90. *The Influence of Pressure on a Number of Organic Reactions in the Liquid Phase.*

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IT is of interest to consider some of the ways in which a chemical reaction may be influenced by an increase in pressure. In the first place the velocity will be increased, because the concentrations of the reacting substances will increase as the system is compressed. Owing to the small compressibilities of liquids, the increases in concentration will be far smaller for reactions in a liquid than for those in a gaseous phase. On the other hand, the velocity is a function of the collision rate between the molecules of the reactants, and this rate is proportional to the product of the concentrations in the case of a gas, in which the space occupied by the molecules is negligible in comparison with the total volume (cf. Hinshelwood, " Kinetics of Chemical Changes in Gaseous Systems," 3rd Ed., p. 28, 1933). Besides this, in the case of a highly compressed gas or of a liquid, the probability of a collision taking place increases as the space occupied by the molecules becomes comparable with the total volume (cf. Enskog, *K. Svenska Vetenskapsakad. Hand.*, 1921, **63**, No. 4, p. 8). If the latter factor is taken into account, it would seem that an increase in pressure may exert a greater influence on the velocity of a liquid reaction than would be expected from a consideration of the small increase in concentration alone.

The velocity would also be influenced by pressure if the potential energy gained by the system as a result of the isothermal compression is available as part of the activation energy necessary for reaction. If this be so, there would be an increase in the concentration of the molecules possessing the requisite minimum energy of activation, and the velocity of the reaction would therefore be increased.

In a reversible reaction a further influence of pressure follows from the principle of Le Chatelier : if such a reaction involves a change in volume, the application of pressure will shift the position of equilibrium to the side of lesser volume. Even if there is no such change in volume at atmospheric pressure, the compressibilities of the reactants and resultants may be different, so that there may be a change in volume under pressure, and, therefore, a corresponding shift in the equilibrium. The position of equilibrium will also be shifted if the application of pressure leads to a change in the specific heat of the reacting substances, and hence, to a change in the heat quantities involved in the reaction. Calculations from the compressibility data of certain gases have shown that such a change in specific heat should occur (Deming and Shupe, *Physical Rev.*, 1931, **37**, 638; **38**, 2245 ; 1932, **40**, 848), and this has been confirmed experimentally in some cases (Krase and Mackey, *Ind. Eng. Chem.*, 1930, **22**, 1060).

Besides the above influences, Michels (*Proc. Roy. Soc.*, 1930, *A*, **127**, 258) has suggested that the application of a sufficiently high pressure may, by forcing the molecules into close contact, result, *inter alia*, in an alteration in the electrostatic fields round the molecules. Such an alteration might become evident in an induced or an increased polarity, possibly resulting in enhanced chemical reactivity, or in a change in the degree of ionisation. In the latter connexion, it is of interest that Tammann and other workers (*Z. anorg. Chem.*, 1929, **182**, 353; **183**, 1) have found that pressures up to 3000 atm. influence the electrical conductivity of aqueous and non-aqueous solutions of electrolytes to a greater degree than can be accounted for by the volume changes and the effect on the mobility of the ions.

Little systematic work has so far been carried out on the effect of high pressures on chemical reactions in the liquid phase. Cohen and his collaborators (cf. *Z. physikal. Chem.*, 1928, **138**, 169, for references), following a number of earlier workers, have, however, made an extensive study of the effect of pressures up to 1500 atm. on the hydrolysis of esters and of sucrose in aqueous and other solutions, in the presence of different acids and bases as catalysts. It was found that pressure had a marked effect on the velocity of such reactions, especially in mixed solvents, and that the effect was positive or negative according to the catalyst used. Moesveld (*ibid.*, 1923, **103**, 486) has also shown that the reaction between bromic and hydrobromic acids in aqueous solution is retarded by pressure.

Bridgman and Conant (*Proc. Nat. Acad. Sci.*, 1929, **15**, 680) have made a preliminary study of the effect of pressures up to 12,000 atm. on a number of organic substances. They found that amylene, pinacol, *tert.*-amyl alcohol, diacetone alcohol, aniline acetate dissolved in aniline, solid maleic acid, benzoquinone in *iso*propyl alcohol, and phenol in 20% aqueous formaldehyde were not appreciably affected, whilst isoprene, dimethylbutadiene, styrene, and indene were partly polymerised, and *n*- and *iso*-butaldehyde were converted into unstable polymerides which reverted to the original aldehydes at atmospheric pressure. Further, Conant and Tongberg (*J. Amer. Chem. Soc.*, 1930, **52**, 1659) and Conant and Peterson (*ibid.*, 1932, **54**, 629) have made a more detailed study of the effect of pressures up to 12,000 atm. on the polymerisation of the conjugated dienes (isoprene, etc.) and of the butaldehydes, and Tammann (*Z. anorg. Chem.*, 1931, **200**, 113) has studied the velocity of polymerisation of isoprene under pressures up to 3000 atm.

Except for the work of Bridgman and Conant, no attempts have been made to study the effect of pressure on organic reactions in general, and we have therefore undertaken a survey of such pressure effects in the light of the possible influences discussed above. For instance, a reaction such as the Diels reaction, which occurs between substances of high reactivity at atmospheric pressure in the absence of catalysts, might occur under high pressure between similar substances of lower reactivity. Again, a reaction which proceeds readily at atmospheric pressure in the presence of a catalyst might proceed readily without that catalyst under pressure. Finally, a reaction proceeding at atmospheric pressure in the absence of catalysts might proceed faster under pressure.

The choice of reactions was somewhat limited, for it was desired, in the first instance, to study reactions in the absence of solvents, whilst it was considered desirable that part, at least, of the reaction mixture should be liquid at the highest pressures to be used. It had therefore to be borne in mind that a pressure of 3000 atm. increases the melting points of most substances by 40—80°. It was also necessary that the reagents should not react with the mercury used to transmit the pressure.

The survey now covers some 50 reactions of different types which have been studied under pressures up to 3000 atm. and at temperatures up to 180°. An outline of the results obtained is given below.

Results.—From a study of the reactions between maleic anhydride and aromatic compounds it was found that reactions of this type, which do not proceed at atmospheric pressure (in the absence of catalysts), do not proceed at a pressure of 3000 atm. and the same conditions of temperature; *e.g.*, although maleic anhydride and anthracene condense readily at 200° and slowly in toluene solution at 40° at atmospheric pressure, no reaction occurs at either atmospheric pressure or 3000 atm. between maleic anhydride and the less reactive naphthalene, toluene, or benzene at temperatures up to 180°.

The study was then extended to reactions between phthalic anhydride and aromatic hydrocarbons, which are known to occur only in the presence of aluminium chloride. It was again found that there was no reaction under pressure in the absence of catalysts or in the presence of milder catalysts.

In view of these negative results some reactions which normally proceed in the presence of milder catalysts were next tried, and it was found that the reactions between aromatic amines and benzaldehyde, which are catalysed by acids, were markedly influenced by pressure; *e.g.*, the reaction between dimethylaniline and benzaldehyde (with no great precautions to remove the last traces of benzoic acid) proceeded slowly at atmospheric pressure at 150°, but the yield in the same time was increased about 8-fold at 3000 atm. at the same temperature, and that the pressure effect persisted in the presence of 1% of benzoic acid. On the other hand, the less reactive aromatic ketones did not react with dimethylaniline at 180° either at atmospheric pressure or at 3000 atm. in the absence of added catalysts.

Owing to the great difficulty of ensuring the absence of acids in reactions involving benzaldehyde, and because of the failure of ketones to react with aromatic amines, a similar type of acid-catalysed reaction, *viz.*, the acetal reaction, was now studied. It was found that acetaldehyde and ethyl alcohol (both freed from acid substances) reacted slowly at atmospheric pressure at 60° but gave a 9-fold yield in the same time at 3000 atm. at the same temperature.

Attempts to prepare acetal from the less reactive ethyl ether by the reaction $CH_3{\cdot}CHO + Et_2O \longrightarrow CH_3{\cdot}CH(OEt)_2$, which is not known to occur under any conditions at atmospheric pressure, were unsuccessful at 3000 atm.

In view of the positive pressure effects found with acid-catalysed reactions, some examples of base-catalysed reactions were tried, but the effects were less marked. Acetaldehyde and ethyl malonate or acetoacetate showed no detectable reaction either at atmospheric pressure or at 3000 atm. in the absence of a catalyst, and similarly the tautomeric change of *o*-xylylene dicyanide into iminocyanohydrindene, which is only known to occur in the presence of sodium ethoxide, could not be made to proceed under pressure without this catalyst. Benzaldehyde and chloroform, which react very slowly at atmospheric pressure, showed a small increase in reaction rate at 3000 atm.

The investigation was now extended to reactions which are known to proceed at atmospheric pressure in the absence of catalysts, *e.g.*, those involving quaternary ammonium salt formation. Cetyl bromide and pyridine react at a moderate rate at atmospheric pressure and the yield in the same time was found to be 4—8 times as great at 3000 atm. Cetyl chloride, which is less reactive than the bromide, showed a similar pressure effect. Attempts to prepare alkylpyridinium hydroxides directly from pyridine and cetyl alcohol or methyl alcohol, however, gave negative results under all conditions. It is interesting to note in the reaction between ethylene dichloride and pyridine that, whilst at atmospheric pressure and 80° the main product is β-chloroethylpyridinium chloride, the application of high pressure strongly favours the addition of a second molecule of pyridine to give *ethylenedipyridinium dichloride*. 8 : 8′-Dichloro-5 : 5′-diquinolyl, which does not form a quaternary halide with ethyl iodide, could not be induced to do so at a high pressure. Triethanolamine and cetyl bromide do not form a quaternary salt at atmospheric pressure, but removal of hydrogen bromide from the cetyl bromide takes place to give hexadecene and the hydrobromide of the base. Under pressure, no quaternary salt formation was observed, whilst the known reaction was accelerated. Another class of reaction of this type is the addition of organic acids to olefins to give esters of the corresponding alcohols. Several examples of this class were studied, and the pressure effects were of the same order as those previously found.

A number of reactions of various types have also been investigated, and all those which proceeded at atmospheric pressure were accelerated by pressure. Of these, the most interesting is the hydrolysis of benzonitrile in the presence of alkalis, in which pressure exercises a selective effect on the two possible reactions; conditions may be realised under which at atmospheric pressure a small yield of benzamide is obtained whilst under pressure the product is benzoic acid, or, alternatively, so that benzamide is obtained under pressure whilst there is no appreciable reaction at atmospheric pressure.

The effect of pressures up to 3000 atm. on the polymerisation of some unsaturated substances has been studied. With acetaldehyde and acraldehyde pressure effects were found, but reversible polymerides similar to those obtained by Bridgman and Conant from the butaldehydes at pressures of 12,000 atm. were not found.

In addition to the study of the effect of pressure on reaction rates, an attempt has also been made to study the effect on the position of equilibrium of the reversible tautomeric change γδ-*iso*heptenoic acid $\rightleftarrows$ δδ-dimethyl-δ-valerolactone. It was found, as anticipated, that the equilibrium was shifted towards the side of greater density; increasing temperature at atmospheric pressure shifted the equilibrium in the opposite direction.

Conclusions.—The following conclusions may be drawn from a consideration of the results so far obtained.

(1) *All the reactions which proceeded slowly at atmospheric pressure showed increased velocity at the same temperature under higher pressure.*

These reactions may be divided into two classes, those which are not susceptible to catalysis, and those which are normally carried out in the presence of catalysts but proceed slowly at atmospheric pressure in the absence of added catalysts. Those of the latter class were found to proceed under pressure at rates which, in some cases, approached the rates of the catalysed reactions at atmospheric pressure. Two of these reactions were carried out in the presence of added catalysts to mask the possible effect of the presence of fortuitous catalysts, and the pressure effect was found to persist.

An increase in the pressure to 3000 atm. increased the rate of reaction by 5—10 times in nearly all cases. The effect on polymerisations was, however, considerably greater, whilst in the reaction between benzaldehyde and chloroform the increase was only about 10%.

(2) *The reactions which did not proceed at atmospheric pressure* (*in the absence of catalysts*) *did not proceed at pressures up to* 3000 *atm.*

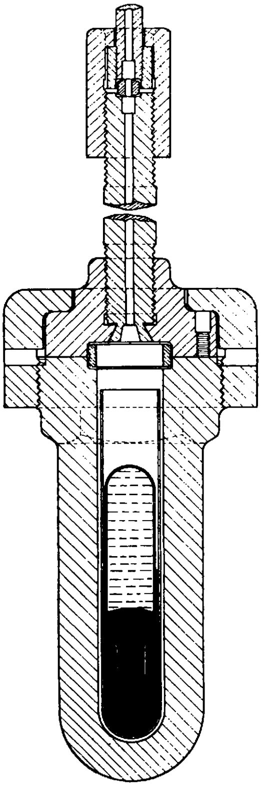
This is not surprising in view of the order of the pressure effects found in most cases. The only exception was the condensation and polymerisation of acetaldehyde, which showed no detectable reaction at atmospheric pressure at the temperature studied, although it is possible that the reaction may proceed slowly at higher temperatures.

It is interesting to note that reactions which proceed at atmospheric pressure only in the presence of aluminium chloride, showed no signs of proceeding at pressures up to 3000 atm., either in the absence of catalysts or in the presence of mild acid or basic catalysts.

Before the observed pressure effects can be ascribed to one or more of the possible influences already discussed, it would seem necessary both to extend this survey to discover how far the effects are general and hold for all reactions, and to undertake a comprehensive quantitative study of these effects.

EXPERIMENTAL.

The apparatus used is shown in the fig. The reactants were placed in small glass tubes of 10—15 c.c. capacity, which were inverted with the open ends under mercury contained in glass liners fitting into the steel pressure vessels as shown. These vessels were placed in oil thermostats maintained at the required temperature, and pressure was transmitted to the samples under investigation through the mercury by means of a light mineral oil, the pressure of which was measured by means of calibrated Bourdon gauges. The pressure was obtained either by means of a Cailletet-type screw press designed by Dr. A. Michels of the University of Amsterdam, and built by Dikkers & Co. of Hengelo, Holland, or by means of a hydraulic intensifier designed and built in these laboratories. The few experiments recorded which were made at pressures above 3000 atm. were carried out in an apparatus similar to that described by Bridgman ("Physics of High Pressures," p. 42, Bell, 1931), also designed and built in these laboratories (*Engineering*, 1933, **136**, 32).



Check experiments at about atmospheric pressure were carried out alongside the pressure experiments either in sealed glass tubes, or in small tubes inverted over mercury, as described above, placed in low-pressure metal vessels fitted with spring-loaded relief valves set at about 5 atm.

Some trouble was at first experienced with the fracture of the glass reaction tubes after one or two applications of pressure. The glass flaked away from the inner surface and produced a structure honeycombed with fine cracks. This phenomenon is no doubt due to the penetration of the glass by the organic liquids under pressure (cf. Poulter, *Physical Rev.*, 1932, **40**, 877). It was found that tubes made of Pyrex glass had a much longer life than those of soft glass.

Reactions between Acid Anhydrides and Aromatic Hydrocarbons.—*Maleic anhydride and hydrocarbons.* Attempts to detect the combination of maleic anhydride (1 mol.) with benzene, toluene, or naphthalene (1 mol.) were unsuccessful, the anhydride being recovered substantially unchanged. The reactions were investigated up to 180° and at 3000 atm. for periods up to 40 hours. The anhydride, however, underwent slow decomposition on being heated for long periods at 180°, carbon dioxide being evolved while the anhydride darkened; extraction of the residue with benzene left a sparingly soluble brown powder which has not been identified. This decomposition is possibly analogous to that of succinic anhydride (Volhard, *Annalen*, 1889, **253**, 206, 233; 1891, **267**, 60, 94; Bredt, *ibid.*, 1890, **256**, 330).

The reaction between anthracene and maleic anhydride, which proceeds at atmospheric pressure at 200° (Diels, *ibid.*, 1931, **486**, 191), was not studied under pressure owing to the high m. p.'s of the reactants. It was, however, found that the reaction proceeds at a moderate rate at ordinary pressures in toluene solution, and the effect of pressure on the yield of the condensation product was determined at 60° and 40°. The yield was determined by adding the product to water, basifying with 10% sodium hydroxide, and heating to 80° for ½ hour to decompose the anhydride. The toluene layer was then removed, and the acid precipitated by acidification with hydrochloric acid (Congo-red), dried at 100°, and weighed. The yields were identical at 3000 atm. and at atmospheric pressure at 60°, whilst in 16 hours at 40° the yield at 3000 atm.

was 20% smaller than that at atmospheric pressure. This retardation by pressure was probably due to the reduced solubility of the reactants in the solvent at 40° and under the high pressure.

Phthalic anhydride and hydrocarbons. There was no reaction when mixtures of phthalic anhydride and benzene, toluene, chlorobenzene, or naphthalene were heated at 3000 atm. to 180° for 40 hours, or when these substances were heated under similar conditions in the presence of boric acid, zinc chloride, piperidine, and amalgamated aluminium powder, which might be expected to act as catalysts. In all cases the reaction product was added to a little hot sodium hydroxide solution and the hydrocarbon layer removed. On acidification, phthalic acid (identified by titration with *N*/10-sodium hydroxide and conversion into the anhydride) was the only acid recovered.

Reactions between Amines and Aldehydes or Ketones.—Benzaldehyde and dimethylaniline. Benzaldehyde (1 mol.) and dimethylaniline (2 mols.) were heated to 150° at 3000 atm. for 20 hours. The product was a viscous liquid containing water. The yield of condensation product was determined by distilling off any unchanged material in steam, extracting the residue with ether, removing the ether on a steam-bath, and weighing the residue after drying in a vacuum desiccator. The residue was pure leuco-malachite green (m. p. 102°; mixed m. p. 101—102°). The first seven results in the following table illustrate the magnitude of the pressure effect observed, the same samples of materials being used throughout :

	No added benzoic acid.							Added benzoic acid.		
Dimethylaniline, g. ...	7·5	7·4	7·8	7·6	7·4	7·8	8·0	8·2	7·4	7·4
Benzaldehyde, g.	3·7	3·6	3·8	3·8	3·6	3·6	3·8	4·0	3·6	3·8
Benzoic acid, g.	—	—	—	—	—	—	—	1·0	1·0	—
Temperature	150·1°	150·0°	150·2°	150°	150°	161·2°	161°	150·1°	150·3°	150·0°
Pressure, atm.	40	1000	2000	3000	3000	80	2990	70	2240	3000
Time, hrs.	20	20	20	20	20	20	20	20	4½	4½
Yield of leuco-malachite green, g.	0·5	3·1	5·7	8·7	8·2	1·1	8·9	2·1	7·6	3·8

By working at 100—120°, the rate of reaction was reduced, but the product contained large proportions of *p*-dimethylaminobenzhydrol. A cursory examination of the temperature and pressure variables in this range did not disclose conditions under which products containing more than 85% of the hydrol could be obtained.

The respective yields of the hydrol and the triphenylmethane derivative were estimated, in cases where incomplete reaction had taken place, by determining the benzaldehyde in the steam distillate by means of phenylhydrazine in dilute acetic acid solution (Dennis and Dunbar, *J. Ind. Eng. Chem.*, 1909, **1**, 256).

The benzaldehyde used in the above experiments was washed with dilute sodium hydroxide solution (2%), dried, and distilled in a current of nitrogen, but it is possible that traces of benzoic acid were present. The reaction was therefore investigated in the presence of added benzoic acid, as shown in the second set of results in the table, the last experiment being a control. The pressure effect was found to persist, although the reaction was certainly catalysed by the acid.

An unexpected difficulty arose, for different samples of benzaldehyde did not give reproducible results. This was not entirely connected with the percentage of benzoic acid present as determined by titration with *N*/100-sodium hydroxide, since samples of benzaldehyde sealed in glass tubes and stored in the dark were found to react more slowly than before such storage. It would appear that, with reactions of this type proceeding in the absence of added catalysts, the rate is very sensitive to the fortuitous presence of traces of catalytic material. It is possible that peroxide catalysts may have a considerable effect on the reactions of benzaldehyde, as in the case of unsaturated hydrocarbons (Kharasch and Mayo, *J. Amer. Chem. Soc.*, 1933, **55**, 2468). No explanation of the variation of the reaction rate has been found, although numerous experiments have been carried out.

Monomethylaniline and benzaldehyde. This reaction does not appear to have been investigated at atmospheric pressure. Investigation at high pressures showed the presence of a similar pressure effect to the last reaction. The product, presumably 4 : *4′-dimethylaminotriphenylmethane*, was a white solid, m. p. 100—101°, becoming green on exposure to air (Found : C, 83·4; H, 7·4; N, 9·2. $C_{21}H_{20}N_2$ requires C, 83·4; H, 7·3; N, 9·26%).

The following table shows the reaction rate between monomethylaniline (2 mols.) and benzaldehyde (1 mol.) at various temperatures and pressures. The yields were determined as in the similar reaction with dimethylaniline described above.

Press., atm.	1.	1000.	2000.	3000.
Temp.	Yield, % of complete reaction.			
150°	35·5	62·5	76·5	87·0
140	26·0	55·0	71·5	81·0
130	22·5	40·0	56·0	—
110°	10·5	30·4	45·0	57·5
90	2·0	22·7	39·0	48·0

At 110° and 90° a determination of both the condensation product and unchanged benzaldehyde showed that considerable quantities of *p*-methylaminobenzhydrol had been formed. The above figures, however, have all been calculated on the basis of complete reaction to the triphenylmethane derivative.

Benzaldehyde and diphenylamine. Reaction occurred between these substances on heating to 150° for 16 hours at 3000 atm., but it was very slow at atmospheric pressure. The product was, however, a mixture, and its constitution was not determined.

Ketones and dimethylaniline. Attempts to condense dimethylaniline with benzophenone or Michler's ketone at 180° at 3000 atm. were unsuccessful. In the first case, after 40 hours the product was entirely volatile in steam, and in the second reaction, both reagents were recovered quantitatively.

Acetal Formation, etc.—Acetaldehyde and ethyl alcohol. Reaction normally proceeds between alcohols and aldehydes in the presence of acid catalysts at atmospheric pressure. In the absence of such catalysts the reaction is very slow at atmospheric pressure, but it is considerably accelerated under high pressure, as shown by the following data for the yield % for the reaction between acetaldehyde (1 mol.) and ethyl alcohol (2 mols.) : At 1 atm., 8·8 at 80°, 1·2 at 60°; at 3000 atm., 32·1 at 80°, 10·8 at 60°. In these experiments the alcohol and aldehyde were freed from acid substances by distillation over quick-lime, followed by fractional distillation. The yield of acetal was determined by the sulphite method (cf. Seywetz and Bardin, *J. Soc. Chem. Ind.*, 1906, **25**, 202; Childs and Adkins, *J. Amer. Chem. Soc.*, 1923, **45**, 3020), bromothymol-blue being used as indicator.

Benzaldehyde and ethyl alcohol. This reaction was negligibly slow with pure benzaldehyde (1 mol.) and ethyl alcohol (2 mols.), but with alcohol containing 1% of dry hydrogen chloride the reaction at 150° was 14·7% complete at atmospheric pressure, and 31·7% complete at 3000 atm. in 16 hours.

The yields of acetal were determined as follows : The reaction product was treated with 1½ mols. of hydroxylamine solution, prepared by adding the theoretical quantity of 10% sodium hydroxide to a 10% solution of the hydrochloride. After standing for 20 minutes, the solution was made alkaline with 1 mol. of 10% sodium hydroxide, the benzaldehyde-acetal removed by extraction with a little petroleum ether (b. p. 40—60°), the extract dried (magnesium perchlorate), the solvent removed on a water-bath (the last traces under 100 mm.), and the residue weighed.

Acetaldehyde and ethyl ether. No ethylacetal was formed when equimolar proportions were heated to 150° at 3000 atm., although slight polymerisation of the acetaldehyde occurred. There was no reaction at 40° at 9000 atm.

Benzaldehyde (1 *mol.*) *and acetic anhydride* (2 *mols.*). This reaction was complete after 16 hours' heating at 150° under 3000 atm., whilst at atmospheric pressure only 32% of benzylidene diacetate was formed. The yield was determined by distilling off the unchanged acetic anhydride in a vacuum, hydrolysing the product with boiling water, and determining the acetic acid by titration with *N*/10-baryta. The product had m. p. 46° (mixed m. p. 46°). The acetic anhydride probably contained some acetic acid, and this is no doubt a case of pressure acceleration of a reaction catalysed by acids.

Quaternary Ammonium Salt Formation.—Pyridine and cetyl halides. Cetyl bromide (1 mol.) and pyridine (1 mol.) react readily at 70° in the absence of catalysts. Under pressure the reaction is accelerated, the yields under various pressures in 20 hours at 50° being shown below ;

Pressure, atm.	1	1000	2000	3000
Yield, % of complete reaction	22·0	33·5	60·0	81·1

Cetyl chloride is less reactive than the bromide, but reaction proceeds at 110°. There is a similar pressure effect, the yield in 20 hours being :

Pressure, atm.	1	1000	2000	3000
Yield, % of complete reaction	11·5	29·7	54·0	72·0

The analytical methods employed are described in the following paper.

Pyridine and alcohols. Attempts to prepare quaternary ammonium hydroxides directly from pyridine and methyl alcohol and cetyl alcohol at temperatures up to 150° at 3000 atm. were fruitless, the pyridine determined by titration being recovered quantitatively.

Pyridine and ethylene dichloride. This reaction proceeds slowly at atmospheric pressure, and in 20 hours at 80°, 38% of the pyridine has reacted. Determination of the unchanged pyridine (as above) and the ethylene dichloride (by distillation and direct weighing) showed that the product was a mixture of the two possible quaternary salts (70% β-chloroethylpyridinium chloride). At 3000 atm. the reaction is accelerated, and after 16 hours at 80° no pyridine was recovered, the product being entirely *ethylenedipyridinium dichloride*, white hygroscopic needles which decomposed without melting (Found : Cl, 27·8. $C_{12}H_{14}N_2Cl_2$ requires Cl, 27·6%).

Triethanolamine and cetyl bromide. The reaction at atmospheric pressure is described on p. 389. At 3000 atm. and 80° in 16 hours, triethanolamine (1 mol.) and cetyl bromide (1 mol.) yielded mainly a dark brown, viscous product containing some solid material. On addition of ether a white crystalline precipitate was obtained, which proved to be triethanolamine hydrobromide (0·6 mol.) (Found : Br, 34·3. Calc. for $C_6H_{16}O_3NBr$: Br, 34·6%). Removal of the ether from the solution and extraction with water left an oil which decolorised bromine, whilst the aqueous extract on evaporation gave only a trace of solid residue, which was found to be triethanolamine hydrobromide. The yield of the hydrobromide under pressure was about double that obtained at atmospheric pressure.

8 : 8′-*Dichloro*-5 : 5′-*diquinolyl* [*] *and ethyl iodide.* This base does not form quaternary salts under any known conditions. It also failed to react when heated to 150° with ethyl iodide at 3000 atm. for 100 hours.

Reactions between Acids and Unsaturated Hydrocarbons.—Nernst (*Z. physikal. Chem.*, 1893, **11**, 353) studied the reactions between the chloroacetic acids and *tert.*-amylene; at 30° the amyl esters are formed quantitatively, but at higher temperatures (100—150°) an equilibrium is attained. A few experiments have been carried out with these and similar reactions under high pressures, and in each case pressure effects have been observed. The reactions were followed by titration of the unchanged acid with *N*/10-baryta.

Trichloroacetic acid (1 *mol.*) *and* tert.-*amylene* (1 *mol.*). In 16 hours at 30°, 18·6% of the acid was esterified under 1 atm. and 33·9% under 3000 atm.

Acetic acid (1 *mol.*) *and* tert.-*amylene* (1 *mol.*). In 16 hours at 100°, 1·1% of acid was esterified under 1 atm. and 6·6 under 3000 atm.; the corresponding data at 110° were 0·4% and 4·5% respectively. The equilibrium corresponds with almost complete dissociation of the ester (cf. Nernst, *loc. cit.*).

Trichloroacetic acid and cyclo*hexene.* In the same way the reaction between this acid (1 mol.) and hydrocarbon (2 mols.) has been investigated.

Temp.	Time, hours.	Press., atm.	Acid esterified, %.	Temp.	Time, hours.	Press., atm.	Acid esterified, %.
30°	16	1	nil	60°	40	1	37·9
30	16	3000	7·8	60	40	2000	68·6
110	88	1	81·7	60	40	3000	74·7
110	88	3000	92·3				

Dichloroacetic acid (1 *mol.*) *and* cyclo*hexene* (2 *mols.*). At 100° in 16 hours 20·9% of acid was esterified under 1 atm. and 54·1% under 3000 atm.; in 32 hours the corresponding values were 27·2% and 60·3%.

Miscellaneous Reactions.—*Acetaldehyde and ethyl malonate, etc.* This condensation is normally carried out in the presence of a trace of a strong base (piperidine, etc.). Acetaldehyde (1 mol.) was heated to 60° for 40 hours with ethyl malonate (2 mols.) at 3000 atm., the unchanged acetaldehyde distilled off, absorbed in water, and determined by the sulphite method. No reaction had occurred. At 150° decomposition occurred and large quantities of gas were evolved. An identical result was obtained with acetaldehyde and ethyl acetoacetate.

Benzonitrile and phenol. There was no combination when equimolar weights were heated to 150° at 3000 atm.

Benzonitrile and resorcinol. There was no measurable reaction when these compounds were heated to 150° for long periods (100 hours) at atmospheric pressure in the absence of catalysts, although the mixture became red. When this experiment was repeated at 3000 atm., reaction occurred and the product separated into a viscous red lower layer and a mobile colourless layer

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[*] This base, which is not recorded in the literature, has m. p. 296° and was prepared by I.C.I. (Dyestuffs), Ltd.

of mainly unchanged benzonitrile. The lower layer on treatment with ether yielded a bright red solid. This consisted of a number of substances, but some condensation to 2 : 4-dihydroxybenzophenoneimine had taken place for, on treatment with water, a small quantity of 2 : 4-dihydroxybenzophenone was isolated (m. p. 143°; mixed m. p. 144°). Complete separation of the remaining material was not achieved, but by fractional crystallisation from methyl ethyl ketone various coloured fractions giving strongly fluorescent solutions in alkalis were obtained, some of which contained no nitrogen and were condensation products of resorcinol itself, identical with or similar to those reported by Hesse (*Annalen*, 1896, **289**, 62).

No nitrogenous fraction was isolated in a pure condition, but it is probable that the small yield of 2 : 4-dihydroxybenzophenone did not represent the total true condensation.

o-Xylylene cyanide. *o*-Xylylene cyanide on treatment with a little sodium ethoxide in alcohol changes smoothly into iminocyanohydrindene (Moore and Thorpe, J., 1908, **93**, 175). Samples of the nitrile alone were heated at 3000 atm. at 50°, 100°, and 150°, but the m. p. was unchanged at 60° (mixed m. p. with the original material 60°), and the products did not give the characteristic colour reaction of the hydrindene with concentrated sulphuric acid containing a trace of selenic acid.

Benzaldehyde and toluene. Benzaldehyde (1 mol.) and toluene (2 mols.) were heated to 150° for 40 hours at 3000 atm., but subsequent distillation through a small column gave unchanged material and no residue.

Benzaldehyde and chloroform. Reaction normally proceeds in the presence of basic catalysts at room temperature to yield phenyltrichloromethylcarbinol. At 150° without a catalyst the reaction is extremely slow. Chloroform (1 mol.) and benzaldehyde (1 mol.) were heated to 150° at 3000 atm. for 16 hours; fractional distillation then afforded chloroform in quantity denoting that 11% of the carbinol had been formed, and this (m. p. 51°) was isolated in 9% yield by adding ligroin to the residue; the major portion of the unchanged benzaldehyde was recovered by distillation under 2 mm.

Phthalic anhydride and tert.*-amyl alcohol.* This reaction was investigated in order to discover whether the *tert.*-alkyl hydrogen phthalates could be prepared under high pressure, but the results were negative, although some phthalic acid was isolated from the experiments at both 1 atm. and 3000 atm.; the yield of the acid from the pressure experiments was consistently greater than from those at atmospheric pressure.

Diphenylamine and ethylene oxide. There is little reaction when diphenylamine (1 mol.) and ethylene oxide (1 mol.) are heated together at 150° at atmospheric pressure, but at 3000 atm. the product after·40 hrs. is a viscous liquid. This was distilled in a vacuum and gave, first unchanged diphenylamine, and then a series of liquid fractions containing nitrogen. One fraction, b. p. 150—152°/15 mm., contained N, 6·9 (Calc. for diphenyl-β-hydroxyethylamine: N, 6·9%). The remaining fractions of higher b. p. were probably products formed by further addition of ethylene oxide to this substance.

Hydrolysis of benzonitrile. No reaction occurred when benzonitrile was heated with water to 150° for 40 hours at 1 atm. or at 3000 atm. The reaction was next investigated in the presence of ½% sodium hydroxide solution. 1·8 G. of benzonitrile and 1·8 c.c. of this solution were heated to 150° for 60 hours at 2000 atm. 0·4 G. of unchanged benzonitrile was recovered and 1·3 g. of a solid product; the latter was a mixture of benzamide and benzoic acid containing 33·7% of the acid, as determined by titration with *N*/10-baryta.

When 1·5 g. of benzonitrile and 1·5 c.c. of the solution were similarly heated in a sealed tube, only 0·2 g. of solid product was isolated, consisting of pure benzamide (m. p. 125·5—126·5°; mixed m. p. 125°). At 130° for 60 hours at 3000 atm., 2·2 g. of nitrile and 5 c.c. of 3% sodium hydroxide solution gave 1·1 g. of pure benzoic acid (as determined by titration). The same mixture at atmospheric pressure gave 0·4 g. of benzamide.

With 1% alcoholic potash (7 c.c.) and water (1 c.c.) as the hydrolytic agent, 2·1 g. of benzonitrile gave 1·3 g. of pure benzamide (m. p. and mixed m. p. 125°) in 60 hours at 120° and 2000 atm., but from a similar experiment carried out at atmospheric pressure no solid product could be isolated.

Polymerisations.—Acetaldehyde. In contrast to the behaviour of the butaldehydes (Bridgman, *loc. cit.*), this substance is unchanged at 40° and 9000 atm. for periods up to 100 hours. At 150° and at 3000 atm. polymerisation occurred in 16 hours to a viscous liquid containing water and smelling strongly of crotonaldehyde. On distillation under 5 mm. a wide range of products—mobile liquids (b. p. 80—150°) and a resinous residue—was obtained. The quantity of material was too small for complete examination, but the analytical figures of the fractions agreed substantially with those of crotonaldehyde, indicating that the main reaction was condensation to this aldehyde, followed by its polymerisation. There was no sign of this reaction when acetaldehyde was heated to 150° under its own v. p.

Acraldehyde. Acraldehyde polymerises readily under pressure to a white, slightly plastic solid. The polymeride is not of the type found by Bridgman (*loc. cit.*) in the case of the butaldehydes, as it does not revert to the monomeride on reduction of pressure. The presence of quinol retards, but does not entirely prevent, the polymerisation. The approximate yield of polymerides was determined by addition of ligroin to the product, filtration, and direct weighing. These yields were also checked in duplicate experiments by vacuum distillation of the unchanged acraldehyde and by weighing the residue.

Substance.	Temp.	Press., atm.	Time, hours.	Percentage polymerised.
Acraldehyde	70°	1	16	0
„ + 0·1% quinol	70	3000	16	3·5
„	70	3000	16	20·2
„	110	1	16	3·8
„ + 0·1% quinol	110	3000	16	56·5
„	110	3000	16	87

Miscellaneous polymerisations. Ethylene oxide, *tert.*-amylene, and *cyclo*hexene were recovered unchanged when heated for 16 hours to 150° at 3000 atm.

*Change of Equilibrium.—The tautomeric change γδ-*iso*heptenoic acid* $\rightleftharpoons$ *δδ-dimethyl-δ-valerolactone.* γδ-*iso*Heptenoic acid on heating to 200° for 10 hours yields an equilibrium mixture containing about 60% of the lactone (Linstead and Rydon, J., 1933, 580). Samples of the acid, kindly supplied by Professor J. F. Thorpe and Dr. R. P. Linstead, showed no such change when heated at 30° at either atmospheric pressure or 3000 atm. After 16 hours at 160° at 3000 atm. and at atmospheric pressure, the samples were found by Dr. Linstead to contain 55·0% and 20·2% of the lactone respectively. The position of the equilibrium at different temperatures and pressures has been followed in a dilatometer constructed to fit inside a high-pressure vessel. After a given time under the required conditions of temperature and pressure, the dilatometer was removed, and the volume of the system measured at atmospheric pressure and 30°. The dilatometer was kept under the required conditions until no further change in the volume at 30° was observed, *i.e.*, until the volume was that of the equilibrium mixture for the given conditions of temperature and pressure. The change in the volume of the equilibrium mixture at 170° with pressure, and with temperature at atmospheric pressure, compared to the volume at 170° and atmospheric pressure, is shown by the following data :

Temp.	Press., atm.	Change of volume, %.	Temp.	Press., atm.	Change of volume, %.
170°	1	—	150°	1	0·20 decrease
	500	0·12 decrease	160		0·10 „
	1000	0·23 „	170		—
	2000	0·39 „	180		0·09 increase
	3000	0·52 „			

The system was not perfectly reversible, possibly owing to a very slow side reaction, and it did not return exactly to the volume for the equilibrium at a given pressure and temperature after measurements had been made of the equilibria under other conditions.

SUMMARY.

The possible influences of pressure on a chemical reaction are discussed.

The results are given of the effect of pressures up to 3000 atm. and temperatures up to 180° on about fifty organic reactions in the liquid phase.

All the reactions which proceeded slowly at atmospheric pressure were accelerated at the same temperature under high pressure, whilst those which did not proceed at atmospheric pressure (in the absence of catalysts) did not proceed at pressures up to 3000 atm. With a few exceptions, the effect of pressure was to increase the rates of reaction by 5—10 times for an increase of pressure of 3000 atm.

The position of equilibrium of the tautomeric system γδ-*iso*heptenoic acid $\rightleftharpoons$ δδ-dimethyl-δ-valerolactone is shifted towards the lactone by an increase in pressure.

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