

MODIFIED METHYL-ORANGE INDICATOR IN TITRATING PHOSPHORIC ACID AND PHOSPHATES.*

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In a paper on "Methyl-orange as an Indicator in Presence of Indigo-carmin" presented this year to the Pennsylvania Pharmaceutical Association attention was called to this combination indicator in which the various shades of yellow to red given by methyl-orange are changed by the addition of indigo-carmin to green in alkaline solution and to violet or purplish in acid solution and giving at one stage a "neutral tint" in which neither green nor violet can be seen.

This paper contains the literature of this modified indicator and mentions various acid and alkaline substances which gave sharp and uniform color changes. In the discussion which followed the reading of the paper the question was raised as to the value of the indicator in titrating phosphoric acid; the answer given was that for the same solution sharp and uniform end reactions were obtainable but that comparison with other methods had not been made.

The modified indicator used for the determinations in this paper was made by dissolving 0.1 Gm. methyl-orange and 0.3 Gm. indigo-carmin in 100 Cc. water; after several months' standing the end-reactions were found to be less distinct, so this led to the use of separate solutions of the two substances preserving, however, the strength stated. Alkaline hydroxides were found to cause decomposition of the indigo-carmin, the end-reaction then being due to the methyl-orange alone; for this reason it is best to run the alkaline hydroxide solutions into acid solutions. Phosphoric acid titrated in presence of excess of calcium chloride or of lead nitrate also gave end-reactions due to the methyl-orange alone, the indigo-carmin being precipitated with the insoluble phosphates. In titrating phosphoric acid in presence of excess silver nitrate the latter apparently oxidized the indigo-carmin and more slowly in some way changed the methyl-orange so that a colorless supernatant liquid resulted.

Two methods of using the modified indicators will be mentioned: (1) Add to two portions of 100 Cc. water, four drops of the modified indicator (or four drops of each solution if they be kept separately; delivered from a one Cc. pipette the four drops are practically equal to 0.2 Cc.) and then add to the green or greenish yellow solution just enough of a weak acid volumetric solution to discharge this color without producing a violet or red color (should either of the latter colors show add enough of a dilute alkali volumetric solution to discharge it). The object is to produce a "neutral tint" showing neither alkalinity nor acidity; disregard the quantities of volumetric solutions necessary to accomplish this.

Reserve one of these solutions and to the other add the substance to be titrated (a violet or purplish color indicates an acid substance, a yellow or green color an alkaline substance); titrate with an alkaline or acid volumetric solution, as the case may require, until the color matches that of the reserved portion.

It is next possible to add to the reserved solution another portion of the substance to be titrated and check this against the previously titrated solution. (2) Use 10 Cc. water, add one drop of the indicator and proceed as above; in this case the neutral tint gives practically a colorless solution.

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The following determinations are arranged in series, the equivalents of the volumetric solutions being given in tabular form:

- 100 Cc. H_2O , or other specified liquid, treated according to method (1).
 1 Cc. $NaOH$ V. S. = 0.05303345 Gm. $NaOH$
 = 0.12997925 Gm. H_3PO_4 in H_2O or $NaCl$ solution
 = 0.06498962 Gm. H_3PO_4 in presence of $CaCl_2$ solution
 1 Cc. HCl V. S. = 0.04713283 Gm. HCl
 = 0.18358078 Gm. Na_2HPO_4 in H_2O or $NaCl$ solution

H_3PO_4 .40.631 Gm. (a) diluted to 100 Cc.

- 10 Cc. with H_2O required 26.5 Cc. $NaOH$ V. S. = 84.76%
 10 Cc. with H_2O required 26.5 Cc. $NaOH$ V. S. = 84.76%
 10 Cc. with $CaCl_2$ (10%) required 53 Cc. $NaOH$ V. S. = 84.76%
 10 Cc. with $CaCl_2$ (10%) required 53 Cc. $NaOH$ V. S. = 84.76%

In these $CaCl_2$ experiments no precipitate was produced until after the addition of the $NaOH$ V. S.; the precipitate redissolved in stirring until 26 Cc. had been added, after which the precipitate increased with every drop of $NaOH$; the final color obtained was yellow, the indigo-carmin being precipitated.

41.7201 Gm. (a) diluted to 100 Cc.

- 10 Cc. with H_2O required 27.2 Cc. $NaOH$ V. S. = 84.74%
 10 Cc. with H_2O required 27.2 Cc. $NaOH$ V. S. = 84.74%
 10 Cc. with $NaCl$ (10%) required 27.7 Cc. $NaOH$ V. S. = 86.29%
 10 Cc. with $NaCl$ (10%) required 27.7 Cc. $NaOH$ V. S. = 86.29%

Na_2HPO_4 dried (Moisture?).

- 2.4328 Gm. with H_2O required 12.35 Cc. HCl V. S. = 93.19%
 2.2724 Gm. with H_2O required 11.5 Cc. HCl V. S. = 92.90%
 2.1618 Gm. with H_2O required 10.95 Cc. HCl V. S. = 92.99%
 2.0120 Gm. with H_2O required 10.35 Cc. HCl V. S. = 94.43%
 1.2626 Gm. with $NaCl$ (10%) required 6.3 Cc. HCl V. S. = 91.60%

The sample apparently was not uniform so a portion was then thoroughly mixed:

- 2.3660 Gm. with H_2O required 12.15 Cc. HCl V. S. = 94.27%
 1.9336 Gm. with $NaCl$ (10%) required 9.7 Cc. HCl V. S. = 92.09%

The experiments show that presence of $NaCl$ gives an increased percentage of H_3PO_4 and a decreased percentage of Na_2HPO_4 .

SERIES B. Comparing methods (1) and (2).

- 1 Cc. HNO_3 V. S. = 0.03149945 Gm. HNO_3
 = 0.07100123 Gm. Na_2HPO_4

Na_2HPO_4 dried (5.92% H_2O) 4 Gm. per 100 Cc.

- adding 10 Cc. of Na_2HPO_4 solution to neutralized mixtures containing
 10 Cc. H_2O with 1 drop modified indicator required 5.3 Cc. HNO_3 V. S.
 10 Cc. H_2O with 2 drops modified indicator required 5.3 Cc. HNO_3 V. S.
 100 Cc. H_2O with 4 drops modified indicator required 5.3 Cc. HNO_3 V. S.

adding 20 Cc. of Na_2HPO_4 solution to neutralized mixture containing 100 Cc. H_2O with 4 drops of modified indicator required 10.6 Cc. HNO_3 V. S. showing 94.07% Na_2HPO_4 in each of the four titrations.

SERIES C.

100 Cc. H_2O , or other specified solution, treated according to method (1).

- 1 Cc. $NaOH$ V. S. = 0.02019829 Gm. $NaOH$
 = 0.04950373 Gm. H_3PO_4 in presence of H_2O
 = 0.01850124 Gm. H_3PO_4 in presence of $AgNO_3$
 1 Cc. HNO_3 V. S. = 0.03149945 Gm. HNO_3
 = 0.07100123 Gm. Na_2HPO_4
 = 0.10454001 Gm. $NaNH_4HPO_4 \cdot 4H_2O$
 = 0.06604289 Gm. $(NH_4)_2HPO_4$
 = 0.01633786 Gm. H_3PO_4 in presence of $AgNO_3$

Na_2HPO_4 dried (contains 5.92% H_2O).

- 1.0346 Gm. with H_2O required 13.7 Cc. HNO_3 V. S. = 94.02%
- 1.1490 Gm. with H_2O required 15.2 Cc. HNO_3 V. S. = 93.93%
- 1.0056 Gm. with H_2O required 13.3 Cc. HNO_3 V. S. = 93.90%
- 0.9668 Gm. with H_2O required 12.8 Cc. HNO_3 V. S. = 94.00%

$\text{NaNH}_4\text{HPO}_4 \cdot 4\text{H}_2\text{O}$.

a, sample frequently used for Bead Tests; *b*, laboratory stock bottle; *c*, cabinet specimen.

- 1.1348 Gm. (*a*) with H_2O required 10.25 Cc. HNO_3 V. S. = 94.42%
- 1.0362 Gm. (*a*) with H_2O required 9.35 Cc. HNO_3 V. S. = 94.33%
- 1.0500 Gm. (*b*) with H_2O required 10.00 Cc. HNO_3 V. S. = 99.56%
- 1.0404 Gm. (*b*) with H_2O required 9.90 Cc. HNO_3 V. S. = 99.47%
- 1.0876 Gm. (*c*) with H_2O required 10.20 Cc. HNO_3 V. S. = 98.04%
- 2.1130 Gm. (*c*) with H_2O required 19.85 Cc. HNO_3 V. S. = 98.21%

$(\text{NH}_4)_2\text{HPO}_4$.

a, sample kept on top shelf of laboratory; *b*, sample from basement stock; *c*, same as (*b*) but sample thoroughly mixed.

- 1.3578 Gm. (*a*) with H_2O required 18.85 Cc. HNO_3 V. S. = 91.69%
- 1.6356 Gm. (*a*) with H_2O required 22.70 Cc. HNO_3 V. S. = 91.60%
- 1.8734 Gm. (*b*) with H_2O required 23.70 Cc. HNO_3 V. S. = 83.55%
- 1.3504 Gm. (*b*) with H_2O required 17.80 Cc. HNO_3 V. S. = 87.05%
- 1.4410 Gm. (*c*) with H_2O required 18.00 Cc. HNO_3 V. S. = 82.50%
- 1.5016 Gm. (*c*) with H_2O required 18.70 Cc. HNO_3 V. S. = 82.24%

All of these samples with phenolphthalein indicator required considerable NaOH V. S. to produce a pink tint.

$\text{NH}_4\text{H}_2\text{PO}_4$.

- 3.3616 Gm. with H_2O required 0.70 Cc. HNO_3 V. S. = 1.38% as $(\text{NH}_4)_2\text{HPO}_4$.

The alkalinity of this sample towards the modified indicator may explain the different results in titrating Na_2HPO_4 in aqueous and NaCl solutions.

H_3PO_4 . 35.5824 Gm. (*b*) diluted to 100 Cc.

- 10 Cc. with H_2O required 60.6 Cc. NaOH V. S. = 84.31%
- 10 Cc. with H_2O required 60.6 Cc. NaOH V. S. = 84.31%

H_3PO_4 .

- 1.0742 Gm. (*c*) with H_2O required 18.40 Cc. NaOH V. S. = 84.79%
- 1.1370 Gm. (*c*) with H_2O required 19.45 Cc. NaOH V. S. = 84.31%
- 0.6106 Gm. (*c*) with 100 Cc. AgNO_3 (3%) required 31.9 Cc. NaOH V. S. = 86.21%

The solution was clear until NaOH V. S. was added when the brown Ag_2O almost immediately changed into yellow Ag_3PO_4 ; as the precipitate became bulkier it promptly settled so that the supernatant liquid could in large part be transferred to another beaker and the titration continued; as the precipitate increased the mixture was transferred back to the original beaker, thoroughly stirred, the liquid decanted and titration continued until finally one drop NaOH produced a brown coloration not changing to yellow upon mixing with more of the supernatant liquid from the original beaker. The indigo-carmine color entirely disappeared in the early stages of the titration while the red color of the methyl-orange more slowly disappeared; on adding a drop of this indicator from time to time an acid reaction could be verified. This was the pioneer experiment with AgNO_3 .

- 0.4106 Gm. (*c*) with 100 Cc. AgNO_3 (2.5%) and four drops methyl-orange required 21.3 Cc. NaOH V. S. = 85.35%

- 0.3962 Gm. (*c*) as preceding required 20.5 Cc. NaOH V. S. = 85.38%

- 0.4258 Gm. (*c*) as preceding but adding one drop methyl-orange indicator at intervals required 22.1 Cc. NaOH V. S. = 85.64%

- 0.4270 Gm. (*c*) with 100 Cc. AgNO_3 (2.5%) to which had been added a few drops NaOH V. S. and the Ag_2O removed by straining through cotton required, without indicator, 22.2 Cc. NaOH V. S. = 85.79%

SERIES D. Titrations in the three previous series show concordant results for uniform material and for the same methods. The results of titration in H_2O or $NaCl$ solution and in presence of $AgNO_3$ seemed worthy of further experimentation.

- 1 Cc. $NaOH$ V. S. = 0.02462267 Gm. $NaOH$
 = 0.06034740 Gm. H_3PO_4 in presence of H_2O or $NaCl$ solution
 = 0.02011580 Gm. H_3PO_4 in presence of $AgNO_3$
 = 0.08741942 Gm. Na_2HPO_4 in presence of $AgNO_3$
 1 Cc. HNO_3 V. S. = 0.03141450 Gm. HNO_3
 = 0.07080973 Gm. Na_2HPO_4

Na_2HPO_4 (dried at 110–115° C.).

- 1.0718 Gm. with 20 Cc. H_2O and two drops modified indicator required 15.2 Cc. HNO_3
 V. S. = 100.42%
 0.8008 Gm. with 50 Cc. H_2O and 4 drops modified indicator required 11.35 Cc. HNO_3
 V. S. = 100.37%

After adding HNO_3 V. S. to total 15 Cc. 60 Cc. $AgNO_3$ (5%) were added and titrated with $NaOH$ V. S. to brown coloration in supernatant liquid; 21.3 Cc. $NaOH$ V. S. required less 12.15 Cc. for the 15 Cc. HNO_3 V. S. gives 9.15 Cc. $NaOH$ V. S. = 99.63%

- 0.903 Gm. with 20 Cc. H_2O and 85 Cc. $AgNO_3$ (5%) required 10.3 $NaOH$ V. S. = 99.71%
 0.4522 Gm. with 50 Cc. $NaCl$ (5%) and 2 drops modified indicator required 6.3 Cc. HNO_3
 V. S. = 98.65%
 1.3688 Gm. with 100 Cc. $NaCl$ (10%) and 4 drops modified indicator required 19 Cc. HNO_3
 V. S. = 98.29%

H_3PO_4 . 15.705 Gm. (d) per 100 Cc. 10 Cc. used for each of the following:
 with 100 Cc. H_2O and 4 drops modified indicator required 21.90 Cc.

$NaOH$ V. S. = 84.17%

with 100 Cc. $NaCl$ (5%) and 4 drops modified indicator required 22.10 Cc.

$NaOH$ V. S. = 84.92%

with 100 Cc. $NaCl$ (10%) and 4 drops modified indicator required 22.35 Cc.

$NaOH$ V. S. = 85.88%

with 150 Cc. $AgNO_3$ (5%), no indicator, required 67.2 Cc. $NaOH$ V. S. = 85.44%

In some other experiments an effort was made to replace the silver nitrate by the cheaper lead nitrate but the results were so discordant that they are not recorded; it had been hoped that the greater insolubility of the lead phosphate would make this an ideal method but the precipitation of the indigo-carmin and the absence of a colored precipitate with excess of $NaOH$ made one entirely dependent upon change in color of the methyl-orange.

From the results in Series D it seems likely that, with the aid of this modified indicator and in presence of sodium chloride, a method will be found for directly titrating phosphoric acid and sodium phosphate; the necessary quantity of sodium chloride will be found to differ for these two substances.

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THE BIOLOGIC STANDARDIZATION OF LOCAL ANAESTHETICS.*

With reference to the Effects of Sterilization on Solutions of Cocaine and Procaine.

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One of the most important duties of the Control Department of a large pharmaceutical manufacturing house is to carefully investigate all complaints received. This is especially true in cases where the physician claims the preparation does not

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