HETEROCYCLES, Vol. 65, No. 12, 2005, pp. 2979 - 2989
Received, 31st August, 2005, Accepted, 13th October, 2005, Published online, 14th October, 2005

AN EFFICIENT SYNTHETIC ROUTE TO NEW IMIDAZO[1,2-*a*]-PYRIDINES BY CROSS-COUPLING REACTIONS IN AQUEOUS MEDIUM

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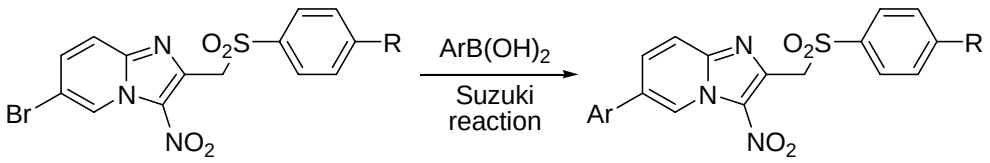
Abstract – The Suzuki cross-coupling reaction of 6-bromo-3-nitro-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridine and 6-bromo-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridine provided an efficient route to the corresponding 6-aryl-3-nitro-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridines and 6-aryl-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridines. The reaction was catalyzed by palladium(0) in aqueous medium.

INTRODUCTION

Over the last thirty years the use of sulfones in organic chemistry and medicinal chemistry has increased dramatically. Sulfones have been employed in many synthetic methodologies as intermediates enabling the preparation of a great number of functionalized products such as natural products and bioactive substances.[1] The Suzuki reaction has proved extremely versatile and has found extensive use in natural products and heterocyclic synthesis.[2] Some examples of Suzuki-type cross-coupling reactions in 3- and 6-haloimidazo[1,2-*a*]pyridine series were described.[3] In continuation of our studies on the reactivity of nitroheterocyclic sulfones,[4,5] we were then interested in the preparation of new sulfones bearing an aryl group. We anticipated to prepare original compounds from 6-bromo-3-nitroimidazo[1,2-*a*]pyridines bearing an arylsulfonylmethyl group in 2-position by Suzuki reaction with various arylboronic acids (Scheme 1).

Scheme 1



R = H, CH_3

To our knowledge, except the pioneer work on the sodium salt of methyl phenylsulfonyl acetate with allylic acetates of either geranyl acetate or neryl acetate in the presence of tetrakis (triphenyl-phosphine)palladium(0) catalyst[6] and the intramolecular version of this reaction for the preparation of medium-ring lactones and macrolides,[6] only the palladium-catalyzed monoarylation of a series of functionalized strongly C-H acidic sulfones by aryl halides has been described.[7]

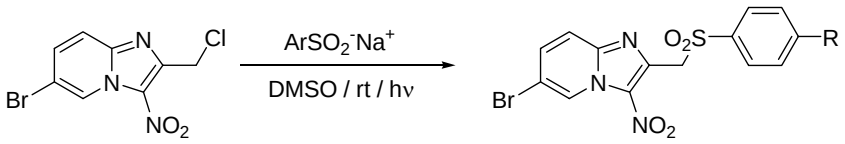
As part of an ongoing research program focused on the synthesis of new pyridinones of pharmaceutical interest for the treatment of central nervous system disorders,[8] we wish to report the results of this study on the functional compatibility in Suzuki reaction of the phenylsulfonylmethyl and tosylmethyl groups in *ortho-like* position of the nitro group in the 6-bromo-3-nitroimidazo[1,2-*a*]pyridine series.

RESULTS AND DISCUSSION

Synthesis of starting materials

The synthesis of 6-bromo-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridine (**2b**) was performed with sodium toluene-4-sulfinate as previously described for the preparation of 6-bromo-3-nitro-2-phenylsulfonyl-methylimidazo[1,2-*a*] pyridine (**2a**) as shown in scheme 2.[3]

Scheme 2



1 **2**

a R = H
b R = CH_3

These two compounds (**2**) served as starting material for the synthesis of several new sulfonyl derivatives (**3a-10b**) obtained by cross-coupling reaction with some arylboronic acids in aqueous medium.

Cross-coupling reactions

Reactions in aqueous media are advantageous for largescale industrial processes because of the simplicity of catalyst-product separation and economy and safety of using water as a solvent.[9] Such reactions in aqueous media are also useful for the biaryl coupling of arylboronic acids.[10]

Furthermore, owing to the fact that the nitroheterocyclic sulfones (**2**) are strongly C-H acidic sulfones, their expected solubility in the basic medium of the Suzuki experimental conditions offers the opportunity to

develop Suzuki reaction in aqueous medium. So, the coupling reactions of the two sulfonyl compounds with bromine atom in position 6 were tested with arylboronic acids according to Suzuki – Miyaura reaction in water with $Pd(PPh_3)_4$ as catalyst. The method, which was tested to carry out cross-coupling reaction, used as catalyst 10 mol% of $Pd(PPh_3)_4$, as base 5 equivalents of Na_2CO_3 and 1.3 equivalent of arylboronic acid. Because of the facile formation of the anion (**2a**) and (**2b**), a large amount of base was employed. The formation of the sulfonyl anion in basic medium could allow a better solubility of the reagent in water, what would allow the cross-coupling reaction to proceed in aqueous medium.

The mixture of 2-arylsulfonylmethyl-6-bromo-3-nitroimidazo[1,2-*a*]pyridine, arylboronic acid, $Pd(Ph_3)_4$, Na_2CO_3 and water was heated under reflux from 1 to 24 h and the disappearance of starting materials was monitored by TLC. No organic solvent or cosolvent were used or investigated. Although the reaction mixtures were nonhomogeneous and aggregated, the yields were good overall. Some yields appeared to suffer due to the difficulties in the workup extractions. The aggregation, coupled with the high surface tension of water, diminishes the surface contact between hydrophobic species and water molecules.[11] These Suzuki couplings in aqueous media were accomplished by the employment of large excess of base for interaction with sulfonyl anions to give **3-10** in moderate to good yields (Scheme 3, Table 1) and the structure of the boronic acid has few influence on the yield.

Scheme 3

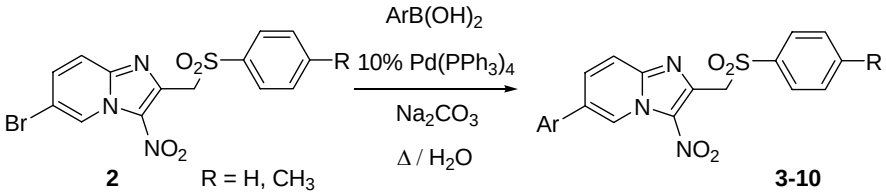
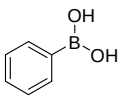
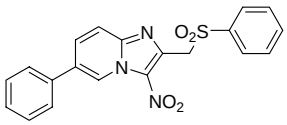
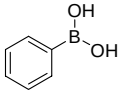
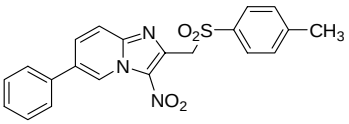
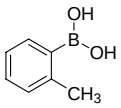
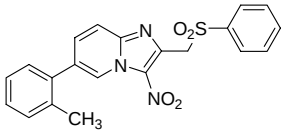
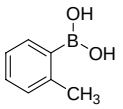
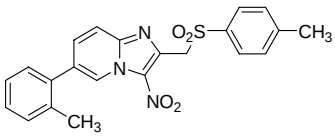
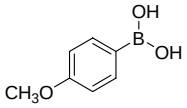
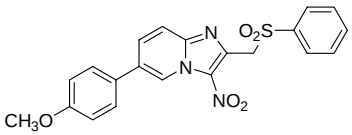
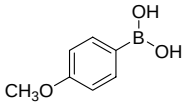
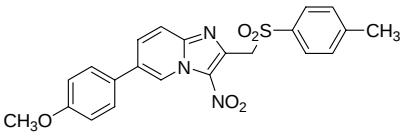
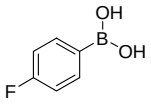
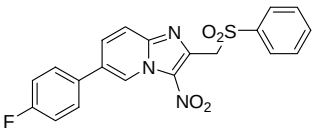
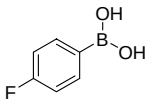
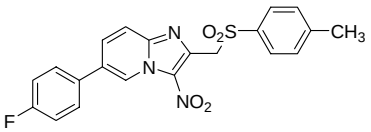
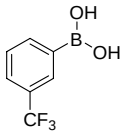
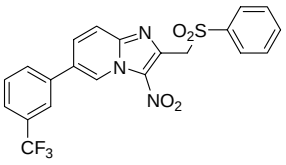
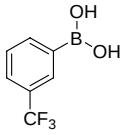
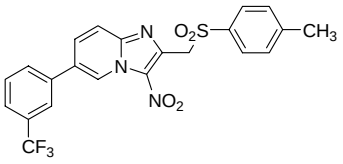
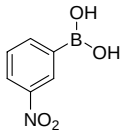
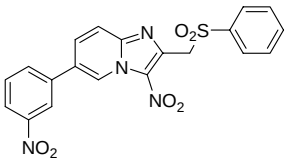
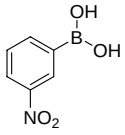
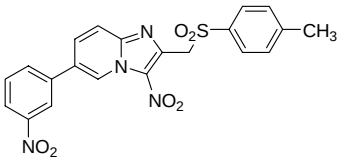
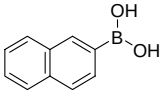
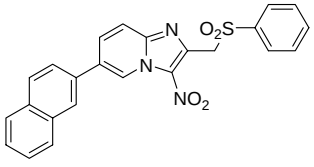
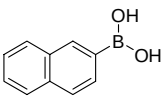
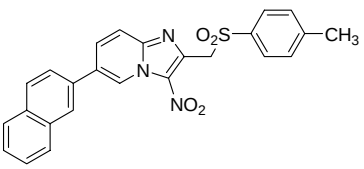
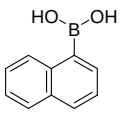
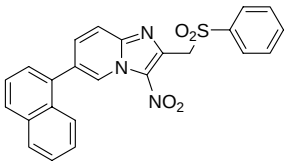
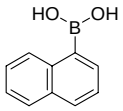
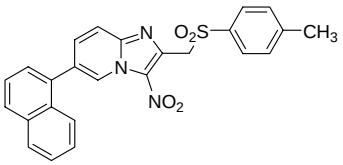


Table 1

Cross-coupling reaction of 2-arylsulfonylmethyl-6-bromo-3-nitroimidazo[1,2-*a*]pyridines with arylboronic acids[a]

Entry	Arylboronic acid	Product	Compound number	*t* (h)	Yield
1			**3a**	20 (3)[b]	60 (70)[b]
2			**3b**	2	60
3			**4a**	2	60
4			**4b**	24	72

5			**5a**	1.75	60
6			**5b**	2	97
7			**6a**	4.5	77
8			**6b**	3	60
9			**7a**	1.5	76
10			**7b**	1.5	55
11			**8a**	5	50
12			**8b**	2	90
13			**9a**	1	63
14			**9b**	20 (3)[b]	20 (90)[b]
15			**10a**	4.5	63

16			**10b**	3	55

[a] Conditions: catalyst $Pd(PPh_3)_4$ 10% mol, 2-arylsulfonylmethyl-6-bromo-3-nitroimidazo[1,2-*a*]pyridine (1 equiv.), arylboronic acid (1.3 equiv.), Na_2CO_3 (5 equiv.), H_2O, 100 °C.

[b] Time reaction and yields in parenthesis correspond to reactions performed under sonication, 74 °C.

In order to optimize the reaction yield, we preliminary investigated cross-coupling reaction performed under sonication at 74 °C on **2a** with phenylboronic acid and **2b** with naphthalen-2-ylboronic acid. These conditions, inspired with significative results were obtained by Toma and coworkers.[12] They assume that the beneficial effect of ultrasound on this heterogeneous reaction can be attributed to a better mass transfer in comparison with magnetically stirred reaction. Sonification seemed to facilitate the treatment and the purification, accelerate the reaction rate and increase the reaction yield. Our results confirm acceleration of reaction rate and increase of the yields (Entries 1 and 14). It is noteworthy that under these experimental conditions, with or without sonication, arylation of the sulfonyl carbanion[7] was not observed or leads to untractable products.

CONCLUSION

In conclusion, a simple general procedure for the preparation of new 6-aryl-3-nitro-2-phenylsulfonyl-methylimidazo[1,2-*a*]pyridines and 6-aryl-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridines has been developed on the basis of palladium-mediated coupling of arylboronic acid. Moreover we have shown in this study the functional compatibility in Suzuki reaction of the phenylsulfonylmethyl and tosylmethyl groups in *ortho-like* position of the nitro group in the 6-bromo- 3-nitroimidazo[1,2-*a*]pyridine series.

EXPERIMENTAL

Melting points were determined with a B-540 Büchi melting point apparatus. 200 MHz ^{1}H NMR and 50 MHz ^{13}C NMR spectra were recorded on a Bruker ARX 200 spectrometer in $CDCl_3$ solution at the Faculté de Pharmacie de Marseille. ^{1}H and ^{13}C NMR chemical shifts (δ) are reported in ppm with respect to $CHCl_3$ 7.26 ppm (^{1}H) and 76.9 ppm (^{13}C) and DMSO-d_6 2.50 ppm (^{1}H) and 39.70 ppm (^{13}C). Elemental analyses were carried out at the Centre de Microanalyses de la Faculté des Sciences et Techniques de Saint-Jérôme and at the Service Central d'Analyse du Centre National de la Recherche Scientifique de Vernaison. The following adsorbent was used for column chromatography: silica gel 60 (Merck, particle size 0.063-0.200 mm, 70-230 mesh ASTM). TLC were performed on 5 cm × 10 cm aluminium plates coated with silica gel 60F-254 (Merck) in an appropriate solvent. Sonochemical experiments were carried out in the ultrasonic

cleaning bath Bioblock Scientific (35 kHz). 6-Bromo-2-chloromethyl-3-nitroimidazo[1,2-*a*]pyridine (**1**) and 6-bromo-3-nitro-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridine (**2a**) were previously described.[3]

Preparation of 6-bromo-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridine (2b)

To a solution of sodium toluene-4-sulfinate (1.78 g, 10 mmol) in DMSO (40 mL) under inert atmosphere (N_2) and irradiation with a tungsten 150W lamp was added 1.45 g (5.0 mmol) of 6-bromo-2-chloromethylimidazo[1,2-*a*]pyridine. The mixture was stirred at rt for 3 h. After disappearance of 6-bromo-2-chloromethyl-3-nitroimidazo[1,2-*a*]pyridine (monitored by TLC), the mixture was poured into an ice-water mixture and a solid precipitated. The solid was collected by filtration and dried in the air to give after purification by recrystallization from propan-2-ol 1.85 g (90%) of **2b** as yellow solid. mp 201 °C. ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H, CH_3); 5.09 (s, 2H, CH_2); 7.31 (d, J = 7.9 Hz, 2H, CH); 7.72 (s, 2H, CH); 7.73 (d, J = 7.9 Hz, 2H, CH); 9.52 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_3); 56.7 (CH_2); 112.4 (C); 119.1 (CH); 127.7 (CH); 128.3 (CHx2); 129.9 (CHx2); 134.5 (CH); 136.2 (C); 139.7 (C); 143.3 (C); 145.3 (C). Anal. Calcd for $C_{15}H_{12}N_3O_4BrS$: C, 43.92; H, 2.95; N, 10.24. Found: C, 43.97; H, 2.67; N, 10.45.

General procedure for cross-coupling reaction of heteroaryl bromides with arylboronic acids

A solution of 2-arylsulfonylmethyl-6-bromo-3-nitroimidazo[1,2-*a*]pyridine (1.26 mmol), arylboronic acid (1.64 mmol), Na_2CO_3 (6.31 mmol), $Pd(PPh_3)_4$ (0.13 mmol) in water was heated under reflux for a time *t*. After disappearance of 2-arylsulfonylmethyl-6-bromo-3-nitroimidazo[1,2-*a*]pyridine (monitored by TLC), the mixture was cooled and the solid was collected by filtration and dried in the air. The crude product was purified by column chromatography on silica gel with appropriate solvent to give 6-aryl-2-arylsulfonylmethyl-3-nitroimidazo[1,2-*a*] pyridine.

3-Nitro-6-phenyl-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridine (3a)

Cross-coupling reaction of phenylboronic acid (200 mg, 1.64 mmol) with **2a** (500 mg, 1.26 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: $CHCl_3$-ethyl acetate 9:1) and recrystallization from ethyl acetate 300 mg (60%) of **3a**. Reaction performed under sonication gave 350 mg (70%) of **3a** as yellow solid. mp 238 °C. ^{1}H NMR ($CDCl_3$) δ 5.17 (s, 2H, CH_2); 7.47-7.90 (m, 12H, CH); 9.55 (m, 1H, CH). ^{13}C NMR ($CDCl_3$): δ 56.9 (CH_2); 118.4 (CH); 125.0 (CH); 127.4 (CHx2); 128.4 (CHx2); 129.1 (CH); 129.3 (CHx2); 129.5 (CHx2); 131.6 (CH); 132.0 (C); 134.2 (CH); 135.7 (C); 139.3 (C); 139.8 (C); 144.2 (C). Anal. Calcd for $C_{20}H_{15}N_3O_4S$: C, 61.06; H, 3.84; N, 10.68. Found: C, 61.30; H, 3.74; N, 10.38.

3-Nitro-6-phenyl-2-tosylmethylimidazo[1,2-*a*]pyridine (3b)

Cross-coupling reaction of phenylboronic acid (190 mg, 1.6 mmol) with **2b** (500 mg, 1.22 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: $CHCl_3$-ethyl acetate 1:1) and recrystallization from propan-2-ol 300 mg (60%) of **5a** as yellow solid. mp 205 °C. ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H); 5.14 (s, 2H, CH_2); 7.32 (d, J = 8.1 Hz, 2H, CH); 7.50-7.64 (m, 5H, CH); 7.76 (d, J = 8.1 Hz, 2H, CH); 7.90 (s, 2H, CH); 9.55 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 21.6

(CH_3); 56.9 (CH_2); 118.4 (CH); 124.9 (CH); 127.3 (CHx2); 128.3 (CHx2); 129.3 (CH); 129.4 (CHx2); 129.8 (CHx2); 131.5 (CH); 131.8 (C); 135.6 (C); 136.3 (C); 139.9 (C); 144.1 (C); 145.2 (C). Anal. Calcd for $C_{21}H_{17}N_3O_4S$: C, 61.90; H, 4.21; N, 10.31. Found: C, 61.68; H, 4.24; N, 10.18.

3-Nitro-2-phenylsulfonylmethyl-6-*o*-tolylimidazo[1,2-*a*]pyridine (4a)

Cross-coupling reaction of *o*-tolylboronic acid (220 mg, 1.64 mmol) with **2a** (500 mg, 1.26 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: CH_2Cl_2) and recrystallization from toluene 300 mg (60%) of **4a** as black solid. mp 191 °C. ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 3H, CH_3); 5.17 (s, 2H, CH_2); 7.25-7.94 (m, 11H, CH); 9.33 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 20.3 (CH_3); 56.8 (CH_2); 117.7 (CH); 126.4 (CH); 126.5 (CH); 128.3 (CHx2); 129.1 (CH); 129.2 (CHx2); 129.9 (CH); 131.0 (CH); 132.1 (C); 133.5 (CH); 134.1 (CH); 135.8 (C); 139.3 (C); 139.6 (C); 144.0 (C). Anal. Calcd for $C_{21}H_{17}N_3O_4S$: C, 61.90; H, 4.21; N, 10.31. Found: C, 62.13; H, 4.24; N, 10.42.

3-Nitro-6-*o*-tolyl-2-tosylmethylimidazo[1,2-*a*]pyridine (4b)

Cross-coupling reaction of *o*-tolylboronic acid (210 mg, 1.6 mmol) with **2b** (500 mg, 1.22 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: $CHCl_3$-ethyl acetate 9:1) and recrystallization from toluene 370 mg (72%) of **4b** as beige solid. mp 249 °C. ^{1}H NMR ($CDCl_3$) δ 2.32 (s, 3H, CH_3); 2.46 (s, 3H, CH_3); 5.16 (s, 2H, CH_2); 7.26-7.91 (m, 10H, CH); 9.35 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 20.4 (CH_3); 21.7 (CH_3); 56.9 (CH_2); 117.7 (CH); 126.4 (CH); 126.6 (CH); 128.4 (CHx2); 129.1 (CH); 129.9 (CHx2); 130.0 (CH); 130.9 (CH); 132.1 (C); 133.4 (CH); 135.8 (Cx2); 136.5 (C); 139.9 (C); 144.0 (C); 145.2 (C). Anal. Calcd for $C_{22}H_{19}N_3O_4S$: C, 62.69; H, 4.54; N, 9.97. Found: C, 62.64; H, 4.54; N, 9.97.

6-(4-Methoxyphenyl)-3-nitro-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridine (5a)

Cross-coupling reaction of 4-methoxyphenylboronic acid (250 mg, 1.64 mmol) with **2a** (500 mg, 1.26 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: CH_2Cl_2-ethyl acetate 4:1) and recrystallization from toluene 320 mg (60%) of **5a** as green solid. mp 249 °C. ^{1}H NMR ($CDCl_3$) δ 3.89 (s, 3H, CH_3); 5.17 (s, 2H, CH_2); 7.06 (d, J = 8.6 Hz, 2H, CH); 7.46-8.00 (m, 9H, CH); 9.52 (m, 1H, CH). ^{13}C NMR ($CDCl_3$): δ 55.5 (CH_3); 56.9 (CH_2); 115.0 (CHx2); 118.3 (CH); 124.3 (CH); 128.0 (C); 128.4 (CHx2); 128.5 (CHx2); 129.2 (CHx2); 131.4 (CH); 131.7 (C); 134.1 (CH); 139.3 (C); 139.7 (C); 144.0 (C); 160.5 (C). Anal. Calcd for $C_{21}H_{17}N_3O_5S$: C, 59.57; H, 4.05; N, 9.92. Found: C, 59.72; H, 4.05; N, 9.83.

6-(4-Methoxyphenyl)-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridine (5b)

Cross-coupling reaction of 4-methoxyphenylboronic acid (240 mg, 1.6 mmol) with **2b** (500 mg, 1.22 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: Petroleum ether-ethyl acetate 3:7) and recrystallization from toluene gave 520 mg (97%) of **5b** as

green solid. mp 221 °C. ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H, CH_3); 3.88 (s, 3H, CH_3); 5.14 (s, 2H, CH_2); 7.04 (d, *J* = 8.8 Hz, 2H, CH); 7.31 (d, *J* = 8.3 Hz, 2H, CH); 7.55 (d, *J* = 8.8 Hz, 2H, CH); 7.75 (d, *J* = 8.3 Hz, 2H, CH); 7.86 (s, 2H, CH); 9.50 (m, 1H, CH); ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_3); 55.4 (CH_3); 56.9 (CH_2); 114.9 (CHx2); 118.3 (CH); 124.3 (CH); 128.4 (CHx2); 128.5 (CHx2); 129.8 (CHx2); 131.3 (CH); 131.6 (C); 134.5 (C); 136.3 (C); 139.8 (C); 143.9 (C); 145.2 (C); 160.5 (C). Anal. Calcd for $C_{22}H_{19}N_3O_5S$: C, 60.40; H, 4.38; N, 9.61. Found: C, 60.79; H, 4.39; N, 9.28.

6-(4-Fluorophenyl)-3-nitro-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridine (6a)

Cross-coupling reaction of 4-fluorophenylboronic acid (230 mg, 1.64 mmol) with **2a** (500 mg, 1.26 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: CH_2Cl_2) and recrystallization from propan-2-ol 400 mg (77%) of **6a** as yellow solid. mp 229 °C. ^{1}H NMR ($CDCl_3$) δ 5.17 (s, 2H, CH_2); 7.19-7.94 (m, 11H, CH); 9.53 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 56.9 (CH_2); 116.4 (CH); 116.8 (CH); 118.6 (CH); 124.9 (CH); 128.4 (CHx2); 129.1 (CH); 129.3 (CHx3); 131.0 (CH); 131.3 (CH); 131.8 (C); 134.2 (C); 139.3 (C); 139.8 (C); 144.1 (C); 163.5 (C). Anal. Calcd for $C_{20}H_{14}N_3O_4FS$: C, 58.39; H, 3.43; N, 10.21. Found: C, 58.52; H, 3.57; N, 10.19.

6-(4-Fluorophenyl)-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridine (6b)

Cross-coupling reaction of 4-fluorophenylboronic acid (220 mg, 1.6 mmol) with **2b** (500 mg, 1.22 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: CH_2Cl_2) and recrystallization from propan-2-ol 306 mg (60%) of **6b** as yellow solid. mp 241 °C. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H, CH_3); 5.15 (s, 2H, CH_2); 7.20-7.94 (m, 10H, CH); 9.54 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 21.8 (CH_3); 56.9 (CH_2); 116.4 (CH); 116.8 (CH); 118.6 (CH); 124.9 (CH); 128.4 (CHx2); 129.1 (CH); 129.3 (CH); 129.9 (CHx2); 131.0 (C); 131.3 (CH); 131.9 (C); 136.4 (C); 140.0 (C); 144.1 (C); 145.3 (C); 161.9 (C). Anal. Calcd for $C_{21}H_{16}N_3O_4FS$: C, 59.29; H, 3.79; N, 9.88. Found: C, 59.42; H, 3.92; N, 9.87.

3-Nitro-2-phenylsulfonylmethyl-6-(3-trifluoromethylphenyl)imidazo[1,2-*a*]pyridine (7a)

Cross-coupling reaction of 3-trifluoromethylphenylboronic acid (310 mg, 1.64 mmol) with **2a** (500 mg, 1.26 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: $CHCl_3$-ethyl acetate 7:3) and recrystallization from propan-2-ol 440 mg (76%) of **7a** as yellow solid. mp 221 °C. ^{1}H NMR ($CDCl_3$) δ 5.18 (s, 2H, CH_2); 7.51-7.99 (m, 11H, CH); 9.59 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 56.8 (CH_2); 118.9 (CH); 123.8 (C); 124.2 (CH); 125.3 (CH); 125.8 (CH); 128.4 (CHx2); 129.3 (CHx2); 130.1 (CH); 130.5 (C); 130.7 (CH); 131.1 (CH); 132.1 (C); 134.2 (CH); 136.6 (C); 139.2 (C); 140.0 (C); 144.2 (C). Anal. Calcd for $C_{21}H_{14}N_3O_4F_3S$: C, 54.66; H, 3.06; N, 9.11. Found: C, 54.63; H, 3.06; N, 9.11.

3-Nitro-2-tosylmethyl-6-(3-trifluoromethylphenyl)imidazo[1,2-*a*]pyridine (7b)

Cross-coupling reaction of 3-trifluoromethylphenylboronic acid (300 mg, 1.6 mmol) with **2b** (500 mg,

1.22 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: CH_2Cl_2) and recrystallization from propan-2-ol 310 mg (55%) of **7b** as yellow solid. mp 221 °C. ^{1}H NMR ($CDCl_3$) δ 2.46 (s, 3H, CH_3); 5.16 (s, 2H, CH_2); 7.32-7.99 (m, 10H, CH); 9.60 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_3); 56.9 (CH_2); 118.8 (CH); 123.7 (C); 124.2 (CH); 125.3 (CH); 125.8 (CH); 128.3 (CHx2); 129.9 (CHx2); 130.1 (CH); 130.4 (C); 130.7 (C); 131.1 (CH); 132.0 (C); 136.3 (C); 136.7 (C); 140.2 (C); 144.2 (C); 145.3 (C). Anal. Calcd for $C_{22}H_{16}N_3O_4F_3S$: C, 55.58; H, 3.39; N, 8.84. Found: C, 55.54; H, 3.43; N, 8.79.

3-Nitro-6-(3-nitrophenyl)-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridine (8a)

Cross-coupling reaction of 3-nitrophenylboronic acid (270 mg, 1.64 mmol) with **2a** (500 mg, 1.26 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: CH_2Cl_2-ethyl acetate 9:1) and recrystallization from toluene 280 mg (50%) of **8a** as green solid. mp 252 °C. ^{1}H NMR (DMSO-d_6) δ 5.28 (s, 2H, CH_2); 7.58-8.59 (m, 11H, CH); 9.57 (m, 1H, CH). ^{13}C NMR (DMSO-d_6) δ 56.3 (CH_2); 118.2 (CH); 122.3 (CH); 123.6 (CH); 126.3 (CH); 128.1 (CHx2); 128.3 (CH); 129.5 (CHx2); 131.4 (CH); 131.9 (CH); 134.1 (CH); 134.4 (CH); 137.5 (C); 139.1 (C); 140.1 (C); 143.9 (C); 148.3 (C). Anal. Calcd for $C_{20}H_{14}N_4O_6S$: C, 54.79; H, 3.22; N, 12.78. Found: C, 54.78; H, 3.25; N, 12.65.

3-Nitro-6-(3-nitrophenyl)-2-tosylmethylimidazo[1,2-*a*]pyridine (8b)

Cross-coupling reaction of 3-nitrophenylboronic acid (270 mg, 1.6 mmol) with **2b** (500 mg, 1.22 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: $CHCl_3$-ethyl acetate 9:1) and recrystallization from toluene 500 mg (90%) of **8b** as yellow solid. mp 249 °C. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H, CH_3); 5.15 (s, 2H, CH_2); 7.35-8.49 (m, 10H, CH); 9.64 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_3); 56.9 (CH_2); 119.1 (CH); 122.3 (CH); 123.8 (CH); 125.5 (CH); 128.4 (CHx2); 129.5 (C); 129.9 (CHx2); 130.6 (CH); 130.7 (CH); 133.2 (CH); 136.3 (C); 137.5 (C); 140.3 (C); 144.2 (C); 145.3 (C); 149.0 (C). Anal. Calcd for $C_{21}H_{16}N_4O_6S$: C, 55.75; H, 3.56; N, 12.38. Found: C, 56.06; H, 3.63; N, 12.49.

6-Naphthalen-2-yl-3-nitro-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridine (9a)

Cross-coupling reaction of naphthalen-2-ylboronic acid (230 mg, 1.31mmol) with **2a** (400 mg, 1.01 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: $CHCl_3$-ethyl acetate 9:1) and recrystallization from toluene 280 mg (63%) of **9a** as yellow solid. mp 220 °C. ^{1}H NMR ($CDCl_3$) δ 5.18 (s, 2H, CH_2); 7.17-8.07 (m, 15H, CH); 9.65 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 56.9 (CH_2); 118.5 (CH); 124.5 (CH); 125.2 (CH); 126.7 (CH); 127.1 (CH); 127.8 (CH); 128.2 (CH); 128.3 (CH); 128.4 (CHx2); 129.2 (CHx2); 129.4 (CH); 131.6 (CH); 131.8 (C); 132.8 (C); 133.2 (C); 133.5 (CH); 134.1 (CH); 139.2 (C); 139.8 (C); 144.1 (C). Anal. Calcd for $C_{24}H_{17}N_3O_4S$: C, 65.00; H, 3.86; N, 9.48. Found: C, 65.39; H, 3.75; N, 9.22.

6-Naphthalen-2-yl-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridine (9b)

Cross-coupling reaction of naphthalen-2-ylboronic acid (140 mg, 0.8 mmol) with **2b** (250 mg, 0.61 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: CH_2Cl_2-ethyl acetate 9:1) and recrystallization from ethyl acetate 55 mg (20%) of **9b**. Reaction performed under sonication gave 250 mg (90%) of **9b** as yellow solid. mp 277 °C. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H, CH_3); 5.17 (s, 2H, CH_2); 7.31-8.09 (m, 13H, CH); 9.69 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_3); 57.0 (CH_2); 118.5 (CH); 124.6 (CH); 125.2 (CH); 126.7 (CH); 127.1 (CH); 127.8 (CH); 128.2 (CH); 128.3 (CHx2); 128.4 (CH); 129.5 (CH); 129.9 (CHx2); 131.6 (CH); 131.8 (C); 132.9 (C); 133.2 (C); 133.5 (C); 136.4 (C); 140.0 (C); 144.2 (C); 145.2 (C). Anal. Calcd for $C_{25}H_{19}N_3O_4S$: C, 65.63; H, 4.10; N, 9.18. Found: C, 65.67; H, 4.21; N, 9.12.

6-Naphthalen-1-yl-3-nitro-2-phenylsulfonylmethylimidazo[1,2-*a*]pyridine (10a)

Cross-coupling reaction of naphthalen-1-ylboronic acid (280 g, 1.64 mmol) with **2a** (500 mg, 1.26 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: CH_2Cl_2) and recrystallization from ethyl acetate 350 mg (63%) of **10a** as yellow solid. mp 249 °C. ^{1}H NMR ($CDCl_3$) δ 5.21 (s, 2H, CH_2); 7.49-7.97 (m, 14H, CH); 9.50 (m, 1H, CH). ^{13}C NMR ($CDCl_3$) δ 56.9 (CH_2); 117.7 (CH); 124.6 (CH); 125.4 (CH); 126.5 (CH); 127.1 (CH); 127.2 (CH); 127.9 (CH); 128.4 (CHx2); 128.8 (CH); 129.3 (CHx2); 129.6 (CH); 131.2 (C); 131.4 (C); 133.8 (C); 133.9 (C); 134.2 (CHx2); 139.4 (C); 139.7 (C); 144.2 (C). Anal. Calcd for $C_{24}H_{17}N_3O_4S$: C, 65.00; H, 3.86; N, 9.48. Found: C, 65.24; H, 3.88; N, 9.29.

6-Naphthalen-1-yl-3-nitro-2-tosylmethylimidazo[1,2-*a*]pyridine (10b)

Cross-coupling reaction of naphthalen-1-ylboronic acid (270 mg, 1.6 mmol) with **2b** (500 mg, 1.22 mmol) according to the general procedure gave after purification by column chromatography (silica gel, eluent: $CHCl_3$-ethyl acetate 9:1) and recrystallization from toluene 300 mg (55%) of **10b** as yellow solid. mp 266 °C. ^{1}H NMR ($CDCl_3$) δ 2.45 (s, 3H, CH_3); 5.18 (s, 2H, CH_2); 7.37-8.01 (m, 13H, CH); 9.49 (m, 1H CH). ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_3); 56.9 (CH_2); 117.7 (CH); 124.7 (CH); 125.4 (CH); 126.5 (CH); 127.1 (CH); 127.2 (CH); 127.9 (CH); 128.4 (CHx2); 128.8 (CH); 129.6 (CH); 129.9 (CHx2); 131.1 (C); 131.3 (C); 133.8 (C); 133.9 (C); 134.1 (C); 136.5 (C); 139.9 (C); 144.2 (C); 145.2 (C). Anal. Calcd for $C_{25}H_{19}N_3O_4S$: C, 65.63; H, 4.19; N, 9.18. Found: C, 65.92; H, 4.23; N, 9.11.

ACKNOWLEDGMENTS

This paper is dedicated to Dr Michel P. Crozet for his retirement. This work was supported by the CNRS and the Universities of Aix-Marseille. C. Castera thanks the AP-HM for hospital appointment.

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