the base from the lower rotating salt was roughly the calculated for an equimolecular mixture of apocupreine and a chlorine derivative of apocupreine such as hydrochloroapocupreine.

Anal. Calcd. for $C_{19}H_{22}O_2N_2$ + $C_{19}H_{23}O_2N_2Cl$: Cl, 5.1. Found: Cl, 6.1.

The base from the higher rotating salt contained about 1% chlorine. Pure chlorine-free α-apocupreine was eventually obtained from this material by extracting with acetone and discarding the acetone insoluble substance, specific rotation −215°. It gave a dihydrochloride of specific rotation −223°.[2]

The Preparation of α- and β-Apocupreines by the Sulfuric Acid Method.—A solution of 50 g. of dried U. S. P. quinine in 200 cc. of 60% sulfuric acid was boiled gently under a reflux condenser for five hours.[6] The crude base was obtained as previously described; yield 37 g.

On attempting to repeat the crystallization of apocupreine monohydrochloride as described by Jarzyński, Ludwiczakówna and Suszko[6] a yield of only 2 g. of salt of specific rotation −145° was obtained. The rest of the material separated repeatedly from water as a gum. However, the crystallization proceeded quite satisfactorily from alcohol as described below.

A solution of 30 g. of dried crude base in 95% alcohol was neutralized with the calculated quantity of aqueous concentrated hydrochloric acid. After evaporation to dryness the salt was ground with a little absolute alcohol, filtered, washed several times with small portions of absolute alcohol and dried; yield, 27 g.; specific rotation −159°. On recrystallization 23 g. of pure α-apocupreine monohydrochloride was obtained; specific rotation −163°.

In many subsequent experiments 100-g. batches of crude apocupreine yielded on one crystallization, monohydrochloride of rotation from −149 to −158°. This material on repeated recrystallization from alcohol yielded 18 g. to 24 g. of β-apocupreine monohydrochloride, specific rotation −145 to −147°; 6 g. to 23 g. of an intermediate fraction, specific rotation −154 to −155°; and 18 g. to 42 g. of α-apocupreine monohydrochloride, specific rotation −163 to −165°.

The bases prepared from α- and β-apocupreine salts had specific rotations −215 and −194°, respectively. Both melted with decomposition at 180 to 190°.

The acid sulfates were prepared by neutralization with the calculated quantity of sulfuric acid and purified by crystallization from alcohol. They had specific rotations of −224 and −208°, for the α- and β-salts, respectively.

Anal. Monohydrochlorides. Calcd. for $C_{19}H_{22}O_2N_2 \cdot HCl$: Cl, 10.2; N, 8.1. Found: Cl, α-salt, 10.2; β-salt, 10.2; intermediate fraction, 10.2. N, α-salt, 7.9; β-salt, 7.8; intermediate fraction 8.0. Dihydrochlorides. Calcd. for $C_{19}H_{22}O_2N_2 \cdot 2HCl$: Cl, 18.5; N, 7.3. Found: Cl, α-salt, 18.3; β-salt, 18.0. N, α-salt, 7.3; β-salt, 7.1. Acid sulfates. Calcd. for $C_{19}H_{22}O_2N_2 \cdot H_2SO_4$: S, 7.85. Found: S, α-salt, 7.8; β-salt, 7.8.

Summary

Evidence has been presented for the existence of apocupreine and its salts in two isomeric forms (possibly geometric). The two bases have been named α- and β-apocupreines. Some properties of these substances have been described.

PITTSBURGH, PENNA. RECEIVED MARCH 18, 1935

[CONTRIBUTION FROM THE SCHOOL OF ENGINEERING RESEARCH, UNIVERSITY OF TORONTO]

Studies of Some Hydrazone and Osazone Reactions

BY E. G. R. ARDAGH AND F. C. RUTHERFORD

Introductory

This research is a continuation, into the field of the sugars, of the investigation of the effect of hydrogen-ion concentration on the rates of formation of phenylhydrazones previously published.[1,2]

The velocity constant, k_1, for the reaction

$C_6H_5NHNH_2 + C_6H_{12}O_6 \rightleftharpoons C_6H_5NHN{:}C_6H_{12}O_5 + H_2O$

was determined, polarimetrically, for *d*-glucose, levulose and *d*-galactose under carefully controlled conditions of hydrogen-ion and buffer concentration, using phosphate and acetate buffers.

Experimental

The solutions polarized were made up from solutions of the sugar (Kahlbaum), freshly prepared water-white solutions of pure phenylhydrazine which had been filtered to remove any turbidity, and the indicated buffer solutions made up from stock solutions of either mono-, di- or tri-potassium phosphate with phosphoric acid or potassium acetate with acetic acid. The buffers were prepared from accurately weighed quantities of the salts, and the *p*H of each was determined by means of the quinhydrone electrode to ±0.05 unit. The temperature during each polarization was accurate to ±0.1° as read from a thermometer in the polarimeter tube.

The velocity constants were calculated using the bimolecular formula[3]

$$k_1 t = \frac{2.303}{c} \log \left(\frac{X + c}{X} \right) + C$$

(1) Ardagh and Williams, THIS JOURNAL, **47**, 2976, 2983 (1925).

(2) Ardagh, Kellam, Rutherford and Walstaff, *ibid.*, **54**, 721 (1932).

(3) Conant and Bartlett, *ibid.*, **54**, 2881 (1932).

in which X is the concentration of the sugar at time t, e is the excess of the phenylhydrazine concentration over that of the sugar, and C is the integration constant.

The initial concentration of the sugar for all determinations was 0.200 M, and of the base, 0.407 M, the buffer concentrations ranging from 0.06 to 0.38 M as specified.

TABLE I

COMPARISON OF k_1 VALUES FOR THE TWO BUFFERS: pH 6.00, BUFFERS 0.38 M

Sugar	Temp., °C.	Phosphate k_1	Phosphate % Max. dev.[a]	Acetate k_1	Acetate % Max. dev.[a]
d-Glucose	22.5	0.1093	4.45	0.00906	5.13
Levulose	22.5	.0486	4.33	.00385	[b]
d-Galactose	23.4	.6505	4.15	.0659	5.01

[a] Maximum deviation (%) of any one value from mean of run.

[b] k_1 only approximate, as only initial portion of the reaction course used due to darkening of polarized solution.

A series of k_1 determinations for *d*-galactose was performed under varying but known pH and buffer concentration values, using phosphate buffers only. The results are plotted as Fig. 1, each point thereon being the average of from six to ten k_1 values calculated during the velocity run.

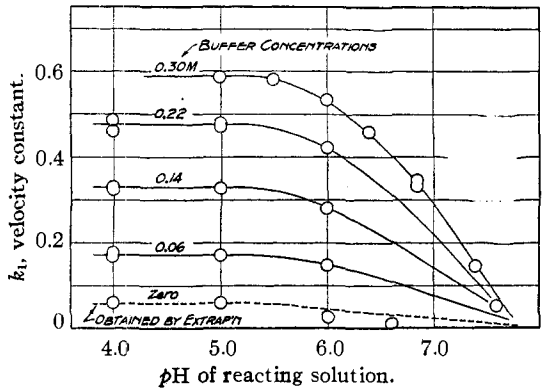

Fig. 1.—Effect of pH at various phosphate buffer concentrations on the rate of formation of *d*-galactose phenylhydrazone at 25°.

Figure 2 shows the variations of k_1 with the buffer concentration at constant pH values, the points indicated being taken from the data used in Fig. 1.

A qualitative comparison of the rates of formation of the corresponding osazones showed no parallelism with those of the hydrazones other than that the ten-fold superiority of the phosphate buffer over the acetate held. To this superiority of the phosphate buffer we wish to draw the attention of all those laboring with the task of preparing hydrazones and osazones.

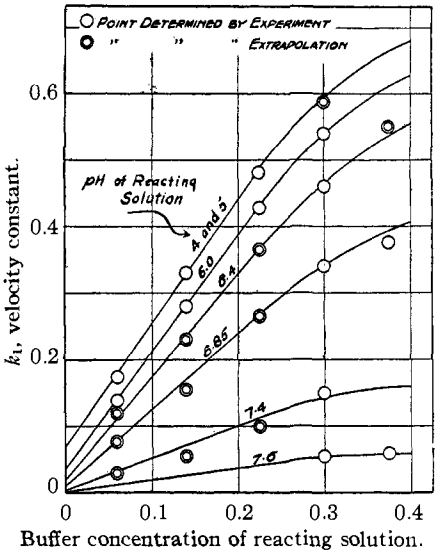

Fig. 2.—Effect of phosphate buffer concentration at various pH's on the rate of formation of *d*-galactose phenylhydrazone.

The specific rotation of *d*-glucose phenylhydrazone was determined as $[\alpha]^{22.5}D$ −52.55° (aqueous solution, 0.200 M). This is obviously the rotation of the equilibrated mixture of the α- and β-forms: no value was located in the literature for this mixture. For *d*-galactose phenylhydrazone $[\alpha]^{23.4}D$ was determined to be −24.21°, compared with the only reported figure located of $[\alpha]^{20}D$ −21.6°.[4] The above values should not be susceptible to any considerable error because they were determined in relatively high concentration in aqueous solution in which the hydrazone had been formed, rather than by dissolving a minute sample, which is difficult to isolate in the pure state, in pyridine or the like. No value for the levulose phenylhydrazone was obtained, since the solution became too dark to permit polarimeter readings before 100% conversion of the sugar was obtained, but the value used was $[\alpha]^{20}D$ −4.22°[5] which, from the constancy of the k_1 values obtained therewith would appear to be an accurate figure.

The temperature coefficient of the *d*-galactose phenylhydrazone reaction was determined from the integrated van't Hoff formula

$$\log \frac{k_2}{k_1} = A\left(\frac{1}{T_1} - \frac{1}{T_2}\right)$$

(4) Mackenzie and Ghosh, *Gazz. chim. ital.*, **36**, 204 (1906).

(5) Hofmann, *Ann.*, 366, 294 (1909).

At a *p*H of 6.00 and with buffer concentrations 0.30 and 0.38 *M*, *A* was found to be 3430 and 3190, respectively, at room temperature.

Discussion

As indicated in Fig. 1, at the *p*H of the free base (approximately 7.8 at the concentration of the experiments, 0.407 *M*) the *d*-galactose phenylhydrazone forms at a very low rate regardless of the buffer concentration. From this minimum value, at buffer concentration of 0.06 *M*, the velocity constant rapidly increases as the *p*H decreases (the hydrogen-ion concentration increases) until a *p*H in the neighborhood of 5.4 is reached, after which it remains constant with increasing hydrogen-ion concentration. For successively higher buffer concentrations each rate of hydrazone formation is proportionately higher, but all of the curves have the same form.

From Fig. 2, by extrapolating the curve for each *p*H through zero buffer concentration, we should obtain the k_1 value due to the hydrogen-ion concentration alone at any *p*H value. These figures have been indicated on Fig. 1 as the broken line, and show that the hydrogen-ion catalysis of the reaction is comparatively slight, but varies with *p*H in the same manner as the salt catalysis.

The constant rate attained at *p*H values below 5.4 appears significant in seeking an explanation of the mechanism of the influence of the buffer on the reaction. It would seem reasonable to suppose that at and below this *p*H value all the base is associated with the acid of the buffer, and a further lowering of the hydrogen-ion concentration can therefore produce no further change in the concentration of this reactant, phenylhydrazine phosphate in the un-ionized form. It follows that the optimum conditions of *p*H and buffer concentration for the reaction are those under which all the phenylhydrazine present is associated with the buffer.

The flattening of the curves of Fig. 2 at the higher buffer concentrations would be expected on the foregoing basis, as large excesses of buffer would be required to convert the last trace of base into the associated compound. It should be noted that at even the highest buffer concentrations used in the experiments of Fig. 1 the total base concentration is in excess of that of the buffer.

Additional weight is lent to the un-ionized acid–base reactant hypothesis by the fact, previously reported,[2] that, in the case of benzophenone phenylhydrazone, the rate of phenylhydrazone formation is higher in alcoholic than in aqueous solution, despite the fact that the hydrazone is more soluble in alcohol than in water. If the salt of the base is more reactive than the free base, the result obtained is precisely the one to be expected, since the alcohol present would no doubt depress somewhat the ionization of the phenylhydrazine phosphate and accordingly increase the concentration of the most reactive substance, at any *p*H.

Conant and Bartlett,[3] dealing with the similar reaction in which semicarbazide instead of phenylhydrazine is involved, believe the ionized base to be the reactant under acid catalysis, but show the theory of the salt as the reactant to be equally tenable.

In an attempt to get further quantitative confirmation of the undissociated salt reactant theory, a series of determinations of the amount of phenylhydrazine extracted from phosphate buffered phenylhydrazine solutions at different hydrogen-ion concentrations by aliquots of benzene shaken with the solutions for equal periods was performed. While these experiments showed conclusively that there was a lowering in the concentration of the free phenylhydrazine from a *p*H of 7.6, at which there was apparently no association of the base with the buffer constituents, to a *p*H of 5.0, at which the indicated association was approximately 10% of the phenylhydrazine present, the decrease in the proportion of free base present was not so great as the reaction velocity curves indicate.

Conclusions

1. Phenylhydrazine will react with aldehydes or ketones to form phenylhydrazones in unbuffered aqueous solution, but the velocity of such reactions is very low.

2. The velocity of phenylhydrazone formation is influenced by the hydrogen-ion concentration and the buffer concentration of the reaction medium. A means of observing the effect of each separately, even though they cannot be experimentally divorced, has been indicated.

3. Phosphate buffers are approximately ten times as effective in catalyzing the formation of phenylhydrazones as are acetate buffers.

4. The undissociated phenylhydrazine salt ap-

pears to be the most active reagent in the formation of phenylhydrazones.

5. The temperature coefficient of the rate of formation of *d*-galactose phenylhydrazone has been determined under acid catalysis, as well as the specific rotation of the phenylhydrazones of *d*-glucose in the equilibrated form and of *d*-galactose.

Since this article was prepared for publication, Compton and Wolfrom[6] have published kinetic data on the acid catalyzed *d*-galactose phenylhydrazone reaction in which a monomolecular formula is used to calculate the k_1 values. In that article reference is made to observations of Bodforss[7] that the reaction between aromatic aldehydes or ketones and phenylhydrazine (in the absence of acid catalysts) is monomolecular when the concentration of the carbonyl compound is in excess of that of the base, and bimolecular when the base is in excess. Compton and Wolfrom explain their monomolecular results, obtained in experiments in which the base was at a concentration higher than that of the sugar, on the basis that the free base is the active reagent. Since the latter will then be present only as that part of the acid–base compound which is dissociated, the sugar will always be in excess of the *free* base.

While we cannot reconcile the fact that our results are in harmony with the opinion that the phenylhydrazone reaction is bimolecular while the work of Compton and Wolfrom appears to show it to be monomolecular, we would point out that our observations confirm those of Bodforss. It should be kept in mind, also, that Conant and Bartlett[3] find the reaction between semicarbazide (the exact counterpart of phenylhydrazine in its reaction with the carbonyl group) and various ketones and aldehydes to be bimolecular regardless of the ratio of the concentrations of the base and the carbonyl compound.

(6) Compton and Wolfrom, THIS JOURNAL, **56**, 1157 (1934).
(7) Bodforss, *Z. physik. Chem.*, **109**, 223 (1924).

TORONTO, CANADA RECEIVED MARCH 21, 1935

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Reactions of the Bromo- and Dibromoolefins[1]

BY G. BRYANT BACHMAN

The reactions studied may be divided into two classes: (1) those in which the bromine is removed or replaced; (2) addition reactions. Reactions of class (1) have been confined to the action of bases in different solvents and of alkali metals in liquid ammonia. Reactions of class (2) include the action of a variety of reagents such as the halogens, oxygen, sulfur, etc.

Action of Bases.—Like the monobromoolefins the dibromoolefins are relatively stable toward water and weak bases. After boiling for several hours with aqueous sodium carbonate or anhydrous pyridine or aniline, they may be recovered almost quantitatively. With strong bases, however, dehalogenation occurs in both cases with the formation of acetylenes. Some oxidizing action is evident in the dehalogenation of the dibromoolefins. If reaction with potassium hydroxide takes place in alcoholic solution acetic acid is one of the products;[2] in other cases the most easily oxidized substance present is attacked. Thus dehalogenation of 1,1-dibromopropene with sodium ethyl mercaptide in alcoholic solution proceeds as follows

$$CH_3CH{=}CBr_2 + 2NaSC_2H_5 \longrightarrow CH_3C{\equiv}CH + C_2H_5SSC_2H_5 + 2NaBr$$

The low yields of acetylenes from the dehalogenation of 1,1-dibromoolefins in mineral oil[3] can probably be explained on this basis as due to the oxidation of some of the product.

Sodium in Liquid Ammonia.—The action of sodium on the monobromoolefins in inert solvents such as ether has already been investigated by Nef[4] and by others, and in liquid ammonia by Kirrmann,[5] Vaughn[6] and Chablay.[7] In the present work the following substances were added separately to sodium dissolved in liquid ammonia until the blue color of the solution just vanished: 1,1-bromopropene, 1-bromooctene, 1,1-dibromo-

(1) Presented before the Organic Section of the Midwest Regional meeting of the American Chemical Society held in Kansas City, May 3–5, 1934.
(2) Valentin, *Ber.*, **28**, 2664 (1895).
(3) Bachman and Hill, THIS JOURNAL, **56**, 2730 (1934).
(4) Nef, *Ann.*, **308**, 267 (1894).
(5) Kirrmann, *Compt. rend.*, **181**, 671 (1925).
(6) Vaughn, THIS JOURNAL, **56**, 2064 (1934).
(7) Chablay, *Ann. chim.*, [9] **1**, 469 (1914).