

477. *The Preparation and Analytical Properties of NN-Di(carboxymethyl)aminomethyl Derivatives of Some Hydroxyanthraquinones.*

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NN-Di(carboxymethyl)aminomethyl derivatives of some hydroxyanthraquinones are prepared by a Mannich-type condensation between the parent material, formaldehyde, and iminodiacetic acid. The monosubstituted derivatives prepared from alizarin and Alizarin Bordeaux R are particularly useful as indicators in complexometric titration, especially the ethylenediaminetetra-acetate titration of Pb^{2+} , Zn^{2+} , Co^{2+} , and In^{3+} in acid solution. The pH limits have been established and the interference of various ions has been examined. The indicators are stable in solution for several months. These substances also show promise as possible colorimetric reagents for Th^{4+} and Ce^{3+} .

INTRODUCTION of the strongly chelating methylamine-*NN*-diacetic acid group, $-\text{CH}_2\cdot\text{N}(\text{CH}_2\cdot\text{CO}_2\text{H})_2$, frequently converts pH-sensitive dyes into indicators suitable for complexometric titration with ethylenediaminetetra-acetic acid.¹ Since many hydroxyanthraquinones show colour changes with pH in both acid and alkaline solution the preparation of complexometric indicators based on these substances was attempted. Accordingly, the *NN*-di(carboxymethyl)aminomethyl derivatives of 1 : 2-dihydroxy-,* 1 : 2 : 5-,* 1 : 2 : 6-, and 1 : 2 : 7-trihydroxy-, and 1 : 2 : 5 : 8-tetrahydroxy-anthraquinone have been prepared.

The preparative method was a Mannich condensation of the hydroxyanthraquinone with formaldehyde and iminodiacetic acid. An excess of the aldehyde and acid was used, but in all cases only a monosubstituted product was obtained; the dicarboxymethylaminomethyl group is assumed to be in position 3 because the reaction tends to occur in positions *ortho* to the hydroxyl groups in aromatic systems.

* Trivial names for these compounds would be alizarin complexone and Alizarin Bordeaux complexone, respectively.

¹ Anderegg, Flaschka, Sallmann, and Schwarzenbach, *Helv. Chim. Acta*, 1954, **37**, 113; Diehl and Ellingboe, *Analyt. Chem.*, 1956, **28**, 882; Tucker, *Analyst*, 1957, **82**, 284; Körbl and Pribil, *Chem. and Ind.*, 1957, 233; *Chemist Analyst*, 1956, **45**, 102.

Very little nitrogenous product was obtained from the corresponding reaction with 2-hydroxy-, 1:4-, 1:5-, or 1:8-dihydroxy-, or 1:2:3- or 1:2:4-trihydroxy-anthraquinone or with a mixture of the 5- and 8-sulphonic acids derived from 1:2-dihydroxy-anthraquinone.

The free acids are yellow or orange-brown powders which in dilute solution are yellow or yellow-pink below pH 4.5, red at *ca.* pH 7, with transition to violet at higher pH's. These substances are also less soluble in ether and alcohol than the starting materials but are more soluble in water.

Analytical Reactions.—Those cations which give coloured compounds with the starting materials still react in a similar fashion with the new derivatives, but in addition several ions which show no colour reaction with the parent substance now form red chelates at pH 4.5. Thus 1:2-dihydroxyanthraquinon-3-ylmethylamine-NN-diacetic acid (A) reacts with ions such as Co^{2+} , Ni^{2+} , Pb^{2+} , Zn^{2+} , La^{3+} , Hg^{2+} , and Cu^{2+} . The indicator itself is red at pH 7–10, mauve at pH 11.5, and violet at pH 12.5 and if added to a solution of any of the above-mentioned ions (pH < 12.5) it assumes the colour characteristic of it in the next higher pH range, *i.e.*, at pH 4.5 it changes to red, at pH 7–10 it changes to mauve, etc. Thus ions which show little tendency to form chelates in acid solution but react in alkaline solution also produce colour reactions; *e.g.*, Ca^{2+} , Ba^{2+} , Sr^{2+} , and Cd^{2+} give rise to mauve chelates at pH 10–11.

Indicator Properties.—Only the analytical reactions of acid (A) are described in this paper. The other compounds behave similarly. The most obvious application of these compounds lies in their potentialities as complexometric indicators. At pH 4.3 good reversible red to yellow end-points were obtained with acid (A) in the EDTA titration of Co^{2+} , Pb^{2+} , and Zn^{2+} . Cu^{2+} was titrated satisfactorily in solutions where its concentration was not very high; in more concentrated solution the intensely blue chelate with EDTA masked the colour change. Ni^{2+} and La^{3+} formed chelates which were sufficiently stable even in boiling solution to offer serious resistance to the action of slight excesses of EDTA. The titration of Pb^{2+} and Zn^{2+} was carried out at room temperature, but the Co^{2+} end-point is best observed at 70–80°. These titrimetric procedures are reproducible within 0.1–0.2%. Indium can also be titrated at 70–80° and pH 4, but a better end-point is obtained with 1:2:5-trihydroxyanthraquinon-3-ylmethylamine-NN-diacetic acid.

Comparison with Other Indicators.—Xylenol Orange which is perhaps the best complexometric indicator hitherto proposed for the titration of Pb^{2+} , Zn^{2+} , and Co^{2+} in acid solution was compared with our acid (A). At pH 5–6 the former gave a better colour response but the latter was preferred in more acid solution (pH 4.3–3.8). Hence use of acid (A) may be of advantage when it is necessary to titrate these ions in solutions of lower pH where, of course, fewer other ions interfere with the titration.

In titrations with acid (A) the yellow to red end-point is improved considerably by screening with Xylene Cyanol FF, a red to green end-point being obtained.

Interferences.—Small amounts of alkaline earths, Mg^{2+} , As^{3+} , Ag^{+} , Be^{2+} , or Cr^{3+} did not cause interference (when up to 5% of them was present). On the other hand Al^{3+} , Fe^{3+} , Sn^{2+} , Sn^{4+} , Ce^{3+} , Ni^{2+} , Mn^{2+} , La^{3+} , Sc^{3+} , Th^{4+} , Zr^{4+} , U^{4+} , and U^{6+} interfered seriously with the colour change. Cu^{2+} , Cd^{2+} , and Bi^{3+} did not unduly affect the quality of the end-point, but added on to the titration for the ion being determined.

Acid (A) can also be used as an indicator for the titration of Ca^{2+} , Ba^{2+} , Cd^{2+} , etc., in alkaline solution but the end-points offer no advantage over those of the many complexometric indicators already available for these ions.

The indicator solutions prepared as described below were stable for several months.

Acid (A) may also have applications as a colorimetric reagent for Ce^{3+} , Th^{4+} , etc., since the chelate compounds formed have an intense colour which is not affected by fluoride and EDTA to the same extent as the Alizarin S chelates which are completely broken down by these ions.

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EXPERIMENTAL

Preparation of 1:2-Dihydroxyanthraquinon-3-ylmethylamine-NN-diacetic Acid.—Alizarin (16 g., 1 mol.) and iminodiacetic acid (22.5 g., 2.5 mol.), suspended in water (30 ml.), were treated with sodium hydroxide (13.5 g., 5 mol.) in water (60 ml.), followed by 37% formaldehyde solution (10 ml.). The mixture was diluted to 230 ml. with water, then kept at 75°, with constant stirring. A further 7 ml. of 37% aqueous formaldehyde were added after 4 hr., bringing the total amount to 3 mol. After a total reaction time of 14 hr., the mixture was diluted to 750 ml. and treated at 45° with 5N-hydrochloric acid dropwise till no more *compound* was precipitated. The precipitate was filtered off, and dissolved in distilled water (500 ml.) by adding the minimum amount of 2N-sodium hydroxide. Reprecipitation was effected at 45° by means of 5N-hydrochloric acid. After 2 hr. the precipitate was filtered off, washed with water containing a small amount of hydrochloric acid, then with a little 1:1-ethanol-ether. The resulting acid cake was dispersed in water (1 l.) lightly buffered at pH 5 (0.8 ml. of acetic acid and 6 g. of sodium acetate trihydrate), treated with a little charcoal at 45° for 2 hr., and filtered through paper pulp. The filtrate was extracted with ether to remove traces of alizarin) acidified with 5N-hydrochloric acid (to precipitate the pure acid) and set aside overnight, after which the precipitate was filtered off, washed as before with ethanol-ether, and dried on a vacuum hot-plate at 70° over P₂O₅. The yield was 13% and the m. p. 180° (decomp.) (Found: C, 59.2; H, 4.5; N, 3.5. C₁₉H₁₆O₈N requires C, 59.2; H, 3.9; N, 3.7%).

The other compounds were prepared similarly, except that for the derivative from 1:2:7-trihydroxyanthraquinone a reaction time of ca. 3 hr. was preferable.

1:2:5-Trihydroxyanthraquinon-3-ylmethylamine-NN-diacetic acid (Found: C, 57.1; H, 3.7; N, 3.5. C₁₉H₁₆O₉N requires C, 56.9; H, 3.7; N, 3.5%) had m. p. 203° (decomp.).

1:2:6-Trihydroxyanthraquinon-3-ylmethylamine-NN-diacetic acid (Found: C, 56.9; H, 3.75; N, 3.7%) had m. p. 200° (decomp.).

1:2:7-Trihydroxy- (Found: C, 54.4, H, 4.1; N, 3.6%), decomp. 184°, and 1:2:5:8-tetrahydroxy-anthraquinon-3-ylmethylamine-NN-diacetic acid (Found: C, 56.8; H, 3.75; N, 3.5. Calc. for C₁₉H₁₆O₁₀N: C, 54.6; H, 3.6; N, 3.4%), m. p. indefinite, were also prepared but were difficult to purify; since they had no unusual indicator properties, further purification was not attempted.

Reagents Required.—0.02M-EDTA solution. This was prepared by dissolving disodium ethylenediaminetetra-acetate dihydrate (7.45 g.) in distilled water (1 l.) and standardised both against a standard calcium solution (prepared from calcium carbonate) with murexide as indicator, and against a standard magnesium solution (prepared from pure magnesium) with Solochrome Black T as indicator.

0.01M-Cobalt solution. This was prepared from "AnalaR" cobalt sulphate and standardised against EDTA solution at pH 8 with Catechol Violet as indicator.

0.02M-Zinc and lead solutions. These were prepared from "AnalaR" lead nitrate and zinc sulphate severally and standardised against EDTA solution at pH 10 with Solochrome Black T as indicator.

0.02M-Indium solution. This was prepared by dissolving metallic indium (2.3 g.) in a two-fold excess of concentrated hydrochloric acid and diluting to 1 l. It was standardised by addition of an excess of 0.02M-EDTA and back-titration at pH 10, with a manganese solution at pH 10 (Solochrome Black T indicator).

Indicator solutions. 0.5% Solutions of the 3-di(carboxymethyl)aminomethyl derivatives of 1:2-di- and 1:2:5-tri-hydroxyanthraquinone were prepared by adding two drops of concentrated ammonia to the powder, followed by 7–8 drops of 20% ammonium acetate solution and dilution to the requisite volume.

Xylene Cyanol FF. This was a 0.1% solution in water.

Buffer solutions. (i) pH 4.3. Sodium acetate trihydrate (105 g.) and glacial acetic acid (100 ml.) were diluted to 1 l. with distilled water. (ii) pH 4–4.1. Sodium acetate trihydrate (70 g.) and glacial acetic acid (120 ml.) were diluted to 1 l. with distilled water.

Titration of Lead and Zinc.—25 ml. of either solution were treated with 3 ml. of pH 4.3 buffer (3 ml.) and a solution of acid (A) (5 drops), and titrated with 0.02M-EDTA to the red through pink to pure yellow end-point. The equivalence point coincides with the disappearance of the last trace of pink. The red to green end-point of the screened indicator is obtained as above, but with the addition of 2–3 drops of 0.1% Xylene Cyanol FF solution.

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Titration of Cobalt and Indium.—25 ml. of 0.01M-cobalt sulphate or of 0.02M-indium solution was treated with a solution of acid (A) (5 drops), 0.1% solution of Xylene Cyanol FF (3 drops), and buffer of pH 4—4.1 (3 ml.), heated to 80°, and titrated with 0.02M-EDTA to the red through grey to green end-point. Because of the colour of the cobalt-EDTA complex the maximum permissible concentration limit is *ca.* 21 mg. of Co^{2+} per 100 ml. Because of this colour, the normal bright green of the screened end-point is replaced by a dull green shade in cobalt titrations.

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