An Improved Synthesis of Alizarin Fluorine Blue

BY K. AL-ANI AND M. A. LEONARD

(Department of Analytical Chemistry, Queen's University, Belfast, BT9 5AG)

The ideas of Hellmann and Opitz concerning optimum conditions for aminomethylation reactions are applied to the synthesis of alizarin fluorine blue. The yield is increased from 13 to 61 per cent. by using an aqueous ethanolic solvent of minimum alkalinity.

THE compound alizarin fluorine blue (1,2-dihydroxyanthraquinon-3-ylmethylamine-NN-diacetic acid) has achieved considerable use as a reagent for the detection of fluoride and certain metal ions, and as a metallochromic indicator.^{1,2} The synthesis formerly suggested by Leonard and West consisted of a Mannich-type condensation between alizarin, formaldehyde and iminodiacetic acid under strongly alkaline, solely aqueous conditions. The yield of the poorly crystalline product was about 13 per cent.

Study of the excellent paper by Hellmann and Opitz³ concerning the optimum conditions required for aminomethylation showed that the Mannich condensation most probably proceeds in this manner:



We therefore repeated the synthesis with pre-formation of the carbonium - immonium intermediate and with aqueous ethanol as the solvent, which enabled a satisfactory alizarin concentration to be used under minimum conditions of alkalinity (the vital cationic intermediate requiring a proton for its formation). Under these conditions the N-ethoxymethyl compound

may be formed, but this also reacts with a proton to give the active carbonium - immonium intermediate.

The total yield by this method of synthesis was 61 per cent.

METHOD OF SYNTHESIS

Dissolve 1 g of alizarin (1,2-dihydroxyanthraquinone, recrystallised from ethanol) in 50 ml of ethanol and add 4 ml of \aleph sodium hydroxide solution dropwise with swirling. Separately dissolve 3.25 g of iminodiacetic acid disodium salt monohydrate in 25 ml of

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ethanol - 4 per cent. sodium hydroxide mixture (11 + 9), add 1 ml of 36 per cent. formaldehyde solution and maintain at 5° C for 12 hours. Mix the two solutions at 20° C in a 100-ml flask fitted with stirrer, reflux condenser and nitrogen inlet. Displace the air in the apparatus with nitrogen and thereafter maintain a slow flow over the surface of the mixture. Heat the mixture to 78° C and maintain it at this temperature for a total of 10 hours, adding further 0.7-ml portions of 36 per cent. formaldehyde solution after 3 and 7 hours.

Dilute the mixture to 250 ml with de-ionised water, heat to 50° C, then add 3 N hydrochloric acid until the pH is 1.8. After 5 hours filter off the precipitate, wash it sparingly with warm water, then dissolve it in 200 ml of water containing 8 ml of N sodium hydroxide solution. Heat the resulting mixture to 50° C and then add dilute acetic acid to bring the pH to 5.5. Maintain it at 50° C for 10 minutes, then filter off the small residue of alizarin or non-carboxylated polymer. Cool the filtrate to 20° C and extract with diethyl ether until the extracts are virtually colourless. Acidify the aqueous phase to pH 1.8, allow it to stand overnight, filter off the clear yellow - orange precipitate, wash it with water followed by a mixture of ethanol - diethyl ether in the ratio (1 + 1) and finally dry under vacuum at 80° C over phosphorus(V) oxide. We obtained a yield of 0.98 g or 61 per cent. by this method.

ELEMENTAL ANALYSIS-

	Percentage of carbon	Percentage of hydrogen	Percentage of nitrogen
Theoretical	 $\begin{array}{c} 59 \boldsymbol{\cdot} 20 \\ 59 \boldsymbol{\cdot} 13 \end{array}$	3·92	3·63
Found		4·07	3·53

MASS SPECTROMETRY-

The mass spectrum showed no parent ion peak at 385 but gave peaks at 326 (10 per cent. abundance) and 254 (100 per cent. abundance; high molecular weight end only) indicating the loss of $-CH_2COOH$ and $-N(CH_2COOH)_2$ radicals from the product.

CONCLUSIONS

Although the product obtained by this method is no purer than rigorously purified material obtained with the old method, a good quality product is much easier to obtain because the conversion yield of alizarin into alizarin fluorine blue is much greater. The products of the old and new methods are identical with respect to thin-layer chromatography (both yielding only one spot), electrophoresis, mass spectrometry, melting-point and reactivity of the lanthanum(III) chelate towards fluoride.

References

- 1.
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Received May 11th, 1970 Accepted June 18th, 1970