[Contribution from the Laboratory of Organic Chemistry, Department of Pharmacology, Hahnemann Medical College]

STUDIES ON ENOL TITRATION. I.[1]

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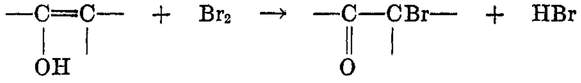
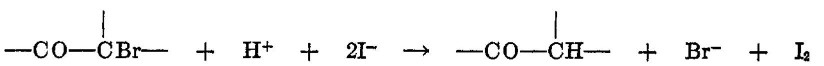
Received October 23, 1953

In its original form (1) the Kurt Meyer titration consisted of titrating the enol content of a ketone directly with a standard bromine solution according to Equation I:



$$-\underset{\substack{|\\ \mathrm{OH}}}{\mathrm{C}}=\underset{|}{\mathrm{C}}- \;+\; \mathrm{Br_2} \rightarrow -\underset{\substack{\|\\ \mathrm{O}}}{\mathrm{C}}-\underset{|}{\mathrm{C}}\mathrm{Br}- \;+\; \mathrm{HBr} \qquad \text{I.}$$

taking for an end point either the appearance of a permanent yellow color from excess bromine or the disappearance of the red color given by enols with ferric ion. Later (2) Meyer preferred to titrate indirectly by adding excess bromine to the tautomeric mixture. In one modification the addition of iodide ion replaces the excess bromine by an equivalent amount of iodine which can be titrated with thiosulfate; in another the excess bromine is destroyed by the addition of some phenol such as α-naphthol, and the bromoketone formed from the enol and bromine is reduced according to Equation II:



$$-\mathrm{CO}-\overset{|}{\mathrm{C}}\mathrm{Br}- \;+\; \mathrm{H^+} \;+\; 2\mathrm{I^-} \rightarrow -\mathrm{CO}-\overset{|}{\mathrm{C}}\mathrm{H}- \;+\; \mathrm{Br^-} \;+\; \mathrm{I_2} \qquad \text{II.}$$

In this case one mole of iodine is liberated for each mole of enol originally present.

While Kurt Meyer preferred this indirect titration, Auwers and Jacobsen (3) criticized his preference and considered results of the direct method to be more reliable. Later Cooper and Barnes (4) improved the indirect method by using diisobutylene instead of α-naphthol and obtained better reproducibility than did Meyer.

Finally, in a modification by Schwarzenbach (5) the enol content is determined by running a ketone solution of known concentration, and a bromine solution of steadily increasing concentration, at controlled rates through a reaction vessel and determining potentiometrically the moment at which excess bromine appears. Simultaneously, the bromine solution is analyzed to determine its content at that moment, thus establishing the amount of bromine equivalent to the enol present in the ketone.

Recently (6) in experiments on a simple olefin, this writer found that mixed halogens, being polar, add more rapidly than the nonpolar bromine, and never cause substitution, which is not true of bromine, Meyer's statement to the contrary notwithstanding. Since speed of addition is essential in order to obtain accurate information on the enol content, it was thought worthwhile to use iodine monochloride—the most polar halogen available—rather than bromine in the Kurt Meyer titration. This, as briefly announced (7), proved feasible. As a

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[1] Presented before the Analytical Division at the 123rd Meeting of the American Chemical Society, Los Angeles, March 1953.

TABLE I

TITRATION WITH ICl

KETONE	ENOL CONTENT, %
Ethyl acetoacetate	13.2
Ethyl benzoylacetate	18.5
Acetylacetone	79.7
Camphor	0.123
Acetone	1.5×10^{-4}

further improvement, an attempt was made to hold down the rate of formation of new enol by eliminating the halogen acid formed according to Equation I. This aim was accomplished by the judicious use of sodium bicarbonate (see experimental part).

Several 1,3-diketones and two simple ketones, camphor and acetone, were titrated by this method. Table I shows the enol contents found.

These results are fairly close to those found in the literature for the same compounds; generally they are rather lower, indicating that previous workers may have been plagued by substitution or acid-catalyzed rearrangement more than they realized. Thus Schwarzenbach (5) found that acetone contains 2.5×10^{-4} % enol, almost twice as much as found here. The values for acetylacetone and ethyl benzoylacetate are well in line with those found by Conant and Thompson (8) and Dieckmann (9), respectively, although Dieckmann, too, observed a slightly higher value. The enol content of camphor does not seem to have been determined previously, but the value of 0.123% is reasonably similar to 0.48% found by Schwarzenbach and Wittwer (10) for cyclopentanone. For ethyl acetoacetate, however, the best-studied of all ketones, this writer finds a value considerably higher than that of K. H. Meyer (1), 6.87%. Apparently bromine addition is noticeably slower in this instance than is the addition of ICl, leading to false results.

The writer has also attempted to find evidence for the existence of vinyl alcohol by applying his method to acetaldehyde. No measurable halogen absorption was detected. In view of the amounts used and of the sensitivity of the method (see below) it can be concluded that the enol content of acetaldehyde, if any, is less than one part in ten million.

EXPERIMENTAL

An amount of ketone known from orienting experiments to contain roughly $\frac{1}{10}$ millimole of enol was mixed with $\frac{1}{10}$ millimole of dry $NaHCO_3$ and 0.1 ml. of a 2.5 *N* solution of ICl in methanol. Immediately after thorough mixing, excess iodide ion was added in the form of 2–3 ml. of a 15% aqueous NaI solution and the liberated iodine was titrated with 0.1 *N* thiosulfate solution.

Methanol as a solvent for the iodine monochloride proved desirable for several reasons: it dissolves both ICl and ketones; it is polar, hence promotes the polar addition reaction; it is miscible with water; and, in contrast to methanol solutions of bromine, solutions of ICl in methanol are quite stable and maintain their titer for a long time.

The addition of sodium bicarbonate has a double purpose; it neutralizes the HCl formed according to Equation I and thus prevents catalysis which would generate new enol, and it keeps up the *p*H of the aqueous solution in which the titration with thiosulfate is carried out. This is quite important: because ICl is more polar than Br_2 it reacts more readily with water and formation of hypoiodite is noticeable even at *p*H 7. On the other hand, at *p*H 5–6 the iodoketone is reduced according to Equation II. It was found that at just below *p*H 7, which was achieved by using the indicated amount of bicarbonate, both the formation of hypoiodite and the reduction of the iodoketone were slow enough to allow more than half a minute to complete the titration.

Camphor, being solid, was moistened with just enough methanol to liquefy it, then bicarbonate and ICl were added and the whole was titrated as usual. In the case of acetone 20 g. were used with the standard amount (0.1 ml.) of ICl solution. This raised the question whether such a large volume of acetone did not dilute the ICl so much that the rate of addition might be lowered sufficiently for the tautomeric rearrangement to interfere with results. In order to decide this question, the determination was repeated using 0.5 ml. of ICl solution. This increase in concentration of ICl should make a noticeable difference in the results if these were too low at first due to dilution. No such difference was observed, however; the enol content of acetone was found to be the same within experimental error, that is, divergences between results were not greater than of the order of 10^{-6} mole.

In the case of acetaldehyde the amount of carbonyl compound titrated was raised to 400 g.; the results were, as stated earlier, entirely negative.

SUMMARY

The Kurt Meyer titration has been improved by the use of the most polar halogen available (iodine monochloride) instead of Kurt Meyer's bromine (to speed up the reaction), and by neutralizing the acid formed in the addition, to eliminate a catalyst which would regenerate enol. The results thus obtained it may be hoped are more representative of the true equilibrium mixture.

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