Unusual Formation of 2,5-Diarylpyrazines from αα′-Dibromoacetophenone Azines and Hydrazine

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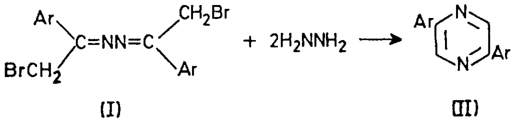
Summary The reaction of αα′-dibromoacetophenone azines (I) with hydrazine results in the formation of the corresponding 2,5-diarylpyrazines; 2,5-diphenylpyrazine was also obtained from the thermolysis of α,α′-diazidoacetophenone azines.

Decomposition of 1,1-dimethyl-1-phenacylhydrazinium bromide to the corresponding 2-aroyl-4- or 2-aroyl-5-arylimidazoles has been recently shown to proceed thermally,[1,2] photolytically,[2] or even upon stirring in dimethyl sulphoxide.[3] The formation of these imidazoles had been reported earlier from the decomposition of phenacylhydrazines[4] and of phenacyl azides.[5] As a continuation of our work in this area, the reaction of the azines (I) with hydrazine was investigated and we now report our initial results.

Treatment of the azine (Ia) with 2 equiv. of hydrazine in ethanol at reflux for 24 h resulted in the formation of amber flakes, m.p. 192—194 °C, which were identified as 2,5-diphenylpyrazine by comparison with an authentic sample.[6] Similarly, 2,5-bis(*p*-tolyl)- and 2,5-bis(*p*-anisyl)-pyrazines, (IIb) and (IIc), were obtained from the corresponding azines [equation (1)]. The 1,4-relationship of the nitrogen atoms of the pyrazine ring makes it unlikely that these nitrogen atoms originated from the starting azines. The formation of 2,5-diphenylpyrazine as a minor product had been observed from the reaction of phenacyl bromide[7] and of phenacylhydrazine[8] with hydrazine. On the basis of the above data, we suggest the mechanism shown in the Scheme to account for the formation of the 2,5-diarylpyrazines.

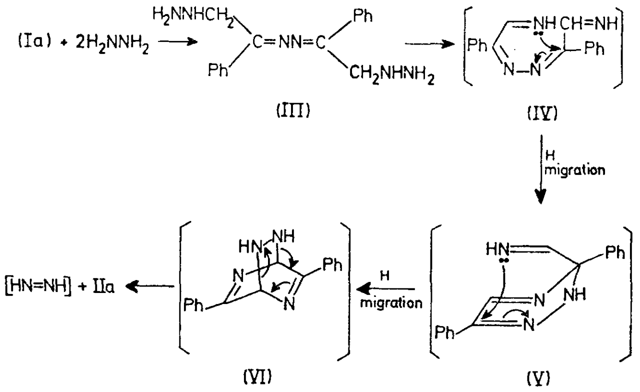


(1)

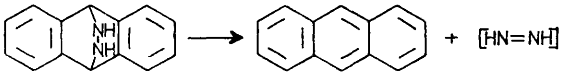
(I) (II)

a, Ar = Ph (22%)
b, Ar = C_6H_4Me-*p* (31%)
c, Ar = C_6H_4OMe-*p* (17%)

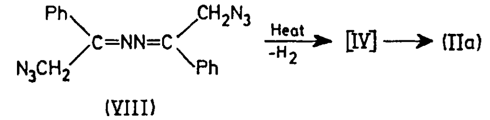
The formation of the αα′-bishydrazino acetophenone azine (III) and its subsequent thermal decomposition to the azine (IV) finds analogy in the study of Busch and Foerst,[4] who were able to isolate phenacylhydrazines from the reaction of phenacyl bromides and hydrazine at *ca.* 0 °C and showed that these phenacylhydrazines underwent thermal fragmentation *via* a cyclic path later suggested by Hauptmann and his co-workers;[9] the resulting arylglyoxaldimines whose intermediacy has been demonstrated[10] then underwent dehydrative self-condensation to the imidazoles. Internal nucleophilic attack of the imino-nitrogen of (IV) on the remote C=N bond of the azine followed by a prototropic shift would give the dihydrotriazine intermediate (V); (V) is itself ideally constructed to suffer a second internal nucleophilic attack to give the bridgehead intermediate (VI) which would then aromatize to the observed pyrazines with expulsion of di-imide. The participation and subsequent aromatization of an intermediate such as (VI) is supported by the isolation of (VII) which was shown to decompose to di-imide and anthracene[11] and the recent isolation and decomposition of a related Diels–Alder adduct between 2,5-dialkyl-3,6-dihydroxypyrazine and dimethyl acetylenedicarboxylate[12] [equations (2) and (3)]. Evidence for the participation of (IV) was adduced from the thermal decomposition of (VIII) in dichlorobenzene at reflux which gave a 55% yield of 2,5-diphenylpyrazine.



Scheme



(VII) (2)



(VIII) (3)

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