This assumption is without theoretical basis, and could only be justified by appeal to experiment. As we have seen, the experimental results do not support it.

Further consideration of Spencer and Boyer's data will even lend support to the conclusion which we reached above, namely, that k' is *not* affected by molecular weight distribution. For each mixture in Table IV take $[\eta]$ equal to the calculated value of η_{sp}/c for $c = 0$, and take $k = k'/2.303$, where k' is the value given in parentheses in the calculated column of Table IV. (These values of k' are average values for the *components* of the mixtures.) Using these values for $[\eta]$ and k, calculate values of η_{sp}/c for each concentration, using equation (5). The results of this procedure are shown in the last column of Table IV, and it is apparent that the values of η_{sp}/c so calculated are in good agreement with those observed by Spencer and Boyer. Statistical analysis shows that the chance that the difference between Spencer and Boyer's values of η_{sp}/c calculated and η_{sp}/c observed is due to random variation is less than 1%, while the same chance for the difference between η_{sp}/c observed and η_{sp}/c calculated from equation (5) as described above is greater than 14%. This means that both the fractions and mixtures thereof most probably obey equation (5) with the same value of k, and must therefore have the same value of k'.

Summary

Original data for cellulose nitrate and data from the literature for cellulose nitrate and polystyrene have been analyzed to show that the slope constant (k or k') in various equations connecting solution viscosity and concentration is a characteristic constant for a given solute–solvent system, and, in particular, is not appreciably affected by the molecular weight distribution of the solute. Cases in which high values of the slope constant are obtained for cellulose nitrate and cellulose acetate can reasonably be attributed to variation in the chemical nature of samples, which are in all cases examined either unfractionated materials, head fractions, or fractions of very low molecular weight.

WILMINGTON, DELAWARE RECEIVED FEBRUARY 3, 1947

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, REICHHOLD CHEMICALS, INC.]

The Esterification Rate of Dibasic Acid Anhydrides with Primary Alcohols at Room Temperature

BY ERNEST F. SIEGEL AND MARGUERITE K. MORAN

In the course of some work carried out with dibasic acid anhydrides it was found that they titrate only half of the expected titer of the dibasic acids when the anhydrides were dissolved in ethanol in the cold. The only plausible explanation for this was that the anhydride formed a half ester leaving only one carboxyl group for titration.

The esterification of dibasic acid anhydrides with polyhydric alcohols has been investigated thoroughly in the past, particularly in reference to the formation of alkyd resins. In this study dibasic acid anhydrides were esterified with polyhydric alcohols at temperatures far above 100°.[1] It was stated that the acidity dropped to half its original value within a matter of minutes and assumed that the acid ester was formed. The literature references[2] concerning the reaction of dibasic acid anhydrides and monohydric alcohols show that the esterification was carried out also at higher temperatures and claim that it could be speeded up by the addition of potassium cyanide as a catalyst. No mention is made anywhere in literature that the esterification of dibasic acid anhydrides proceeds at room temperature.

Incited by our preliminary finding mentioned above, the reaction of phthalic anhydride and maleic anhydride with several primary mono- and polyhydric alochols at room temperature (20–25°) was studied. It was found that the monoester formation was instantaneous and quantitative and its rate almost comparable with that of an ionic reaction, *e. g.*, between an inorganic base and an inorganic acid. The esterification rate is rapid for all primary alcohols under investigation, so rapid as to make a comparison of rates or of the effect of chain length or the functionality of the alcohols impossible. Maleic anhydride reacts as readily with primary *n*-amyl alcohol or ethylene glycol as with methanol. The rapidity of the esterification is not decreased when carried out in presence of an inert diluent. The amount of excess alcohol is of no importance since a 1:1 molecular ratio of alcohol to anhydride gives the same result as that of 2:1 or 4:1. Secondary alcohols, *e. g.*, *i*-propyl alcohol do not esterify at all under our chosen reaction conditions. Therefore no attempt was made to esterify tertiary alcohols.

This investigation found an interesting application in testing the rearrangement of fumaric acid to maleic anhydride in the presence of rosin which

(1) Kienle and Hovey, THIS JOURNAL, **51**, 509 (1929); **52**, 3636 (1930); Kienle, Vander Meulen and Petke, *ibid.*, **61**, 2258 (1939); **61**, 2268 (1939); Kienle and Petke, *ibid.*, **62**, 1053 (1940); Savard and Diner, *Bull. Soc. Chim.*, **51**, 597 (1932); Hirano and Ohashi, *J. Soc. Chem. Ind., Japan*, **41**, Suppl. binding 90 (1938).

(2) Shields, *J. Chem. Soc.*, **59**, 740 (1891); Walker, *ibid.*, **61**, 710, 711 (1892); *Beilstein*, **9**, 797; Sudborough, Roberts, *J. Chem. Soc.*, **87**, 1844 (1905); Goggins and Copenhaver, THIS JOURNAL, **61**, 2909 (1939).

TABLE I

MALEIC ANHYDRIDE

Alcohol	Moles alcohol: anhydride	Percentage of original theoretical titer 1 min.	10 min.	1/2 hr.	1 hr.	1 1/2 hr.	3 hr.	4 1/2 hr.
Methyl[a]	Large excess of alc.	50.0						
Methyl	2:1	49.9	49.6	49.9				51.0
Ethyl	2:1	50.7	50.9	51.4				
Propyl	2:1	45.8	45.0	46.4			46.0	
i-Propyl	2:1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Butyl	2:1	49.0	..	48.8				
Butyl	4:1	52.7	52.7	50.6				
Amyl	2:1	52.8	52.9	52.5	51.5			
Ethylene glycol	2:1	48.3	..	50.4				

[a] Without acetone as solvent to prove that acetone is really inert. In the case of *n*-propyl alcohol, no explanation can be found for the incomplete mono-esterification. All other alcohols followed a consistent pattern.

will be described in more detail in a separate paper. The formation of maleic anhydride could be followed up and proven by the drop in acidity in an alcoholic medium. A mixture of one mole of rosin (based on its carboxyl group) and 0.8 mole of fumaric acid with a total combined acidity of 100% at the start was expected to assume an acidity of only 69.3% when all fumaric acid was converted into maleic anhydride or its adduct. All titrations were carried out in alcoholic medium. The lowest actual acidity obtained was 70.5% which proves that 96% fumaric acid was rearranged to maleic anhydride. It is interesting to note that even complex dibasic acid anhydrides like the rosin–maleic anhydride adduct follow the same pattern as the simple anhydrides with regard to instantaneous monoesterification with primary alcohols.

This reaction was also used as a method to analyze an unknown mixture of a dibasic acid and its anhydride. From the difference in titer between a titration in a non-alcoholic and an alcoholic medium the amount of each ingredient could be calculated. The difference is due to and corresponds to the amount of anhydride present in the mixture which forms immediately the monoester in alcoholic medium and thus gives a lower titer than the non-alcoholic titration. Below is the formula for calculating the mole per cent. of anhydride in a mixture of a dibasic acid and its anhydride:

$$\text{Mole \% anhydride} = 2(A - B)/A \times 100$$

where A = cc. of 0.1 N aqueous KOH
B = cc. of 0.1 N alcoholic KOH

It was also attempted to apply this method to determine acid anhydride together with free acid in the presence of esters but this failed. The accuracy of the titration in non-alcoholic medium is not satisfactory in this case due to the fact that some hydrolysis of the esters takes place on titrating with aqueous alkali and thus the neutralization point is vague. Since unfortunately there is no suitable solvent for alkali besides water and alcohols the method could not be applied in this case.

Experimental

The following materials were used in our experimental work: phthalic anhydride, C. P. (Fisher); maleic anhydride, distilled from a commercial product; and acetone, C. P.

All alcohols employed were C. P. grade except amyl alcohol. The only amyl alcohol available was a practical grade.

The anhydride was dissolved in acetone in a three-necked flask equipped with a thermometer, an agitator and an addition funnel. In order to study the rate of esterification at room temperature (25°), it was necessary to use an inert solvent to ensure a complete solution of anhydride and alcohol initially. The solvent was acetone, but the ratio of acetone to anhydride had to be changed for the two anhydrides. One part acetone and one part maleic anhydride by weight was used, while five parts acetone to one part phthalic anhydride was necessary based on the difference in acetone solubility of the two anhydrides. The mixture of acetone and anhydride was warmed to 25° at which temperature the alcohol, also held at 25°, was added rapidly from the addition funnel. Samples were analyzed at one-, ten- and thirty-minute intervals, and in some cases, even after five hours. The system was closed to prevent any loss of volatile matter.

In order to prevent the possibility of the titration solution acting as an esterifying reagent, we used approximately 0.1 N solutions of potassium hydroxide dissolved in the same alcohol as was used as the reactant alcohol with the anhydride. A sample taken at regular intervals from the reaction mixture was dissolved in acetone and titrated with the corresponding potassium hydroxide–alcohol solution. Phenolphthalein was used as indicator. In calculating the titration results, the slight acidity of acetone and the different alcohols was accounted for. Tables I and II are based on our experimental data.

Since a mutual solvent for glycerol and the anhydrides could not be found, it was impossible to study the reaction at room temperature, although there is no reason to believe that it should not proceed as well as ethylene glycol.

TABLE II

PHTHALIC ANHYDRIDE

Alcohol	Moles Alcohol: anhydride	Percentage of original theoretical titer 1 min.	10 min.	1/2 hr.	1 hr.
Methyl	1:1	50.9	..	51.0	..
Methyl	2:1	50.0	49.7	50.3	50.3
Butyl	2:1	51.1	51.2	49.7	..
Ethylene glycol	2:1	50.6	..	50.8	..

NOTE.—A sample of phthalic acid was titrated in methanolic medium and found to consume the theoretical amount of 0.1 N potassium hydroxide.

Differential Titration Method. A mixture of 0.1 g. of maleic acid and 0.1 g. of maleic anhydride was analyzed by differential titration, and approximately 99% of the original maleic anhydride in the mixture was found. Acetone replaced alcohol as the indicator solvent in the aqueous titration to exclude even traces of alcohol.

Summary

1. Mono-esterification of dibasic acid anhydrides with primary mono- and polyhydric alcohols proceeds instantaneously and quantitatively at room temperature.

2. Even high molecular weight acid anhydrides, for example, rosin–maleic anhydride adduct, proceed readily to mono-esterification.

3. This work serves as the basis for the analytical determination method for dibasic acid anhydrides in a mixture with their acids. It can also serve to determine the rate of rearrangement of fumaric acid to maleic anhydride.

ELIZABETH, NEW JERSEY RECEIVED JANUARY 21, 1947

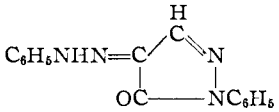
[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY]

The Action of Periodic Acid on Glucose Phenylosazone

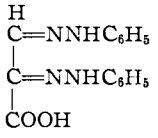
BY ERWIN CHARGAFF AND BORIS MAGASANIK

In the course of studies on the enzymatic dehydrogenation of stereoisomers of the inositol group,[1] which included the use of periodic acid as an analytical tool, it became desirable to examine the action of this oxidant on a phenylosazone of known structure, *viz.*, glucosazone.

The oxidation of this osazone by periodic acid in boiling 50% alcohol had already been studied some time ago.[2] Under the rather vigorous conditions used it had been shown to lead to the formation of 1-phenyl-4-phenylhydrazonopyrazolone-5 (I).[3] This compound was assumed to have been formed by dehydration from the original oxidation product, the 1,2-bisphenylhydrazone of mesoxalic acid semialdehyde (II).[4] But the production of II can hardly be reconciled with what is known at present of the behavior of periodic acid.[5] The oxidative cleavage of glucosazone by periodic acid was therefore studied in greater detail by procedures that had proved satisfactory in previous work in this Laboratory.[6]

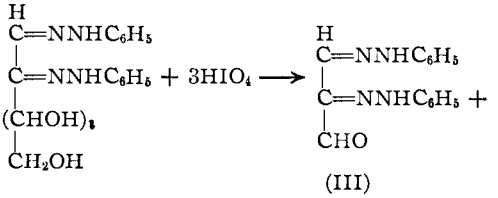


(I)



(II)

When glucose phenylosazone in 66% ethanol was treated with periodic acid *at room temperature* three moles of oxidant were consumed per mole of

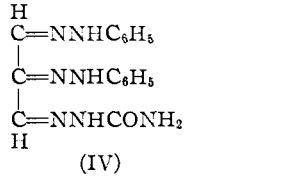


(III)

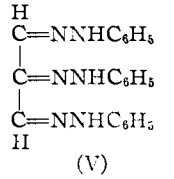
$$2HCOOH + HCHO + H_2O + 3HIO_3$$

osazone and a compound was isolated (yield 85%) whose analytical composition showed it to be the hitherto undescribed *1,2-bisphenylhydrazone of mesoxalaldehyde* (III). Under the experimental conditions employed here the oxidative action of periodic acid appeared, therefore, to proceed in the expected fashion.

Compound III was further characterized by its conversion to the corresponding semicarbazone (IV) and to the known trisphenylhydrazone[7] (V).



(IV)



(V)

The quantitative comparison of the experimental conditions leading, at room temperature, to the formation of the aldehyde III and at an elevated temperature to that of the pyrazolone I gave interesting results. In both cases three moles of periodic acid were consumed; but the titration of the total available oxidizing capacity (*i. e.*, of the sum of excess periodic and iodic acids in the reaction mixtures) with sodium thiosulfate in acidic solution indicated that in boiling alcohol one additional gram-atom of oxygen, derived from the iodic acid, had been used. The conclusion appeared justified that the aldehyde III, formed as the primary oxidation product in both sets of conditions, was further oxidized by the boiling iodic acid solution.

It remained to be shown whether the cyclization to the pyrazolone I proceeded *via* the acid II. When the aldehyde III was heated with iodic acid in 50% ethanol it was converted to I. That the production of the pyrazolone was not due to the dehydration, under acidic conditions, of II, formed as the primary oxidation product, could be shown in experiments in which the acid II was subjected to a similar treatment with 1 *N* hydrochloric acid in 50% ethanol. Under these conditions the unchanged compound II was recovered.

Even more convincing was the direct formation

(1) E. Chargaff and B. Magasanik, *J. Biol. Chem.*, **165**, 379 (1946).

(2) P. Karrer and K. Pfaehler, *Helv. Chim. Acta*, **17**, 766 (1934).

(3) L. Knorr, *Ber.*, **21**, 1201 (1888).

(4) O. Nastvogel, *Ann.*, **248**, 85 (1888).

(5) E. L. Jackson in R. Adams, "Organic Reactions," Vol. 2, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 341.

(6) D. B. Sprinson and E. Chargaff, *J. Biol. Chem.*, **164**, 433 (1946).

(7) H. v. Pechmann and K. Jenisch, *Ber.*, **24**, 3255 (1891).