REACTION OF 8-CHLORO-10-PHENYLHYDRAZONO-10,11-DIHYDRO-DIBENZO[*b*,*f*]THIEPINE WITH AROMATIC ALDEHYDES

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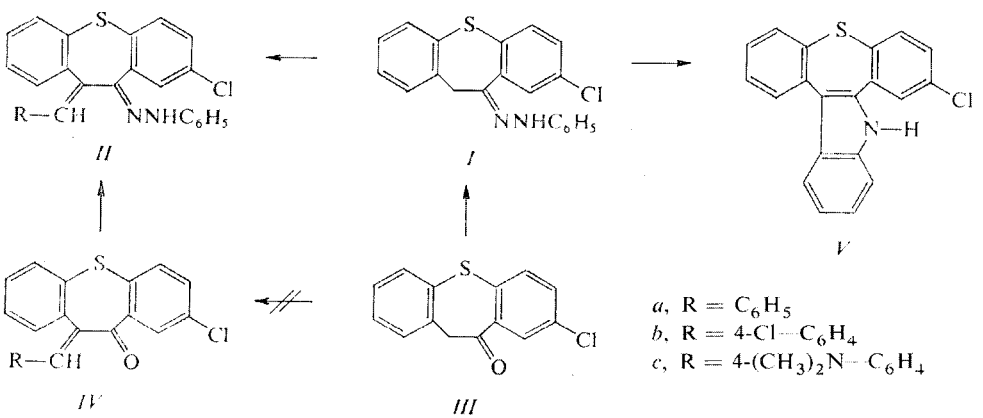
8-Chloro-10-phenylhydrazono-10,11-dihydrodibenzo[*b*,*f*]thiepine (*I*) reacts with benzaldehyde or 4-chlorobenzaldehyde (but not with 4-dimethylaminobenzaldehyde) in boiling acetic acid to afford the corresponding 11-arylidene derivatives *II*. In boiling acetic acid, compound *I* rearranges to compound *V*. 8-Chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-one (*III*) does not react with aromatic aldehydes under analogous conditions.

In connection with investigations on psychotropic substances of the dibenzo[*b*,*f*]thiepine group[1-4] we have reported in an earlier paper[5] reactions of 8-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-one (*III*) and 8-chloro-10-phenylhydrazono-10,11-dihydrodibenzo[*b*,*f*]thiepine (*I*) with aromatic aldehydes under conditions of an alkaline aldolisation and a modified Doebner reaction. It has been observed under conditions of the Doebner reaction that compound *III* reacts with benzaldehyde, 4-chlorobenzaldehyde, and 4-dimethylaminobenzaldehyde whereas compound *I* undergoes this type of reaction in the case of benzaldehyde only. Under the conditions stated, replacement of the carboxylic oxygen atom at position 10 by the phenylhydrazono residue thus results in a lowered reactivity of hydrogen atoms on the methylene group at position 11. In the present paper, the reactivity of compounds *I* and *III* towards aromatic aldehydes is compared with the use of the acid-catalysed aldolisation. In view of the known sensitivity of the phenylhydrazono residue towards mineral acids, acetic acid has been used.

Thus, when compound *I* was refluxed in anhydrous acetic acid with benzaldehyde or 4-chlorobenzaldehyde, the corresponding 11-arylidene derivatives *IIa* and *IIb* were obtained. In contrast to the modified Doebner reaction which takes place in the case of benzaldehyde only, the derivative *IIb* has been now obtained also from the less reactive 4-chlorobenzaldehyde. The structure of compound *IIb* was confirmed by a reversed reaction sequence, namely, by reaction of compound *IVb* with phenylhydrazine in ethanol and acetic acid. When refluxed in acetic acid with 4-dimethylaminobenzaldehyde, compound *I* afforded compound *V* which was also obtained from compound *I* by a simple reflux in acetic acid or conc. formic acid.

As it may be inferred from elemental analysis (*inter alia*, absence of the 4-dimethylaminobenzylidene group) and mass spectra, compound *V* possesses the structure of 8-chloroindolo[*b*,*d*]dibenzo[*b*,*f*]thiepine. The present reaction course resembles somewhat the Fischer preparation of indole derivatives. The increased reactivity of hydrogen atoms on the methylene group at position 11 of compound *I* might be explained in this case by the formation of a positive charge on the nitrogen atom of the phenylhydrazino residue due to protonisation. The inductive effect caused by this charge is considerably higher than effect of the free phenylhydrazono residue which asserts itself in the Doebner reaction. The protonated form affords with reactive aromatic aldehydes the corresponding arylidene derivatives *IIa* and *IIb*. In the case of a poorly reactive aromatic aldehyde such as 4-dimethylaminobenzaldehyde, the protonated form of compound *I* merely rearranges to compound *V*.



When 8-chloro-10,11-dihydrodibenzo[*b*,*f*]thiepin-10-one (*III*) was refluxed in acetic acid with benzaldehyde, 4-chlorobenzaldehyde or 4-dimethylaminobenzaldehyde, only the unreacted starting compound *III* was isolated even in the case of prolonged reaction time. Since the modified Doebner reaction of compound *III* takes place with all the three aldehydes and the alkaline aldolisation may be accomplished with benzaldehyde as the reaction component, it is obvious that in acetic acid as solvent the oxygen atom of the carbonyl group at position 10 of compound *III* does not undergo protonation and consequently, compound *III* cannot react with the above mentioned aldehydes. The present results extend the knowledge on condensation of compounds bearing an active methylene group to systems where the oxygen atom of the carbonyl group is replaced by substituents of the hydrazono type. The present procedure may thus be advantageously used in those cases which fail to undergo the alkaline aldolisation or the Doebner reaction, or applied to less stable systems sensitive to mineral acids serving as aldolisation catalysts.

EXPERIMENTAL

Melting points were taken on a heated microscope stage (Kofler block). Analytical samples were dried at 60°C/20 Torr for 5 h.

8-Chloro-11-benzylidene-10-phenylhydrazono-10,11-dihydrodibenzo[*b,f*]thiepine (*IIa*)

A mixture of compound *I* (1·75 g; 0·005 mol), benzaldehyde (3 ml), and acetic acid (20 ml) was refluxed for 4 h and kept at room temperature overnight. The solid was collected with suction, washed with ethanol, and crystallised from acetic acid (120 ml) to afford 1·86 g (85%) of compound *IIa*, m.p. 250–259°C (decomp.), identical with a specimen obtained by another method[5].

8-Chloro-11-(4-chlorobenzylidene)-10-phenylhydrazono-10,11-dihydrodibenzo[*b,f*]thiepine (*IIb*)

A. A mixture of compound *I* (1·75 g; 0·005 mol), 4-chlorobenzaldehyde (0·70 g; 0·05 mol), and acetic acid (20 ml) was processed analogously to the preparation of compound *IIa*. Yield, 1·96 g (83%) of compound *IIb*, m.p. 253–257°C (ethanol). For $C_{27}H_{18}Cl_2N_2S$ (473·4) calculated: 68·48% C, 3·83% H, 17·98% Cl, 5·92% N, 6·77% S; found: 68·35% C, 3·78% H, 14·71% Cl, 5·69% N, 6·68% S.

B. A mixture of compound *IVb* (1·91 g; 0·005 mol), phenylhydrazine (1·18 g; 0·011 mol), ethanol (30 ml), and acetic acid (2 ml) was refluxed for 5 h and evaporated under diminished pressure. The residue was crystallised from ethanol (150 ml) to afford 1·91 g (81%) of compound *IIb*, m.p. 253–257°C, undepressed on admixture with specimen obtained in paragraph *A*.

8-Chloroindolo[*b,d*]dibenzo[*b,f*]thiepine (*V*)

A solution of compound *I* (1·75 g; 0·005 mol) in acetic acid or formic acid (20 ml each) was processed analogously to preparation of compound *IIa*. Yield, 1·35 g (81%) of compound *V*, m.p. 212–214°C. For $C_{20}H_{12}ClNS$ (333·8) calculated: 71·96% C, 3·62% H, 10·62% Cl, 4·19% N, 9·60% S; found: 71·58% C, 3·57% H, 10·98% Cl, 4·07% N, 9·55% S.

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