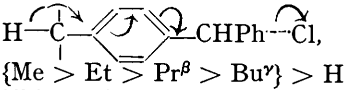
# 33. *Mechanism of Aromatic Side-chain Reactions with Special Reference to the Polar Effects of Substituents. Part XI. The Aldehydecyanohydrin Reaction: Evidence for the Mesomeric Effects of Alkyl Groups.*

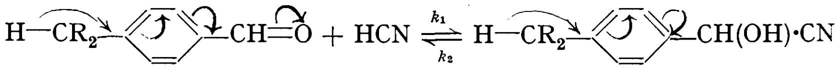
By John W. Baker and (Miss) Mabel L. Hemming.

In the equilibrium (I) $p\text{-}C_6H_4R{\cdot}CHO + HCN \underset{k_2}{\overset{k_1}{\rightleftharpoons}} p\text{-}C_6H_4R{\cdot}CH(OH){\cdot}CN$ (II), where $R = H$, Me, Et, $Pr^{\beta}$, or $Bu^{\gamma}$, conjugation of the alkyl group, necessary for the operation of its mesomeric effect (Baker and Nathan, J., 1935, 1844), extends to the side-chain carbonyl group in (I), but is restricted to the benzene ring in (II). If this effect were predominant, stabilisation of the free aldehyde relative to its cyanohydrin should increase in the order $H < Bu^{\gamma} < Pr^{\beta} < Et < Me$. The values of the dissociation constant of the cyanohydrin $K = k_2/k_1$ have been determined in constant boiling-point alcohol at 20° and 35°, and both series follow the sequence $K = Me > Et > Pr^{\beta} > Bu^{\gamma} > H$, in agreement with the above expectations. The order is confirmed by the corresponding values of $\Delta F = -\boldsymbol{R}T \ln K$, and the data thus provide the first conclusive evidence for an order of mesomeric electron-release $Me > Et > Pr^{\beta} > Bu^{\gamma}$. This, together with the evidence for the same order in the electromeric effect obtained by Hughes, Ingold, and Taher (J., 1940, 949), completes the experimental proof of the original hypothesis of Baker and Nathan (*loc. cit.*).

The values of $k_1$ and $k_2$ have also been determined at 20°, and these results, together with those relating to $K$, find a simple and consistent explanation on the basis of the changes in energy levels effected in the initial, transition, and final states of the reaction by the combined operation of the inductive and tautomeric effects of the alkyl substituents.

The theory of partial conjugation of electrons of a C–H bond with an attached unsaturated system, $\mathrm{H\overset{\curvearrowright}{-}C-C\overset{\curvearrowright}{=}C}$, postulated by Baker and Nathan (J., 1935, 1844) to explain the rate sequence $\{Me > Et > Pr^{\beta} \approx Bu^{\gamma}\} > H$ for the bimolecular, nucleophilic substitution $p\text{-}C_6H_4R{\cdot}CH_2Br + C_5H_5N \longrightarrow p\text{-}C_6H_4R{\cdot}CH_2{\cdot}\overset{+}{N}C_5H_5\}\overset{-}{Br}$, has since been conclusively verified by Hughes, Ingold, and Taher (J., 1940, 949) in the unimolecular solvolysis of $p$-alkylbenzhydryl halides. In this reaction the electron-release by the tautomeric mechanism is of predominating importance in the transition state,  and leads to a well-spaced sequence of velocity coefficients $\{Me > Et > Pr^{\beta} > Bu^{\gamma}\} > H$ supported by a corresponding differentiation in activation energies. This evidence, since it is derived from reaction kinetics, only proves the existence of an *electromeric* (polarisability) effect decreasing in the order $Me > Et > Pr^{\beta} > Bu^{\gamma}$ required by Baker and Nathan's hypothesis. Evidence so far obtained for a corresponding *mesomeric* (polarisation) effect (cf., *inter alia*, Davies and Hammick, J., 1938, 763; Davies, *ibid.*, p. 1865; Baker, Dippy, and Page, J., 1937, 1774; Baker, Nathan, and Shoppee, J., 1935, 1847; Baker, J., 1939, 1150; Baker and Nathan, J., 1936, 236; Burkhardt *et al.*, *ibid.*, pp. 17, 25, 1649, 1654), is inconclusive for one or other of the following reasons: (1) it refers only to incomplete series of alkyl groups, or (2) only partial inversion of the electron-release order $Bu^{\gamma} > Pr^{\beta} > Et > Me > H$, indicated by the inductive effects, has been realised. The object of the present communication is to provide equally conclusive evidence for an order of mesomeric electron-release $Me > Et > Pr^{\beta} > Bu^{\gamma} > H$.

It was considered that investigation of the cyanohydrin equilibrium for the appropriate *p*-alkylbenzaldehyde should achieve this object. An equilibrium state is unaffected by polarisability effects and provides information regarding the permanent states of polarisation and hence of the relative stabilities of the molecules concerned. Lapworth has shown experimentally that, with substituents of the electron-release type, the stability of the cyanohydrin decreases with increasing electron-release. In the *p*-alkylbenzaldehyde the type of conjugation postulated by Baker and Nathan extends to the side-chain carbonyl group (III), whereas in the cyanohydrin (IV) it is restricted to the aromatic nucleus.

(III.)  (IV.)

It was therefore anticipated that the mesomeric electron-release by the *p*-alkyl substituent would stabilise the free aldehyde to a greater extent than it does the cyanohydrin. Moreover, the complete conjugation possible in (III) gave ground for hope that the effect of such mesomeric electron-release might predominate over any inductive effect and thus reveal an order $p\text{-Me} > Et > Pr^{\beta} > Bu^{\gamma} > H$ for stabilisation of the free aldehyde relative to its cyanohydrin.

The cyanohydrin equilibrium was studied quantitatively by Lapworth and Manske (J., 1928, 2533 *et seq.*) in constant boiling-point alcohol as solvent, and the scope of their investigation has now been extended to include the *p*-methyl-, -ethyl-, -*iso*propyl-, and -*tert.*-butyl-benzaldehydes at two temperatures. The values of the cyanohydrin dissociation constants, $K = k_2/k_1$ at 20° and 35°, all of which are the mean of several consistent determinations, are given in Table I, together with the corresponding values for the change in free energy $\Delta F = -\boldsymbol{R}T \ln K$.* A new technique was necessary for the determinations at 35° (see p. 197).

TABLE I.

*Equilibrium constants for the reaction* (I) + HCN $\underset{k_2}{\overset{k_1}{\rightleftharpoons}}$ (II) *in constant-boiling alcohol at* 20° *and* 35°.

| R. | $10^3K$, g.-mol.-l.$^{-1}$ 20°. | $10^3K$, g.-mol.-l.$^{-1}$ 35°. | $\Delta F \times 10^{-2}$, cals. 20°. | $\Delta F \times 10^{-2}$, cals. 35°. |
|---|---|---|---|---|
| H | *4·47 ± 0·12 | 8·80 ± 0·10 | +31·5 | +29·0 |
| Me | *8·98 ± 0·13 | 20·32 ± 0·21 | +27·5 | +23·9 |
| Et | 8·18 ± 0·03 | 17·39 ± 0·09 | +28·0 | +24·8 |
| $Pr^{\beta}$ | 8·04 ± 0·05 | 16·50 ± 0·06 | +28·1 | +25·1 |
| $Bu^{\gamma}$ | 7·49 ± 0·17 | 15·04 ± 0·09 | +28·5 | +25·7 |

* These values are somewhat lower than those, 4·72 and 10·3 respectively, obtained by Lapworth and Manske (*loc. cit.*).

The order of the stabilities of the cyanohydrins, $H > \{Bu^{\gamma} > Pr^{\beta} > Et > Me\}$, relative to their respective aldehydes revealed by the values of $K$ at both temperatures and by the corresponding well-spaced values of $\Delta F$ are completely in accord with theoretical anticipations and provide the first

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* $\Delta F$ is calculated from this thermodynamic relationship and is thus the increase in free energy (at absolute zero) for the dissociation of the cyanohydrin into aldehyde and hydrogen cyanide. It should be noted that, since Lapworth and Manske used $\Delta F = \boldsymbol{R}T \ln K$ in their evaluation of the free energy change, the signs of our values are the opposite of theirs.

conclusive evidence for the order of mesomeric electron-release Me > Et > $Pr^{\beta}$ > $Bu^{\gamma}$ required by Baker and Nathan's hypothesis.*

In order that a more complete theoretical discussion of the problem on the basis of relative energy levels might be possible it was necessary also to evaluate $k_1$ and $k_2$ individually. The determination of such kinetic data presented many difficulties from an experimental point of view. These were due mainly to three factors: (1) The great susceptibility of the reaction to fortuitous catalysts, and the consequent difficulty in obtaining reproducible results. (2) The ready oxidation of the aldehydes, which introduces small, but unknown, concentrations of acids. (3) The volatility and consequent loss of hydrogen cyanide during sampling. Disturbance due to (3) was reduced to a negligible minimum by devising a special apparatus (see p. 197) by means of which the reaction and sampling were carried out in an atmosphere of pure nitrogen under slight positive pressure. The problem of suitable catalysis presented by (1) and (2) was a two-fold one, *viz.*, to discover catalytic conditions which (*a*) gave reaction speeds convenient for measurement, and (*b*) were exactly reproducible. Even small concentrations of tri-*n*-propylamine (the catalyst in the equilibrium experiments) gave inconveniently large velocities: the very weak base acetamide was effective only in such concentrations as would seriously alter the nature of the medium. Pyridine was found to be adequate in small concentrations, but consistent results could not, at first, be obtained, probably owing to the formation of small, unknown amounts of pyridinium *p*-alkylbenzoate. It was shown, experimentally, that pyridinium benzoate has a smaller catalytic effect than pyridine itself. After a long systematic investigation of the effects of all the catalytic entities likely to be present under the reaction conditions, it was concluded that the catalyst used must contain sufficient base to swamp any catalytic effects of fortuitous alkali present (*e.g.*, from the glass vessels) and sufficient benzoate ions to render the small, unknown traces of acid produced by oxidation of the aldehyde negligible in comparison. The kinetic investigations were accordingly effected by using a mixture of 0·01M-pyridine + 0·01M-pyridinium benzoate as the standard catalyst. In several instances the reaction was allowed to proceed to equilibrium and the values of $K$ so determined agreed with those obtained by using tri-*n*-propylamine as a catalyst.

The general reaction type is $A + B \underset{k_2}{\overset{k_1}{\rightleftharpoons}} C$, and the authors are indebted to Dr. W. Wild of the Physical Chemistry Department of this University for the following derivation of the integrated kinetic expression for such a reversible addition.

If $a$ = initial concentration of A (aldehyde), $b$ = initial concentration of B (hydrogen cyanide), and $x$ = concentration of C (cyanohydrin) at time $t$, then

$$dx/dt = k_1(a - x)(b - x) - k_2x \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad \text{(i)}$$

At equilibrium $dx/dt = 0$ and $x = \Delta$, then, from (i)

$$k_2\Delta = k_1(a - \Delta)(b - \Delta)$$

or

$$k_2 = k_1(a - \Delta)(b - \Delta)/\Delta.$$

Substitution of this value in (i) gives

$$dx/dt = k_1(a - x)(b - x) - k_1(a - \Delta)(b - \Delta)x/\Delta$$

which on integration gives

$$k_1t = \frac{2\cdot303}{-\Delta}\log\frac{(x - \alpha)}{\alpha(x - \Delta)}, \text{ where } \alpha = ab/\Delta$$

*i.e.*,

$$\log_{10}\frac{x - \alpha}{x - \Delta} = \frac{k_1(\alpha - \Delta)t}{2\cdot303} - \log_{10}\frac{\Delta}{\alpha}.$$

The slope of the straight line obtained by plotting $f(x) = \log_{10}(x - \alpha)/(x - \Delta)$ against $t$ is equal to $k_1(\alpha - \Delta)/(2\cdot303)$, whence $k_1$ was determined. $k_2$ was then found from

$$K = k_2/k_1, \text{ where } K = (a - \Delta)(b - \Delta)/\Delta.$$

The results agreed accurately with this straight-line relationship for a period of about 100 hours, corresponding to about 80% of the course of the reaction to the equilibrium position.

* The corresponding values of $\Delta H$, calculated from the relationship $\Delta H = T_1T_2/(T_2 - T_1)R \ln K_2/K_1$, for the H, Me, Et, $Pr^{\beta}$, and $Bu^{\gamma}$ compounds are, respectively, 8089, 9752, 8999, 8585, and 8348 cals. This means that the changes in $\Delta F$ depend mainly on changes in $T\Delta S$ and not in $\Delta H$, but it is generally recognised that the values of $\Delta F$ more truly reflect the energy changes in the molecule caused by substitution, and these values form a clear-cut series in harmony with the theoretical predictions.

The values of $k_1$ and $k_2$, each of which is the mean of at least two consistent determinations, at 20° ± 0·01° are given in Table II.

TABLE II.

*Kinetic data for the reaction* (I) + HCN $\underset{k_2}{\overset{k_1}{\rightleftharpoons}}$ (II) *in constant boiling-point alcohol at* 20° : 0·01M-*pyridine* + 0·01M-*pyridinium benzoate as catalyst.*

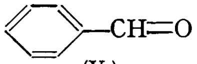
| R = | H. | Me. | Et. | Pr$^\beta$. | Bu$^\gamma$. |
|---|---|---|---|---|---|
| $10^8k_1$, sec.$^{-1}$ g.-mol.$^{-1}$l. .................. | 1·96 | 0·98 | 1·01 | 0·85 | 0·91 |
| $10^{10}k_2$, sec.$^{-1}$ .................................. | $0{\cdot}87_8$ | $0{\cdot}88_3$ | $0{\cdot}82_5$ | $0{\cdot}68_3$ | 0·68 |

DISCUSSION.

The stabilisation of the aldehyde relative to its cyanohydrin will be effected by electron-release from the *p*-alkyl substituent by both the inductive (+ *I*) and the mesomeric (+ *M*) effect. The greater the total electron-release the greater is the relative stability of the free aldehyde. The experimental data clearly reveal an order of decreasing cyanohydrin stability H > Bu$^\gamma$ > Pr$^\beta$ > Et > Me, proving an order of total electron-release, $(I_{\text{Me}} + M_{\text{Me}}) > (I_{\text{Et}} + M_{\text{Et}}) > (I_{\text{Pr}^\beta} + M_{\text{Pr}^\beta}) > (I_{\text{Bu}^\gamma} + M_{\text{Bu}^\gamma})$. The order of electron-release by the inductive effect is, however, known to be $I_{\text{Bu}^\gamma} > I_{\text{Pr}^\beta} > I_{\text{Et}} > I_{\text{Me}}$; hence the order of mesomeric electron-release must be $M_{\text{Me}} > M_{\text{Et}} > M_{\text{Pr}^\beta} > M_{\text{Bu}^\gamma}$, in agreement with the requirement of Baker and Nathan's hypothesis.

Correlated interpretation of both the equilibria and kinetic data is best effected by the method of relative energy levels applied to other side-chain reactions in previous papers in this series * (J., 1939, 1150; 1940, 692; *Trans. Faraday Soc.*, 1941, **37**, 632). It will be convenient to deal first with equilibria which involve only the energy levels of the ground states of the aldehyde and cyanohydrin molecules and then, by consideration of the energy levels of the activated transition complex, to extend the treatment to the interpretation of the velocity data.

(a) *Equilibria.*—In the ground state of benzaldehyde itself resonance will occur between structures of types (V), (VI) and (VII). Introduction of a *p*-alkyl substituent will lower the energy level (increase the stability), since structures of types (VIII) and (IX) can now also be included in the resonance hybrid.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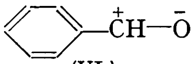
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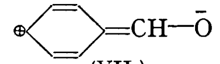
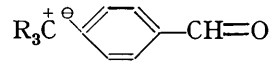
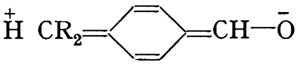

(VII )

Of these, for reasons already given, (IX) is likely to be the more important, and the increased stabilisation will be greater the larger the number of C–H bonds which are directly conjugated with the aromatic ring (*i.e.*, $CH_3$ > $MeCH_2$ > $Me_2CH$ > $Me_3C$), being zero in the case of Bu$^\gamma$. The values assigned to the inductive and mesomeric effects of the various alkyl substituents and their total effect on the relative energy levels of the aldehyde are given in Table III. Because conjugation of the alkyl C–H bonds extends to the side-chain carbonyl group, the values of + *M* are greatly enhanced compared with those

(VIII.)



(IX.)

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* To avoid misconceptions it must be emphasised that the use of numerical values to represent the magnitudes of the inductive and tautomeric effects is merely a concise method of expressing changes in energy levels which result from substitution in the parent molecule, and so avoids (otherwise necessary) long verbal statements or graphical representation. The energy-level changes have a sound basis in physical theory, and the only arbitrary factors in the numerical values are the (unknown) units in which they are measured and their *absolute* magnitudes. The *differences* in magnitudes thus disclosed between various groups are always strictly in at least qualitative agreement with the established relative magnitudes of the inductive and tautomeric effects. The statement that " the stability of benzaldehyde is increased, *i.e.*, its energy level is lowered, by both the inductive and the tautomeric electron-release of a *p*-methyl substituent " is concisely represented by the three sets of figures in the first line of the left-hand column of Table III. " The lowering of the energy level by similar introduction of a *p*-ethyl group will be greater than that of methyl by virtue of its inductive effect, but less than that of methyl by virtue of its tautomeric effect " is again concisely represented in the second line of the same column in Table III, which assigns a larger value (25) to the inductive effect of ethyl than that (10) of methyl, and a smaller value (80 instead of 120, since two C–H bonds instead of three are conjugated with the rest of the molecule) to its tautomeric effect. The figures under " ${}_{\text{A}}E_0$," for example, then indicate concisely that the energy levels of benzaldehyde and its *p*-alkyl derivatives are in the order H > Bu$^\gamma$ > Pr$^\beta$ > Et > Me. The graphical method of representation was used in the first application of this treatment (Baker, J., 1939, 1150) and the adoption of the tabular system used in Table III is merely to avoid the expense of blocks necessitated by the former method.

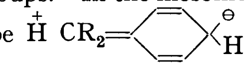
used in the interpretation of the dipole-moment data for *p*-alkylbenzenes in the vapour phase (Baker, J., 1939, 1150) although, of course, the relative magnitudes are still in the ratio Me : Et : $Pr^{\beta}$ : $Bu^{\gamma}$ = 3 : 2 : 1 : 0. The rather large differences in the magnitudes previously assigned to the inductive effects have, however, been reduced for the following reason. The dipole-moment data refer not so much to energy levels as to the charge separation arising from the polar effects of alkyl groups. In the mesomeric component of such electron-release, since it arises from structures of the type  in the resonance hybrid, the distance between the positive and the negative charge is approximately constant for all alkyl substituents. The polar effect of the alkyl group due to the operation of its inductive effect gives rise to a positive charge which will be distributed in the group $CR_3$. As the constitution of this group alters from $CH_3$ to $C(CH_3)_3$ the average location of this positive charge will be situated at an increasing distance from the aromatic nucleus. The arbitrary values assigned to the inductive component on the basis of dipole moments will thus be a measure of the product of charge × effective distance. Since the distance increases in passing from toluene to *tert.*-butylbenzene, the relative magnitudes assigned to the inductive effects of the various alkyl substituents will tend to be too large and the discrepancy will increase as the complexity of the alkyl group increases. Smaller differences between the various values of the $+ I$ components have therefore been assigned in Table III, especially in the higher alkyl groups. The established sequence of magnitude Me < Et < $Pr^{\beta}$ < $Bu^{\gamma}$ is, of course, maintained.

TABLE III.

*Relative energy levels in the ground and the activated states of* $p$-$C_6H_4R{\cdot}CHO$ *and* $p$-$C_6H_4R{\cdot}CH(OH){\cdot}CN$.

(Standard energy level, R = H.)

| | Reductions in energy levels in the ground state of aldehyde. | | | Reductions in energy level in the activated state. | | | Reductions in energy levels in the ground state of cyanohydrin. | | |
|---|---|---|---|---|---|---|---|---|---|
| R. | $+I$. | $+M$. | ${}_{A}E_g$.† | $+I$. | $+M$. | $E_g$.† | $+I$. | $+M$. | ${}_{C}E_g$.† |
| Me | 10 | 120 | 130 | 4 | 100 | 104 | 6 | 99 | 105 |
| Et | 25 | 80 | 105 | 14 | 67 | 81 | 18 | 66 | 84 |
| $Pr^{\beta}$ | 39 | 40 | 79 | 16 | 33 | 49 | 26 | 33 | 59 |
| $Bu^{\gamma}$ | 50 | 0 | 50 | 22 | 0 | 22 | 32 | 0 | 32 |

† Positive values for ${}_{A}E_g$, etc., mean a positive *reduction* in the energy level, *i.e.*, a lower energy level.

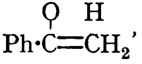
In the ground state of the cyanohydrin, formal conjugation does not extend into the side chain, and hence electron-release by the mesomeric mechanism will be smaller than in the parent aldehyde. A similar, but smaller, reduction has been made in the values assigned to the inductive effects in Table III because of the smaller electron-attraction of the side chain $-CH(OH){\cdot}CN$ than of $-CH{:}O$.

It will be seen that the relative energy levels in the ground states of the free aldehyde (${}_{A}E_g$) and its cyanohydrin (${}_{C}E_g$) are both in agreement with an order of stabilisation H < $Bu^{\gamma}$ < $Pr^{\beta}$ < Et < Me, but that the stabilising effect of any particular alkyl substituent is greater in the free aldehyde than in its cyanohydrin (${}_{A}E_g > {}_{C}E_g$). The differences ${}_{A}E_g - {}_{C}E_g$ * are a measure of the stability of the aldehyde relative to its cyanohydrin, *i.e.*, of the relative values of $K$ : the greater the difference the larger the value of the dissociation constant $K$. These differences are Me 25, Et 21, $Pr^{\beta}$ 20, $Bu^{\gamma}$ 18, in harmony with the observed sequence for $K$, *viz.*, H < $Bu^{\gamma}$ < $Pr^{\beta}$ < Et < Me.

The view that the values of $K$ are determined largely by the relatively greater stabilising effects of the alkyl group conjugated with carbonyl in the free aldehydes receives striking confirmation from the results of Lapworth and Manske (J., 1930, 1978) for phenyl alkyl ketones Ph·COR, which were obtained under exactly the same experimental conditions as our own. They are as follows :

| R = | H. | Me. | Et. | $Pr^{\beta}$. | $Bu^{\gamma}$. |
|---|---|---|---|---|---|
| $10^3K$ | 47 | 1300 | 600 | 250 | 90 |
| $\Delta F \times 10^{-2}$ ‡ | +31 | −2 | +3 | +8 | +14 |

‡ The signs of Lapworth and Manske's values for $\Delta F$ have been reversed to make them correspond with our values based on $\Delta F = -RT \ln K$ (see footnote, p. 192).

The large decrease in stability of the cyanohydrin in passing from benzaldehyde to acetophenone evidently arises from the increased stabilisation of the free carbonyl compound due to structures of the type  $Ph{\cdot}\overset{\bar{O}}{C}{=}\overset{\overset{+}{H}}{C}H_2$, and the order of cyanohydrin stability (R =) H > $Bu^{\gamma}$ > $Pr^{\beta}$ > Et > Me is that anticipated

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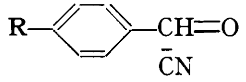
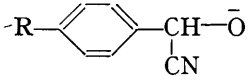
* See footnote on p. 196.

on the basis of the number of C–H bonds in the alkyl group R which are conjugated with C⁚O. When R = Ph the possibilities of conjugation are greatly enhanced, and this should cause much greater stabilisation of the ketone relative to its cyanohydrin. This accords with the fact that Lapworth (J., 1928, 2548) found no measurable formation of the cyanohydrin with benzophenone, *i.e.*, $K$ approaches infinity. This large effect of phenyl only operates when the group is directly conjugated with the carbonyl group, since the equilibrium constants for the cyanohydrin formation of $CH_3{\cdot}CO{\cdot}CH_2Ph$ ($10^3K = 21{\cdot}5$, $10^{-2}\Delta F = +22$) and $CH_3{\cdot}CO{\cdot}CH_2Me$ ($10^3K = 26{\cdot}5$, $10^{-2}\Delta F = +21$) (Lapworth and Manske, *loc. cit.*) are closely comparable in magnitude. In both these ketones there are five C–H bonds conjugated with the C⁚O group.

(b) *Kinetic Data.*—The common activated transition complex for both forward and back reactions will be a resonance hybrid symmetrically related to structures of types (X) and (XI). In this complex,

(X.)



(XI.)

electron-release from the *p*-alkyl substituent by the tautomeric mechanism would presumably be smaller than in the ground state of the free aldehyde owing to the opposing electron displacements initiated by the negative charge in the side chain. A proportionately greater diminution should occur in the inductive component. Account is taken of these factors in the values assigned in Table III.

The differences ${}_{\mathrm{A}}E_g - E_a$ ($\delta E_{k_1}$) * are a qualitative measure of the energies of activation for the forward reaction. They are:

| R = | Me. | Et. | Pr$^\beta$. | Bu$^\gamma$. |
|---|---|---|---|---|
| $\delta E_{k_1}$ ........................................ | 26 | 24 | 30 | 28 |

in agreement with the sequence observed for $k_1$, *viz.*, H > Et > Me > Bu$^\gamma$ > Pr$^\beta$. Similarly, $\delta E_{k_2} = {}_{\mathrm{C}}E_g - E_a$, a measure of the energies of activation for the back reaction, has the values Me 1, Et 3, Pr$^\beta$ 10, Bu$^\gamma$ 10, in harmony with the observed velocity sequence for $k_2$, *viz.*, H $\approx$ Me > Et > Pr$^\beta$ $\approx$ Bu$^\gamma$.

It is thus apparent that not only the regular sequence observed in the equilibria but also the "muddled" sequences of the velocity data receive a complete and consistent explanation on the basis of the same sets of relative energy levels derived from the theoretical concepts of the polar effects of alkyl groups recently developed in this series of papers. In conclusion, it may be noted that a close resemblance can be traced between the cyanohydrin reaction and the electrolytic reduction of the aldehydes at a dropping-mercury cathode (Baker, Davies, and Hemming, J., 1940, 692), and the complex results revealed in the latter investigation also receive a satisfactory explanation on the basis of very closely similar sets of values for the energy levels of ground and activated states (cf. Hemming, Thesis, University of Leeds, 1940).

## EXPERIMENTAL.

*Preparation of Materials.*—The *p*-alkylbenzaldehydes were prepared and purified by the methods given by Baker, Davies, and Hemming (*loc. cit.*). In every case purification involved conversion first into the bisulphite compound and then into the semicarbazone. Regeneration of the aldehyde from the purified semicarbazone was effected by steam-distillation with oxalic acid in an atmosphere of carbon dioxide, followed by repeated fractionation under reduced pressure in a current of nitrogen. All samples were stored in the dark under nitrogen and were redistilled into the weight pipette with the same precautions immediately before use. The samples used had the following b. p.'s: benzaldehyde, 73°/21 mm.; *p*-methyl-, 98°/24 mm.; *p*-ethyl-, 64·2°/1·2 mm.; *p*-*iso*propyl-, 120°/23 mm.; *p*-*tert.*-butyl-benzaldehyde, 80°/0·9 mm.

Liquid hydrogen cyanide was prepared as described in "Organic Syntheses," 1927, VII, 50, and was refractionated from phosphoric oxide in an all-glass apparatus. The standard solution was prepared by dissolving 16 c.c. of the liquid in 400 c.c. of constant boiling-point alcohol, and was stored in well-stoppered brown bottles sealed with paraffin wax. Its concentration (approximately 10 m.-mol./10 c.c.) remained unchanged over long periods.

Aqueous alcohol (64 O.P. = 93·5% by vol.) was refluxed with 2% of oxalic acid, fractionated through a Widmer column, refluxed with 5% by weight of sodium hydroxide, again distilled through a column, and finally repeatedly fractionated, the portion of constant b. p. (78·5°) being stored for use. All-glass apparatus was used throughout.

*Calibration of Apparatus.*—All flasks and pipettes were carefully calibrated by weight and checked against

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* If $x$ and $y$ are, respectively, the energy levels of the ground and activated states in the unsubstituted (reference) compounds, then in, *e.g.*, the methyl compounds the energy level in the ground state is ($x - 130$) and, in the activated state, ($y - 104$). The activation energy for the unsubstituted compound is $y - x$, and for the methyl compound, $(y - 104) - (x - 130) = y - x + 26$ (${}_{\mathrm{A}}E_g - E_a$). The values of $\delta E_k$ are thus measures of the *increases* in the potential energies of activation over the standard reference values for the unsubstituted compound.

each other, those used for alcoholic solutions being calibrated with this solvent. For titrations an N.P.L. standard semi-micro burette, reading to 0·01 c.c., was employed.

*Determination of Equilibrium Constants.*—At 20° the technique of Lapworth and Manske (*loc. cit.*), slightly modified and standardised to minimise loss due to the volatility of hydrogen cyanide, was employed. In preparation of the reaction mixture, exposure of the aldehyde to the air was reduced to a minimum and no appreciable oxidation was possible with the technique used. The titrations on the hydrogen cyanide solution (blank) always agreed to ± 0·02 c.c. and the consistency of the various determinations of $K$ is illustrated by the values obtained with benzaldehyde : $10^3K = 4{\cdot}57, 4{\cdot}51, 4{\cdot}25, 4{\cdot}39, 4{\cdot}27, 4{\cdot}56, 4{\cdot}44, 4{\cdot}70$ : mean $4{\cdot}47 \pm 0{\cdot}12$. The value 4·57 was obtained from one velocity determination which was left until equilibrium was attained. The mean deviations from the mean are recorded in each case in Table I.

At 35° this technique was unsatisfactory, presumably owing to the greater and irregular losses of hydrogen cyanide during sampling. The following sealed-bulb technique was therefore developed, and is regarded as a marked improvement on that of Lapworth and Manske.

A series of bulb tubes (see Fig. 1) were made from 4″ × ½″ test-tubes such that (1) the constricted portion was wide enough for insertion of the stem of a 2-c.c. pipette; (2) they contained 10 c.c. when filled to a mark low down on the constricted portion, and (3) the bulbs were of such thickness that they would withstand the slight pressure developed in the thermostat but could easily be broken under the silver nitrate solution after equilibration was complete. The bulbs, cleaned with the pure solvent, were calibrated in the thermostat with 10 c.c. of pure solvent at 35°, and a mark made on the constricted portion. The appropriate quantity of aldehyde was delivered from a weight pipette, with the usual precautions, into about 3 c.c. of the solvent (containing the requisite amount of tri-*n*-propylamine in solution), the space above this solvent having previously been filled with nitrogen. Any trace of aldehyde in the constriction was immediately washed down with more solvent. 2 C.c. of the standard hydrogen cyanide solution were added and the total volume was adjusted to the 10 c.c. mark in the thermostat. The tube was kept closed with a well-fitting rubber stopper during these operations. The bulb was then cooled in a good freezing mixture, and sealed near the top of the constricted portion. After immersion in the thermostat for 24 hours the outside was well washed with distilled water at 35°, and the bulb broken under an appropriate volume of 0·05N-silver nitrate and nitric acid, also at 35°. The excess of silver nitrate, arranged to be about 5 c.c., was determined with ammonium thiocyanate in the usual manner. The consistency of the results is illustrated by details (Table IV) of the determinations with *p-tert.*-butylbenzaldehyde.

FIG. 1.

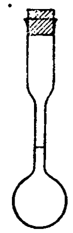
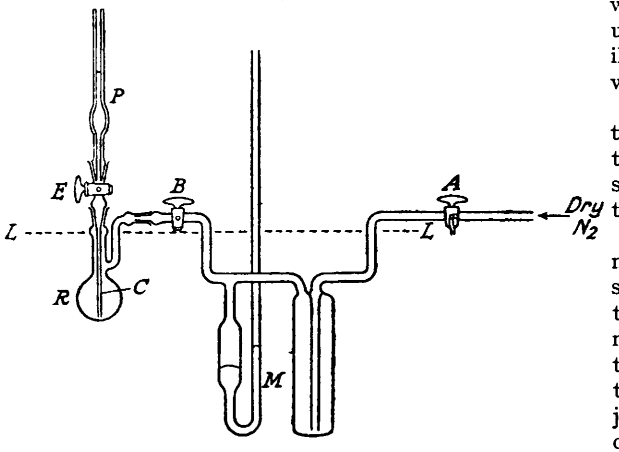


FIG. 2.



*Velocity Determinations.*—The preliminary work to determine suitable experimental conditions and to evaluate the effects of possible errors has been summarised (p. 193). Full details are given in the thesis referred to on p. 196.

The all-glass apparatus used for the kinetic measurements is shown in Fig. 2, devised so that the sample could be transferred from the reaction flask $R$ to the calibrated 2-c.c. pipette $P$ by pressure of nitrogen. The drawn-out end of $P$ was ground into the cone above the tap $E$, the dead space above this tap being as smallas possible. All ground glass joints in the apparatus were standard and interchangeable. The whole apparatus could be immersed in the thermostat to the line $LL$. Immediately before each determination the whole apparatus

TABLE IV.

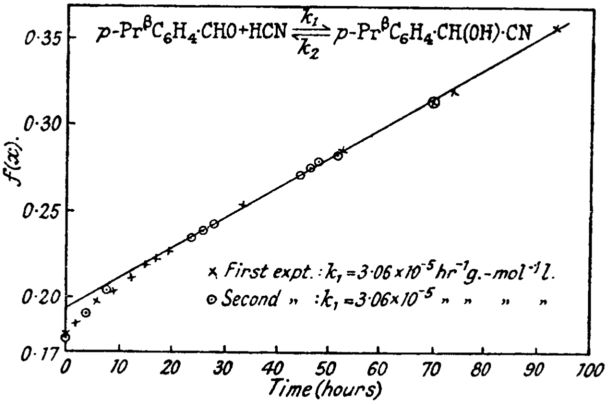
Vol. of HCN solution = 2 c.c. Total vol. = 10 c.c. Temp. 35° ± 0·05°.

| No. | Wt. of aldehyde, g. | 0·05N-AgNO$_3$ used, c.c. | 0·05N-NH$_4$NCS for excess, c.c. | 0·05N-AgNO$_3$ for free HCN, c.c. | $N_A$. | $N_{HCN}$. | $N_{Cyan.}$. | $N_{R \cdot CHO}$. | $10^2K$, g.-mol.-1.$^{-1}$ |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 0·4184 | 10 | 4·69 | 5·31 | 12·905 | 1·328 | 8·220 | 4·685 | 15·14 |
| 2 | 0·4468 | 10 | 5·37$_5$ | 4·62$_5$ | 13·780 | 1·156 | 8·374 | 5·406 | 14·93 |
| 3 | 0·4518 | 10 | 5·40$_5$ | 4·59$_5$ | 13·935 | 1·149 | 8·399 | 5·536 | 15·14 |
| 4 | 0·4470 | 10 | 5·35 | 4·65 | 13·785 | 1·163 | 8·387 | 5·395 | 14·96 |
|  | Blank | 40 (1—3) | 1·88 | 38·12 | — | 9·530 | — | — | — |
|  |  | 40 (4) | 1·80 | 38·20 | — | 9·550 | — | — | — |

$N_A$ is the initial concentration of aldehyde, and $N_{HCN}$, $N_{Cyan.}$, and $N_{R \cdot CHO}$ are the equilibrium concentrations of free HCN, cyanohydrin, and free aldehyde, respectively, in m.-mols./50 c.c.

was swept out with a stream of pure, dry, oxygen-free nitrogen. About 10 mg.-mols. of the aldehyde were transferred from a weight-pipette (with the usual precautions) into 20 c.c. of the solvent alcohol, 0·02M with respect to both pyridine and pyridinium benzoate, in a 25-c.c. calibrated flask, and adjustment to the mark was made with more solvent catalyst after thermal equilibrium had been attained in the thermostat. A solution containing 20 c.c. of the stock alcoholic solution of hydrogen cyanide in 50 c.c. of the pure solvent alcohol was similarly prepared. The concentration of the latter solution was determined by withdrawing 5 c.c. and delivering it under the surface of 40 c.c. of 0·05N-silver nitrate, the excess of which was determined in the usual manner. 20 C.c. of the aldehyde solution were pipetted into the reaction flask *R* (of about 50 c.c. capacity) and, at zero time, 20 c.c. of the hydrogen cyanide solution were added, thus diluting the catalyst concentration to 0·01M. The tap-head *E* with its pipette were immediately inserted, and the reaction flask was attached to the rest of the apparatus. With taps *E* and *B* closed, the nitrogen stream (previously by-passed into the air through the three-way tap *A*) was passed into the apparatus until a pressure of approximately 50 mm. was registered on the manometer *M*. By manipulation of taps *E* and *B*, a sample of the reaction mixture was gently forced into *P*, and the free hydrogen cyanide in this 2-c.c. sample was determined in the usual way. The small amount of liquid remaining in the cone above *E* was dried out with filter-paper, and the column of liquid in the tube *C* was allowed to fall back into the flask by a momentary release of the nitrogen pressure in the apparatus. Between sampling, the cone above *E* was closed with a glass stopper.

FIG. 3.



The reaction was usually followed for about 100 hours, and the plot of about 15 values of $\log_{10}(x - \alpha)/(x - \Delta)$ against *t* always gave a good straight line from the slope of which $k_1$ was determined as indicated on p. 193. At least two consistent values of $k_1$ were obtained with each aldehyde. The reproducibility of the results is illustrated in Fig. 3, which gives the plot of f(*x*) against *t* for *p*-*iso*propylbenzaldehyde, using the actual working units, *viz.*, mg.-mols./40 c.c. and hours.

It will be noticed that a slight divergence from the straight line occurs during the first 10% of the reaction. It was proved that such divergences could not be accounted for by changes in either the value of *K* or of the initial hydrogen cyanide concentration much greater than the probable experimental errors. Since, in isolated examples, strict adherence to the straight-line relationship was observed right from the start of the reaction, these small initial disturbances are regarded as due to purely fortuitous circumstances.

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