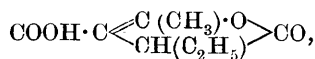## CXI.— *Ketolactonic Acid and its Homologues.*

By CHARLES H. G. SPRANKLING, B.Sc. Lond.

SOME years ago, Young (Trans., 1883, **172**) found that, on heating β-ethylic acetosuccinate, alcohol was removed, and the residue, on hydrolysis with dilute hydrochloric acid, yielded, in addition to α-ethyl-β-acetopropionic acid and a small quantity of ethylsuccinic acid, a crystalline acid which had the empirical formula $C_8H_{10}O_4$; this he termed ketolactonic acid and from it he obtained three barium salts :
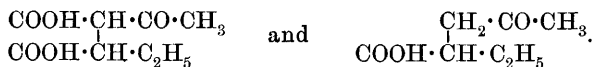
(1) By neutralisation with barium carbonate.
(2) By the action of barium hydroxide in the cold.
(3) By the action of barium hydroxide at 100°.

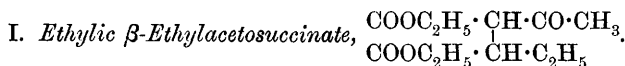From the composition of these salts, he concluded that the constitutional formula of ketolactonic acid was probably

$$COOH \cdot C {<} {\overset{\textstyle C\,(CH_3) \cdot O}{\underset{\textstyle CH(C_2H_5)}{}}} {>} CO,$$

the barium salts (2) and (3) being derived respectively from the acids,

$$\begin{array}{c} \text{COOH·CH·CO·CH}_3 \\ \text{COOH·CH·C}_2\text{H}_5 \end{array} \quad \text{and} \quad \begin{array}{c} \text{CH}_2\text{·CO·CH}_3. \\ \text{COOH·CH·C}_2\text{H}_5 \end{array}$$

As the ketolactonic acid has not been further investigated, Professor Young suggested that I should repeat his experiments, and also endeavour to obtain homologues of the acid by similar reactions.

I. *Ethylic β-Ethylacetosuccinate,* $\begin{array}{c} \text{COOC}_2\text{H}_5\text{·CH·CO·CH}_3. \\ \text{COOC}_2\text{H}_5\text{·CH·C}_2\text{H}_5 \end{array}$

This salt was prepared by the action of sodium ethoxide and ethylic acetoacetate on ethylic α-bromobutyrate in the manner described by Young (*loc. cit.*). In order to obtain, if possible, a larger yield of Young's ethylketolactonic * acid, the acetosuccinate was heated for a considerable time, and after being distilled, during which the boiling point rose considerably, it was hydrolysed by boiling with dilute hydrochloric acid for about 12 hours. The crystals which separated on cooling after recrystallisation melted at 178—179° (181° Young).

On evaporating the ethereal extract of the mother liquors and placing the residue (chiefly α-ethyl-β-acetopropionic acid) in ice for a week, more of the ketolactonic acid, melting at 180°, was obtained.

I. 0·2530 gave 0·5190 CO_2 and 0·1375 H_2O. C = 55·95 ; H = 6·07.
II. 0·1190 ,, 0·2485 CO_2 ,, 0·0665 H_2O. C = 56·95 ; H = 6·21.
$C_8H_{10}O_4$ requires C = 56·47 ; H = 5·89 per cent.

The total weight of recrystallised acid obtained was 5·1 grams.

The action of barium carbonate, and of cold and hot barium hydroxide on the acid gave rise to the barium salts $Ba(C_8H_9O_4)_2$, $BaC_6H_{10}O(COO)_2$, and $Ba(C_6H_{11}O·COO)_2$, thus confirming Young's results.

When the aqueous solution of the first barium salt was allowed to evaporate spontaneously, the crystals contained $5H_2O$ (Young's product, deposited from a hot solution, contained $2H_2O$). The salt was dried at 130° and analysed.

Ba = 28·61 per cent. $Ba(C_8H_9O_4)_2$ requires Ba = 28·84.
H_2O = 15·92 ,, $5H_2O$,, H_2O = 14·41.

The second barium salt is exceedingly unstable. It was, however, obtained in a nearly pure state by evaporating its aqueous solution

* As lower homologues of the acid were prepared, a difficulty of nomenclature arose, and Professor Fittig (in whose laboratory the original work on the ethylic compound was done) agreed that it would be desirable to use the name ketolactonic acid for the simplest one, so that Young's crystalline acid will be called "ethylketolactonic acid" in this paper.

to dryness in a vacuum over sulphuric acid. A small quantity of barium carbonate remained admixed with the product, and was estimated separately.

$0\cdot0685$ gave $0\cdot0502$ $BaSO_4$ the barium carbonate present $0\cdot0002$ $BaSO_4$.
$\quad Ba = 43\cdot28$ per cent. $\quad BaC_8H_{10}O_5$ requires $Ba = 42\cdot41$ per cent.

Hence by the action of barium hydroxide in the cold, the unsaturated lactone ring is broken down, and the salt of an unstable dibasic acid, $C_6H_{10}O(COOH)_2$, is formed.

The barium salt, obtained by the action of barium hydroxide on ethylketolactonic acid at $100°$, agreed in all respects with that described by Young.

$\quad Ba = 32\cdot37$ per cent. $\quad Ba(C_7H_{11}O_3)_2$ requires $Ba = 32\cdot39$.

α-Ethyl-β-acetopropionic Acid.

The acid obtained from the original hydrolysed solutions as a gummy oil, after being boiled with barium hydroxide to decompose any ethylketolactonic acid, was recovered from the barium salt and submitted to fractional distillation ; ultimately $5\cdot6$ grams of lactone were obtained, boiling between $240°$ and $250°$. This was purified by boiling it with water and barium carbonate to remove unaltered acid, and then extracting it from the solution by agitation with ether. The portion distilling at $217—221°$ was left over sulphuric acid for a day, and then analysed.
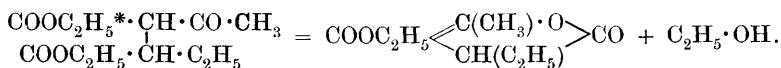
$\quad 0\cdot1602$ gave $0\cdot3915$ CO_2 and $0\cdot1200$ H_2O. $\quad C = 66\cdot73$; $H = 8\cdot33$.
$\quad\quad C_7H_{10}O_2$ requires $C = 66\cdot66$; $H = 7\cdot99$ per cent.

It was therefore nearly pure.

Solubility of the Unsaturated Lactone in Water.—The lactone, when shaken with water, formed an emulsion at the ordinary temperature, but, on warming, the solution rapidly cleared at about $97°$; also on cooling in ice, it cleared at about $2°$. It is therefore more soluble in water at $100°$ and at $0°$ than at intermediate temperatures, and Young's observation, made with a mixture of this lactone with its next homologue, is thus confirmed.

In the formation of the ethylic ethylketolactonate from ethylic β-ethylacetosuccinate by elimination of alcohol, it has been assumed that the reaction takes place according to the equation
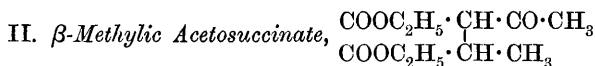
$$\begin{array}{l} COOC_2H_5{}^*\cdot \underset{|}{C}H\cdot CO\cdot CH_3 \\ COOC_2H_5\cdot CH\cdot C_2H_5 \end{array} = COOC_2H_5{<}\begin{array}{l}C(CH_3)\cdot O\\CH(C_2H_5)\end{array}{>}CO + C_2H_5\cdot OH.$$

If that is so, no ethylic ketolactonate should be formed if the hydrogen in the $\equiv CH$ group, marked *, is displaced by an alkyl group.

It was found by Young, however, that neither by using methylic acetoacetate nor by the action of sodium ethoxide and methylic iodide on ethylic β-ethylacetosuccinate, could a product free from unaltered ethylic β-ethylacetosuccinate be obtained.

Analogous experiments, in which ethylic iodide was employed instead of methylic iodide, I also found to yield negative results as regards the formation of a ketolactonate, although large quantities of ethylic ethylsuccinate were formed.

$$\text{II. } \beta\text{-Methylic Acetosuccinate, } \begin{array}{l} COOC_2H_5 \cdot CH \cdot CO \cdot CH_3 \\ COOC_2H_5 \cdot CH \cdot CH_3 \end{array}$$

Seventy grams of ethylic α-bromopropionate was heated for some time with potassium iodide and alcohol. A mixture of 51 grams ethylic acetoacetate and 8·9 grams of sodium dissolved in alcohol was added, and the liquid heated till neutral (20 hours). During the first fractionation, the thermometer was very constant at about 242—$244°$, but, on redistilling, alcohol was given off, and the boiling point rose as by the following table.

Temperature.	I.	II.	III.
$-190°$	8 grams	10 grams	12 grams
190—220	4 ,,	8 ,,	14 ,,
220—240	11 ,,	5 ,,	3 ,,
240—245	29 ,,	9 ,,	1 ,,
245—255	10 ,,	12 ,,	6 ,,
255—270	9 ,,	26 ,,	33 ,,

Hence the decomposition of the acetosuccinate into alcohol and ethylic methylketolactonate takes place much more readily than in the case of the ethyl compound; the hydrolysis was also much more rapid, being complete in about 6 hours. The product, after recrystallisation from alcohol melted at $176°$.

I. $0·2239$ gave $0·4438$ CO_2 and $0·0985$ H_2O. $C = 53·21$; $H = 4·87$.
II. $0·0877$,, $0·1709$ CO_2 ,, $0·0415$ H_2O. $C = 53·33$; $H = 5·26$.
$C_7H_8O_4$ requires $C = 53·84$; $H = 5·12$ per cent.

The yield in this case was very much better, amounting to 8·9 grams of recrystallised methylketolactonic acid. This acid, like the ethyl derivative, gave three barium salts, which were prepared in the manner already described.

The first barium salt (from $BaCO_3$) was much more soluble than the ethyl derivative. It was dried at 100—$120°$, and analysed.

I. 0·2134 gave 0·1103 $BaSO_4$. $Ba = 30·38$.

II. 0·0731   ,,   0·0379 $BaSO_4$. $Ba = 30·50$.

$Ba(C_7H_7O_4)_2$ requires $Ba = 30·64$ per cent.

The second salt (from barium hydroxide in the cold) was even more unstable than that of ethylketolactonic acid.

I. 0·0580 gave 0·0392 $BaSO_4$ and 0·0053 $BaSO_4$ from the barium carbonate. $Ba = 45·10$.

II. 0·1000 gave 0 0697 $BaSO_4$ and 0·0056 $BaSO_4$ from the carbonate. $Ba = 44·27$.

$BaC_7H_8O_5$ requires $Ba = 44·33$ per cent.

Hence the barium salt of the dibasic acid, $C_5H_8O(COOH)_2$, is formed.

The third salt (by the action of barium hydroxide at 100°) gave

I. 0·2479 gave 0·1462 $BaSO_4$. $Ba = 34·67$.

II. 0·2219   ,,   0·1301 $BaSO_4$. $Ba = 34·47$.

$Ba(C_6H_9O_3)_2$ requires $Ba = 34·68$ per cent.

The salt is therefore that of the monobasic acid, $C_5H_9O·COOH$.

α-Methyl-β-acetopropionic Acid.

By extracting the hydrolysed solution and filtrate with ether as before, 19 grams of α-methyl-β-acetopropionic acid, mixed with methyl ketolactonic acid were obtained. After the latter (m. p. $= 176—176·5°$) had crystallised out, the oil was treated in the manner described on p. 1160; the lactone thus obtained boiled at 210—214°.

I. 0·0807 gave 0·1890 CO_2 and 0·0523 H_2O. $C = 63·87$; $H = 7·22$.

II. 0·0920   ,,   0·2156 CO_2 ,, 0·0594 H_2O. $C = 63·90$; $H = 7·17$.

$C_6H_{10}O_2$ requires $C = 64·28$; $H = 7·14$ per cent.

The lactone is formed according to the equation

$$CH_3·CO·CH_2·CH(CH_3)·COOH = CH{\Large<}{{CH(CH_3)}\atop{C(CH_3)O}}{\Large>}CO + H_2O.$$
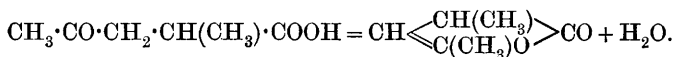
Solubility.—The lactone was much less soluble in water than that obtained from α-ethyl-β-acetopropionic acid, but exhibited the same peculiarity, namely, it was more soluble at 0° and 100° than at intermediate temperatures.

III. *Ethylic β-Isopropylacetosuccinate,* $\dfrac{COOC_2H_5·CH·CO·CH_3}{COOC_2H_5·CH·CH(CH_3)_2}$.
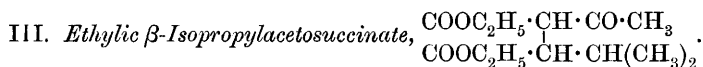
One hundred and thirty-two grams of ethylic α-bromisovalerate, $CH(CH_3)_2·CHBr·COOC_2H_5$, was heated with a mixture of 14·4 grams

of sodium dissolved in absolute alcohol, and 82 grams ethylic aceto-acetate for 7 days, when it became nearly neutral. The product was then treated as usual.

Fractionation gave the following results.

	Temperature.	I.	II.	III.
A.	—170°	16 grams	12 grams	14 grams
B.	170—190	16 ,,	25 ,,	20 .,,
C.	190—200	25 ,,	23 ,,	26 ,,
D.	200—210	24 ,,	27 ,,	27 ,,
E.	210—240	27 ,,	19 ,,	17 ,,
F.	240—260	11 ,,	8 ,,	8 ,,

The boiling point was therefore considerably lower than that of any of the corresponding compounds; this was probably due to the presence of unaltered ethylic α-bromisovalerate (b. p. 186°), and possibly also of a little ethylic isopropylsuccinate.

Each fraction, except A, was then heated for about 6 days (a very little alcohol was given off in all cases except F). After hydrolysis, crystals appeared in D, E, and F, but not in B or C; these after recrystallisation from benzene and light petroleum melted at 115—116°. (Kachler, *Ann.*, **169**, 168, and Hlasiwitz and Grabowski, *Ann.*, **145**, 205, give 114° as the melting point of isopropylsuccinic acid prepared from camphoric acid.)

0·1443 gave 0·2765 CO_2 and 0·0983 H_2O.   C = 52·21; H = 7·57.
   $C_7H_{12}O_4$ requires C = 52·50; H = 7·50 per cent.

The barium salt was obtained as an amorphous powder.

0·2142 gave 0·1685 $BaSO_4$.   Ba = 46·60.
   $C_7H_{10}O_4Ba$ requires Ba = 46·44 per cent.

These results show that the acid is isopropylsuccinic acid, $CH(CH_3)_2 \cdot CH(COOH) \cdot CH_2COOH$.

This acid gave no precipitate of barium carbonate on boiling with excess of barium hydroxide. On adding calcium chloride to a solution of the barium salt and warming, a white, amorphous precipitate of the calcium salt was formed.

On boiling the original hydrolysed solutions with excess of barium hydroxide, only very slight precipitates were obtained, showing that an isopropylketolactonic acid had been formed, but in *very* slight amount.

The benzene and light petroleum mother liquors from which the isopropylsuccinic acid had crystallised were evaporated, and the acid

residue converted into the barium salts, and analysed after drying at 120°.

0·1400 gave 0·0894 $BaSO_4$. $Ba = 38·03$ per cent.
    Barium isopropylketolactonate requires $Ba = 27·23$ per cent.
        ,,   isopropylsuccinate   ,, $Ba = 46·44$,,
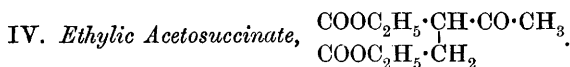
The barium salt was regenerated and treated with silver nitrate, when a white precipitate was formed, which proved to be chiefly silver isopropylsuccinate. The mother liquors from this solution possibly contained silver isopropylketolactonate ; the acid from this, on being boiled with excess of barium hydroxide, gave a distinct precipitate. This was collected and weighed, and from the result it was calculated that the quantity of isopropylketolactonic acid formed would not exceed 3 per cent.

The filtrate from the barium carbonate gave an amorphous barium salt.

0·1519 gave 0·0780 $BaSO_4$. $Ba = 30·65$.
Barium a-isopropyl-β-acetopropionate, $Ba(C_8H_{13}O_3)_2$, requires $Ba = 30·38$ per cent.

Owing to an accident, the aqueous solutions from which the isopropylsuccinic acid had crystallised were lost, and the a-isopropyl-β-acetopropionic acid, which they probably contained, could not therefore be further investigated.

$$\text{IV. } \textit{Ethylic Acetosuccinate,} \quad \begin{array}{l} COOC_2H_5 \cdot \underset{|}{C}H \cdot CO \cdot CH_3 \\ COOC_2H_5 \cdot CH_2 \end{array}.$$

Ethylic sodacetoacetate was first prepared by treating ethylic acetoacetate, 113 grams, with 19·95 grams sodium dissolved in alcohol ; after cooling, 145 grams ethylic bromacetate was added.

The condensation was exceedingly rapid, much heat being developed, and the whole of the sodium bromide separating out in about 5 minutes ; no external heating was required, as the solution was quite neutral after that time.   On fractionation, the following results were obtained.

	Temperature.	I.	II.	III.
A.	—190°	23 grams	25 grams	29 grams
B.	190—240	13 ,,	10 ,,	8 ,,
C.	240—260	20 ,,	11 .,	4 ,,
D.	260—270	30 ,,	45·5 ,,	59 ,,
E.	270—280	24 ,,	14 ,,	4 ,,
F.	280—300	13 ,,	10 ,,	8 ,,

The boiling point would therefore appear to lie between 260° and 270°. The fraction D was then heated for some time; alcohol was eliminated, and the residue distilled between 225° and 290°.

The hydrolysis was performed with very dilute hydrochloric acid and was complete in 45 minutes, but no crystals appeared, either on cooling or after extraction with ether; the ketolactonic acid appeared to be an oil.

A portion of the ethereal extract was treated with barium carbonate as usual; the salt obtained was a deliquescent, gummy mass, which became brittle on cooling. After drying at $100-120°$, it was analysed.

I. 0·3555 gave 0·2011 $BaSO_4$. $Ba = 32·93$.
II. 0·7267 ,, 0·4016 $BaSO_4$. $Ba = 32·85$.
$Ba(C_6H_5O_4)_2$. $Ba = 32·69$ per cent.

The acid liberated from the salt did not crystallise. After heating at 100° and leaving it in a vacuum over sulphuric acid for a short time, it was analysed.

I. 0·1649 gave 0·3039 CO_2 and 0·0611 H_2O. $C = 50·27$; $H = 4·12$.
II. 0·3726 ,, 0·6908 CO_2 ,, 0·1483 H_2O. $C = 50·56$; $H = 4·39$.
$C_6H_6O_4$ requires $C = 50·70$; $H = 4·22$ per cent.

A second portion of the acid was then treated with a slight excess of barium hydroxide in the cold, the excess being removed in the usual way, and the filtrate evaporated in a vacuum. The amount of barium carbonate which separated during the evaporation was negligible.

I. 0·2782 gave 0·2138 $BaSO_4$. $Ba = 45·85$.
II. 0·5448 ,, 0·4225 $BaSO_4$. $Ba = 46·18$.
$BaC_6H_6O_5$ requires $Ba = 46·44$ per cent.

A third portion of the acid was heated with a slight excess of barium hydroxide; barium carbonate began to be precipitated at about 80—85°, and after boiling for 5 minutes the decomposition was complete. The barium β-acetylpropionate (levulinate) was left as a deliquescent gum, which was dried at 120° and analysed.

I. 0·2439 gave 0·1515 $BaSO_4$. $Ba = 37·00$.
II. 0·4453 ,, 0·2776 $BaSO_4$. $Ba = 37·12$.
$Ba(C_5H_7O_3)_2$ requires $Ba = 37·32$ per cent.

GENERALISATIONS.

1. *Action of Brominated Ethylic Salts on Ethylic Sodacetoacetate.*—The condensation was very rapid with ethylic bromacetate. The rate diminishes rapidly with rise of molecular weight.

		Approximate time required.
Ethylic bromacetate	....	5 minutes.
,,	α-bromopropionate	10 hours.
,,	α-bromobutyrate	20 hours.
,,	α-bromisovalerate	7 days.

2. *Action of Heat on Alkylic Acetosuccinates.*—The removal of alcohol with the formation of a ketolactonate is most rapid with methylic acetosuccinate, the rate diminishing very rapidly as the methyl is replaced by ethyl and isopropyl groups respectively. Ethylic acetosuccinate itself gives up alcohol much more rapidly than the ethyl derivatives, but apparently less rapidly than the methyl derivative.

		Approximate time required.
Ethylic acetosuccinate	....	less than 4 days.
,,	methylacetosuccinate	on distillation.
,,	ethylacetosuccinate	5 days.
,,	isopropylacetosuccinate	about 6 days.

3. *Rate of Hydrolysis of Ethylic Ketolactonates, &c., with Dilute Hydrochloric Acid.*—The members of the series are not quite comparable in this case, for ethylic acetosuccinate was completely converted into ethylic ketolactonate, whilst the substituted ethylic acetosuccinates were only partially converted into the corresponding ethylic ketolactonates.

Neglecting this difference in composition, the rate of hydrolysis diminishes with rise of molecular weight.

		Approximate time required.
Ethylic acetosuccinate	....	45 minutes.
,,	β-methylacetosuccinate	6 hours.
,,	β-ethylacetosuccinate	12 hours.
,,	β-isopropylacetosuccinate	about 2 days.

4. *Products of Hydrolysis of Unaltered Ethylic Acetosuccinates.*— By the hydrolysis of the ethylic ketolactonates, the corresponding acids are formed, and the other acids obtained by the hydrolysis of the mixture of ethylic ketolactonates and unaltered acetosuccinates are in all probability derived from the latter.

Leaving these, the ketolactonic acids, out of account, the only acid obtained by the hydrolysis of ethylic β-methylacetosuccinate was α-methyl-β-acetopropionic acid, no indication of the presence of methylsuccinic acid having been observed.

In the case of ethylic β-ethylacetosuccinate, the chief product is α-ethyl-β-acetopropionic acid, but Young, after removing this acid by reduction and conversion into the lactone, was able to show that a small quantity of ethylsuccinic acid was left unacted on by the sodium amalgam.

By the hydrolysis of ethylic β-isopropylacetosuccinate, isopropyl-succinic acid is obtained in large quantity. As the aqueous solution from which the crystals separated was lost, it is impossible to say how much α-isopropyl-β-acetopropionic acid was formed, but the quantity was certainly relatively smaller than in the case of the lower homologues. As the ethylic acetosuccinate itself was completely converted into ethylic ketolactonate, only ketolactonic acid was obtained by hydrolysis. It appears, then, that by the hydrolysis of the alkyl derivatives of ethylic acetosuccinate with hydrochloric acid, more and more of the alkyl derivatives of succinic acid are formed, and less and less of the alkyl derivatives of acetopropionic acid.
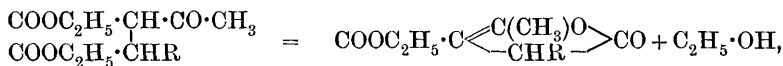
Constitution of the Acids.

The simplest ketolactonic acid has the empirical formula $C_6H_6O_4$ and the constitution (I),

I. $COOH \cdot C {<} {\overset{C(CH_3)O}{\underset{-CH_2-}{}}} {>} CO$ II. $COOH \cdot C {<} {\overset{C(CH_3)O}{\underset{CH(CH_3)}{}}} {>} CO.$
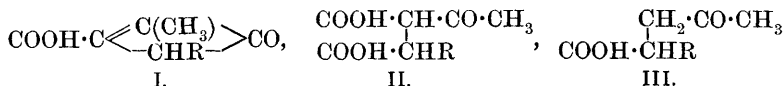
The next one would have the graphic formula (II), and would be termed methylketolactonic acid, and so on for the others.

The formation of the ketolactonic ethers from the acetosuccinic ethers may be represented generally as below.

$\begin{matrix} COOC_2H_5 \cdot CH \cdot CO \cdot CH_3 \\ COOC_2H_5 \cdot CHR \end{matrix}$ $=$ $COOC_2H_5 \cdot C {<} {\overset{C(CH_3)O}{\underset{-CHR-}{}}} {>} CO + C_2H_5 \cdot OH,$

and the three barium salts are in each case derived from the acids,

$COOH \cdot C {\ll} {\overset{C(CH_3)}{\underset{-CHR-}{}}} {>} CO,$ $\begin{matrix} COOH \cdot CH \cdot CO \cdot CH_3 \\ COOH \cdot CHR \end{matrix}$, $\begin{matrix} CH_2 \cdot CO \cdot CH_3 \\ COOH \cdot CHR \end{matrix}$

I.   II.   III.

R representing in each case an alkyl group (or hydrogen).

In conclusion, I tender Dr. Young my sincere thanks for the kind way in which he has given me his advice and assistance whenever required.

UNIVERSITY COLLEGE,
    BRISTOL.