578. *Alicyclic Compounds. Part III.* Ultra-violet Absorption, Acidity, and Ring Fission of* cyclo*Hexane-1 : 3-diones.*

By Eric G. Meek, J. H. Turnbull, and Walter Wilson.

Ultra-violet absorption studies of several *cyclo*hexane-1 : 3-diones, in ethanol and over a range of pH in 50% ethanol, confirm the view that the monoenols and the corresponding ions are the only major species involved. From these data, pK_a values are calculated and compared with values obtained electrometrically. The extension of Woodward's empirical rules for the calculation of $\lambda_{max.}$ to various enolised α- and β-diketones is discussed. Bathochromic displacements in the absorption of certain cyclic α-diketones and acyclic β-diketones can be correlated with intramolecular hydrogen bonding. The ring fission of several *cyclo*hexane-1 : 3-diones by alkali has been followed spectroscopically.

Woodward and Blout recognised that 5 : 5-dimethyl*cyclo*hexane-1 : 3-dione (dimedone) had the ultra-violet absorption characteristics of a (mono)enolised β-diketone (*J. Amer. Chem. Soc.*, 1943, **65**, 562; cf. Heywood and Kon, *J.*, 1940, 713). *cyclo*Hexane-1 : 3-dione (I) exhibited concentration-dependent absorption in alcohol (Bastron, Davis, and Butz, *J. Org. Chem.*, 1943, **8**, 515), an effect later attributed to reversible ionisation of the acidic enol (Blout, Eager, and Silverman, *J. Amer. Chem. Soc.*, 1946, **68**, 566). However apart from the work of Valyashko and Shcherbak (*J. Gen. Chem. U.S.S.R.*, 1938, **8**, 1629), whose data appear to be incomplete and even self-contradictory, the influence of pH on the ultra-violet absorption of *cyclo*hexane-1 : 3-diones has not been studied in detail.

Table 1. *Light absorption* (0·001% *solutions in ethanol*).

	Dione (enol)		Enol ethyl ether [1]	
*cyclo*Hexane-1 : 3-dione :	$\lambda_{max.}$ (mμ)	ε	$\lambda_{max.}$ (mμ)	ε
Unsubstituted	253	22,300	249	18,700
2-Methyl	261	18,800	265	20,800
4- or 6-Methyl [2]	255	12,700 [3]	249	16,100
5 : 5-Dimethyl	255	17,800	250	19,200
2 : 5 : 5-Trimethyl	264	13,600	268	19,200
2 : 2 : 5 : 5-Tetramethyl [4]	207	1,100	—	—
	274	240	—	—

[1] Part II. [2] Possibly a mixture of the two isomers. [3] The sample contained some α-methylglutaric acid, which is transparent at 255 mμ; hence the low ε value. [4] Concn., 0·01%.

The ultra-violet absorptions of several *cyclo*hexane-1 : 3-diones in absolute ethanol have been measured by us (Table 1). The 2 : 2 : 5 : 5-tetramethyl compound cannot

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* Part II, *J.*, 1953. 811.

enolise to a conjugated system, and has the weak absorption expected for two isolated carbonyl groups; the remaining diones exhibit intense absorption, similar to that of the corresponding enol ethers. These results therefore confirm the view that the diones are substantially monoenolic in ethanol.

An extended series of measurements was made on each dione, at different pH's in 50% aqueous ethanol (Table 2); the absorption of the 2 : 2 : 5 : 5-tetramethyl compound was independent of pH, and is not included. Numerous extinction curves were drawn; those for *cyclo*hexane-1 : 3-dione are typical (see Figure). The form of these curves, and particularly the single, sharp, isosbestic point show that only two significant species are involved. These can only be the enol (II) and its ion (III), which predominate in acid and in alkaline solutions respectively. The extinction coefficients at $\lambda_{\text{max.}}^{\text{enol}}$ and $\lambda_{\text{max.}}^{\text{enol ion}}$ vary greatly with pH changes between 4·5 and 8, but approach limiting values at higher or lower pH; this can be demonstrated graphically in each case. The similarity of the λ and ε values of a given enol seen on comparing Tables 1 and 2 shows that negligible ionisation occurred in

TABLE 2. *Light absorption and* pK_a *in* 50% *aqueous ethanol.*

		$E_{1\text{ cm.}}^{1\%}$		pK_a		
pH	$\lambda_{\text{max.}}$ (mμ)	at $\lambda_{\text{max.}}^{\text{enol}}$	at $\lambda_{\text{max.}}^{\text{enol ion}}$	Spectroscopic [1]	Mean	Electrometric [5]
		cyclo*Hexane*-1 : 3-*dione* (8·29 *mg./l.*; I.P.[2] 264 mμ, $E_{1\text{ cm.}}^{1\%}$ 1182)				
1·98	255 [3]	1569	182			
		(ε 1·76 × 10^4)				
4·60	256	1552	213	6·43		
5·52	260	1342	661	6·05		
5·90	278	1123	1001	6·05		
6·22	280	966	1318	6·09	6·21	5·89
6·84	280	749	1722	6·24		
7·27	280	672	1809	6·42		
7·59	280	592	1984	6·13		
7·99	280	565	2204			
9·50	280	538	2280			
10·30	280 [4]	528	2283			
			(ε 2·56 × 10^4)			
		2-*Methyl*cyclo*hexane*-1 : 3-*dione* (5·05 *mg./l.*; I.P. 274 mμ, $E_{1\text{ cm.}}^{1\%}$ 1010)				
2·27	264 [3]	1512	202			
		(ε 1·905 × 10^4)				
4·40	264	1367	226	6·33		
5·60	265	1218	303	6·73		
6·26	265	1194	586	6·79		
6·50	267	1099	836	6·83		
6·68	270	1006	891	6·81	6·63	6·76
6·84	287	901	1139	6·74		
7·17	290	867	1420	6·80		
7·37	290	717	1564	6·79		
7·64	290	578	1802	6·31		
7·84	290	560	1956	6·19		
8·42	290	541	2115			
11·50	290 [4]	541	2158			
			(ε 2·72 × 10^4)			
		2 : 5 : 5-*Trimethyl*cyclo*hexane*-1 : 3-*dione* (5·42 *mg./l.*; I.P. 276 mμ, $E_{1\text{ cm.}}^{1\%}$ 748)				
2·0	265 [3]	978	125			
		(ε 1·53 × 10^4)				
5·19	265	954	148	6·98		
5·56	266	928	185	6·91		
6·16	267	881	317	7·01		
6·25	268	841	377	6·90		
6·48	271	701	620	6·70	6·91	6·76
6·97	292	609	891	6·88		
7·46	294	465	1251	6·91		
7·97	294	386	1416	7·01		
9·10	294	362	1550			
12·20	295 [4]	321	1550			
			(ε 2·42 × 10^4)			

TABLE 2. (*Continued.*)

		$E^{1\%}_{1\,\mathrm{cm.}}$		pK_a		
pH	$\lambda_{\mathrm{max.}}$ (mμ)	at $\lambda^{\mathrm{enol}}_{\mathrm{max.}}$	at $\lambda^{\mathrm{enol\ ion}}_{\mathrm{max.}}$	Spectroscopic [1]	Mean	Electrometric [5]
	4-*Methyl*cyclo*hexane*-1 : 3-*dione* (7·43 *mg./l.*; I.P. 265 mμ, $E^{1\%}_{1\,\mathrm{cm.}}$ 626)					
1·90	255 [3]	827	118			
		(ε 1·04 × 10^4)				
3·94	255	814	124			
5·05	255	828	188	6·22		
5·31	257	781	232	6·23		
5·77	258	713	353	6·31		
6·07	260	630	491	6·30	6·30	6·81
6·21	263	602	549	6·34		
6·50	279	563	740	6·41		
7·00	280	415	922	6·29		
8·13	280	312	1170			
9·30	281	276	1225			
12·40	281 [4]	320	1265			
			(ε 1·59 × 10^4)			
	5 : 5-*Dimethyl*cyclo*hexane*-1 : 3-*dione* (5·5 *mg./l.*; I.P. 266 mμ, $E^{1\%}_{1\,\mathrm{cm.}}$ 973)					
3·76	257 [3]	1235	181			
		(ε 1·73 × 10^4)				
4·01	258	1196	245	5·40		
4·66	258	1170	262	5·85		
4·86	259	1162	273	6·08		
5·04	259	1142	318	6·06		
5·37	260	1091	473	6·11		
5·67	261	1036	600	6·10	6·20	6·05
5·75	262	1011	636	6·13		
5·98	262	984	704	6·27		
6·22	268	920	882	6·29		
6·46	278	813	1109	6·22		
6·74	280	765	1396	6·26		
7·10	282	745	1654	6·46		
7·43	282	582	1764	6·20		
8·40	282	619	1774			
12·50	282 [4]	624	1898			
			(ε 2·66 × 10^4)			

[1] Let A_e and B_e be $E^{1\%}_{1\,\mathrm{cm.}}$ of the pure enol at $\lambda^{\mathrm{enol}}_{\mathrm{max.}}$ and $\lambda^{\mathrm{enol\ ion}}_{\mathrm{max.}}$ respectively, and let A_i and B_i be the corresponding values for the enol ion. Then, at a given pH, if A and B are $E^{1\%}_{1\,\mathrm{cm.}}$ at $\lambda^{\mathrm{enol}}_{\mathrm{max.}}$ and $\lambda^{\mathrm{enol\ ion}}_{\mathrm{max.}}$,

$$\mathrm{p}K_a = \mathrm{pH} - \log_{10}\left(\frac{B - B_e}{B_i - B_e}\right)\left(\frac{A_i - A_e}{A_i - A}\right)$$

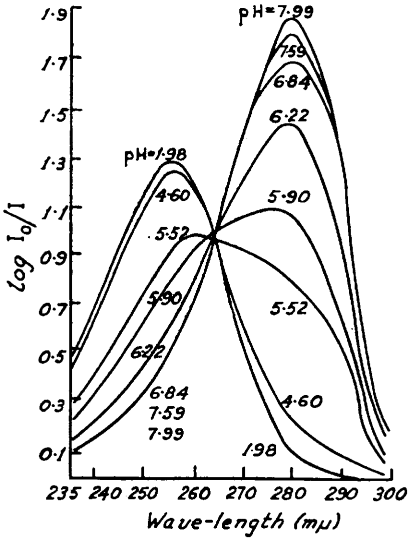
[2] Isosbestic point. [3] $\lambda^{\mathrm{enol}}_{\mathrm{max.}}$. [4] $\lambda^{\mathrm{enol\ ion}}_{\mathrm{max.}}$. [5] The dione (*ca.* 0·001 mole) in 50% aqueous ethanol was titrated with 0·1N-sodium hydroxide solution, and the pH measured at intervals. The pK_a value was read in the usual way from the graph of pH against volume of sodium hydroxide added.

the absolute ethanol. The enol maxima in 50% ethanol are at slightly longer wavelengths than in absolute ethanol; the difference has the magnitude expected (1—2 mμ).

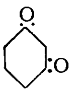
Further considerations confirm the view that monoenols and their ions are the only significant species in solutions of *cyclo*hexane-1 : 3-diones. By an ingenious experimental method, Schwarzenbach and Felder (*Helv. Chim. Acta*, 1944, **27**, 1044) showed that dimedone existed as 95·3% monoenol in water (0·01—0·001M). On theoretical grounds diketo-forms (*e.g.*, I) of *cyclo*hexane-1 : 3-diones should be less stable than their conjugated isomers (II) and (IV); the monoenol (II) is *s-trans* and would therefore be favoured instead of the dienol (IV), which is *s-cis* (cf. Braude, Jones, Koch, Richardson, Sondheimer, and Toogood, *J.*, 1949, 1890). The α-diketone (V; R = H) has been shown to enolise no further than the monoenol stage, even in strongly alkaline solutions (French and Holden, *J. Amer. Chem. Soc.*, 1945, **67**, 1239).

From the results in Table 2, the pK_a's (in 50% alcohol) of the diones have been calculated; values were also determined by an independent electrometric method. The introduction of a 2-methyl substituent notably decreases the acidity of these compounds.

Extension of Woodward's Rules.—The following discussion applies to solutions in absolute ethanol. Empirical rules enunciated by Woodward (*J. Amer. Chem. Soc.*, 1941, **63**, 1123; 1942, **64**, 76) permit the calculation of $\lambda_{max.}$ for αβ-unsaturated ketones. *cyclo*Hexane-1 : 3-dione enols and enol ethers are 3-hydroxy- and 3-ethoxy-*cyclo*hex-2-enones respectively; extending the principles used by Woodward, the bathochromic displacements ($\Delta\lambda_{OH}$ and $\Delta\lambda_{OEt}$) which accompany the introduction of these substituents into the *cyclo*hexenone system, have been calculated (Table 3). A preliminary estimate of $\Delta\lambda_{OH}$ in certain steroids has already been made by Fieser and Fieser (" Natural Products Related to Phenanthrene," Reinhold, New York, 3rd Edn., 1949, p. 195). Comparison of the $\lambda_{max.}$ values of the enols (Table 1) confirms the validity of Woodward's rules in this series, as a 2-methyl substituent produces a bathochromic displacement of 8—9 mμ. The $\Delta\lambda_{OH}$ values (Table 3) are reasonably uniform. However, the $\Delta\lambda_{OEt}$ values fall into two groups, 24—25 and 30—33 mμ; the higher value obtained with 2-methyl compounds is possibly a result of steric interaction between the fairly large ethoxy-group and the 2-methyl substituent although steric hindrance is not commonly associated with bathochromic shifts (cf. Braude *et al.*, *loc. cit.*).



Ultra-violet absorption of cyclo*hexane-1 : 3-dione in* 50% *ethanol.*



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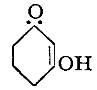

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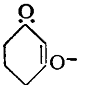

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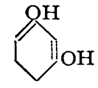

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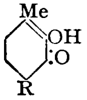

(V)

TABLE 3.

*cyclo*Hexane-1 : 3-dione :	$\Delta\lambda_{OH}$ [1]	$\Delta\lambda_{OEt}$ [2]	*cyclo*Hexane-1 : 3-dione :	$\Delta\lambda_{OH}$ [1]	$\Delta\lambda_{OEt}$ [2]
Unsubstituted	28	24	5 : 5-Dimethyl	30	25
2-Methyl	26	30	2 : 5 : 5-Trimethyl	29	33
4-Methyl	30	24	(Mean)	(28·5)	

[1] $\Delta\lambda_{OH} = \lambda^{enol}_{max.} - \lambda^{C}_{max.}$. [2] $\Delta\lambda_{OEt} = \lambda^{enol\ ether}_{max.} - \lambda^{C}_{max.}$. $\lambda^{C}_{max.}$ refers to the *cyclo*hexenone from which the enols and enol ethers are derived by the introduction of OH or OEt. $\lambda_{max.}$ for *cyclo*hexenone is taken as 225 mμ; this value appears reasonable from data for related compounds (as in Woodward's work, 10 mμ is allowed for a methyl group on the ethylenic centre): 5-*iso*propyl*cyclo*hexenone, $\lambda_{max.}$ 226·5 (Frank and Hall, *J. Amer. Chem. Soc.*, 1950, **72**, 1645); 3-methyl*cyclo*hexenone, $\lambda_{max.}$ 235 (Evans and Gillam, *J.*, 1941, 816); piperitone, $\lambda_{max.}$ 235·5 mμ (Gillam, Lynas-Gray, Penfold, and Simonsen, *J.*, 1941, 60).

It is instructive to compare values of $\lambda_{max.}$ observed for the enols of several acyclic β-diketones and cyclic α-diketones (Table 4) with those computed by using the above value of $\Delta\lambda_{OH}$. It is assumed that the bathochromic shifts resulting from the introduction of α- and β-hydroxyl groups into the system $>C{:}\overset{|}{C}{\cdot}\overset{|}{C}{:}O$ are similar (in the absence of hydrogen bonding). Intramolecular hydrogen-bonding is impossible in *cyclo*hexane-1 : 3-diones (Wheland, " Advanced Organic Chemistry," Wiley, New York, 1949, p. 616), but is possible in all the compounds listed in Table 4. The $\lambda_{max.}$ values observed for these compounds are usually much higher than those calculated, owing it is believed to intramolecular hydrogen-bonding. The variation in $\Delta\lambda$ seen in Table 4 can be attributed to variations in the extent of intramolecular hydrogen-bonding, especially owing to solvent–solute interaction. Intramolecular hydrogen-bonding is well established for acetylacetone; a similarity between acetylacetone and enolised α-diketones is suggested by the relative pK_a values of acetylacetone, the α-diketone (V; R = H), and *cyclo*hexane-1 : 3-dione (Schwarzenbach *et al.*, *Helv. Chim. Acta*, 1940, **23**, 1147, 1162; 1947, **30**, 663; cf., however, Wheland, *op. cit.*, pp. 611, 616).

Several earlier observations have an important bearing on these general conclusions. Heywood and Kon (*J.*, 1940, 713) referred to unpublished experiments showing that enolised cyclic α- and β-diketones have similar spectra, but the α-maxima are displaced to longer wave-lengths, and Berson (*J. Amer. Chem. Soc.*, 1952, **74**, 5172) has pointed out that derivatives of enolised β-diketones in which hydrogen-bonding is prevented (as in enol ethers or acetates) show a pronounced hypsochromic displacement. The concept of hydrogen-bonding has been used in the interpretation of several other spectra (*e.g.*, by Morton and Stubbs, *J.*, 1940, 1347, and Burawoy and Chamberlain, *J.*, 1952, 3734).

TABLE 4. $\lambda_{\text{max.}}$ (mμ) *in ethanol.*

	Found	Calc.[1]	$\Delta\lambda$ [2]
Diosphenol (V; R = Pr^i)	274 [3]	263·5	+10·5
(V; R = H)	268·5 [4]	263·5	+ 5
Hydroxymethylenecamphor	264·5 [3]	258·5	+ 6
Acetylacetone (enol)	273 [5]	253·5	+19·5
Cholestane-2 : 3-dione, enol (*B*)	270 [5]	255·5	+14·5
,, ,, enol (*A*)	272 [6]	255·5	+16·5
Cholestane-3 : 4-dione enol	281 [10]	272·5	+ 8·5
3β-Acetoxycholestane-6 : 7-dione enol	274·5 [7]	272·5	+ 2
5-Hydroxyergost-7-ene-3 : 6-dione [9]	253 [8]	244	+ 9
11 : 12-Diketocholanic acid enol	290 [11]	272·5	+17·5

[1] Woodward's (1942) constants were used in calculations for the simpler compounds, and Fieser and Fieser's revised constants for steroids (*op. cit.*, p. 192). An increment of 28·5 mμ was added for a hydroxyl group ($\Delta\lambda_{\text{OH}}$). [2] $\Delta\lambda = \lambda$ (Found − Calc.). [3] Gillam, Lynas-Gray, Penfold, and Simonsen, *J.*, 1941, 60. [4] French and Holden, *loc. cit.* [5] Blout, Eager, and Silverman, *loc. cit.* [6] Stiller and Rosenheim, *J.*, 1938, 353. [7] Heilbron, Jones, and Spring, *J.*, 1937, 801. [8] Fieser and Fieser (*op. cit.*, p. 181) give $\lambda_{\text{max.}}^{\text{CHCl}_3}$ 252 mμ; hence $\lambda_{\text{max.}}^{\text{EtOH}} = 253$ mμ, by applying the solvent correction factor given by the same authors (p. 184). [9] This compound is neither an α- nor a β-diketone; the 7-en-6-one chromophore, however, could be modified by intramolecular hydrogen-bonding between the 5-hydroxy- and the 6-keto-group. [10] Butenandt *et al.* (*Ber.*, 1936, **69**, 2779) give $\lambda_{\text{max.}}^{\text{CHCl}_3}$ 280 mμ; hence $\lambda_{\text{max.}}^{\text{EtOH}} = 281$ mμ, Fieser and Fieser's solvent correction factor being used. [11] Barnett and Reichstein (*Helv. Chim. Acta*, 1938, **21**, 926) give $\lambda_{\text{max.}}^{\text{hexane}}$ 279 mμ; hence $\lambda_{\text{max.}}^{\text{EtOH}} = 290$ mμ (Fieser and Fieser's solvent correction factor).

Ring Fission of cyclo*Hexane*-1 : 3-*diones*.—The well-known formation of γ-acylbutyric acids from *cyclo*hexane-1 : 3-diones by alkali has been studied kinetically by Hinkel, Ayling, Dippy, and Angel (*J.*, 1931, 814). These experiments have now been extended; and a spectroscopic method was used for analysis of dione solutions, being more convenient and probably more reliable than the permanganate titration used by the earlier workers. The velocity constants (Table 5) demonstrate an apparent stabilising effect of a 5 : 5-*gem*-dimethyl group on the ring; for example, no detectable hydrolysis occurred with the 2 : 5 : 5-trimethyl dione. It has been reported also that the 4 : 5 : 5-trimethyl dione is not hydrolysed by barium hydroxide solution (Crossley, *J.*, 1901, 138). The stabilities of *cyclo*-

TABLE 5. *Rates of ring fission at* 100°.

	10^5k (min.$^{-1}$)			10^5k (min.$^{-1}$)	
*cyclo*Hexane-1 : 3-dione	Hinkel [1] *et al.*	Present work	*cyclo*Hexane-1 : 3-dione	Hinkel [1] *et al.*	Present work
Unsubstituted	95·6	133	5 : 5-Dimethyl	6·67	5·4
2-Methyl	—	136—216 [2]	2 : 5 : 5-Trimethyl	—	0
4-Methyl	—	132			

[1] Only those values relevant to the present work are quoted. [2] Not computed graphically; *k* was calculated at each time interval; mean value, 169. See Experimental section.

hexane-1 : 3-diones in air and in alkali are not parallel, as the spontaneous decomposition which occurs in air is probably an oxidative ring fission (Part II).

EXPERIMENTAL

The *cyclo*hexane-1 : 3-diones were freshly purified samples of those described in Part II. Spectroscopic data were measured with a Unicam SP. 500 Spectrophotometer, with 10-mm. cells. The ethanol used was the "commercial absolute" grade. pH's were measured with a Cambridge meter, and calomel and glass electrodes.

*Ring Fission of 2-Methyl*cyclo*hexane-1 : 3-dione.*—The dione (4·2 g.), water (35 c.c.) and sodium hydroxide (2·6 g.) were heated at 100° for 8 hr. Acidification (pH 3) precipitated the original dione (3·0 g., 72%); ether-extraction of the filtrate afforded 5-ketoheptanoic acid (1·1 g., 26%), b. p. 90—102°/0·01 mm., m. p. 47—49°, $\lambda_{max.}$ 262 mμ (ε 73) (semicarbazone, m. p. 185—186°) (Blaise and Maire, *Bull. Soc. chim.*, 1908, **3**, 421, give m. p. 50° and semicarbazone, m. p. 196°). In a similar experiment with the 2 : 5 : 5-trimethyl dione, no change was detected after 20 hr.' refluxing.

Kinetic Measurements.—The diones were hydrolysed in a 100-c.c. 2-necked flask, fitted with an efficient reflux condenser, on a steam-bath, in a slow stream of moist, CO_2-free nitrogen, which stirred the mixture; losses by evaporation were negligible. The dione (1 g.) was dissolved in 2N-sodium hydroxide (100 c.c.), and about three-quarters of the solution put in the reaction vessel. At suitable intervals, small portions of liquid were removed and acidified to pH 2—3, suitably diluted with 50% aqueous ethanol, and the ultra-violet extinction at $\lambda_{max.}^{enol}$ measured. First-order rate constants were computed by means of the equation $k = (2{\cdot}303/t) \log_{10} (E_0/E_t)$ where E_t is $E_{1\,cm.}^{1\%}$ (at $\lambda_{max.}^{enol}$) after t min. and E_0 is the initial value, at a convenient time soon after the attainment of thermal equilibrium. Plots of t against log (E_0/E_t) were usually linear, and k could be read off. In hydrolyses in which considerable proportions of γ-acylbutyric acids were formed, E_t values were corrected for the (small) absorption of these acids.

2-Methyl*cyclo*hexane-1 : 3-dione gave plots which deviated from linearity, by much more than reasonable experimental error. Similar deviations were observed by Hinkel *et al.* in the hydrolysis of certain other 2-substituted *cyclo*hexane-1 : 3-diones.

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CHEMISTRY DEPARTMENT, THE UNIVERSITY,
EDGBASTON, BIRMINGHAM 15.

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