

STUDIES PERTAINING TO THE MECHANISM OF THE HETEROGENEOUS CANNIZZARO REACTION¹

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INTRODUCTION

The previous literature relating to the mechanism of the Cannizzaro reaction has been reviewed by Geissman (1) and by Alexander (2). The formulation of an adequate mechanistic hypothesis must integrate three salient facts.

1. The homogeneous reactions are characterized by third-order kinetics, the rates being representable by the equation: $d(\text{ArCHO})/dt = k(\text{ArCHO})^2(\text{OH}^-)$ (3, 4, 5, 6).

2. As demonstrated by the experiments of Fredenhagen and Bonhoeffer (7), performed in deuterated aqueous media, the hydrogen transfer involved in the Cannizzaro reaction takes place directly between aldehyde molecules, without intervention of the medium.

3. Benzyl benzoate has been isolated from benzaldehyde Cannizzaro reaction mixtures by Lachmann (8), and is therefore, under certain reaction conditions at least, an intermediate. No simple mechanistic formulation as yet proposed takes account of all three of these facts.

The present study of the heterogeneous Cannizzaro reaction, undertaken with the objectives of supplementing and, if possible, correlating the known facts, encountered special problems not ordinarily met in studies of the homogeneous reaction. The most significant of these, the elucidation of which constitutes the subject-matter of the present report, are: (a) anomalous variations in reaction rate dependent on the origin and history of the aldehyde; (b) abnormal variations in reaction rate with changing alkali concentration; (c) autocatalysis of the reaction; (d) the question of the locus of the reaction; and (e) abnormal differences in the reaction rates of substituted benzaldehydes.

To spare the reader unnecessary suspense and to facilitate his assimilation of the discussion that follows it may be stated at this point that, as conducted in this study, and as ordinarily employed preparationally, the so-called heterogeneous Cannizzaro reaction is essentially a composite of two homogeneous reactions occurring simultaneously in the two phases, the non-aqueous phase reaction being catalyzed by a product of the aqueous phase reaction.² Appar-

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² There is considerable evidence to suggest that, under certain experimental conditions, there may also be a Cannizzaro dismutation of the free-radical chain-reaction type. See *e.g.*: Haber and Willstätter, *Ber.*, **69**, 2844 (1931); Kharasch and Foy, *J. Am. Chem. Soc.*, **57**, 1510 (1935); Urushibara and Takebayashi, *Bull. Chem. Soc. Japan*, **12**, 328 (1937); Weiss, *Trans. Faraday Soc.*, **37**, 782 (1941). That problem is under further investigation in this laboratory.

ently the phase interface plays no significant part in any rate-determining step of the over-all reaction.

DESCRIPTION OF THE PRESENT STUDY

Anomalous variations in reaction rate with origin and history of the aldehyde. Moderate precautions suffice to insure highly reproducible reaction rates for the homogeneous Cannizzaro reaction in dilute solutions. Moreover, despite repeated attempts, no accelerators or inhibitors for the homogeneous reaction have been found except in the special case of formaldehyde. For the heterogeneous Cannizzaro reaction, on the other hand, reproducible rates are attainable only with rigorous application of special precautions.

Earlier studies in this laboratory by Kharasch and Foy (9) and Kharasch and Chenicek (10) revealed that no two samples of aldehyde were likely to undergo reaction at the same rate, and that for a given sample the reaction rate might vary erratically with aging. It was shown that, in general, the reaction rate was increased by exposure of the aldehyde to air or light, and that the

TABLE I
EFFECT OF ULTRAVIOLET ILLUMINATION OF BENZALDEHYDE ON RATE OF HETEROGENEOUS CANNIZZARO REACTION

CHARACTER OF SAMPLE	% CONVERSION (1 HR., 25°)
Purified benzaldehyde.....	11
Purified, irradiated benzaldehyde.....	88
Irradiated, redistilled benzaldehyde.....	14
Purified benzaldehyde with distillation residue from irradiated benzaldehyde added.....	82

increase in rate was roughly proportional to the duration and intensity of exposure. Slow, reproducible reaction rates were eventually obtained with aldehyde samples which had been subjected to low-temperature, low-pressure distillation in the dark.

It was shown by Kharasch and Richlin (11) that ultraviolet irradiation of degassed benzaldehyde in evacuated quartz vessels produces a relatively non-volatile accelerator (or accelerators) of the heterogeneous Cannizzaro reaction. The data of Table I, taken from unpublished work of Kharasch and Richlin (11), relating to experiments in which 5 cc. each of 48.2% aqueous potassium hydroxide and benzaldehyde were agitated in 18-cc. sealed tubes, indicate qualitatively the rate-accelerating effect of the photochemical product(s).

In experiments preliminary to the present study it was found that sunlight irradiation of benzaldehyde gives rise to a complex mixture of products which includes high-molecular-weight "polymer", benzoic acid, stilbene, benzoin, mesohydrobenzoin, mesohydrobenzoin dibenzoate, and, very probably, benzoin benzoate and benzil. Tests for accelerating properties revealed that mesohydrobenzoin significantly increases the rate of the heterogeneous reaction of benzaldehyde with 46% aqueous potassium hydroxide. Surprisingly enough

dl-hydrobenzoin was found to effect a considerably greater rate-acceleration.³ Representative data relating to experiments conducted at room temperature are presented in Table II.

Geib's (12) suggestion that the increase in heterogeneous Cannizzaro reaction rates when primary, or, to a lesser extent when secondary, alcohols are added to the reaction system is attributable to alterations in phase relationships scarcely seems adequate in this instance. The rate-accelerating influence of the hydrobenzoin has the appearance of a catalytic effect. Accordingly, several more or less similar glycols were tested for accelerating properties. In one series of experiments phenylethylene glycol and 1-phenyl-1,3 propanediol were both

TABLE II
EFFECT OF HYDROBENZOINS ON RATE OF HETEROGENEOUS REACTION OF PURIFIED
BENZALDEHYDE (5 CC.) WITH 46% AQUEOUS POTASSIUM HYDROXIDE (5 CC.)

HYDROBENZOIN	% CONVERSION (1.75 HR.)
None.....	3.6
Meso- (100 mg.).....	23.5
Racemic (100 mg.).....	41.9

TABLE III
EFFECT OF VARIOUS GLYCOLS ON RATE OF HETEROGENEOUS REACTION OF PURIFIED
BENZALDEHYDE (5 CC.) WITH 40% AQUEOUS POTASSIUM HYDROXIDE (5 CC.)

GLYCOL	REACTION TIME (HRS.)	% CONVERSION
None.....	1.5	3.6
Phenylethylene glycol.....	1.5	55.0
1-Phenyl-1,3-propanediol.....	1.5	48.5
None.....	2.0	8.2
Ethylene glycol.....	2.0	5.8
Glycerol.....	2.0	7.2
Pinacol.....	3.0	8.2

found to be somewhat superior to the hydrobenzoin as accelerators; in another series ethylene glycol, glycerol, and pinacol were found to be ineffective. Relevant data are presented in Table III.

Analysis of the nature of the catalytic action of the glycols is deferred to a later portion of this discussion. However, two conclusions may be drawn at this point.

1. The heterogeneous reaction is subject to accelerating influences which do not affect the homogeneous reaction in more or less aqueous solutions.
2. Some members of the classes of compounds which accelerate the heterogeneous reaction are normal impurities in benzaldehyde (and probably in substituted benzaldehydes as well).

³ *dl*-Hydrobenzoin has not been isolated from irradiated benzaldehyde but is, nonetheless, a probable photochemical reaction product.

It follows that the rate of a heterogeneous Cannizzaro reaction has no significance unless the purity of the aldehyde is rigidly controlled.

Abnormal variations in rate of the heterogeneous Cannizzaro reaction with changing alkali concentration. It is well established that the rate of the heterogeneous Cannizzaro reaction is extraordinarily sensitive to changes in the concentration of the base. The reaction of benzaldehyde in contact with 45% aqueous potassium hydroxide is complete in a few hours at room temperature; when 30% aqueous potassium hydroxide is used, several days may be required to effect the same conversion. If the over-all reaction rate showed a first-order dependence on the base concentration, a 33% decrease in the base strength

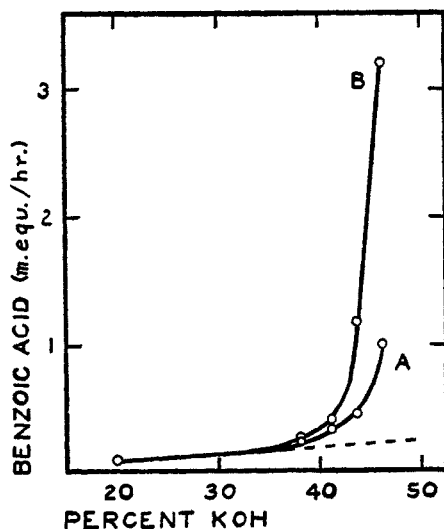


FIGURE 1. EFFECT OF ALKALI CONCENTRATION ON RATE OF CONVERSION

should only decrease the reaction rate by the same factor. Even if the dependence were second-order, the rate of reaction should not be reduced by much more than one-half. The observed decrease in rate under these circumstances is more nearly tenfold.

To study these variations, a series of experiments in which only the initial base concentration was varied was performed. To avoid substantial change in the initial concentrations of the reactants, the reactions were carried only to about 7.5% conversion, and the average rates thus determined were then plotted as a function of the initial alkali concentration (Curve A of Figure 1).

By inspection of the curve it is apparent that in the range of 20–38% potassium hydroxide, and presumably over the range of 0–38%, the reaction is slow and shows a nearly linear dependence on the base concentration. However, at about 38% potassium hydroxide some other factor intervenes to effect a relatively large increase in rate with slight increase in base concentration. The factor responsible for the marked sensitivity of the reaction rate to increasing alkali concentration in this range is the onset of *autocatalysis* by benzyl alcohol.

Autocatalysis of the heterogeneous alkaline dismutation of benzaldehyde by benzyl alcohol. The autocatalytic character of the heterogeneous Cannizzaro reaction (when the critical or a higher concentration of alkali is used) is apparent in a plot of the percentage aldehyde conversion as a function of time. In Figure 2 the variation in rate of reaction of a system initially composed of benzaldehyde and 2.44 molecular equivalents of 46.2% aqueous potassium hydroxide is recorded in this way. Notwithstanding the continuous decrease in the amount of benzaldehyde present and in the alkali concentration, the instantaneous reaction rate, as measured by the slope of the curve, continues to increase beyond 50% conversion. That the continuous increase in the reaction

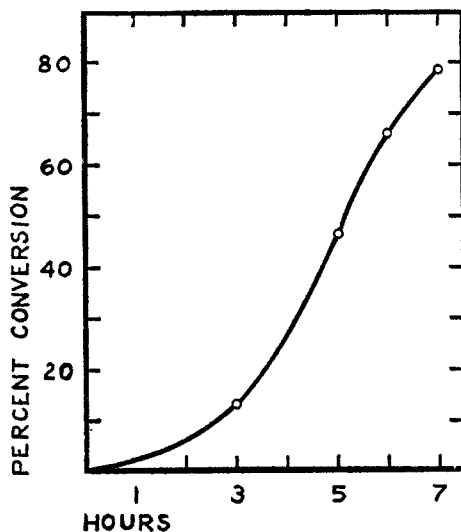


FIGURE 2. AUTOCATALYSIS OF THE HETEROGENEOUS CANNIZZARO REACTION

rate is attributable to the continuous increase in the amount of benzyl alcohol present is shown by the effect of small quantities of added benzyl alcohol upon the initial reaction rate.

In Figure 1, Curve B records a set of experiments performed under the same conditions as the experiments recorded in Curve A except that the benzaldehyde used contained 4 weight percent of benzyl alcohol. It is to be noted that vertically-corresponding points on the two curves were determined for identical reaction periods. In the 20–38% alkali range Curves A and B are experimentally indistinguishable, indicating that in this range the reaction rate is not appreciably affected by small amounts of initially-present benzyl alcohol. Beyond 38% potassium hydroxide concentration the curves diverge rapidly, and the vertical intervals between corresponding alkali-concentration points on the two curves are indicative of the autocatalytic effect of benzyl alcohol.

In the range of alkali concentrations where benzyl alcohol is without catalytic effect the average rate of reaction over the first 7.5% of conversion may fairly well approximate the true initial rate of reaction. The most probable value

for the true initial rate of reaction in the experiments in which autocatalysis occurs is approximated by extrapolation to high alkali concentrations of the rectilinear, coincident portions of Curves A and B of Figure 1.

Locus of the reaction. It is obvious that there is a critical point at which the nature of the reaction changes as the alkali concentration is increased. Understanding of the change must include some knowledge of the reaction site, which, *a priori*, could be in either the liquid phase, at the phase interface, or in some combination of these. In order to ascertain whether or not the over-all reaction rate shows an unequivocal dependence on the volume of either phase, a series of experiments in which a constant volume (5 cc.) of aqueous alkali was agitated with varying volumes (2 cc., 5 cc., 10 cc.) of benzaldehyde was undertaken.

TABLE IV
EFFECT OF VARYING PHASE-VOLUME RATIOS ON OVER-ALL CONVERSION RATE

EXPERIMENT	KOH (5 cc.) CONC'N (%)	C ₆ H ₅ CHO (cc.)	TIME (HRS.)	AVERAGE OVER-ALL ^a CONVERSION RATE
I A	20.3	2	13.0	0.095
B		5		.098
C		10		.101
II A	29.6	2	12.0	.131
B		5		.136
C		10		.125
III A	46.2	2	2.0	1.27
B		5		1.21
C		10		1.04
IV A	46.2	2 ^b	1.5	0.90
B		5 ^b		1.13
C		10 ^b		1.44

^a $d C_6H_5CO_2H/dt$, expressed in milliequivalents per hour.

^b Containing 2 weight percent of benzyl alcohol.

In two sets of experiments in which 20% and 30% potassium hydroxide solutions were used the over-all conversion rates (in terms of milliequivalents of benzoic acid produced per hour) did not vary (beyond the limits of experimental error) with variation in the volume of the benzaldehyde phase. The relevant data are summarized in sections I and II of Table IV. These results imply that at relatively low alkali concentrations the amount of benzaldehyde that disappears depends upon the volume and hydroxyl ion concentration (or activity) of the aqueous phase, and are consistent with the hypothesis that reaction takes place exclusively in the aqueous phase. Under the experimental conditions imposed the rate of diffusion of benzaldehyde into the aqueous phase evidently is not a rate-controlling factor. Other interfacial effects are not necessarily excluded (for the interfacial area presumably varies but little), but there is no evident compulsion to assume such effects.⁴

⁴ Supplementary experiments, described later in this discussion showed that interfacial variations do not materially affect the relationships here described.

When the described technique was extended to the reaction with 46.2% potassium hydroxide it became apparent that at higher alkali concentrations the over-all rate of the reaction is no longer determined by the volume and alkali concentration of the aqueous phase (section III, Table IV). Not only had the rate increased out of all proportion to the (first-power) increase in hydroxyl ion concentration of the aqueous phase; it now showed an inverse dependence on the volume of the benzaldehyde phase. These facts suggest the initiation of a catalyzed concurrent reaction in the benzaldehyde phase.

In a fourth series of experiments, varying volumes of benzaldehyde containing 2 weight percent of benzyl alcohol were treated with a fixed volume of 46.2% aqueous potassium hydroxide (section IV, Table IV). The over-all rate of reaction then showed an increase with increasing benzaldehyde volume.

These observations are consistent with the hypothesis that: (a) at all alkali concentrations there is a relatively slow⁵ hydroxide ion-catalyzed reaction in the aqueous phase, the rate of which is limited by the solubility of benzaldehyde in that phase; (b) above a critical alkali concentration of the aqueous phase there is a concurrent relatively rapid⁵ benzylate ion-catalyzed reaction in the benzaldehyde phase.

Re-examination of the data of sections III and IV of Table IV in the light of the proposed hypothesis may serve to clarify and substantiate the foregoing statement. In the absence of benzyl alcohol the dismutation of benzaldehyde begins in the aqueous phase, and in the early stage of the reaction benzyl alcohol is produced at the same rate regardless of the volume of the benzaldehyde phase. As the concentration of benzyl alcohol builds up, however, and benzylate ions are transferred to the benzaldehyde phase, the *concentration* of benzylate ions, which determines the rate of reaction in the non-aqueous phase is initially greater when the benzaldehyde volume is small, and correspondingly smaller when the benzaldehyde phase is large. For low percentage conversions, therefore, the over-all rate of conversion for the "heterogeneous" reaction is greater when the aldehyde phase is relatively small and less when the benzaldehyde phase is relatively large (section III, Table IV).

When a constant small amount of benzyl alcohol is initially present in the benzaldehyde, the two phase reactions proceed concurrently from the first, and the over-all rate of conversion ($d C_6H_5CO_2H/dt$) for small percentage conversions is greatest when the benzaldehyde phase is largest (section IV, Table IV). As the reaction proceeds, and as the benzylate ion concentration is increased more rapidly by transfer from the aqueous phase into the smaller benzaldehyde phase, the over-all rates of conversion in the three experiments should tend to converge.

That the nature and extent of the interfacial area do not materially affect any rate-determining step of the over-all reaction was shown with the aid of emulsifying agents. Although not ideal, fatty acid soaps were used as emulsifiers and proved fairly effective. In 46% alkali solution, potassium stearate and lau-

⁵ "Slow" and "rapid" are here used in the special sense implying contribution to the over-all reaction rate in terms of $d C_6H_5CO_2H/dt$.

rate were without perceptible effect on the over-all rate. In more dilute alkali solution, potassium laurate did increase the rate of reaction, but only by increasing the solubility of benzaldehyde in the aqueous phase.

Abnormal differences in reaction rates of substituted benzaldehydes. It is well known that substituted benzaldehydes undergo the homogeneous Cannizzaro reaction at varying rates (3). According to Weissberger and Haase (13) the homogeneous reaction rates of the *meta*- and *para*-substituted benzaldehydes may be related to the acid dissociation constants of the respective corresponding benzoic acids (the *ortho*-substituted benzaldehydes exhibit an "ortho effect"). In the heterogeneous reaction the relative reactivities of the aldehydes fall in the same order, but the differences in over-all rates of conversion are greatly exaggerated. For example, the data of Molt (3) indicate that in methanol at 100° the third-order constant for the rate of reaction of benzaldehyde with

TABLE V
EFFECT OF ADDED BENZYL ALCOHOLS ON OVER-ALL RATE OF REACTION OF BENZALDEHYDE WITH 46.2% AQUEOUS POTASSIUM HYDROXIDE

ADDED ALCOHOL	TIME (MIN.)	% CONVERSION
None.....	60	4.1
Benzyl.....	60	15.6
<i>p</i> -Nitrobenzyl.....	60	48.1
None.....	100	11.2
Anisyl.....	100	28.9
Benzyl.....	100	43.7
<i>p</i> -Chlorobenzyl.....	100	48.6

sodium hydroxide is greater than that of anisaldehyde for the analogous reaction by a factor of 20–25. In the heterogeneous reaction with 46% aqueous potassium hydroxide, the initial over-all rate of conversion for benzaldehyde is rapid, whereas that for anisaldehyde is almost negligibly slow, the difference factor being estimated as of the order of 200–500.⁶ *p*-Nitrobenzaldehyde, on the other hand, is more reactive than benzaldehyde.

Taken in conjunction with the facts set forth in the foregoing discussion, these observations suggest that the respective benzylate ions differ considerably in their ability to catalyze the aldehyde-phase reaction. In two sets of experiments designed to test this point small constant molar percentages of several benzyl alcohols were added to samples of benzaldehyde, which were then treated with 46% aqueous potassium hydroxide (Table V).

The catalytic effectiveness of the respective benzylate ions would appear to be related to the probable acidities of the respective alcohols.

Assuming that the abnormally low reactivity of anisaldehyde in the heterogeneous reaction with 46% aqueous potassium hydroxide is attributable to

⁶ It should be noted that the quantities mentioned, namely, the third-order rate constant (k) for the homogeneous reaction and the overall rate of conversion ($d \text{RCO}_2\text{H}/dt$) for the heterogeneous reaction, are not directly comparable.

the relatively feeble autocatalytic properties of the anisylate ion, it should be possible to accelerate the conversion by the addition of suitable aldehyde-phase reaction catalysts. This possibility was realized in two sets of experiments summarized in Table VI.

Methanol and benzyl alcohol proved relatively weak accelerators; the glycols tested were much more effective. Phthalyl alcohol and phenylethylene glycol are probably even better than the data of Table VI would indicate, for in the quantities used they were not completely soluble in anisaldehyde. It seems likely that with suitable catalysts the heterogeneous conversion of other relatively unreactive aldehydes could be accelerated.

TABLE VI

EFFECT OF ALDEHYDE-PHASE CATALYSTS ON THE RATE OF CONVERSION OF ANISALDEHYDE IN THE PRESENCE OF 46.2% AQUEOUS POTASSIUM HYDROXIDE

CATALYST, MOLE % ^a	TIME (HOURS)	% CONVERSION
None.....	28	0.95
Benzyl alcohol, 5.0.....	28	2.24
Phthalyl alcohol, 5.0.....	28	5.38
1-Phenyl-1,3-propanediol, 5.3.....	18	22.8
1-Phenyl-1,3-propanediol, 11.5.....	18	50.9
None.....	70	5.65
Methanol, 12.2.....	70	3.84
Methanol, 24.4.....	70	6.08
Methanol, 36.6.....	70	20.8
Phenylethylene glycol, 11.5.....	70	74.3

^a Based on moles of anisaldehyde used.

DISCUSSION

Concerning the major problems peculiar to the heterogeneous Cannizzaro reaction (as outlined in the Introduction) the following facts have been established.

1. Unlike the homogeneous reaction, the heterogeneous Cannizzaro reaction is remarkably susceptible to the catalytic effects of small amounts of polyhydroxy compounds ordinarily present as impurities in benzaldehyde that has been aged under ordinary laboratory conditions.

2. Benzyl alcohol, although a much less effective catalyst than some of the glycols investigated, is responsible for the autocatalytic character of the heterogeneous benzaldehyde Cannizzaro reaction when highly concentrated alkaline solutions are used.

3. The alcoholic (or glycolic) catalysts function by effecting an aldehyde-phase reaction which contributes much more toward the over-all rate of conversion than does the concurrent aqueous-phase reaction.

4. The marked variation in the reactivity of substituted benzaldehydes is largely due to the relative catalytic efficiencies of the corresponding benzylate ions.

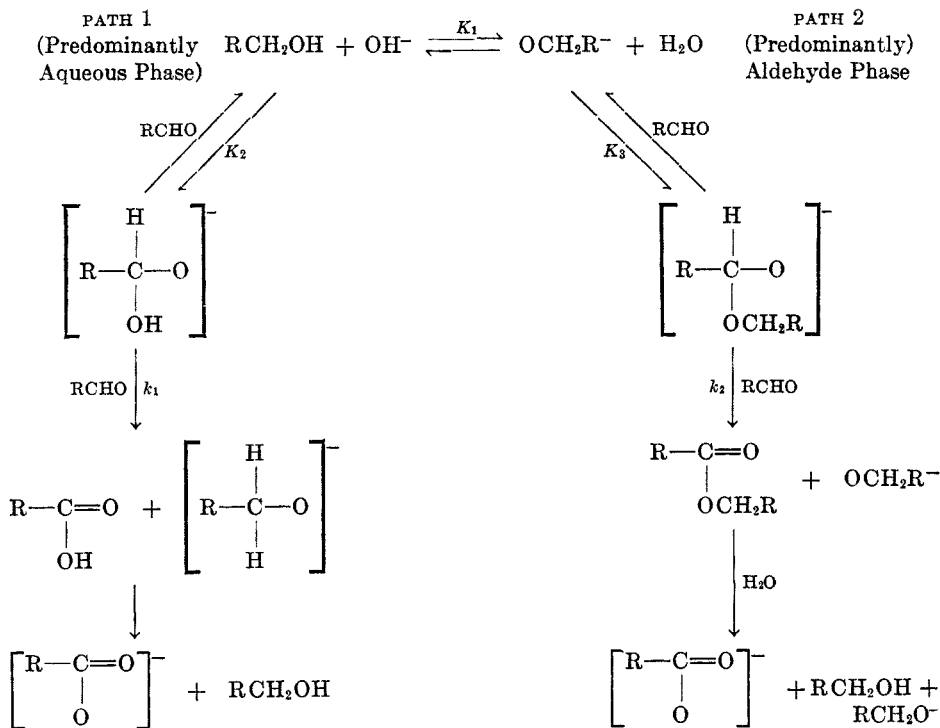
5. The rate of conversion of relatively unreactive aldehydes (such as anisaldehyde) may be materially accelerated by suitable catalysts.

Proposed reaction scheme, and some verifiable implications thereof. These facts, together with the results of kinetic studies of the homogeneous Cannizzaro reaction, supply a basis for the formulation of the proposed reaction scheme outlined in Diagram I.

At all alkali concentrations the reversible metathetical reaction, to which the equilibrium constant K_1 has been assigned, takes place. Within the limits of

DIAGRAM I

PROPOSED REACTION SCHEME FOR THE HETEROGENEOUS ALKALINE DISMUTATION OF AROMATIC ALDEHYDES



solubility of the components, the extent of displacement of the equilibrium toward the right will be determined primarily by the acidity of the alcohol (RCH_2OH) and the concentration of the hydroxyl ion. At low alkali concentrations the metathetical reaction has no significant effect upon the rate of conversion of aldehyde. There is negligible diffusion of alkoxide ions into the non-aqueous phase, and conversion by Path 2 in the aqueous phase must be very slight, and may proceed at a rate not greatly different from that of conversion by Path 1. At higher alkali concentrations the relative solubilities of alkoxide ion in the aqueous and non-aqueous phases alter sharply, and there is

partial, or perhaps even preferential, distribution in the non-aqueous phase. Disproportionation of aldehyde to ester then takes place rapidly in the non-aqueous phase. The total concentration of alkoxide ions is further increased by hydrolysis of the ester, in part by diffusion of water into the aldehyde phase, but probably much more by diffusion of ester to the interface or into the aqueous phase.

The over-all conversion rate implied by the reaction scheme suggested in Diagram I may be defined by the expression:

$$d(\text{RCHO})/dt = k_1 (\text{OH}^-) (\text{RCHO})^2 + k_2 (\text{OCH}_2\text{R}^-) (\text{RCHO})^2.$$

No attempt has been made as yet to estimate the relative values of k_1 and k_2 , but it is evident that if k_1 is not enormously greater than k_2 the rate of conversion by Path 2 will greatly exceed the rate of conversion by Path 1, which is sharply limited by the solubility of the aldehyde in the aqueous phase.

Apparent conflicts in hitherto available evidence as to whether or not benzyl benzoate is an intermediate in the alkaline dismutation of benzaldehyde are satisfactorily resolved by the reaction scheme proposed (Diagram I). In essentially aqueous-phase reactions the ester is a possible, but not a necessary intermediate. In view of the rapidity with which benzyl benzoate undergoes saponification (2a) it would not be an isolable intermediate. In essentially non-aqueous-phase reactions the ester is a probable (though again not a necessary) intermediate. Under properly chosen conditions it is unquestionably isolable.

It was shown in section III of Table IV that in the early stages of the heterogeneous dismutation of benzaldehyde by 46% aqueous potassium hydroxide there is a slight inverse dependence of the over-all rate of conversion on the volume of the aldehyde phase. The kinetic scheme outlined in Diagram I requires that all experiments in section III of Table IV should show the same over-all rate. (This follows from the fact that during the early stage of the reaction the same amount of benzyl alcohol will be present in all reaction mixtures, owing to the fixed volume of the aqueous phase. The concentration of benzylate ion in the oil phase will then vary inversely as the volume of the oil phase. However, the over-all amount of reaction in the oil phase depends upon the product of the benzylate concentration and the volume of benzaldehyde, and therefore should remain constant in all experiments.) The discrepancy between the theory and the experimental results is to be attributed to a differential in the time lag involved in hydrolyzing benzyl benzoate to the catalytically effective benzyl alcohol. This is borne out by the fact that addition of potassium laurate to a similar series of reaction mixtures (to facilitate equilibrium between the two phases) brings the results in closer accord with theory, as shown in Table VII.

In section IV of Table IV a different situation prevails, and it is to be noted that initially the over-all rate of reaction by Path 2 (Diagram I) will vary directly as the volumes of benzaldehyde present (for the benzylate ion concentration will be the same in the benzaldehyde). However the constant increment of benzyl alcohol contributed by the aqueous phase exerts a leveling effect, and the total over-all rates of reaction converge with increasing conversion.

According to the reaction scheme proposed (Diagram I), the effectiveness of a hydroxylic compound as a catalyst for the heterogeneous Cannizzaro reaction must depend upon: (a) the facility with which it forms alkoxide, and (b) the possibility of transfer of the alkoxide to the aldehyde phase. For a given alkali concentration, the first of these factors is a function of the acidity of the hydroxylic compound. The second is a function of the distribution coefficient, which is to say, of the solubilities in the aqueous and aldehydic phases, respectively.

For structurally similar alcohols (whose alkoxides presumably would not differ greatly in solubility properties), the relative acidities should be the controlling factor. This has already been seen to be true of the benzyl alcohols (Table VI). Supplementary experiments with a variety of miscellaneous alcohols (Table VIII) tend to substantiate this view. For example, the strongly acidic phenol is an excellent catalyst, the mildly acidic benzyl alcohol a fair catalyst, and the very weakly acidic *t*-butyl alcohol and benzohydrol are substantially ineffective.

TABLE VII
OVER-ALL RATES OF CONVERSION OF VARYING VOLUMES OF BENZALDEHYDE BY 46.2%
AQUEOUS POTASSIUM HYDROXIDE (5 CC.) IN THE PRESENCE OF POTASSIUM LAURATE
(47.6 MG.) IN TWO HOURS

VOL. C ₆ H ₅ CHO (cc.)	<i>d</i> C ₆ H ₅ CO ₂ H (MILLI EQUIV. PER HR.)
2	0.93
5	1.02
10	1.05

Relative solubilities, however, exert a modifying effect on the behavior of structurally dissimilar alcohols. At first thought it might seem improbable that a salt would undergo appreciable distribution between an aqueous phase and a relatively non-polar non-aqueous phase. There is reasonable question, however, that 46% aqueous potassium hydroxide should be regarded as an essentially aqueous medium. Thermodynamic studies by Akerlof and Bender (14) indicate that at high alkali concentrations—*i.e.*, about 7 *molar* (31%), or higher—there is a “structural constancy” of the solutions. In other words it is doubtful that such solutions contain any “free” water at all.

It was noted visually in the course of this study that catalytically effective alkoxides, although often soluble in water, are virtually insoluble in concentrated aqueous potassium hydroxide solutions. On the other hand, it was found that the potassium salts of some catalytically ineffective polyhydroxy compounds, which must be relatively acidic (*e.g.*, ethylene glycol, glycerol, pinacol), are not salted out of concentrated alkali solutions.

It was found that the highly effective catalyst potassium phenolate is very slightly soluble in concentrated aqueous potassium hydroxide solution, from which it separates as the dihydrate. The dihydrated salt dissolves readily in

TABLE VIII
EFFECT OF MISCELLANEOUS HYDROXY COMPOUNDS ON RATE OF HETEROGENEOUS
REACTION OF BENZALDEHYDE (5 CC.) WITH 46.2% AQUEOUS POTASSIUM HYDROXIDE
(5 CC.)

COMPOUND, MOLE %	TEMP. (°C)	TIME (HRS.)	% CONVERSION
None	24.0	2.25	8.2
Methanol, 4.00			11.6
<i>n</i> -Amyl alcohol, 4.00			33.7
Lauryl alcohol, 4.00			39.1
None	26.2	2.25	8.9
Methanol, 6.00			23.4
<i>n</i> -Amyl alcohol, 6.00			62.4
None	27.5	2.25	11.2
Methanol, 8.00			71.0
<i>n</i> -Amyl alcohol, 8.00			67.8
Isopropyl alcohol, 8.00			37.1
Benzyl alcohol, 3.92	25.0	1.40	34.3
Methanol, 13.24			69.9
<i>n</i> -Amyl alcohol, 4.80			20.7
<i>t</i> -Butyl alcohol, 5.72			6.3
Benzyl alcohol, 3.92	27.0	1.00	19.8
Benzyl alcohol, 19.60			59.6
<i>n</i> -Amyl alcohol, 4.80			15.8
<i>n</i> -Amyl alcohol, 24.00			54.3
None	24.0	3.00	12.1
Benzyl alcohol, 3.92			78.6
Benzohydrol, 2.32			14.0
None	25.0	3.00	12.8
Phenylbenzylmethanol, 2.16			11.4
α -Phenylethanol, 3.48			11.0
Phenethyl alcohol, 3.48			51.7
None	25.0	3.00	10.6
Hydrocinnamyl alcohol, 2.00			38.9
Phenethyl alcohol, 3.48			61.8
None	24.5	2.00	7.2
Phenethyl alcohol, 3.48			37.0
Benzyl alcohol, 3.92			48.6
Phthalyl alcohol, 3.08			88.5
None	26.9	2.75	21.2
Phenol, 4.20			68.9
Stearyl alcohol, 3.70 ^a			28.9

TABLE VIII—*Concluded*

COMPOUND, MOLE %	TEMP. (°C)	TIME (HRS.)	% CONVERSION
None	25.0	2.00	7.8
Stearyl alcohol, 1.48			9.4
1,10-Decanediol, 2.44			23.0
Oleyl alcohol, ^a 0.16			41.6
None	24.5	2.00	6.5
Oleyl alcohol, ^b 0.16			5.8
None	24.5	2.10	5.3
Oleyl alcohol, ^b 0.32			10.1
Oleyl alcohol, ^a 0.32			62.8
None	26.0	3.00	11.0
Cumene hydroperoxide, 0.14			15.1
None	26.0	2.00	6.8
Tung oil, 4.0 ^d			37.0
Linseed oil, 4.0 ^d			41.9

^a Containing peroxides.

^b Peroxide-free.

^c Incompletely soluble.

^d Weight percent.

benzaldehyde at room temperature and initiates a rapid exothermic reaction which yields potassium benzoate and benzyl alcohol. The anhydrous salt is not appreciably soluble in benzaldehyde at room temperature, but at 100° catalyzes a reaction which yields benzyl benzoate.

EXPERIMENTAL

Purification of aldehydes. Commercial *benzaldehyde* (Merck's N.F. quality) in five-pound brown bottles, used as a source of supply, was always kept under nitrogen in a dark closet. The methods of purification of the benzaldehyde were essentially the same as those used by Chenicek (10), Foy (9), and Richlin (11). The benzaldehyde to be used in any given set of experiments was always purified immediately before use. A 100-cc. portion was washed with two 10-cc. portions of 10% aqueous potassium hydroxide (to remove phenolic antioxidants and benzoic acid) and with two 10-cc. portions of a saturated sodium sulfite solution (to remove peroxidic materials), was dried over sodium sulfate under nitrogen in the dark, and was then transferred to a distillation apparatus. The distillation apparatus consisted of two 125-ml. flasks connected by a yoke of 18-mm. glass tubing. A side-arm of 10-mm. tubing was inserted at the center of the yoke to permit connection to the vacuum line. The benzaldehyde which had been placed in one bulb of the distillation apparatus was cooled to -80°, and the apparatus was then evacuated to about 10⁻⁵ mm. pressure. The benzaldehyde was degassed by the usual vacuum-line technique. It was then distilled from the one bulb to the other by cooling the second bulb to -80° while allowing the first bulb to warm to room temperature. The distillation and subsequent operations with the aldehyde were carried out in the dark.

The purification of *anisaldehyde* was carried out in a manner similar to that described for benzaldehyde.

Preparation of potassium hydroxide solution. Potassium hydroxide stock solutions varying in concentration from 20 to 53% were prepared by dissolving the requisite quantities of U.S.P. potassium hydroxide pellets (containing *ca.* 3% of potassium carbonate) in freshly boiled distilled water. The solutions were standardized by titration with standard acid, using phenolphthalein indicator, and were stored in Pyrex bottles which had previously contained strong alkali solutions. The potassium hydroxide solutions were standardized from time to time to ascertain whether the normality decreased owing to attack on the glass; no changes were ever noted.

Purity of compounds tested for catalytic activity. The melting points of all crystalline compounds were determined and compared with those recorded in the literature. Liquid compounds were distilled prior to use.

Preparation of potassium phenolate. The preparation of potassium phenolate requires special mention because of its novelty as a reagent. The *dihydrate* was prepared by adding 40% aqueous potassium hydroxide to molten phenol at 60–70° to the point of incipient precipitation. On cooling to 0° the salt crystallized in large white plates which were filtered and washed successively with 20% aqueous potassium hydroxide, a small quantity of water, and ether. The crystals were allowed to stand in a desiccator over calcium chloride before use.

Two different methods were used to prepare *anhydrous* potassium phenolate.

(A) Distilled phenol (94 g., 1 mole) contained in a 150-cc. flask was heated to 45°. The air in the flask was displaced by nitrogen; 3.9 gms. (0.1 mole) of potassium metal was then added to the phenol. To avoid too violent a reaction it was necessary to cool the reaction intermittently with a Dry Ice–ether bath while the potassium dissolved. The temperature should be maintained somewhere between the melting points of phenol and potassium. Aliquot samples of this stock solution of potassium phenolate in phenol were transferred to empty reaction vessels, and the excess of phenol was removed by evaporation at reduced pressure (10^{-3} mm.).

(B) To distilled phenol (141 g., 1.5 mole) contained in a 250-cc. flask under a nitrogen atmosphere and heated to 45° was added 33.6 g. of a 50% aqueous potassium hydroxide solution. Suitable aliquots of this stock solution were pipetted into reaction vessels, and the water and excess phenol were removed at reduced pressure. To insure the complete absence of water additional molten phenol was added to the residue, and the phenol was again removed by distillation at 10^{-3} mm. and 130°. This procedure yielded potassium phenolate which was considered satisfactory for experimental purposes.

Methods of operation. All the Cannizzaro reactions with aqueous potassium hydroxide recorded in this paper were carried out in Pyrex glass tubes (120 × 18 mm.). The reactants were pipetted into the reaction tubes which had been previously swept out with nitrogen. The denser alkali solution was added first and then frozen in a Dry Ice–chloroform bath to prevent premature mixing with the aldehyde. The additive, if any, and the aldehyde were next added, and the reaction mixture was chilled to –80°. The vessel was then evacuated, and the reactants were degassed, after which the tube was sealed off. The reaction mixtures were then warmed to room temperature and agitated in a horizontal position on a horizontal shaking machine with a frequency of about 200 cycles per minute.⁷

Method of analysis. The percentage conversion was followed by determination of the amount of *benzoic acid* formed. The reaction vessels were opened, and the contents were transferred to 100-ml. separatory funnels. The reaction mixtures were each extracted with three 50-cc. portions of ether to remove benzyl alcohol and unchanged benzaldehyde. The alkaline solutions were then acidified with hydrochloric acid and reextracted with three 50-cc. portions of ether. The latter ether extracts were evaporated to dryness in tared

⁷ Thermostatic control of the reaction temperature was not employed because, until the factors affecting the rate of reaction had been elucidated, it was thought that valid comparisons could be made only among individual experiments of a set which were run simultaneously.

flasks, dried in a vacuum desiccator overnight and then weighed. Occasionally the results of this gravimetric analysis were checked by titrating the weighed acid with standard base; no disagreement was ever noted. Experiments with known mixtures have indicated that the method is accurate to within $\pm 3\%$.

CANNIZZARO REACTIONS WITH POTASSIUM PHENOLATE

(a) *Potassium phenolate dihydrate*. To 21.2 g. (0.2 mole) of benzaldehyde, contained in a 50-cc. flask under nitrogen, was added 16.8 g. (0.1 mole) of potassium phenolate dihydrate. The resultant solution rapidly warmed to about 50° and almost immediately a bulky precipitate of potassium benzoate appeared. No attempt was made at a quantitative estimation of the degree of conversion, but both benzoic acid and benzyl alcohol were identified as reaction products [The benzyl alcohol was isolated by extraction of the reaction product with water, treatment of the remaining oil with sodium bisulfite (to remove excess benzaldehyde), further washing of the residue with alkali solution (to remove phenol), followed by distillation].

(b) *Anhydrous potassium phenolate*. To 1.32 g. (0.01 mole) of anhydrous potassium phenolate, contained in a 50-cc. flask, was added 50 g. (0.47 mole) of benzaldehyde. The flask was sealed off and was then heated at 100° for 18 hours. The reaction products were worked up as follows. The reaction mixture was filtered, and the filtrate was distilled in a Hickman still to remove residual salts. The distillate was redistilled through a Vigreux distilling-column at 10 mm. pressure to yield 15 g. of benzyl benzoate (m.p. 19°). The ester was further identified by its refractive index and saponification equivalent.

The incomplete conversion of aldehyde to ester is attributable to the fact that a small amount of condensation to form resins occurs between phenol and benzaldehyde under the reaction conditions employed, the net effect of which is to destroy the catalyst. It is believed that a more careful search for optimum reaction conditions would lead to quantitative conversions.

SUMMARY

1. The heterogeneous Cannizzaro reaction has been investigated, and the following problems peculiar to it have been explained:

(a) the anomalous variations in reaction rate with differences in the origin and history of the aldehyde; (b) the abnormal sensitivity of the reaction rate to changing alkali concentration; (c) the influence of autocatalysis on the reaction rate; (d) the locus of the reaction; and (e) abnormal differences in the reaction rates of substituted benzaldehydes.

2. The Cannizzaro reaction is shown to occur exclusively in the aqueous phase at low alkali concentrations.

3. At high alkali concentrations a concurrent, but much faster, oil-phase conversion is shown to take place.

4. The oil-phase reaction is shown to be subject to catalysis by some alcohols and glycols, and the conditions for catalytic effectiveness are set forth.

5. A comprehensive mechanism to explain all the known facts about the Cannizzaro reaction is outlined.

6. Potassium phenolate dihydrate is shown to be an effective reagent for the dismutation of benzaldehyde to the conventional Cannizzaro reaction products.

7. Anhydrous potassium phenolate is shown to be an effective catalyst for the conversion of benzaldehyde to benzyl benzoate.

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