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Synthesis of 1-Aryl - 3, 3-disubstituted Triazenes on Ion-exchange resin support

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Abstract : Diazonium ions have been immobilized on a cation exchanger followed by N-coupling on a 2-amine to give the 3,3-disubstituted-1-aryltriazenes as the only product. Reaction is clean and work up procedure simple.

INTRODUCTION

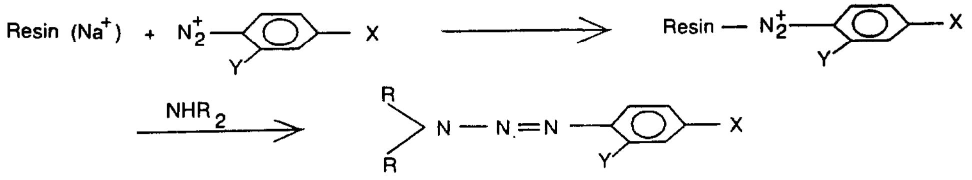
1,2,3-triazenes are useful synthetic intermediate and finds application as cytotoxic agents[1,2]. In the classical synthetic method, triazenes were synthesized by N-coupling of amines with diazonium ions in acidic or alkaline medium. This method is unsatisfactory due to multiple product formation coupled with instability of the triazene in the medium leading to its low yield[3]. It has been reported that synthesis of triazene is favoured under neutral condition[4].

We have been successful in synthesizing the 1,2,3-triazenes in good yield by first immobilizing diazonium ions, prepared in the usual way, onto a cation exchanger and subsequently carrying out the diazocoupling reaction in 'solid phase' with DPA[5] in cyclohexane and DEA[5] in deionized water. The neutrality of the reaction medium was thus maintained eliminating the possibility of by product formation and decomposition of triazene formed.

RESULTS & DISCUSSION

Primary aim of the study was to ascertain whether diazonium ions could be immobilized on polymeric support so that 'solid phase' diazocoupling reactions could be possible. To ascertain whether diazonium ions were indeed grafted onto an ion exchanger, the well documented N-coupling reactions of diazonium ions with amines was selected. 2°-amines were used so as to eliminate the possibility of formation of by-products resulting from possible tautomers[6]. DPA gave coloured crystalline triazenes whereas DEA products were coloured viscous oils, except **2a** (Scheme-1). The study has yielded important results. Firstly, we have been able to immobilize diazonium ions on cation exchangers much in the same fashion as other resin based reagents, which are well documented[7,8,9]. This technique is convenient because it enables us to carry out the diazocoupling reaction in neutral medium which was

SCHEME - 1



1, 2

For1, R=Phenyl and for2, R=Ethyl

1a	X=NO_2,	Y=H	2a	X=NO_2,	Y=H
1b	X=Cl ,	Y=H	2b	X=CH_3,	Y=H
1c	X=Br,	Y=H	2c	X=Y=Cl	
1d	X=CH_3,	Y=H	2d	X=Cl,	Y=NO_2
1e	X=Y=NO_2				
1f	X=Y=Cl				
1g	X=Cl,	Y=NO_2			
1h	X=COOH,	Y=H			

earlier possible only in acidic or alkaline medium with consequent disadvantages mentioned. Secondly, decomposition of the target molecule could be prevented leading to a higher yield, TLC shows the presence of only one product. Thirdly, the resin could be reused and finally, isolation and purification procedures are simple.

EXPERIMENTAL SECTION

Aromatic amines, DEA and DPA were purified before use. Amberlite-IR-120 (Na$^+$) macroporous type according to Rohm & Haas specification with type analysis SO_3^- 20-50 mesh, Na$^+$ form styrene-DVB 8% was choosen as the cation exchanger. The resin beads were washed several times with distilled water before use.

Immobilization of Diazonium ions onto cation exchanger. Aromatic amine (0.01 mole) was dissolved in 50 ml of conc. HCl and diazotised with a solution of sodium nitrite at 0-5°C. The diazonium salt solution was filtered through Celite-545 filter aid and the filtrate passed through a column slurry packed with 15 gms of the cation exchanger, Amberlite-IR-120 (Na$^+$ form) at the rate of 2ml/min. The resin was recovered and washed several times with distilled water till free of diazonium ions (alkaline β- naphthol test). The loaded resin was then dried over P_2O_5 at 50°C under reduced pressure (50 mm Hg).

The dried resin was analysed for diazonium ion content by reductometric titration procedure using 57% hydroiodic acid[10,11] where the liberated iodine was titrated with sodium thiosulphate solution using starch as indicator. The average capacity was found to be 2.4 m.mol of ArN_2^+/gm of the resin. This experiment was done with the diazonium ions obtained from p-toluidine and may be taken as representative. The dry resin was stored at room temperature and the diazonium ion capacity was found to remain constant over a period of 10 weeks. Immobilization of diazonium ions on cation exchange resin is in fact an excellent procedure for their stabilization..

General procedure for Synthesis of Triazene. DPA (0.05 mole) in 75 ml cyclohexane added to the loaded resin (5 gms.) and stirred for 30 mins. Immediate change in colour of the resin indicated instantaneous reaction of the DPA with the immobilized diazonium ions. The resin beads were recovered, washed with water and then with cyclohexane till free of DPA. Cyclohexane was found to be the most suitable solvent as the triazenes were insoluble in it whereas DPA was. This prevented the triazenes from leaving the surface of the resin and eliminating the possibility of the product being contaminated with DPA. The triazenes were then extracted with 95% EtOH from the loaded beads in a soxhlet apparatus and reduced pressure removal of solvent gave coloured crystalline compounds (Table-1) in 55-75% yield.

Identical procedure was followed for synthesis of triazenes of DEA. Aqueous solution of DEA was taken as the triazenes formed were insoluble in water whereas DEA was. In this case triazenes were extracted from the loaded beads with petroleum spirit (40-60°C) and solvent removed under reduced pressure to give compounds **2** which were deep coloured viscous oils except **2a**.

TLC of all the products in silica gel H with benzene as eluent gave a single spot indicating that only the triazene was formed. As no by products were obtained elaborate purification procedure was not necessary.

TABLE - 1

Product	Colour of Product	Y%*	m.p.(°C)[i]	Rf[ii]	N% found	Calc.	ir(cm^{-1})[iii] in KBr	^{1}H-nmr
1a	Red	60	127	0.85	17.36	17.61	1395 1520(-NO_2)	7.3(m),10H; 7.9(m),4H
1b	Orange	64	122	0.80	13.36	13.65	1394	7.3(m),10H; 7.9(m),4H
1c	Yellow	72	50	0.87	11.73	11.93	1404	7.3(m),10H; 7.9(m),4H
1d	Yellow	54	44	0.85	14.39	14.63	1400	1.8(s),3H; 7.2(m),4H; 7.6(m), 10H
1e	Brown	58	49	0.64	19.21	19.28	1400	7.3(m),10H; 7.9(m),3H
1f	Orange	60	47	0.82	12.23	12.28	1399 1545 (-NO_2)	7.2(m),10H; 7.8(m),3H
1g	Red	64	48	0.79	15.66	15.88	1398 1520 (-NO_2)	7.4(m),10H; 7.9(m),3H;
1h	Yellow	69	224	0.75	13.12	13.24	1393 1680 (-COOH)	7.2(m),10H; 7.6(m),4H 11.8(s), 1H

* Yield % is determined with respect to the average capacity of the diazonium ion content of the loaded resin.

[i] determined by open capillaries.

[ii] eluent Benzene, TLC on Silica gel-H plates.

[iii] characteristic -N=N- str. freq. of triazene[15]

The uv-vis spectra obtained in Hitachi U 3210 spectrophotometer ; i.r. taken in Perkin Elmer 1600 FT-IR spectrophotometer; ^{1}H-nmr in Jeol JNM-PMX 60 using TMS as internal standard in acetone-d_6. ^{1}H-nmr of compounds **2** were taken in CCl_4 solution with the same internal standard. Molecular weights of compounds **1** obtained from Mass spectra taken in Jeol JMSD 300, a low intensity molecular ion peak was observed and nitrogen analysis was carried out in Elemental Analyser Carbo Erba 1106 (Table-1).

Interestingly addition of conc. H_2SO_4 to compounds **1** (in EtOH solution) gave violet coloured solutions with consequent shift in absorption maxima (Table-2). This shift in the absorption maxima was possibly due to the protonation of the triazene[12]. This observation was typical of the triazenes of DPA hence may be taken as a test to detect them.

TABLE - 2

uv-vis spectral studies of compounds-1

Compound	λmax (95% EtOH)	λmax^{iv}
1a	449 nm	523 nm
1b	411 nm	535 nm
1c	411 nm	539 nm
1d	402 nm	544 nm
1e	432 nm	527 nm
1f	425 nm	536 nm
1g	440 nm	542 nm
1h	439 nm	533 nm

iv - on addition of conc. H_2SO_4 to EtOH solution of compounds.

Compounds **2** are well documented, however, compounds **1** were, to our knowledge, not reported earlier. Triazenes of DEA were detected by their photochemical decomposition when exposed to sunlight especially in case of **2a,b** [13,14]. The uv spectra gave λmax at 310-320 nm and i.r. showed the characteristic triazene absorption at 1410-1390 cm^{-1} as reported in literature[15]. In ^{1}H-nmr δ values for compounds **2** are **2a** 1.4(t), 2.9(q), 7.2(m); **2b** 1,4(t), 2.3(s), 3.0(q), 7.4(m); **2c** 1.5(t), 2.8(q), 7.3(m); **2d** 1.6(t), 2.9(q), 7.3(m).

CONCLUSION

The results have shown that the diazonium ions can be immobilized on cation exchangers and consequently diazocoupling reaction can conveniently be carried out under neutral condition so that multiplicity of products can be eliminated. Further studies on utilization of resin based diazonium ions for carrying out diazocoupling reaction under neutral condition is being investigated. The procedure adopted gives the desired product in good yield.

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