

A NEW SYNTHESIS OF 1-ACETYL-3-ARYLIDENE(ALKYLIDENE)
PIPERAZINE-2,5-DIONES

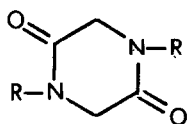
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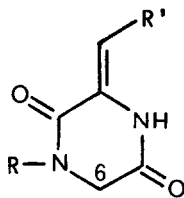
3,6-Diarylidenepiperazine-2,5-diones can be prepared¹⁾ by condensation of piperazine-2,5-dione(I) with aromatic aldehydes. Dialkylidene as well as monoalkylidene and monoarylidene derivatives were not accessible through this route and have been prepared, only recently, by independent methods^{2,3)}.

We have reinvestigated the condensation reaction and used the more reactive 1,4-diacetylpiperazine-2,5-dione(II) instead of I. Not only the aromatic aldehydes, but even the aliphatic terms underwent condensation to give the 1-acetyl-3-arylidene(alkylidene) derivatives III^{4,5)}, when reacted as indicated below.



I R = H

II R = COCH₃



III R = COCH₃

IV R = H

- a) R' = C₆H₅
- b) R' = pCH₃OC₆H₄
- c) R' = pO₂NC₆H₄
- d) R' = CH₃
- e) R' = C₂H₅
- f) R' = nC₃H₇
- g) R' = iC₃H₇

A) 2 M.moles of aldehyde, 2 m.moles of II and 2 m.moles of triethylamine in 4 ml of DMF, 12 hr at room temperature.

B) The same, 6 hr at 130°.

C) 8 M.moles of aldehyde, 2 m.moles of II in 4 ml of DMF and 4 ml of 0.5 N tBuOK in tBuOH added with stirring at 0°; than 6 hr at room temperature.

The reaction mixtures were acidified with 0.5 ml of acetic acid, poured into water, the products extracted with EtOAc and crystallized from ethyl acetate. The results are reported in Table 1. The deacylated derivatives IVa³⁾, IVb,c⁴⁾, and IVd,e,f,g²⁾ were obtained by treatment with hydrazine in DMF.

TABLE 1

Compound	Mp °C	Method	Yield %	UV(EtOH)	
				nm	ϵ
IIIa	200-201	C	85	229,316	14500,15300
IIIb	179-180	B	75	230,334	15800,20900
IIIc	213-215	A	100	229,331	13300,15500
IIId	182-184	C	37 ⁷	222	14100
IIIe	154-156	C	90 ⁷	222	14600
IIIf	137-138	C	92 ⁷	222	14500
IIIg	146-147	C	95 ⁷	222	14200

The 1-acetyl-3-arylidene(alkylidene)derivatives(III) can be further condensed with aromatic aldehydes under the same conditions to give symmetrical or unsymmetrical 3,6-diarylidene-piperazine-2,5-diones or 3-alkylidene-6-arylidene-piperazine-2,5-diones. It is apparent that our modification makes the condensation of aldehydes with piperazine-2,5-dione a stepwise reaction easy to control simply by changing the ratios of reagents, and allows ready access to both monoarylidene and monoalkylidene piperazine-2,5-diones.

FOOTNOTES AND REFERENCES

- 1) R.Sasaki, Chem.Ber.,1921,54,163.
- 2) C.Shin, M.Fujii, and J.Yoshimura, Tetrahedron Letters, 1971,2499.
C.Shin, Y.Chigira, and M.Otha, Bull.Chem.Soc.Japan, 1969,42,191.
- 3) B.W.Dominy, and G.Lawton, J.Org.Chem., 1969,34,2013.
- 4) All new compounds had satisfactory microanalytical and spectral properties.
- 5) Trans geometry was assigned to the 3-arylidene derivatives on the basis of UV absorption according to Sammes and Blake⁸) and is suggested for 3-alkylidene derivatives. The position of the acetyl group was indicated by NMR spectra of the series III and IV (for solutions in CDCl₃ or D₃C-SO-CD₃, chemical shifts reported as δ values relative to TMS as internal standard). In the series IV, the signal of the proton at C6 appeared as a doublet (J 2.0-2.1 cps) in the range 3.96-4.08 δ and became a singlet when D₂O was added. In the series III, a singlet (4.42-4.50 δ) was uniformly observed, indicating that the adjacent nitrogen atom is attached to the acetyl group rather than to an exchangeable hydrogen.
- 6) Excess of aliphatic aldehyde in view of base-catalysed self-condensations.
- 7) Based on the 1,4-diacetylpiperazine-2,5-dione.
- 8) K.W.Blake, and P.G.Sammes, J.Chem.Soc.(C), 1970,980.