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REACTION OF N-ARYLHYDROXYLAMINES WITH ETHYL AECTOACETATE[1]

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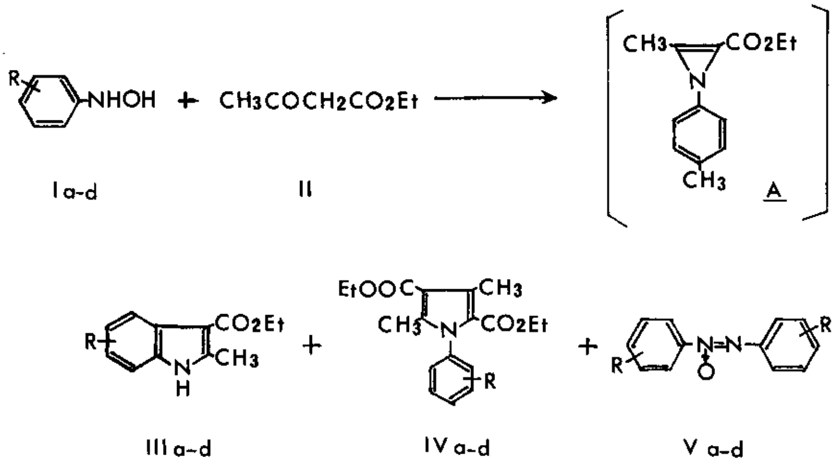
Reaction of N-p-tolylhydroxylamine (Ia) with ethyl acetoacetate (II) at room temperature for 30 days or in boiling ether for 5 h affords 2,5-dimethyl-3-ethoxycarbonylindole (IIIa), N-p-tolyl-2,4-dimethyl-3,5-diethoxycarbonylpyrrole (IVa) and azoxy-p-touene (Va). Some other N-arylhydroxylamines also undergo similar reaction.

Early in 1907, Scheiber and Wolf[2] have described that N-p-tolylhydroxylamine reacts with ethyl acetoacetate to give a 1-substituted azirine derivative (A). The fact that no 1H-azirine has been obtained because of its antiaromatic character of 4π-electron system[3] and also our research interest in the chemistry of hydroxylamine have stimulated to re-examine this reaction.

A mixture of N-p-tolylhydroxylamine (Ia) and 1 equivalent of ethyl acetoacetate (II) was allowed to react at room temperature for 30 days. Chromatography on silica gel afforded three products, IIIa, IVa and Va, in 24, 17 and 25% yields, respectively.



a: R= p-CH_3, b: R=H, c: R= p-Cl, d: R= o-Cl

The product IIIa melts at 173-174° (lit.[2] mp 172°) and has the same empirical formula $C_{13}H_{15}O_2N$ with that reported by Scheiber and Wolf.[2] However, its uv spectrum [λ_{max}^{EtOH} nm(log ε): 235 (4.04), 255 (3.70), 285 (3.70)] is closely similar to that of 2-methyl-3-ethoxycarbonylindole[4], and its ir spectrum shows a band attributable to NH group at 3290 cm^{-1} besides a carbonyl band at 1600 cm^{-1}. On the basis of these observations and also the nmr spectrum [$\tau(CDCl_3)$: 8.58 (3H, t, J=7.0 Hz, $CO_2CH_2C\underline{H}_3$), 7.56 (3H, s, 5-$C\underline{H}_3$), 7.31 (3H, s, 2-$C\underline{H}_3$), 5.58 (2H, q, J=7.0 Hz, $CO_2C\underline{H}_2CH_3$), 2.0-3.0 (3H, m, aromatic protons), 1.7 (1H, b.s., $N\underline{H}$)], we deduced IIIa to be 2,5-dimethyl-3-ethoxycarbonylindole, and finally this was confirmed by its identity with an authentic sample prpared by the Fischer's methos from p-tolylhydrazone of II.[5] Accordingly the structure A must be corrected as the structure IIIa.

The compound IVa, mp 68°, has the empirical formula $C_{19}H_{23}O_4N$ which indicates that IVa is a condensation product from 1 molar Ia and 2 moles of II. The structure can be reasonably assumed to be N-p-tolyl-2,4-dimethyl-3,5-diethoxycarbonylpyrrole from the following spectral data ; λ_{max}^{EtOH} nm(log ε): 256 (sh)(4.18), 2.67 (4.18); $\nu_{C=O}^{Nujol}$: 1710 cm^{-1}; τ ($CDCl_3$): 8.92 (3H, t, J=7.5 Hz, 5-$CO_2CH_2C\underline{H}_3$), 8.60 (3H, t, J=6.7 Hz, 3-$CO_2CH_2C\underline{H}_3$), 7.74 (3H, s, 2-$C\underline{H}_3$), 7.55 (3H, s, p-Ph-$C\underline{H}_3$), 7.35 (3H, s, 4-$C\underline{H}_3$), 5.94 (2H, q, J=7.5 Hz, 5-$CO_2C\underline{H}_2CH_3$), 5.65 (2H, q, J=6.7 Hz, 3-$CO_2C\underline{H}_2CH_3$), 2.65-3.10 (4H, m, aromatic protons).

The compound Va was proved to be azoxy-p-toluene[6].

It was also found that treatment of Ia with II in boiling ether for 5 h gave IIIa, IVa and Va, but the amount of IIIa was appreciably decreased and that of Va was conversely increased.

From similar reactions with some other N-arylhydroxylamines (Ib,c,d), the corresponding IIIb,c,d, IVb,c,d and Vb,c,d were obtained, though in similarly unsatisfactory yields (Table I).

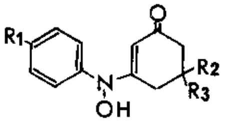
The structures of these products were established by elemental analyses, uv, ir and nmr spectra. Although attempted reactions with p-methoxy- and p-methoxycarbonylphenylhydroxylamines did not give any products and the starting materials were recovered, this type of reaction appears to be fairly general to N-arylhydroxylamine.

Table I. Reactions of N-Arylhydroxylamines with Ethyl Acetoacetate

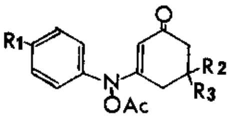
I	Procedure1)	Products(%)		
		III	IV	V
a: R= p-CH_3	i	24	17	25
	ii	3	10	41
b: R=H	i	15	7	9
	ii	4	8	22
c: R= p-Cl	ii	1.3	3	18
d: R= o-Cl	i	2.6	7	5

1) Procedure i : allowed to react at room temperature for 30 days.
Procedure ii : refluxed in ether for several hours.

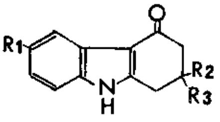
Okamoto and Shudo[7] have recently reported that N-arylhydroxylamines react with cyclohexa-1,3-diones in boiling benzene to give N,N-disubstituted products (B), which are readily cyclized to carbazole derivatives (D) directly upon treatment with trifluoroacetic acid and its anhydride or through acetates of B (C).



B



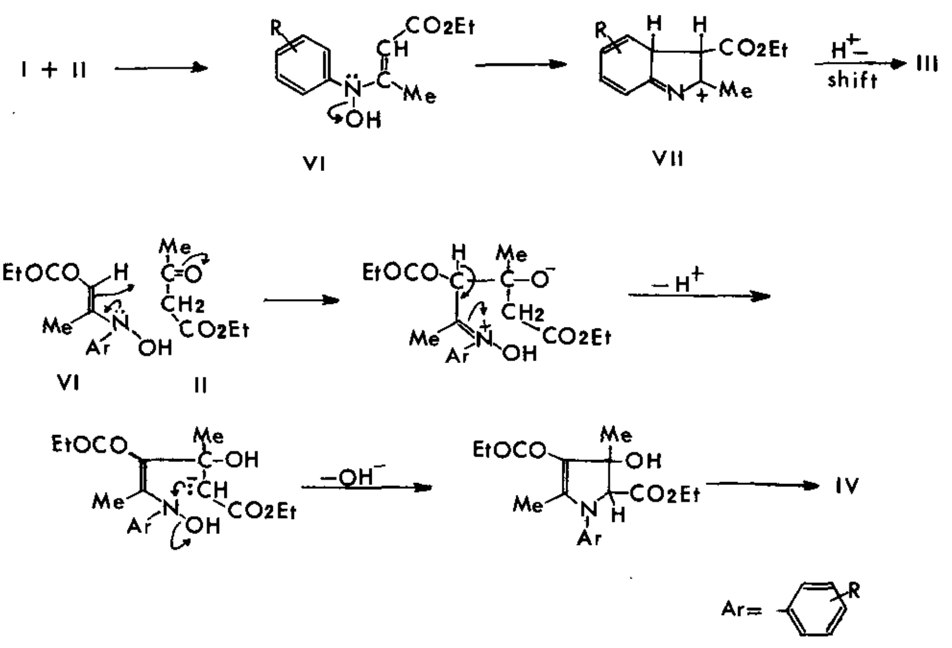
C



D

The formation of III is quite similar to that of D and may be explained by the course which involves the N-O bond cleavage of the intermediate VI corresponding to C and subsequent cyclization to VII as described by Okamoto and Shudo[7]. However the details of the mechanism remain to be further explored. On the other hand, the formation of IV can be rationalized by the following reaction sequence from VI and another mole of II.

Further work on extending this type of reaction is in progress.



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