In one instance the alkali-insoluble fraction was isolated by drying and evaporating the ether solution. From the residue was obtained a 2,4-dinitrophenylhydrazone melting at 238–239°. Its equal mixture with authentic benzophenone 2,4-dinitrophenylhydrazone (m. p. 238–239°) melted at 238–239°.

Hydrogenolysis of Catechol Diphenylmethylene Ethers.—Palladium oxide was prepared according to the directions of Starr and Hixon.[14] Ten mg. of this catalyst took up 2.5 cc. of hydrogen. The activity of the catalyst with respect to the splitting of benzyl ethers was established by the hydrogenolysis of benzyl tetra-acetyl-β-glucoside ($[\alpha]_D$ −52.3°) kindly furnished for the purpose by Dr. N. K. Richtmyer. This compound was cleaved quantitatively under the conditions already described by Dr. Richtmyer and in duplication of his results.[5]

To 1.0 g. of the catechol diphenylmethylene ether in 100 cc. of absolute alcohol was added 0.5 g. of palladium oxide. This mixture took up the theoretical quantity of hydrogen in ten to twelve hours. After completion of the reduction the alcohol was evaporated; the residue was dissolved in ether and extracted as described above. The sublimed products possessed the melting points of the pure catechols and these were not depressed by mixture with the corresponding authentic catechol. The yields were 80–85% of the theoretical. The alkali-insoluble fraction in the ether solution was a low melting solid, presumably diphenylmethane. which was not further investigated.

Action of Alkali on Catechol Diphenylmethylene Ethers.—One gram of the cyclic ether was added to 25 cc. of a 25% solution of potassium hydroxide in methanol and the mixture, protected from atmospheric carbon dioxide, was refluxed for seventy-two hours. It was then cooled at 0° for forty-eight hours; the crystals which formed were filtered off and washed with ice-cold methanol. The product was identical with the starting material and was recovered in 90–95% yields.

Action of the Grignard Reagent on Catechol Diphenylmethylene Ethers.—The Grignard reagent was formed from 1 g. of 1-bromobutane, b. p. 100–101°, and 0.2 g. of magnesium turnings in 50 cc. of dry ether. To this reagent. protected by dry nitrogen, was added 1 g. of the catechol diphenylmethylene ether; the mixture was refluxed for forty-eight hours. At the end of this period, the solution was thrown on ice and exactly neutralized with 1 *N* hydrochloric acid. The ether layer was dried and evaporated and the residue was recrystallized from absolute alcohol. The original cyclic ether was recovered in 90–95% yield.

Summary

The preparation and properties of the diphenylmethylene ethers of catechol, 3-*n*-propylcatechol, and 4-*t*-butylcatechol, have been studied. Although these ethers are resistant to alkali and to the Grignard reagent, they are cleaved by dilute mineral acid and by catalytic hydrogenation.

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[14] Starr and Hixon, "Organic Syntheses," A. H. Blatt, Editor, John Wiley and Sons, New York, N. Y., 1943, Coll. Vol. II, p. 566.

[Contribution from the Department of Chemistry, Carnegie Institute of Technology]

A Comparative Study of the Kinetics and Mechanisms of Formation of the Phenylhydrazone, Semicarbazone and Oxime of *d*-Carvone[1,2]

By G. H. Stempel, Jr., and Gerson S. Schaffel

The assumption that the reactions of a ketone with the carbonyl reagents, such as phenylhydrazine, semicarbazide and hydroxylamine, proceed by identical mechanisms has heretofore been generally accepted without direct experimental evidence.[3,4] The object of this investigation was to determine the correctness of this assumption by means of a comparative study of the kinetics of these reactions, as well as to obtain data which could lead to a better picture of such a common mechanism.

The kinetics of these reactions were followed by observing the change of rotation during the reactions of the carbonyl reagents with the optically active ketone, *d*-carvone. One of the more important considerations which led to the choice of *d*-carvone is that the optically active center of the molecule is not alpha to the carbonyl group, and consequently enolization of the ketone does not bring about racemization[5] as it does in the case of *l*-menthone.

In order to compare these reactions, the following four characteristics were studied: (1) effect of added neutral salts upon the velocity constants; (2) dependence of their rates upon the carvone concentration; (3) dependence of their rates upon carbonyl reagent concentration; and (4) determination of whether the reactions are general or specific acid catalyzed.

Experimental

Reagents.—The *d*-carvone used in these experiments was an Eastman Kodak Co. product which was further purified by the method of Wallach[6] through the formation of a "hydrosulfide" with hydrogen sulfide which was recrystallized several times from alcohol and then reconverted to *d*-carvone by refluxing with aqueous alkali. The regenerated *d*-carvone was carefully distilled, after which it exhibited the following properties: b. p. 230°, corrected to 760 mm. pressure; $[\alpha]^{30}_{5461}$ 73.33°; n^{20}_D 1.5005 ± 0.0003. In 83% aqueous alcohol, a solvent in which many of the rate experiments were performed, a 0.4000-g. sample dissolved in sufficient 83% alcohol to make 100 ml. of solution gave $[\alpha]^{30}_{5461}$ 68.53°.

The semicarbazide, phenylhydrazine and hydroxylamine hydrochlorides employed were Eastman Kodak Co. products which were recrystallized several times from

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[1] Presented before the Division of Organic Chemistry of the American Chemical Society at Detroit in April, 1943.

[2] Abstracted from the thesis submitted by Gerson S. Schaffel to the Committee on Graduate Instruction at Carnegie Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Science.

[3] Conant and Bartlett, This Journal, **54**, 2881 (1932).

[4] Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940. pp. 333–334.

[5] Bartlett and Vincent, This Journal, **55**, 4992 (1933).

[6] Wallach, *Ann.*, **305**, 224 (1899).

aqueous alcohol and carefully dried over calcium chloride and sodium hydroxide. The semicarbazone, phenylhydrazone and oxime were prepared, and exhibited the following properties: *d*-carvone semicarbazone, m. p. 143°, $[\alpha]^{30}_{5461}$ 181.3° in 83% aqueous alcohol; *d*-carvone phenylhydrazone, m. p. 110°, $[\alpha]^{30}_{5461}$ 268.31° in 83% aqueous alcohol; and *d*-carvone oxime, m. p. 73°, $[\alpha]^{30}_{5461}$ 38.2° in 83% aqueous alcohol.

The water and alcohol used in making solutions were warmed under reduced pressure to remove dissolved oxygen and were stored under an atmosphere of nitrogen in automatic filling burets. All materials used in preparing buffers, etc., were standard C. P. reagents.

Apparatus.—The optical measurements were made with a Hilger M-8 polarimeter using the Hg green line (5461 Å.). On this instrument static readings are reproducible to 0.01°. The kinetic runs were made in a specially designed Pyrex polarimeter tube. The tube proper consisted of a 50-cm. Pyrex glass tube to which were sealed flat Pyrex end pieces. At one end of the tube a 100 ml. bulb was attached by means of capillary tubing; at the other end, a side arm containing a stopcock. The tube was completely enclosed by a water jacket made of 2-inch micarta tubing with end windows placed in brass end caps, and provided with an inlet and outlet permitting the circulation of water thermostatically controlled at 30 ± 0.05°.

Procedure.—When making an experimental run, the solution was prepared in a flask equipped with a gas inlet through which nitrogen was continually bubbled into the mixture. The carbonyl reagent hydrochloride was weighed into the flask, the requisite quantity of standard potassium hydroxide was added, and the proper amounts of absolute alcohol and distilled water at 30° were added to bring the volume to a predetermined value. The *d*-carvone was weighed into a small weighing bottle, which was dropped into the flask as the timing was begun. The polarimeter tube was thoroughly swept out with nitrogen, the solution was poured into the bulb on the tube while the nitrogen was still flowing, and the solution was stirred by the gas for a short time. Then the gas flow was discontinued and a slight suction was applied to draw the solution into the tube. The elapsed time from the mixing of the reagents until the first reading was taken was from one to two minutes. Subsequent readings consisted of the time at which a given rotation was observed. All runs were made at 30° and all concentrations here reported are in moles per liter.

In order to avoid any complicating extraneous effects which might arise from the use of external buffers, the *p*H was maintained constant by the buffering action of the carbonyl reagent and its hydrochloride, according to the method suggested by Orning and Stempel.[7] Experimentally, this was accomplished by dissolving a known quantity of the hydrochloride and then adding less than the stoichiometric amount of standard base. The concentration of the carbonyl reagent, BNH_2, was then equal to the concentration of the added inorganic base, and the concentration of the ion of the hydrochloride, BNH_3^+, was equal to the difference between the gross initial concentration of BNH_3^+ and the concentration of the added base.

By utilization of such a buffer, the concentration of the BNH_2 was kept at such a high value that the reaction became pseudo-unimolecular. Therefore, the rate equation for a first order, reversible reaction expressed in terms of optical rotations was used. For the reaction

$$R_2CO + BNH_2 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} R_2C{=}NB + HOH$$

we have

$$k_{\text{observed}} = k_1 + k_2 = \frac{1}{t}\ln\frac{\alpha_e - \alpha_0}{\alpha_e - \alpha_t}$$

where α_e is the final rotation, α_0 is the initial rotation, and α_t is the rotation at any time.

Now, $\log(\alpha_e - \alpha_t) = \log(\alpha_e - \alpha_0) - (k_{\text{obs.}}\, t/2.303)$, from which it follows that if $\log(\alpha_e - \alpha_t)$ is plotted against t, a straight line will be obtained whose slope is $k_{\text{obs.}}$, -2.303. Figure 1 shows the plot of $\log(\alpha_e - \alpha_t)$ against time for typical runs with each of the carbonyl reagents. Determinations of the equilibrium constants, K, of these reactions showed that K is of the order of 300 or more and since $k_1 = k_{\text{obs.}}/(1 + 1/K)$, then k_1 may be set equal to $k_{\text{obs.}}$. In order to obtain the true rate constant, k_0, independent of the constant carbonyl reagent concentration, k_1 was divided by the carbonyl reagent concentration. It is this k_0 that has been recorded in all of the following tables.

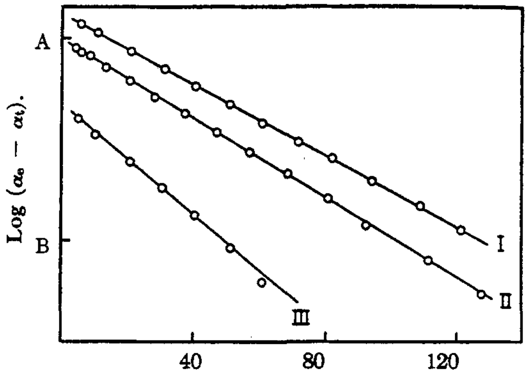

Fig. 1.—Typical log ($\alpha_e - \alpha_t$) *vs.* time plots for kinetic runs of *d*-carvone with: I, phenylhydrazine (A, 0.625; B, 0.325); II, semicarbazide (A, 0.3; B, −0.3); and III, hydroxylamine (A, 0.0; B, −0.6).

Experimental Results

Equilibrium Constants.—Equilibrium constants were obtained from equilibrium rotation readings of typical kinetic runs and were calculated from the expression: $K = x/(1 - x)(b - ax)$, in which a and b are, respectively, the initial ketone and carbonyl reagent concentrations and $x = (\alpha_e - \alpha_0)/(\alpha_\infty - \alpha_0)$, where α_∞ is the rotation calculated for complete conversion of ketone to phenylhydrazone, semicarbazone or oxime. Typical values of K are: for the phenylhydrazine–*d*-carvone reaction: 614, 576 and 572; for the hydroxylamine–*d*-carvone reaction: 410, 310 and 380; for the semicarbazide–*d*-carvone reaction: 310, 330 and 430.

Kinetic Salt Effect.—The absence of any effect upon k_0 by changing ionic strength is shown in Table I, in which are shown k_0 values for a series

TABLE I

CONSTANCY OF k_0 WITH CHANGING IONIC STRENGTH

Concentrations in moles per liter: (A) phenylhydrazine 0.138, phenylhydrazine hydrochloride 0.010, carvone 0.020; (B) semicarbazide 0.054, semicarbazide hydrochloride 0.050, carvone 0.022; (C) hydroxylamine 0.088, hydroxylamine hydrochloride 0.090, carvone 0.065. Solvent: A and B, 83% aqueous alcohol; C, 50% aqueous alcohol.

(A) Phenylhydrazine Ionic strength	$k_0 \times 10^3$	(B) Semicarbazide Ionic strength	$k_0 \times 10$	(C) Hydroxylamine Ionic strength	$k_0 \times 10$
0.010	2.37	0.013	3.12	0.178	2.39
.020	2.00	.032	3.18	.246	2.35
.023	2.13	.041	3.18	.315	2.39
.038	2.13	.067	3.14		
.066	2.30				

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(7) Orning and Stempel, *J. Org. Chem.*, 4, 410 (1939).

of kinetic runs in which all variables except ionic strength were kept constant. The ionic strength was varied by adding calculated amounts of potassium chloride.

Dependence of Rate on Ketone Concentration.—In Table II are shown the values for k_0 for the reactions of the three carbonyl reagents with various initial concentrations of *d*-carvone. The dependence of the rates on the *d*-carvone concentration is shown by the constancy of k_0 in Table II.

TABLE II

VALUES OF k_0 WITH DIFFERENT STARTING CONCENTRATIONS OF CARVONE

Concentrations of carbonyl reagent and its hydrochloride both 0.05 mole/liter; solvent, 83% aqueous alcohol.

Phenylhydrazine		Hydroxylamine		Semicarbazide	
Molar concn. of carvone	$k_0 \times 10$	Molar concn. of carvone	$k_0 \times 10$	Molar concn. of carvone	$k_0 \times 10$
0.0062	1.26	0.0065	2.78	0.0203	1.87
.0106	1.24	.0158	2.74	.0228	1.88
.0140	1.23	.0247	2.72	.0268	1.88
.0178	1.20				
.0232	1.24				

Dependence of Rate on Carbonyl Reagent Concentration.—In Table III are shown the values of k_0 for runs with various initial concentrations of carbonyl reagent. These values of k_0, found by dividing the observed k by the carbonyl reagent concentration, should remain constant if the rates are proportional to the first power of the carbonyl reagent concentration. That this is approximately true can be seen from the nearly constant values of k_0 in Table III. The small drift in k_0 is attributable to the somewhat increased pH as the concentrations of the basic carbonyl reagents are increased.

TABLE III

VALUES OF k_0 WITH DIFFERENT STARTING CONCENTRATIONS OF CARBONYL REAGENT

Concentrations in moles per liter: (A) $C_6H_5NH{\cdot}NH_3Cl$ 0.05, carvone 0.0203; (B) $NH_2{\cdot}CO{\cdot}NH{\cdot}NH_3Cl$ 0.05, carvone 0.0221; (C) NH_3OHCl 0.113, carvone 0.0385; solvent, 83% aqueous alcohol.

(A) Phenylhydrazine		(B) Semicarbazide		(C) Hydroxylamine	
Molar concn. of phenylhydrazine	$k_0 \times 10^2$	Molar concn. of semicarbazide	$k_0 \times 10$	Molar concn. of hydroxylamine	$k_0 \times 10^2$
0.052	11.2	0.054	3.18	0.071	2.4
.074	9.5	.069	2.63	.097	2.0
.092	9.1	.086	2.58	.128	1.7

Demonstrations of General Acid Catalysis.—These runs were made to show that the reaction of the ketone with each carbonyl reagent is subject to general acid catalysis. The method used was that of Brönsted and Guggenheim[8] in which the same pH is maintained in each of several solutions containing different amounts of an acid HA. This is accomplished by adding to each solution enough of the anion of the acid, A^-, to make the ratio of the concentration of A^- to that of HA the same in all solutions.

Since the carbonyl reagents are bases, the following equilibria exist

$$\begin{array}{rcl} \mathrm{HA} \rightleftarrows & \mathrm{H^+} & + \mathrm{A^-} \\ & + & \\ & \mathrm{BNH_2} & \\ & \upharpoonleft\!\downharpoonright & \\ & \mathrm{BNH_3^+} & \end{array}$$

It is apparent that the effect on the pH by small changes in the concentration of BNH_2, which is used up in the reaction, can be minimized by choosing HA so that its acid dissociation constant is nearly the same as that of BNH_3^+. A comparison of K_{acid} for the BNH_3^+ ion with that of the acid of the buffer pair chosen in each case is shown in Table IV. In all runs, the ionic strength was maintained constant by the addition of potassium chloride.

TABLE IV

COMPARISON OF DISSOCIATION CONSTANTS OF THE HYDROCHLORIDES OF CARBONYL REAGENTS AND CERTAIN ORGANIC ACIDS

Carbonyl reagent	K_a for ion, BNH_3^+	Acid chosen	K_a for acid
Phenylhydrazine	0.6×10^{-6}	Acetic	1.9×10^{-5}
Semicarbazide	2.2×10^{-4}	Formic	2.0×10^{-4}
Hydroxylamine	8×10^{-7}	Sodium hydrogen maleate	4×10^{-7}

Table V shows the experimental results along with glass electrode readings to show the approximate constancy of the pH in the solutions. It

TABLE V

DATA SHOWING THE INCREASE OF k_0 WITH ACIDITY AT CONSTANT pH

Phenylhydrazine

Concentration of phenylhydrazine 0.149, of carvone 0.0203 mole per liter; solvent, 80% aqueous alcohol; ionic strength, 0.0719.

Acetic acid concentration	Acetate ion concentration	k_0	E. m. f.
0.0128	0.0112	0.0199	0.090
.0256	.0223	.0346	.087
.0384	.0335	.0468	.083

Semicarbazide

Concentration of semicarbazide 0.098, of carvone 0.018 mole per liter; solvent, 74% aqueous alcohol; ionic strength, 0.398.

Formic acid concentration	Formate ion concentration	k_0	E. m. f.
0.076	0.074	0.550	0.0350
.114	.111	.618	.0338
.152	.148	.691	.0329

Hydroxylamine

Concentration of hydroxylamine 0.097, of carvone 0.066 mole per liter; solvent, 48% aqueous alcohol; ionic strength, 0.225.

Hydrogen maleate concentration	Maleate ion concentration	k_0	E. m. f.
0.032	0.032	0.183	0.379
.048	.048	.206	.368
.064	.064	.233	.360

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(8) Brönsted and Guggenheim, THIS JOURNAL, **49**, 2554 (1927).

was not possible to convert these readings to actual *p*H values because of the unknown liquid junction potentials in the alcohol–water solutions.

It can be seen that the k_0's increase with increasing acid concentration although the *p*H remains constant. This shows that these reactions are general acid catalyzed.

Discussion

These experiments indicate that there can be little doubt that the reactions of *d*-carvone with phenylhydrazine, semicarbazide and hydroxylamine proceed by the same mechanism. The experimental facts which must be satisfied by a proposed mechanism may be summarized as follows: the reaction rates are proportional to the concentration of the ketone and to the concentration of the carbonyl reagent; the reactions are general acid catalyzed; and none of the reactions show any kinetic salt effect, which can be interpreted only as showing that the rate controlling step cannot be one between ions, but may be one between uncharged molecules or between an ion and an uncharged molecule.

Accordingly, the velocity expression common to all three of these reactions, and which must therefore be the velocity expression for the rate controlling step, appears to be

$$v = [R_2CO][BNH_2]k_i\Sigma[HA_i]$$

as has been shown by Conant and Bartlett[3] for the semicarbazide reaction. Since in our experiments the catalyzing acid was the conjugate acid, BNH_3^+, of the carbonyl reagent, this velocity expression becomes

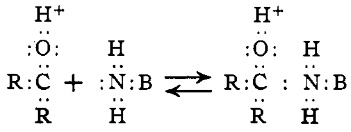
$$v = k_i[R_2CO][BNH_2][BNH_3^+]$$

Our experimental data are in agreement with the following mechanism, which is a slightly modified version of that proposed by Hammett.[4]

It seems probable that the function of the acid catalyst is to increase the positive charge density on the carbonyl carbon. Hence, the first step in the reaction is

$$(1)\quad R_2C::\ddot{\underset{..}{O}} + BNH_3^+ \rightleftharpoons R_2C:\ddot{\underset{..}{O}}:H^+ + BNH_2$$

which facilitates the acceptance of the free electron pair from the nitrogen of the carbonyl reagent

(2) 

$$R:\underset{\underset{R}{..}}{\overset{\overset{\overset{H^+}{..}}{:O:}}{C}} + :\underset{\underset{H}{..}}{\overset{\overset{H}{..}}{N}}:B \rightleftharpoons R:\underset{\underset{R}{..}}{\overset{\overset{\overset{H^+}{..}}{:O:}}{C}} : \underset{\underset{H}{..}}{\overset{\overset{H}{..}}{N}}:B$$

The remaining steps are

$$(3)\quad R_2C(OH)NH_2B^+ + BNH_2 \rightleftharpoons R_2C(OH)NHB + BNH_3^+$$

$$(4)\quad R_2C(OH)NHB + BNH_3^+ \rightleftharpoons R_2C(OH_2)NHB^+ + BNH_2$$

$$(5)\quad R_2C(OH)_2NHB^+ \rightleftharpoons R_2C{=}NHB^+ + H_2O$$

$$(6)\quad R_2C{=}NHB^+ + BNH_2 \rightleftharpoons R_2C{=}NB + BNH_3^+$$

A mathematical analysis of these reactions shows that if the first step is rate controlling, the velocity expression for the reaction would be

$$(1)\qquad v_1 = k_1[R_2CO][BNH_3^+]$$

If, instead, one of the other steps is rate controlling, the velocity expression would be

For (2): $v_2 = k_2K_1[R_2CO][BNH_3^+]$
For (3): $v_3 = k_3K_1K_2[R_2CO][BNH_2][BNH_3^+]$
For (4): $v_4 = k_4K_1K_2K_3[BNH_3^+][BNH_2][R_2CO]$
For (5): $v_5 = k_5K_1K_2K_3K_4[BNH_3^+][R_2CO]$
For (6): $v_6 = k_6K_1K_2K_3K_4K_5[BNH_2][R_2CO][BNH_3^+]$

where K_5 includes the relatively large constant concentration of water.

It follows that steps 1, 2 and 5 cannot be rate controlling since they do not yield the necessary velocity expression. There are no data to decide between steps 3, 4 and 6, all of which have the proper velocity expression.

Summary

1. A comparative polarimetric study of the reactions between hydroxylamine, phenylhydrazine and semicarbazide with *d*-carvone shows that these reactions are general acid catalyzed, show no salt effect, and that their velocities are proportional to the concentrations of the ketone and carbonyl reagent.

2. These results indicate that these three reactions proceed by the same mechanism.

3. The data here presented are in agreement with Hammett's mechanism for the semicarbazide reaction.

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