DYES CONTAINING THE INDOLE RING-I

TRINUCLEAR PENTAMETHINCYANINES

J. R. MAJER

The Chemistry Department, The University of Birmingham

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Abstract—Indole trimethincyanines prepared as described previously¹ and also by the interaction of indoles containing unsubstituted NH- and β -positions with acetylenic aldehyde acetals have been found to condense with homocyclic and heterocyclic aldehydes to yield trinuclear dyes. A simple method of preparing unsymmetrical trimethincyanines is described.

It was shown in a previous paper that indoles containing unsubstituted NH- and β -positions react with a large excess of a carbonyl compound and a molecular equivalent of concentrated sulphuric acid to yield yellow crystalline salts having the structure I (R = hydrocarbon residue, R' = H or a hydrocarbon residue). When the carbonyl compound contains the group --CO·CH₂-- the products, such as 2-methyl-3-isopropylidene indolenine sulphate, condense with homocyclic and heterocyclic aldehydes to yield trimethincyanines II. Because the two methyl groups in the isopropylidene groups are essentially equivalent, it seemed probable that the trimethincyanine II should be capable of further reaction with a second molecule of aldehyde to yield the trinuclear dye III. When, however, I was refluxed in acetic acid with an excess of 2-methyl-3-indole aldehyde for a prolonged period, only the purple trimethincyanine II was obtained.

It is concluded that when the first methyl group has reacted and the trimethincyanine has been formed, the reactivity of the remaining methyl group is reduced, possibly owing to steric effects. Bis-(2-methyl-3-indole)- α -methyl trimethincyanine sulphate was therefore refluxed with 2-methylindole-3-aldehyde in a 1 : 1 mixture of acetic anhydride and glacial acetic acid. The original purple colour of the solution was rapidly replaced by a deep blue colour and green crystals were deposited. These were shown by analysis to be the expected trinuclear dye III. A similar dye was obtained when the aldehyde used was Fischer's base aldehyde.

Because of the tedious nature of the preparation of indole-3-aldehydes, alternative routes to the trimethincyanines were investigated. König² described the use of propargyl aldehyde diethyl acetal in the preparation of indole and pyrrole trimethincyanines and his method was extended to the substituted acetylenic acetals. An alternative route employing acetylenic ketones has been described by Johnson.³ Crotonaldehyde was brominated and the resulting dibromide acetalized with ethyl orthoformate. Debromination with alcoholic caustic potash gave α -methyl propargyl aldehyde diethyl acetal. This compound reacted readily in glacial acetic acid solution with both

¹ A. H. Cook and J. R. Majer, J. Chem. Soc. 486 (1944).

⁸ W. König, Angew. Chem. 38, 743 (1925).

^{*} A. W. Johnson, J. Chem. Soc. 1626 (1947).

pyrroles and indoles in the presence of mineral acid to yield trimethincyanines. α -Phenol propargyl aldehyde diethyl acetal was prepared similarly from cinnamaldehyde.⁴ Crystalline trimethincyanines were obtained from propargyl aldehyde diethyl acetal with 2,4-diphenylpyrrole, and 2-methyl-3-carbethoxy-4-phenylpyrrole- α -methyl propargyl aldehyde diethyl acetal with 2-phenyl-4-o-chlorophenylpyrrole,



2-methyl-3-carbethoxy-4-phenylpyrrole, 2,4-diphenylpyrrole, 2-methylindole and 2phenylindole, and a-phenyl propargyl aldehyde diethyl acetal with 2-phenyl-4-panisylpyrrole, 2,4-diphenylpyrrole, 2-methyl-4-phenylpyrrole and 2-methyl-3-carbethoxy-4-phenylpyrrole. In each case the dye obtained was identical with that prepared by the original method. In the case of pyrrole itself only an insoluble amorphous precipitate was obtained when mineral acid was added to a solution in the presence of an acetylenic acetal although there was an initial development of the expected purple colour. This is believed to be due to the rapid resinification of the pyrrole by the acid. Attempts to prepare dyes from N-substituted pyrroles were equally unsuccessful; when an acetic acid solution of 1,2-dimethyl-3-carbethoxy-4phenylpyrrole was treated with mineral acid in the presence of an acetylenic acetal a deep blue colour developed but there was no precipitate. Addition of water or ether decolourized the solution and deposited a whitish solid. On standing in glacial acetic acid solution the colour slowly faded. Similar fugitive colours were obtained with α -substituted β -free pyrroles such as 2,5-dimethyl-, 2,5-dimethyl-1-cyclohexyland 2,5-dimethyl-1-stearyl-pyrroles.

Attempts were made to condense the pyrrole trimethincyanines prepared from α -methyl propargyl aldehyde diethyl acetal with aldehydes, but on prolonged refluxing in the acetic acid-acetic anhydride mixture the original blue colour of the trimethincyanine gradually faded without the appearance of any deposit. It is concluded that the

4 Org. Synth. 25, 92.

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trinuclear dyes derived from pyrrole are unstable. Bis-3-(2-phenyl indole)- α -methyl trimethincyanine sulphate, however, reacted readily with 2-methylindole-3-aldehyde although the resulting trinuclear dye was so insoluble that it was precipitated without imparting any colour to the refluxing solution.

Unsymmetrical indole trimethincyanines were prepared by the addition of a hot solution of an indole in ethyl orthoformate to a boiling solution of I in glacial acetic acid, thus avoiding the use of the indole-3-aldehydes. The exact course of this reaction is not clear:— β -free indoles do not react with boiling ethyl orthoformate and on



addition of mineral acid the di-indolyl methene IV is formed. The same product is obtained even if a ketone such as acetone is present, so that the most rapid reaction must be the formation of the methene. This is not the case with pyrroles, where in the presence of ketones, trimethincyanines are formed.¹ The most plausible explanation is that the indolenine salt I reacts with the ortho ester to form V which then condenses with the indole to produce the trimethincyanine. Attempts to isolate V have been unsuccessful.

Unsymmetrical trimethincyanines were prepared by the condensation of 2methyl-3-isopropylidene indolenine sulphate with ethyl orthoformate and indole, 2,4-diphenylpyrrole and 2-phenylindole; 2-phenyl-3-isopropylidene indolenine sulphate was condensed with ethyl orthoformate and indole. The unsymmetrical trimethincyanines were converted to the trinuclear dyes by refluxing with aldehydes in glacial acetic acid-acetic anhydride mixture. Indole-3-aldehyde was condensed with 3-(2-methylindole)-3-indole- α -methyl trimethincyanine sulphate and with 3-(2-methylindole)-3-(2-phenylindole)- α -methyl trimethincyanine sulphate. In the latter case the product contained three different nuclei connected by a chain of five carbon atoms. In order to simplify the nomenclature of these trinuclear dyes they are treated as derivatives of indole pentamethincyanines although their nearest relatives in the true cyanines are the trinuclear neocyanines.⁵

⁵ F. M. Hamer, R. J. Rathbone and B. S. Winton, J. Chem. Soc. 1434 (1947); 1872 (1948).

EXPERIMENTAL

Symmetrical trimethincyanines

2-Diphenylpyrrole (2·19 g) and propargyl aldehyde diethyl acetal (0·6 g) were refluxed in glacial acetic acid (10 ml) and 50% hydrobromic acid in glacial acetic acid (0·81 ml) added. A deep blue colour appeared and green crystals were precipitated. On crystallization from chloroform bis-2-(3,5-diphenylpyrrole) trimethincyanine bromide (1·1 g) was obtained as bronze octahedra m.p. 260°. (Found: Br, 14·35%; C₃₈N₃₈N₃Br requires: Br, 14·35%).

2-Methyl-3-carbethoxy-4-phenylpyrrole $(2\cdot 3 \text{ g})$ gave bis-2-(3-phenyl-4-carbethoxy-5-methylpyrrole) trimethincyanine bromide as green rods from formic acid m.p. 200°.

2-Phenyl-4-o-chlorophenylpyrrole (2.53 g) and methyl propargyl aldehyde diethyl acetal (1.02 g) gave bis-2-(3-o-chlorophenyl-5-phenylpyrrole)- α -methyl-trimethincyanine bromide (0.9 g) as black needles from glacial acetic acid m.p. 158°. (Found: Br, 12.2%; C₄₁H₂₂N₂Cl₂Br requires: Br, 12.5%).

2-Methyl-3-carbethoxy-2-phenyl pyrrole (2.3 g) gave bis-2-(3-phenyl-4-carbethoxy-5-methylpyrrole)- α -methyl-trimethincyanine bromide as matted green needles from formic acid m.p. 198°.

2-Methylindole (1.3 g) and methyl propargyl aldehyde diethyl acetal (0.71 g) and sulphuric acid (0.28 ml) gave bis-3-(2-methylindole)- α -methyl-trimethincyanine sulphate as long green needles from glacial acetic acid m.p. 168°.

2-Phenylindole (7.7 g) gave bis-3-(2-phenylindole)- α -methyl-trimethincyanine sulphate (6.2 g) as copper crystals from acetic acid-ether m.p. 178°. (Found: S, 5.9%; C₃₃H₃₆O₄N₃S requires: S, 5.99%).

2-Phenyl-4-*p*-anisylpyrrole (2·49 g), phenyl propargyl aldehyde diethyl acetal (1·02 g) and 50% hydrobromic acid gave bis-2-(3-*p*-anisyl-5-phenylpyrrole)- α -phenyl-trimethincyanine bromide as dark green crystals from glacial acetic acid m.p. 240°. (Found: Br, 11·7%; C₄₅H₃₅O₅N₂ Br requires: Br, 11·55%).

2-Methyl-3-carbethoxy-4-phenylpyrrole gave bis-2-(3-phenyl-4-carbethoxy-5-phenylpyrrole)- α -phenyl-trimethincyanine bromide as green needles from ethyl formate m.p. 202°.

2,4-Diphenylpyrrole gave bis-2-(3,5-diphenylpyrrole)- α -phenyl-trimethincyanine bromide as brassy crystals from chloroform m.p. 247°.

Unsymmetrical trimethincyanines

2-Methyl-3-isopropylidene indolenine sulphate (5.86 g) was dissolved in glacial acetic acid (20 ml) and the mixture heated to boiling. A boiling solution of indole (2.3 g) in ethyl orthoformate (3 ml) was added when a vigorous reaction occurred and the solution became deep red. On cooling and dilution with ether an oil was precipitated which hardened to a brown solid when ground with water. Crystallization from acetic acid-ether yielded 3-(2-methylindole(-3'-indole- α -methyl-trimethincyanine sulphate (6.2 g) as brown metallic needles m.p. 172°. (Found: S, 8.0%; C₂₁H₂₀O₄N₂S requires: S, 8.08%).

2-Phenylindole (3.86 g) gave 3-(2-methylindole)-3'-(2-phenylindole)- α -methyl-trimethincyanine sulphate (6.4 g) as purple brown needles m.p. 106°. (Found: S, 6.6%; C₁₇H₁₄O₄N₁S requires: S, 6.78%).

2,4-Diphenylpyrrole (2·2 g) gave 3-(2-methylindole)-2'-(3,5-diphenylpyrrole)- α -methyl-trimethincyanine sulphate (0·6 g) as copper octahedra from chloroform-ether m.p. 136°. (Found: S, 6·3%; C₂₅H₂₅O₄N₂S requires: S, 6·42%).

2-Phenylindole (3.86g) was dissolved in acetone (5ml) and A.R. conc sulphuric acid (1.1ml) added. The excess acetone was removed under reduced pressure and the residue dissolved in glacial acetic acid (20 ml). The solution was refluxed and a boiling solution of indole (2.3 g) in ethyl orthoformate (3 ml) added. After refluxing for 5 min the red dye was precipitated by addition of ether and the resulting oil ground with water. On crystallization from acetic acid-ether 3-(2-phenylindole)-3'indole- α -methyl-trimethincyanine sulphate was obtained as purple needles m.p. 174°. (Found: S, 6.98%; C₂₈H₂₂O₄N₂S requires: S, 6.99%).

Trinuclear dyes

Indole-3-aldehyde (1.0 g) and 3-(2-methylindole)-3'-(2-phenylindole)- α -methyl-trimethincyanine sulphate (3.6 g) were refluxed for 2 min in a 1 : 1 mixture of acetic acid and acetic anhydride (20 ml).

The solution became an intense brown colour and deposited a black solid. On crystallization from methanol, 3-(2-phenylindole)-3'-indole- γ -3"-(2-methylindole) pentamethincyanine sulphate (3 g) was obtained as black metallic needles m.p. 143°. (Found: S, 5·3%; C₁₆H₁₀O₄N₂S requires: S, 5·34%).

Indole-3-aldehyde (1.0 g) and 3-(2-methylindole)-3'-indole α -methyl-trimethincyanine sulphate (3.3 g) gave bis-3-(indole)- γ -3-(2-methylindole) pentamethincyanine sulphate (2.3 g) as black metallic needles from methanol m.p. 120°. (Found: S, 6.0% N, 8.0%; C₂₀H₂₈O₄N₂S requires: S, 6.12%, N, 8.03%). Treatment with ammonia solution gave the free base as a brown solid m.p. 2480°. (Found: N, 10.0%; C₂₀H₂₈N₃ requires: N, 9.08%).

2-Methyl-3-indole aldehyde (0.74 g) and bis-(2-phenylindole)- α -methyl-trimethincyanine sulphate (2.6 g) gave (2-phenylindole)-3'-(2-methylindole)- γ -3"-(2-phenylindole) pentamethincyanine sulphate (2.0 g) as black metallic needles from methanol m.p. 310°. (Found: S, 4.4%, N, 6.2%; C₄₃H₃₅O₄N₃S requires: S, 4.74%, N, 6.34%).

Bis-3-(2-methylindole)- α -methyl-trimethincyanine sulphate (0.6 g) and Fischer's base aldehyde (0.3 g) gave 3-(2-methylindole)-2'-(1,3,3'-trimethylindolenine)- γ -3"-(2-methylindole) hexamethincyanine sulphate (0.5 g) as copper octahedra from acetic acid-ether m.p. 184°. (Found: S, 5.25%, N, 7.0%; C₁₅H₂₈O₄N₂S requires: S, 5.4%, N, 7.08%).

2-Methyl-3-indole aldehyde (0.4 g) and bis-3-(2-methylindole)- α -methyl-trimethincyanine sulphate (1.02 g) gave bis-3-(2-methylindole)- γ -3'-2-methylindole) pentamethincyanine sulphate (0.86 g) as small green needles from acetic acid m.p. 281°. (Found: S, 5.7%, 7.5%; C₁₁H₂₀O₄N₃S requires: S, 5.81%, N, 7.62%).