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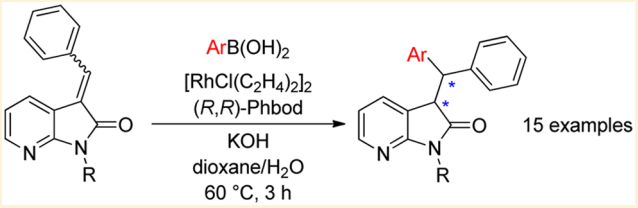
Rhodium-Catalyzed 1,4-Addition of Arylboronic Acids to 3-Benzylidene-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-one Derivatives

Cécile Croix, Gildas Prié, Charlotte Chaulet, and Marie-Claude Viaud-Massuard*

GICC UMR 7292, Equipe 4 "Innovation Moléculaire et Thérapeutique", Université de Tours, Labex SYNORG, Faculté de Pharmacie, 31 avenue Monge, 37200 Tours, France

Supporting Information

ABSTRACT: 7-Azaindoles are versatile building blocks, especially in medicinal chemistry, where they serve as bioisosteres of indoles or purines. Herein, we present a novel rhodium-catalyzed asymmetric 1,4-addition of arylboronic acids to 3-benzylidene-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-ones, as these substrates are exocyclic methylene lactamyl Michael acceptors. Ten new original derivatives of 1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-one have been obtained.



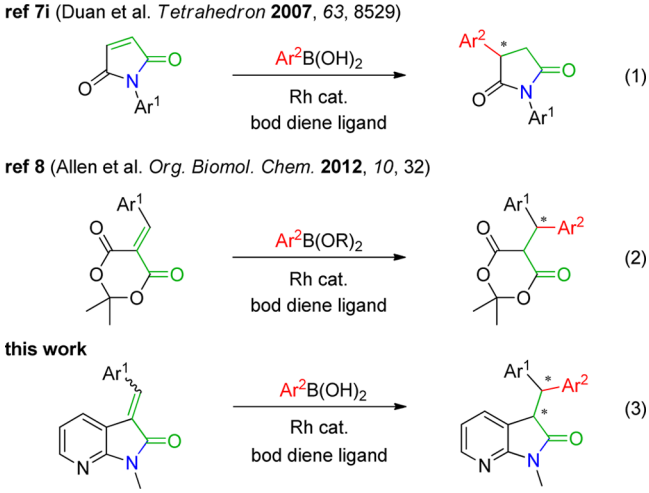
Because of their specific chemical behavior, 7-azaindole (1*H*-pyrrolo[2,3-*b*]pyridine) derivatives have become an important subject of several synthetic studies. Moreover, due to their particular biological activity, interest in the synthesis of compounds derived from 7-azaindole has arisen in numerous recent pharmacological programs within diverse therapeutic areas,[1] where they serve as bioisosteres of indole, oxoindole, or purine ring systems. Consequently, as a part of our medicinal chemistry research program, we have been interested in the preparation of new 7-azaoxindole compounds.

The 1,4-conjugate addition of organometallic reagents to enones is a widely used process of carbon−carbon bond formation giving *β*-substituted carbonyl compounds which are versatile substrates used in further organic transformations.[2] It is therefore of high value to achieve such a transformation in a catalytic and asymmetric fashion, which has been developed in the past few years using a large number of strategies.[3]

While transition-metal-catalyzed asymmetric transformations in the presence of chiral ligands have proved to be one of the most efficient methods for the construction of enantioenriched chiral compounds from achiral precursors,[4] rhodium-catalyzed synthesis, including 1,4-conjugate addition of aryl- and alkenylboronic acids to enones, has experienced considerable growth over the past two decades.[5]

Indeed, a variety of chiral ligands in Rh-catalyzed asymmetric reactions have been used and developed including phosphorus, diene, and sulfoxide structures.[6] In the last 10 years, chiral dienes ligands have emerged due to their efficiency in rhodium-catalyzed 1,4-addition. These new ligands are superior to conventional chiral bis(phosphine) ligands in some cases, allowing the easier insertion of the boronic acid permitting a better control of regioselectivity. In particular, Hayashi et al. have developed a new class of ligands based on the bicyclo[2.2.2]octa-2,5-diene (bod) skeleton as good candidates for asymmetric 1,4-addition, for instance, on maleimide derivatives (Scheme 1, eq 1).[7] Herein we report an uncommon rhodium-catalyzed asymmetric 1,4-addition of organoboronic acids to 7-azaoxindoles (3-benzylidene-1*H*-pyrrolo[2,3-*b*]-pyridine-2(3*H*)-ones) using a chiral diene ligand (Scheme 1, eq 3). Indeed, as far as we know, it is the first time that this kind of reaction has been used on exocyclic methylene of lactam as Michael acceptor substrates. This 1,4-addition has been performed once toward exocyclic methylene on benzylidene Meldrum acid derivatives (Scheme 1, eq 2).[8]

Scheme 1. Rh/bod-Catalyzed 1,4-Addition of Boron Species



We began our studies by synthesizing 3-benzylidene-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-ones by condensation between 7-azaoxindoles with various aldehydes (Table 1).[9]

Compounds **1a−e** have been obtained in a mixture of *E* and *Z* isomers with moderate to good yields. The NMR studies and comparisons with the literature have shown that the *E* isomer is the major one.[10] Several attempts have been made to separate

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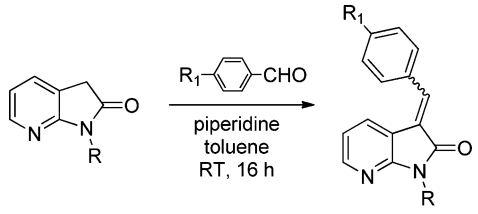
Table 1. Synthesis of 3-Benzylidene-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-ones



entry	R	R_1	product	yield (%)	*E*/*Z* ratio[a]
1	Me	COMe	**1a**	76	82/18
2	Me	H	**1b**	85	94/6
3	Me	OMe	**1c**	70	80/20
4	H	H	**1d**	52	90/10
5	Bn	H	**1e**	72	93/7

[a]Determined by ^{1}H NMR analysis immediately after column chromatography.

isomers by classical chromatography and semipreparative chiral HPLC, but none of them was successful. Indeed, as an example, ^{1}H NMR and HPLC studies have shown that each isomer of **1b** isomerizes in solution to an approximately 70/30 (*E*/*Z*) ratio after 1 week.[11] However, 3-benzylidene-1*H*-pyrrolo[2,3-*b*]-pyridin-2(3*H*)-ones **1a**–**e** did not isomerize when they were retained in the solid state.

The addition of phenylboronic acid to 3-benzylidene-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-one derivatives **1a**–**e** was used to study the reaction (Table 2).

From previous unpublished biological results, the first stereoselective 1,4-addition reactions attempts were made on the 3-(4-acetoxybenzylidene)-1-methyl-1*H*-pyrrolo[2,3-*b*]-pyridin-2(3*H*)-one **1a**. In the presence of chlorobis(ethylene)-rhodium(I) dimer and BINAP ligand, generally used in various organocatalysis combined with metal catalysis reactions, the 1,4-addition reaction on **1a** did not occur, nor did it occur with the nonsubstituted **1b** substrate (Table 2, entries 1–3). According to Hayashi's work, the use of (*R*,*R*)-Phbod* ligand gave better results. Indeed, 1,4-addition adducts starting from **1b**, **1c**, and **1e** (Table 2, entries 5, 6, and 8) were obtained in good yields. However, these conditions have not been successful with **1a** and **1d** (Table 2, entries 4 and 7), so it seems that **1a** is not a good Michael acceptor as it presents an electron-withdrawing group on the aromatic ring which may lead to a relocation of the double bond in the α, β positions of the amide to the aromatic ring. Finally, the addition was performed toward **1b** and **1e** with the nonchiral catalytic system $[(Rh(cod)Cl]_2$ and gave the adducts with modest yields (Table 2, entries 9 and 10).

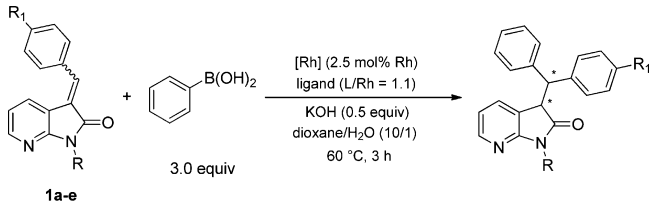
Thereafter, to exemplify this reaction, these optimized experimental conditions with (*R*,*R*)-Phbod* as the ligand and $[(RhCl(C_2H_4)_2]_2$ as the catalyst have been tested with various arylboronic acids toward compounds **1b** and **1e** as the Michael acceptor to furnish 1,4-adducts **2a**–**j** (Table 3).

Employing the optimized set of reaction conditions with classical para- or meta-substituted arylboronic acids, the 1,4-adducts **2b**–**f** were obtained with good yields (Table 3, entries 2–6). In contrast, use of ortho-substituted arylboronic acids did not promote the reaction, and starting material was fully recovered (Table 3, entries 7 and 8). As seen before, the low reactivity of the boronic acids can be dependent on the steric hindrance.[8]

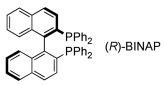
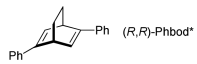
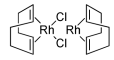
In order to obtain new interesting potential pharmaceutical derivatives, various heteroarylboronic acids have also been tested (Table 3, entries 9–13). Moreover, to the best of our knowledge, none of them have been described in rhodium-catalyzed 1,4-addition. Several attempts have been done without success using 2-thiophenylboronic acid (Table 3, entry 10). In contrast, the reaction with the 3-substituted thiophene gave the adduct **2h**. This difference of reactivity is classical in heteroarylboronic acids. The lack of reactivity of the 2-pyridinylboronic acid was therefore expected, but surprisingly, no reaction occurred with 3-pyridinylboronic acid, whatever the quantity of rhodium catalyst used (Table 3, entries 12 and 13).

Then, starting from **1e**, we synthesized compounds **2i** and **2j**, protected by a benzyl group with good yields (Table 3, entries 14 and 15). Indeed, as the nonprotected 7-azaoxindole derivative did not react (Table 1), we could use *N*-benzyl substrates **2i** and **2j** as precursors of unprotected adducts.

Table 2. Rhodium-Catalyzed 1,4-Addition of Phenylboronic Acid to 7-Azaoxindoles 1a–e: Study of Reaction Conditions



Entry	**1a-e**	[Rh]	Ligand[a]	Yield (%)	Entry	**1a-e**	[Rh]	Ligand[a]	Yield (%)
1	**1a**	$[(RhCl(C_2H_4)_2]_2$	(*R*)-BINAP	0	6	**1c**	$[(RhCl(C_2H_4)_2]_2$	(*R*,*R*)-Phbod*	85
2	**1a**	$[(RhCl(C_2H_4)_2]_2$[b]	(*R*)-BINAP	0	7	**1d**	$[(RhCl(C_2H_4)_2]_2$	(*R*,*R*)-Phbod*	0
3	**1b**	$[(RhCl(C_2H_4)_2]_2$	(*R*)-BINAP	0	8	**1e**	$[(RhCl(C_2H_4)_2]_2$	(*R*,*R*)-Phbod*	90
4	**1a**	$[(RhCl(C_2H_4)_2]_2$	(*R*,*R*)-Phbod*	0	9	**1b**	$[(Rh(cod)Cl]_2$		45
5	**1b**	$[(RhCl(C_2H_4)_2]_2$	(*R*,*R*)-Phbod*	93	10	**1e**	$[(Rh(cod)Cl]_2$		48

[a]  (*R*)-BINAP  (*R*,*R*)-Phbod*  $[(Rh(cod)Cl]_2$

[b] 10 mol% in Rh catalyst were used

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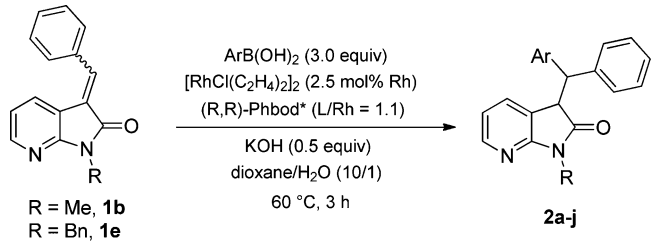
Table 3. Rhodium-Catalyzed 1,4-Addition of Boronic Acids to 7-Azaoxindoles 1b and 1e

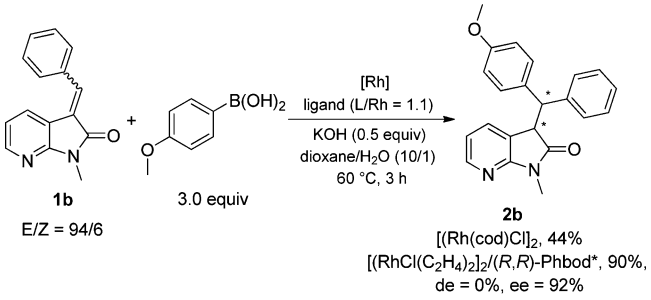


Entry	1b/1e	Ar	Product	Yield (%)	Entry	1b/1e	Ar	Product	Yield (%)
1	**1b**		**2a**	93	9	**1b**		**2g**	86
2	**1b**		**2b**	90	10	**1b**		-	n.r.[a]
3	**1b**		**2c**	86	11	**1b**		**2h**	35 71[b]
4	**1b**		**2d**	89	12	**1b**		-	n.r.[a]
5	**1b**		**2e**	86	13	**1b**		-	n.r.[a]
6	**1b**		**2f**	73	14	**1e**		**2i**	90
7	**1b**		-	n.r.[a]	15	**1e**		**2j**	90
8	**1b**		-	n.r.[a]					

[a] no reaction; [b] 10mol% in Rh catalyst were used

As our optimized conditions used an asymmetric catalyst, we decided to study by chiral HPLC the reaction enantioselectivity on our best example in term of yield (Table 3, entry 2). The addition of 4-methoxyphenylboronic acid on 3-benzylidene-1-methyl-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-one **1b** was considered, using either $[(Rh(cod)Cl]_2$ or $[(RhCl(C_2H_4)_2]_2$/(*R*,*R*)-Phbod* as the catalytic system (Scheme 2).

Scheme 2. Reaction Enantioselectivity Study



To begin, we optimized the separation of the four stereoisomers adducts obtained with the nonchiral addition using $[(Rh(cod)Cl]_2$ (Table 2, entry 9) in order to confirm the results of the chiral reaction (i.e., peak attribution).[12] Unexpectedly, the enantioselective version using $[(RhCl(C_2H_4)_2]_2$/(*R*,*R*)-Phbod* gave only two isomers.[13] This high enantioselectivity (ee = 92%) showed us that the *E*/*Z* isomer distribution in the starting material might not be responsible for the stereoisomer adduct distribution. This hypothesis was proven by performing the same addition with a different *E*/*Z* ratio (85/15) of the starting **1b**, yielding the two isomers in the same enantiomeric ratio.[14] It seems that a dynamic resolution or an enantioconvergent process operates and provides high enantioselectivity whatever the *E*/*Z* ratio of the starting material. There is no diastereomeric excess, which is not surprising considering that the protonation of Rh-enolates in the Hayashi reaction is often nonselective. Furthermore, the acidity of the C-3 hydrogen is likely to lead to epimerization under the reaction conditions.

Finally, we have extended this study to compounds described in Table 3. The results are mentioned in Figure 1.

In summary, we have identified a novel effective and highly stereoselective approach for the preparation of original 7-azaoxindole derivatives using a rhodium-catalyzed asymmetric 1,4-addition of various arylboronic acids toward 3-benzylidene-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-ones.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise noted, all reagents were purchased from commercial suppliers and used without purification. All 1,4-addition reactions were performed under inert atmosphere. Silica gel (230−400 mesh) was used for column chromatography. ^{1}H NMR spectra were referenced internally to the residual proton resonance in $CDCl_3$ (δ 7.26 ppm) or with TMS (δ 0.00 ppm) as the internal standard. Chemical shifts (δ) were reported as parts per million (ppm) on the δ scale downfield from TMS. ^{13}C NMR spectra were referenced to $CDCl_3$ (δ 77.0 ppm, the middle peak). Coupling constants (*J*) are reported in hertz.

High-resolution mass spectra (HRMS) were performed using Orbitrap. HPLC analysis were carried out with a LaChrom Elite system using 25 nm UV detection to quantify diastereoisomers.

General Procedure for the Condensation of Aldehyde on 7-Azaoxindole. A solution of the 1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-one (6.75 mmol), the appropriate aldehyde (13.5 mmol), and piperidine (2.7 mmol) in toluene (15 mL) under an Ar atmosphere was stirred at ambient temperature for 16 h. The reaction mixture was treated with H_2O, and the aqueous layer was extracted with EtOAc. The organic layers were dried over $MgSO_4$, filtered, concentrated in vacuo, and purified by flash chromatography (SiO_2, DCM/AcOEt) to afford the desired 3-benzylidene-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-one derivative.

*3-(4-Acetylbenzylidene)-1-methyl-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**1a**):* yellow solid; 1.43 g (76%); mp 152−153 °C; ^{1}H NMR ($CDCl_3$) δ 8.17 (dd, *J* = 5.2, 1.5 Hz, 1H), 8.07−8.02 (m, 2H), 7.93 (s, 1H), 7.72−7.69 (m, 3H), 6.81 (dd, *J* = 7.6, 5.3 Hz, 1H), 3.36 (s, 3H), 2.65 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 197.3, 167.8, 157.4, 148.4,

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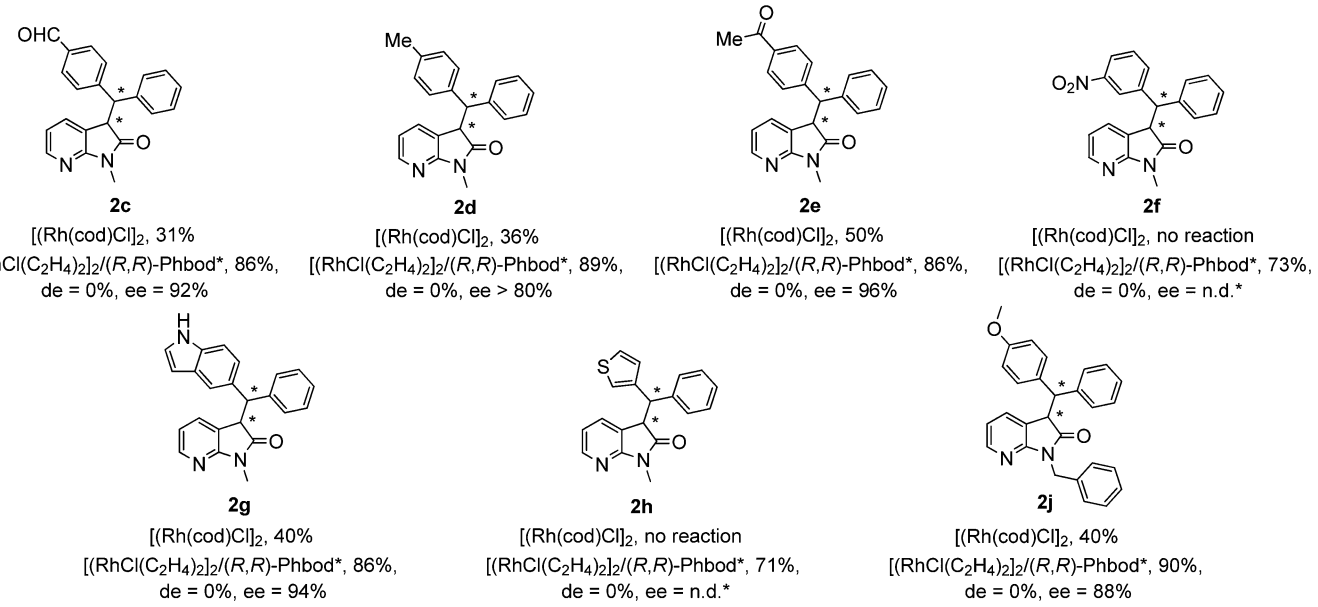

* n.d.: non determined [15]

Figure 1. de and ee values for compounds **2c–h** and **2j**.

147.6, 139.2, 137.9, 137.3, 137.2, 132.1, 129.8, 129.6, 128.9, 128.3, 117.7, 26.8, 25.6; HRMS (ESI) m/z calcd for $C_{17}H_{15}N_2O_2$ (M + H) 279.11280, found 279.11246

*3-Benzylidene-1-methyl-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**1b**):* yellow solid. 1.35 g (85%); mp 98–99 °C; ^{1}H NMR ($CDCl_3$) δ 8.15 (dd, J = 5.3, 1.5 Hz, 1H), 7.96 (s, 1H), 7.82 (dd, J = 7.5, 1.3 Hz, 1H), 7.62–7.59 (m, 2H), 7.51–7.44 (m, 3H), 6.81 (dd, J = 7.6, 5.3 Hz, 1H), 3.37 (s, 3H); ^{13}C NMR ($CDCl_3$) 168.2, 157.0, 147.7, 139.3, 134.5, 130.2, 129.6, 129.5, 128.9, 125.5, 117.6, 116.1, 25.5; HRMS (ESI) m/z calcd for $C_{15}H_{13}N_2O$ (M + H) 237.10224, found 237.10143.

*3-(4-Methoxybenzylidene)-1-methyl-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**1c**):* yellow solid; 1.26 g (70%); mp 114–116 °C; ^{1}H NMR ($CDCl_3$) δ 8.16 (dd, J = 5.2, 1.5 Hz, 1H), 7.95–7.92 (m, 2H), 7.63–7.60 (m, 2H), 7.03–6.97 (m, 2H), 6.84 (dd, J = 7.5, 5.2 Hz, 1H), 3.89 (s, 3H), 3.38 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 168.5, 161.4, 156.7, 147.1, 139.5, 135.1, 131.8, 129.1, 123.3, 117.5, 114.4, 114.1, 55.6, 25.6; HRMS (ESI) m/z calcd for $C_{16}H_{15}N_2O_2$(M + H) 267.11280, found 267.11176.

*3-Benzylidene-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**1d**):* yellow solid; 0.78 g (52%); mp 166–168 °C; ^{1}H NMR (DMSO) δ 11.26 (s, 1H), 8.10 (d, J = 5.1 Hz, 1H), 7.82 (d, J = 7.6 Hz, 1H), 7.77 (s, 1H), 7.72 (d, J = 7.3 Hz, 2H), 7.52 (m, 3H), 6.95–6.86 (m, 1H); ^{13}C NMR (DMSO) δ 168.2, 157.0, 148.2, 137.8, 134.0, 130.2, 129.6, 128.9, 128.3, 126.0, 117.4, 115.3; HRMS (ESI) m/z calcd for $C_{14}H_{11}N_2O$ (M + H) 223.08659, found 223.08614.

*1-Benzyl-3-benzylidene-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**1e**):* yellow solid; 1.51 g (72%); mp 118–120 °C; ^{1}H NMR ($CDCl_3$) δ 8.18 (dd, J = 5.2, 1.5 Hz, 1H), 8.00 (s, 1H), 7.85 (dd, J = 7.6, 1.4 Hz, 1H),, 7.65–7.62 (m, 2H), 7.53–7.49 (m, 5H), 7.32 (ddt, J = 7.0, 5.5, 2.2 Hz, 3H), 6.83 (dd, J = 7.6, 5.2 Hz, 1H), 5.12 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 168.1, 156.6, 148.1, 139.3, 136.9, 134.6, 132.3, 130.2, 129.6, 129.5, 129.0, 128.7, 128.6, 127.7, 125.6, 117.7, 42.8. HRMS (ESI) m/z calcd for $C_{21}H_{17}N_2O$ (M + H) 313.13354, found 313.13272.

General Procedure for the Rh(I)-Catalyzed 1,4-Conjugate Addition of Arylboronic Acid to 7-Azaoxindole. A solution of $[RhCl(C_2H_4)_2]_2$ (8 mg, 0,04 mmol Rh) and (*R*,*R*)-Ph-bod* (12 mg, 0,046 mmol) in 2 mL of 1,4-dioxane was stirred for 10 min at room temperature under Ar. A 0.21 mL portion of a 1 M KOH solution (0,21 mmol) was then added, and the resulting solution was stirred for 3 min at room temperature. After addition of $ArB(OH)_2$ (1,27 mmol), the mixture was stirred for an additional 3 min at room temperature. The substrate **1**, 3-benzylidene-1-methyl-1*H*-pyrrolo[2,3-*b*]pyridin-2(3*H*)-one (100 mg, 0.42 mmol), was then added to this with additional 2 mL of 1,4-dioxane, and the resulting mixture was stirred for 3 h at 60 °C. The solvent was removed under vacuum, and the resulting mixture was purified by silica gel flash chromatography with cyclohexane/EtOAc to afford the desired 1,4-adduct.

*3-Benzhydryl-1-methyl-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**2a**):* oil; 122 mg (93%); ^{1}H NMR ($CDCl_3$) δ 8.12 (ddd, J = 5.2, 1.6, 0.8 Hz, 1H), 7.38–7.27 (m, 5H), 7.19–7.14 (m, 3H), 7.01–6.95 (m, 2H), 6.89–6.84 (m, 1H), 6.77 (dd, J = 7.3, 5.2 Hz, 1H), 4.91 (d, J = 5.7 Hz, 1H), 4.37 (d, J = 5.7 Hz, 1H), 3.08 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 175.7, 157.8, 147.1, 141.0, 139.4, 132.5, 129.3, 128.6, 128.4, 128.4, 127.3, 127.0, 122.0, 117.7, 51.5, 49.5, 25.2; HRMS (ESI) m/z calcd for $C_{21}H_{19}N_2O$ (M + H) 315.14919, found 315.14816.

*3-((4-Methoxyphenyl)(phenyl)methyl)-1-methyl-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**2b**):* oil; 130 mg (90%); ^{1}H NMR ($CDCl_3$) δ 8.14 (dd, J = 5.3, 0.8 Hz, 2H), 7.41–7.26 (m, 5H), 7.26–7.14 (m, 5H), 7.05–6.66 (m, 12H), 4.91 (d, J = 5.5 Hz, 1H), 4.86 (d, J = 5.8 Hz, 1H), 4.36 (t, J = 5.6 Hz, 2H), 3.83 (s, 3H), 3.75 (s, 3H), 3.13 (s, 3H), 3.12 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 175.7, 158.7, 146.4, 141.4, 139.7, 132.9, 131.2, 130.4, 129.5, 129.2, 128.7, 128.4, 128.4, 127.3, 127.0, 122.4, 117.7, 114.0, 113.8, 55.4, 55.27, 50.9, 50.6, 49.7, 25.5; HRMS (ESI) m/z calcd for $C_{22}H_{21}N_2O_2$ (M + H), 345.15975, found 345.15878.

*4-((1-Methyl-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-3-yl)-(phenyl)methyl)benzaldehyde (**2c**):* oil; 122 mg (86%); ^{1}H NMR ($CDCl_3$): δ 10.02 (s, 1H), 9.94 (s, 1H), 8.18–8.13 (m, 2H), 7.88 (d, J = 8.3 Hz, 2H), 7.74–7.68 (m, 2H), 7.52 (d, J = 8.2 Hz, 2H), 7.40–7.16 (m, 10H), 7.12–6.97 (m, 3H), 6.81 (m, 3H), 5.07 (d, J = 5.1 Hz, 1H), 4.82 (d, J = 6.6 Hz, 1H), 4.43 (d, J = 5.8 Hz, 2H), 3.13 (s, 3H), 3.11 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 191.9, 191.9, 175.3, 175.1, 157.7, 148.3, 147.3, 147.2, 146.6, 139.9, 139.0, 135.4, 135.3, 132.6, 132.5, 130.1, 130.0, 129.8, 129.2, 128.9, 128.8, 128.4, 127.8, 127.5, 121.7, 121.4, 117.9, 117.8, 52.2, 51.4, 49.2, 48.9, 25.4; HRMS (ESI) m/z calcd for $C_{22}H_{19}N_2O_2$ (M + H) 343.14410, found 343.14325.

*1-Methyl-3-(phenyl(p-tolyl)methyl)-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**2d**):* oil; 122 mg (89%); ^{1}H NMR ($CDCl_3$) δ 8.14 (d, J = 5.2 Hz, 2H), 7.42–7.27 (m, 6H), 7.24–7.14 (m, 6H), 7.02–6.96 (m, 4H), 6.89 (ddd, J = 11.0, 5.3, 3.7 Hz, 4H), 6.79 (dd, J = 7.3, 5.3 Hz, 2H), 4.89 (t, J = 6.1 Hz, 2H), 4.37 (d, J = 5.4 Hz, 2H), 3.12 (s, 3H), 3.11 (s, 3H), 2.37 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (CDCl3) δ 175.7, 157.7, 146.6, 141.3, 139.6, 138.0, 136.9, 136.7, 136.2, 132.8, 129.3, 129.3, 129.2, 129.1, 128.6, 128.4, 128.4, 128.3, 127.3, 127.0, 122.3,

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117.7, 51.2, 51.1, 49.6, 49.5, 25.4, 21.1; HRMS (ESI) m/z calcd for $C_{22}H_{21}N_2O$ (M + H) 329.16484, found 329.16397.

*3-((4-Acetylphenyl)(phenyl)methyl)-1-methyl-1H-pyrrolo[2,3-b]-pyridin-2(3H)-one (**2e**):* oil; 127 mg (86%); ^{1}H NMR ($CDCl_3$) δ 8.13 (d, J = 4.9 Hz, 2H), 7.93 (d, J = 8.4 Hz, 2H), 7.81−7.70 (m, 2H), 7.47−7.15 (m, 10H), 7.11 (t, J = 8.9 Hz, 2H), 7.07−6.98 (m, 2H), 6.94 (t, J = 8.3 Hz, 1H), 6.78 (ddd, J = 10.1, 7.3, 5.3 Hz, 3H), 5.02 (d, J = 5.2 Hz, 1H), 4.81 (d, J = 6.4 Hz, 1H), 4.39 (d, J = 5.9 Hz, 2H), 3.10 (s, 3H) 3.09 (s, 3H), 2.59 (s, 3H), 2.53 (s, 3H); ^{13}C NMR ($CDCl_3$): δ 197.8, 197.7, 175.3, 175.2, 157.6, 147.1, 147.0, 146.6, 145.0, 140.1, 139.0, 136.1, 135.9, 132.7, 132.6, 129.6, 129.2, 128.8, 128.8, 128.7, 128.6, 128.5, 128.4, 127.7, 127.4, 121.8, 121.6, 117.9, 117.8, 51.9, 51.2, 49.3, 49.0, 26.7, 26.7, 25.5; HRMS (ESI) m/z calcd for $C_{23}H_{21}N_2O_2$ (M + H) 357.15975, found 357.15869.

*1-Methyl-3-((3-nitrophenyl)(phenyl)methyl)-1H-pyrrolo[2,3-b]-pyridin-2(3H)-one (**2f**):* oil; 109 mg (73%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.25 (s, 1H), 8.14 (dd, J = 6.3, 3.5 Hz, 3H), 8.11−8.00 (m, 1H), 7.87 (t, J = 1.8 Hz, 1H), 7.70 (d, J = 7.8 Hz, 1H), 7.53 (t, J = 7.9 Hz, 1H), 7.47−7.18 (m, 10H), 7.12 (dd, J = 9.0, 5.5 Hz, 3H), 6.91−6.68 (m, 3H), 5.12 (d, J = 4.6 Hz, 1H), 4.72 (d, J = 7.3 Hz, 1H), 4.43 (d, J = 5.2 Hz, 2H), 3.14 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2, 174.9, 157.6, 148.4, 148.1, 147.5, 147.4, 143.5, 141.7, 139.4, 139.1, 135.6, 134.7, 132.6, 132.5, 129.5, 129.3, 129.0, 129.0, 128.5, 128.0, 127.7, 124.2, 123.2, 122.4, 122.2, 121.4, 121.0, 118.0, 117.9, 52.0, 50.9, 49.2, 48.6, 25.4, 25.4; HRMS (ESI) m/z calcd for $C_{21}H_{18}N_3O_3$ (M + H) 360.13427, found 360.13358.

*3-((1H-Indol-5-yl)(phenyl)methyl)-1-methyl-1H-pyrrolo[2,3-b]-pyridin-2(3H)-one (**2g**):* oil; 127 mg (86%); ^{1}H NMR ($CDCl_3$) δ 8.35 (s, 1H), 8.24 (s, 1H), 8.13 (ddd, J = 5.2, 1.5, 0.7 Hz, 2H), 7.54 (d, J = 0.8 Hz, 1H), 7.43−7.31 (m, 6H), 7.31−7.26 (m, 1H), 7.24−7.21 (m, 1H), 7.20−7.13 (m, 6H), 7.06−6.97 (m, 2H), 6.97−6.87 (m, 1H), 6.84−6.71 (m, 3H), 6.51 (ddd, J = 3.0, 2.0, 0.9 Hz, 1H), 6.42 (ddd, J = 3.0, 2.0, 0.9 Hz, 1H), 5.11 (d, J = 5.4 Hz, 1H), 4.99 (d, J = 6.0 Hz, 1H), 4.51−4.42 (m, 2H), 3.11 (s, 3H), 3.10 (s, 3H); ^{13}C NMR (75 MHz) δ 176.1, 176.0, 157.9, 156.0, 146.8, 146.8, 142.2, 140.2, 135.0, 134.8, 132.9, 132.8, 132.7, 132.4, 130.9, 129.4, 128.5, 128.5, 128.3, 128.0, 127.9, 127.1, 126.8, 124.9, 124.6, 123.5, 122.9, 122.6, 122.4, 121.4, 120.4, 119.7, 117.7, 111.3, 110.9, 102.9, 102.8, 51.8, 51.4, 50.1, 49.8, 25.3, 25.3; HRMS (ESI) m/z calcd for $C_{23}H_{20}N_3O$ (M + H) 355.16344, found 355.15955.

*1-Methyl-3-(phenyl(thiophene-3-yl)methyl)-1H-pyrrolo[2,3-b]-pyridin-2(3H)-one (**2h**):* oil; 95 mg (71%); ^{1}H NMR ($CDCl_3$) δ 8.20−8.11 (m, 2H), 7.43−7.23 (m, 5H), 7.20−7.09 (m, 5H), 7.05−6.91 (m, 4H), 6.90−6.78 (m, 3H), 6.57 (dd, J = 5.0, 1.3 Hz, 1H), 5.14 (d, J = 4.9 Hz, 1H), 4.96 (d, J = 4.2 Hz, 1H), 4.32 (d, J = 4.9 Hz, 1H), 4.25 (d, J = 5.0 Hz, 1H), 3.12 (s, 3H), 3.06 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 175.5, 175.3, 157.8, 157.7, 146.7, 146.5, 142.2, 140.6, 138.9, 138.5, 132.8, 132.6, 129.1, 128.7, 128.3, 128.3, 128.3, 127.9, 127.6, 127.2, 126.5, 125.6, 123.2, 122.6, 122.2, 121.9, 117.8, 50.3, 50.2, 47.7, 46.8, 25.5, 25.4; HRMS (ESI) m/z calcd for $C_{19}H_{17}N_2OS$ (M + H) 321.10561, found 321.10538.

*3-Benzhydryl-1-benzyl-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**2i**):* oil; 143 mg (90%); ^{1}H NMR ($CDCl_3$): δ 8.14 (ddd, J = 5.2, 1.5, 0.8 Hz, 1H), 7.41−7.27 (m, 5H), 7.24−7.10 (m, 6H), 7.06−6.95 (m, 5H), 6.80 (dd, J = 7.3, 5.3 Hz, 1H), 5.04 (d, J = 5.2 Hz, 1H), 4.97 (d, J = 14.9 Hz, 1H), 4.79 (d, J = 14.9 Hz, 1H), 4.46 (d, J = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 175.4, 157.3, 147.3, 141.0, 139.0, 136.2, 132.5, 129.6, 128.4, 127.7, 127.3, 127.2, 127.0, 121.8, 117.8, 51.2, 49.7, 42.5; HRMS (ESI) m/z calcd for $C_{27}H_{23}N_2O$ (M + H), 391.18049, found 391.17896.

*1-Benzyl-3-((4-methoxyphenyl)(phenyl)methyl)-1H-pyrrolo[2,3-b]pyridin-2(3H)-one (**2j**):* oil; 157 mg (90%); ^{1}H NMR ($CDCl_3$) δ 8.15−8.08 (m, 2H), 7.38−7.24 (m, 6H), 7.23−7.08 (m, 10H), 7.05−6.90 (m, 7H), 6.90−6.73 (m, 7H), 6.67−6.59 (m, 2H), 5.02−4.88 (m, 4H), 4.75 (d, J = 14.9 Hz, 2H), 4.39 (t, J = 5.3 Hz, 2H), 3.80 (s, 3H), 3.74 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 175.6, 175.5, 158.8, 158.5, 157.4, 157.3, 147.3, 147.2, 141.4, 139.5, 136.3, 136.3, 133.0, 132.6, 132.5, 130.7, 129.5, 129.5, 128.6, 128.5, 128.4, 127.8, 127.8, 127.3, 127.2, 126.9, 122.1, 121.9, 117.8, 114.0, 113.8, 55.4, 55.2, 50.7, 50.4, 50.0, 49.9, 42.5; HRMS (ESI) m/z calcd for $C_{28}H_{25}N_2O_2$ (M + H) 421.19105, found 421.18958.

■ ASSOCIATED CONTENT

Supporting Information

Scanned NMR spectra of all new products and HPLC analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: marie-claude.viaud-massuard@univ-tours.fr.

Notes

The authors declare no competing financial interest.

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(11) After semipreparative HPLC purification, each isomer of **1b** has been isolated and analyzed over the course of a week by NMR spectroscopy in $CDCl_3$ (the product was kept in solution during the study). For the major *E* isomer, the evolution of the *E*/*Z* ratio was as follows: 5 min (94/6), 3 h (90/10), 6 h (85/15), 72 h (81/19), 1 week (73/24). For the minor *Z* isomer, the evolution of the *E*/*Z* ratio was as follows: 5 min (28/72), 3 h (42/58), 6 h (61/39), 72 h (62/38), 1 week (66/34).
(12) ChiralPak 1A column, hexane/ethanol 95/5 at 10 °C. Retention times of the four expected stereoisomers are as follows: 21.0 min, 23.4 min, 24.5 min (two isomers) (see the Supporting Information).
(13) ChiralPak 1A column, hexane/ethanol 95/5 at 10 °C. Retention times of the two stereoisomers are as follows: 20.9 min, 24.4 min (see the Supporting Information).
(14) ChiralPak 1A column, hexane/ethanol 95/5 at 10 °C. Retention times of the two stereoisomers are as follows: 21.1 min, 24.7 min (see the Supporting Information).
(15) Due to the lack of reactivity with $[Rh(cod)Cl]_2$ for compounds **2f** and **2h**, it was impossible to determine an accurate ee value, even if we obtained two majors peaks (see the Supporting Information) giving, respectively, estimated ee > 80% and ≈ 88%.

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