View Article Online View Journal

# Organic & Biomolecular Chemistry

## Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: S. Sengmany, A. Ollivier, E. Le Gall and E. Léonel, *Org. Biomol. Chem.*, 2018, DOI: 10.1039/C8OB00500A.



This is an Accepted Manuscript, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this Accepted Manuscript with the edited and formatted Advance Article as soon as it is available.

You can find more information about Accepted Manuscripts in the **author guidelines**.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard <u>Terms & Conditions</u> and the ethical guidelines, outlined in our <u>author and reviewer resource centre</u>, still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this Accepted Manuscript or any consequences arising from the use of any information it contains.



rsc.li/obc

# Journal Name

### ARTICLE



**Biomolecular Chemistry Accepted Manuscript** 

৵

rganic

## A mild electroassisted synthesis of (hetero)arylphosphonates

Stéphane Sengmany,<sup>a</sup> Anthony Ollivier,<sup>a</sup> Erwan Le Gall<sup>a</sup> and Eric Léonel<sup>\*a</sup>

Received 00th January 20xx, Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

The electrochemically-assisted synthesis of (hetero)arylphosphonates from (hetero)aryl halides and dimethyl phosphite is described. Very mild and simple conditions are employed as the cross-coupling is carried out under galvanostatic mode, in an undivided cell at room temperature, using NiBr<sub>2</sub>bpy as easily available pre-catalyst and acetonitrile as the solvent. In addition, both aryl bromides and iodides can be used as well, providing the corresponding (hetero)arylphosphonates in generally good yields. A mechanism involving the *in situ* generation of a Ni ate complex is proposed.

#### Introduction

As a possible alternative to classic organic synthesis, electroorganic synthesis<sup>1</sup> has benefited of constant interest<sup>2</sup> in the last decades, leading therefore to multiple innovative works.<sup>3</sup> The emergence of conceptually-new synthetic methodologies based on single electron transfer like photoredox catalysis<sup>4</sup> has also undoubtedly aroused a resurgence of interest for this field, comparable concepts being involved in both domains. In this context, and to the best of our knowledge, the use of electrosynthetic procedures for the preparation of arylphosphonates has not been disclosed to date. Though, aromatic phosphorus-containing compounds are widespread in materials science<sup>5</sup> and can also exhibit many interesting applications in biochemistry<sup>6</sup> and catalysis.<sup>7</sup> Most convenient methods for their synthesis generally involve C-P coupling between aryl halides and nucleophilic phosphoruscontaining reagents.<sup>8</sup> Since Hirao's pioneering work,<sup>9</sup> mostly encountered procedures are based on Pd-catalyzed cross-coupling reactions,<sup>10</sup> but copper catalysis has also been developed, to a lesser extent though.<sup>11</sup> Although nickel can represent a valuable alternative to more toxic and/or costly metals, methods employing this metal catalysis are more and more developed.<sup>12</sup> Recently, Han and coworkers described a very elegant reductant-free crosscoupling of aryl halides with dialkyl phosphites.<sup>12a</sup> However, the coupling is carried out at high temperature and aryl moieties substituted by electron-donating groups seem less efficient in the process. Han and Chen's group reported the phosphonylation of pivalates at reflux of toluene (Scheme 1a). In this case, the catalyst in of Ni(cod)<sub>2</sub> was used the presence 1.2bis(dicyclohexylphosphino)-ethane as external ligand and the dialkyl phosphite had to be introduced in two steps, separated by 12 h for a total 24 h reaction time.<sup>12b</sup> A few years ago, Yamagishi described the synthesis of arylphosphinates by zinc mediated Ni-catalyzed coupling of aryl halides and *H*-phosphinate under mild conditions (Scheme 1b).<sup>12c</sup> However, there was no mention on the possible use of dialkyl phosphites in the reaction and the couplings were only efficient with aryl iodides. Consequently, most methods involving Ni-catalysis can be experimentally-demanding or may require long reaction times at high temperatures to afford phosphorus derivatives. Therefore, a mild, rapid and general method employing simple Ni-precatalyst for the synthesis of aromatic phosphonates remains desirable.

In our group, the electroassisted Ni-catalyzed activation of aryl halides is of constant interest. In previous works, we described the electrochemical reductive cross-coupling of heteroaromatic amines or diazines with aromatic halides using a sacrificial iron or iron/nickel anode process.<sup>13</sup> In this contribution, we disclose the first electrochemically-assisted Ni-catalyzed coupling of aryl bromides with dimethyl phosphite (Scheme 1c). Beyond valuable synthetic applicability, the use of an electrochemical procedure provides new interesting insights into the possible reaction mechanism.





<sup>&</sup>lt;sup>a</sup> Électrochimie et Synthèse Organique, Université Paris Est, ICMPE (UMR 7182), CNRS, UPEC, F- 94320 Thiais France. E-mail: leonel@icmpe.cnrs.fr

<sup>&</sup>lt;sup>+</sup> Electronic Supplementary Information (ESI) available: Detailed general procedures, characterization and copies of the <sup>1</sup>H, <sup>13</sup>C, <sup>19</sup>F and <sup>31</sup>P NMR spectra of all compounds. See DOI: 10.1039/x0xx00000x

#### ARTICLE

#### **Results and discussion**

Table 1 Optimization of the experimental conditions<sup>a</sup>

			MeO	−X + H−P(OMe) <sub>2</sub>	e <sup>-</sup> , nickel foam cathode sacrificial anode [Ni] cat, NEt <sub>3</sub> solvent, rt, intensity	MeO-	P(OMe)₂		
1a (X=Br) 1a' (X=I) 2 2 equiv				3a					
entry	Х	anode	electrolyte	solvent	[Ni] cat (%)	i (A)	NEt₃ (equiv)	time (h) <sup>b</sup>	yield (%) <sup>c</sup>
1	T	Fe	LiCl	DMF	NiBr <sub>s</sub> bpy (10)	0.2	2	3	<10 <sup>d</sup>
2	Ι	Fe/Ni	LiCl	DMF	NiBr <sub>2</sub> bpy (10)	0.2	2	2	60
3	Ι	Ni	LiCl	DMF	NiBr <sub>2</sub> bpy (10)	0.2	2	1.7	56
4	Ι	Zn	LiCl	DMF	NiBr, bpy (10)	0.2	2	3.5	$13^d$
5	Ι	Fe/Ni	Nal	DMF	NiBr <sub>2</sub> bpy (10)	0.2	2	2	46
6	Ι	Fe/Ni	$Bu_a NBF_a$	DMF	NiBr, bpy (10)	0.2	2	2	53
7	Ι	Fe/Ni	Bu <sub>a</sub> NBr	DMF	NiBr <sub>2</sub> bpy (10)	0.2	2	2	64
8	I.	Fe/Ni	Bu₄NBr	DMF	-	0.2	2	3	_e
9	I.	Fe/Ni	Bu₄NBr	DMF	NiBr <sub>2</sub> .xH <sub>2</sub> O (10)	0.2	2	3	_ <sup>e</sup>
10	Ι	Fe/Ni	Bu₄NBr	DMF	NiBr <sub>2</sub> dppe (10)	0.2	2	3	<5 <sup><i>d,f</i></sup>
11	T	Fe/Ni	Bu₄NBr	DMF	NiBr, bpy (10)	0.1	2	4	51
12	I.	Fe/Ni	Bu₄NBr	DMF	NiBr <sub>2</sub> bpy (10)	0.3	2	1	60
13	T	Fe/Ni	Bu <sub>A</sub> NBr	DMF	NiBr, bpy (10)	0.2	-	1	10 <sup><i>d,g</i></sup>
14	T	Fe/Ni	Bu₄NBr	DMF	NiBr <sub>2</sub> bpy (10)	0.2	1	2	54
15	T	Fe/Ni	Bu₄NBr	DMF	NiBr <sub>2</sub> bpy (10)	0.2	3	1.5	58
16	T	Fe/Ni	Bu <sub>a</sub> NBr	DMF/py (9/1)	NiBr, bpy (10)	0.2	-	2	46
17	Ι	Fe/Ni	Bu NBr	CH,CN	NiBr, bpy (10)	0.2	2	2	68
18	Br	Fe/Ni	Bu₄NBr	CH <sub>3</sub> CN	NiBr, bpy (10)	0.2	2	3	86
19	Cl	Fe/Ni	Bu <sub>2</sub> NBr	CH <sub>3</sub> CN	NiBr, bpy (10)	0.2	2	5	_e
20	Br	Fe/Ni	Bu₄NBr	CH <sub>3</sub> CN	NiBr, bpy (5)	0.2	2	3	42 <sup><i>h</i></sup>
21	Br	Fe/Ni	Bu₄NBr	CH <sub>3</sub> CN	NiBr <sub>2</sub> bpy (10)	-	2	5	n.r.

<sup>*a*</sup> Conditions: Reactions were performed under galvanostatic mode in an undivided cell fitted with a metal rod anode surrounded by a nickel foam cathode, starting from 4-anisole halide (4 mmol) and dimethyl phosphite (8 mmol) at room temperature. <sup>*b*</sup> Reactions were monitored by GC and stopped when all the starting halide had been consumed. <sup>*c*</sup> Isolated yield. <sup>*d*</sup> Hydro-dehalogenation product of iodoanisole as the major compound. <sup>*e*</sup> Almost no conversion, only traces of the expected coupling product. <sup>*f*</sup> Partial conversion. <sup>*g*</sup> Corresponding biaryl as the major compound. <sup>*h*</sup> 56% conversion of the starting material after 3 h.

At the outset of the study, the electrochemical cross-coupling of bromoanisole **1a** or iodoanisole **1a'** with dimethyl phosphite **2** was examined, under nickel catalysis, in an undivided cell fitted with a nickel foam cathode and a consumable metal anode. The experimentally reliable galvanostatic mode (no reference electrode, simple power supply) was chosen for the electrolysis. Results are reported in Table 1.

First attempts were carried out at 0.2 A in DMF using LiCl as the supporting electrolyte, NiBr<sub>2</sub>bpy as the catalyst, and triethylamine as a base (Table 1, entries 1-4). Only very limited yield of the coupling product **3a** were obtained when Fe (Table 1, entry 1) or Zn anode (Table 1, entry 4) were used, whereas Fe/Ni (Table 1, entry 2) or Ni (Table 1, entry 3) anodes provided satisfactory yields. Switching the supporting electrolyte to Nal (Table 1, entry 5) or Bu<sub>4</sub>NBF<sub>4</sub> (Table 1, entry 6) did not result in improved yields. However, using Bu<sub>4</sub>NBr instead of LiCl resulted in a slight yield improvement (Table 1, entry 7). Since LiCl is more hygroscopic than Bu<sub>4</sub>NBr, this latter quaternary ammonium salt was thus retained for the rest of the study. Following experiments indicated that the

presence of a nickel pre-catalyst (Table 1, entry 8) as well as a ligand are both mandatory (Table 1, entry 9). However, bpy was found undoubtedly more efficient that a bidentate phosphorus ligand like dppe (Table 1, entry 10), which rather seems to impede the reaction. The effect of the applied current was also analyzed, by first decreasing it to 0.1 A (Table 1, entry 11) and then increasing it to 0.3 A (Table 1, entry 12). These modifications to the initial procedure did not result in the improvement of the reaction yield. The effect of the amount of the base was then examined (Table 1, entries 13-15). Thus, it was observed that a very low yield is obtained in the absence of NEt<sub>3</sub> (Table 1, entry 13), whereas the use of 1 (Table 1, entry 14) or 3 equivalents (Table 1, entry 15) of the amine results in slightly decreased yields. The use of an alcaline cosolvent like pyridine, expected to improve conditions by both acting as a Ni ligand and as a base (Table 1, entry 16), resulted in a failure. However, the reaction yield could be increased to 68% by using acetonitrile as the solvent instead of DMF (Table 1, entry 17). Another important improvement of the reaction was observed by using bromoanisole 1a instead of iodoanisole 1a' (Table 1, Published on 01 June 2018. Downloaded by University of Reading on 01/06/2018 10:52:11.

#### Journal Name

entry 18). In this case, a very good 86% yield was obtained for the coupling product. However, chloroanisole did not react at all (Table 1, entry 19). Finally, the pre-catalyst amount was reduced to 5 mol%, resulting in the important decrease of the reaction yield (Table 1, entry 20). An attempt of coupling in the absence of electricity (Table 1, entry 21) revealed that the reaction did not occur.

The scope of the reaction was then examined under the above optimized conditions (Entry 18 of Table 1). Results are outlined in Table 2.

 Table 2 Scope of (hetero)aryl halides<sup>a,b</sup>



<sup>*a*</sup> General conditions: Iron/nickel (64/36) rod anode, nickel foam cathode, acetonitrile (20 mL), tetrabutylammonium bromide (0.15 mmol), 1,2-dibromoethane (0.3 mmol), NiBr<sub>2</sub>bpy complex (10 mol%), (hetero)aryl halide (4 mmol), dimethylphosphite (8 mmol), I = 0.2 A (1.9-3.7 F/mol), room temperature. <sup>*b*</sup> Isolated yield. <sup>*c*</sup> Hydrodehalogenation product of the (hetero)aryl bromide as the major compound. <sup>*d*</sup> Incomplete conversion. <sup>*e*</sup> The same result was obtained starting from 3-chlorobenzonitrile. <sup>*f*</sup> Complex mixture. <sup>*g*</sup> The coupling was performed with 4 equiv. of dimethyl phosphite and 4 equiv. of trimethylamine in the presence 10 mol% of NiBr<sub>2</sub>bpy.

The reaction was found general and tolerated an important set of aryl halides. Indeed, both electron-rich and electron-deficient aryl bromides underwent the coupling with dimethyl phosphite, providing the corresponding coupling products in good to high yields. Contrary to what had been observed by Han and View Article Online DOI: 10.1039/C8OB00500A ARTICLE

coworkers,<sup>12a</sup> phenyl moieties substituted with electron-donating groups gave best yields of coupling products (3a-3h). It is interesting to note that the coupling can be performed efficiently when phenyl is substituted by 1,2-(methylenedioxy) (3f). However, steric hindrance may play a significant role, as 2-substituted arylphosphonates were obtained in only limited yields with methoxy, ethyl and trifluoromethyl (3c, 3i, 3p). With 1-Bromo-2ethyl substituent, only 20% of the substrate is converted after 4h of electrolysis. It can be noted that 4-fluorobromobenzene, 3fluorobromobenzene and 3-chlorobromobenzene could be successfully employed in the process, the C-F bond (3I and 3m) and, more importantly, the C-Cl bond remaining intact at the end of the coupling reaction (3k).<sup>14</sup> Unfortunately, cyano and oxo substituents seem to hamper the reaction, as the hydro-dehalogenation product or complex mixtures were observed starting from the corresponding bromides, respectively. 1-Bromonaphthalene proved to be usable in the reaction, the coupling product being isolated in satisfactory yield (3u). Moreover, 1,4-dibromobenzene can be phosphonylated in presence of 4 equiv. of dimethyl phosphite to favor dual cross-coupling on the starting substrate (3v). Although the diphosphonylation product 3v proved to be the major product of the reaction, the yield was somewhat limited. This result seems quite logical as we have reported above that electron-deficient aryl bromides furnish the coupling products in more limited yield. In addition, the monophosphonylated bromobenzene and the monophosphonylated debromo-hydrogenation products were also detected in the reaction medium. Finally, heteroaromatic bromides were also explored in the coupling. Unfortunately, whereas 3bromothiophene underwent the reaction with good yield (3w), 3bromopyridine was less efficient, the corresponding coupling product 3x being obtained in far more limited yield. Attempts of performing this latter reaction either in an acetonitrile/pyridine (90/10) mixture or in DMF/pyridine (90/10) did not result in improved yield.<sup>15</sup> In addition other nitrogenated heteroaromatic halides (5-bromopyrimidine, 3-chloro-6-methoxypyridazine, 2chloroquinoline) did not react with dimethyl phosphite. Only reduction products of these substrates were observed.

At the same time, as trimethyl phosphite is supposed to afford the same coupling product than dimethyl phosphite, this was assessed in the electrochemical coupling with 4-bromoanisole under the above-described optimized conditions in the absence of triethylamine (Scheme 2). Unfortunately, low conversion of the starting bromide was noticed after 3 h at 0.2 A.



**Scheme 2** Nickel catalyzed C-P coupling of 4-bromoanisole and trimethyl phosphite.

In the last part of the study, the coupling was applied to other dialkyl phosphites starting from 4-bromoanisole as the model substrate (Scheme 3). Except from di*iso*propyl phosphite where only 25% of conversion is observed, the phosphonylation affords the expected products with good yields.



Scheme 3 Nickel catalyzed C-P coupling of 4-bromoanisole and dialkyl phosphites.

Finally, extension of the process to vinylic bromides was performed (Scheme 4).  $\beta$ -Bromostyrene as well as 1-bromoprop-1-ene provided the corresponding coupling products **5a** and **5b** in good yields without isomerization of the double bond.

	e <sup>-</sup> , nickel foam cathode sacrificial Fe/Ni anode NiBr <sub>2</sub> bpy (10 mol%)	O //~~ <sup>H</sup> (OMe) <sub>2</sub>
R = Ph (dr:92/8), <b>4a 2</b> (2 equiv)	NEt₃ (2 equiv)	R = Ph (dr:92/8), <b>5a</b> , 77%
Me (dr: 90/10), <b>4b</b>	MeCN, rt, 0.2 A, 2 h	Me (dr: 90/10), <b>5b</b> , 58%

**Scheme 4** Nickel catalyzed C-P coupling of vinylic bromides with dimethyl phosphite.

A possible reaction mechanism (Scheme 5) would imply an initial cathodic reduction of the Ni<sup>II</sup> pre-catalyst to lead to the active Ni<sup>0</sup> species, followed by oxidative addition of the halide (step (a)) and reductive electron transfer (step (b)) to generate a Ni<sup>I</sup> species I.<sup>16</sup> Dimethyl phosphite would then add (step (c)) to form a nickel-phosphorus ylide II. Proton abstraction on the OH group of II by triethylamine (step (d)) would lead to the key nickel ate complex III, which would be oxidized (possibly at the anode or more probably by metal salts,<sup>17</sup> step (e)) to form Ar-Ni<sup>II</sup>P(O)(OMe)<sub>2</sub> IV. Reductive elimination (step (f)) from this intermediate would afford the final product **3** together with the catalyst of the process Ni<sup>0</sup>.



Scheme 5 Possible reaction mechanism.

#### Conclusions

In summary, the results reported herein indicate that electrochemistry can represent a mild and efficient methodology to access to aromatic and heteroaromatic phosphonates by cross-coupling of aryl and heteroaryl bromides with dimethyl phosphite. The process can be extended to other dialkyl phosphites. Among the previously described Ni-catalyzed procedures, this is the sole allowing such kind of cross-coupling at room temperature and providing access to the final compounds within hours. The proposed mechanism involves a Red/Ox process through the formation of a transient Ni ate complex. The extension of this electrochemical process to other vinyl bromides derivatives is currently underway.

#### **Conflicts of interest**

There are no conflicts to declare.

#### Acknowledgements

The authors are grateful to the CNRS and the Université Paris-Est Créteil for financial support on this work. AO acknowledges the Institut Universitaire de Technologie de Créteil-Vitry for a temporary Assistant Professor position.

#### Notes and references

- For some recent reviews, see: (a) R. Francke and R. D. Little, *Chem. Soc. Rev.*, 2014, **43**, 2492; (b) R. Francke, *Beilstein J. Org. Chem.*, 2014, **10**, 2858; (c) M. Yan, Y. Kawamata and P. S. Baran, *Chem. Rev.*, 2017, **117**, 13230; (d) Y. Jiang, K. Xu and C. Zeng, *Chem. Rev.*, 2017, DOI: 10.1021/acs.chemrev.7b00271; (e) Y. Okada and K. Chiba, *Chem. Rev.*, 2017, DOI: 10.1021/acs.chemrev.7b00400.
- For some selected examples, see: (a) J.-Y. Nédélec, J. 2 M. Troupel, in *Electrochemistry* Périchon and Electroorganic Synthesis: Bond Formation at Anode and Cathode, ed. E. Steckhan, Springer Berlin Heidelberg, 1997, 141-173; (b) E. Duñach, D. Franco and S. Olivero, Eur. J. Org. Chem., 2003, 1605; (c) H. Wu and K. D. Moeller, Org. Lett., 2007, 9, 4599; (d) J. A. Miranda, C. J. Wade and R. D. Little, J. Org. Chem., 2005, 70, 8017; (e) B. A. Frontana-Uribe, R. D. Little, J. G. Ibanez, A. Palma and R. Vasquez-Medrano, Green Chem., 2010, 12, 2099; (f) J.-i. Yoshida, K. Kataoka, R. Horcajada and A. Nagaki, Chem. Rev., 2008, 108, 2265; (g) C. Gütz, M. Selt, M. Bänziger, C. Bucher, C. Römelt, N. Hecken, F. Gallou, T. R. Galvão and S. R. Waldvogel, Chem. Eur. J., 2015, 21, 13878; (h) L. Schulz, M. Enders, B. Elsler, D. Schollmeyer, K. M. Dyballa, R. Franke and S. R. Waldvogel, Ang. Chem. Int. Ed., 2017, 56, 4877; (i) T. Gieshoff, A. Kehl, D. Schollmeyer, K. D. Moeller and S. R. Waldvogel, Chem. Commun., 2017, 53, 2974; (j) P. Wang, S. Tang, P. Huang and A. Lei, Angew. Chem. Int. Ed., 2017, 56, 3009; (k) S. Zhang, F. Lian, M. Xue, T. Qin, L. Li, X. Zhang and K. Xu, Org. Lett., 2017, 19, 6622; (/) N. Sauermann, T. H. Meyer, C. Tian and L. Ackermann, J. Am. Chem. Soc., 2017, 139, 18452; (m) S. Zhang, L. Li, H. Wang, Q. Li, W. Liu, K. Xu and C. Zeng, Org. Lett., 2018, 20, 252.
- 3 (a) E. J. Horn, B. R. Rosen, Y. Chen, J. Tang, K. Chen, M. D. Eastgate and P. S. Baran, *Nature*, 2016, **533**, 77; (b) C. Li, Y. Kawamata, H. Nakamura, J. C. Vantourout, Z. Liu, Q. Hou, D. Bao, J. T. Starr, J. Chen, M. Yan and P. S. Baran, *Angew. Chem. Int. Ed.*, 2017, **56**, 13088; (c) Y. Kawamata, M. Yan, Z. Liu, D.-H. Bao, J. Chen, J. T. Starr and P. S. Baran, *J. Am. Chem. Soc.*, 2017, **139**, 7448; (d) A. G. O'Brien, A. Maruyama, Y. Inokuma, M. Fujita, P. S. Baran and D. G. Blackmond, *Angew. Chem. Int. Ed.*, 2014, **53**, 11868; (e) B. R. Rosen, E. W. Werner, A. G. O'Brien and P. S. Baran, *J. Am. Chem. Soc.*, 2014, **136**, 5571.
- For recent reviews, see: (a) N. A. Romero and D. A. Nicewicz, Chem. Rev., 2016, 116, 10075; (b) C. K. Prier, D. A. Rankic and D. W. C. MacMillan, Chem. Rev., 2013, 113, 5322. (c) For an example of photocatalytic C-P coupling, see: R. S. Shaikh, S. J. S. Düsel and B. König, ACS Catalysis, 2016, 6, 8410.

Page 4 of 5

DOI: 10.1039/C8OB00500A

Journal Name

Published on 01 June 2018. Downloaded by University of Reading on 01/06/2018 10:52:11

Published on 01 June 2018. Downloaded by University of Reading on 01/06/2018 10:52:11

- (a) T. Bock, H. Möhwald and R. Mülhaupt, Macromol. Chem. Phys., 2007, 208, 1324; (b) F.-M. Hsu, C.-H. Chien, C.-F. Shu, C.-H. Lai, C.-C. Hsieh, K.-W. Wang and P.-T. Chou, Adv. Funct. Mater., 2009, 19, 2834; (c) O. R. Evans, D. R. Manke and W. Lin, Chem. Mater., 2002, 14, 3866; (d) S. M. Zakeeruddin, M. K. Nazeeruddin, P. Pechy, F. P. Rotzinger, R. Humphry-Baker, K. Kalyanasundaram, M. Grätzel, V. Shklover and T. Haibach, Inorg. Chem., 1997, 36, 5937; (e) S. Edizer, G. Sahin and D. Avci, J. Polym. Sci. A: Polym. Chem., 2009, 47, 5737.
- 6 (a) Q. Dang, Y. Liu, D. K. Cashion, S. R. Kasibhatla, T. Jiang, F. Taplin, J. D. Jacintho, H. Li, Z. Sun, Y. Fan, J. DaRe, F. Tian, W. Li, T. Gibson, R. Lemus, P. D. van Poelje, S. C. Potter and M. D. Erion, J. Med. Chem., 2011, 54, 153; (b) P. Lassaux, M. Hamel, M. Gulea, H. Delbrück, P. S. Mercuri, L. Horsfall, D. Dehareng, M. Kupper, J.-M. Frère, K. Hoffmann, M. Galleni and C. Bebrone, J. Med. Chem., 2010, 53, 4862; (c) K. Moonen, I. Laureyn and C. V. Stevens, Chem. Rev., 2004, 104, 6177; (d) R. Engel, Chem. Rev., 1977, 77, 349; (e) C. Liu, S. G. Dumbre, C. Pannecouque, C. Huang, R. G. Ptak, M. G. Murray, S. De Jonghe and P. Herdewijn, J. Med. Chem., 2016, 59, 9513; (f) S. J. Hecker and M. D. Erion, J. Med. Chem., 2008, 51, 2328; (g) V. Pham, W. Zhang, V. Chen, T. Whitney, J. Yao, D. Froese, A. D. Friesen, J. M. Diakur and W. Haque, J. Med. Chem., 2003, 46, 3680; (h) J.-J. Shie, J.-M. Fang, S.-Y. Wang, K.-C. Tsai, Y.-S. E. Cheng, A.-S. Yang, S.-C. Hsiao, C.-Y. Su and C.-H. Wong, J. Am. Chem. Soc., 2007, 129, 11892.
- 7 (a) M.-N. Birkholz, Z. Freixa and P. W. N. M. van Leeuwen, *Chem. Soc. Rev.*, 2009, **38**, 1099; (b) M. McCarthy and P. J. Guiry, *Tetrahedron*, 2001, **57**, 3809; (c) W. Tang and X. Zhang, *Chem. Rev.*, 2003, **103**, 3029; (d) D. S. Surry and S. L. Buchwald, *Chem. Sci.*, 2011, **2**, 27; (e) H. Fernández-Pérez, P. Etayo, A. Panossian and A. Vidal-Ferran, *Chem. Rev.*, 2011, **111**, 2119.
- 8 For some reviews, see: (a) F. M. J. Tappe, V. T. Trepohl and M. Oestreich, *Synthesis*, 2010, 3037; (b) C. S. Demmer, N. Krogsgaard-Larsen and L. Bunch, *Chem. Rev.*, 2011, **111**, 7981; (c) A. L. Schwan, *Chem. Soc. Rev.*, 2004, **33**, 218; (d) S. Van der Jeught and C. V. Stevens, *Chem. Rev.*, 2009, **109**, 2672.
- 9 (a) T. Hirao, T. Masunaga, Y. Ohshiro and T. Agawa, *Tetrahedron Lett.*, 1980, 21, 3595; (b) T. Hirao, T. Masunaga, Y. Ohshiro and T. Agawa, *Synthesis*, 1981, 56; (c) H. Toshikazu, M. Toshio, Y. Naoto, O. Yoshiki and A. Toshio, *Bull. Chem. Soc. Jpn*, 1982, 55, 909.
- 10 (a) M. Kalek, M. Jezowska and J. Stawinski, Adv. Synth. Cat., 2009, 351, 3207; (b) W. Xu, G. Hu, P. Xu, Y. Gao, Y. Yin and Y. Zhao, Adv. Synth. Cat., 2014, 356, 2948; (c) O. Berger, C. Petit, E. L. Deal and J.-L. Montchamp, Adv. Synth. Cat., 2013, 355, 1361; (d) K. Xu, H. Hu, F. Yang and Y. Wu, Eur. J. Org. Chem., 2013, 319; (e) Y. Belabassi, S. Alzghari and J.-L. Montchamp, J. Organomet. Chem., 2008, 693, 3171; (f) M. Kalek, A. Ziadi and J. Stawinski, Org. Lett., 2008, 10, 4637; (g) E. L. Deal, C. Petit and J.-L. Montchamp, Org. Lett., 2011, 13, 3270; (h) A. J. Bloomfield and S. B. Herzon, Org. Lett., 2012, 14, 4370; (i) L. J. Gooßen and M. K. Dezfuli, Synlett, 2005, 445.
- (a) B. Xiong, M. Li, Y. Liu, Y. Zhou, C. Zhao, M. Goto, S.-F. Yin and L.-B. Han, Adv. Synth. Cat., 2014, **356**, 781; (b) J. Ballester, J. Gatignol, G. Schmidt, C. Alayrac, A.-C. Gaumont and M. Taillefer, ChemCatChem, 2014, **6**, 1549; (c) H. Rao, Y. Jin, H. Fu, Y. Jiang and Y. Zhao, Chem. Eur. J., 2006, **12**, 3636; (d) C. Huang, X. Tang, H. Fu, Y. Jiang and Y. Zhao, J. Org. Chem., 2006, **71**, 5020; (e) D. Gelman, L. Jiang and S. L. Buchwald, Org. Lett., 2003, **5**, 2315; (f) M. Stankevič and A. Włodarczyk, Tetrahedron, 2013, **69**, 73.
- 12 (a) Y.-L. Zhao, G.-J. Wu, Y. Li, L.-X. Gao and F.-S. Han, Chem. Eur. J., 2012, 18, 9622; (b) J. Yang, J. Xiao, T. Chen and L.-B. Han, J. Org. Chem., 2016, 81, 3911; (c) A. Kinbara, M. Ito, T.

Abe and T. Yamagishi, *Tetrahedron*, 2015, **71**, 7614; (*d*) X. Zhang, H. Liu, X. Hu, G. Tang, J. Zhu and Y. Zhao, *Org. Lett.*, 2011, **13**, 3478; (*e*) C. Shen, G. Yang and W. Zhang, *Org. Biomol. Chem.*, 2012, **10**, 3500; (*f*) Q. Yao and S. Levchik, *Tetrahedron Lett.*, 2006, **47**, 277.

- 13 (a) S. Sengmany, E. Léonel, F. Polissaint, J.-Y. Nédélec, M. Pipelier, C. Thobie-Gautier and D. Dubreuil, J. Org. Chem., 2007, 72, 5631; (b) S. Sengmany, E. Le Gall and E. Léonel, Molecules, 2011, 16, 5550; (c) S. Sengmany, A. Vitu-Thiebaud, E. Le Gall, S. Condon, E. Léonel, C. Thobie-Gautier, M. Pipelier, J. Lebreton and D. Dubreuil, J. Org. Chem., 2013, 78, 370; (d) S. Sengmany, S. Vasseur, A. Lajnef, E. Le Gall and E. Léonel, Eur. J. Org. Chem., 2016, 4865.
- 14 To the best of our knowledge, this is the first example of a nickel-catalyzed phosphonylation reaction preserving such aromatic C-Cl bond.
- 15 Addition of pyridine to the medium revealed beneficial effects in related reaction systems involving heteroaryl halides. For details, see: R. Rahil, S. Sengmany, E. Le Gall and E. Léonel, *Synthesis*, 2018, **50**, 146.
- 16 It can be noted that the formation of transient Ni<sup>1</sup> species has already been reported by our group in reductive couplings involving aryl or heteroaryl halides, see ref. (13c).
- 17 No cross-coupling occurs when the reaction is performed in a divided cell or with non oxidable anode materials like platinum or graphite. In addition, it was found that after 3 h electrolysis (2160 C), the anode has lost 490 mg (approx. 8.6 mmol) of its mass and conversely, the cathode has gained 440 mg of its mass. The major part of the electrogenerated metal salts is reduced at the surface of the cathode (black particles cover).