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ARTICLE TYPE

Ionic liquid effect: Selective aniline oxidative coupling to azoxybenzene by TiO_2

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Simple commercially available TiO_2 in ionic liquids (ILs) promote the oxidative catalytic coupling of anilines to diazo compounds. For example, the reaction of aniline with molecular oxygen (5 bars) in the presence of TiO_2 and functionalised imidazolium-based ILs affords azoxybenzene up to an 85% yield. The catalytic selectivity and activity are mainly related to the viscosity, oxygen solubility, and stability of the superoxide ion ($O_2^{\bullet-}$) and ionic species provided by the IL (IL effect). This effect is evident since most of the reactions performed in the presence of ILs gave as a major product the azoxybenzene zwitterions. This is in opposition to that performed in toluene, which gave almost exclusively azobenzene.

Introduction

There is no doubt that the aerobic oxidation of aniline is an important reaction for the preparation of its oxygenated derivatives such as nitroso, azo, hydroxylamine, nitro, and azoxy aromatic compounds. Aromatic azoxy compounds are of great interest in view of their large applications such as dyes, reducing agents, chemical stabilisers, liquid crystal in electronic display, and therapeutic medicines.[1] In the same vein, aromatic azo compounds are widely used in the industry as pigments, indicators, food additives, and radical reaction initiators.[2-4] Although several methods for the synthesis of azo and azoxy derivatives have been reported, challenges remain to afford high yields and selectivities. Moreover, their preparation from aromatic amines usually requires the use of large amounts of lead salts,[5] mercury salts,[6] manganese salts,[7] ferrates,[8] or diazonium salts.[9]

However, the catalytic oxidation of anilines could be achieved using supported gold nanoparticles on TiO_2 under oxygen at 100 °C.[10] More recently, supported transition-metal nanoparticles have also been successfully used for the aerobic oxidation of anilines.[11] The employment of noble and expensive metals may limit their application. Although these catalytic methods represent a significant improvement as compared with classical ones, they use noble metals that are still a major drawback. Nonetheless, simple titanium dioxide is also active for the oxidation of aniline in toluene at 100 °C, giving diazobenzene a 52.5% yield.[10] It is accepted that the aerobic oxidation of the anilines involves radical and/or ionic species. In this respect, the use of compounds that can stabilise such species may generate more active and selective catalytic systems. It is well known that some imidazolium-based ionic liquids (ILs) are able to have a strong influence on the stability of radical and ionic species.[12, 13]

We report herein that simple ILs associated with commercially available titanium dioxide (P25) indeed make up a highly active noble-metal-free catalyst system for the oxidation of anilines. Moreover, we demonstrate that selectivity is strongly dependent on the nature of both the cation and anion of the IL.

Results and discussion

The screening of the ILs was performed using the same reaction conditions employed in the oxidation of aniline by P25 in toluene (i.e., at 100 °C for 24 h under 5 bars of molecular oxygen).[10] The reaction was performed by simple mixing of P25 (3.1 mmol) and aniline (10.7 mmol) in 1 g of various ILs (Figure 1). The results are summarised in Table 1.

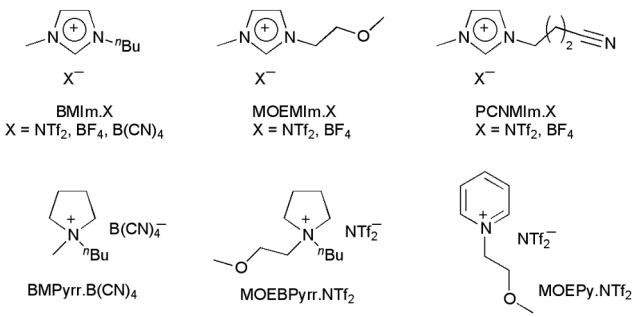

Figure 1. Structure of the ILs employed in the oxidative coupling of anilines.

It is clear from the data on Table 1 that regardless of the nature of the IL, aniline is oxidised (conversion from 64% to 95%) into only three products: azoxybenzene (**2a**), azobenzene (**3a**), and nitrobenzene (**4a**). In opposition to the reaction performed in toluene (entry 11, Table 1), nitrosobenzene was not detected, indicating that the IL induces the formation of nitrobenzene.

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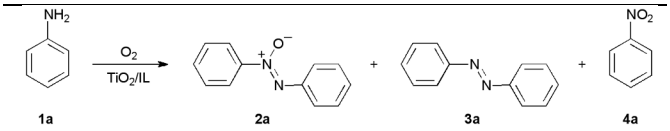
Table 1. Results of the aerobic oxidation of aniline (**1a**) in ILs catalysed by TiO_2[a]



Entry	Medium	Conv.(%)[b]	Selectivity (%)[b]		
			2a	**3a**	**4a**
1	MOEMIm.NTf_2	95	85	9	6
2	MOEMIm.BF_4	86	77	6	7
3	BMIm.BF_4	78	46	12	42
4	BMIm.NTf_2	73	76	18	6
5	BMIm.$B(CN)_4$	86	70	8	22
6	PCNMIm.NTf_2	75	23	22	55
7	PCNMIm.BF_4	89	2	3	95
8	MOEPy.NTf_2	94	20	8	72
9	MOEBPyrr.NTf_2	67	75	6	19
10	BMPyrr.$B(CN)_4$	64	36	7	57
11[c]	Toluene	53	0	52.5	0
12	CH_3CN	9	0	100	0
13	DMSO	3	0	100	0
14	THF	37	43	36	21

[a] Reaction conditions: aniline (10.7 mmol) dissolved in IL (1.0 g), TiO_2-P25 (3.1 mmol), 5 bars of O_2, 100 °C for 24 h. [b] Determined by gas chromatography using *n*-Undecane as an internal standard. [c] Data from reference 10.

The IL effect[14] is more pronounced in the selectivity since in most of the reactions performed in ILs, the major product is azoxybenzene (**2a**) zwitterions (see entries 1–5 and 9). This fact is in opposition to that performed in toluene, acetonitrile and DMSO, which yields almost exclusively azobenzene (**3a**) (entries 11-13, Table 1), and no azoxybenzene (**2a**) was observed. This is probably related to the stabilisation of ionic species promoted by the ILs.[15] Moreover, even in the cases where the selectivity is towards nitrobenzene (**4a**), the azobenzene (**3a**) is mostly the minor product (see entries 6, 8, and 10, Table 1) in the reactions performed in ILs. It is important to note that using THF the conversion was low and the selectivity was slightly superior for product **2a** (entry 14, Table 1).

The highest conversions are observed with methoxy-functionalised-based imidazolium (MOEIm.NTf_2) and pyridinium (MOEPy.NTf_2) ILs (see entries 1 and 8, respectively). This relatively higher catalytic activity is likely to be related to the lower viscosity and higher oxygen solubility displayed by these ILs as compared with the nonfunctionalised ones.[16] Moreover, it is known that the imidazolium-based ILs are able to stabilise superoxide ion ($O_2^{\bullet-}$),[12] and this is probably not the case for the nonconjugated pyrrolidinium cation (see entries 9 and 10, Table 1). In fact, the highest aniline conversion (95%) and selectivity (85%) on azoxybenzene (**2a**) was attained in the reaction performed in MOEIm.NTf_2 (entry 1), which has the relative lowest viscosity, the higher oxygen solubility, and the imidazolium ring that can stabilise the superoxide ion and catalyse the aniline oxidative coupling.

For the evaluation of the scope of reaction, it was decided that the IL MOEMIm.NTf_2 be used as a standard solvent because of its superior performance in terms of conversion and selectivity. Control experiments showed that the thermal oxidation of aniline does not occur. The effect of oxygen was also elucidated in an experiment performed under N_2, which showed no reaction. Then the presence of oxygen has been found to be essential for the oxidation of aniline. At 1 bar of oxygen pressure, 40% conversion was obtained, with 42% azoxybenzene, 9% azobenzene, and 49% nitrobenzene. As expected, increasing the oxygen pressure increases the conversion, with the selectivity of azoxybenzene reaching up to 85% at 5 bars (Figure 2). The higher selectivity of azoxybenzene compared with azobenzene even at 1 bar of oxygen suggests that it may be difficult to control the overoxidation of the preformed azobenzene to azoxybenzene using IL as a solvent. To investigate this hypothesis, the oxidation of azobenzene was carried out under the standard reaction conditions in MOEMIm.NTf_2 achieving 30% of conversion and total selectivity of azoxybenzene. This low conversion indicates that the overoxidation of azobenzene is not easy and that it is unlikely that the obtained azoxybenzene might come in its major amount from the oxidation of the preformed azobenzene (see the discussion below).

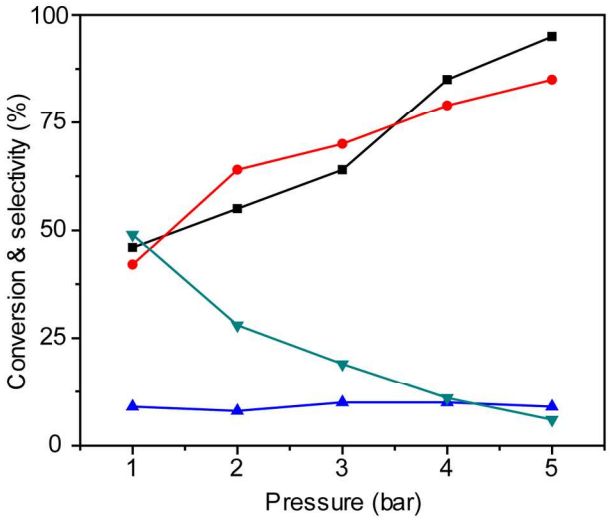


Figure 2. Graph showing the conversion/selectivity versus the O_2 pressure for aniline oxidation: (black) conversion, (red) **2a**, (blue) **3a**, and (green) **4a**. Aniline (10.7 mmol) dissolved in MOEMIm.NTf_2 (1.0 g), TiO_2-P25 (3.1 mmol), desired O_2 pressure at 100 °C for 24 h.

In addition, the selectivity of the products was followed during the oxidation of aniline in MOEMIm.NTf_2 at 5 bars of O_2 and at 100 °C (Figure 3).

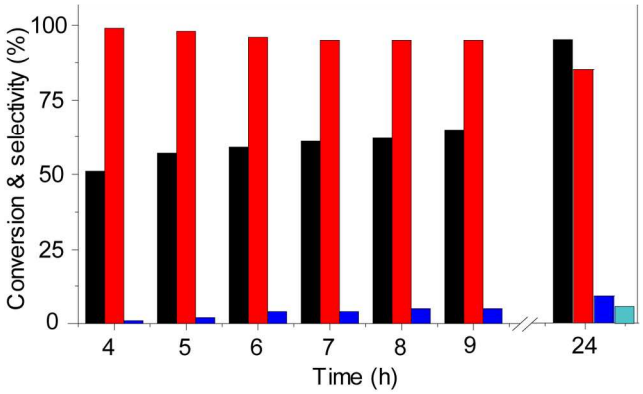


Figure 3. Conversion/selectivity versus time for aniline oxidation: (black) conversion, (red) **2a**, (blue) **3a**, and (green) **4a**. Aniline (10.7 mmol) dissolved in MOEMIm.NTf_2 (1.0 g), TiO_2-P25 (3.1 mmol), 5 bars of O_2 pressure at 100 °C.

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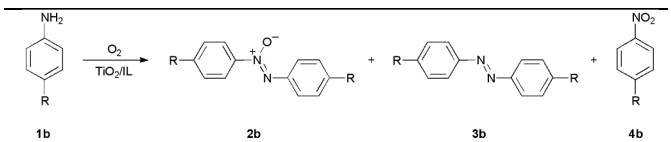
The reaction started only after 3 h, and the selectivity of azoxybenzene was always much higher than that of azobenzene. This fact indicates that the IL is stabilising the ionic transition species favouring the formation of the azoxy compound. Interestingly, nitrobenzene was not observed even after 9 h of reaction, suggesting that it is not a preferred product in this case.

To demonstrate the general applicability of aerobic catalytic oxidation, a screening of some primary aromatic substituted anilines was performed (Table 2). In most of the cases, the reaction was found to be selective for the azobenzene product. The reaction rate depended qualitatively on the Hammett constant of the substituent since the oxidation reaction is favoured in the presence of electron-donor substituents. The homocoupling of anilines with electron-donating substituents is faster than that with electron-withdrawing substituents. Under the optimised conditions, *p*-methylaniline and *p*-methoxyaniline gave 99% and 90% of conversion, respectively. Interestingly, *p*-bromoaniline showed 50% of conversion with total selectivity to the azo derivative **3b** after a long reaction time (66 h). Moreover, no coupling was seen using *p*-nitroaniline, *m*-nitroaniline, and 2-methoxyaniline. Unfortunately, attempts to produce only heterocoupling products from the reaction using different couples of anilines failed because a mixture of homo- and heterocoupled products was observed in the system.

Table 2. Results of the aerobic oxidation of substituted anilines (**1b**) in the presence of TiO_2[a]



Entry	R	Time (h)	Conv.(%)[b]	Selectivity (%)[b]		
				2b	**3b**	**4b**
1	CH_3	24	99	34	45	21
2	OCH_3	24	90	56	31	13
3	Br	66	50	0	100	0
4	NO_2	66	0	0	0	0

[a] Reaction conditions: **1b** (5.5 mmol) dissolved in MOEMIm.NTf_2 (1.0 g), TiO_2-P25 (3.1 mmol), 5 bars of O_2 at 100 °C. [b] Determined by gas chromatography using *n*-Undecane as an internal standard.

The proposed mechanism for the oxidation of aniline probably involves the defect sites or vacancies on TiO_2 as active catalytic sites that are able to abstract an electron from aniline, activate the oxygen molecule, and also produce O_2^- radicals after the adsorption of oxygen on reduced titania.[17] After single electron abstraction, the coupling of a cationic aniline radical with a neutral aniline leads to the formation of a hydrazine-derived compound.[18-22] This hydrazine-derived compound undergoes overoxidation by the IL-stabilised superoxide ion ($O_2^{\bullet-}$)[12] to yield azoxybenzene and/or nitrobenzene.[23, 24] The presence of a radical species was confirmed by using CCl_4 and hydroquinone as scavenger agents.

Conclusions

In conclusion, we have developed an efficient new heterogeneous catalytic method for the aerobic oxidation of anilines to aromatic azoxy compounds by using ILs as a surface modifier. The preferred selectivity of azoxy instead of azo compounds in ILs may be related to the intrinsic properties of ILs in stabilising ionic species (IL effect). Indeed, it was found that the cage lifetime for radical ion pairs in ionic liquid was estimated to be much longer than the neutral radical pairs in the same fluid.[25] The nature of IL has a significant influence on the conversion and selectivity of products. In particular, the IL cation seems to play a major role during the oxidation reaction. A higher catalytic activity and selectivity was attained in ILs displaying lower viscosity and higher oxygen solubility, such as in the case of MOEMIm.NTf_2, which can also stabilise superoxide ion ($O_2^{\bullet-}$) formed after the adsorption of oxygen on reduced titania.

Experimental section

General

The ILs were prepared following the procedures previously reported: MOEMIm.NTf_2,[26] MOEMIm.BF_4,[26] PCNMIm.BF_4,[27] PCNMIm.NTf_2,[27] BMIm.BF_4,[28] BMIm.NTf_2,[28] MOEBPyrr.NTf_2,[29, 30] and MOEPy.NTf_2.[31] In particular, BMIm.$B(CN)_4$ and BMPyrr.$B(CN)_4$ were purchased from EMD Chemicals Inc. All the other chemicals were purchased from commercial sources. The substrates were distilled, degassed, and stored under argon prior to use. Mass spectra were obtained using a GC-MS Shimadzu QP-5050 (EI, 70 eV), and gas chromatography (GC) analyses were performed with an Agilent 6820 gas chromatograph with a flame ionisation detector and 30 m capillary column with a dimethylpolysiloxane stationary phase. For GC analysis, n-Undecane was used as an internal standard. The catalytic oxidation reactions were carried out in a modified Fischer-Porter steel bottle immersed in a silicon oil bath. Caution: oxygen can form explosive mixtures with organic vapours in particular working under pressure in the presence of a catalyst, caution must be taken to avoid explosion.

Oxidation reactions

In a typical oxidation reaction, the IL (1.0 g) was mixed with TiO_2-P25 (3.1 mmol) in a Fischer-Porter reactor. After stirring for 10 minutes, distilled aniline (10.7 mmol) was added, and the reactor was loaded with oxygen (5 bars). The mixture was heated at 100 °C under magnetic stirring (650 rpm). After the desired time, the reactor was cooled at room temperature and depressurised. Aliquots were removed and analysed by GC and GC-MS. The validity of the identification and quantification of the GC peak were verified through a comparison of the mass spectra and gas chromatographic retention time with those of authentic compounds using *n*-Undecane as a standard.

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Notes and references

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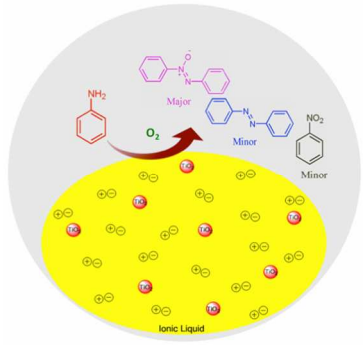
Graphical Abstract

TiO_2 promote the oxidative catalytic coupling of anilines to diazo compounds. In ionic liquids azoxybenzene is formed in high selectivity whereas in toluene azobenzene is formed almost exclusively.



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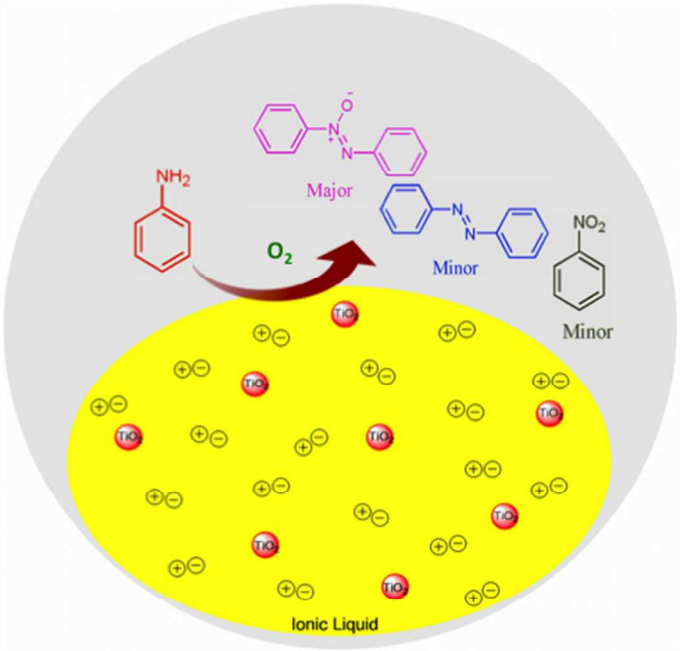

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