

CONDENSATION OF AROMATIC ALDEHYDES
WITH γ -PICOLINE METHIODIDE

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An earlier paper from these laboratories (1) reported the preparation of a series of α -stilbazole methiodides by the condensation of aromatic aldehydes with α -picoline methiodide. A similar series of compounds has now been made from γ -picoline methiodide. These compounds were made primarily for testing in a search for substances possessing curare-like activity. Incidental to the main purpose, certain correlations of possible theoretical interest have been noted in this and the earlier publication.

EXPERIMENTAL

All melting points are uncorrected.

Preparation of the γ -stilbazole methiodides. The general method of preparation is the same as that described for the α -stilbazole methiodides (1).

γ -Picoline methiodide, 5 g. (0.021 *M*), and 5 g. (0.03-0.04 *M*) of the aldehyde to be condensed were mixed and dissolved in 30 cc. of methanol. Piperidine (1 cc.) was added and the reaction mixture was refluxed on the steam-bath for a period of from one to four hours. After cooling, the solid was collected, washed with and recrystallized from methanol. Yields reported are in most cases those obtained after a single recrystallization from methanol of the first and second (obtained by partial evaporation of the original mother liquors) crops. Results are compiled in Table I.

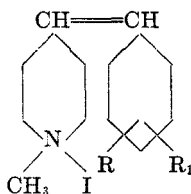
Acknowledgment. The microanalytical results included were obtained by Mr. Samuel W. Blackman and absorption spectra were obtained by Miss Gertrude Elion. Their help is much appreciated.

DISCUSSION

The compounds presented here manifest the same general relationship between color, yields obtained, and resonance possibilities of the products which was described previously for the α -series (1). Corresponding compounds from the two series were of about the same color.

With the highly colored members, the 4'-dialkylaminostilbazole methiodides, the γ -isomers appeared to be of a slightly deeper shade than their α -isomers. This observation, questionable as applied to visual examination of the solid substances, was supported by absorption spectra, for compound XIX (see Table I) had its characteristic maximum in the visible at 4540 Å [Clemo and Swan (2) reported a maximum at 4800 Å for this substance] as compared with 4440 Å for the α -isomer. Similarly the 4'-hydroxystilbazole methiodide, compound XI (Table I), which is highly colored in alkaline solution, had its maximum at 4450 Å in alkali as compared with 4350 Å for its α -analog in the same medium. Even in neutral medium a significant difference in the position of the maxima is observed for these two compounds: XI, 3750 Å; its α -analog, 3630 Å.

TABLE I
DERIVATIVES OF γ -STILBAZOLE METHIODIDE



COMP'D. NO.	SUBSTITUENTS ON BENZENE RING	M.P., °C.	YIELD%	ANALYSIS				ABSORPTION MAXIMUM, Å	
				Calc'd		Found			
				C	H	C	H		
I	None	220-221	82	52.00	4.37	52.12	4.39	3350 ^a	
II	4-CH ₃ -	235-236	75	53.40	4.78	53.22	4.69		
III	2-Cl-	218-219	65	46.98	3.66	47.19	3.95		
IV	4-Cl-	250-251	70	46.98	3.66	46.95	3.63		
V	3-NO ₂ - ^b	>290	90	45.64	3.56	45.73	3.72		
VI	4-NO ₂ -	235-236	68	45.64	3.56	45.29	3.59		
VII	2-CH ₃ O-	194-195	94	50.98	4.57	51.15	4.42		
VIII	4-CH ₃ O-	214-215	98	50.98	4.57	50.72	4.68		3680 ^a
IX	2-HO-	218-219	78	49.54	4.16	49.82	4.32		
X	3-HO-	260-261	90	49.54	4.16	49.47	4.14		4510 ^c
XI	4-HO-	265-266	80	49.54	4.16	49.23	4.10		3430 ^a
								3450 ^c	
								4450 ^c	
XII	3,4-CH ₂ O ₂ <	283-284	93	49.03	3.84	49.16	3.77		
XIII	3,4-(CH ₃ O-) ₂	253-254	81	50.12	4.72	50.04	4.76		
XIV	2,5-(CH ₃ O-) ₂	246-247	96	50.12	4.72	50.38	4.64		
XV	3-CH ₃ O-4-HO-	275-276	64	48.77	4.36	48.92	4.62		
XVI	3-C ₂ H ₅ O-4-HO-	258-259	80	50.12	4.72	50.20	4.54		
XVII	2-HO-3-CH ₃ O-	247-248	94	48.77	4.36	48.98	4.29		
XVIII	2-HO-3-C ₂ H ₅ O-	236-237	90	50.12	4.72	50.36	4.72		
XIX	4-(CH ₃) ₂ N- ^d	258-259	100	52.43	5.24	52.65	5.44	4540 ^a	
								3275 ^c	
XX	4-(C ₂ H ₅) ₂ N-	221-222	100	54.79	5.88	54.52	6.14	4710 ^c	
								3310 ^c	
XXI	α -Furyl ^f	202-203	46	45.99	3.86	46.04	4.10		
XXII	α -Thienyl ^f	232-233	68	43.76	3.68	43.85	3.78		

^a Absorption spectrum of a solution in distilled water.

^b Crystallized from hot water.

^c Absorption spectrum in aqueous sodium hydroxide.

^d Previously described by Clemo and Swan, reference (2).

^e Absorption spectrum in aqueous hydrochloric acid.

^f This ring in place of phenyl above.

With less highly colored compounds, where the resonance contribution of the styryl side chain would be expected to be of relatively lesser importance, the absorption maxima for the two analogous series show remarkably close agreement. Compound I (Table I), the simple styryl derivative, has its maximum at 3350 Å, its α -isomer at 3340 Å.

The significantly deeper color, absorption maxima at longer wave lengths, of the highly colored members of the γ -stilbazole methiodide group, as compared with the corresponding members of the α -group can probably be accounted for in

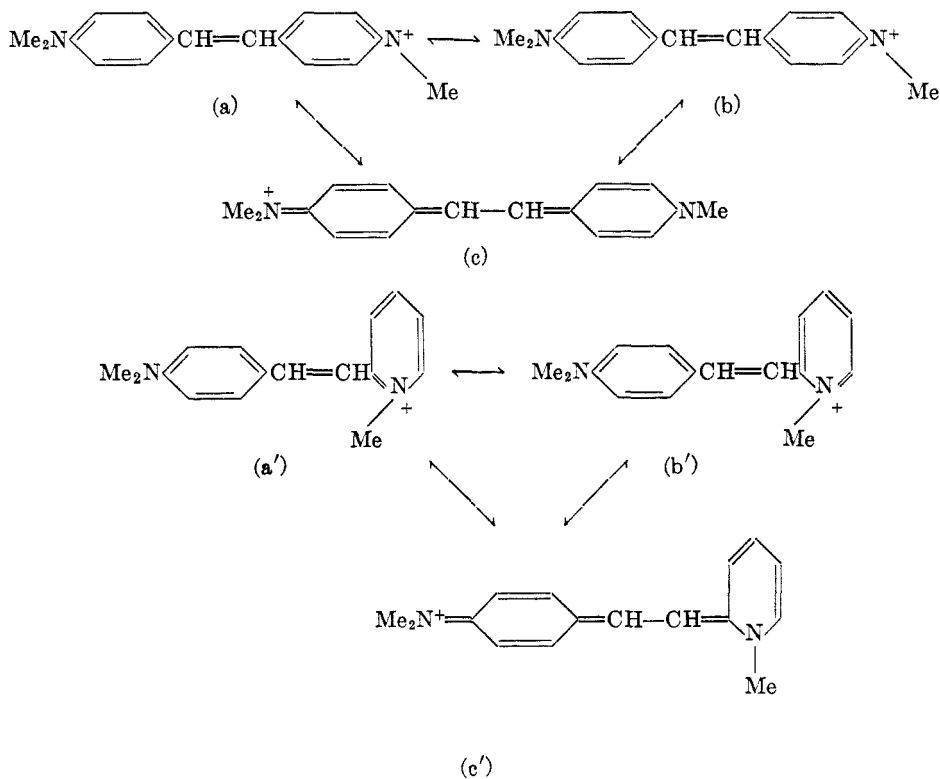


FIG. 1

terms of a more favorable resonance situation in the γ compounds, as indicated in Fig. 1.

By use of the principal resonance variants shown in Fig. 1, the deeper color for the γ -isomer could reasonably be attributed to one or the other, or both, of two effects: 1. the variants for the γ -series (a, b, c) would afford an average longer chain of conjugated double bonds (mobile electronic system) since each possesses five conjugated double bonds between the cationic and tertiary nitrogens. On the other hand, in the α -system (a', b', c') a' has four double bonds between nitrogens, b' has six, while c' could be counted as either four or six, but with the possibility of the shorter route there seems no reason for weighing the longer

route as more important; 2. the energy contents of a and b would be identical, with c differing by some small amount. In contrast a', b', and c' should all be of different energy and as a result resonance in the former groups of variants would be expected to be more favorable.

3'-Hydroxy- γ -stilbazole methiodide had absorption maxima for neutral and alkaline media at 3430 Å and 3450 Å, respectively, again confirming the visually observed and theoretically predicted result, equally applicable to either α or γ series, of no appreciable color change between the two media.

A number of aldehydes seemed to give significantly greater yields of condensation product with γ -picoline methiodide than they had with α -picoline methiodide. In spite of earlier reports (3) of the greater reactivity of the α -methylpyridines and quinolines (as compared to the γ -analogs) this observation is in accord with theory as interpreted earlier in this paper to explain the deeper color of the γ -isomers, and in the earlier paper (1) describing the relationships between structure and yields. However, a careful check has revealed that although this observation is doubtless correct in several cases, a more careful control of reaction time, ratio of reactants, and a modification of the method of isolating products is desirable to obtain more comparable results. These results, for a few selected aldehydes, will be presented in the near future.

SUMMARY

In the preparation of a series of γ -stilbazole methiodides the same general relationship between color, yields and resonance possibilities of the products has been observed as was reported previously for the α -isomers.

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REFERENCES

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