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Oxidation of Primary Aromatic Amines under Irradiation with Ultrasound and/or Microwaves

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Abstract: The oxidation of primary aromatic amines, p-methylaniline, p-ethylaniline and p-chloroaniline to the corresponding azo- and azoxy-compounds has been observed in ultrasound and/or microwaves systems. The individual irradiation of microwaves and its simultaneous irradiation with ultrasound obviously elevate the conversion of amines, as compared with the individual irradiation of ultrasound and the heating in a plain water bath. However, the formation of formamidine resulted in poor selectivity toward azo and azoxy products in the presence of dimethylformamide (DMF).

Aromatic azo and azoxy compounds are important dyes and are widely used in biological and chemical research as analytical reagents, reducing agents, stabilizers, and polymerization inhibitors. Aromatic azo compounds are traditionally synthesized by coupling diazo compounds with amines or phenols, oxidation of hydrazine and hydrazo compounds, the reduction of nitro compounds in alkaline solution, or molecular rearrangement of diazoamines. Azo compounds are converted into azoxy compounds by oxidizing agents.

The formation of azobenzene by oxidation of aniline in basic solution has also been long known, and its mechanism was clarified in the 1960s.[1,2]

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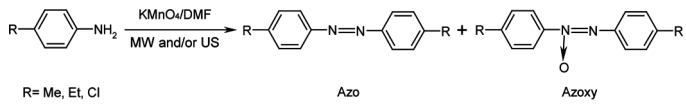
The catalytic oxidation of primary aromatic amines to azo derivatives with H_2O_2 in the presence of titanium silicate molecular sieves, sodium periodate in the presence of manganese(III) tetraphenylporphyrin, or titania pillared montmorillonite clays was recently reported.[3–7] Primary aromatic amines can also be oxidized to azo compounds by permanganate under solvent-free conditions, a green method.[8]

The reaction mechanism in which azobenzene is formed by oxidation of aniline in aqueous solution under irradiation with 21-kHz ultrasound (US) was explained.[9] Sonically generated H· and OH· radicals convert aniline to PhNH· and PhN· radicals that can combine to yield PhNHNHPh and PhN=NPh. Microwave (MW) irradiation has afforded another new procedure for the selective oxidation of aromatic amines. Using alumina as a solid support, azobenzene was prepared in 75% yield in 5 h at room temperature.[8] The oxidation of aniline with MnO_2/SiO_2 under MW irradiation (420 W) for just 4 min gave azobenzene in 84% yield.[10] Although the existing catalytic methods can achieve comparable yields of azo and azoxy compounds, the use of MW–US has the advantage of reducing catalyst load or dispensing with it altogether, besides facilitating the separation of products and significantly shortening production times.

The chemoselective reduction of nitroarenes to azo and azoxy compounds under US/MW irradiation has also been reported.[11] Either energy source, as well as their combination, promoted the reactions and increased their yields. The simultaneous use of US and MW represent an emerging technological innovation that deserves wider attention in fine chemical and pharmaceutical research. Although cavitation and MW effects are not fully understood, there is no doubt that processes requiring enhanced heat transfer and mass transport can greatly benefit from the use of this technique.[12]

The present communication deals with the use (so far unreported) of the simultaneous irradiation of microwaves and ultrasound for the selective oxidation of primary aromatic amines to azo and azoxy compounds (Scheme 1).

Reactions were carried out in batches in a 100-ml specially designed glass vessel placed in the center of a professional multimode MW oven



Scheme 1. Oxidation of primary aromatic amines under irradiation with ultrasound and/or microwaves.

Table 1. Conversion rates and product distribution for the oxidation of aromatic amines under MW and/or US irradiation[a]

Amine	Irradiation	Conversion (%)	Product distribution (%)				
			Formamidine	Diphenylamine	Azo	Azoxy	Other
p-Methylaniline	MW–US	71	8	6	47	6	33
	MW	80	13	11	44	9	23
	US	73	6	10	43	4	37
p-Ethylaniline	MW–US	72	16	2	45	16	21
	MW	80	17	9	45	11	18
	US	57	12	9	49	18	12
	Water bath	54	27	7	38	12	16
p-Chloroaniline	MW–US	47	20	0	40	19	21
	MW	40	34	0	25	14	27
	US	34	15	1	61	14	9

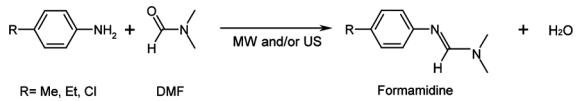
[a]2 mmol of amine, 4 mmol of $KMnO_4$, 25 ml of DMF, 5 ml of H_2O. MW: MLS-Ethos MW system; 1 min at 1000 W to heat the mixture to 95 °C and further irradiated for 19 min at 70 W to maintain this temperature. US: 20 kHz with a Pyrex® horn (Φ 15 mm), nominal power 50 W, reaction vessel standing in a water bath heated at 95 °C.

where a Pyrex® horn was directly inserted in the vessel.[11] In a typical run, 4 mmol of $KMnO_4$ were dispersed in a solution of 2 mmol of amine in 30 ml of DMF–water (25:5). After the reaction was completed (20 min) and the mixture had cooled down to room temperature, MnO_2 was filtered off, and the reaction mixture was extracted with ethyl acetate (3×20 ml). The organic layer was dried over anhydrous $MgSO_4$, then the solvent was removed in a rotavapor and 10 ml of ethyl acetate were added to redissolve the residue for GC analysis. The solution was analyzed in a gas chromatograph (HP-5890) fitted with a HP-5 capillary column (30 m × 0.32 mm × 0.25 μm) using H_2 as carrier gas. The temperature was held at 70 °C for 3 min, then raised to 250 °C at the rate of 10 °C/min, and finally kept at 250 °C for 4 min. The identity of the products was established by GC-MS (Agilent Technologies mass spectrometer, GC 6890N with MS detector 5973), fitted with a HP-5MS capillary column (30 m × 0.25 mm × 0.25 μm) using He as carrier gas.

Results of the oxidation of amines under individual and simultaneous irradiations of MW and US are summarized in Table 1. More than 70% conversions of p-methylaniline and p-ethylaniline were obtained in 20 min by irradiating with MW or simultaneously with MW and US, whereas 57 and 54% conversions of p-ethylaniline were respectively observed with US irradiation as well as plain heating in a water bath. As expected, the simultaneous irradiation with MW and US significantly enhanced the conversion of p-chloroaniline as well.

The extent of conversion for p-methylaniline and p-ethylaniline under different irradiation was found to vary in the order MW > MW–US > US > heating in a plain water bath. Yields of azo products did not vary significantly except in the case of p-chloroaniline. The extent of conversion for p-chloroaniline under different irradiation varied in the order MW–US > MW > US; however, yields of 4,4′-dichlorazobenzene followed the order US > MW–US > MW.

Because DMF is a good polar, aprotic solvent with a high boiling point, its use is common in MW irradiation chemistry. However, in its presence formation of formamidine and other by-products resulted in poor selectivity toward azo and azoxy products (Scheme 2). No by-product was formed when the amount of water in the medium was increased from 15 to 35 ml. However, the yields of azo and azoxy compounds also decreased.



Scheme 2. Formation of formamidine in the presence of DMF.

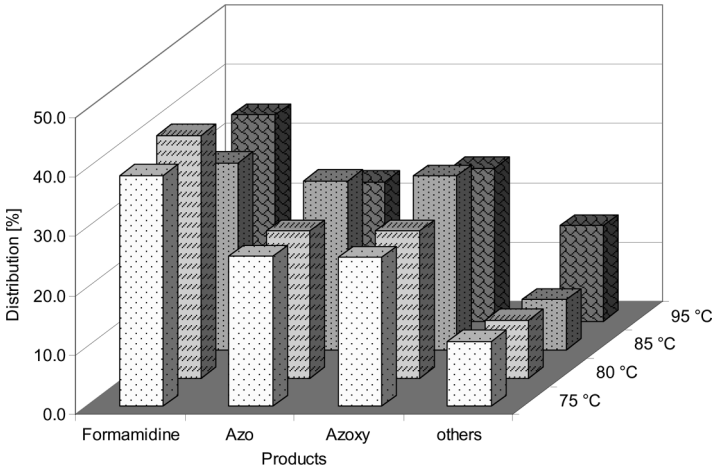


Figure 1. Product distribution in the oxidation of p-ethylaniline under simultaneous irradiation with MW–US, as a function of temperature; 1 mmol of p-ethylaniline, 4 mmol of $KMnO_4$, 25 ml of DMF, 5 ml of H_2O. MW: MLS-Ethos MW system: 1 min at 1000 W to heat the mixture to 95°C and further irradiated for 19 min at 70 W to maintain this temperature. US: 20 kHz with a Pyrex horn® (Φ 15 mm), nominal power 50 W.

Figure 1 shows how product distribution varied as a function of temperature for the oxidation of p-ethylaniline under simultaneous MW–US irradiation. As temperature increased from 75 to 95 °C, the conversion increased from 74 to 94% while product distribution for azo and azoxy products increased slightly. As shown in Fig. 1, less formanidine and other products were formed at 85 °C than at 95 °C.

To improve the conversion rate under simultaneous MW–US irradiation, 2, 4, and 6 mmol of $CuSO_4 \cdot 5H_2O$ were added as catalyst to 30 ml of DMF–water (25:5) mixtures containing 1 mmol of p-ethylaniline. As expected, the conversion at 85 °C increased from 70 to 81%. The product distribution to azo compound increased from 27 to 36%, and the product distribution to azoxy compound increased from 22 to 35% while formation of formamidine decreased from 39 to 1%.

In conclusion, a high conversion rate for amines can be achieved under MW or simultaneous MW–US irradiation. An efficient MW–US procedure for the preparation of azo and/or azoxy compounds from primary aromatic amines has been presented. In the future, the effect of other solvents such as dimethyl sulfoxide (DMSO), acetonitrile, and ethanol will be investigated, with the aim to avoid the formation of formamidine and other by-products.

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