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REACTION OF SULFOXIDES WITH NITRILES IN PRESENCE OF TRIFLUOROACETIC ANHYDRIDE AND TRIFLUOROACETIC ACID A CASE OF RITTER REACTION ON PUMMERER INTERMEDIATE.

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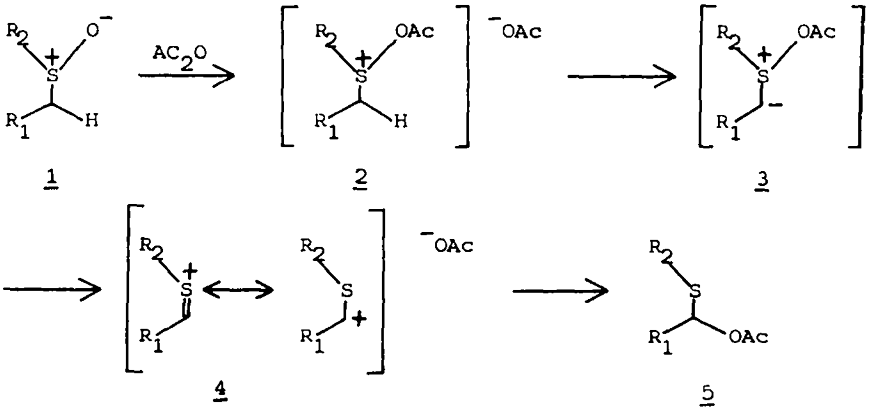
Abstract. Reaction of various sulfoxides 9, with nitriles 10 in presence of trifluoroacetic anhydride and trifluoroacetic acid gave the corresponding amides 11 via a Ritter reaction on Pummerer intermediate derived from the sulfoxides.

Sulfoxides bearing atleast one α-hydrogen undergo[1] a facile rearrangement, when treated with an electrophilic reagent, to give the corresponding α-functionalised sulfides. This reaction has been studied[2] in detail and is known to proceed via the initial formation of the sulfonium salt 2 (see scheme 1, where acetic anhydride is used as a typical electrophile) which is converted to an ylide 3 followed by a rapid elimination of acetate ion to form the sulfenium ion 4. Reaction of 4 with acetate ion gives the observed α-acetoxy sulfide 5.

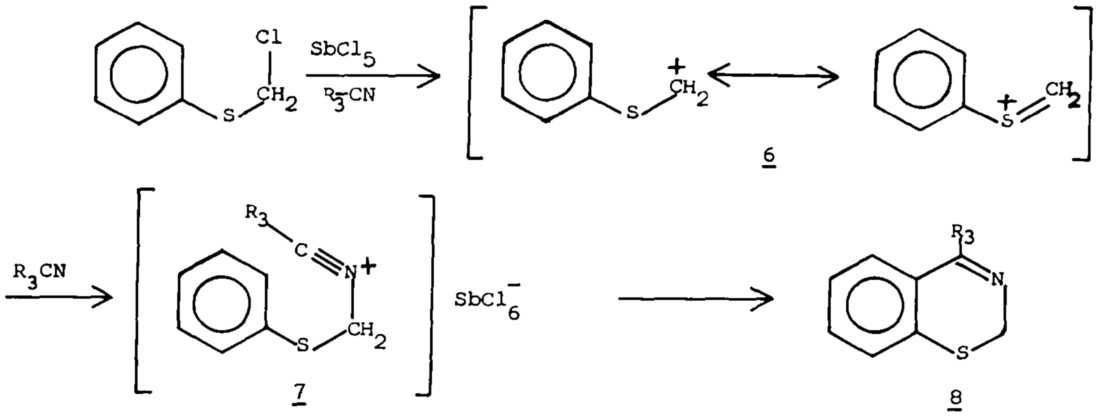


Scheme 1

It is apparent that the intermediate 4 is responsible in bringing out the functionalisation at α-carbon. A variety of nucleophiles have been reported[3] to trap 4 in both inter and intramolecular fashion. However, there is no report where a Ritter reaction has been carried out on such an intermediate derived from a sulfoxide.

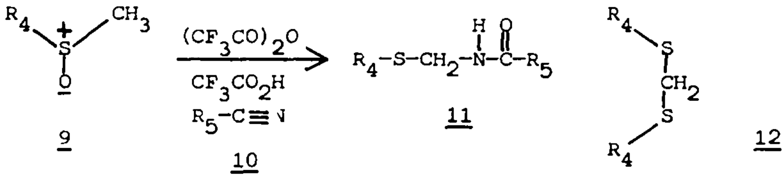
Recently we reported[4] the synthesis of 2H-benzothiazine derivatives 8 starting from chloromethyl aryl sulfide and nitrile in presence of $SbCl_5$ (see scheme 2).

It was presumed that the reaction probably involved the formation of an intermediate 6 which is trapped by the nitrile to produce another intermediate 7 followed by its cyclization to give 8.



Scheme 2

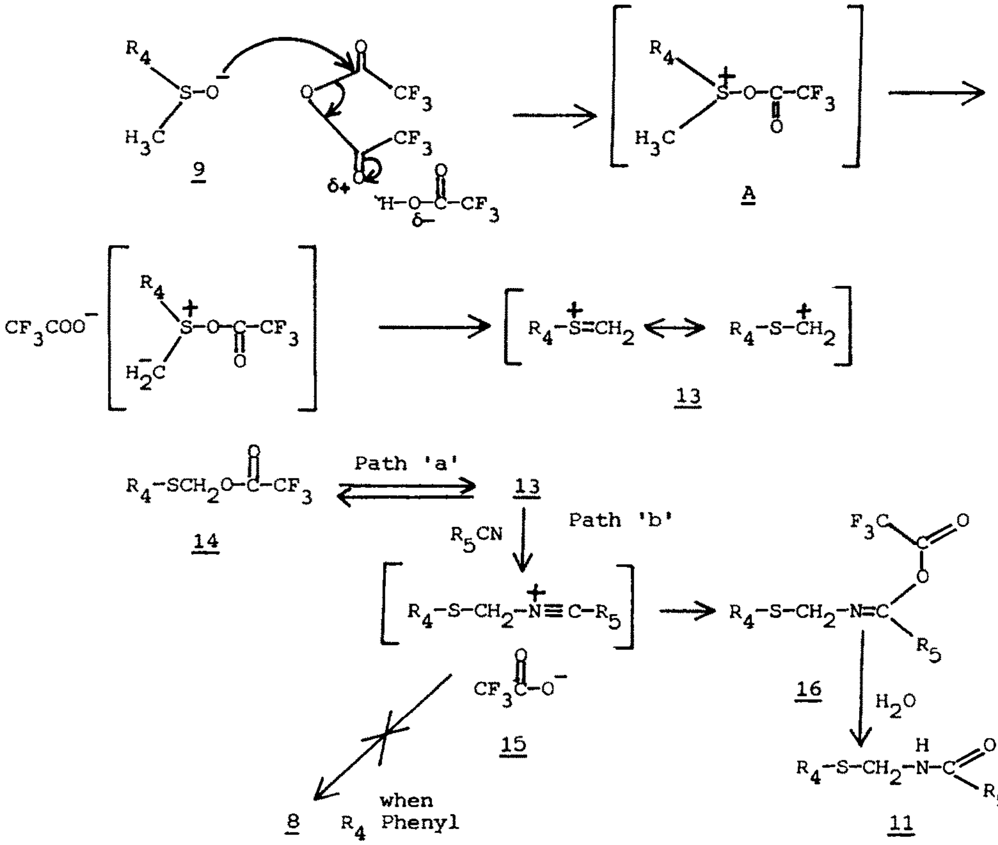
The structural similarity of 6 with that of Pummerer intermediate 4 prompted us to investigate the reaction of nitriles with sulfoxides in presence of an electrophile. In this paper we wish to report the trapping of a Pummerer intermediate, derived from sulfoxides 9, by a variety of nitriles 10, in presence of trifluoroacetic anhydride and trifluoroacetic acid to yield the corresponding amides 11 analogous to Ritter reaction (scheme 3). Results are summarized in the



Scheme 3

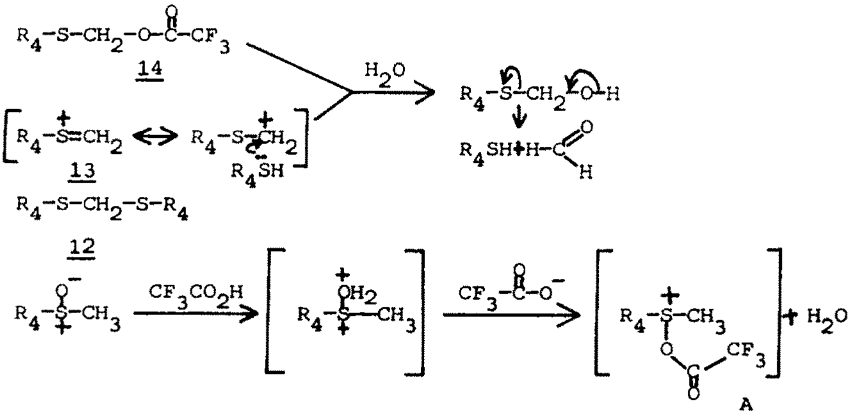
table. To our knowledge this is the first report of Ritter reaction on a Pummerer intermediate, derived from a sulfoxide. Use of approximately 4-5 equivalents of trifluoroacetic acid is necessary for the success of reaction or else only the trifluoroacetyl derivative 14 is obtained (see path 'a', scheme 4). A probable mechanism is shown in Scheme 4.

Unfortunately, the intermediate 15, unlike 7 did not undergo any cyclization even in cases where the phenyl ring (if R_4 phenyl ring) carried a methoxy group meta to the sulfoxide moiety. It is likely that 15 is easily trapped by the trifluoroacetate anion to yield 16 which, under the reaction conditions, does not cyclize but undergoes hydrolysis, during work up, to give the amide.



Scheme 4

Interestingly a reasonable amount of disulfide 12 was obtained in every case examined (see table). This is possible only if free R_4SH is somehow produced in the reaction to react with 13. In view of the fact[5] that the intermediate 13 and the trifluoroacetyl derivative 14 both react with water to produce formaldehyde and free R_4SH (scheme 5), it is likely that some water is produced in the reaction. Literature survey[6] indicates that sulfoxides do ionise in strongly acidic medium to produce sulfonium salts of type 'A' (see scheme 4 and scheme 5) by eliminating H_2O. It is, therefore, not surprising that under the present reaction conditions some ionisation of sulfoxides of this type is possible which eventually results into the formation of disulfide 12 (see scheme 5).



Scheme 5

Table

Physical and Spectral Data of 11

Entry	R_4	R_5	Reaction Time (Hrs.)	Yield		M.P. °C	Lit. M.P. °C	IR $\nu_{-NH-\overset{O}{\overset{\parallel}{C}}-}$ (cm^{-1})	H^1NMR ($CDCl_3$) δ[PPM]	M.S. m/e (M)	Analysis (%)					
											Required			Found		
				11	14						C	H	N	C	H	N
1	C_6H_5	CH_3	48	45	36	45	45.46[7]	1675	1.9(s,3H); 4.6(d,2H)	181	59.67	6.08	7.73	59.92	5.71	7.39
2	C_6H_5	$CH_2{=}CH$	48	57	38	–[a]	–[b]	1670	4.56(d,2H); 5.4–6.26(m,3H)	193	62.18	5.70	7.25	62.71	5.78	7.41
3	C_6H_5	C_6H_5	72	46	38	66	67[8]	1660 1630	4.51(d,2H)	243	69.14	5.35	5.76	68.25	5.27	5.51
4	$(p\text{-}CH_3)C_6H_4$	CH_3	72	40	36	97	–[b]	1675	1.86(s,3H); 2.26(s,3H); 4.36(d,2H)	195	61.54	6.67	7.18	60.98	6.57	7.53
5	$(p\text{-}CH_3)C_6H_4$	$CH_2{=}CH$	48	43	48	77	–[b]	1675	2.27(s,3H); 4.66(d,2H); 5.47–6.97 (m,3H)	207	63.77	6.28	6.76	64.18	6.58	6.90
6	$(p\text{-}CH_3)C_6H_5$	C_6H_5	48	46	35	106–108	–[b]	1660	2.27(s,3H); 4.76(d,2H)	257	70.04	5.84	5.45	69.49	5.57	5.19
7	CH_3	CH_3	24	32	–[c]	–[a]	–	1665	2.0(s,3H); 2.1(s,3H); 4.3(d,2H)	119	40.34	7.56	11.76	40.84	6.98	11.37
8	CH_3	$CH_2{=}CH$	24	30	–[c]	–[a]	–	1670	2.16(s,3H); 4.42(d,2H); 5.58–6.45 (m,3H)	131	45.80	6.87	10.69	46.31	6.79	10.48
9	CH_3	C_6H_5	24	53	–[c]	104	105[9]	1660	2.1(s,3H); 4.33(d,2H)	181	59.67	6.08	7.73	58.34	6.81	6.95

a: Thick oil b: Unknown c: Not isolated

EXPERIMENTAL

^1H spectra were recorded at HA100, WP80 and EM90 spectrometer in $CDCl_3$ solution with TMS as internal standard. IR spectra were recorded at Perkin Elmer 580 instrument.

General Procedure for the preparation of compounds 11 and 14

(i) Corresponding to entries 1,2,4 and 5

To a stirred solution of a sulfoxide (2.5 mmol) in 5 ml freshly distilled nitrile at 0°C was added a mixture of trifluoroacetic anhydride (3.25 mmol) and trifluoroacetic acid (1.0 ml) in 2 ml of dry dichloromethane (dried over P_2O_5) over a period of 30 minutes. It was allowed to stir at 0°C for 8 hrs. and then at room temperature for the time indicated in the table. At the end the reaction mixture was cooled to 0°C and a cold 8 aqueous solution of sodium hydroxide was slowly added to it till it was just basic to litmus. The reaction mixture was then diluted with water (10 ml) and extracted with dichloromethane (3x20 ml). The combined organic layers were washed with water (10 ml), then with brine (10 ml) and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude product containing 11 and 14 which were separated by thick layer chromatography using silica gel (eluents benzene acetone, 80 20) and characterised by spectral means.

(ii) Corresponding to entries 3 and 6

The reaction was carried out in the same manner as indicated above except that the excess of benzonitrile and trifluoroacetic acid were removed under vacuum prior to the treatment with base.

(iii) Corresponding to entries 7,8 and 9

The reaction was carried out in the same manner as above cf. (i). At the end excess of benzonitrile and trifluoroacetic acid were removed under vacuum and the residue treated with 8 aqueous cold NaOH solution until it was just basic to litmus. About 2 gms of solid sodium chloride was then added to it and extracted with ethyl acetate (3x15 ml). The combined organic layers were washed with brine (10 ml) and dried over anhydrous sodium sulfate. Evaporation of the solvent gave a crude product which was washed twice with pentane (5 ml). The pentane layer was discarded and the crude compound was purified by thick layer chromatography using silica gel (eluents benzene acetone, 80 20) and characterized by spectral means.

Acknowledgement

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