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PHASE TRANSFER CATALYSIS IN INTRAMOLECULAR DIELS-ALDER REACTION OF TERTIARY FURFURYLAMINES

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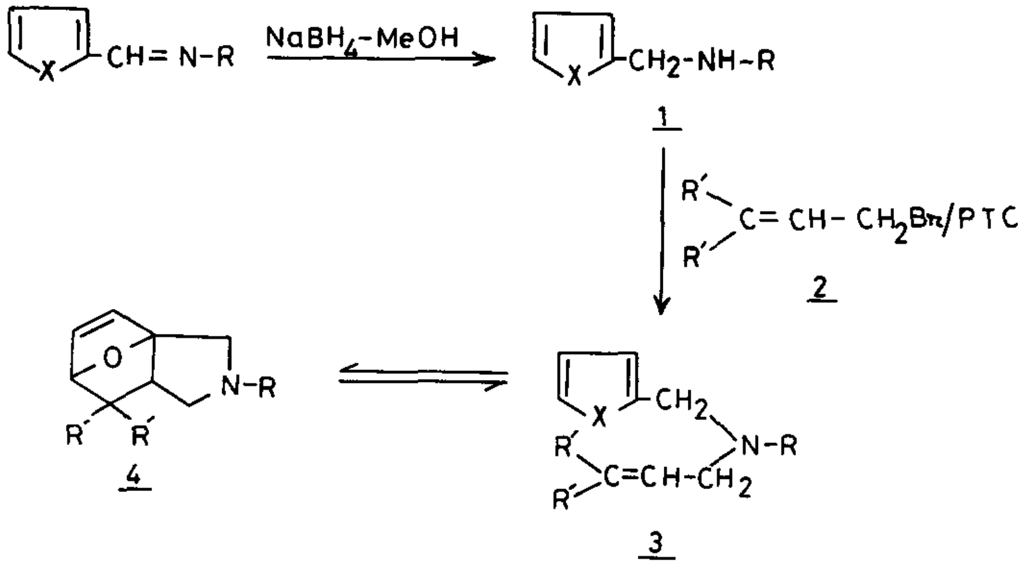
Abstract - One pot Intramolecular Diels-Alder reaction of tertiary furfurylamines using phase transfer catalysis is reported and cycloadducts are obtained in good yields.

Furan moiety occupies a position of unique significance because of its presence in a variety of naturally occurring substances[1,2]. Moreover the facile extrusion of oxygen[3] from the cycloadducts of this heterocycle affording carbocyclic ring annelated products have always been attractive synthetic strategy to build complex natural products. Properly functionalised furans when reacted with suitably substituted dienophiles resulted in 1,4-cycloadducts, one such approach was the synthesis of oxygenated A-ring of polycyclic terpenoids such as gibberellins[4]. More recently emphasis has been on intramolecular Diels-Alder reaction (IMDA)[5-7] to synthesise complex alkaloids[8] as well as terpenoids[9,10]. In continuation to our studies on furan analogues[11,12], here we wish to describe one pot synthesis of N-aryl-4H-5,7-epoxyisoindolines in a high yield via IMDA reaction of tertiary furfurylamines 1 under phase transfer condition.

Furfurylamines 1 were readily available in two steps from the corresponding furfural imines followed by sodium borohydride reduction in high yields[13]. The secondary amines 1 and allyl bromide (R'= H) 2 were refluxed in dry benzene over anhydrous potassium carbonate in the presence of a catalytic amount of phase transfer catalysis (TEBA) for 8 h and work up of the reaction mixture yielded IMDA products 4 in 70-85% yields. The characteristics and other data of products 4a-f are recorded in the Table.

In this reaction when prenyl bromide was used in place of allyl bromide no IMDA products were observed. The reaction did not proceed (vide tlc) even if the reaction mixture was kept at room temperature for several weeks, however corresponding linear products were obtained. Also when thiophene analogues of 1 were used in this reaction only N-allylation could be observed and no IMDA products were formed.



X	R'	R	
O	H	p-Phenethyl	Gives IMDA Product 4a
O	H	p-Anisyl	" " " 4b
O	H	p-Tolyl	" " " 4c
O	H	Phenyl	" " " 4d
O	H	p-Bromophenyl	" " " 4e
O	H	p-Chlorophenyl	" " " 4f
S	H	p-Anisyl	" Linear Product 3
O	CH_3	p-Anisyl	" " " 3
S	CH_3	p-Anisyl	" " " 3

It is worth mentioning here product 4d, 4b and 4c were reported earlier in poor yields[14] and the reaction sequence completed in two steps and over a period of several days. Also it was reported the adducts 4b-d undergo retro Diels-Alder reaction if tried to purify through distillation.

Therefore our method has the following advantages

(a) Reaction is complete in few hours affording high yields of IMDA products.

(b) The reaction is not at least reversible at the reflux temperature of benzene

(c) Instead of isolating salts and neutralising the intermediate salts, the present method reaction is taken to completion in one step in excellent yields.

We believe this reaction could offer considerable synthetic potential because of two main reasons, firstly giving an oxygenated cyclohexene ring fused to nitrogen heterocycles and secondly the availability of a large number of functionalised furans.

Table : Physical Data of N-Aryl-4H-5,7-epoxyisoindolines (4a-f)

Product 4	R	Yield (%)	Mp (°C)	Conditions Temp./time	Molecular formula	Recryst. Solvent
a	$C_6H_4OC_2H_5$-p	85	97-99	80°C/8 h	$C_{16}H_{19}NO_2$ (259)	n-hexane
b	$C_6H_4OCH_3$-p	80	138-39	80°C/7 h	$C_{15}H_{17}NO_2$ (245.3)	Petroleum ether
c	$C_6H_4CH_3$-p	79	108-10	80°C/8 h	$C_{15}H_{17}NO_2$ (229.2)	benzene-hexane
d	C_6H_5	75	120-21	80°C/6 h	$C_{14}H_{15}NO$ (215.3)	benzene-pet. ether
e	C_6H_4Br-p	70	129-30	80°C/6 h	$C_{14}H_{14}NOBr$ (294.1)	Petroleum ether
f	C_6H_4Cl-p	85	118-20	90°C/10 h	$C_{14}H_{14}NOCl$ (249.3)	Petroleum ether

[a] All the compounds reported here gave satisfactory spectral analyses, i.e. NMR & mass spectra.

[b] The microanalyses of these compounds were in satisfactory agreement with the expected results (C ± 0.38, H ± 0.25, N ± 0.21).

N-Aryl-4H-5,7a-epoxyisoindolines 3a-f (General Procedure)

To a flask fitted with a reflux condenser is added (2-furfuryl)-p-phenetidine (1a ; 2.59 g, 0.01 mol) in dry benzene (30 ml), anhydrous potassium carbonate (1.38 g, 0.01 mol), allyl bromide (2.42 g, 0.02 mol) in dry benzene (10 ml) and finally added 50 mg of TEBA (Triethylbenzyl ammoniumchloride). The resulting mixture is then stirred at room temperature for 1 h. This solution under stirring was then heated in an oil bath and the temperature increased slowly to reflux the reaction mixture. After refluxing for 8 h, benzene was distilled off under reduced pressure, the residue was washed with water and treated with n-hexane to obtain 4a in 85% yield. If the proper control of the temperature not observed, the yield was only 60%. The product 4a is then purified by recrystallisation from n-hexane. Other products 4b-f were prepared similarly and their characteristics are recorded in the Table.

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