287. *Prototropy in Relation to the Exchange of Hydrogen Isotopes. Part I. Rates of Isomerisation and of Hydrogen Isotope Exchange in Unsaturated Nitriles.*

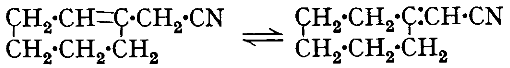
By Christopher K. Ingold, Eduardo de Salas, and Christopher L. Wilson.

This paper initiates an extension, which it is planned considerably to develop, of a general investigation ("Optical Activity in Relation to Tautomeric Change," Parts I—VI, J., **1933**, 1493, *et seq.*) into what has been called the "intimate" mechanism of prototropic change. The evidence hitherto brought to bear on the problem consists essentially in certain comparisons of reaction rates. For instance, we have compared the rate of loss of the optical activity which arises from a centre of asymmetry in a prototropic system with the chemically determined rate of isomerisation of the system. We have also compared the rate of racemisation of a prototropic system with the rate at which the mobile hydrogen atom is replaced by a halogen, where, as in enolisable ketones, the latter rate is independent of the halogen. There is a fourth kind of reaction rate which can be made to serve the general purpose underlying such comparisons, and that is the rate of isotopic exchange of the mobile hydrogen atom. In the work now to be described we compare the chemically measured rate of isomerisation of a prototropic system with the rate at which it exchanges hydrogen with the medium in which isomerisation occurs.

Observations are already on record which show that the mobile hydrogen of tautomeric compounds is readily exchanged with deuterium either during isomerisation or at least under conditions known to favour prototropic change. This has been proved for acetylacetone (Klar, *Z. physikal. Chem.*, 1934, **26**, *B*, 335), acetone (Schwarz and Steiner, *ibid.*, 1934, **25**, *B*, 153; Klar, *loc. cit.*; Halford, Anderson, Bates, and Swisher, *J. Amer. Chem. Soc.*, 1934, **56**, 491; 1935, **57**, 663), the acetate ion (Hall, Bowden, and Jones, *ibid.*, 1934, **56**, 750; Goldfinger and Lasareff, *Compt. rend.*, 1935, **200**, 1671), and the vinylacetate ion (Ives and Rydon, J., 1935, 1735). None of these demonstrations has, however, been accompanied by rate comparisons of the kind contemplated.

Our previous work with optically active substances has shown that prototropic systems are divisible into two broad classes. The first class contains all the highly mobile or moderately mobile systems for which the change proceeds through kinetically independent ions, these being produced and re-associated in distinct steps. This mechanism (Ingold, Shoppee, and Thorpe, J., 1926, 1477) has been distinguished by Pedersen as the "bimolecular" mechanism (*J. Physical Chem.*, 1934, **38**, 541). It appears to be operative in all systems the anions of which are stable enough to exist, *i.e.*, all systems capable of being alkylated, *e.g.*, keto-enols. The second class contains those slightly mobile prototropic systems the anions of which are so unstable or so difficult to form that they never attain kinetic independence, but are dissociated from one proton and re-associated in a different place with another in a single synchronised act (Hsü, Ingold, and Wilson, J., 1935, 1778). Pedersen calls this the "termolecular" mechanism, and it was originally suggested by Lowry (J., 1927, 2554). So far as is known it applies only to systems the anion of which cannot exist in the solvated state, *i.e.*, to systems which are incapable of being directly alkylated, *e.g.*, derivatives of benzylidenebenzylamine and presumably αγ-diphenylpropene.

The present research relates to the class of systems which use the bimolecular mechanism, and as an example we have chosen the unsaturated nitriles (I) $\rightleftharpoons$ (II). These were

(I.)  (II.)

$$\begin{array}{l} CH_2\cdot CH{=}C\cdot CH_2\cdot CN \\ CH_2\cdot CH_2\cdot CH_2 \end{array} \rightleftharpoons \begin{array}{l} CH_2\cdot CH_2\cdot C{:}CH\cdot CN \\ CH_2\cdot CH_2\cdot CH_2 \end{array}$$

selected because interconversion proceeds at a convenient rate, and because we thought at the outset that the equilibrium constant was known. The interconversion was first investigated by Kandiah and Linstead (J., 1928, 2139), who obtained 95% as the equilibrium proportion of (II) in *N*-ethyl-alcoholic sodium ethoxide at 25°. Using 0·1*N*-alcoholic sodium ethoxide at 25°, we obtained a figure practically indistinguishable from 100%. There is thus considerable uncertainty about the equilibrium constant, and although the rate of the change (I) $\longrightarrow$ (II) can be measured with adequate precision, nothing better than a rough upper limit can be given for the rate of the reverse reaction (II) $\longrightarrow$ (I). Hence we are able only to compare the measured rate (I) $\longrightarrow$ (II) with the rates at which the separate compounds (I) and (II), and the changing system (I) $\rightleftharpoons$ (II), exchange their hydrogen with the isotopically distinguished hydrogen of the medium in which isomerisation takes place. We have used " light " nitriles and " heavy " alcohol, *i.e.*, ordinary nitriles and ethyl alcohol with considerably more than the normal proportion of ionisable deuterium, *i.e.*, of $C_2H_5{\cdot}OD$.

The essential result is this : compound (I) interchanges hydrogen with the medium much more rapidly than it becomes converted into (II), and this conversion is in turn much more rapid than hydrogen exchange between (II) and the medium.

Described in more detail, the observations were as follows. When dissolved in " heavy " 0·1*N*-ethyl-alcoholic sodium ethoxide at 25°, compound (I) reached pseudo-equilibrium with respect to the uptake of deuterium very rapidly. The speed of exchange was much too great for measurement, but we know that this phase of the reaction was finished before measurable isomerisation had occurred. If we assume that two hydrogen atoms are thus rapidly exchanged, the isotopic compositions lead to an exchange equilibrium constant which agrees satisfactorily with the constant calculated by approximate methods from the bonding forces. This rapid isotopic interchange was succeeded by a slow conversion of (I) into (II), and a contemporaneous *diminution* in the deuterium content of the total nitrile, (I) + (II), isolated after successive intervals of time. The deuterium content of these mixed nitriles was an approximately linear function of the mol.-fractions of the isomerides. When the conversion into compound (II) was complete, the deuterium content had fallen to about three-quarters of what it was immediately after (I) had been dissolved in the medium. When compound (II) was dissolved in the same medium, there was an initial, very small uptake of deuterium, which we believe to be due to an impurity. No further deuterium was taken up during a period of time which would have sufficed for a considerable conversion of (I) into (II).

In interpreting these results, it is convenient to consider first the broad outcome as stated in the last paragraph but one. It will be simplest at the outset to suppose that the changes occur in a deuterium-free medium; we imagine, however, that we have some method of labelling the individual protons. The first point to be observed is that the greater rate of hydrogen exchange than of isomerisation is consistent with our classification of the unsaturated nitrile system as one of those which should undergo isomerisation by the so-called bimolecular mechanism. Evidently if one hydrion could enter the molecule only whilst another is being withdrawn from a different position, there should be agreement between the rates of exchange and isomerisation. On the other hand, if ionisation and ionic association occur as separate steps, then the exchange must be faster than the isomerisation, and might be much faster; for not every anion that is formed from (I) will yield (II) because some will revert to (I), whereas every anion that is formed leads to hydrogen exchange with the medium.

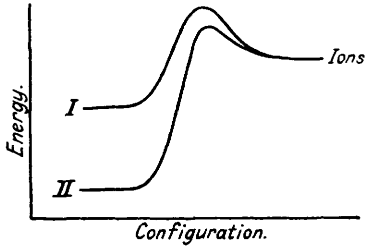
The distinction can be represented symbolically if we write the mechanism thus :

$$\text{(I.)}\quad \underset{\kappa_3}{\overset{\kappa_1}{\rightleftharpoons}}\ \text{Ions}\ \underset{\kappa_4}{\overset{\kappa_2}{\leftrightharpoons}}\quad \text{(II.)}$$

Since (I) and (II) are very weak acids, we may assume that their rates of ionisation are very much smaller than the rates of their formation from the ions. It follows that the rate of proton exchange of (I) is measured simply by the rate constant κ_1. The proportion of ions which, having been formed from (I), pass into (II) is evidently $\kappa_4/(\kappa_3 + \kappa_4)$. Hence the rate constant for the conversion of (I) into (II) is $\kappa_1[\kappa_4/(\kappa_3 + \kappa_4)]$. It is clear that the factor, $\kappa_4/(\kappa_3 + \kappa_4)$, by which the rate of isomerisation differs from the rate of hydrogen exchange, must be less than unity and might be much less.

That it appears to be much less is consistent with analogy. We are familiar with the idea that in a ψ-acid one form attains equilibrium with its ions rapidly whilst the other comes into equilibrium with the same ions much more slowly. This is shown for the formation of the ions by the instantaneous reaction of an *aci*-form with alkali and the slow reaction of the corresponding ψ-form. It is shown for the recombination of the ions by the circumstance that cautious addition of acid to an alkali-metal salt will often give the *aci*-form first, even although this may be the less thermodynamically stable modification. Now, Hugh and Kon (J., 1930, 775) have shown that this kind of relationship holds for certain αβ- and βγ-unsaturated esters: cautious acidification of the solution of either in alcoholic sodium ethoxide gives the βγ-unsaturated ester first even when the αβ-unsaturated isomeride is the more stable. Our isomeride (I) is a βγ-unsaturated nitrile, and hence we should expect the ions on recombination to give (I) much more rapidly than (II), notwithstanding that (II) is thermodynamically more stable than (I). This is equivalent to saying that we would expect that $\kappa_4/(\kappa_3 + \kappa_4)$ would be much less than unity for the unsaturated nitriles; in short that $\kappa_3 \gg \kappa_4$.

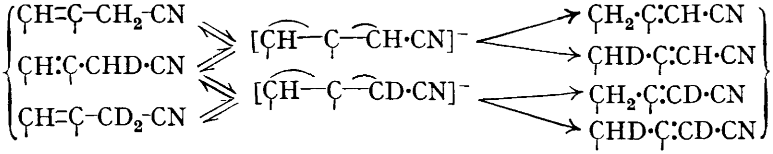
The system is strongly unbalanced with respect to velocities. From the assumption that (I) and (II) are very weak acids, it follows that their rates of conversion into ions are equal respectively to their rates of proton exchange. In each case this rate will be somewhat greater than the observed rate of deuterium uptake, for, as we shall show in detail later, deuterons are transferred more slowly than are protons from the medium containing both to the anion of the nitriles. However, for each nitrile the rate of proton exchange will be of the same order of magnitude as the rate of replacement of a proton by a deuteron, and hence our observation that for nitrile (I) the uptake of deuterium was too rapid to be measured, whilst for nitrile (II) it was too slow to be detected, proves that there must be a similarly marked distinction between the rates at which the two nitriles exchange ordinary hydrogen, and therefore between their rates of ionisation: in symbols $\kappa_1 \gg \kappa_2$. Concerning the recombination of the ions to give the nitriles, we have already seen that $\kappa_3 \gg \kappa_4$.



We have next to consider the meaning of the observation that the rate constant for the isomerisation, besides being much smaller than κ_1, is also much greater than κ_2. We have seen that the isomerisation rate constant is given by $\kappa_1[\kappa_4/(\kappa_3 + \kappa_4)]$; the conclusion that κ_3 is much greater than κ_4 allows us to replace this expression by $\kappa_1\kappa_4/\kappa_3$. The observation is that this is much greater than κ_2: in symbols $(\kappa_1\kappa_4/\kappa_3) \gg \kappa_2$. Dividing through by κ_1 and taking reciprocals, we obtain $(\kappa_1/\kappa_2) \gg (\kappa_3/\kappa_4)$. Thus there is a greater proportionate disparity between the rates of ionisation of the nitriles than between the rates of their formation from the ions. This is just what we should expect from the theory (see figure) that the ions are common to the two nitriles, and that ionisation involves large energies of activation whilst ionic recombination requires only small activation energies. The ionisation can evidently accommodate a large difference between the energies of activation for the two compounds, whilst for the ionic associations there is room only for a small difference. The critical states must be more nearly alike than the nitriles themselves, since the former represent a stage on the way to absolute identity.

We have still to consider the meaning of the slow fall of deuterium content during isomerisation, and for this purpose it is necessary to set out the isomerisations and exchanges in further detail. They may be represented as follows:

(I.)



(II.)

This scheme does not show all the possible reactions, but it contains all those which can occur to an appreciable extent under the conditions employed: for instance, we omit the ionisations of (II), which in complete equilibrium would lead to two more ions (with γ-deuterium atoms), and thence to three more forms of (I) (each with a γ-deuterium atom), and to two more forms of (II) (each with two γ-deuterium atoms). It is the imperfection of the equilibrium, as shown by the above scheme, which is the essential cause of the effect we have to explain.

The scheme shows that two hydrogen atoms in (I) can be successively ionised and exchanged, and this is what we assumed from the magnitude of the initial rapid uptake of deuterium by (I). From this uptake we can calculate an " equivalent " exchange equilibrium constant, *i.e.*, a constant defined in terms of equivalent concentrations, and therefore in terms of half-mol. concentration of those species which can contain two atoms of deuterium :

$$K_{\text{eq.}} = \{[(C_8H_9N)_{\frac{1}{2}}D]/[(C_8H_9N)_{\frac{1}{2}}H]\}/\{[EtOD]/[EtOH]\}$$

The value is 0·67, which is close to what would be estimated from the frequencies characteristic of C—H, C—D, O—H, and O—D links.

The equilibrium constant has been formulated in a manner which brings out its interpretation as the ratio in equilibrium of the D : H ratio in one exchanging position of the nitrile to the D : H ratio in the exchanging position of the ethyl alcohol. We shall now make the assumption that substantially the same value of the constant, 0·67, can be applied separately to *each* exchanging position, not only of nitrile (I), but also of the ion and of nitrile (II) : for each position the ratio in equilibrium of the D : H ratio to the D : H ratio in the hydroxyl group of the medium will be taken as 0·67. This is an approximation, but nevertheless it must be nearly true, because all these equilibrium constants are determined substantially by the vibrational frequencies of the links, and we know that the frequencies of links such as C—H and C—D are only slightly constitutive.

By expanding the scheme given above until it represents complete equilibrium, one can see that in the course of establishing such an equilibrium a third hydrogen atom becomes exchangeable. Under the assumption of the preceding paragraph, therefore, the deuterium content of nitriles should rise during *complete* equilibrium by nearly 50% above the value which obtains after the initial rapid exchange of two atoms (exactly 50% if the quantity of medium were infinite). In our experiments this does not happen, because the first step in the replacement of the third hydrogen atom would be the ionisation of (II), and this change is altogether too slow. Therefore, in nitrile (II), as in nitrile (I), there are effectively only two hydrogen atoms replaceable by deuterium.

Now if the isotope ratios for these two hydrogen atoms in (II) could be determined by chemical equilibria, just as the isotope ratios are for the two replaceable hydrogen atoms of (I), then we should expect the deuterium content of the nitriles to remain substantially unchanged during isomerisation. We shall see that the reason why it changes is that the isotope ratio of only one of the two replaceable atoms of (II) is fixed by equilibria, whilst that of the other is determined by the relative rates of effectively irreversible reactions.

The total D : H ratio for the two relevant positions of (II) may be represented by $(\{D_\alpha\} + \{D_{\gamma'}\})/(\{H_\alpha\} + \{H_{\gamma'}\})$, where the braces { } signify the total number of atoms of the kind and in the position indicated which are contained in some fixed number of molecules of (II); the subscripts α and γ' indicate position, and the dash distinguishes that individual γ-position which is filled by the addition of a proton or deuteron to the ion. This total D : H ratio for nitrile (II) can be regarded as a kind of average between the D : H ratio for the α-position and the D : H ratio for the γ'-position, and its numerical value must obviously lie between those of the separate ratios for the two positions. The D : H ratio for the α-position is easily deduced, for, as the scheme shows, the hydrogen and deuterium atoms in this position in (II) are identically those which were in the α-position of the ion; and here the D : H ratio is established by a rapidly attained equilibrium, which we have given reasons for assuming is governed by the exchange equilibrium constant 0·67. Therefore the α-D : H ratio in (II) will be 0·67 times the average D : H ratio in the hydroxyl group of the medium in which (II) is formed. This statement takes care also of a minor point, which is that, as the quantity of medium is limited, it becomes slightly enriched in deuterium during the slow loss of this isotope from the interchanging nitriles, so that we must calculate with the average isotope composition of the medium, not its composition at the commencement of the interconversion.

The D : H ratio in the γ'-position of (II) is governed, not by any equilibrium, but by the relative rates at which deuterons and protons are irreversibly taken from the medium into this position. One can see qualitatively that if this ratio of rates happened to be just 0·67 : 1, then the γ'-D : H ratio in (II) would be 0·67 times the average D : H ratio of the hydroxyl group of the medium, and the total deuterium content of (II) would then be just the same as if both positions had been filled by completely established exchange equilibria, all, of course, subject to the constant 0·67 ; *i.e.*, the deuterium content of (II) would be the same as that of (I). The fact that the deuterium content of (II) is appreciably smaller than that of (I) merely means that there is a greater disparity between the rates of uptake of the deuteron and the proton than would be represented by the velocity ratio 0·67 : 1 ; in other words, the proton must enter the γ'-position of (II) more than 1·5 times faster than the deuteron.

We can calculate the ratio of the rates of uptake. Our isotopic analysis of the product (II) gives the value of $(\{D_\alpha\} + \{D_{\gamma'}\})/(\{H_\alpha\} + \{H_{\gamma'}\})$, and we have deduced the value of $\{D\}_\alpha/\{H\}_\alpha$. The other two relations which are necessary in order to solve for the four unknowns, $\{D_\alpha\}$, etc., come from the conditions that the numbers of atoms occupying the α- and γ'-positions are the same, $\{D_\alpha\} + \{H_\alpha\} = \{D_{\gamma'}\} + \{H_{\gamma'}\}$, and that each is equal to the number of molecules under consideration. Thus we can calculate $\{D_{\gamma'}\}/\{H_{\gamma'}\}$, and a comparison of this ratio with the mean D : H ratio of the medium gives the ratio of the rates. We find that the proton is transferred 4·1 times as fast as the deuteron from the alcoholic medium to the γ'-position of (II), and this figure is consistent with what is already known about the relative rates of proton and deuteron transference (cf. Wynne-Jones, *J. Chem. Physics*, 1934, **2**, 381).

This explanation of the lower deuterium content of (II) than of (I) may be summarised as follows. Of the two positions concerned with exchange in each nitrile, both of those in (I) and one of those in (II) attain isotopic equilibrium with the medium ; the second position in (II), however, is filled irreversibly, and is relatively poor in deuterium because the proton is taken up so much more rapidly than the deuteron. The reason why the positions which come into isotopic equilibria are considerably richer in deuterium is that, although for these positions likewise the proton is taken up more rapidly than the deuteron, the proton is also withdrawn the more rapidly, and this largely compensates for the faster uptake.

We can deduce the ratio of the rates of withdrawal if we assume that the equilibrium constant 0·67 would apply to the γ'-position of (II) if equilibrium were attained, or alternatively, that the uptake velocity ratio 4·1 applies to the other exchanging positions of (I) and (II) in which equilibrium is attained. The equilibrium equation

$$\mathrm{DO{\cdot}Et} + \mathrm{HC}\vdots \rightleftharpoons \mathrm{HO{\cdot}Et} + \mathrm{DC}\vdots \text{ with } K = [\mathrm{DC}\vdots][\mathrm{HOEt}]/[\mathrm{DOEt}][\mathrm{HC}\vdots]$$

can be decomposed into the equations

$$\mathrm{Et}\ddot{\bar{\mathrm{O}}}\left\{\begin{matrix} + \mathrm{HC}\vdots \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} \mathrm{HO{\cdot}Et} \\ + \mathrm{DC}\vdots \underset{k_2''}{\overset{k_1''}{\rightleftharpoons}} \mathrm{DO{\cdot}Et} \end{matrix}\right\} + \bar{\mathrm{C}}\vdots \text{ with } \left\{\begin{matrix} K' = [\mathrm{HOEt}][\bar{\mathrm{C}}\vdots]/[\mathrm{Et}\bar{\mathrm{O}}][\mathrm{HC}]\vdots \\ K'' = [\mathrm{DOEt}][\bar{\mathrm{C}}\vdots]/[\mathrm{Et}\bar{\mathrm{O}}][\mathrm{DC}\vdots] \end{matrix}\right\}$$

and hence

$$K = K'/K'' = (k_1'/k_2')/(k_1''/k_2'') = (k_1'/k_1'')/(k_2'/k_2'')$$

We have $K = 0{\cdot}67$ and $k_2'/k_2'' = 4{\cdot}1$; hence $k_1'/k_1'' = 2{\cdot}75$. In words, the proton is withdrawn from the nitrile molecule 2·75 times as fast as the deuteron by the ethoxide ions of the medium.

EXPERIMENTAL.

Materials.—Ethyl *cyclo*hexan-1-ol-1-acetate was prepared by the Reformatski condensation of *cyclo*hexanone and ethyl bromoacetate (Wallach, *Annalen*, 1906, **347**, 329 ; Wilson, *Chem. and Ind.*, 1935, 558). Dehydration of the hydroxy-ester by means of potassium hydrogen sulphate gave ethyl Δ^1-*cyclo*hexenylacetate, which was hydrolysed to the corresponding acid (Wallach, *Annalen*, 1905, **343**, 51). The hydroxy-ester was also hydrolysed to the hydroxy-acid, which was converted into *cyclo*hexylideneacetic acid by boiling with acetic anhydride (*idem, ibid.*, 1909, **365**, 255). The unsaturated acids were converted into their chlorides by means of thionyl chloride, and thence into their amides (cf. *idem, ibid., Annalen*, 1907, **353**, 292). The latter gave the respective nitriles in 70—73% yield when treated by Kandiah and Linstead's method (J., 1929, 2139).

Anhydrous Ethyl Deuteralcohol.—Dry ethyl alcohol (Lund and Bjerrum, *Ber.*, 1931, **64**, 210, who give $d_{4°}^{25°}$ 0·78503) had $d_{4°}^{25°}$ 0·78506. A mixture of this material (115 c.c.) and water (10 c.c.) was refluxed for 6 hours with freshly ignited lime (50 g.), and distilled in a vacuum in an all-glass apparatus. The product (90 c.c.) had $d_{4°}^{25°}$ 0·78530, which corresponds with a water content of 0·1%. The water content was reduced to less than 0·01% ($d_{4°}^{25°}$ 0·78506) by refluxing with three times the necessary weight of magnesium amalgam. Repetition of the experiment, but upon deuterium oxide (10 c.c., 99·2 atoms %), gave anhydrous deuteralcohol.

Determination of Ionisable Deuterium in the Alcohol.—A sample of the deuteralcohol (b g.), diluted with " light " alcohol (a g.) was burnt over red-hot copper oxide, and the isotopic composition of the water produced was determined by measurement of density. If the latter corresponds to P atoms % of deuterium in the combustion water, then the atomic percentage of deuterium in the hydroxyl group of the deuteralcohol is $x = 6P(a + b)/(b - 0{\cdot}001302aP)$. In an actual experiment with the alcohol prepared as above, $a = 8{\cdot}7437$; $b = 0{\cdot}73391$, and $P = 0{\cdot}485$; and thus $x = 37{\cdot}4$.

Metallic sodium was dissolved in the deuteralcohol to give a 0·1*N*-solution of sodium ethoxide. A separation coefficient of 3 being assumed for this reaction, it follows that the ethoxide solution has an ionisable deuterium content of 37·5 atoms %.

Analysis of Mixtures of the Nitriles (cf. Linstead and May, J., 1927, 2565).—Two solutions were prepared : A, iodine (6·76 g.) in ethyl alcohol (100 c.c.), and B, mercuric chloride (10·14 g.) in ethyl alcohol (100 c.c.). Equal volumes of A and B were mixed, and the mixture was diluted with its own volume of ethyl alcohol. After the mixture had been kept in the dark for 24 hours, potassium iodide was added, and the solution was titrated with 0·05*N*-thiosulphate solution.

An accurately weighed portion of the mixed nitriles was treated at 25·0° with the equivalent amount of iodine chloride solution calculated for complete addition. After one hour water (300—400 c.c.) and potassium iodide were added, and the solution was titrated with thiosulphate. The error of the method is a few units %.

Artificial mixtures of the two nitriles gave the following amounts of addition :

βγ-Unsaturated nitrile (%)	100·0	55·0	38·5	0·0
Iodine addition (%)	81·7	53·1	43·2	17·0

Isolation of Nitriles from the Reaction Mixtures.—The sodium ethoxide solution of the nitriles was poured into a large excess of distilled water and extracted with ether, the extract being shaken several times with water. The recovered nitrile mixture was distilled in a high vacuum without ebullition. On keeping, the nitriles developed an acid reaction and the iodine absorption fell; it was necessary therefore to carry out the iodine chloride addition as soon as possible after isolation.

Isotopic Composition of the Nitriles.—The nitrile mixture (*ca.* 2·5 g.) was introduced into a silica boat, and burnt in a stream of air over heated copper oxide. The combustion water, collected in a trap at − 78°, was distilled from silver oxide without ebullition in an all-glass apparatus. The density was determined with a 1 c.c. pyknometer, which gave an accuracy of a few parts per million.

Isomerisation of the βγ-Unsaturated Nitrile in " Light " Solvent.—The change is represented by the following figures for 0·1*N*-sodium ethoxide at 25·0° :

Time (hours)	0·0	1·0	3·0	17·0
βγ-Unsaturated nitrile (%)	100·0	96·5	77·6	19·1

The corresponding unimolecular velocity constant is $0{\cdot}27 \times 10^{-4}$ sec.$^{-1}$.

Isotopic Exchange and Isomerisation in the " Heavy " Solvent.—In all the experiments, n g. of the βγ-unsaturated nitrile were treated at 25° with 2·5n c.c. of 0·1*N*-ethoxide solution. A portion of the isolated and purified nitriles was submitted to iodination, and the remainder burnt. The results are in the following table :

Original nitrile		$\beta\gamma$-.				$\alpha\beta$-.	
Time (hours)		*ca.* 0·0	3·0	6·0	51·0	0·02	3·0
$\beta\gamma$-Unsaturated nitrile (%)		*ca.* 100·0	84·8	66·5	0·8	—	—
Combustion water	Excess density (p.p.m.)	3607	3464	3300	2694	161	159
	D (atoms %)	3·903	3·748	3·572	2·916	0·174	0·172

We thank the Royal Society for a grant for materials, and the Academia de Ciencias de Madrid for financial assistance accorded to one of us.

UNIVERSITY COLLEGE, LONDON.

[*Received, July 3rd,* 1936.]