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C-N, C-O and C-S Ullmann-Type Coupling Reactions of Arenediazonium *o*-Benzenedisulfonimides

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Abstract: Arenediazonium *o*-benzenedisulfonimides have been used as efficient electrophilic partners in Cu(I) catalysed Ullmann-type coupling. The synthetic protocols are mild and easy, and produced either N-alkylanilines, aryl ethers, or thioethers in fairly good yields (18 positive examples, average yield 66%). *o*-Benzenedisulfonimide was recovered at the end of the reactions and was reused to prepare the starting salts for further reactions. It is noteworthy that diazonium salts have been used as electrophilic partners in the Ullmann-type protocol for the first time.

Keywords: Ullmann-type coupling; copper catalysis; arenediazonium salts

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1. Introduction

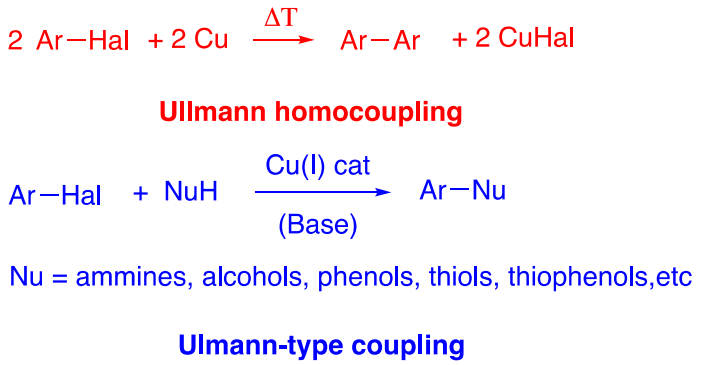
In recent years, the considerable efforts made in understanding the mechanism of Ullmann reaction [1,2], together with the urgency of cross-coupling protocols based on generally less costly and toxic first row transition metals [3] (e.g., iron [4], nickel [5], and copper [6,7]) rather than palladium, has led to a resurgence of this reaction. Indeed, although the classical Ullmann reaction is perhaps the most ancient cross coupling protocol [8,9], harsh reaction conditions (generally > 200 °C) and low yields drastically limited its applications, and consequently, its industrial employment.

Apart from being a powerful tool for the formation of a $C(sp^2)$-$C(sp^2)$ bond between two aromatic rings (Ullmann homocoupling of aryl halides), even under mild reaction conditions [10,11], in optimal yields and excellent functional group tolerance [12–16], the Ullmann protocol also proved its usefulness and versatility in broader applications, including Cu-catalyzed nucleophilic aromatic substitution between various nucleophiles with aryl halides, known as Ullmann-type (or hetero-Ullmann) coupling (Scheme 1) [17–28]. These reactions can lead to moieties that are building blocks of active molecules in the life sciences [29] and in different material precursors [30]. Recent studies suggested that the copper catalyst may play a significant role in the activation of the aryl halide with evidence for an oxidative addition/reductive elimination process through a copper (III) intermediate (Scheme 1); however, in spite of this progress, the role of the ligand in the catalytic cycle remains relatively unresolved [12].

Aryl halides are generally the preferred electrophilic partners for Ullmann couplings; other types of compounds have only rarely been used. In particular, arenediazonium salts, which, in other coupling reactions, turn out to be a valid alternative to aryl halides [31,32], have been employed only sporadically in classical Ullmann homocoupling [33].

The industrial use of diazonium compounds has historically been limited from their intrinsic hazard [34] and instability, which depends, to a large extent on the reaction medium [35,36], the nature of the substrate (i.e., alkyl diazonium salts cannot be isolated), and of the counteranion [37], which has prompted the investigation of their decomposition kinetics [38]. As a result, the knowledge acquired on the chemistry of diazonium salts has even allowed for their application within the framework of particular reaction set-ups, such as flow reactors [39]. Once these issues have been pointed out, arenediazonium salts offer a series of advantages with respect to aryl halides. First of all, they possess

better reactivity, due to the fact that the diazonium group is a better nucleofuge than the halide, which allows the use of mild reaction conditions. Second, as the nucleofuge is a gaseous species, it can work around the issue of high COD/BOD in wastewater, due to the presence of halide anions. Finally, reactions often do not require a base or additional ligands. Furthermore, our previous research has resulted in a large family of dry diazonium salts, namely, arenediazonium *o*-benzenedisulfonimides (Figure 1) [40–51]. The properties of these compounds indicate that they have great potential in numerous synthetic applications, as they are easy to prepare and isolate, they are extremely stable (in some cases more than the corresponding tetrafluoroborates), and they can be stored for an unlimited time. Moreover, they react smoothly both in water and organic solvents.



Scheme 1. Ullmann homocoupling and Ullmann-type coupling.

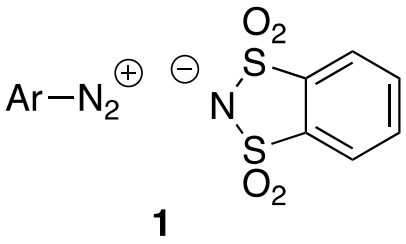
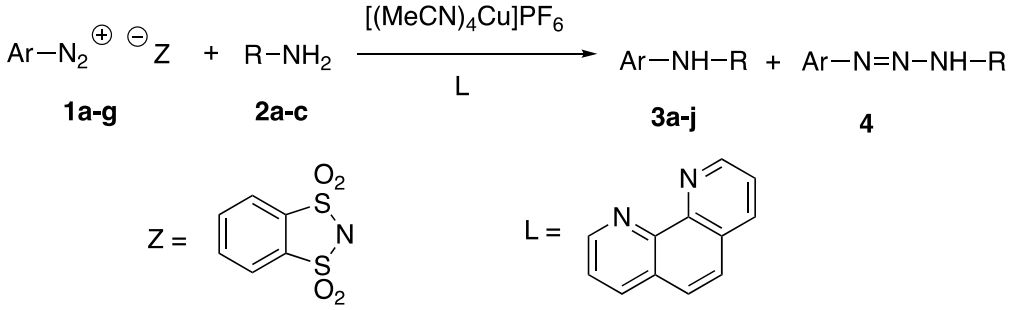


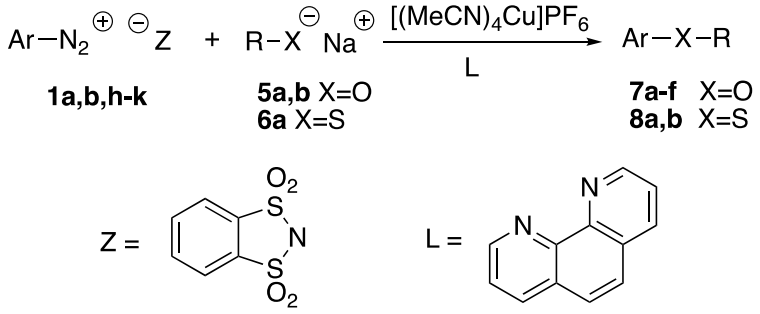
Figure 1. Arenediazonium *o*-benzenedisulfonimides **1**.

In light of this, in this study, we propose a mild, easy, and efficient revisitation of Ullmann-type couplings carried out by reacting suitable arenediazonium *o*-benzenedisulfonimides **1** with primary aliphatic amines **2a**–**c**, in the presence of tetrakis(acetonitrile)copper hexafluorophosphate and 1,10-phenanthroline as a ligand (Scheme 2). It must be stressed that, to the best of our knowledge, diazonium salts have been used here as electrophilic partners in an Ullmman-type protocol for the first time.

The reaction, in the same conditions, was also extended to primary alcoholates **5a**,**b** and thiolate **6a** (Scheme 3).



Scheme 2. Ullmann-type coupling between arenediazonium *o*-benzenedisulfonimides **1** and amines **2**.



Scheme 3. Ullmann-type coupling between arenediazonium *o*-benzenedisulfonimides **1** and primary alcoholates **5a**,**b** and thiolate **6a**.

2. Materials and Methods

2.1. General Informations

All the reactions were carried out in open air. Analytical grade reagents and solvents were used and reactions were monitored by GC, GC-MS, and TLC. Column chromatography and TLC were performed on Merck silica gel 60 (70–230 mesh ASTM) and GF 254, respectively. Petroleum ether refers to the fraction boiling in the range 40–70 °C. Room temperature is 22 °C. Mass spectra were recorded on an HP 5989B mass selective detector connected to an HP 5890 GC with a methyl silicone capillary column. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Jeol ECZR spectrometer at 600 and 150 MHz, respectively. IR spectra were recorded on an IR PerkinElmer UATR-two spectrometer. Tetrakis(acetonitrile)copper hexafluorophosphate was prepared as reported in the literature [52]. Dry arenediazonium *o*-benzenedisulfonimides **1** were prepared as described previously by us [40]. The crude salts **1** were virtually pure (by ^{1}H NMR spectroscopy) and were used in subsequent reactions without further crystallization. All the other reagents were purchased from Sigma-Aldrich or Alfa-Aesar. Structures and purity of all the products obtained in this research were confirmed by their spectral (NMR, MS) and physical data, which are substantially identical to those reported in the literature. Yields of the pure (GC, above 96%; GC-MS; TLC and NMR) isolated compounds **3**, **7, 8** are collected in Tables 1 and 2. NMR spectra of **3**, **7, 8** are reported in the Supplementary Materials.

*2.2. N-(n-Hexyl)-4-Nitroaniline (**3a**): Representative procedure for the Ullmann-Type Coupling Reactions of Arenediazonium o-Benzenedisulfonimides*

Moreover, 4-Nitrobenzenediazonium *o*-benzenedisulfonimide (**1a**, 0.74 g, 2 mmol) was added to hexan-1-amine (**2a,** 0.22 g, 2.2 mmol), tetrakis(acetonitrile)copper hexafluorophosphate $[(Me_3CN)_4Cu]PF_6$ (0.75 g, 2 mmol) and 1,10-phenanthroline (0.36 g, 2 mmol) in DMSO (5 mL). The resulting mixture was stirred at room temperature for 3 h; the completion of the reaction was confirmed by the absence of azo coupling with 2-naphthol. Then, the reaction mixture was poured into diethyl ether/water (100 mL, 1:1). The aqueous layer was separated and extracted with diethyl ether (50 mL). The combined organic extracts

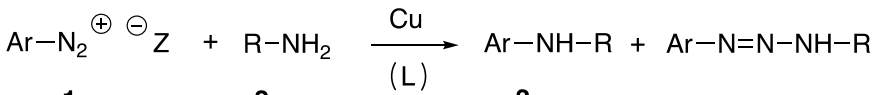
were washed with water (50 mL), dried with Na_2SO_4, and evaporated under reduced pressure. GC-MS analyses of the crude residue showed N-(n-hexyl)-4-nitroaniline (**3a**), MS (EI): m/z 222 (M^+) as the major product, as well as traces of 4,4′-dinitrobiphenyl, MS (EI): m/z 244 (M^+), 3-hexyl-1-(4-nitrophenyl)triaz-1-ene (**4a**), MS (EI): m/z 250 and nitrobenzene MS (EI): m/z 123 (M^+). The crude residue was purified on a short column, eluting with petroleum ether/diethyl ether (9:1). The title compound **3a** was obtained in 87% yield (0.39 g).

The aqueous layer and aqueous washings were collected and evaporated under reduced pressure. The tarry residue was passed through a column of Dowex HCR-W2 ion exchange resin (1.6 g/1 g of product), eluting with water (about 50 mL). After removal of water under reduced pressure, virtually pure (^{1}H NMR) *o*-benzenedisulfonimide was recovered (0.360 g, 81% yield; mp 192–194 °C. Lit. 190–193 °C).

3. Results and Discussion

A model reaction between 4-nitrobenzenediazonium *o*-benzenedisulfonimmide (**1a**) and hexan-1-amine (**2a**) were studied under various conditions (Table 1), in order to optimize the reaction conditions. First of all, the reaction carried out in absence of copper, with THF as a solvent, only provided the corresponding triazene **4**, as it is logical to expect, on the basis of the well-known reactivity of the diazonium salts with aliphatic amines (Table 1; entry 1) [53,54].

Table 1. Ullmann-type coupling between arenediazonium *o*-benzenedisulfonimides **1** and amines **2**.



1 **2** **3** **4**

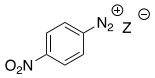
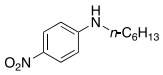
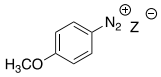
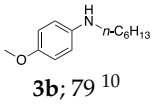
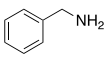
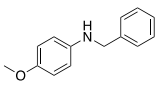
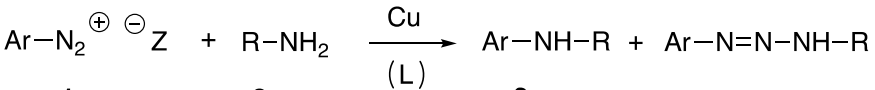
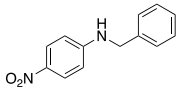
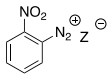
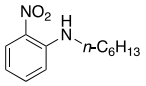
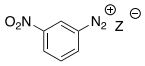
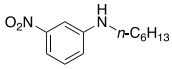
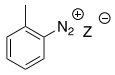
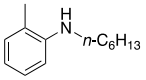
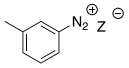
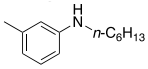
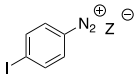
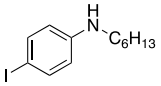
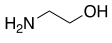
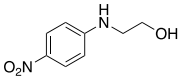
Entry	Salt 1	Amines 2	Cu and Ligand (L)	Solvent	T (°C)	Time (h)	Products 3 and Yields (%) [1]	Literature Yields (%)
1	 **1a**	*n*-$C_6H_{13}NH_2$ **2a**	-	THF	rt	3	- [2]	
2	**1a**	**2a**	Cu	THF	rt	3	- [3]	
3	**1a**	**2a**	CuCl	THF	rt	3	- [4]	
4	**1a**	**2a**	CuI	THF	rt	2	- [5]	
5	**1a**	**2a**	Cu_2O	THF	rt	3	- [6]	
6	**1a**	**2a**	$[(MeCN)_4Cu]PF_6$	THF	rt	2	 **3a**; 27 [7]	
7	**1a**	**2a**	$[(MeCN)_4Cu]PF_6$	THF	50	1	- [8]	
8	**1a**	**2a**	$[(MeCN)_4Cu]PF_6$	EtOH	rt	2	**3a**; 34 [7]	
9	**1a**	**2a**	$[(MeCN)_4Cu]PF_6$	MeCN	rt	3	**3a**; 30 [7]	
10	**1a**	**2a**	$[(MeCN)_4Cu]PF_6$	DMSO	rt	2	**3a**; 48 [7]	
11	**1a**	**2a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	2	**3a**; 87 [7,9]	87 [55]
12	 **1b**	**2a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	4	 **3b**; 79 [10]	94 [55]
13	**1b**	 **2b**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	3	 **3c**; 73 [10]	95 [20]

Table 1. *Cont.*



1 **2** **3** **4**

Entry	Salt 1	Amines 2	Cu and Ligand (L)	Solvent	T (°C)	Time (h)	Products 3 and Yields (%) [1]	Literature Yields (%)
14	**1a**	**2b**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	3.5	 **3d**; 85 [10]	91 [56]
15	 **1c**	**2a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	4	 **3e**; 51 [10]	85 [57]
16	 **1d**	**2a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	2	 **3f**; 86 [10]	78 [58]
17	 **1e**	**2a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	5	 **3g**; 46 [10]	56 [59]
18	 **1f**	**2a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	3	 **3h**; 51 [10]	98 [22]
19	 **1g**	**2a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	3	 **3i**; 86 [10]	87 [60]
20	**1a**	 **2c**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	2	 **3j**; 79 [10]	78 [61]
21	**1a**	**2d**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	2	- [11]	
22	**1a**	**2e**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	3	- [11]	

[1] The reactions were carried out with 2 mmol of **1**, 2.2 mmol of **2**, 2 mmol of Cu(I) adduct, and 2 mmol of ligand. Yields refer to pure and chromatographic column isolated **3**. [2] The main product was 3-hexyl-1-(4-nitrophenyl)triaz-1-ene (**4a**). [3] GC-MS analyses of crude residues showed the presence of **4a**, 4,4′-dinitrobiphenyl and nitrobenzene. [4] GC-MS analyses of crude residues showed the presence of **4a**, 4,4′-dinitrobiphenyl, nitrobenzene 1-chloro-4-nitrobenzene. [5] GC-MS analyses of crude residues showed the presence of **4a**, 4,4′-dinitrobiphenyl, nitrobenzene and 1-iodo-4-nitrobenzene. [6] GC-MS analyses of crude residues showed the presence of **4a**, 4,4′-dinitrobiphenyl, nitrobenzene and **3a**. [7] GC-MS analyses of crude residues showed, as well as **3a** as the main product, the presence of **4a**, 4,4′-dinitrobiphenyl, and nitrobenzene. [8] Decomposition of **1a** occurred. [9] Lower amounts of $[(MeCN)_4Cu]PF_6$ and 1,10-phenanthroline led to significantly lower yields. [10] GC-MS analyses of crude residues always showed the presence of triazenes **4**, arenes and symmetrical biaryls as by-products. [11] The only product was corresponding triazene **4**.

In order to favor the hetero-Ullmann coupling, a number of copper derivatives such as powdered Cu (Table 1; entry 2) or Cu (I) (copper chloride, copper iodide or cuprous oxide) were added (Table 1; entries 3−5) in stoichiometric amounts. The products were triazene **4a**, together with variable amounts of 1-chloro or 1-iodo-4-nitrobenzene, nitrobenzene, 4,4′-dinitrobiphenyl. Traces of target **3a** were formed only in the presence of cuprous oxide (Table 1; entry 6). At this point we decided to use another Cu (I) adduct, namely tetrakis(acetonitrile)copper hexafluorophosphate (easily prepared from $Cu(II)SO_4$ and Cu powder, in the presence of KPF_6 and NCMe [52]), which was unable to favor the classic

Sandmeyer reaction [53,54]. GC-MS analyses showed the formation of the desired coupling adduct **3a**. (Table 1; entry 6). Other solvents were then tested and the best results were obtained in DMSO (Table 1; entry 10). A suitable ligand (1,10-phenanthroline: Table 1; entry 11) was then added, in a stoichiometric amount; to our delight, the main product of the reaction was **3a**, obtained with a good yield (87%), after carrying out the reaction at room temperature and in a relatively short time. It is interesting to note that the reactions were carried out without additional bases and that lower amounts of $[(MeCN)_4Cu]PF_6$ and 1,10-phenanthroline led to significantly lower yields (Table 1, entry 11: footnote 9).

The amine **2a** was then reacted with other diazonium salts, **1a**–**f**, which were variously substituted with electron donor groups or electron-withdrawing groups. The target compounds, **3b**–**j** (Table 1; entries 12–20), were obtained in fair to good yields and selectivity while producing relatively low amounts of by-products, among which, the main one is always the triazene. The reaction was chemoselective; diazonium salt **1g**, bearing a iodine atom that could potentially react as a diazonium group, only furnished target product **3i** (Table 1; entry 19); no traces of possible diamine were detected. The reaction was also regioselective; in fact, where the amino group and the hydroxyl group are present in the same structure **2c**, only the first reacted, with the formation of compound **3j**. (Table 1; entry 20) Good results were also achieved with another primary amine, such as benzylamine (**2b**: Table 1; entries 13 and 14). Finally, we decided to change the type of amine and use a secondary amine, namely, diethylamine (**2d**). The reaction failed; the only obtained product, even in the presence of catalyst and ligands, was triazene (Table 1; entry 21). The same results were obtained using aniline (**2e**: Table 1; entry 22).

In order to expand the scope of our research, we also decided to study C-O and C-S Ullmann coupling.

It is well known that arenediazonium salts undergo the O-coupling reaction with alcohols, mainly under acidic conditions [53,54]. The products of this coupling, namely, diazo ethers, (Ar-N=N-O-R), initiate a radical mechanism, which, through the formation of aryl radicals, yield reduction products (arenes).

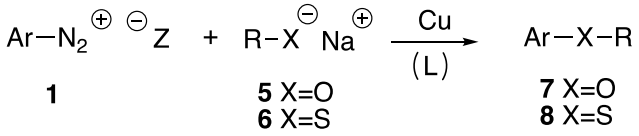
However, some synthetic protocols, allow aryl alkyl ethers to be obtained via the reaction (usually at high temperature) of diazonium salts with various alcohols, are reported in the literature [62,63].

On this basis, a model reaction between 4-nitrobenzenediazonium (**1a**) and hexan-1-ol was studied (Table 2). Unfortunately, the hexan-1-ol did not react under the optimum conditions set up above (Table 2; entries 2 and 3).

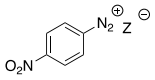
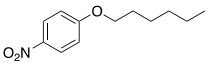
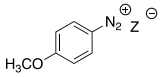
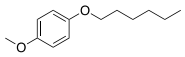
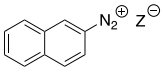
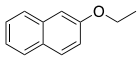
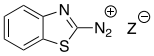
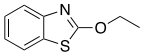
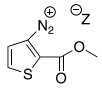
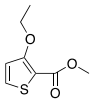
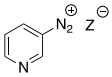
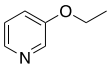
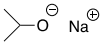
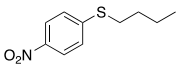
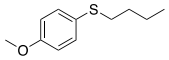
Moreover, we decided to previously treat the hexanol with sodium hydride to transform it into the corresponding alcoholate, **5a**. To our surprise, we obtained the target product, **7a**, with a good yield (Table 2; entry 4). It must be stressed that the reaction that was carried out with a secondary alkoxide (Table 2; entries 12 and 13) did not lead to significant results. In this case, the only product was nitrobenzene.

Heteroarene tetrafluoroborate is rather unstable and sometimes are difficult to isolate [34]; in the light of this, we synthesized three, more stable and easy to handle, heteroarene diazonium *o*-benzenedisulfonimides, **1i**–**k**, and, as reported in Table 2, the reactions carried out in the presence of these salts and sodium ethoxide (**5b**) in ethanol provided ethers **7d**–**f** in fairly good yields (Table 2; entries 9–11).

Table 2. Ullmann-type coupling between arenediazonium *o*-benzenedisulfonimides **1** and alcoholates **5** and thiolate **6**.



1 **5** X=O, **6** X=S → **7** X=O, **8** X=S

Entry	Salt 1	Alcolholates 5 or Thiolate 6	Cu(I) and Ligand (L)	Solvent	T (°C)	Time (h)	Products 7 and 8 and Yields (%) [1]	Literature Yields (%)
1	 **1a**	*n*-$C_6H_{13}OH$	-	DMSO	rt	24	- [2]	
2	**1a**	*n*-$C_6H_{13}OH$	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	24	- [3]	
3	**1a**	*n*-$C_6H_{13}OH$	$[(MeCN)_4Cu]PF_6$/L	DMSO	50	3	- [4]	
4	**1a**	*n*-$C_6H_{13}O^{\ominus}Na^{\oplus}$ **5a**	$[(MeCN)_4Cu]PF_6$	DMSO	rt	24	 **7a**; 34 [3]	
5	**1a**	**5a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	3	**7a**; 67 [5,6]	
6	 **1b**	**5a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	6	 **7b**; 49 [7]	78 [19]
7	 **1h**	EtO Na **5b**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	4	 **7c**; 64 [7]	
8	**1h**	**5b**	$[(MeCN)_4Cu]PF_6$/L	EtOH	rt	2	**7c**; 67 [7]	74 [64]
9	 **1i**	**5b**	$[(MeCN)_4Cu]PF_6$/L	EtOH	rt	4	 **7d**; 66 [7]	100 [65]
10	 **1j**	**5b**	$[(MeCN)_4Cu]PF_6$/L	EtOH	rt	4	 **7e**; 51 [7]	
11	 **1k**	**5b**	$[(MeCN)_4Cu]PF_6$/L	EtOH	rt	3	 **7f**; 60 [7]	
12	**1a**	 **5c**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	24	- [8]	
13	**1a**	**5c**	$[(MeCN)_4Cu]PF_6$/L	DMSO	50	4	- [8]	
14	**1a**	**5c**	$[(MeCN)_4Cu]PF_6$/L	*i*PrOH	rt	24	- [8]	
15	**1a**	*n*-C_4H_9SH	-	DMSO	rt	24	- [2]	
16	**1a**	*n*-C_4H_9SH	$[(MeCN)_4Cu]PF_6$/L	DMSO	50	8	- [3]	
17	**1a**	*n*-$C_4H_9S^{\ominus}Na^{\oplus}$ **6a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	2	 **8a**; 65 [7]	
18	**1b**	**6a**	$[(MeCN)_4Cu]PF_6$/L	DMSO	rt	6	 **8b**; 48 [7]	65 [66]

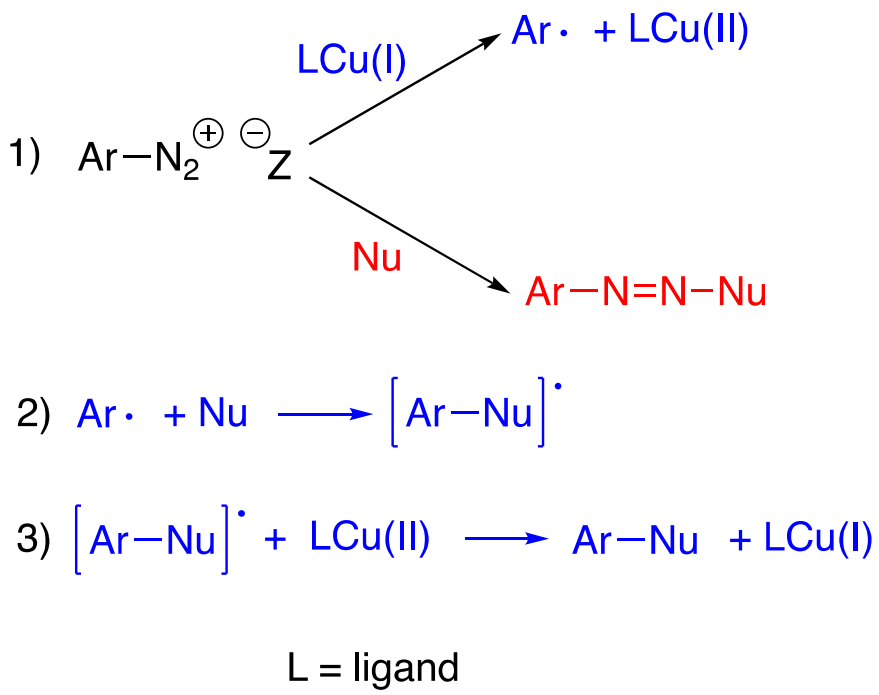
[1] The reactions were carried out with 2 mmol of **1**, 2.2 mmol of **5** and **6**, 2 mmol of Cu(I) adduct, and 2 mmol of ligand. Yields refer to pure and chromatographic column isolated, **7,8**. [2] After 24 h, **1a** had not reacted. GC-MS analyses of a sample showed the presence of nitrobenzene. [3] After 24 h, **1a** had still not reacted. GC-MS analyses of a sample showed the presence of nitrobenzene and **7a.** [4] Decomposition of **1a** occurred. [5] GC-MS analyses of crude residues also showed the presence of nitrobenzene and 4,4′-dinitrobiphenyl. [6] Lower amounts of $[(MeCN)_4Cu]PF_6$ and 1,10-phenanthroline, which led to significantly lower yields.[7] GC-MS analyses of crude residues always showed the presence of arenes and symmetrical biaryls as by-products. [8] Only traces of isopropyl phenyl ether were detected. The main product was nitrobenzene.

Finally, under the same conditions as the primary alcoholates, primary thiolate **6a** was prepared and gave good yields of the C-S coupling product, aryl alkyl sulfide **8a**,**b** (Table 2; entries 17 and 18).

In conclusion, the target products, **3**, **7**, **8**, were obtained in discrete yields, but sometimes, the yields were lower than those reported in the literature for the same products obtained with different Ullmann-type reactions, using aryl halides as electrophiles (Tables 1 and 2); however, it is necessary to highlight that generally, these latter reactions are carried out at high temperatures under strictly controlled conditions (e.g., in an inert atmosphere and/or in a sealed vial) with long reaction times. On the contrary, by using diazonium salts as an alternative to aryl halides, the reactions can be carried out in milder conditions (for example, at room temperature, in open air vials and with shorter reaction times)

It is worth noting that it was possible to recover *o*-benzenedisulfonimide at a yield of more than 80% from all the reactions described above. It was also possible to recycle it for the preparation of other salts **1**, with economic and ecological benefits.

In order to formulate a convincing hypothesis on the mechanism of this Ullmann-type coupling, two reactions, reported in Table 1 (entry 11) and Table 2 (entry 5), were carried out in the presence of TEMPO, a well-known radical scavenger; a sharp decrease in the yields of **3a** and **7a** were observed. In light of this, and inspired by Kochi's previous mechanistic studies [1,67], we hypothesized a radical S_{RN1}-type mechanism, as shown in Scheme 4. It must be stressed that dediazoniations initiated by an electron transfer are well-known reactions of diazonium salts [7,35,53].



Scheme 4. Ullmann-type coupling: hypothesis of mechanism.

We believe that in step 1, there may be competition between the Cu (I) adduct and the nucleophile (ammine, alcoholate or thiolate). This could explain why a stoichiometric amount of Cu (I) adduct is needed, so that the coupling products **3**, **7**, **8** can be formed. On the other hand, the ligand 1,10-phenanthroline, stabilizing the Cu (I) adduct, would facilitate its interaction with the diazonium salt, and consequently step 3. Indeed, copper catalysis is not necessary to produce aryl alkyl sulfides **8**; they can be easily obtained with the classic Stadler–Ziegler reaction [68]; however, this reaction is dangerous to carry out as a result of the intermediate formation and accumulation of the highly explosive diazosulfides. In our previous paper [68], we developed an efficient and safe modification

of the Stadler–Ziegler reaction, in which the formation of disulfides always occurred as by-products. Carrying out the reaction in the presence of Cu(I) as a catalyst, we never observed the formation of disulfides. This leads us to believe that the reaction mechanism, shown in Scheme 4, may also be plausible with thiolates **6**.

4. Conclusions

We have proposed a mild, easy and efficient Ullmann-type coupling of arenediazonium and heteroarenediazonium *o*-benzenedisulfonimides. The target products were generally obtained in fairly good yields (18 positive examples, 66% average yield). To the best of our knowledge, in this study, diazonium salts have been used as electrophilic partners in an Ullmman-type protocol for the first time.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/reactions3020022/s1, Physical and NMR data of anilines **3**, NMR spectra of anilines **3**, Physical and NMR data of ethers **6**, NMR spectra of ethers **6**, Physical and NMR data of thioethers **7**, NMR spectra of thioethers **7**. Figures S1–S18, such as Figure S1: NMR spectra of N-(*n*-Hexyl)-4-Nitroaniline (**3a**). Figure S2: NMR spectra of N-(*n*-Hexyl)-4-Methoxyaniline (**3b**). Figure S3: NMR spectra of N-(*n*-Benzyl)-4-Methoxyaniline (**3c**). Figure S4: NMR spectra of N-(*n*-Benzyl)-4-Nitroaniline (**3d**). Figure S5: NMR spectra of N-(*n*-Hexyl)-2-Nitroaniline (**3e**). Figure S6: NMR spectra of N-(*n*-Hexyl)-3-Nitroaniline (**3f**). Figure S7: NMR spectra of N-(*n*-Hexyl)-2-Toluidine (**3g**). Figure S8: NMR spectra of N-(*n*-Hexyl)-3-Toluidine (**3h**). Figure S9: NMR spectra of NMR spectra of N-(*n*-Hexyl)-4-Iodoaniline (**3i**). Figure S10: NMR spectra of 2-[(4-Nitrophenyl)amino]Ethan-1-ol (**3j**). Figure S11: NMR spectra of 1-(*n*-Hexyloxy)-4-Nitrobenzene (**7a**). Figure S12: NMR spectra of 1-(n-Hexyloxy)-4-Methoxybenzene (**7b**). Figure S13: NMR spectra of 2-Ethoxynaphthalene (**7c**). Figure S14: NMR spectra of 2-Ethoxybenzo[d]thiazole (**7d**). Figure S15: NMR spectra of Methyl 3-Ethoxythiophene-2-carboxylate (**7e**). Figure S16: NMR spectra of 3-Ethoxypyridine (**7f**). Figure S17: *n*-Butyl 4-Nitrophenyl Sulfide (**8a**). Figure S18: *n*-Butyl 4-Tolyl Sulfide (**8b**). References [69–72] are cited in the supplementary materials.

Author Contributions: Conceptualization, S.D. and A.A.; methodology, S.D.; software, S.D.; validation, S.D. and A.A.; formal analysis, S.D.; investigation, S.D. and A.A.; resources, S.D.; data curation, S.D. and A.A.; writing—original draft preparation, S.D. and A.A.; writing—review and editing, S.D. and A.A.; visualization, S.D. and A.A.; supervision, S.D.; project administration, S.D.; funding acquisition, S.D. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflict of interest.

References

1. Sperotto, E.; van Klink, G.P.M.; van Koten, G.; de Vries, J.G. The mechanism of the modified Ullmann reaction. *Dalton Trans.* **2010**, *39*, 10338–10351. [CrossRef] [PubMed]
2. Ribas, X.; Güell, I. Cu(I)/Cu(II) catalytic cycle involved in Ullmann-type cross-coupling reactions. *Pure Appl. Chem.* **2014**, *86*, 345–360. [CrossRef]
3. Cahiez, G.; Moyeux, A.; Cossyc, J. Grignard Reagents and Non-Precious Metals: Cheap and Eco-Friendly Reagents for Developing Industrial Cross-Couplings. A Personal Account. *Adv. Synth. Catal.* **2015**, *357*, 1983–1989. [CrossRef]
4. Neidig, M.L.; Carpenter, S.H.; Curran, D.J.; DeMuth, J.C.; Fleischauer, V.E.; Iannuzzi, T.E.; Neate, P.G.N.; Sears, J.D.; Wolford, N.J. Development and Evolution of Mechanistic Understanding in Iron-Catalyzed Cross-Coupling. *Acc. Chem. Res.* **2019**, *52*, 140–150. [CrossRef] [PubMed]
5. Diccianni, J.B.; Diao, T. Mechanisms of Nickel-Catalyzed Cross-Coupling Reactions. *Trends Chem.* **2019**, *1*, 830–844. [CrossRef]
6. Chemley, S.R. Copper catalysis in organic synthesis. *Beilstein J. Org. Chem.* **2015**, *11*, 2252–2253. [CrossRef]
7. Antenucci, A.; Barbero, M.; Dughera, S.; Ghigo, G. Copper catalysed Gomberg-Bachmann-Hey reactions of arenediazonium tetrafluoroborates and heteroarenediazonium o-benzenedisulfonimides. Synthetic and mechanistic aspects. *Tetrahedron* **2020**, *76*, 131632. [CrossRef]
8. Ullmann, F.; Bielecki, J. Ueber Synthesen in der Biphenylreihe. *Chem. Ber.* **1901**, *34*, 2174–2185. [CrossRef]
9. Ullmann, F. Ueber eine neue Bildungsweise von Diphenylaminderivaten. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382–2384. [CrossRef]

10. Ding, X.; Bai, J.; Wang, H.; Zhao, B.; Li, J.; Ren, F. A mild and regioselective Ullmann reaction of indazoles with aryliodides in water. *Tetrahedron* **2017**, *73*, 172–178. [CrossRef]
11. Wu, Q.; Wang, L. Immobilization of Copper(II) in Organic-Inorganic Hybrid Materials: A Highly Efficient and Reusable Catalyst for the Classic Ullmann Reaction. *Synthesis* **2008**, *13*, 2007–2012. [CrossRef]
12. Lo, Q.A.; Sale, D.; Braddock, D.C.; Davies, R.P. Mechanistic and Performance Studies on the Ligand-Promoted Ullmann Amination Reaction. *ACS Catal.* **2018**, *8*, 101–109. [CrossRef]
13. Clavè, G.; Garel, C.; Renard, C.P.B.-L.; Olszewski, T.-K.; Lange, B.; Shutcha, M.; Faucon, M.-P.; Grison, C. Ullmann reaction through ecocatalysis: Insights from bioresource and synthetic potential. *RSC Adv.* **2016**, *6*, 59550–59564. [CrossRef]
14. Ferlin, F.; Trombettoni, V.; Luciani, L.; Fusi, S.; Piermatti, O.; Santoro, S.; Vaccaro, L. A waste-minimized protocol for copper-catalyzed Ullmann-type reaction in a biomass derived furfuryl alcohol/water azeotrope. *Green Chem.* **2018**, *20*, 1634–1639. [CrossRef]
15. Yashwantrao, G.; Saha, S. Sustainable strategies of C–N bond formation via Ullmann coupling employing earth abundant copper catalyst. *Tetrahedron* **2021**, *97*, 132406. [CrossRef]
16. Zuo, Z.; Kim, R.S.; Watson, A.D. Synthesis of Axially Chiral 2,2′-Bisphosphobiarenes via a Nickel-Catalyzed Asymmetric Ullmann Coupling: General Access to Privileged Chiral Ligands without Optical Resolution. *J. Am. Chem. Soc.* **2021**, *143*, 1328–1333. [CrossRef]
17. Dai, L. Ullmann Reaction, A Centennial Memory and Recent Renaissance Related Formation of Carbon Heteroatom Bond. *Prog. Chem.* **2018**, *30*, 1257–1297. [CrossRef]
18. Chen, Y.-J.; Chen, H.-H. 1,1,1-Tris(hydroxymethyl)ethane as a New, Efficient, and Versatile Tripod Ligand for Copper-Catalyzed Cross-Coupling Reactions of Aryl Iodides with Amides, Thiols, and Phenols. *Org. Lett.* **2006**, *8*, 5609–5612. [CrossRef]
19. Altman, R.A.; Shafir, A.; Lichtor, P.A.; Buchwald, S.L. An Improved Cu-Based Catalyst System for the Reactions of Alcohols with Aryl Halides. *J. Org. Chem.* **2008**, *73*, 284–286. [CrossRef]
20. Zhang, Y.; Yang, X.; Yao, Q.; Ma, D. CuI/DMPAO-Catalyzed N-Arylation of Acyclic Secondary Amines. *Org. Lett.* **2012**, *14*, 3056–3059. [CrossRef]
21. Zhou, W.; Fan, M.; Yin, J.; Jiang, Y.; Ma, D. CuI/Oxalic Diamide Catalyzed Coupling Reaction of (Hetero)Aryl Chlorides and Amines. *J. Am. Chem. Soc.* **2015**, *137*, 11942–11945. [CrossRef] [PubMed]
22. Gao, J.; Bhunia, S.; Wang, K.; Gan, L.; Xia, S.; Ma, D. Discovery of N-(Naphthalen-1-yl)-N′-alkyl Oxalamide Ligands Enables Cu-Catalyzed Aryl Amination with High Turnovers. *Org. Lett.* **2017**, *19*, 2809–2812. [CrossRef] [PubMed]
23. Quivelli, A.F.; Vitale, P.; Perna, F.M.; Capriati, V. Reshaping Ullmann Amine Synthesis in Deep Eutectic Solvents: A Mild Approach for Cu-Catalyzed C-N Coupling Reactions with No Additional Ligands. *Front. Chem.* **2019**, *7*, 723. [CrossRef] [PubMed]
24. Quivelli, A.F.; Marinò, M.; Vitale, P.; Álvarez, J.G.; Perna, F.M.; Capriati, V. Ligand-Free Copper-Catalyzed Ullmann-Type C O Bond Formation in Non-Innocent Deep Eutectic Solvents under Aerobic Conditions. *ChemSusChem* **2022**, *15*, e202102211. [CrossRef]
25. Liu, W.; Xu, J.; Chen, X.; Zhang, F.; Xu, Z.; Wang, D.; He, Y.; Xia, X.; Zhang, X.; Liang, Y. CuI/2-Aminopyridine 1-Oxide Catalyzed Amination of Aryl Chlorides with Aliphatic Amines. *Org. Lett.* **2020**, *22*, 7486–7490. [CrossRef]
26. van Emelen, L.; Henrion, M.; Lemmens, R.; de Vos, D. C–N coupling reactions with arenes through C–H activation: The state-of-the-art *versus* the principles of green chemistry. *Catal. Sci. Technol.* **2022**, *12*, 360–389. [CrossRef]
27. Ji, R.; Jie, X.; Zhou, Y.; Wang, Y.; Li, B.; Liu, X.; Zhao, J. Light-Assisted Ullmann Coupling of Phenols and Aryl Halides: The Synergetic Effect Between Plasmonic Copper Nanoparticles and Carbon Nanotubes from Various Sources. *Chem. Eur. J.* **2022**, *28*, e202103703. [CrossRef]
28. Rajabzadeh, M.; Najdi, N.; Zarei, Z.; Khalifeh, R. CuI Immobilized on Tricationic Ionic Liquid Anchored on Functionalized Magnetic Hydrotalcite (Fe_3O_4/HT-TIL-CuI) as a Novel, Magnetic and Efficient Nanocatalyst for Ullmann-Type C–N Coupling Reaction. *J. Inorg. Organomet. Polym. Mater.* **2022**, 1–16. [CrossRef]
29. Quivelli, A.F.; Rossi, F.V.; Vitale, P.; Álvarez, J.G.; Perna, F.M.; Capriati, V. Sustainable and Scalable Two-Step Synthesis of Thenfadil and Some Analogs in Deep Eutectic Solvents: From Laboratory to Industry. *ACS Sust. Chem. Eng.* **2022**, *10*, 4065–4072. [CrossRef]
30. Sawant, S.Y.; Somani, R.S.; Cho, M.H.; Bajaj, H.C. A low temperature bottom-up approach for the synthesis of few layered graphene nanosheets via C–C bond formation using a modified Ullmann reaction. *RSC Adv.* **2015**, *5*, 46589–46597. [CrossRef]
31. Roglans, A.; Pla-Quintana, A.; Moreno-Mañas, M. Diazonium Salts as Substrates in Palladium-Catalyzed Cross-Coupling Reactions. *Chem. Rev.* **2006**, *106*, 4622–4643. [CrossRef] [PubMed]
32. Felpin, F.-X.; Sengupta, S. Biaryl synthesis with arenediazonium salts: Cross- coupling, CH-arylation and annulation reactions. *Chem. Soc. Rev.* **2019**, *48*, 1150–1193. [CrossRef] [PubMed]
33. Cepanec, I.; Litvic, M.; Udikovic, J.; Pogorelic, I.; Lovric, M. Copper(I)-catalysed homo-coupling of aryldiazonium salts: Synthesis of symmetrical biaryls. *Tetrahedron* **2007**, *63*, 5614–5621. [CrossRef]
34. Sheng, M.; Frurip, D.; Gorman, D. Reactive chemical hazards of diazonium salts. *J. Loss Prev. Process Ind.* **2015**, *38*, 114–118. [CrossRef]
35. Antenucci, A.; Bonomo, M.; Ghigo, G.; Gontrani, L.; Barolo, C.; Dughera, S. How do arenediazonium salts behave in deep eutectic solvents? A combined experimental and computational approach. *J. Mol. Liq.* **2021**, *339*, 116743. [CrossRef]

36. Ghigo, G.; Bonomo, M.; Antenucci, A.; Reviglio, C.; Dughera, S. Copper-Free Halodediazoniation of Arenediazonium Tetrafluoroborates in Deep Eutectic Solvents-like Mixtures. *Molecules* **2022**, *27*, 1909–1924. [CrossRef]
37. Firth, J.D.; Fairlamb, J.S. A Need for Caution in the Preparation and Application of Synthetically Versatile Aryl Diazonium Tetrafluoroborate Salts. *Org. Lett.* **2020**, *22*, 7057–7059. [CrossRef]
38. Xie, C.; Yuan, Y.; Wang, B.; Du, L. Research on the decomposition kinetics and thermal hazards of aniline diazonium salt. *Thermochim. Acta* **2022**, *709*, 179156. [CrossRef]
39. Oger, N.; Le Grognec, E.; Felpin, F.-X. Handling diazonium salts in flow for organic and material chemistry. *Org. Chem. Front.* **2015**, *2*, 590–614. [CrossRef]
40. Barbero, M.; Crisma, M.; Fochi, I.D.R.; Perracino, P. New Dry Arenediazonium Salts, Stabilized to an Exceptionally High Degree by the Anion of o-Benzenedisulfonimide. *Synthesis* **1998**, 1171–1175. [CrossRef]
41. Barbero, M.; Degani, I.; Dughera, S.; Fochi, R. Halodediazoniations of Dry Arenediazonium *o*-Benzenedisulfonimides in the Presence or Absence of an Electron Transfer Catalyst. Easy General Procedures to Prepare Aryl Chlorides, Bromides, and Iodides. *J. Org. Chem.* **1999**, *64*, 3448–3453. [CrossRef] [PubMed]
42. Artuso, E.; Barbero, M.; Degani, I.; Dughera, S.; Fochi, R. Arenediazonium *o*-benzenedisulfonimides as efficient reagents for Heck-type arylation reactions. *Tetrahedron* **2006**, *62*, 3146–3157. [CrossRef]
43. Dughera, S. Palladium-Catalyzed Cross-Coupling Reactions of Dry Arenediazonium *o*-Benzenedisulfonimides with Aryltin Compounds. *Synthesis* **2006**, *2006*, 1117–1123. [CrossRef]
44. Barbero, M.; Cadamuro, S.; Dughera, S.; Giaveno, C. Reactions of Dry Arenediazonium *o*-Benzenedisulfonimides with Triorganoindium Compounds. *Eur. J. Org. Chem.* **2006**, *2006*, 4884–4890. [CrossRef]
45. Barbero, M.; Cadamuro, S.; Dughera, S. Palladium-Catalyzed Cross-Coupling Alkylation of Arenediazonium *o*-Benzenedisulfonimides. *Synthesis* **2008**, *2008*, 474–478. [CrossRef]
46. Barbero, M.; Cadamuro, S.; Dughera, S.; Ghigo, G. Reactions of Arenediazonium *o*-Benzenedisulfonimides With Aliphatic Triorganoindium Compounds. *Eur. J. Org. Chem.* **2008**, *2008*, 862–869. [CrossRef]
47. Barbero, M.; Cadamuro, S.; Dughera, S. Negishi cross-coupling of arenediazonium *o*-benzenedisulfonimides. *Tetrahedron* **2014**, *70*, 8010–8016. [CrossRef]
48. Barbero, M.; Cadamuro, S.; Dughera, S. Copper- and Phosphane-Free Sonogashira Coupling of Arenediazonium *o*-Benzenedisulfonimides. *Eur. J. Org. Chem.* **2014**, *2014*, 598–605. [CrossRef]
49. Barbero, M.; Cadamuro, S.; Dughera, S. Copper-free Sandmeyer cyanation of arenediazonium *o*-benzenedisulfonimides. *Org. Biomol. Chem.* **2016**, *14*, 1437–1441. [CrossRef]
50. Barbero, M.; Dughera, S. Gold catalyzed Heck-coupling of arenediazonium o-benzenedisulfonimides. *Org. Biomol. Chem.* **2018**, *16*, 295–301. [CrossRef]
51. Barbero, M.; Dughera, S. Gold catalysed Suzuki-Miyaura coupling of arenediazonium *o*-benzenedisulfonimides. *Tetrahedron* **2018**, *74*, 5758–5769. [CrossRef]
52. Kritchenkov, I.S.; Shakirova, J.R.; Tunik, S.P. Efficient one-pot green synthesis of tetrakis(acetonitrile)copper(I) complex in aqueous media. *RSC Adv.* **2019**, *9*, 15531–15535. [CrossRef]
53. Zollinger, H. *Diazochemistry: Aromatic and Heteroaromatic Compounds*; Wiley-VCH: Weinheim, Germany, 1994. [CrossRef]
54. Saunders, K.H.; Allen, R.L.M. *Aromatic Diazo Compounds*; Edward Arnold: London, UK, 1985.
55. Wang, D.; Zheng, Y.; Yang, M.; Zhang, F.; Mao, F.; Yu, J.; Xia, X. Room-temperature Cu-catalyzed N-arylation of aliphatic amines in neat water. *Org. Biomol. Chem.* **2017**, *15*, 8009–8012. [CrossRef]
56. Yang, H.; Xi, C.; Miao, Z.; Chen, R. Cross-Coupling Reactions of Aryl Halides with Amines, Phenols, and Thiols Catalyzed by an N,N′-Dioxide–Copper(I) Catalytic System. *Eur. J. Org. Chem.* **2011**, *2011*, 3353–3360. [CrossRef]
57. Yang, K.; Qiu, Y.; Li, Z.; Wang, Z.; Jiang, S. Ligands for Copper-Catalyzed C-N Bond Forming Reactions with 1 Mol% CuBr as Catalyst. *J. Org. Chem.* **2011**, *76*, 3151–3159. [CrossRef] [PubMed]
58. F Y Kwong, S.B. Mild and Efficient Copper-Catalyzed Amination of Aryl Bromides with Primary Alkylamines. *Org. Lett.* **2003**, *5*, 793–796. [CrossRef] [PubMed]
59. Feng, Y.-S.; Man, Q.-S.; Pan, P.; Pan, Z.-Q.; Xu, H.-J. CuCl-catalyzed formation of C–N bond with a soluble base. *Tetrahedron Lett.* **2009**, *50*, 2585–2588. [CrossRef]
60. Yang, M.; Liu, F. An Ullmann Coupling of Aryl Iodides and Amines Using an Air-Stable Diazaphospholane Ligand. *J. Org. Chem.* **2007**, *72*, 8969–8971. [CrossRef]
61. Costa, M.V.; Viana, G.M.; de Souza, T.M.; Malta, L.F.B.; Aguiar, L.C.S. Copper-catalyzed C–N cross-coupling reactions for the preparation of aryl diamines applying mild conditions. *Tetrahedron Lett.* **2013**, *54*, 2332–2335. [CrossRef]
62. DeTar, D.F.; Turetzky, M.N. The Mechanisms of Diazonium Salt Reactions. I. The Products of the Reactions of Benzenediazonium Salts with Methanol. *J. Am. Chem. Soc.* **1955**, *77*, 1745–1750. [CrossRef]
63. Shriver, J.A.; Flaherty, D.P.; Herr, C.C. Aryl Ethers from Arenediazonium Tetrafluoroborate Salts: From Neat Reactions to Solvent-mediated Effects. *J. Iowa Acad. Sci. JIAS* **2009**, *116*, 27–35.
64. Huang, J.; Chen, Y.; Chan, J.; Ronk, M.L.; Larsen, R.D.; Faul, M.M. An Efficient Copper-Catalyzed Etherification of Aryl Halides. *Synlett* **2011**, *10*, 1419–1422. [CrossRef]
65. Murru, S.; Mondal, P.; Yella, R.; Patel, B.K. Copper(I)-Catalyzed Cascade Synthesis of 2-Substituted 1,3-Benzothiazoles: Direct Access to Benzothiazolones. *Eur. J. Org. Chem.* **2009**, *2009*, 5406–5413. [CrossRef]

66. Sakai, N.; Maeda, H.; Ogiwara, Y. Copper-Catalyzed Three-Component Coupling Reaction of Aryl Iodides, a Disilathiane, and Alkyl Benzoates Leading to a One-Pot Synthesis of Alkyl Aryl Sulfides. *Synthesis* **2019**, *51*, 2323–2330. [CrossRef]
67. Kochi, J.K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, NY, USA, 1978.
68. Barbero, M.; Degani, I.; Diulgheroff, N.; Dughera, S.; Fochi, R.; Migliaccio, M. Alkyl- and Arylthiodediazoniations of Dry Arenediazonium o-Benzenedisulfonimides. Efficient and Safe Modifications of the Stadler and Ziegler Reactions to Prepare Alkyl Aryl and Diaryl Sulfides. *J. Org. Chem.* **2000**, *65*, 5600–5608. [CrossRef] [PubMed]
69. Gaur, P.; Yamajala, K.D.B.; Banerjee, S. Efficient synthetic route to aromatic secondary amines via Pd/RuPhos/TBAB-catalyzed cross coupling. *New J. Chem.* **2017**, *41*, 6523–6529. [CrossRef]
70. Petricci, E.; Santillo, N.; Castagnolo, D.; Cini, E.; Taddei, M. Iron-Catalyzed Reductive Amination of Aldehydes in Isopropyl Alcohol/Water Media as Hydrogen Sources. *Adv. Synth. Catal.* **2018**, *360*, 2560–2565. [CrossRef]
71. Yang, C.; Zhang, F.; Deng, G.-J.; Gong, H. Amination of Aromatic Halides and Exploration of the Reactivity Sequence of Ar-omatic Halides. *Synthesis* **2019**, *84*, 181–190. [CrossRef]
72. Meo, P.L.; D'Anna, F.; Gruttadauria, M.; Riela, S.; Noto, R. Thermodynamics of binding between α- and β- cyclodextrins and some p-nitroaniline derivatives: Reconsidering the enthalpy–entropy compensation effect. *Synthesis* **2004**, *60*, 9099–9111. [CrossRef]