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A NEW CYCLIZATION TO INDOLE DERIVATIVES FROM ARYLHYDROXYLAMINES

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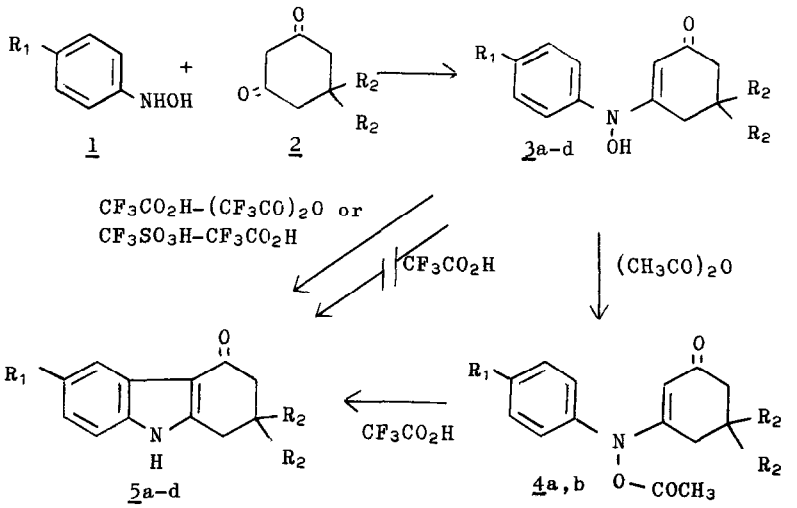
In the course of our studies on arylhydroxylamines,[1] we found a novel cyclization which leads to an indole derivative. When arylhydroxylamines (1, R_1= H, CH_3, Cl) and 0.8-1.0 molar equivalent of cyclic 1,3-diones (2, R_2= H, CH_3) were heated in benzene for 5-10 hr, adducts (3) formed from dehydration between 1 and 2 were obtained in 26-36% yields. In the condensation reaction, the yields increased up to 93%, when a small amount of ascorbic acid was suspended in the reaction solution. Ascorbic acid seems



a:R_1=H, R_2=CH_3; b:R_1=CH_3, R_2=H; c:R_1=CH_3, R_2=CH_3; d:R_1=Cl, R_2=CH_3

to supress the adverse decomposition of phenylhydroxylamines rather than to accelerate the reaction rate, because the rate in the presence of ascorbic acid was slower when the reaction was monitored by tlc.

The chemical analyses, infrared (3200-2200 cm^{-1}, OH: ca. 1550 and 1480 cm^{-1}, enol-carbonyl) and nmr spectra (an olefinic hydrogen which can be slowly substituted by D_2O, an active hydrogen (OH), and five aromatic hydrogens) show the structure 3 for the adducts.

Though 3 were stable in refluxing trifluoroacetic acid, the acetates (4, IR^{KBr}: 1780-1790 cm^{-1}, $-N-O-\overset{\overset{O}{\|}}{C}-CH_3$) easily cyclised to 1,2,3,4-tetrahydro-4-oxo-carbazoles (5) in trifluoroacetic acid. More conveniently, 3 can be readily converted directly to 5 in trifluoroacetic acid-trifluoroacetic anhydride at room temperature or below in good yields.

Table.

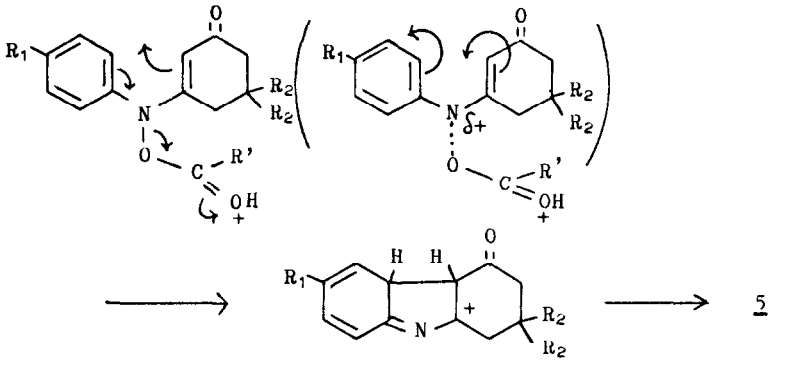
1, R_1=	2, R_2=	3, yield % in the presence of ascorbic acid	5, yield % from 3
H	CH_3	52 (36)*	87 (66)**
H	H	93	(69)
CH_3	CH_3	36 (29)	91
Cl	CH_3	70 (25)	85

* yields in the absence of ascorbic acid
** yields via acetates

The structures of 5 were supported from the characteristic ultraviolet spectra,[2] microanalyses and infrared spectra. 5b was compa red with the authentic sample.[2]

The cyclization can be explained by an acid catalysed elimination of the acetoxy group as shown (or an electrocyclic ring closure of an 3-aza-pentadienyl cation system),[3] followed by the hydrogen rearrangement. When a stronger acid, trifluoromethanesulfonic acid[4] in trifluoroacetic acid

was used as an acid, 3a directly afforded the indole 5a in a 9% yield. Therefore, the acylation step is not always necessary if the acid is strong enough.



In addition to synthetic utilities, the above reaction shows the heterolytic behabiour of an N-O bond.[5] The mechanism shown may have a suggestive insight into the mechanism of Fisher indole synthesis.[6]

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