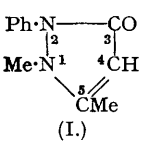
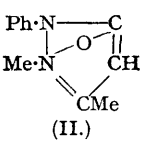
592. *Dielectric Polarisation and Spectroscopic Data for Antipyrin, Certain of its Derivatives, and Phenyl*isooxazolone.

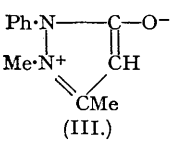
By R. D. Brown, A. A. Hukins, R. J. W. Le Fèvre, (Miss) Jean Northcott, and I. R. Wilson.

Antipyrin, and its 4-bromo-, 4-dimethylamino-, and 4 : 4′-dinitro-derivatives have moments (in benzene) of 5·5, 6·0, 5·2, and 4·6 D., respectively. These results are explicable in terms of the mesomerism of the N–C=C–C=O system. Phenyl*iso*oxazolone (μ = 5·0 D.) seems unperturbed. Ultra-violet spectra (in alcohol) of the above and also of 4-nitrosoantipyrin are recorded.

Two formulæ have been proposed for antipyrin : (I) by Knorr (*Annalen*, 1887, **238**, 160, 205; 1896, **293**, 1, 26, 40; 1903, **328**, 78), and (II) by Michaelis (*Annalen*, 1902, **320**, 45). Thoms


(I.)


(II.)


(III.)

and Schnupp (*Annalen*, 1923, **434**, 296) considered (II) to be misleading, and concluded " Das Antipyrin stellt also ein heterovicinales Oxo-Derivat des dihydrierten Pyrazols dar. Es besitzt eine dipolare Struktur in Form einer ' Ringdipolarität,' die eine grosse Beständigkeit der

Molekul bedingt und ist als (1)-Phenyl-(2,3)-dimethyl-(5)-oxo-(3,4)-dihydropyrazol zu kennzeichnen." However, (III) is the modern enol-betaine version of (II) and that it may contribute to the real structure of antipyrin is understandable from Ingold's discussion of polarisation mechanisms (*J.*, 1933, 1120) in which displacements in the system $R_2N{-}C{=}C{-}C{=}O$ are explicitly mentioned; that (III) participates as an activated form in certain chemical reactions has also been indicated experimentally (Michaelis, *loc. cit.*; *Ber.*, 1903, **36**, 3271; Stolz, *ibid.*, p. 3279).

It therefore seemed relevant to investigate possible physical evidence bearing on the point. There appeared to be some analogy with the sydnones (Earl, Leake, and Le Fèvre, *J.*, 1948, 2269; Earl, Le Fèvre, and Wilson, this vol., p. S 103) for which the bicyclic formulation originally proposed (Earl and Mackney, *J.*, 1935, 899) may be satisfactorily replaced by one which is monocyclic and mesomeric between various activated, radicaloid, and covalent extremes (cf. also Baker and Ollis, *Nature*, 1946, **158**, 703; Earl, *ibid.*, p. 909; Kenner and Mackay, *ibid.*, p. 909; Earl, Leake, and Le Fèvre, *ibid.*, 1947, **160**, 366; Baker, Sutton, *et al.*, *ibid.*, p. 366).

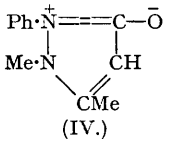
Dipole Moments.—From the data tabulated later the following have been evaluated :

Antipyrin	$\mu = 5{\cdot}5$ D.	4-Dimethylaminoantipyrin	$\mu = 5{\cdot}2$ D.
4-Bromoantipyrin	$5{\cdot}9_7$	4 : 4′-Dinitroantipyrin	$4{\cdot}6$

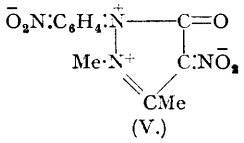
Attempts to construct a scale model of (I) (using distances : C–C, 1·54; C=C, 1·34; N–N, 1·48; N–C, 1·47 A.) lead to most unlikely N–N–CO angles unless those at each end of the double bond are *ca.* 110° (contrast Mills and Nixon, *J.*, 1930, 2510). The heterocyclic nucleus then becomes an approximately regular pentagon. Very roughly the four C–N bond moments at the two N-atoms will mutually cancel. The resultant moment of (I) should therefore be of the order of that expected for an αβ-unsaturated ketone (*e.g.*, 3 : 5-dimethyl*cyclo*hex-2-enone, $\mu = 3{\cdot}8$—$4{\cdot}0$; cf. *Trans. Faraday Soc.*, 1934, **30**, Appendix, 44). The value actually found is *ca.* 1·5 D. higher than this.

Further, it is qualitatively obvious that the direction of action of the resultant in (I) is roughly parallel to the axis of the C=O group, and has its negative end remote from the heteronucleus. Support for this is found in the moment of the 4-bromo-derivative which, on the pentagonal structure mentioned above, should be the resultant of two vectors, 5·5 and 1·5 D., interacting at 72°, *i.e.*, 6·1 D. (compared with 6·0, found). Likewise the 4-dimethylamino-group appears to be equivalent to a component of 1·5—2 D. (operating as $Me_2N \longrightarrow C$, *i.e.*, in the same sense and value as in various dimethylanilines studied by Marsden and Sutton, *J.*, 1936, 599) since calculation as for the bromo-analogue yields 5·2—5·3 D., compared with 5·2 D., found). However, substitution of the 4 : 4′-hydrogen atoms by nitro-groups which should produce a substantial component *augmenting* that of the parent structure, notably does not do so—the polarity of dinitroantipyrin is *ca.* 1 D. *less* than that of antipyrin (this is more significant since such derivatives are likely to have an " anomalous " high moment, due to atomic polarisation, cf. Sutton, *Ann. Reports*, 1940, **37**, 57; Coop and Sutton, *J.*, 1938, 1269).

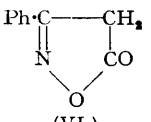
We submit that these results may be understood if antipyrin is viewed as a resonance structure, to which the two chief polar contributors are (III) and (IV). A 4-bromo-atom will not seriously affect either of the conjugated systems connecting nitrogen to the (ketonic)



(IV.)



(V.)



(VI.)

oxygen. A 4-dimethylamino-group may depress the polarisation producing (III) (by allowing an electron excess at $C_{(5)}$), but still allow that leading to (IV). In the dinitro-derivative simultaneous permanent duplet displacements (such as are commonly believed to occur in, *e.g.*, *p*-nitroaniline) would contravene the " adjacent charge " rule, cf. (V). Each is better written separately, thus providing two further contributing structures. This molecule therefore may contain a nearly unperturbed ketonic group. We note that two $C \longrightarrow NO_2$ vectors of 4 D. each, interacting at 144°, produce a resultant of only 2·2 D. This, added to 2·3 D. for the C=O link (Eucken and Meyer, *Physikal. Z.*, 1929, **30**, 397), would give a value close to that observed experimentally.

We also have examined 4-nitrosoantipyrin, which might be expected to display a strong polarisation of the type N—C=C—N=O [cf. lower part of (V)], since the nitroso-group has previously been found to be a powerful cause of such mesomerisation (Le Fèvre, *J.*, 1931, 810; Le Fèvre and Smith, *J.*, 1932, 2239; Le Fèvre, *Nature*, 1932, **129**, 400; Marsden and Sutton, *loc. cit.*). The solubility of 4-nitrosoantipyrin in non-polar solvents proved too small for other than spectroscopic measurements. In this fact, however, lies qualitative evidence of abnormally high polarity.

Ultra-violet Spectra.—These (taken in alcohol) are shown in Fig. 1, and summarised in Table I. The first two substances have been examined previously by Valyashko and Bliznynkov

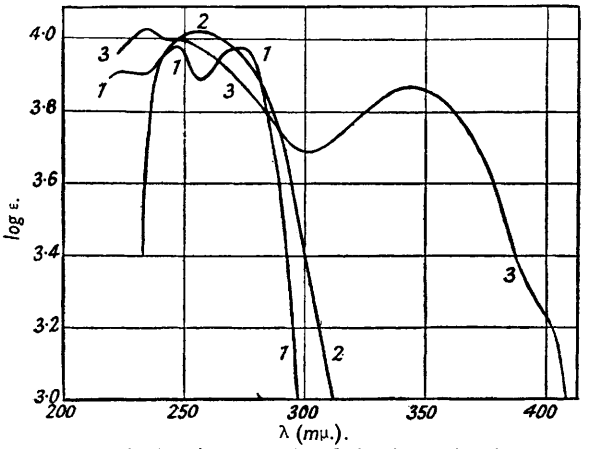
TABLE I.

	$\lambda_{max.}$	$\log_{10}\varepsilon$.	$\lambda_{max.}$	$\log_{10}\varepsilon$.	$\lambda_{max.}$	$\log_{10}\varepsilon$.
Antipyrin	223	3·91	247	3·97	273	3·98
4-Dimethylaminoantipyrin	—	—	255	4·04	—	—
4-Nitrosoantipyrin	233	4·03	250	4·00 *	343	3·88
					397	3·23

* Inflection only.

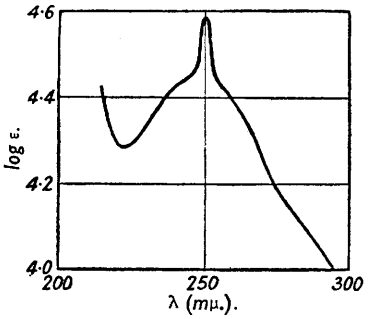
(*J. Gen. Chem. Russia*, 1940, **10**, 1342) and Biquard and Grammaticakis (*Bull. Soc. chim.*, 1941, [v], **8**, 246). Our results are less congruent with those of the Russian than with the French

FIG. 1.



1. *Antipyrin.* 2. *Dimethylaminoantipyrin.*
3. 4-*Nitrosoantipyrin.*

FIG. 2.



3-*Phenyl*isooxazol-5-*one.*

authors, who emphasised the spectral resemblance to phenylhydrazine (240 mμ., 3·8; 285 mμ., 3·2). It would, we submit, be better to seek among α-acylphenylhydrazines for analogies. These show no maxima between 240 and 400 mμ. (Biquard and Grammaticakis, *ibid.*, 1939, [v], **6**, 1606). On the other hand, acetanilide absorbs at 240 mμ. (4·2), 273 mμ. (3·0), and 280 mμ. (2·7) (Ramart Lucas, *ibid.*, 1936, **3**, 726; West and Gillam, *J.*, 1945, 432), *iso*propylideneacetone at 237 mμ. (4·06) and 313 mμ. (1·76) (Burawoy, *J.*, 1939, 1177), and crotonanilide at 268 mμ. (4·2) (Biquard and Grammaticakis, 1939, *loc. cit.*).

Glickman and Cope (*J. Amer. Chem. Soc.*, 1945, **67**, 1018) list the following which are relevant :

	$\lambda_{max.}$ (mμ.).	$\log_{10}\varepsilon_{max.}$.		$\lambda_{max.}$ (mμ.).	$\log_{10}\varepsilon_{max.}$.
NH_2·CMe:CH·C(OEt):O ...	274	4·31	NHMe·CMe:CH·C(OEt):O	284	4·51

Accordingly the absorption in antipyrin and pyramidon appears to arise more from the systems MeN—CMe=CH—C=O and PhN—C=O than from the Ph–N–N portion of the molecule.

4-Nitrosoantipyrin presents a more complex spectrum, for which there do not appear to be any very direct comparisons. It is reasonable to suppose that conjugation of –N=O with

an olefinic double bond will shift $\lambda_{max.}$ to longer-wave regions and increase $\log_{10}\varepsilon$. Some comparisons supporting this are :

C_6H_6	198 mμ.	(3·6)		420·5	(4·37)
C_6H_5·NO	280	(3·9	*p*-NMe_2·C_6H_4·NO	310	(3·1) *
				270	(3·7)

* Inflexion.

3-*Phenyl*iso*oxazol-5-one*.—This compound (VI) was studied as a possible " sydnone " model. Its dipole moment (in benzene) has been measured as $4{\cdot}9_7$ D. This value is of the order to be expected from simple vector addition on the basis of (VI), but since the literature (Beilstein, " Handbuch," XXVII, 200; XXVII, Ergänzungsband, p. 278) cites chemical evidence for the keto–enol mobility of (VI) we wish to withhold discussion pending further work.

The absorption spectrum of (VI) (in alcohol) is shown in Fig. 2. A maximum is seen at 250 mμ. ($\log_{10}\varepsilon$, 4·58), with points of inflection at 244 (4·46) and 257 mμ. (4·41). Comparison may be made with *N*-methylbenzaldimine (247 mμ., 4·23; Biquard and Grammaticakis, 1939, *loc. cit.*), and the shorter-wave-length maximum of benzaldoxime at 250 mμ. (4·15) although the oxime has also another maximum at 290 mμ. (3·0) and a point of inflection at 282 mμ. (3·23) (Ramart Lucas, *loc. cit.*).

Experimental.

Dipole-moment Determinations.—Antipyrin and its 4-dimethylamino-derivative (pyramidon) were commercial specimens. The remaining substances were prepared by methods indicated by Beilstein's " Handbuch." All were recrystallised and had m. p.s in agreement with the recorded values.

The apparatus, methods, and symbols used have been described before (Le Fèvre and Calderbank, *J.*, 1948, 1949). The data of Tables II and III refer to benzene as solvent. They have been taken at different seasons, and it has not always been possible easily to maintain baths at 25°.

Table II.

Refractivities.

10^6w_1.	n_D^{30}.	d_D^{30}.	r_{12}, c.c.	$[R_L]_D$, c.c.	10^6w_1.	n_D^{30}.	d_D^{30}.	r_{12}, c.c.	$[R_L]_D$, c.c.
	Antipyrin.					Dinitroantipyrin.			
0	1·4913	0·86718	0·33415	—	0	1·4913	0·86848	0·33375	—
25635	$1{\cdot}4937_8$	0·87347	0·33317	55·7	3282·7	1·4920	0·87031	0·33335	6·66
	3-Phenyl*iso*oxazol-5-one.								
0	$1{\cdot}4916_4$	0·86718	0·33435	—					
13274	$1{\cdot}4921_5$	0·87081	0·33325	40·5					

Table III.

Dielectric constant and density coefficients.

10^6w_1.	ε^{30}.	$\alpha\varepsilon_2$.	d_4^{30}.	βd_2.	10^6w_1.	ε^{30}.	$\alpha\varepsilon_2$.	d_4^{30}.	βd_2.
	Antipyrin (30°).					4-Dimethylaminoantipyrin (25°).			
0	2·2628	—	0·86718	—	0	2·2725	—	0·87378	—
6713_5	$2{\cdot}3786_5$	17·3	$0{\cdot}86887_5$	0·2525	9745·5	2·4089	14·0	0·88016	0·655
16325_5	$2{\cdot}5480_5$	17·5	0·87111	0·241	9817·8	2·4102	14·0	0·88017	0·651
26853	2·7384	17·7	0·87371	0·243	14426	$2{\cdot}4721_5$	13·8	0·88321	0·654
	Dinitroantipyrin (30°).				14880	2·4823	14·1	—	—
0	2·2628	—	0·86848	—	15267	2·4847	13·9	0·88374	0·652
1639	2·2769	8·60	0·86939	0·555	24939	2·6142	13·7	0·89012	0·656
2069	2·2804	8·51	0·86963	0·556		4-Bromoantipyrin (25°).			
2327	2·2828	8·60	0·86977	0·554	0	2·2725	—	0·87378	—
2492	2·2842	8·59	—	—	5391	2·3531	15·0	0·87577	0·369
3282·7	2·2911	8·62	0·87031	0·557	10247	2·4269	15·1	0·87763	0·376
	3-Phenyl*iso*oxazol-5-one (30°).				15150	2·5021	$15{\cdot}1_5$	0·87977	0·395
0	2·2628	—	0·86718	—	20085	2·5638	14·5	0·88159	0·389
2971	—	—	0·86799	0·273					
4432	2·3364	16·6	0·86838	0·271					
6563	2·3707	16·4	0·86900	0·277					
13274	2·4805	16·4	—	—					

Calculation of Results.—The equations, ${}_\infty P_1 = M_1[P_2(1-\beta) + c\alpha\varepsilon_2$ (cf. Le Fèvre and Vine, *J.*, 1937, 1805), and $\mu = 0{\cdot}01273\,({}_\infty P_1 - R)^{\frac{1}{2}}T^{\frac{1}{2}}$, were used.

TABLE IV.

Compound.	M_1.	Temp.	Mean $\alpha\varepsilon_2$.	Mean β.	$_{\infty}P_1$.	$[R_L]_D$.	μ., D.
Antipyrin.....	188·2	30°	17·5	0·283	672_5	55·7	5·5
Dinitroantipyrin	278·2	30	8·58	0·642	489	66·6	4·6
Phenyl*iso*oxazolone	161·1	30	16·5	$0{\cdot}315_5$	543_5	40·5	$4{\cdot}9_7$
Pyramidon	231·3	25	13·9	0·748	625	69 *	5·2
4-Bromoantipyrin	267	25	14·9	0·437	801	62 *	$5{\cdot}9_7$

* Calculated from data for antipyrin.

The moment of antipyrin has been previously observed by Jensen and Friediger (*Kgl. Danske Videnskabernes Selskab*, 1943, **20**, No. 20). Working at 25° they reported 5·4 D., with which our value is in satisfactory agreement.

Absorption Spectra.—These were recorded in absolute ethanol, at first with the Hilger medium spectrograph in conjunction with a rotating-sector photometer and condensed tungsten-steel spark, and were later checked on a Beckman photoelectric quartz spectrophotometer, model DU.

Our thanks are due to the Chemical Society for permission to retain apparatus originally purchased from a research grant and to the Commonwealth Science Committee for financial assistance.

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, June 27th*, 1949.]