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UNEXPECTED REACTION OF α-ARYL-N-(β-PHENYLETHYL) NITRONES WITH CHLORINATING AGENTS

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ABSTRACT

The α-aryl-N-(β-phenylethyl)nitrones when subjected to SO_2Cl_2/Et_3N and NCS/NaOMe treatment independently, gave unexpectedly the corresponding amides. These procedures form an alternative route for the rearrangement of nitrones to amides.

In our attempt to synthesise the heterodienes of the type C=N-C=C, we have already reported the preparation of the precursor, α-aryl-N-(β-phenylethyl)nitrones.[1] It was planned to effect dehydrogenation either directly or after funtionalising the α- or β- methylene of N-ethyl substituent of the nitrones. Selenium dioxide failed to effect the dehydrogenation, instead leads to the formation of arylaldoxime and styrene. N-bromosuccinimide treatment has also led to such a cleavage at elevated temperature.

In the process of attempting chlorination followed by dehydrochlorination on **1**, we wanted to make use of SO_2Cl_2 - Et_3N[2] and NCS - NaOMe[3] separately which was found to be successful in nitro compound[2] and surprisingly the end product has been found to be an amide **2**. Neither the chlorinating agents

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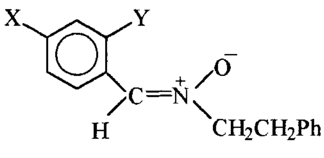
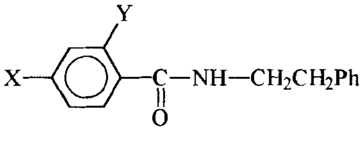
SO_2Cl_2/NCS nor the bases Et_3N/NaOMe alone could effect the rearrangement of **1** to **2**. The perusal of the literature reveals that the conversion of nitrone to amide has been effected by light,[4] PCl_3,[5,6] acid chlorides[7] and more often by acetic anhydride.[8-10] Our present study of nitrones with chlorinating agent and base leading to the formation of amide seems to involve a simple procedure with mild reaction conditions. In light induced rearrangements,[4] it has been noticed that the transient intermediate formed underwent transformations to other products in addition to the amides. PCl_3[6] and other phosphorus compounds are no good choice as they lead to competitive deoxygenation reaction which would produce imines along with the amides.



1



2

a) X = NO_2; Y = H **b)** X = Cl; Y = H

c) X = NMe_2; Y = H **d)** X = OMe; Y = H

e) X = H; Y = H f) X = H; Y = OH

The conventional acetic anhydride[8-10] method takes 3h at 120° C to effect this rearrangement. Thus, SO_2Cl_2 - Et_3N and NCS - NaOMe are alternate reagents to effect the nitrone - amide rearrangement requiring mild reaction conditions and simple workup with good yield.

Incidently this reaction leads to a new method of synthesising the amides **2**, which has already been synthesised by benzoylating the corresponding amines[11] and very recently by amidation of benzyl esters by *Pseudomonas cepacia lipase*[12]. The derivatives of these amides have shown to be anticonvulsant agent[13].

Table : Yield and melting point of the amides 2

Compound	M.pt.(oC)	Yield(%)
2a	144 - 45	84
2b	133 - 34	82
2c	218 - 19	88
2d	146 - 47	87
2e	viscous liquid	82
2f	viscous liquid	80

EXPERIMENTAL

To a solution of α-(*p*-nitrophenyl)-N-(2-phenylethyl)nitrone (5 mmol) in 20 ml of dichloromethane was added a solution of sulphurylchloride (5 mmol). Immediately a precipitate was formed and some more dichloromethane was added to dissolve the precipitate. This solution was stirred at room temperature for 15 - 20 minutes. Then triethylamine (5 mmol) was added and stirred for 15 minutes. The reaction mixture was then poured into water and the organic layer was washed with dil. HCl, with water and dried with magnesium sulphate. Evaporation of the solvent gave **2a**, yield 84%.

^{1}H NMR($CDCl_3$, δ scale) : 2.8,t,2H,C$\underline{H_2}$Ph; 3.6,q,2H,NHC$\underline{H_2}$; 6.4,b,1H,NH (disappears on D_2O treatment); 7.1,s,5H,Ar-$\underline{H}$; 7.6,d,2H,Ar-H(*meta* to nitro); 8.0,d,2H,Ar-H(*ortho* to nitro)

IR : 1640 cm^{-1} due to amide carbonyl; 3270 - 3260 cm^{-1} due to ν_{NH}

A solution of α-(*p*-chlorophenyl)-N-(2-phenylethyl)nitrone (5 mmol) and NCS (5 mmol) in 40 ml of carbontetrachloride was refluxed for 2 h. The reaction mixture was then filtered, concentrated and treated with water. The precipitate formed was filtered, dried and then treated with a solution of sodium (5 mmol) in 40 ml of methanol. The reaction mixture was then refluxed for 2h and then poured into water. The solid, **2b**, separated was filtered and recrystallised from ethanol, yield 82%.

^{1}H NMR ($CDCl_3$, δ scale) : 2.8,t,2H,$C\underline{H}_2$Ph; 3.55,q,2H,$NHC\underline{H}_2$; 6.3,b,1H,NH (disappears on D_2O treatment); 6.9 - 7.5,9H,Ar-H

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