

# Ullmann reaction in tetraethyl orthosilicate: a novel synthesis of triarylamines and diaryl ethers†

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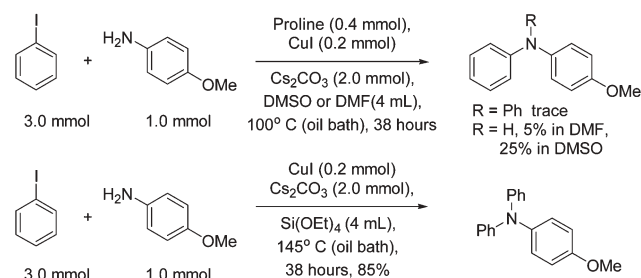
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A novel synthesis of triarylamines and diaryl ethers is reported; a feature of this process is the ligand-free copper-catalysed C–N and C–O bond formation in tetraethyl orthosilicate.

High boiling point solvents are frequently required as reaction media for better yields in organic synthesis. These solvents generally provide the high temperature that is sometimes crucial for the synthesis of triarylamines, an important type of electronic materials,<sup>1</sup> by a copper-promoted Ullmann reaction.<sup>2</sup> Although numerous high boiling point organic solvents have been used as reaction media for this transformation, relatively few are in general use. As a consequence, the utilization of high boiling point solvents suffers from the difficulty of purifying the desired products and is occasionally problematic, with several chromatographic separations being required to separate a desired product from the residue of a high boiling point solvent. As reaction “media”, solvents are used in large excess. Unavoidably, this brings the environmental problem of atmospheric emissions and the contamination of aqueous effluents. It is therefore highly desirable to find suitable solvents for high-temperature Ullmann reactions that don't suffer the shortcomings of traditional high boiling point solvents such as DMF and DMSO.

In our studies towards the synthesis of triarylamines, we decided to carry out a proline–copper complex-catalysed Ullmann amination, as indicated in Scheme 1. Although proline–copper complex-promoted amination had been successfully applied to the preparation of diarylamines in the literature,<sup>3</sup> no examples concerning triarylamines have been reported.



**Scheme 1** Attempts towards the synthesis of triarylamines.

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To our disappointment, besides low yields (5% in DMF and 25% in DMSO), the purification of diarylamines from the residue of DMF or DMSO was troublesome. In the literature,<sup>4</sup> tetraethyl orthosilicate (TEOS) has been utilized as a dehydration reagent for the synthesis of enaminoesters<sup>4a</sup> and sterically-hindered imines.<sup>4b</sup> We perceived that TEOS could be used as a solvent for Ullmann reactions. As shown in Scheme 1, when switching to TEOS, the desired triarylamine, which was generally obtained by the utilization of a ligated palladium or copper complex-catalysed Ullmann reaction,<sup>5</sup> was obtained in one step with high yield in the presence of copper(I) iodide.‡ No ligand was necessary in this new solvent.<sup>6</sup>

Encouraged by this result, we carried out a number of reactions in TEOS in order to optimise the reaction conditions (Table 1). We found that the copper-catalysed amination of aryl iodide in TEOS could lead to triarylamines in good yield, even in the presence of only a 10% equivalent amount of copper(I) iodide (Table 1, entry 4). In order to understand the role that TEOS plays, we also carried out reactions in traditional solvents, but with TEOS as an additive. It is worthwhile noting that TEOS might serve as a promoting ligand for Ullmann coupling (Table 1, entries 8 and 9). The yields of triarylamines dramatically decreased when bromobenzene was used instead of iodobenzene.

Although the palladium complex-catalysed “one-pot” synthesis of triarylamines has been realized by Buchwald,<sup>5h</sup> to the best of

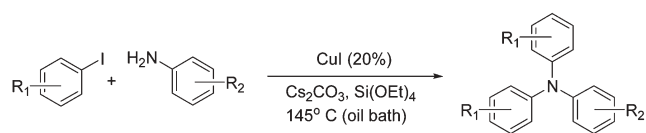
**Table 1** Studies on the CuI-catalysed formation of triarylamines<sup>a</sup>

Entry	Base	Solvent	Aryl halide	Yield (%)
1	<sup>t</sup> BuOK	Si(OEt) <sub>4</sub>	Iodobenzene	(complex)
2	K <sub>2</sub> CO <sub>3</sub>	Si(OEt) <sub>4</sub>	Iodobenzene	65
3	Cs <sub>2</sub> CO <sub>3</sub>	Si(OEt) <sub>4</sub>	Iodobenzene	82
4	Cs <sub>2</sub> CO <sub>3</sub>	Si(OEt) <sub>4</sub>	Iodobenzene	67 <sup>b</sup>
5	Cs <sub>2</sub> CO <sub>3</sub>	Si(OEt) <sub>4</sub>	Bromobenzene	5
6	Cs <sub>2</sub> CO <sub>3</sub>	DMF	Iodobenzene	7
7	Cs <sub>2</sub> CO <sub>3</sub>	DMSO	Iodobenzene	5
8	Cs <sub>2</sub> CO <sub>3</sub>	DMF	Iodobenzene	70 <sup>c</sup>
9	Cs <sub>2</sub> CO <sub>3</sub>	DMSO	Iodobenzene	55 <sup>c</sup>

<sup>a</sup> Reaction conditions: Aryl halide (3 mmol), CuI (20% mol equiv.), aryl amine (1 mmol) and base (2 mmol) in commercially available organic solvents (4 mL) were de-gassed and purged with nitrogen, and then stirred at 145 °C (oil bath) for 20 h. <sup>b</sup> Reactions were carried out under identical conditions, except with less CuI (10% mol equiv.).

<sup>c</sup> Reactions were carried out under identical conditions, except in the presence of TEOS (1.0 mmol). Yields quoted are isolated yields.

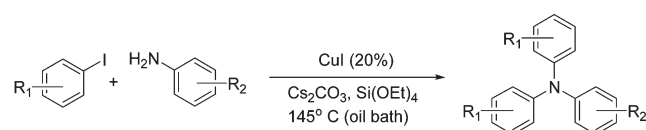
**Table 2** CuI-catalysed synthesis of triarylamines in TEOS with primary arylamines and aryl iodides<sup>a</sup>



Entry	Product	Time/h	Yield (%)
1		48	61
2		42	70
3		40	75
4		24	85
5		30	83
6		18	89
7		24	90
8		40	81
9		24	80

our knowledge, our procedure represents the first general method for the one-step synthesis of triarylamines with catalytic amounts of copper (20%) in the absence of a promoting additive ligand under relatively mild reaction conditions (145 °C oil bath and Cs<sub>2</sub>CO<sub>3</sub> as a base). Complete removal of the solvent (TEOS) was easily realized by treatment of the reaction mixture with freshly prepared aqueous NH<sub>4</sub>F (6.25%) absorbed onto silica gel in the presence of ethanol. The solvent was completely converted to silica gel, and the desired product was obtained by filtration and washing with a regular organic solvent. With a 20% amount of copper(I) iodide as the catalyst, a number of triarylamines were prepared with TEOS as the reaction media. The results are summarised in Table 2.

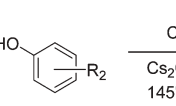
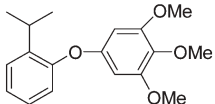
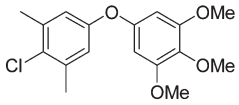
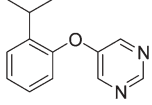
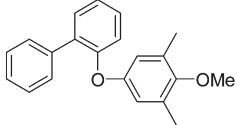
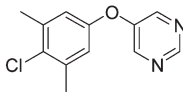
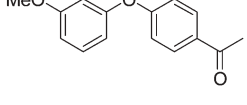
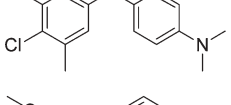
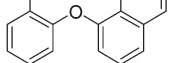
**Table 2** CuI-catalysed synthesis of triarylamines in TEOS with primary arylamines and aryl iodides<sup>a</sup> (Continued)



Entry	Product	Time/h	Yield (%)
10		30	81
11		24	94
12		24	85
13		120	87
14		32	84
15		28	93
16		24	88

<sup>a</sup> Reagents and conditions: Aryl iodide (3 mmol), CuI (38 mg, 0.2 mmol), aryl amine (1 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (652 mg, 2 mmol) in commercially available TEOS (3–5 mL) were de-gassed and purged with nitrogen, and then stirred at 145 °C (oil bath) for 18–120 h. Yields quoted are isolated yields.

**Table 3** CuI-catalysed formation of diarylethers in TEOS<sup>a</sup>

Entry	Product	Yield (%)
1		79
2		86
3		89
4		84
5		78
6		85
7		88
8		88
9		81

<sup>a</sup> *Reagents and conditions:* Aryl bromide (1 mmol), CuI (95 mg, 0.5 mmol), respective phenol (1.2–1.3 mmol) and Cs<sub>2</sub>CO<sub>3</sub> (652 mg, 2 mmol) in commercially available TEOS (3–5 mL) were de-gassed and purged with nitrogen, and then stirred at 145 °C (oil bath) for 18–20 h. Yields quoted are isolated yields.

The synthesis of diaryl ethers by copper-catalysed Ullmann coupling reactions are of current interest, and a number of new protocols have recently been developed.<sup>7</sup> To our pleasant surprise, our triarylamine synthetic process could also be applied to the synthesis of diarylether by the direct coupling of phenols with aryl bromides. A notable feature of our method is that it is free of a promoting additive ligand. A number of diaryl ethers were synthesized with high yields. The results are shown in Table 3.

In summary, a versatile reaction medium for the synthesis of triaryl amines and diaryl ethers by a ligand-free copper-catalysed Ullmann reaction, tetraethyl orthosilicate (TEOS), is disclosed. TEOS can serve as a promoting ligand in copper-catalysed Ullmann coupling reactions. Separation of the desired product from the solvent medium is also greatly facilitated. For applications in industry, TEOS could be recycled by distillation under reduced pressure, while the TEOS residue could be hydrolysed easily to silica gel and ethanol, therefore making it an economic and green process. Utilization of this solvent in other organic reactions is currently under way in our laboratory.

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## Notes and references

‡ *General procedure for the synthesis of triaryl amines:* A mixture of CuI (38 mg, 0.2 mmol), Cs<sub>2</sub>CO<sub>3</sub> (652 mg, 2 mmol, 2.0 equiv.), primary aryl amine (1 mmol) and aryl iodide (3 mmol) in TEOS (3–5 mL) was de-gassed and purged with nitrogen (2 times). The resulting mixture was then stirred at 145 °C (oil bath) under nitrogen. The reaction was monitored by thin layer chromatography (TLC). After cooling to room temperature, the residue was diluted with ethyl acetate (5 mL) and 95% ethanol (10 mL). NH<sub>4</sub>F–H<sub>2</sub>O on silica gel [5 g, pre-prepared by the addition of NH<sub>4</sub>F (10 g) in water (150 mL) to silica gel (50 g, 100–200 mesh)] was added, and the resulting mixture was kept at room temperature for 3–5 h. The solidified material was filtered and washed with ethyl acetate. After removal of the solvents, the residue was chromatographed on silica gel (ethyl acetate–petroleum ether) to afford the products.

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