This point was settled satisfactorily when it was found that ether alone could be used as a solvent if the time of shaking was prolonged to from eighteen to twenty-four hours. Purified dioxane could also be used alone but then the reaction likewise proceeded at a very slow rate. The sodium used in the procedure served merely as a drying agent, since anhydrous calcium sulfate (Drierite) could be substituted for it without affecting the yield. When sodium was used and the solid sodium hydroxide omitted, a very low yield of α-glucose pentaacetate was obtained. This small amount of conversion was undoubtedly due to the slight quantity of sodium hydroxide produced by unavoidable contamination with moisture. All of these experiments pointed to the conclusion that the active interconverting agent was the sodium hydroxide. When α-*d*-glucose pentaacetate was used initially, it was recovered unchanged in approximately 50% yield but no β-form was isolated. This would indicate either that the equilibrium was displaced to favor the α-form or that the β-isomer was more readily deacetylated.

α-*d*-Galactose Pentaacetate.—Pure β-*d*-galactose pentaacetate (3.0 g.) was treated exactly as described for β-*d*-glucose pentaacetate except that the time of shaking was from five to seven hours. The acidified filtrate showed a specific rotation of from +60 to +80°. The sirup obtained after solvent removal under reduced pressure was dissolved in ethanol, treated with Carboraffin, filtered and the ethanol removed under reduced pressure. The residual sirup was dissolved in chloroform and the solution washed successively with 5% hydrochloric acid, 5% aqueous sodium bicarbonate and then with water, dried, the solvent removed under reduced pressure and the residual sirup crystallized from a small amount of hot ethanol; yield 0.8 to 1.0 g.; m. p. 94–95° (mixed m. p. unchanged); $[\alpha]^{27}$ +104° (*c*, 3.7; $CHCl_3$). Hudson and Parker[8] record for α-*d*-galactose pentaacetate the constants: m. p. 96°; $[\alpha]^{20}$ +107° ($CHCl_3$).

(8) C. S. Hudson and H. O. Parker, THIS JOURNAL, **37**, 1589 (1915).

α-*d*-Mannose Pentaacetate.—Pure β-*d*-mannose pentaacetate (3.0 g.) was treated exactly as described for β-*d*-glucose pentaacetate except that the time of shaking was from four to four and one-half hours. The acidified filtrate showed a specific rotation of approximately +45°. The sirup obtained after solvent removal was crystallized from hot water; yield 1.2 g.; m. p. 73–74°; $[\alpha]^{23}$ +59° (*c*, 2.6; $CHCl_3$; 2-dm. semimicro tube). After one further recrystallization the substance showed the constants: m. p. 74–75° (mixed m. p. unchanged); $[\alpha]^{28}$ +60° (*c*, 3.3; $CHCl_3$; 2-dm. semimicro tube). Levene and Bencowitz[9] record for α-*d*-mannose pentaacetate the constants: m. p. 75°; $[\alpha]^{22}$ +55° ($CHCl_3$).

α-Lactose Octaacetate.—Pure β-lactose octaacetate (3.0 g.; m. p. 90°; $[\alpha]$ −4.2°, $CHCl_3$) was treated exactly as described for β-*d*-glucose pentaacetate and the sirup obtained after solvent removal was dissolved in ethanol (Carboraffin) and the ethanol removed under reduced pressure. The residual sirup was triturated with several portions of cold water and obtained crystalline from either ethanol or ether by slow evaporation of the solvent. α-Lactose octaacetate is difficult to crystallize and the yield was very low; m. p. 149–150°; $[\alpha]^{21}$ +51° (*c*, 2.9; $CHCl_3$; 2-dm. semimicro tube). On one further recrystallization the melting point was 152° (mixed m. p. unchanged). Hudson and Johnson[1b] record for α-lactose octaacetate the constants: m. p. 152°; $[\alpha]^{20}$ +54° ($CHCl_3$).

Summary

1. A method was found for converting β-*d*-glucose pentaacetate to the α-form, using sodium hydroxide as the reagent.

2. The method was extended to the corresponding fully acetylated derivatives of *d*-galactose, *d*-mannose and lactose. It is probably of general application.

(9) P. A. Levene and I. Bencowitz, *J. Biol. Chem.*, **72**, 627 (1927)

COLUMBUS, OHIO RECEIVED NOVEMBER 19, 1936

[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Configurations of α- and β-*p*-Bromobenzophenone Oximes

BY RAYMOND WRIGHT JOHNSON AND JOE GOLENTERNEK

An earlier contribution by Johnson and Stieglitz[1] from this Laboratory reported the details of an empirical method for the determination of the velocity of hydrolysis of oximes. Data were reported which showed that the individual members of the pair of stereoisomeric oximes of *p*-methylbenzophenone hydrolyzed at considerably different rates.

The purpose of this study was, first, to test the generality of this difference in rates by the investigation of another pair of stereoisomeric oximes and, second, to extend the study to include a comparison of the rates of hydrolysis of the stereoisomeric forms with those of the corresponding symmetrical oximes. It was hoped that this might throw some light on the configurations of the stereoisomeric compounds. The compounds selected were the α and β forms of *p*-bromobenzophenone oxime and the related oximes of benzophenone and *p,p'*-dibromobenzophenone.

(1) Johnson and Stieglitz, THIS JOURNAL, **56**, 1904 (1934).

Preparation of Materials

Benzophenone Oxime.—This compound was prepared by the method of Fischer.[2]

(2) Fischer, "Anleitung zur Darstellung organ. Prepärate," Braunschweig, 1908, p. 68.

p,p'-**Dibromobenzophenone Oxime.**—A mixture of the ketone (10 g.) and hydroxylamine hydrochloride (6.5 g.) dissolved in ethyl alcohol (700 cc. of 95%) to which a solution of sodium carbonate (10 g. in 30 cc. of water) had been added was refluxed on a steam-bath for ten hours and then allowed to cool. The unreacted ketone (about 25% of the original amount) and sodium carbonate was removed by filtration. The filtrate was diluted with water (2500 cc.) and chilled. Crystals of the crude oxime (7.5 g., m. p. 140–145°) were obtained. Two recrystallizations from ligroin (b. p. 90–100°) produced the pure oxime (m. p. 150–152°).

Anal. (Micro) Calcd. for $C_{13}H_9ONBr_2$: N, 3.94. Found: N, 3.94, 4.02.

α- and β-*p*-**Bromobenzophenone Oximes.**—Anhydrous sodium acetate (100 g.) was added to a solution of the ketone (50 g.) and hydroxylamine hydrochloride (60 g.) in ethyl alcohol (400 cc. of 95%). The mixture was refluxed for six hours on a steam-bath. The alcohol was removed by distillation and the residue was washed several times with warm water. The crude mixture of the two oximes (51 g.) when dry had a melting point of 102–160°. The method used for the separation of the two forms was based on the difference in their solubility in solutions of sodium hydroxide. The crude mixture of oximes was extracted with successive portions (700, 150, 85 and 50 cc.) of a hot (90°) solution of sodium hydroxide (2 *N*). The undissolved oxime (m. p. 160–165°) on recrystallization from ethyl alcohol produced the pure α-oxime. The melting point of this pure α-form (m. p. 168–170°) was higher than that reported (165–166°) previously by Schäfer.[3] The combined alkaline extract was saturated with carbon dioxide gas to precipitate the oxime in solution. This material was washed with water until free from alkali. The dried material was dissolved in hot ethyl alcohol (absolute). Fractional crystallization was obtained by means of the addition of small quantities of water from time to time. Relatively small amounts of the pure β-form (m. p. 109–111°) were obtained.

Anal. (Micro) Calcd. for $C_{13}H_{10}ONBr$: N, 5.07. Found: (α-form), N, 5.01, 4.93; (β-form), 5.03, 4.88.

Method

The method used for the determination of the velocity of hydrolysis of the oximes was essentially that of Johnson and Stieglitz.[1] The limited solubility of these bromo compounds in an acetic–hydrochloric acid mixture such as was used by them required the use of a mixture richer in acetic acid. This necessitated a slight change in the extraction procedure. The procedure followed in each of the determinations listed below was identical. A weighed quantity of the oxime was dissolved in glacial acetic acid (140 cc. of reagent quality) at 25° in a 200-cc. graduated flask. At a definite noted time exactly 50 cc. of hydrochloric acid (1.899 *N*) at 25° was run in. The volume of the solution was quickly made up to 200 cc. by the addition of glacial acetic acid. After it was thoroughly mixed, the solution was placed in a thermostat at 25 ± 0.02°. From time to time a sample (25 cc.) of the solution was pipetted into a Squibb separatory funnel. At a definite noted time 35 cc. of water was added and the procedure from that point on was the same as that described by Johnson and Stieglitz.[1] The concentration of the oxime in the various determinations ranged from 0.03 to 0.045 *N*.

Tests with known solutions showed that this procedure yields quantitative results with acetic–hydrochloric acid solutions of hydroxylamine such as were obtained in this investigation.

The fact that the reactions in each case were normal and yielded only the respective ketone and hydroxylamine was proved when examinations of the content of completely hydrolyzed solutions yielded only these two substances.

Results

The average of at least two determinations of the velocity of hydrolysis of each of the oximes studied is given in Table I.

TABLE I

VELOCITY OF HYDROLYSIS OF OXIMES (25°)

Compound, oxime	Concn. of HCl in hydrolyzing solution, *N*	$K \times 10^5$
Benzophenone	0.4747	60.21
α-*p*-Bromobenzophenone	.4747	67.49
β-*p*-Bromobenzophenone	.4747	55.85
p,p'-Dibromobenzophenone	.4747	46.83

Discussion

In the article by Johnson and Stieglitz[1] the hydrolysis of oximes tentatively was assumed to consist of at least two consecutive reactions, the first reaction consisting of the addition of a molecule of water to the double bond between carbon and nitrogen in the oxime or its salt, followed by the decomposition of this intermediate hydrated form to produce the normal end products. Furthermore, it was pointed out that, if such is the true mechanism for the reaction, the experimentally determined rate of hydrolysis of the stereoisomeric oximes must be that of the addition of water to form the intermediate hydrated compound. The data reported in this paper are most logically explained by this theory. The fact that the rate of hydrolysis of chloral oxime[4] is very much less than the rate of hydrolysis of the hydrate of chloral oxime supports this general theory.

If this simple mechanism is valid, and, if *cis* addition of the molecule of water takes place, one might expect that that one of the two stereoisomeric oximes investigated which has the *syn*-phenyl configuration would hydrolyze at a rate more nearly approximating the rate of hydrolysis of benzophenone oxime than the rate for *p,p'*-dibromobenzophenone oxime. Similarly of the two the rate of hydrolysis of the form with the *syn*-*p*-bromophenyl configuration might be ex-

(3) Schäfer, *Ann.*, **264**, 152 (1891).

(4) Unpublished data.

pected to approximate more nearly the rate of hydrolysis of *p,p'*-dibromobenzophenone oxime. An examination of the data in Table I shows that the rate of hydrolysis of *α*-*p*-bromobenzophenone oxime more nearly approximates the rate for benzophenone oxime than it does that for *p,p'*-dibromobenzophenone oxime. Thus this criterion of configuration would assign the *syn*-phenyl configuration to the *α*-*p*-bromobenzophenone oxime. Similarly, the closer relationship between the rates of hydrolysis of the *β*-*p*-bromobenzophenone oxime and *p,p'*-dibromobenzophenone oxime would assign the *syn*-*p*-bromophenyl configuration to the *β*-*p*-bromobenzophenone oxime. These configurations agree with those assigned to the *α*- and *β*-forms of this oxime by the method of Hantzsch, based on the products of the Beckmann rearrangement of the individual oximes. However, if *trans* addition of water occurs, the interpretation of the above data would reverse the assigned configurations. Thus no claim can be made for the validity of this method until further investigations have been made on other pairs of oximes. In particular data on the rates of hydrolysis of oximes whose configurations have been determined by other means are needed. This work will be done in this Laboratory.

Summary

1. The velocities of hydrolysis of benzophenone oxime, *p,p'*-dibromobenzophenone oxime and the stereoisomeric *α*- and *β*-*p*-bromobenzophenone oximes were determined under identical conditions.

2. A possible tentative method for the assignment of configurations to stereoisomeric oximes, based on a comparison of velocity of hydrolysis constants, is discussed.

CHICAGO, ILL. RECEIVED SEPTEMBER 28, 1936

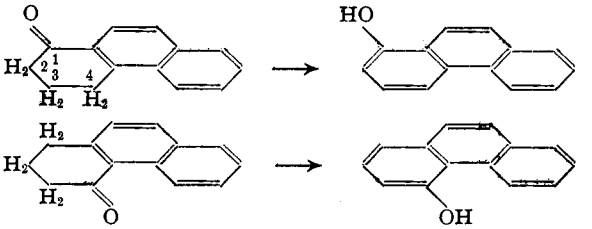
[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Studies in the Phenanthrene Series. XIV. The Preparation of 1- and 4-Phenanthrol

BY ERICH MOSETTIG AND HARRY M. DUVALL[1]

As starting material for the synthesis of new compounds which might possess oestrogenic activity, we were in need of several of the phenanthrols. While all five of the possible monohydroxyphenanthrenes are known, heretofore there has been no satisfactory method of preparing the 1- and 4-isomers. The total synthesis of 1- and 4-methoxyphenanthrene by Pschorr's method[2] can hardly be considered for large scale preparation. The synthesis of the 1-hydroxy- and in particular of the 4-hydroxyphenanthrene by the pyrolysis of *α*- and *β*-naphthylparaconic acid,[3] respectively, appears quite impracticable. The more recent preparations of 1-phenanthrol by potassium hydroxide fusion of the rare 1-sulfonic acid[4] and by diazotization of 1-aminophenanthrene[5] do not appear feasible.

In a previous communication of this series[6] we stated that 1-phenanthrol can be obtained from 1-keto-2-bromo-1,2,3,4-tetrahydrophenanthrene in a yield of about 50% by elimination of hydrogen bromide, while 4-phenanthrol is obtained only in small amounts by an analogous reaction. A more direct way, however, appeared to be dehydrogenation of the 1- and 4-ketotetrahydrophenanthrenes themselves, according to the scheme



The principle of this method is not new and has been applied successfully by Darzens and Levy[6,7] in the preparation of phenols from the corresponding hydroaromatic ketones, using sulfur and selenium as dehydrogenating agents. Since we found the application of these agents to the ketotetrahydrophenanthrenes not very successful,

(1) E. R. Squibb and Sons Research Fellow.

(2) (a) Pschorr, Wolfes and Buckow, *Ber.*, **33**, 162 (1900); (b) Pschorr and Jäckel, *ibid.*, **33**, 1826 (1900).

(3) (a) Shoesmith and Guthrie, *J. Chem. Soc.*, 2332 (1928); (b) Behrend and Ludewig, *Ann.*, **379**, 351 (1911).

(4) Fieser, THIS JOURNAL, **51**, 2460 (1929).

(5) Backmann and Boatner, *ibid.*, **58**, 2194 (1936).

(6) Mosettig and Burger, *ibid.*, **57**, 2180 (1935).

(7) Darzens and Levy, *Compt. rend.*, **194**, 181 (1932); Levy, *ibid.*, **194**, 1749, 1952 (1932). See also Ruzicka, *Helv. Chim. Acta*, **19**, 419 (1936); Fieser, Hershberg and Newman, THIS JOURNAL, **57**, 1509 (1935).