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Microwaves and Aqueous Solvents Promote the Reaction of Poorly Nucleophilic Anilines with a Zincke Salt

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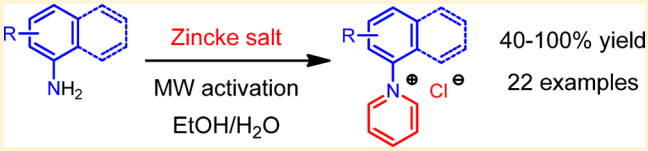
Supporting Information

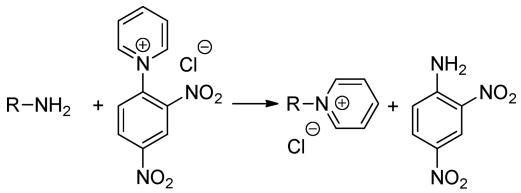
ABSTRACT: The Zincke reaction allows the transformation of primary amines into their respective *N*-alkylated or *N*-arylated pyridinium salts. While nucleophilic primary amines (typically, aliphatic primary amines) often lead to quantitative reactions and has been documented profusely, the use of poorly nucleophilic amines still requires an in depth account. To date, the lack of nucleophilicity of the amines is redhibitory. The subject addressed in this article is a series of primary amines deriving from aniline having been engaged in Zincke reactions. Efficient transformations were obtained, even when conducted on electronically deactivated, eventually also sterically hindered, substrates. This was achieved by the combined use of microwave activation and aqueous solvents. Under our conditions, the role of water revealed indeed crucial to avoid the self-degradation of the Zincke salt, the reagent of the reaction.



INTRODUCTION

The Zincke reaction allows the transformation of primary amines **1** into their respective *N*-alkyl- or *N*-aryl-pyridinium salts **2** (Scheme 1).[1,2] This reaction usually requires *N*-(2,4-dinitrophenyl)-pyridinium chloride **3** as reagent, the latter being commonly called Zincke salt.[3] Following a S_N(ANRORC) mechanism (i.e., a nucleophilic substitution by adding the nucleophile, ring opening, and ring closure),[4−6] the Zincke reaction consists of a transannulation reaction by transferring the Zincke salt pyridinium ring carbon chain onto the nitrogen atom of the primary amine. Concomitantly, 2,4-dinitroaniline **4** is released as byproduct. The Zincke reaction is typically performed under thermal activation but also proceeds under unconventional activation methods such as microwaves or ultrasonic activation.[7−10] The ease with which this reaction is carried out makes it the reaction of choice when preparing *N*-substituted pyridinium salts either in solution or on solid-phase.[11,12] The extensive applicability of pyridinium salts, prepared per se or as intermediates in heterocyclic chemistry, explains the abundant literature mentioning the use of the Zincke reaction.[13]

Scheme 1. Zincke Reaction



The Zincke reaction commonly results in good to excellent yields, especially when using aliphatic primary amines. However, an overview of the literature allows identifying conditions leading to moderate or even low yields. Such situations are typically associated with the formation of macrocycles[14,15] and/or the use of aniline derivatives as primary amines.[16−20]

Recently, we described the preparation of an *N*-arylated pyridinium.[21] Later, the toxicological evaluation of this compound showed its ability to induce cell death by apoptosis on human neuroblastoma cells (SH-SY5Y).[22] Based on these preliminary results, we next aimed to prepare a series of *N*-arylated pyridiniums by Zincke reaction, including challenging compounds deriving from poorly nucleophilic anilines. In order to obtain these target pyridinums in good yields, we logically envisioned the microwave activation.[23,24] Under these conditions however and when poorly nucleophilic anilines are used as primary amines, side reactions turn into a challenge as they are also significantly accelerated.

In the present article, we describe the efficient synthesis by the Zincke reaction of *N*-arylated pyridiniums with a focus on compounds deriving from poorly nucleophilic anilines, most of which remain inaccessible under conventional activation methods and consequently constitute a sparsely described class of compounds. We also demonstrate the crucial role of water used as cosolvent in order to achieve their preparation.

RESULTS AND DISCUSSION

Stability Study on the Zincke Salt 3. As the microwave heating allows reaching very high temperatures, a stability study was conducted on the Zincke salt **3** (Scheme 1). For this, the salt was dissolved in different solvents and then heated under microwave irradiation and under pressure at 130 and 150 °C.

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The degradation of the salt **3** was measured by ^{1}H NMR in DMSO-d_6, in the presence of dichloroethane used as external standard (Table 1).

Table 1. Stability of the Zincke Salt 3 in Various Solvents[a]

		degradation of **3** [%][b]	
entry	solvent	130 °C	150 °C
1	MeCN	95	98
2	*i*-PrOH	50	97
3	EtOH	20	76
4	H_2O	0	0

[a]Conditions: MW activation under pressure, 5 min, Zincke salt **3** (0.2 mmol), solvent (1 mL). [b]Measured by ^{1}H NMR in DMSO-d_6 in the presence of dichloroethane as external standard.

The stability study first showed that the Zincke salt **3** disappeared almost completely after 5 min of heating in MeCN at 130 and 150 °C (entry 1). The presence of chlorodinitrobenzene and pyridine highlighted by ^{1}H NMR led to conclude unambiguously that a S_NAr reaction occurred by *ipso* substitution of the pyridinium ring by chloride ions—which is in fact the reverse reaction of the formation reaction of the Zincke salt. It should be noted that this reaction of self-degradation, consecutive to the nucleophilic attack of chloride ions, has already been reported. The solution proposed to avoid this self-degradation was a replacement by salt metathesis of chloride ions by non-nucleophilic alkyl sulfates.[11,25]

The stability study also showed that protic solvents such as alcohols were able to minimize this reaction of self-degradation due to their ability to solvate chloride ions.[26] As expected, the more the solvation was effective, the more the self-degradation was limited. Thus, EtOH, more acidic than *i*-PrOH, revealed to be also more efficient to preserve the Zincke salt **3** (entries 2 and 3). The increase of molecular agitation due to the raising of the temperature, by minimizing the solvation effect, also resulted in a significant increase of the self-degradation. It should be noted that the solvents commonly used for the Zincke reaction are C1−C5 alcohols, typically EtOH or *n*-BuOH. The fact that excellent yields can be obtained with this type of solvent suggests that in the presence of sufficiently nucleophilic primary amines (typically, aliphatic amines) this possibly competitive self-degradation reaction—in reality—remains limited, even under microwave activation.[7]

Considering the use of water as solvent, it was found that in this medium, the Zincke salt **3** remained intact after 5 min of heating at 130 and even 150 °C (entry 4). It should be noted that the use of water as solvent for the Zincke reaction has already been described, including under microwave irradiation. However, its protective effect by solvation of chloride ions has, to our knowledge, never been demonstrated nor even mentioned.[8,27] The lipophilicity of some primary amines unfortunately made it impossible to use only water as the reaction solvent. Considering logically using a EtOH/H_2O binary solvent, we endeavored to determine the optimal proportion of these two cosolvents for an effective implementation of the Zincke reaction.

Optimization of the Binary Solvent. The optimization of the EtOH/H_2O binary solvent was performed under microwave irradiation at 150 °C and under pressure on a reaction between the Zincke salt **3** and *p*-toluidine **1a**, the latter being chosen precisely for its lipophilicity (Figure 1). The yields in the expected salt **2a** and of the self-degradation of the Zincke salt **3** were measured after 5 min of reaction by ^{1}H NMR in DMSO-d_6, in the presence of diethyl fumarate used as external standard.

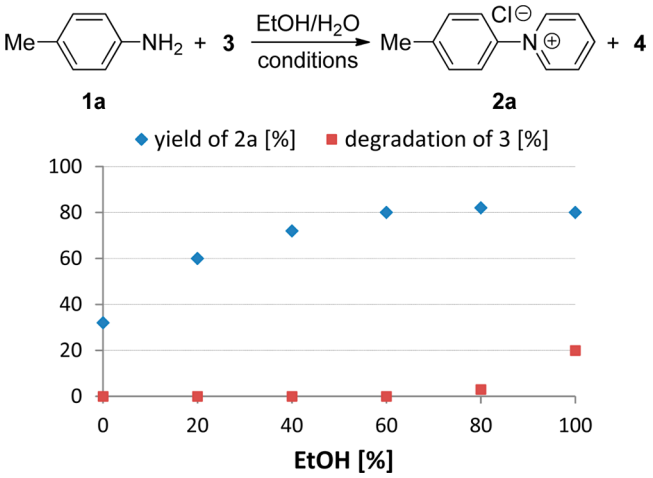

Figure 1. Determination of the optimal composition of the EtOH/H_2O binary solvent. Conditions: MW activation (150 °C, under pressure), 5 min, Zincke salt **3** (0.2 mmol), **1a** (2 equiv), solvent (1 mL). Yields and degradation were measured by ^{1}H NMR in DMSO-d_6 in the presence of diethyl fumarate as external standard.

This study showed that the use of water as single reaction solvent preserved the Zincke salt **3**, merely gave a limited yield of 32% of the expected salt **2a**. The lack of solubility of the aniline **1a** in the reaction mixture presumably explains this result. The addition of EtOH helped to significantly improve the yields while limiting the self-degradation of the Zincke salt **3**. From this study, it appeared that a EtOH/H_2O mixture, with volume ratio in the range of (60/40) to (80/20), was the optimal solvent to carry out Zincke reactions.

Reactivity Study on the Aniline Derivative Used as Primary Amine. As second partner of the reaction, the aniline derivative used as primary amine was also subjected to a preliminary study. More precisely, it appeared useful to identify the parameters relevant to anticipate its reactivity with the Zincke salt **3**. For this, a series of variously functionalized monosubstituted anilines was engaged in a Zincke reaction, under conventional heating at 80 °C, for 96 h, in an EtOH/H_2O (60/40) binary solvent. Yields were measured by ^{1}H NMR in DMSO-d_6, in the presence of diethyl fumarate used as external standard.

This study showed a good correlation between the yield of the reaction and the pK_a of the conjugate acid of the considered aniline derivative (Figure 2).[28−31] In our conditions, compounds associated with pK_a superior to 3.75 gave the corresponding salt in quantitative yields. Conversely, aniline derivatives associated with pK_a inferior to 2.75, characterized by the electronic deactivation of the nitrogen atom, eventually associated with a steric hindrance, gave the expected salts in low yields of about 20% maximum. It should be noted that when no or incomplete conversions were observed, the amount of starting materials was measured by NMR. The measured quantities were consistent with those expected, thus confirming the absence of any competitive self-degradation reaction.

It should be noted that a reaction was carried out in the presence of a larger excess of nonreactive aniline. The Zincke salt **3** (0.1M) was thus engaged with 6 equiv of *o*-trifluoromethyl aniline **1b**. After 18 weeks of reaction under

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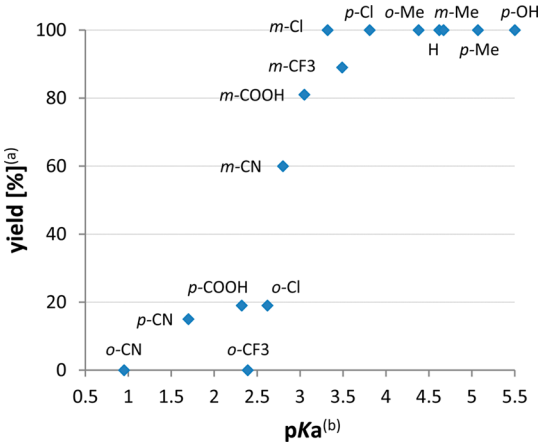


Figure 2. Reactivity study on aniline derivatives. Conditions: conventional heating (80 °C), 96 h, Zincke salt **3** (0.2 mmol), $RC_6H_4NH_2$ (2 equiv), EtOH/H_2O: 60/40 (1 mL). (a) Yields were measured by ^{1}H NMR in DMSO-d_6 in the presence of diethyl fumarate as external standard. (b) For pK_a values, see refs 28−31.

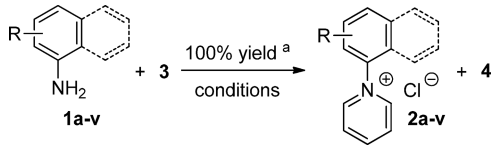
conventional heating in refluxing EtOH, an inseparable (and thus unusable) mixture of Zincke salt and expected salt **2b** was obtained. The incomplete conversion of about 78% measured by NMR confirmed the need to develop a protocol both applicable to poorly nucleophilic primary amines and reasonably feasible from a practical viewpoint.

Implementation of the Zincke Reaction with Aniline Derivatives. A series of aniline derivatives **1** was put to react with the Zincke salt **3**, under microwave irradiation and under pressure in an EtOH/H_2O (60/40) binary solvent. Three different protocols were set up depending on the pK_a of the primary amine used. The monitoring of the reactions was carried out by ^{1}H NMR in DMSO-d_6, in the presence of diethyl fumarate used as external standard. To avoid obtaining mixtures of salts, reaction times were adjusted so that the yields in expected salts **2** were quantitative (Table 2).

Reactions involving aniline derivatives whose pK_a of conjugate acids is inferior to 2.75 required experimental conditions defined in protocol A, with the noticeable exception however of the *p*-aminobenzoic acid **1f** (entry 4). Leading quantitatively to the expected salts, protocol A was characterized by the use of a large excess of amine (12 equiv vs Zincke salt **3**) and prolonged heating times (60−75 min) at 150 °C (entries 1, 2, 3, 5, and 6). The large excess of amine was necessary in order to complete the reaction. The competing nucleofugalities of the dinitroaniline and of the amine to be quaternized may result in the establishment of an equilibrium in solution, which only a large excess of amine is able to completely displace. In this series, 4′-aminoacetophenone **1e** which has revealed to be totally unreactive under conventional activation,[24] was successfully converted into its corresponding salt (entry 3). It should be also noted that because of its lipophilicity, *o*-trifluoromethyl aniline **1b** revealed to be slightly soluble in the EtOH/H_2O (60/40) binary solvent. For this reason, a (80/20) mixture enriched in EtOH was used. This resulted in a partial self-degradation of the Zincke salt **3** into chlorodinitrobenzene and the formation of salt **2b** in 50% yield before purification (entry 5).

In the case of reactions involving this kind of poorly nucleophilic aniline derivatives, the S_NAr between pyridine and the corresponding chlorinated derivatives could be considered

Table 2. Quantitative Zincke Reactions with Aniline Derivatives 1a−v



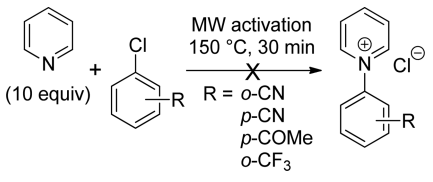
entry	pK_a	R	aniline	protocol[b]	time [min]	isolated yield [%]
1	0.95[28]	*o*-CN	**1c**	A	60	84
2	1.70[31]	*p*-CN	**1d**	A	60	88
3	2.19[28]	*p*-COMe	**1e**	A	60	84
4[c]	2.32[29]	*p*-COOH	**1f**	B	60	38[90][g]
5[d]	2.39[30]	*o*-CF_3	**1b**	A	60	8[16][g]
6	2.62[29]	*o*-Cl	**1g**	A	75	84
7	2.80[31]	*m*-CN	**1h**	B	60	100
8	3.05[29]	*m*-COOH	**1i**	B	60	78
9	3.32[29]	*m*-Cl	**1j**	B	40	91
10	3.49[29]	*m*-CF_3	**1k**	B	60	73
11	nd	*p*-$CONH_2$	**1l**	B	60	80
12	nd	*m*-$CONH_2$	**1m**	B	20	64
13	3.81[29]	*p*-Cl	**1n**	C	30	93
14	3.92[29]	1-naphtyl	**1o**	B	20	70
15[e]	4.17[29]	*m*-OH	**1p**	C	40	63[84][g]
16	4.38[29]	*o*-Me	**1q**	C	15	94
17	4.49[29]	*o*-OMe	**1r**	C	30	80
18	4.62[29]	H	**1s**	C	20	100
19	4.67[29]	*m*-Me	**1t**	C	20	95
20[f]	4.72[29]	*o*-OH	**1u**	C	30	31[77][g]
21	5.07[29]	*p*-Me	**1a**	C	15	96
22	5.50[29]	*p*-OH	**1v**	C	20	63

[a]Chemical yields were measured by ^{1}H NMR in DMSO-d_6 in the presence of diethyl fumarate as external standard. [b]Conditions: MW activation, under pressure, Zincke salt **3** (0.2 mmol), EtOH/H_2O: 60/40 (1 mL). Protocol A: 150 °C, **1** (12 equiv). Protocol B: 150 °C, **1** (3 equiv). Protocol C: 130 °C, **1** (1.2−2 equiv). [c]The salt **2f** was obtained in 42% chemical yield in mixture with side products. [d]Reaction conducted in a 80/20 mixture of EtOH/H_2O; the salt **2b** was obtained in 50% chemical yield (a partial decomposition of the Zincke salt **3** into chlorodinitrobenzene was observed by NMR). [e]The salt **2p** was obtained in 85% chemical yield in mixture with side products. [f]The salt **2u** was obtained in 40% chemical yield in mixture with side products. [g]Corrected yield, taking into account the chemical yield inferior to 100%.

for the preparation of pyridinium salts. For this purpose, reactions were conducted under microwaves and under pressure at 150 °C in an EtOH/H_2O (60/40) binary solvent (Scheme 2).

Despite the drastic conditions (150 °C in the presence of 10 equiv of pyridine), no traces of the desired salts could be observed after 30 min of reaction. Consequently, the use of the S_NAr reaction as an alternative to the Zincke reaction revealed

Scheme 2. Possible Access to Pyridinium Chlorides by S_NAr



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to be totally ineffective, even in the case of these electronically deactivated substrates.

Reactions involving aniline derivatives **1h−k**, whose pK_a of conjugate acids is between 2.75 and 3.75, required the use of only 3 equiv of amine at 150 °C (these conditions characterizing protocol B) to give quantitatively the corresponding salts **2h−k** (entries 7−10). The salt deriving from the *p*-aminobenzoic acid **1f** was obtained by observing these experimental conditions. According to protocol B, anilines derivatives **1l** and **1m**, bearing an aminocarbonyl substituent (pK_a unknown), gave the corresponding salts **2l−m** (entries 11−12).

Aniline derivatives whose pK_a of conjugate acids is superior to 3.75, were quantitatively converted into their corresponding salts following protocol C, characterized by the use of a slight excess of amine (from 1.2 to 2 equiv), the reaction temperature lowered to 130 °C and reaction time limited to 40 min (entries 13, 15−22). It should be noted, however, that despite a pK_a of 3.92, naphthylamine **1o** quantitatively gave the corresponding salt **2o** following the protocol B set up for less reactive aniline derivatives **1h−m** (entry 14). This is in accordance with a previous study showing the total lack of reactivity of **1o** when engaged in a Zincke reaction under ultrasonic activation.[10] This behavior, presumably explained by the steric hindrance of the naphtyl group, illustrates the limits of considering only pK_a values to anticipate the reactivity of primary amines engaged in the Zincke reaction. In this series, aminophenols revealed a variable reactivity, depending on their substitution pattern. Engaged in reaction with the Zincke salt **3**, *o*-, *m*- and *p*-aminophenols **1u**, **1v** and **1p** gave indeed the expected salts in 40, 85 and 100% yield respectively (entries 20, 15 and 22). The purification of the crude mixture obtained from the *o*-aminophenol **1u**, allowed isolating a major side-product, fully characterized after recrystallization in *i*-PrOH, and unambiguously attributed to be the diarylamine **5** (Figure 3).

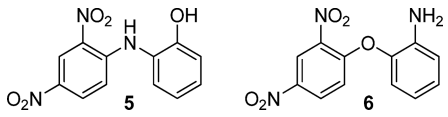

Figure 3. Identification of a side-product of the Zincke reaction.

Resulting from a S_NAr reaction, the diarylamine **5** may be formed as a consequence of the direct nucleophilic attack of the amino group of the aminophenol **1u**. Alternatively, it may also resulted from a first substitution led by the hydroxyl group of **1u**,[32] thus giving the intermediate diaryl ether **6**. In such hypothesis, the subsequent Smiles rearrangement of **6** into **5** demonstrated at room temperature and in the presence of water, would occur.[33,34] Whatever the mechanism involved, it seems that the possibility to form such diarylamines explains the variable yields in the expected salt, obtained when using aminophenols as primary amine. Interestingly, the protection of the hydroxyl group under the form of a methyl ether (as in the case of *o*-anisidine **1r**) prevented the formation of any side-products and gave quantitatively the expected salt **2r** (entry 17).

Due to their polarity, salts obtained by the Zincke reaction are known to be purified with difficulty.[35] When reactions are conducted on large scale, however, the expected salts can be purified by recrystallization.[36] Regarding compounds **2a−v**, they could be separated from the dinitroaniline **4** and from the excess of amine by chromatography on reversed phase.[37] Purification yields were generally good, ranging from 63 to 100%. It should be noted that salt **2b** was isolated with an overall yield of 8% (of 16% taking into consideration the yield of only 50% measured in the crude mixture) indicating a significant loss of material during the purification step (entry 5). Deriving from an aniline derivative among the less basic, it is possible that this salt degraded during purification due to its electrophilicity.

CONCLUSION

This work allowed pointing out the limit of the Zincke reaction when conducted under conventional heating. It also allowed identifying the kind of primary amines for which the use of more efficient activation methods was not only useful but also necessary. In this regard, microwave activation revealed to be the ideal method of obtaining quantitative reactions, even when conducted on substrates for which the conventional heating or even unconventional methods, such as ultrasonic activation, remain inoperative. Under these conditions, however, the use of water is crucial in order to preserve Zincke salt **3** from self-degradation by solvation of chloride ions. With exception to the particularly hindered substrates, as highlighted in this study, the good correlation observed between pK_a values and the reactivity of anilines derivatives should enable to choose the correct protocol for the quantitative transformation of any primary amine of known pK_a. The present study should consequently help to significantly extend the scope of the Zincke reaction, especially regarding poorly nucleophilic primary amines.

EXPERIMENTAL SECTION

Materials and Methods. All chemicals and solvents were used as received without purification. EtOH purity was of analysis grade (water ≤200 mg/kg) and water was distillated. The Zincke salt **3** was prepared according to the reported procedure.[38] Reactions were carried out in closed vials using a CEM-Discover apparatus, provided with a fiber optic temperature control. Automated purification of salts **2a−v** was performed on C18 reversed-phase (40 g cartridges). NMR spectra were recorded in DMSO-d_6 or MeOH-d_4. Chemical shifts (δ) are reported in part per million (ppm) relative to the residual no-deuterated solvent signal. Coupling constant values (J) are given in hertz (Hz) and refer to apparent multiplicities indicated as follows: s (singlet); d (doublet); t (triplet); q (quadruplet); m (multiplet); dd (doublet of doublets); td (triplet of doublets); bp (broad peak). IR spectra were recorded on a spectrometer equipped with a diamond ATR unit, between 500 and 4000 cm^{-1}. Wavenumbers (ν) are expressed in cm^{-1} at their maximum intensity. LC−MS analyses were performed with a reversed-phase chromatographic system (MeOH was used as eluent in isocratic mode) coupled with a single-quadrupole mass spectrometer (ESI^+ mode, 50 V, 400 °C). GC−MS analysis was performed in ionization mode (EI^+).

General Procedure for the Synthesis of Pyridinium Salts 2a−v. Into a microwave vial (10 mL) equipped with a magnetic stirrer, were successively added the Zincke salt **3**, the specified quantity of aniline derivative **1**, and the EtOH/H_2O binary solvent (1 mL). Unless specified, the reaction was conducted on 0.2 mmol (56.2 mg) of Zincke salt **3**, in a EtOH/H_2O (60/40) mixture. The reaction was performed in closed vial for the specified time, and under microwaves (150 W) at the specified temperature. After completion of the reaction, the mixture was concentrated under vacuum. The crude product was purified by chromatography on reverse phase, according to the specified method (vide infra). The expected salt was obtained after evaporation of the mobile phase.

General Procedure for the Purification of Pyridinium Salts 2a−v. Method 1: impurities were eluted by successively Et_2O (5

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column volumes) and MeCN (5 column volumes); the expected salt was obtained after elution with MeOH (3 column volumes). Method 2: impurities were eluted by MeCN (5 column volumes) and the expected salt was obtained after elution with MeOH (3 column volumes). Method 3: the expected salt was obtained in the very first fraction eluted with a H_2O/MeOH (95/5) mixture.

*1-(p-Tolyl)pyridin-1-ium chloride (**2a**).*[36,39] **2a** was prepared from **1a** (25.7 mg, 0.24 mmol, 1.2 equiv) after 20 min of heating under microwaves at 130 °C, and purified according to method 2. **2a** was obtained under the form of a beige powder (39.5 mg, 96%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.26 (dd, 2H, J = 7.5, 1.2 Hz), 8.80 (tt, 1H, J = 7.5, 1.2 Hz), 8.31 (t, 2H, J = 7.5 Hz), 7.75 (d, 2H, J = 8.3 Hz), 7.75 (d, 2H, J = 8.3 Hz), 2.51 (s, 3H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 147.6, 146.0, 143.6, 142.2, 132.1, 129.6, 125.2, 21.2. IR (neat) ν 3451, 3397, 3015, 1778, 1477, 1453, 833, 787, 694. LC−MS m/z (%) 170 (100), 171 (12). Anal. calcd for $C_{12}H_{12}ClN{\cdot}4/3H_2O$: C, 62.75; H, 6.44; N, 6.10. Found: C, 62.58; H, 6.19; N, 6.51.

*1-(2-(Trifluoromethyl)phenyl)pyridin-1-ium chloride (**2b**).* **2b** was prepared from **1b** (386.7 mg, 2.4 mmol, 12 equiv) after 60 min of heating under microwaves at 150 °C in a EtOH/H_2O (80/20) mixture. **2b** was purified according to method 1 and obtained under the form of a brown powder (4.0 mg, 8%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.31 (d, 2H, J = 7.0 Hz), 8.96 (t, 1H, J = 7.0 Hz), 8.40 (t, 2H, J = 7.0 Hz), 8.12 (dd, 1H, J = 7.0, 1.7 Hz), 8.08−7.99 (bp, 3H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 149.7, 148.1, 140.7, 135.8, 133.9, 129.9, 129.3, 129.1 (q, J = 4.9 Hz), 126.2 (q, J = 32.0 Hz), 124.0 (q, J = 273.0 Hz). ^{19}F NMR (376 MHz, MeOH-d_4) δ −59.81. IR (neat) ν 3385, 3033, 1502, 1486, 1469, 1129, 1109, 1074, 793, 685. LC−MS m/z (%) 224 (100). Anal. calcd for $C_{12}H_9ClF_3N{\cdot}1/2H_2O$: C, 53.65; H, 3.75; N, 5.21. Found: C, 53.27; H, 3.70; N, 5.40.

*1-(2-Cyanophenyl)pyridin-1-ium chloride (**2c**).* **2c** was prepared from **1c** (283.5 mg, 2.4 mmol, 12 equiv) after 60 min of heating under microwaves at 150 °C, and purified according to method 1. **2c** was obtained under the form of a very hygroscopic turquoise powder (36.5 mg, 84%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.40−9.34 (m, 2H), 8.95 (tt, J = 7.8, 1.3 Hz, 1H), 8.42 (dd, J = 7.8, 6.8 Hz, 2H), 8.17 (dd, J = 7.6, 1.3 Hz, 1H), 8.11−8.01 (m, 2H), 7.97 (td, J = 7.6, 1.5 Hz, 1H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 149.8, 147.3, 144.9, 136.4, 135.7, 133.6, 129.8, 128.5, 115.3, 110.6. IR (neat) ν 3357, 3016, 2240, 1494, 1469, 1356, 779, 689. LC−MS m/z (%) 181 (100), 182 (13). Anal. calcd for $C_{12}H_9ClN_2{\cdot}5/4H_2O$: C, 60.26; H, 4.85; N, 11.71. Found: C, 60.43; H, 4.85; N, 11.63.

*1-(4-Cyanophenyl)pyridin-1-ium chloride (**2d**).*[36] **2d** was prepared from **1d** (283.5 mg, 2.4 mmol, 12 equiv) after 60 min of heating under microwaves at 150 °C, and purified according to method 1. **2d** was obtained under the form of a white powder (38.1 mg, 88%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.38 (d, 2H, J = 7.6 Hz), 8.83 (t, 1H, J = 7.6 Hz), 8.35 (t, 2H, J = 7.6 Hz), 8.30 (d, 2H, J = 8.7 Hz), 8.12 (d, 2H, J = 8.7 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ 147.4, 145.6, 145.1, 134.3, 128.1, 126.3, 117.6, 114.1. IR (neat) ν 3366, 3031, 3006, 2235, 1486, 1471, 784, 678. LC−MS m/z (%) 181 (100), 182 (14), 183 (1), 246 (17), 247 (2). Anal. calcd for $C_{12}H_9ClN_2{\cdot}5/4H_2O$: C, 60.26; H, 4.85; N, 11.71. Found: C, 60.70; H, 4.96; N, 11.25.

*1-(4-acetylphenyl)pyridin-1-ium chloride (**2e**).* **2e** was prepared from **1e** (324 mg, 2.4 mmol, 12 equiv) after 60 min of heating under microwaves at 150 °C, and purified according to method 2. **2e** was obtained under the form of a brown powder (40.3 mg, 84%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.37 (d, 2H, J = 7.1 Hz), 8.88 (t, 1H, J = 7.1 Hz), 8.38 (t, 2H, J = 7.1 Hz), 8.34 (d, 2H, J = 7.9 Hz), 8.05 (d, 2H, J = 7.9 Hz), 2.73 (s, 3H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 198.7, 148.5, 147.2, 146.0, 140.5, 131.6, 129.7, 126.2, 27.1. IR (neat) ν 3334, 3031, 1674, 1597, 1475, 1362, 1257, 786. LC−MS m/z (%) 198 (100), 199 (19). Anal. calcd for $C_{13}H_{12}ClNO{\cdot}7/5H_2O$: C, 60.31; H, 5.76; N, 5.41. Found: C, 60.35; H, 6.04; N, 5.25.

*1-(4-Carboxyphenyl)pyridin-1-ium chloride (**2f**).* **2f** was prepared from **1f** (82.3 mg, 0.6 mmol, 3 equiv) after 60 min of heating under microwaves at 150 °C, and purified according to method 1. **2f** was obtained under the form of a brown solid (18.1 mg, 38%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.32 (d, 2H, J = 7.8 Hz), 8.84 (t, 1H, J = 7.8 Hz), 8.34 (bp, 4H), 7.96 (d, 2H, J = 8.5 Hz). ^{13}C NMR (100 MHz, MeOH-d_4) δ 168.1, 148.4, 147.3, 146.1, 135.5, 132.8, 129.6, 125.9. IR (neat) ν 3382, 3015, 2776, 2584, 1699, 1624, 1473, 1385, 1328, 1236, 791, 682. LC−MS m/z (%) 200 (100), 202 (13). Anal. calcd for $C_{12}H_{10}ClNO_2{\cdot}H_2O$: C, 56.81; H, 4.77; N, 5.52. Found: C, 56.83; H, 4.64; N, 5.49.

*1-(2-Chlorophenyl)pyridin-1-ium chloride (**2g**).*[40] **2g** was prepared from **1g** (306.2 mg, 2.4 mmol, 12 equiv) after 75 min of heating under microwaves at 150 °C, and purified according to method 1. **2g** was obtained under the form of a very hygroscopic green solid (38.0 mg, 84%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.22 (d, 2H, J = 7.1 Hz), 8.92 (t, 1H, J = 7.1 Hz), 8.39 (t, 2H, J = 7.1 Hz), 7.91 (d, 1H, J = 7.8 Hz), 7.85 (d, 1H, J = 7.8 Hz), 7.79 (t, 1H, J = 7.8 Hz), 7.72 (t, 1H, J = 7.8 Hz). ^{13}C NMR (100 MHz, MeOH-d_4) δ 149.3, 147.2, 141.3, 134.5, 132.3, 130.3, 129.8, 129.7, 128.9. IR (neat) ν 3363, 3024, 1470, 762, 681. LC−MS m/z (%) 190 (100), 191 (16), 192 (49). Anal. calcd for $C_{11}H_9Cl_2N{\cdot}H_2O$: C, 54.12; H, 4.54; N, 5.74. Found: C, 53.80; H, 4.48; N, 5.57.

*1-(3-Cyanophenyl)pyridin-1-ium chloride (**2h**).* **2h** was prepared from **1h** (70.8 mg, 0.6 mmol, 3 equiv) after 60 min of heating under microwaves at 150 °C, and purified according to method 2. **2h** was obtained under the form of a brown powder (43.3 mg, 100%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.37 (d, 2H, J = 7.0 Hz), 8.90 (t, 1H, J = 7.0 Hz), 8.40 (s, 1H), 8.37 (d, 2H, J = 7.0 Hz), 8.26 (d, 1H, J = 8.1 Hz), 8.17 (d, 1H, J = 8.1 Hz), 7.99 (t, 1H, J = 8.1 Hz). ^{13}C NMR (100 MHz, MeOH-d_4) δ 148.7, 146.3, 144.6, 136.3, 132.9, 130.6, 129.8, 129.7, 118.0, 115.4. IR (neat) ν 3389, 3015, 2234, 1490, 1468, 776, 681. LC−MS m/z (%) 181 (100), 182 (14). Anal. calcd for $C_{12}H_9ClN_2{\cdot}7/8H_2O$: C, 62.01; H, 4.66; N, 12.05. Found: C, 62.00; H, 4.39; N, 12.27.

*1-(3-Carboxyphenyl)pyridin-1-ium chloride (**2i**).* **2i** was prepared from **1i** (82.2 mg, 0.6 mmol, 3 equiv) after 60 min of heating under microwaves at 150 °C, and purified according to method 2. **2i** was obtained under the form of a purple solid (36.7 mg, 78%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.27 (dd, 2H, J = 6.9, 1.3 Hz), 8.78 (tt, 1H, J = 7.8, 1.3 Hz), 8.28 (bp, 3H), 8.24 (m, 1H), 7.85 (ddd, 1H, J = 7.8, 2.3, 1.1 Hz), 7.74 (t, 1H, J = 7.8 Hz). ^{13}C NMR (100 MHz, MeOH-d_4) δ 172.0, 147.8, 146.2, 144.1, 142.2, 133.2, 131.3, 129.5, 126.8, 126.0. IR (neat) ν 3378, 3041, 2688, 2535, 1704, 1625, 1469, 1443, 1378, 1290, 1257, 756, 682. LC−MS m/z (%) 200 (100), 201 (13). Anal. calcd for $C_{12}H_{10}ClNO_2{\cdot}H_2O$: C, 56.81; H, 4.77; N, 5.52. Found: C, 56.78; H, 4.69; N, 5.53.

*1-(3-Chlorophenyl) pyridin-1-ium chloride (**2j**).*[39] **2j** was prepared from **1j** (76.5 mg, 0.6 mmol, 3 equiv) after 40 min of heating under microwaves at 150 °C, and purified according to method 2. **2j** was obtained under the form of a brown solid (41.1 mg, 91%). ^{1}H NMR (400 MHz, DMSO) δ 9.39 (d, J = 5.6 Hz, 2H), 8.82 (t, J = 7.8 Hz, 1H), 8.37−8.27 (m, 2H), 8.15 (t, J = 2.0 Hz, 1H), 7.92−7.75 (m, 3H).^{13}C NMR (100 MHz, DMSO-d_6) δ 147.1, 145.1, 143.6, 134.1, 131.8, 131.2, 128.0, 125.3, 123.9. IR (neat) ν 3360, 3071, 3025, 1627, 1588, 1471, 1093, 874, 780. LC−MS m/z (%) 190 (100), 192 (29). Anal. calcd for $C_{11}H_9Cl_2N{\cdot}8/7H_2O$: C, 53.56; H, 4.61; N, 5.68. Found: C, 53.05; H, 4.49; N, 6.17.

*1-(3-(Trifluoromethyl)phenyl)pyridin-1-ium chloride (**2k**).* **2k** was prepared from **1k** (96.7 mg, 0.6 mmol, 3 equiv) after 60 min of heating under microwaves at 150 °C, and purified according to method 1. **2k** was obtained under the form of a brown powder (37.9 mg, 73%).^{1}H NMR (400 MHz, MeOH-d_4) δ 9.32 (dd, J = 6.8, 1.3 Hz, 2H), 8.84 (tt, J = 7.8, 1.3 Hz, 1H), 8.35−8.30 (m, 2H), 8.28 (s, 1H), 8.12 (t, J = 7.3 Hz, 2H), 7.98 (t, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 148.8, 146.4, 144.7, 133.5 (q, J = 33.6 Hz), 132.9, 130.1, 129.9, 129.7, 129.4 (q, J = 3.6 Hz), 124.6 (q, J = 221.1 Hz), 123.2 (q, J = 3.9 Hz). ^{19}F NMR (376 MHz, MeOH-d_4) δ −63.87. IR (neat) ν 3301, 3003, 1502, 1474, 1326, 1176, 1102, 775, 680. LC−MS m/z (%) 224 (100), 225 (13). Anal. calcd for $C_{12}H_9ClF_3N{\cdot}3/2H_2O$: C, 50.28; H, 4.22; N, 4.89. Found: C, 50.35; H, 4.25; N, 5.22.

*1-(4-Carbamoylphenyl)pyridin-1-ium chloride (**2l**).* **2l** was prepared from **1l** (81.6 mg, 0.6 mmol, 3 equiv) after 60 min of heating under microwaves at 150 °C, and purified according to method 2. **2l** was obtained under the form of a brown powder (40.0 mg, 85%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.32 (d, 2H, J = 6.9 Hz), 8.84 (t, 1H, J

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= 6.9 Hz), 8.33 (t, 2H, J = 6.9 Hz), 8.23 (d, 2H, J = 8.6 Hz), 7.97 (d, 2H, J = 8.6 Hz). ^{13}C NMR (100 MHz, MeOH-d_4) δ 170.0, 148.4, 146.5, 146.1, 138.2, 131.0, 129.7, 126.0. IR (neat) ν 3392, 3034, 1683, 1466, 1389, 711, 672. LC−MS m/z (%) 199 (100), 200 (13). Anal. calcd for $C_{12}H_{11}ClN_2O{\cdot}1/2H_2O$: C, 59.14; H, 4.96; N, 11.50. Found: C, 59.06; H, 4.50; N, 11.59.

*1-(3-Carbamoylphenyl)pyridin-1-ium chloride (**2m**).* **2m** was prepared from **1m** (81.6 mg, 0.6 mmol, 3 equiv) after 20 min of heating under microwaves at 150 °C, and purified according to method 2. **2m** was obtained under the form of a brown powder (32.2 mg, 68%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.31 (dd, J = 6.8, 1.3 Hz, 2H), 8.83 (tt, J = 7.9, 1.3 Hz, 1H), 8.36−8.28 (m, 3H), 8.27−8.21 (m, 1H), 8.02 (ddd, J = 8.0, 2.4, 0.9 Hz, 1H), 7.86 (t, J = 8.0 Hz, 1H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 169.6, 148.3, 146.2, 144.4, 137.7, 132.0, 131.6, 129.7, 128.6, 125.1. IR (neat) ν 3471, 3118, 2923, 1661, 1499, 1487, 764, 673. LC−MS m/z (%) 199 (100), 200 (14). Anal. calcd for $C_{12}H_{11}ClN_2O{\cdot}2H_2O$: C, 53.24; H, 5.58; N, 10.35. Found: C, 53.42; H, 5.24; N, 10.49.

*1-(4-Chlorophenyl)pyridin-1-ium chloride (**2n**).*[36,39] **2n** was prepared from **1n** (51.0 mg, 0.4 mmol, 2 equiv) after 30 min of heating under microwaves at 130 °C, and purified according to method 1. **2n** was obtained under the form of a light brown powder (41.9 mg, 93%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.34 (d, 2H, J = 7.5 Hz), 8.79 (t, 1H, J = 7.5 Hz), 8.31 (t, 2H, J = 7.5 Hz), 7.94 (d, 2H, J = 8.9 Hz), 7.86 (d, 2H, J = 8.9 Hz). ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.9, 145.1, 141.6, 136.1, 130.1, 128.1, 126.8. IR (neat) ν 3626, 3363, 3093, 3020, 1625, 1590, 1474, 1093, 870, 843, 777. LC−MS m/z (%) 190 (100), 191 (13), 192 (26), 415 (4), 418 (7). Anal. calcd for $C_{11}H_9Cl_2N{\cdot}H_2O$: C, 54.12; H, 4.54; N, 5.74. Found: C, 54.55; H, 4.58; N, 5.72.

*1-(Naphthalen-1-yl) pyridin-1-ium chloride (**2o**).*[40] **2o** was prepared from **1o** (85.9 mg, 0.6 mmol, 3 equiv) after 20 min of heating under microwaves at 150 °C, and purified according to method 1. **2o** was obtained under the form of a very hygroscopic red solid (33.7 mg, 70%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.29−9.23 (m, 2H), 8.93 (tt, J = 7.9, 1.4 Hz, 1H), 8.39 (dd, J = 7.8, 6.7 Hz, 2H), 8.32 (d, J = 8.4 Hz, 1H), 8.21−8.15 (m, 1H), 7.92 (dd, J = 7.4, 1.1 Hz, 1H), 7.82−7.67 (m, 3H), 7.39−7.35 (m, 1H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 148.8, 147.9, 140.4, 135.6, 133.4, 130.4, 129.9, 129.8, 129.1, 128.4, 126.5, 125.5, 121.3. IR (neat) ν 3364, 3034, 1509, 1469, 774, 684. LC−MS m/z (%) 206 (100), 207 (15). Anal. calcd for $C_{15}H_{12}ClN{\cdot}H_2O$: C, 69.36; H, 5.43; N, 5.39. Found: C, 69.49; H, 5.38; N, 5.41.

*1-(3-Hydroxyphenyl)pyridin-1-ium chloride (**2p**).* **2p** was prepared from **1p** (43.6 mg, 0.4 mmol, 2 equiv) after 40 min of heating under microwaves at 130 °C, and purified according to method 2. **2p** was obtained under the form of a very hygroscopic black solid (26.4 mg, 63%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.22 (d, 2H, J = 6.5 Hz), 8.78 (t, 1H, J = 6.5 Hz), 8.27 (t, 2H, J = 6.5 Hz), 7.54 (t, 1H, J = 9.8 Hz), 7.24 (d, 1H, J = 9.8 Hz), 7.22 (s, 1H), 7.15 (d, 1H, J = 9.8 Hz). ^{13}C NMR (100 MHz, MeOH-d_4) δ 160.6, 147.9, 146.0, 145.5, 132.6, 129.5, 119.6, 115.9, 112.4. IR (neat) ν = 3485, 3047, 3026, 1567, 1480, 1335, 1297, 1252, 805, 794. LC−MS m/z (%) 172 (100), 173 (13), 343 (17). Anal. calcd for $C_{11}H_{10}ClNO{\cdot}2H_2O$: C, 54.22; H, 5.79; N, 5.75. Found: C, 54.59; H, 5.88; N, 5.59.

*1-(o-Tolyl)pyridin-1-ium chloride (**2q**).*[40] **2q** was prepared from **1q** (42.8 mg, 0.4 mmol, 2 equiv) after 15 min of heating under microwaves at 130 °C, and purified according to method 2. **2q** was obtained under the form of a brown powder (38.9 mg, 94%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.13 (dd, 2H, J = 6.7, 1.3 Hz), 8.86 (tt, 1H, J = 6.7, 1.3 Hz), 8.34 (t, 2H, J = 6.7 Hz, 7.68−7.53 (bp, 4H), 2.21 (s, 3H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 148.3, 147.3, 143.8, 133.9, 133.2, 132.9, 129.7, 129.0, 126.9, 17.0. IR (neat) ν 3365, 3118, 2923, 1487, 1469, 1385, 767, 717, 685. LC−MS m/z (%) 170 (100), 171 (13). Anal. calcd for $C_{12}H_{12}ClN{\cdot}7/4H_2O$: C, 60.76; H, 6.59; N, 5.90. Found: C, 60.93; H, 6.28; N, 5.99.

*1-(2-Methoxyphenyl)pyridin-1-ium chloride (**2r**).*[40] **2r** was prepared from **1r** (49.3 mg, 0.4 mmol, 2 equiv) after 30 min of heating under microwaves at 130 °C, and purified according to method 2. **2r** was obtained under the form of a light brown powder (35.5 mg, 80%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.24 (dd, 2H, J = 6.5, 1.2 Hz), 8.81 (tt, 1H, J = 6.5, 1.2 Hz), 8.32 (t, 2H, J = 6.5 Hz), 7.77 (d, 1H, J = 7.9 Hz), 7.72 (t, 1H, J = 7.9 Hz), 7.46 (d, 1H, J = 7.9 Hz), 7.28 (t, 1H, J = 7.9 Hz), 3.86 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 151.8, 147.1, 146.7, 133.0, 131.2, 127.9, 126.9, 121.2, 113.4, 56.6. IR (neat) ν 3440, 3380, 3031, 2841, 1606, 1440, 1277, 1020, 763, 684, 694. LC−MS m/z (%) 186 (100), 187 (17). Anal. calcd for $C_{12}H_{12}ClNO{\cdot}4/3H_2O$: C, 58.66; H, 6.02; N, 5.70. Found: C, 58.82; H, 5.66; N, 5.86.

*1-Phenylpyridin-1-ium chloride (**2s**).*[36] **2s** was prepared from **1s** (22.3 mg, 0.24 mmol, 1.2 equiv) after 20 min of heating under microwaves at 130 °C, and purified according to method 2. **2s** was obtained under the form of a brown powder (38.3 mg, 100%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.37 (d, 2H, J = 7.1 Hz), 8.79 (t, 1H, J = 7.1 Hz), 8.32 (t, 2H, J = 7.1 Hz), 7.90 (dd, 2H, J = 5.9, 1.9 Hz), 7.75 (bp, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 146.6, 145.0, 142.8, 131.2, 130.2, 128.2, 124.8. IR (neat) ν 3626, 3363, 3093, 3020, 1625, 1590, 1474, 870, 843, 777. LC−MS m/z (%) 190 (100), 191 (13), 192 (26), 415 (4), 418 (7). Anal. calcd for $C_{11}H_{10}ClN{\cdot}3/2H_2O$: C, 60.42; H, 5.99; N, 6.41. Found: C, 60.35; H, 5.68; N, 6.14.

*1-(m-Tolyl)pyridin-1-ium chloride (**2t**).*[36] **2t** was prepared from **1t** (25.7 mg, 0.24 mmol, 1.2 equiv) after 20 min of heating under microwaves at 130 °C, and purified according to method 2. **2t** was obtained under the form of a very hygroscopic brown solid (39.2 mg, 95%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.28 (d, 2H, J = 6.9 Hz), 8.82 (t, 1H, J = 6.9 Hz), 8.33 (t, 2H, J = 6.9 Hz), 7.73 (s, 1H), 7.68−7.58 (bp, 3H), 2.54 (s, 3H). ^{13}C NMR (100 MHz, MeOH-d_4) δ 147.8, 146.0, 144.5, 142.6, 133.3, 131.5, 129.6, 125.9, 122.5, 21.3. IR (neat) ν 3409, 3360, 3032, 1492, 1382, 808, 774, 717. LC−MS m/z (%) 170 (100), 171 (12). Anal. calcd for $C_{12}H_{12}ClN{\cdot}5/2H_2O$: C, 57.49; H, 6.83; N, 5.59. Found: C, 57.85; H, 6.47; N, 5.65.

*1-(2-Hydroxyphenyl)pyridin-1-ium chloride (**2u**).* **2u** was prepared by reacting 0.4 mmol (112.4 mg) of Zincke salt **3** with **1u** (85.3 mg, 0.8 mmol, 2 equiv) after 30 min of heating under microwaves at 130 °C, and purified according to method 3. **2u** was obtained under the form of a very hygroscopic yellow solid (25.5 mg, 31%). ^{1}H MNR (400 MHz, MeOH-d_4) δ 9.09 (d, 2H, J = 6.8 Hz), 8.76 (t, 1H, J = 6.8 Hz), 8.27 (t, 2H, J = 6.8 Hz), 7.59 (d, 1H, J = 7.8 Hz), 7.52 (t, 1H, J = 7.8 Hz), 7.21 (d, 1H, J = 7.8 Hz), 7.10 (t, 1H, J = 7.8 Hz). ^{13}C NMR (100 MHz, MeOH-d_4) δ 152.3, 147.7, 147.7, 134.0, 132.0, 129.1, 127.2, 121.1, 118.7. IR (neat) ν 3252, 3024, 2924, 1595, 1453, 1384, 1284, 1203, 839, 776. LC−MS m/z (%) 172 (100), 173 (13). Anal. calcd for $C_{11}H_{10}ClNO{\cdot}H_2O$: C, 58.54; H, 5.36; N, 6.21. Found: C, 58.22; H, 5.46; N, 5.89.

*1-(4-Hydroxyphenyl)pyridin-1-ium chloride (**2v**).*[36] **2v** was prepared from **1v** (26.2 mg, 0.24 mmol, 1.2 equiv) after 20 min of heating under microwaves at 130 °C, and purified according to method 2. **2v** was obtained under the form of a light brown powder (26.4 mg, 63%). ^{1}H NMR (400 MHz, MeOH-d_4) δ 9.17 (dd, 2H, J = 7.8, 2.1 Hz), 8.72 (tt, 1H, J = 7.8, 2.1 Hz), 8.24 (t, 2H, J = 7.8 Hz), 7.66 (d, 2H, J = 8.1 Hz), 7.08 (d, 2H, J = 8.1 Hz). ^{13}C NMR (100 MHz, MeOH-d_4) δ 161.9, 147.0, 145.9, 136.4, 129.5, 126.8, 117.9. IR (neat) ν 3307, 3111, 3054, 1594, 1512, 1478, 1312, 1293, 1233, 850, 776. LC−MS m/z (%) 172 (100), 173 (12), 197 (1). Anal. calcd for $C_{11}H_{10}ClNO{\cdot}6/5H_2O$: C, 57.62; H, 5.45; N, 6.11. Found: C, 57.96; H, 5.37; N, 5.69.

*2-((2,4-Dinitrophenyl)amino)phenol (**5**).*[33,41] The salt-free fractions obtained after the purification of **2u** were collected and concentrated. **5** was isolated by chromatography on silica gel (PE/EtOAc 75/25). Recrystallization in *i*-PrOH gave **5** under the form of an orange powder (41.0 mg, 19%, mp 202−204 °C). ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.01 (s, 1H), 9.95 (s, 1H), 8.90 (d, J = 2.7 Hz, 1H), 8.24 (dd, J = 9.6, 2.8 Hz, 1H), 7.30 (dd, J = 7.8, 1.6 Hz, 1H), 7.26−7.19 (m, 1H), 7.02 (dd, J = 8.2, 1.3 Hz, 1H), 6.93 (td, J = 7.6, 1.3 Hz, 1H), 6.88 (d, J = 9.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 152.2, 146.9, 136.0, 130.7, 129.8, 128.5, 127.2, 124.2, 123.3, 119.7, 117.1, 116.7. IR (neat) ν 3364, 3295, 3098, 1619, 1585, 1494, 1282, 1129, 741, 625, 507. GC−MS m/z (%) 127 (42), 128 (31), 140 (25), 154 (46), 155 (77), 156 (25), 167 (82), 183 (55), 207 (29), 275 (100).

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■ ASSOCIATED CONTENT

Supporting Information

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NMR, IR and MS spectra of purified compounds **2a**–**v** and **5**. (PDF)

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Notes

The authors declare no competing financial interest.

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