 (d, $J$ = 29.6 Hz), 29.3 (d, $J$ = 29.6 Hz), 24.3 (d, $J$ = 28.1 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 78.6. Following the general procedure B, **2e** was prepared from **1e** as white solid (44.3 mg, 72%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44−7.42 (m, 1H), 6.93 (dd, $J$ = 2.5, 1.5 Hz, 1 H), 6.64 (d, $J$ = 2.6 Hz, 1H), 6.57 (dd, $J$ = 3.3, 1.4 Hz, 0.86 H), 3.84 (s, 3H), 2.80 (d, $J$ = 2.1 Hz, 0.24 H), 1.22 (d, $J$ = 12.6 Hz, 18H). IR (film) 2941, 2360, 1578, 1495, 1473, 1267, 1167, 1123, 1106, 812, 752, 512 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{18}H_{26}D_3NOP$ (M + H)$^+$: 309.2170, found 309.2175. According to $^1$H NMR, According to $^1$H NMR, 14% deuterium incorporation C3 position and 94% deuterium incorporation at C7 position was generated in product **2e**.

**1-(Di-*tert*-butylphosphanyl)-6-methoxy-7-methyl-1*H*-indole (2f′) and 1-(Di-*tert*-butylphosphanyl)-6-methoxy-7-(methyl-$d_3$)-1*H*-indole (2f).** Following the general procedure A, **2f′** was prepared from **1f** as white solid (44.5 mg, 73%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43−7.38 (m, 2H), 6.90 (d, $J$ = 8.5 Hz, 1H), 6.57 (dd, $J$ = 3.4, 1.4 Hz, 1H), 3.90 (s, 3H), 2.83 (d, $J$ = 2.9 Hz, 3H), 1.26 (d, $J$ = 12.6 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 154.4, 142.2 (d, $J$ = 13.5 Hz), 132.1 (d, $J$ = 5.7 Hz), 124.8 (d, $J$ = 1.7 Hz), 117.5, 112.5, 107.3, 105.2 (d, $J$ = 1.1 Hz), 57.4, 35.9 (d, $J$ = 30.4 Hz), 29.4 (d, $J$ = 17.4 Hz), 14.6(d, $J$ = 30.1 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 79.4. Following the general procedure B, **2f** was prepared from **1f** as white solid (44.9 mg, 73%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.46 (d, $J$ = 8.4 Hz, 1H), 7.31 (d, $J$ = 3.4 Hz, 1H), 6.87 (d, $J$ = 8.5 Hz, 1H), 6.56 (dd, $J$ = 3.2, 0.8 Hz, 1H), 3.83 (s, 3H), 1.19 (d, $J$ = 12.8 Hz, 18H). IR (film) 2940, 2360, 1580, 1495, 1473, 1267, 1167, 1223, 1106, 812, 603 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{18}H_{26}D_3NOP$ (M + H)$^+$: 309.2170, found 309.2174. According to $^1$H NMR, According to $^1$H NMR, 99% deuterium incorporation at C7 position was generated in product **2f**.

**4-(Benzyloxy)-1-(di-*tert*-butylphosphanyl)-7-methyl-1*H*-indole (2g′) and 4-(Benzyloxy)-1-(di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indole (2g).** Following the general procedure A, **2g′** was prepared from **1g** as white solid (52.2 mg, 68%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.55 (d, $J$ = 7.3 Hz, 2H), 7.47−7.39 (m, 3H), 7.38−7.32 (m, 1H), 6.92−6.81 (m, 2H), 6.56 (d, $J$ = 7.9 Hz, 1H), 5.22 (s, 2H), 2.84 (d, $J$ = 4.6 Hz, 3H), 1.26 (d, $J$ = 12.6 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 150.7 (d, $J$ = 1.4 Hz), 142.1 (d, $J$ = 16.1 Hz), 137.8, 130.8 (d, $J$ = 6.2 Hz), 128.4, 127.6, 127.3, 125.8, 120.6 (d, $J$ = 3.4 Hz), 116.9, 102.7 (d, $J$ = 2.2 Hz), 101.5, 69.9, 35.7 (d, $J$ = 29.8 Hz), 29.3 (d, $J$ = 17.3 Hz), 24.0 (d, $J$ = 28.3 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 78.5. Following the general procedure B,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**2g** was prepared from **1g** as white solid (51.4 mg, 67%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.52 (d, $J$ = 7.3 Hz, 2H), 7.43−7.37 (m, 3H), 7.37−7.27 (m, 1H), 6.90−6.80 (m, 1.9H), 6.54 (d, $J$ = 7.9 Hz, 1H), 5.19 (s, 2H), 2.83−2.72 (m, 0.14H), 1.23 (d, $J$ = 12.6 Hz, 18H). IR (film) 2940, 2360, 1654, 1579, 1472, 1364, 1184, 1122, 752, 696, 603 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{24}H_{30}D_3NOP$ $(M + H)^+$: 385.2483, found 385.2488. According to $^1$H NMR, 10% deuterium incorporation C3 position and 95% deuterium incorporation at C7 position was generated in product **2g**.

**1-(Di-*tert*-butylphosphanyl)-4-fluoro-7-methyl-1*H*-indole (2h′) and 1-(Di-*tert*-butylphosphanyl)-4-fluoro-7-(methyl-$d_3$)-1*H*-indole (2h).** Following the general procedure A, **2h′** was prepared from **1h** as colorless oil (46.2 mg, 79%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43 (d, $J$ = 3.4 Hz, 1H), 6.85 (dd, $J$ = 7.5, 6.0 Hz, 1H), 6.76−6.52 (m, 2H), 2.81 (d, $J$ = 4.5 Hz, 3H), 1.23 (d, $J$ = 12.7 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 156.2 (dd, $J$ = 244.4, 1.7 Hz), 142.9 (dd, $J$ = 16.2, 9.4 Hz), 132.0 (d, $J$ = 6.2 Hz), 125.6 (d, $J$ = 7.3 Hz), 119.5 (d, $J$ = 3.7 Hz), 118.7 (dd, $J$ = 22.0, 3.3 Hz), 104.7 (d, $J$ = 18.0 Hz), 101.2 (d, $J$ = 2.5 Hz), 35.8 (d, $J$ = 29.9 Hz), 29.3 (d, $J$ = 17.3 Hz), 23.9 (d, $J$ = 28.7 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 79.2. $^{19}$F NMR (377 MHz, $CDCl_3$) $\delta$ −127.2. Following the general procedure B, **2h** was prepared from **1h** as colorless oil (46.7 mg, 79%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43 (d, $J$ = 3.4 Hz, 1H), 6.85 (dd, $J$ = 8.0, 5.6 Hz, 1H), 6.75−6.66 (m, 1.92H), 2.78 (s, 0.15H), 1.23 (d, $J$ = 12.7 Hz, 18H). IR (film) 2941, 2360, 1493, 1473, 1364, 1253, 1144, 1117, 1027, 755, 601 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{17}H_{23}D_3FNP$ $(M + H)^+$: 297.1970, found 297.1973. According to $^1$H NMR, 8% deuterium incorporation C3 position and 95% deuterium incorporation at C7 position was generated in product **2h**.

**1-(Di-*tert*-butylphosphanyl)-6-fluoro-7-methyl-1*H*-indole (2i′) and 1-(Di-*tert*-butylphosphanyl)-6-fluoro-7-(methyl-$d_3$)-1*H*-indole (2i).** Following the general procedure A, **2i′** was prepared from **1i** as colorless oil (38.0 mg, 65%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.42 (d, $J$ = 3.4 Hz, 1H), 7.35 (dd, $J$ = 8.2, 5.6 Hz, 1H), 6.90 (dd, $J$ = 10.2, 8.5 Hz, 1H), 6.58 (dd, $J$ = 3.4, 1.5 Hz, 1H), 2.79 (t, $J$ = 2.8 Hz, 3H), 1.23 (d, $J$ = 12.7 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 159.7 (d, $J$ = 234.0 Hz), 141.4 (dd, $J$ = 14.1, 7.7 Hz), 132.6 (dd, $J$ = 5.8, 3.3 Hz), 126.0 (d, $J$ = 2.7 Hz), 117.9 (d, $J$ = 11.1 Hz), 110.5 (d, $J$ = 20.5 Hz), 109.1 (d, $J$ = 27.8 Hz), 105.5 (d, $J$ = 1.3 Hz), 36.0 (d, $J$ = 29.9 Hz), 29.3 (d, $J$ = 17.3 Hz), 13.8 (dd, $J$ = 29.9, 7.5 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 79.8. $^{19}$F NMR (377 MHz, $CDCl_3$) $\delta$ −120.8. Following the general procedure B, **2i** was prepared from **1i** as colorless oil (37.3 mg, 63%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43−7.40 (m, 1H), 7.34 (ddd, $J$ = 8.5, 5.5, 1.2 Hz, 1H), 6.90 (dd, $J$ = 10.3, 8.5 Hz, 1H), 6.58 (dd, $J$ = 3.4, 1.5 Hz, 0.85H), 2.75 (dd, $J$ = 11.6, 9.2 Hz, 0.15H), 1.23 (d, $J$ = 12.7 Hz, 18H). IR (film) 2940, 2360, 1487, 1473, 1364, 1253, 1134, 1121, 1077, 755, 601 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{17}H_{23}D_3FNP$ $(M + H)^+$: 297.1970, found 297.1975. According to $^1$H NMR, 15% deuterium incorporation C3 position and 95% deuterium incorporation at C7 position was generated in product **2i**.

**4-Chloro-1-(di-*tert*-butylphosphanyl)-7-methyl-1*H*-indole (2j′) and 4-Chloro-1-(di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indole (2j).** Following the general procedure A, **2j′** was prepared from **1j** as white solid (50.6 mg, 82%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.50 (d, $J$ = 3.4 Hz, 1H), 7.04 (d, $J$ = 7.7 Hz, 1H), 6.88 (d, $J$ = 7.8 Hz, 1H), 6.77 (dd, $J$ = 3.4, 1.5 Hz, 1H), 2.84 (d, $J$ = 4.4 Hz, 3H), 1.23 (d, $J$ = 12.7 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 141.6 (d, $J$ = 15.8 Hz), 132.8 (d, $J$ = 6.0 Hz), 128.4 (d, $J$ = 2.9 Hz), 126.3, 123.5 (d, $J$ = 1.4 Hz), 122.6, 120.0, 104.1 (d, $J$ = 2.4 Hz), 35.9 (d, $J$ = 30.0 Hz), 29.3 (d, $J$ = 17.3 Hz), 24.2 (d, $J$ = 28.9 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 80.1. Following the general procedure B, **2j** was prepared from **1j** as white solid (52.4 mg, 84%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.5 (d, $J$ = 3.4 Hz, 1H), 7.0 (d, $J$ = 7.7 Hz, 1H), 6.9 (d, $J$ = 7.7 Hz, 1H), 6.8 (dd, $J$ = 3.4, 1.5 Hz, 0.94H), 2.85−2.77 (m, 0.14H), 1.22 (d, $J$ = 12.7 Hz, 18H). IR (film) 2941, 2360, 1684, 1560, 1480, 1363, 1253, 1144, 1117, 1027, 755, 601 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{17}H_{22}D_3ClNNaP$ $(M + Na)^+$: 335.1494, found 335.1497. According to $^1$H NMR, 6% deuterium incorporation C3 position and 95% deuterium incorporation at C7 position was generated in product **2j**.

**4-Bromo-1-(di-*tert*-butylphosphanyl)-7-methyl-1*H*-indole (2k′) and 4-Bromo-1-(di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indole (2k).** Following the general procedure A, **2k′** was prepared from **1k** as white solid (52.2 mg, 74%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.51 (d, $J$ = 3.4 Hz, 1H), 7.20 (d, $J$ = 7.7 Hz, 1H), 6.83 (d, $J$ = 7.8 Hz, 1H), 6.72 (dd, $J$ = 3.4, 1.5 Hz, 1H), 2.83 (d, $J$ = 4.4 Hz, 3H), 1.23 (d, $J$ = 12.7 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 141.2 (d, $J$ = 15.7 Hz), 132.7 (d, $J$ = 5.8 Hz), 130.1 (d, $J$ = 2.2 Hz), 126.7, 123.4. 123.2, 112.1, 105.9 (d, $J$ = 1.8 Hz), 35.8 (d, $J$ = 30.0 Hz), 29.3 (d, $J$ = 17.3 Hz), 24.2 (d, $J$ = 29.0 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 80.4. Following the general procedure B, **2k** was prepared from **1k** as white solid (56.9 mg, 80%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.50 (d, $J$ = 3.4 Hz, 1H), 7.19 (d, $J$ = 7.7 Hz, 1H), 6.82 (d, $J$ = 7.7 Hz, 1H), 6.71 (dd, $J$ = 3.4, 1.5 Hz, 0.91H), 2.79 (d, $J$ = 2.1 Hz, 0.12H), 1.22 (d, $J$ = 12.7 Hz, 18H). IR (film) 2361, 2343, 1698, 1654, 1558, 1508, 1362, 1149, 762, 669 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{17}H_{23}D_3BrNP$ $(M + H)^+$: 357.1169, found 357.1170. According to $^1$H NMR, 9% deuterium incorporation C3 position and 96% deuterium incorporation at C7 position was generated in product **2k**.

**6-Bromo-1-(di-*tert*-butylphosphanyl)-7-methyl-1*H*-indole (2l′) and 6-Bromo-1-(di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indole (2l).** Following the general procedure A, **2l′** was prepared from **1l** as white solid (49.4 mg, 70%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45 (d, $J$ = 3.4 Hz, 1H), 7.36 (d, $J$ = 8.3 Hz, 1H), 7.29 (d, $J$ = 8.3 Hz, 1H), 6.58 (dd, $J$ = 3.3, 1.4 Hz, 1H), 3.05 (d, $J$ = 1.6 Hz, 3H), 1.22 (d, $J$ = 12.7 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 141.8 (d, $J$ = 13.0 Hz), 133.2 (d, $J$ = 5.5 Hz), 129.2 (d, $J$ = 1.8 Hz), 125.2, 123.5 (d, $J$ = 0.6 Hz), 121.2, 119.1, 105.6 (d, $J$ = 2.4 Hz), 36.0 (d, $J$ = 30.9 Hz), 29.3 (d, $J$ = 17.4 Hz), 22.8 (d, $J$ = 32.0 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 81.2. Following the general procedure B, **2l** was prepared from **1l** as white solid (52.7 mg, 74%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44 (d, $J$ = 3.4 Hz, 1H), 7.35 (d, $J$ = 8.3 Hz, 1H), 7.29 (dd, $J$ = 8.3, 1.2 Hz, 1H), 6.58 (dd, $J$ = 3.3, 1.3 Hz, 1H), 2.99 (d, $J$ = 2.1 Hz, 0.09H), 1.22 (d, $J$ = 12.7 Hz, 18H). IR (film) 2940, 2360, 2213, 1673, 1654, 1553, 1508, 1364, 1184, 762, 669, 601 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{17}H_{23}D_3BrNP$ $(M + H)^+$: 357.1169, found 357.1163. According to $^1$H NMR, 32% deuterium incorporation C3 position and 97% deuterium incorporation at C7 position was generated in product **2l**.

**1-(Di-*tert*-butylphosphanyl)-7-methyl-1*H*-indole-4-carbonitrile (2m′) and 1-(Di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indole-4-carbonitrile (2m).** Following the general procedure A, **2m′** was prepared from **1m** as light yellow solid (37.8 mg, 63%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.62 (d, $J$ = 3.4 Hz, 1H), 7.37 (d, $J$ = 7.5 Hz, 1H), 6.99 (d, $J$ = 7.6 Hz, 1H), 6.86 (dd, $J$ = 3.4, 1.5 Hz, 1H), 2.92 (d, $J$ = 4.1 Hz, 3H), 1.22 (d, $J$ = 12.8 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 140.6 (d, $J$ = 15.4 Hz), 134.8 (d, $J$ = 5.9 Hz), 131.3 (d, $J$ = 2.6 Hz), 129.8, 125.9, 125.5, 119.0, 104.4 (d, $J$ = 2.5 Hz), 100.9, 35.8 (d, $J$ = 30.0 Hz), 29.2 (d, $J$ = 17.3 Hz), 24.7 (d, $J$ = 29.1 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 81.9. Following the general procedure B, **2m** was prepared from **1m** as light yellow solid (38.2 mg, 63%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.62 (d, $J$ = 3.4 Hz, 1H), 7.37 (d, $J$ = 7.5 Hz, 1H), 6.99 (d, $J$ = 7.5 Hz, 1H), 6.86 (dd, $J$ = 3.4, 1.5 Hz, 0.94H), 2.89 (dd, $J$ = 5.3, 3.2 Hz, 0.24H), 1.22 (d, $J$ = 12.8 Hz, 18H). IR (film) 2941, 2360, 2219, 1698, 1653, 1541, 1474, 1364, 1274, 1143, 766, 632, 421 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{18}H_{23}D_3N_2P$ $(M + H)^+$: 304.2016, found 304.2022. According to $^1$H NMR, 6% deuterium incorporation C3 position and 92% deuterium incorporation at C7 position was generated in product **2m**.

**1-(Di-*tert*-butylphosphanyl)-7-methyl-3-phenyl-1*H*-indole (2n′) and 1-(Di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-3-phenyl-1*H*-indole (2n).** Following the general procedure A, **2n′** was prepared from **1n** as white solid (52.6 mg, 75%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.77 (d, $J$ = 7.8 Hz, 1H), 7.67 (dd, $J$ = 8.2, 1.2 Hz, 2H), 7.59 (s, 1H), 7.48 (t, $J$ = 7.7 Hz, 2H), 7.36−7.29 (m, 1H), 7.13 (t, $J$ = 7.5 Hz, 1H), 7.05 (d, $J$ = 7.1 Hz, 1H), 2.93 (d, $J$ = 4.5 Hz, 3H), 1.29 (d, $J$ = 12.6 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 141.9 (d, $J$ = 14.9 Hz), 135.4, 129.9 (d, $J$ = 6.2 Hz), 128.7, 128.0,


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127.9, 126.4, 126.2, 124.1, 120.7, 120.6 (d, $J$ = 2.0 Hz), 117.3, 35.9 (d, $J$ = 30.1 Hz), 29.4 (d, $J$ = 17.3 Hz), 24.6 (d, $J$ = 28.7 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 79.8. Following the general procedure B, **2n** was prepared from **1n** as white solid (53.8 mg, 76%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.76 (dt, $J$ = 7.9, 1.4 Hz, 1H), 7.72−7.61 (m, 2H), 7.58 (s, 1H), 7.52−7.42 (m, 2H), 7.38−7.29 (m, 1H), 7.18−7.09 (m, 1H), 7.04 (dd, $J$ = 7.1, 1.2 Hz, 1H), 2.89 (s, 0.27H), 1.28 (d, $J$ = 12.6 Hz, 19H); IR (film) 2941, 2360, 1678, 1653, 1636, 1540, 1478, 1360, 1243, 1151, 765, 630, 421 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{23}H_{28}D_3NP$ (M + H)$^+$: 355.2377, found 355.2377. According to $^1$H NMR, 91% deuterium incorporation at C7 position was generated in product **2n**.

**1-(1-(Di-*tert*-butylphosphanyl)-7-methyl-1*H*-indol-3-yl)-ethan-1-one (2o′) and 1-(1-(Di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indol-3-yl)ethan-1-one (2o).** Following the general procedure A, **2o′** was prepared from **1o** as white solid (45.6 mg, 72%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.29 (d, $J$ = 7.9 Hz, 1H), 8.11 (s, 1H), 7.18 (t, $J$ = 7.6 Hz, 1H), 7.05 (d, $J$ = 7.2 Hz, 1H), 2.86 (d, $J$ = 4.5 Hz, 3H), 2.56 (s, 3H), 1.26 (d, $J$ = 12.8 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 193.1, 141.8 (d, $J$ = 13.9 Hz), 139.8 (d, $J$ = 6.0 Hz), 127.6, 127.0 (d, $J$ = 2.2 Hz), 123.9, 122.8, 120.1 (d, $J$ = 2.7 Hz), 120.0, 35.9 (d, $J$ = 31.4 Hz), 29.2 (d, $J$ = 17.3 Hz), 27.7, 24.4 (d, $J$ = 28.3 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 84.6. Following the general procedure B, **2o** was prepared from **1o** as white solid (47.3 mg, 74%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.33−8.24 (m, 1H), 8.11 (s, 1H), 7.19 (dd, $J$ = 7.8, 7.3 Hz, 1H), 7.05 (dd, $J$ = 7.2, 1.3 Hz, 1H), 2.82 (s, 0.09H), 2.68−2.32 (m, 1.2H), 1.26 (d, $J$ = 12.8 Hz, 18H). IR (film) 2941, 2360, 1698, 1652, 1558, 1488, 1473, 1398, 1225, 1168, 1147, 765, 669, 421 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{19}H_{23}D_6NOP$ (M + H)$^+$: 324.2358, found 324.2359. According to $^1$H NMR, 97% deuterium incorporation at C7 position was generated in product **2o**.

**Methyl 1-(di-*tert*-butylphosphanyl)-7-methyl-1*H*-indole-3-carboxylate (2p′) and Methyl 1-(di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indole-3-carboxylate (2p).** Following the general procedure A, **2p′** was prepared from **1p** as white solid (48.6 mg, 73%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.16 (s, 1H), 8.09 (d, $J$ = 7.9 Hz, 1H), 7.17 (t, $J$ = 7.6 Hz, 1H), 7.04 (d, $J$ = 7.2 Hz, 1H), 3.92 (s, 3H), 2.87 (d, $J$ = 4.6 Hz, 3H), 1.24 (d, $J$ = 12.8 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 165.3, 141.6 (d, $J$ = 14.3 Hz), 139.1 (d, $J$ = 6.0 Hz), 127.4 (d, $J$ = 1.5 Hz), 127.1, 124.1, 122.2, 119.2, 110.8 (d, $J$ = 2.3 Hz), 51.1, 35.8 (d, $J$ = 31.0 Hz), 29.2 (d, $J$ = 17.4 Hz), 24.5 (d, $J$ = 28.6 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 84.4. Following the general procedure B, **2p** was prepared from **1p** as white solid (50.4 mg, 75%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.16 (s, 1H), 8.09 (d, $J$ = 7.9 Hz, 1H), 7.17 (t, $J$ = 7.6 Hz, 1H), 7.06−6.99 (m, 1H), 3.92 (s, 3H), 2.83 (s, 0.18H), 1.24 (d, $J$ = 12.8 Hz, 18H). IR (film) 2947, 2360, 1714, 1542, 1399, 1303, 1211, 1139, 1058, 913, 882, 748, 669 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{19}H_{26}D_3NO_2P$ (M + H)$^+$: 337.2119, found 337.2125. According to $^1$H NMR, 94% deuterium incorporation at C7 position was generated in product **2p**.

**2-(1-(Di-*tert*-butylphosphanyl)-7-methyl-1*H*-indol-3-yl)-acetonitrile (2q′) and 2-(1-(Di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indol-3-yl)acetonitrile (2q).** Following the general procedure A, **2q′** was prepared from **1q** as light yellow solid (50.2 mg, 80%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.50 (s, 1H), 7.38 (d, $J$ = 7.7 Hz, 1H), 7.11 (t, $J$ = 7.5 Hz, 1H), 7.04 (d, $J$ = 7.1 Hz, 1H), 3.83 (d, $J$ = 1.0 Hz, 2H), 2.88 (d, $J$ = 4.4 Hz, 3H), 1.24 (d, $J$ = 12.7 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 141.6 (d, $J$ = 15.2 Hz), 130.3 (d, $J$ = 6.4 Hz), 127.8 (d, $J$ = 2.8 Hz), 126.9, 124.4, 120.7, 118.0, 115.6, 107.2 (d, $J$ = 3.0 Hz), 35.8 (d, $J$ = 30.0 Hz), 29.3 (d, $J$ = 17.3 Hz), 24.4 (d, $J$ = 28.3 Hz), 14.49. $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 80.4. Following the general procedure B, **2q** was prepared from **1q** as light yellow solid (52.6 mg, 83%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.49 (s, 1H), 7.37 (d, $J$ = 7.8 Hz, 1H), 7.11 (t, $J$ = 7.5 Hz, 1H), 7.06−7.01 (m, 1H), 3.83 (s, 2H), 2.84 (d, $J$ = 1.9 Hz, 0.21H), 1.23 (d, $J$ = 12.7 Hz, 18H). IR (film) 2939, 2360, 2221, 1472, 1400, 1365, 1282, 1170, 1135, 1077, 806, 757, 671, 513 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{19}H_{24}D_3N_2NaP$ (M + Na)$^+$: 340.1992, found 340.1996. According to $^1$H NMR, 93% deuterium incorporation at C7 position was generated in product **2q**.

**3-(1-(Di-*tert*-butylphosphanyl)-7-methyl-1*H*-indol-3-yl)-1-morpholinopropan-1-one (2r′) and 3-(1-(Di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indol-3-yl)-1-morpholinopropan-1-one (2r).** Following the general procedure A, **2r′** was prepared from **1r** as white solid (52.4 mg, 63%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.40 (d, $J$ = 7.7 Hz, 1H), 7.28 (s, 1H), 7.04 (t, $J$ = 7.4 Hz, 1H), 6.97 (d, $J$ = 7.1 Hz, 1H), 3.61 (s, 4H), 3.49−3.44 (m, 2H), 3.36−3.30 (m, 2H), 3.13 (t, $J$ = 7.5 Hz, 2H), 2.85 (d, $J$ = 4.3 Hz, 3H), 2.71−2.64 (m, 2H), 1.21 (d, $J$ = 12.6 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 171.3, 141.5 (d, $J$ = 15.4 Hz), 129.6 (d, $J$ = 6.3 Hz), 129.1 (d, $J$ = 2.6 Hz), 126.0, 124.0, 119.9, 117.5 (d, $J$ = 1.7 Hz), 116.1, 66.7, 66.4, 45.9, 41.8, 35.8 (d, $J$ = 29.7 Hz), 33.5, 29.3 (d, $J$ = 17.3 Hz), 24.6 (d, $J$ = 28.3 Hz), 21.0. $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 78.1. Following the general procedure B, **2r** was prepared from **1r** as white solid (50.3 mg, 60%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.40 (dt, $J$ = 7.7, 1.4 Hz, 1H), 7.27 (s, 1H), 7.04 (t, $J$ = 7.4 Hz, 1H), 6.96 (dd, $J$ = 7.1, 1.1 Hz, 1H), 3.61 (s, 4H), 3.48−3.44 (m, 2H), 3.35−3.30 (m, 2H), 3.12 (t, $J$ = 7.5 Hz, 2H), 2.82 (s, 0.3H), 2.72−2.65 (m, 2H), 1.20 (d, $J$ = 12.6 Hz, 18H). IR (film) 2939, 2360, 1698, 1652, 1558, 1541, 1508, 1457, 1117, 747, 669 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{24}H_{35}D_3N_2O_2P$ (M + H)$^+$: 420.2854, found 420.2858. According to $^1$H NMR, 90% deuterium incorporation at C7 position was generated in product **2r**.

**9-(Di-*tert*-butylphosphanyl)-1-methyl-9*H*-carbazole (2s′) and Methyl 9-(Di-*tert*-butylphosphanyl)-1-(methyl-$d_3$)-9*H*-carbazole (2s).** Following the general procedure A, **2s′** was prepared from **1s** as white solid (52.0 mg, 80%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.07 (d, $J$ = 7.7 Hz, 1H), 7.95 (d, $J$ = 8.4 Hz, 2H), 7.43−7.37 (m, 1H), 7.24 (ddd, $J$ = 24.6, 10.9, 6.1 Hz, 3H), 3.05 (d, $J$ = 6.1 Hz, 3H), 1.36 (d, $J$ = 13.4 Hz, 18H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 145.8 (d, $J$ = 21.6 Hz), 143.6 (d, $J$ = 10.3 Hz), 130.6, 126.8 (d, $J$ = 2.1 Hz), 125.7 (d, $J$ = 3.6 Hz), 120.3, 119.5, 117.4, 116.0, 36.8 (d, $J$ = 37.2 Hz), 30.8 (d, $J$ = 19.4 Hz), 26.5 (d, $J$ = 35.3 Hz). $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 81.7. Following the general procedure B, **2s** was prepared from **1s** as white solid (53.7 mg, 82%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.15−8.00 (m, 1H), 8.00−7.87 (m, 2H), 7.39 (ddd, $J$ = 8.4, 7.1, 1.4 Hz, 1H), 7.34−7.12 (m, 3H), 3.02 (d, $J$ = 6.9 Hz, 0.21H), 1.35 (d, $J$ = 13.4 Hz, 18H). IR (film) 2941, 2360, 1653, 1558, 1473, 1450, 1397, 1364, 1196, 1079, 960, 751, 476 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{21}H_{26}D_3NP$ (M + H)$^+$: 329.2220, found 329.2224. According to $^1$H NMR, 93% deuterium incorporation at C7 position was generated in product **2s**.

**Bis(1-(di-*tert*-butylphosphanyl)-7-methyl-1*H*-indol-3-yl)-methane (2t′) and Bis(1-(di-*tert*-butylphosphanyl)-7-(methyl-$d_3$)-1*H*-indol-3-yl)methane (2t).** Following the general procedure A, **2t′** was prepared from **1t** as white solid (58.4 mg, 52%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43 (d, $J$ = 7.6 Hz, 2H), 7.08 (s, 2H), 6.99 (dt, $J$ = 14.3, 7.0 Hz, 4H), 4.19 (s, 2H), 2.87 (d, $J$ = 4.3 Hz, 6H), 1.11 (d, $J$ = 12.5 Hz, 36H); $^{13}$C{1H} NMR (101 MHz, $CDCl_3$) $\delta$ 141.7 (d, $J$ = 15.6 Hz), 130.1 (d, $J$ = 6.2 Hz), 129.5 (d, $J$ = 2.9 Hz), 125.9, 123.7, 119.8, 117.7 (d, $J$ = 1.8 Hz), 117.0, 35.6 (d, $J$ = 29.4 Hz), 29.3 (d, $J$ = 17.3 Hz), 24.5 (d, $J$ = 28.2 Hz), 21.5. $^{31}$P NMR (162 MHz, $CDCl_3$) $\delta$ 77.8. Following the general procedure B, **2t** was prepared from **1t** as white solid (56.8 mg, 50%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43 (d, $J$ = 7.6 Hz, 2H), 7.08 (s, 2H), 7.03−6.93 (m, 4H), 4.20 (s, 2H), 2.84 (s, 0.6 H), 1.12 (d, $J$ = 12.5 Hz, 36H). IR (film) 2941, 2360, 1698, 1684, 1653, 1558, 1508, 1457, 749, 669, 421 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{35}H_{47}D_6N_2P_2$ (M + H)$^+$: 569.4055, found 569.4059. According to $^1$H NMR, 90% deuterium incorporation at C7 position was generated in product **2t**.

**4-Methoxy-7-methyl-1*H*-indole (3d′) and 4-Methoxy-7-(methyl-$d_3$)-1*H*-indole (3d).** Following the general procedure **C**, **3d′** was prepared from **2d′** as white solid (11.4 mg, 71%): $^1$H NMR (400 MHz, CDCl3) $\delta$ 8.07 (s, 1H), 7.14−7.09 (m, 1H), 6.91 (d, $J$ = 7.7 Hz, 1H), 6.69 (dd, $J$ = 3.1, 2.2 Hz, 1H), 6.47 (d, $J$ = 7.8 Hz, 1H), 3.96 (s, 3H), 2.44 (s, 3H). $^{13}$C{1H} NMR (101 MHz, CDCl3) $\delta$ 151.8, 136.6, 122.6, 122.4, 118.0, 113.2, 100.4, 99.6, 55.4, 16.0. **3d** was prepared from **2d** as white solid (11.8 mg, 72%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.08 (s, 1H), 7.19−7.11 (m, 1H), 6.90 (d, $J$ = 7.8 Hz, 1H), 6.67 (dd, $J$ = 3.1, 2.2 Hz, 1H), 6.45 (d, $J$ = 7.8 Hz, 1H), 3.94 (s, 3H), 2.41 (m, 0.21 H). IR (film) 3395, 3110, 2962, 2941, 1684, 1653, 1524, 1508, 1262 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{10}H_9D_3NO$ (M


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+ H)$^+$: 165.1102, found 165.1105. According to $^1$H NMR, 93% deuterium incorporation at C7 position was generated in product **3d**.

**7-Methyl-3-phenyl-1*H*-indole (3n′) and 7-(Methyl-$d_3$)-3-phenyl-1*H*-indole (3n).** Following the general procedure **C**, **3n′** was prepared from **2n′** as white solid (16.6 mg, 80%): $^1$H NMR (400 MHz, CDCl3) $\delta$ 8.11 (s, 1H), 7.88 (d, $J$ = 8.0 Hz, 1H), 7.73 (d, $J$ = 7.8 Hz, 2H), 7.51 (t, $J$ = 7.7 Hz, 2H), 7.35 (q, $J$ = 6.2 Hz, 2H), 7.19 (t, $J$ = 7.5 Hz, 1H), 7.12 (d, $J$ = 7.0 Hz, 1H), 2.54 (s, 3H). $^{13}$C{1H} NMR (101 MHz, CDCl3) $\delta$ 136.1, 135.7, 128.7, 127.4, 125.9, 125.2, 122.9, 121.5, 120.5, 120.5, 118.7, 117.5, 16.6. **3n** was prepared from **2n** as white solid (16.8 mg, 80%): $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 8.17 (s, 1H), 7.81 (d, $J$ = 7.9 Hz, 1H), 7.73−7.64 (m, 2H), 7.50−7.42 (m, 2H), 7.39 (d, $J$ = 2.5 Hz, 1H), 7.33−7.26 (m, 1H), 7.17−7.10 (m, 1H), 7.10−7.04 (m, 1H), 2.52 (m, 0.3H). IR (film) 3394, 3110, 2965, 2941, 1678, 1653, 1636, 1474, 1364, 1243, 1151 cm$^{-1}$; HRMS $m/z$ (ESI) calcd for $C_{15}H_{11}D_3N$ (M + H)$^+$: 211.1309, found 211.1315. According to $^1$H NMR, 90% deuterium incorporation at C7 position was generated in product **3n**.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.9b01114.

Experimental procedures and full spectroscopic data for all new compounds (PDF)

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### Notes

The authors declare no competing financial interest.

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