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A NOVEL SYNTHESIS OF UNSYMMETRICAL AZO AROMATICS INACCESSIBLE BY DIAZO-COUPLING REACTION[+]

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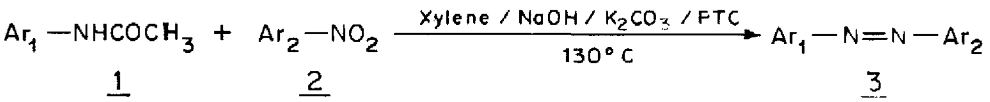
Summary: A novel synthesis of unsymmetrical azo aromatics inaccessible by diazo-coupling reaction is reported. The synthesis involved the reaction of acetanilides with nitroarenes under moderate reaction conditions. A reaction pathway via a nitrosoarene intermediate involving elimination of the elements of the acetate anion, is proposed.

In analogy with the facile procedure for the N-alkylation of benzanilides and acetanilides under phase transfer catalysis (PTC) conditions recently reported by us,[1] acetanilide was reacted with p-nitrochlorobenzene (PNCB) instead of alkyl halide. There was no trace of the expected p-nitrodiphenylamine. The reaction, however, afforded p-chloroazobenzene in excellent yield. Surprisingly, nitro group had entered into the reaction in preference to the activated chloro group (Chlorobenzene under similar conditions did not react with acetanilide).

Although anilines react with nitroarenes to yield azo aromatics, the generation of a nitrogen anion from the aniline for its reaction with electrophilic nitrogen of the nitro group was achieved at high temperatures (175°-200°C) in the presence of a strong base. The condensations with the nitroarenes were found to be sluggish resulting in low yields, loss of selectivity and formation of significant amounts of tarry material. However, the reactions involving nitrosoarenes generally prepared from the corresponding nitroarenes are relatively more facile but still low yielding when performed under similar conditions. In typical cases, the reactions with nitrosoarenes gave azo compounds in satisfactory yields but this involved the use of expensive and toxic reagents such as triphenylarsine phenylimine.[2]

In this paper, we report a novel method for the preparation of unsymmetrical azo aromatics **3** inaccessible by conventional diazo-coupling reaction The yields are good and the selectivity high. Our synthesis makes use of the less basic acetanilides **1** instead of the anilines as starting materials. Easy generation of nitrogen anions under moderate conditions in inert non-polar solvents such as xylene are, thus achieved. The amines reacted with the readily available nitroarenes **2** to yield the azo aromatics **3** in high selectivity (Scheme 1).



$$\underset{\underline{1}}{Ar_1-NHCOCH_3} + \underset{\underline{2}}{Ar_2-NO_2} \xrightarrow[130°C]{Xylene / NaOH / K_2CO_3 / PTC} \underset{\underline{3}}{Ar_1-N{=}N-Ar_2}$$

Scheme -1.

In a typical experiment, a mixture of substituted acetanilide **1** (0.1 mole), finely powdered sodium hydroxide (0.4 mole), potassium carbonate (0.1 mole) and tris(methoxyethoxyethyl)amine (TDA-1) as PTC (0.004 mole) in distilled xylene (150 ml) was stirred at 100°C for 1 h. The nitroarene **2** (0.1 mole) was then added. The mixture was stirred vigorously at 130°C for 8 h. and the contents were filtered hot (The pH of this filtrate was ~13). The residual liquid after removal of solvent at reduced pressure was chromatographed through a silica-gel column using pet. ether as eluent. The yield data are recorded in the Table. A facile reaction was observed even without the use of PTC when the azo aromatics **3** were obtained in lower (50% to 75%) yields. Acetanilide did not react with PNCB at 100°C, and hence the temperature was raised to 130°C to yield p-chloroazobenzene (**3b**) in excellent yield (88%). It should be emphasized that the reaction proceeded even without PTC to afford the azo aromatics in significant yield (67%). The PTC helped in enhancing the yield. The use of other PTC such as tetrabutylammonium bromide (TBAB), triethylbenzylammonium chloride (TEBA) and polyethylene glycol (PEG-400) gave **3b** in lowered yield (60%). The lower yield may be partly attributed to the instability of TBAB and TEBA at 130°C. The individual use of bases such as sodium t-butoxide, potassium hydroxide, sodium hydroxide, and potassium carbonate instead of the combination of bases as mentioned above gave a poor yield of **3** (0-15%). Thus, the reaction parameters such as temperature and specific composition of the base appears to have played a key role in the success of the reaction. The reaction has been used for the synthesis of several unsymmetrical azo aromatics including azo-naphthalenes and azo-heterocycles (Table). In all cases the azo aromatics were observed to be the major products and the complete recovery of the unreacted starting materials indicated high selectivity of the reaction. The reaction did not proceed when p-nitroaniline or p-nitrophenol was used as the nitroarene. The decrease in electrophilicity of the nitro group by electron-donating substituents at the para-position may have rendered these substrates inactive.

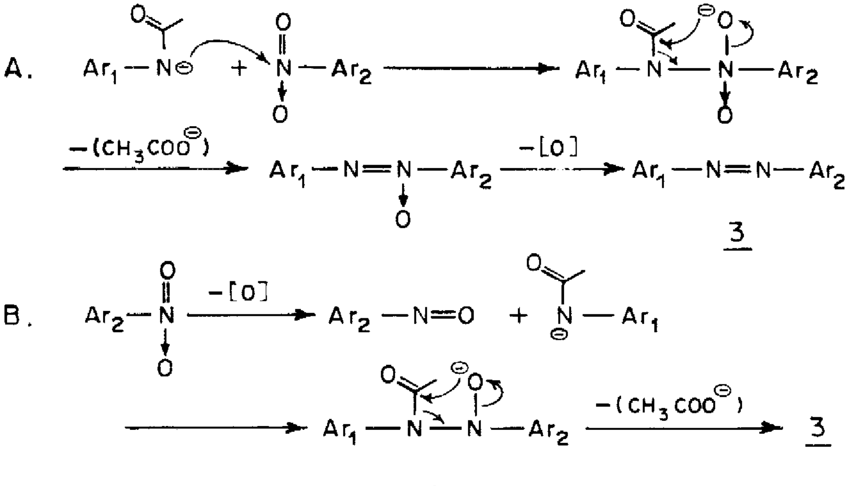
It is reasonable to assume that the reaction will follow one of the two more probable pathways (A or B) as shown in Scheme-2. A loss of oxygen can either occur from an azoxybenzene intermediate (pathway A) or from nitrobenzene (pathway B). The intermediate azoxybenzene which would be expected by pathway A could not be detected in the reaction mixture in spite of our best attempts to do so. Moreover, the pure trans-

Table: Synthesis of azo aromatics 3[3]

3	Ar_1	Ar_2	Yield[4] (%)	m.p. (°C)	λ_{max} (log ε) (nm)
3a	Phenyl	Phenyl	77	68-69	315(4.3), 440(2.7)
3b	Phenyl	p-Chlorophenyl	88	91	320(4.3), 440(2.7)
3c	Phenyl	o-Chlorophenyl	69	29-30	320(4.1), 450(2.9)
3d	Phenyl	m-Chlorophenyl	97	67	315(4.3), 440(2.9)
3e	m-Chlorophenyl	p-Chlorophenyl	65*	120	330(4.1), 435(2.8)
3f	p-Methoxyphenyl	p-Chlorophenyl	82	121	350(4.4), 430(3.2)
3g	Phenyl	p-Bromophenyl	77	88-89	322(4.3), 445(2.8)
3h	β Naphthyl	Phenyl	81	83-84	370(3.9), 455(3.0)
3i	α Naphthyl	Phenyl	64	69	335(3.9), 465(2.8)
3j	[illegible]-Benzoylphenyl	Phenyl	78	106	322(4.5), 445(2.7)
3k	4-Pyridyl	Phenyl	69	99	310(4.2), 453(2.5)
3l	4-Pyridyl	p-Chlorophenyl	76	99	320(4.2), 445(2.7)
3m	4-Pyridyl	m-Chlorophenyl	55*	65	311(3.9), 455(2.3)
3n	4-Pyridyl	o-Chlorophenyl	63	60-61	312(4.2), 460(2.6)
3o	4-Pyridyl	4-Pyridyl	65	107	282(4.2), 460(2.3)

* New Compounds

or the cis-azoxybenzene[5] (the latter likely to be formed by a cis-elimination of the elements of acetate anion as shown in pathway A) did not deoxygenate under the reaction conditions. This rules out pathway A. A blank reaction with nitrobenzene and all other reagents except acetanilide under similar



Scheme—2.

conditions yielded azoxybenzene (20%) and azobenzene (5%). This observation shows the intermediate formation of nitrosobenzene in the reaction since the azoxybenzene and azobenzene could have only been formed by the reaction of nitrosobenzene with phenyl hydroxylamine and aniline (the other reduction products) respectively. Moreover, the aqueous extract of the reaction mixture tested positive for peroxides (liberation of iodine from acidified potassium iodide solution, detected by starch solution). These observations indicate the reaction course as shown in pathway B.[6] The nitrosobenzene, as soon as it is formed by deoxygenation of nitrobenzene reacts with the nitrogen anion of the acetanilide salt pushing the reaction more and more towards the right giving rise to the azo aromatics in good yields.

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References and Notes

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3. All the compounds (**3a** - **3o**) gave satisfactory elemental analyses and spectroscropic data, and their m.ps were comparable with those reported in literature.

4. The yields refer to isolated products and are calculated on the basis of nitroarene converted. More than 80% of the nitroarene in each case was converted to products.

5. *cis*-Azoxybenzene was prepared as per the method reported by G.M. Badger, G.E. Lewis, and R.G. Buttery, *J. Chem. Soc.*, 1953, 2143.

6. Nitrosobenzene also reacted with acetanilide to give **3a** under identical conditions.

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