

### 601. Structure of 3-Alkyl-4-arylazoisoxazol-5-ones and Related Compounds

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On spectral evidence 3-alkyl-4-arylazoisoxazol-5-ones are shown to exist essentially as 3-alkyl-4-arylhydrazonoisoxazol-5-ones.<sup>1</sup> This conclusion is supported by a study of alkyl derivatives of three of the four possible tautomeric forms. 3-Alkyl-4-arylazoisoxazole-5-thiones also favour the aryl-hydrazono-form.

ALTHOUGH 3-alkyl-4-arylazoisoxazol-5-ones have been known for many years<sup>2</sup> no reports have been made of attempts to establish the predominant tautomer(s) of the four possible forms (Ia), (IIa), (IIIa), and (IVa). In contrast, the structure of the related dyestuff, 3-methyl-1-phenyl-4-phenylazopyrazol-5-one, has been the subject of several conflicting reports.<sup>3</sup>

Our interest in the chemistry of arylazoisoxazolones stemmed from the continuation of our study of azo-compounds as fungicides<sup>4</sup> and was aroused by the discovery<sup>5</sup> that some of the isoxazolones gave excellent control of a number of plant pathogenic micro-organisms. During this investigation many 3-alkyl-4-arylazoisoxazol-5-ones were prepared by the well-known method of coupling diazotised anilines with acylacetoacetates followed by ring closure with hydroxylamine, and these are briefly recorded in Table 2.

The infrared spectra of 3-methyl-4-phenylazoisoxazol-5-one and its *o*-chlorophenylazo- and *m*-chlorophenylazo-analogues in the solid state and in solution showed absorption maxima at 1710—1720 and 3200—3210 cm.<sup>-1</sup>, which were assigned to CO and NH stretching

<sup>1</sup> Preliminary communication, L. A. Summers and D. J. Shields, *Chem. and Ind.*, 1964, 1264.

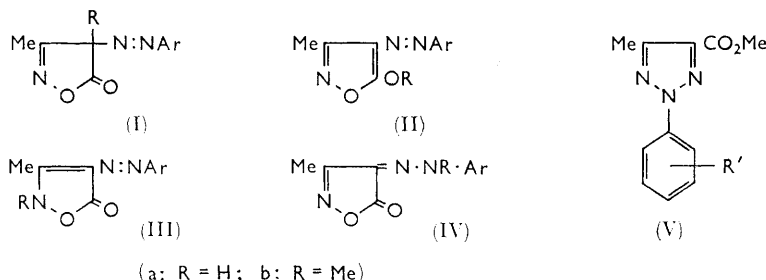
<sup>2</sup> L. Knorr and B. Reuter, *Ber.*, 1894, **27**, 1174; see review by A. Quilico, in "Five- and Six-Membered Compounds with Nitrogen and Oxygen," Wiley, Interscience, New York and London, 1962, p. 140.

<sup>3</sup> R. Jones, A. J. Ryan, S. Sternhall, and S. E. Wright, *Tetrahedron*, 1963, **19**, 1497; F. A. Snavelly, W. S. Trahanovsky, and F. H. Suydam, *J. Org. Chem.*, 1962, **27**, 994; W. Pelz, W. Puschel, H. Schellenberger, and K. Löffler, *Angew. Chem.*, 1960, **72**, 967; S. Toda, *J. Chem. Soc. Japan*, 1959, **80**, 402.

<sup>4</sup> H. M. Fox, M. J. Geoghegan, J. A. Silk, and L. A. Summers, *Ann. Appl. Biol.*, 1963, **52**, 33.

<sup>5</sup> Imperial Chemical Industries Limited, Belgian P. 617,389/1962; M. J. Geoghegan, L. A. Summers, and J. A. W. Turner, *B.P. Appl.* 37,645/1960.

frequencies, respectively (see Table 1). As the NH frequency was low for an unbonded amino-group and was also independent of the concentration of the solution it was inferred that the NH group was involved in intramolecular hydrogen bonding. The nuclear magnetic resonance spectra also showed, in addition to absorptions assigned to methyl



and aromatic protons, a broad absorption,  $\delta \sim 12.7$  p.p.m., which was independent of concentration and which was consistent with an intramolecularly bonded NH proton. There was no evidence for the presence of more than one tautomer for the nuclear magnetic resonance spectra and the ultraviolet absorption curves of freshly prepared solutions in ethanol or hexane were identical with those of solutions which had been kept for one week. These findings could not be reconciled with structures (Ia) and (IIa). Moreover, models showed that intramolecular hydrogen bonding was unlikely in structure (IIIa) but was highly probable between the CO and NH groups of structure (IVa). The evidence indicated therefore, that the compounds examined exist essentially as structure (IVa) with intramolecular bonding between the CO and NH groups. Since the infrared spectra of many of the compounds listed in Table 2 showed the presence of similar CO and NH groups, this structure is apparently the favoured one for most 3-alkyl-4-arylazoisoxazol-5-ones.

Additional evidence in support of structure (IVa) was obtained from a study of the *O*- and *N*-alkyl derivatives (IIb), (IIIb), and (IVb). Unlike 3-phenyl-4-phenylazoisoxazol-5-one, which is unaffected<sup>6</sup> by treatment with alkaline dimethyl sulphate, 4-aryla-3-methylisoxazol-5-ones were converted by this reagent into 4-aryla-2,3-dimethylisoxazol-5-ones (IIIb) in 25–40% yield. The same products were also obtained by the use of methyl iodide in acetone in the presence of potassium carbonate. The structure of the 4-aryla-2,3-dimethylisoxazol-5-ones was proved by unambiguous synthesis of authentic samples from the appropriate ethyl  $\alpha$ -aryla-2-oxoacetate and *N*-methylhydroxylamine (cf. Boulton and Katritzky<sup>7</sup>). As expected, their ultraviolet absorption spectra were different from those of the analogous 4-aryla-3-methylisoxazol-5-ones, thus furnishing convincing evidence that the latter do not exist as structure (IIIa).

Treatment of 4-(3-chlorophenylazo)-3-methylisoxazol-5-one and the 2-chlorophenylazo-analogue in chloroform-ethanol with an excess of ethereal diazomethane gave, in each case, three distinct products (cf. Meyer<sup>6</sup>), which were conveniently separated by fractional crystallisation. One of the products from each source was obtained in about 20% yield and was identified as the corresponding 3-methyl-4-[methyl(chlorophenyl)hydrazono]-isoxazol-5-one (IVb). In both cases this structure was assigned to the product on the basis of a negative methoxyl determination, infrared absorption at  $1740\text{ cm}^{-1}$  (CO), and the nuclear magnetic resonance spectrum. The last had, in addition to signals ascribed to the 3-methyl and the aromatic protons, a single methyl absorption ( $\delta \sim 4.0$  p.p.m.) which, since methoxy-groups were absent, could only be attributed to a methyl group attached to a nitrogen atom. As the products were different from the fully authenticated 4-chlorophenylazo-2,3-dimethylisoxazol-5-ones, they can only have the assigned structure. The

<sup>6</sup> M. A. Meyer, *Ann. Chim.*, 1914, **1**, 289.

<sup>7</sup> A. J. Boulton and A. R. Katritzky, *Tetrahedron*, 1961, **12**, 41.

ultraviolet spectrum of 3-methyl-4-[methyl(3-chlorophenyl)hydrazono]isoxazol-5-one,  $\lambda_{\text{max}}$  243 and 390  $\text{m}\mu$  ( $\epsilon$  8650 and 20,400) closely resembled that of the parent arylazoisoxazolone (compound 16, Table 1) and this provides strong supporting evidence for our representation of the latter as structure (IVa). The ultraviolet absorption maxima of 3-methyl-4-[methyl-(2-chlorophenyl)hydrazono]isoxazol-5-one,  $\lambda_{\text{max}}$  238 and 358  $\text{m}\mu$  ( $\epsilon$  5800 and 13,900) (cf. compound 17), on the other hand, showed pronounced hypsochromic shifts with reduced intensities, thus affording another example of the influence of bulky *ortho*-substituents on the ultraviolet spectra of *N*-substituted *N*-methyl anilines.<sup>8</sup>

The second product from each isoxazolone (5–20% yield) was identified as the appropriate 4-(chlorophenylazo)-5-methoxy-3-methylisoxazole (IIb) by the absence of a

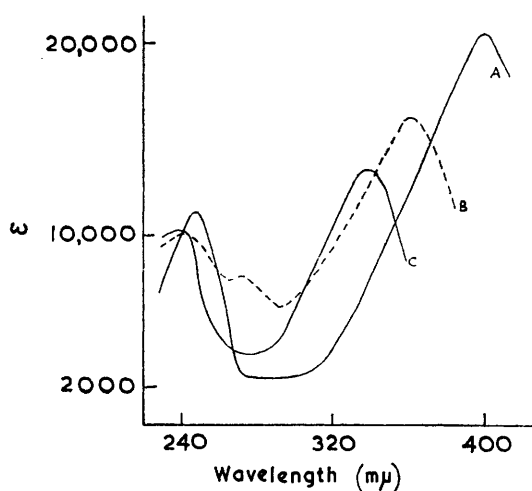


FIGURE 1. Ultraviolet absorption spectra of:  
(A) 4-(2-chlorophenylazo)-3-methylisoxazol-5-one in ethanol  
(B) 4-(2-chlorophenylazo)-2,3-dimethylisoxazol-5-one in ethanol  
(C) 4-(2-chlorophenylazo)-5-methoxy-3-methylisoxazole in hexane

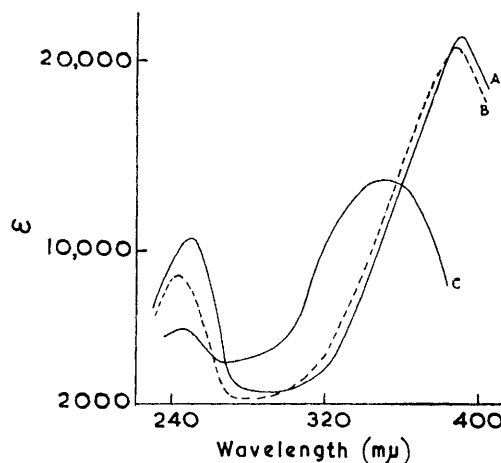


FIGURE 2. Ultraviolet absorption spectra of:

- (A) 4-(3-chlorophenylazo)-3-methylisoxazol-5-one in ethanol  
(B) 3-methyl-4-[methyl-(3-chlorophenyl)hydrazono]isoxazol-5-one in ethanol  
(C) 3-methyl-4-[methyl-(2-chlorophenyl)hydrazono]isoxazol-5-one in hexane

carbonyl absorption band (infrared) and by a methoxyl determination. The ultraviolet spectrum was different from that of the parent arylazoisoxazolone. The third product in each case was obtained in 15–25% yield and had an elemental analysis consistent with a monomethyl derivative of the starting material or an isomer thereof. The nuclear magnetic resonance spectrum showed singlets due to two methyl groups ( $\delta$  ~2.6 and 4.5 p.p.m.) in addition to aromatic signals. Moreover, the infrared spectrum showed an absorption band in the 1725–1740  $\text{cm}^{-1}$  region (CO) and a Zeisel determination showed that there was one methoxy-group per molecule. These findings cannot be reconciled with any of the structures (Ib), (IIb), (IIIb), and (IVb) but are in accord with structure (V;  $\text{R}' = 3$  or 2-Cl), the compound which would be expected to arise from a 4-(chlorophenylazo)-5-methoxy-3-methylisoxazole by a transformation analogous to the known thermal isomerisation of 3-methyl-5-phenyl-4-phenylazoisoxazole to 5-benzoyl-4-methyl-2-phenyl-1,2,3-triazole.<sup>9</sup> In confirmation of this, 2-(3-chlorophenyl)-4-methoxycarbonyl-5-methyl-1,2,3-triazole (V;  $\text{R}' = 3\text{-Cl}$ ) was hydrolysed to 4-carboxy-2-(3-chlorophenyl)-5-methyl-1,2,3-triazole, the ultraviolet spectrum  $\lambda_{\text{max}}$  278  $\text{m}\mu$  ( $\epsilon$  20,040), of which was similar to that

<sup>8</sup> H. H. Jaffe and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," Wiley, New York and London, 1962, p. 407; P. Grammaticakis, *Bull. Soc. chim. France*, 1951, 534.

<sup>9</sup> G. Wittig, F. Bangert, and H. Kleiner, *Ber.*, 1928, **61**, 1140.

reported<sup>10</sup> for 4-carboxy-2-(3-chlorophenyl)-1,2,3-triazole  $\lambda_{\max}$ , 270 m $\mu$  ( $\epsilon$  19,050). It was subsequently ascertained that the arylazomethoxymethylisoxazoles were converted into the triazoles to the extent of ~50% (infrared evidence) merely by boiling with light petroleum for one hour. It seems likely therefore, that most, if not all, of the rearrangement occurred during fractional crystallisation and not during methylation. Three analogous ethyl derivatives were obtained similarly from the reaction between 4-(3-chlorophenylazo)-3-methylisoxazol-5-one and diazoethane.

4-(2-Chlorophenylazo)-3-methylisoxazol-5-one was converted into the corresponding isoxazole-5-thione by treatment with phosphorus pentasulphide in toluene. The infrared spectrum of the product ( $\nu_{\max}$ , 3100 cm.<sup>-1</sup>, NH) and the nuclear magnetic resonance spectrum (a broad absorption at  $\delta$  = 15.6 p.p.m., independent of concentration) indicate that this compound also exists predominately as structure (IVa; CS for CO) with strong intramolecular bonding between the CS and NH groups.

## EXPERIMENTAL

Light petroleum refers to the fraction b. p. 60–80° unless otherwise stated. Infrared spectra were determined for Nujol mulls with a Perkin-Elmer Infracord spectrophotometer model 137, and for potassium bromide discs and chloroform solutions with a Perkin-Elmer model 237 instrument. Ultraviolet absorption measurements were made with a Perkin-Elmer model 137 spectrophotometer and 0.000085M-solutions. Nuclear magnetic resonance spectra were determined on a A.E.I. RS2 spectrometer at 60 Mc./sec. with deuteriochloroform as solvent and tetramethylsilane as internal reference.

TABLE I  
Spectra of 4-arylaizoxazol-3-methylisoxazol-5-ones and their methylation products

Compound No. (see Table 2 or text)	I.r. stretching frequencies (cm. <sup>-1</sup> )		U.v. absorptions		N.m.r. absorptions ( $\delta$ values, p.p.m.)		
	CO	NH	$\lambda_{\max}$	$\epsilon$	Me	Aromatic	NH
1	1710	3210 <sup>abc</sup>	247	9360 <sup>e</sup>	2.33	7.3—7.5	12.8
			398	20,400			
16	1720	3210 <sup>abc</sup>	251	10,560 <sup>e</sup>	2.38	7.3—7.5	12.6
			392	21,240			
17	1720	3200 <sup>abc</sup>	248	11,300 <sup>e</sup>	2.35	7.4—7.8	12.8
			398	20,600			
(111b; Ar = 2-chlorophenyl)			238	10,300 <sup>d</sup>			
			338	13,300			
(111b; Ar = 2-chlorophenyl)	1740 <sup>b</sup>		242	10,200 <sup>e</sup>			
			272	7800			
			362	16,200			
					Me	Aromatic	
(111b; Ar = 3-chlorophenyl)	1740 <sup>a</sup>		237	8400 <sup>e</sup>	2.64 (C—Me)	7.25—7.5	
			279	7200	3.68 (N—Me)		
			351	17,200			
(IVb; Ar = 2-chlorophenyl)	1740 <sup>b</sup>		238	5800 <sup>d</sup>	2.3 (C—Me)	7.3—7.6	
			358	13,900	4.1 (N—Me)		
(IVb; Ar = 3-chlorophenyl)	1740 <sup>a</sup>		243	8650 <sup>e</sup>	2.3 (C—Me)	7.3—7.5	
			390	20,400	4.2 (N—Me)		
(Vb; R' = 2-chloro)	1740 <sup>b</sup>		259	14,500 <sup>d</sup>	2.64 (C—Me)	7.3—7.5	
					4.50 (O—Me)		
(Vb; R' = 3-chloro)	1725 <sup>b</sup>		278	19,400 <sup>d</sup>	2.6 (C—Me)	7.3—7.5	
					4.02 (O—Me)		

<sup>a</sup> In Nujol. <sup>b</sup> KBr disc. <sup>c</sup> In chloroform. <sup>d</sup> In hexane. <sup>e</sup> In ethanol.

3-Alkyl-4-arylaizoxazol-5-ones (Table 2).—(a) Compounds 1—23 were prepared essentially as described by Schiff<sup>11</sup> by adding aqueous sodium nitrite to a cold mixture of ethyl acetoacetate, a substituted aniline, and hydroxylamine in aqueous hydrochloric acid. The arylazo-methylisoxazolones, which varied in colour from yellow to red, precipitated after 2—24 hr. (40—65%).

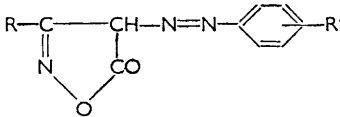
(b) Compounds 24—77 were obtained by a modification of the method of Bulow and Hecking.<sup>12</sup> Substituted anilines were diazotised and coupled with ethyl acylacetates. The

<sup>10</sup> H. El Khadem, Z. M. El-Shafei, and M. H. Meshreki, *J.*, 1961, 2957.

<sup>11</sup> R. Schiff, *Ber.*, 1895, **28**, 2731.

<sup>12</sup> C. Bulow and A. Hecking, *Ber.*, 1911, **44**, 238.

TABLE 2  
3-Alkyl-4-arylazoisoxazol-5-ones



No.	R	R'	M. p.	Sol-vent *	Formula	Found (%)		Reqd. (%)		Stretching frequencies (i.r. in Nujol; cm. <sup>-1</sup> )	
						C	H	C	H	CO	NH
1	Me	—	190° <sup>a</sup>	A						See Table 1	
2	Me	4-Me	204 <sup>b</sup>	A						1720	3230
3	Me	3-Me	172	B	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	60.7	5.0	60.8	5.1	1710	3220
4	Me	2-Me	160 <sup>c</sup>	A						1725	3240
5	Me	4-MeO	208	B	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>3</sub>	56.0	4.7	56.5	4.7	1700	3200
6	Me	3-MeO	193	B	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>3</sub>	56.8	4.8	56.5	4.7	1710	3200
7	Me	2-MeO	178 <sup>d</sup>	A						1700	3200
8	Me	2,4-Me <sub>2</sub>	126 <sup>e</sup>	A						1700	'
9	Me	2,6-Me <sub>2</sub>	150	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	62.6	5.8	62.3	5.6	1700	
10	Me	2,5-Me <sub>2</sub>	142	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	62.4	5.5	62.3	5.6		
11	Me	3,4-Me <sub>2</sub>	199	B	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	61.8	5.4	62.3	5.6	1710	3240
12	Me	2,3-Me <sub>2</sub>	136	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	62.3	5.5	62.3	5.6	1710	3200
13	Me	3,5-Me <sub>2</sub>	171	C	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	61.7	5.8	62.3	5.6	1700	3200
14	Me	2,4,6-Me <sub>3</sub>	128	B	C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	63.9	6.1	64.0	6.1	1710	'
15	Me	4-Cl <sup>j</sup>	192	B	C <sub>10</sub> H <sub>9</sub> ClN <sub>3</sub> O <sub>2</sub>	50.5	3.4	50.5	3.4	1720	3220
16	Me	3-Cl	162	B	C <sub>10</sub> H <sub>9</sub> ClN <sub>3</sub> O <sub>2</sub>	50.8	3.7	50.5	3.4	See Table 1	
17	Me	2-Cl <sup>j</sup>	168	C	C <sub>10</sub> H <sub>9</sub> ClN <sub>3</sub> O <sub>2</sub>	50.4	3.4	50.5	3.4	See Table 1	
18	Me	4-EtO	150	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub>	58.4	5.3	58.4	5.25	1710	3210
19	Me	2-EtO	140	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub>	58.9	5.3	58.4	5.25	1700	3200
20	Me	4-NO <sub>2</sub>	176 <sup>f</sup>	A						1740	3250
21	Me	3-NO <sub>2</sub> <sup>j</sup>	205	B	C <sub>10</sub> H <sub>9</sub> N <sub>4</sub> O <sub>4</sub>	48.4	3.5	48.6	3.3	1700	3250
22	Me	2-NO <sub>2</sub>	214	B	C <sub>10</sub> H <sub>9</sub> N <sub>4</sub> O <sub>4</sub>	49.0	3.4	48.6	3.3		
23	Me	2-COOH	228 <sup>g</sup>	B						{ 1680 1740	'
24	Me	3-Cl, 4-Me	192	A	C <sub>11</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>2</sub>	52.8	4.2	52.5	4.0	1720	3240
25	Me	4-Cl, 2-Me	148	A	C <sub>11</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>2</sub>	52.8	4.1	52.5	4.0	1710	'
26	Me	3-Cl, 2-Me	194	B	C <sub>11</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>2</sub>	52.8	4.4	52.5	4.0	1715	3220
27	Me	2-Cl, 6-Me	148	B	C <sub>11</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>2</sub>	52.0	4.4	52.5	4.0	1710	3200
28	Me	5-Cl, 2-Me	168	B	C <sub>11</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>2</sub> ·0.5EtOH	51.7	4.4	51.6	4.5	1730	3220
29	Me	4-Et	156	C	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	62.7	6.0	62.3	5.6	1710	3210
30	Me	2-Et	122	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	62.7	5.8	62.3	5.6	1710	3200
31	Me	3,4-Cl <sub>2</sub>	193	A	C <sub>10</sub> H <sub>7</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	44.6	2.7	44.1	2.6	1725	3230
32	Me	2,3-Cl <sub>2</sub>	170	B	C <sub>10</sub> H <sub>7</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub> ·EtOH	45.4	4.0	45.3	4.1		
33	Me	2,5-Cl <sub>2</sub> <sup>j</sup>	182	B	C <sub>10</sub> H <sub>7</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub> ·EtOH	45.5	4.3	45.3	4.1	1700	3220
34	Me	2,4-Cl <sub>2</sub>	160	A	C <sub>10</sub> H <sub>7</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub> ·EtOH	45.6	3.8	45.3	4.1		
35	Me	3-Br	163	A	C <sub>10</sub> H <sub>9</sub> BrN <sub>3</sub> O <sub>2</sub>	42.9	2.5	42.5	2.8	1730	3240
36	Me	2-Br	145	A	C <sub>10</sub> H <sub>9</sub> BrN <sub>3</sub> O <sub>2</sub> ·0.5EtOH	43.7	3.4	43.3	3.6	1710	3210
37	Me	3-COOEt	122 <sup>k</sup>	A	C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub>	56.9	4.7	56.7	4.7	1720 1740	3220
38	Me	2-COOEt	120	A	C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> ·EtOH	56.5	5.8	56.1	5.9	{ 1680 1700	3200
39	Me	4-N=N-Ph	208	A	C <sub>16</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	62.0	4.4	62.5	4.2		
40	Me	3-CF <sub>3</sub>	198	A	C <sub>11</sub> H <sub>9</sub> F <sub>3</sub> N <sub>3</sub> O <sub>2</sub>	49.0	3.0	48.7	2.95		
41	Me	3-Br, 4-F	182	A	C <sub>10</sub> H <sub>7</sub> BrFN <sub>3</sub> O <sub>2</sub>	39.9	2.3	40.0	2.3	1720	3200
42	Me	3-F	200	A	C <sub>10</sub> H <sub>9</sub> FN <sub>3</sub> O <sub>2</sub>	54.0	3.8	54.4	3.6	1720	3210
43	Me	4-F	165	A	C <sub>10</sub> H <sub>9</sub> FN <sub>3</sub> O <sub>2</sub>	54.4	3.6	54.4	3.6	1710	3200
44	Me	2-Bu <sup>n</sup>	49	A	C <sub>14</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub>	64.4	6.4	64.9	6.6		
45	Me	4-Bu <sup>n</sup>	92	A	C <sub>14</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub>	64.3	6.6	64.9	6.6	1720	3200
46	Me	4-C <sub>12</sub> N <sub>25</sub> <sup>n</sup>	91	A	C <sub>22</sub> H <sub>33</sub> N <sub>3</sub> O <sub>2</sub>	71.4	8.7	71.0	8.9	1730	3240
47	Me	3-EtO	162	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub>	58.3	5.2	58.4	5.25	1720	3220
48	Me	2-I	199	B	C <sub>10</sub> H <sub>9</sub> IN <sub>3</sub> O <sub>2</sub>	36.6	2.6	36.4	2.4	1710	3200
49	Me	2,5-(EtO) <sub>2</sub>	151	A	C <sub>14</sub> H <sub>17</sub> N <sub>3</sub> O <sub>4</sub> ·EtOH	57.6	6.8	57.0	6.8	1680	3230
50	Me	2-MeO, 5-Me	146	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> ·EtOH	55.5	6.6	55.9	6.1	1675	3230
51	Me	2-MeO, 4-NO <sub>2</sub>	210	B	C <sub>11</sub> H <sub>10</sub> N <sub>4</sub> O <sub>5</sub> ·EtOH	47.9	5.3	48.1	4.9	1680	3220
52	Me	4-MeO, 2-NO <sub>2</sub>	184	B	C <sub>11</sub> H <sub>10</sub> N <sub>4</sub> O <sub>5</sub> ·EtOH	48.2	5.4	48.1	4.9	1690	3200
53	Me	4-COOEt	211	A	C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub>	56.75	4.6	56.7	4.7		
54	Me	2,5-(PrO) <sub>2</sub>	125	A	C <sub>16</sub> H <sub>21</sub> N <sub>3</sub> O <sub>4</sub> ·EtOH	58.8	7.5	59.2	7.4		
55	Me	2-Me, 4-NO <sub>2</sub>	190	D	C <sub>11</sub> H <sub>10</sub> N <sub>4</sub> O <sub>4</sub> ·EtOH	50.3	5.4	50.65	5.1	1700	3240
56	Me	4-Me, 2-NO <sub>2</sub>	177	D	C <sub>11</sub> H <sub>10</sub> N <sub>4</sub> O <sub>4</sub>	50.8	4.2	50.4	3.8	1700	3250
57	Me	2-Me, 5-NO <sub>2</sub>	175	A	C <sub>11</sub> H <sub>10</sub> N <sub>4</sub> O <sub>4</sub>	50.1	4.2	50.4	3.8	1710	'
58	Me	4-SO <sub>2</sub> NH <sub>2</sub>	226	A	C <sub>10</sub> H <sub>10</sub> N <sub>4</sub> O <sub>4</sub> S	42.6	3.8	42.55	3.5		

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TABLE 2 (Continued)

No.	R	R'	M. p.	Sol-vent *	Formula	Found (%)		Reqd. (%)		Stretching frequencies (i.r. in Nujol; cm. <sup>-1</sup> )	
						C	H	C	H	CO	NH
59	Me	4-Ph	194	C	C <sub>16</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> ·0.25MeOH	67.6	4.9	67.9	4.9	1720	3230
60	Me	4-Br	194	E	C <sub>10</sub> H <sub>6</sub> BrN <sub>3</sub> O <sub>2</sub>	42.5	2.8	42.55	2.8	1720	3220
61	Me	2,5-(MeO) <sub>2</sub>	166 <sup>k</sup>	B	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>4</sub> ·EtOH	54.0	6.2	54.4	6.15	1680	3220
62	Me	4-Me, 3-NO <sub>2</sub>	199	B	C <sub>11</sub> H <sub>10</sub> N <sub>4</sub> O <sub>4</sub>	50.9	3.7	50.4	3.8	1740	3260
63	Me	2,6-Et <sub>2</sub>	60	A	C <sub>14</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub>	64.2	6.6	64.9	6.6	1720	3220
64	Me	4-NMe <sub>2</sub>	170	B	C <sub>12</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub>	59.1	6.1	58.5	5.7	1690	3200
65	Me	4-OH	230	A	C <sub>10</sub> H <sub>9</sub> N <sub>3</sub> O <sub>3</sub>	54.5	3.9	54.8	4.1	1720	3230
66	Me	2,4,5-Cl <sub>3</sub>	151	A	C <sub>10</sub> H <sub>6</sub> Cl <sub>3</sub> N <sub>3</sub> O <sub>2</sub>	38.7	2.0	39.1	2.0		
67	Me	4-NHCOMe	187	A	C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>3</sub>	55.0	5.0	55.4	4.6	1690 } 1725 }	3250 } 3375 }
68	Me	2-Pr <sup>i</sup>	140	A	C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	64.3	6.4	63.7	6.1	1720	3250
69	Me	3-Me, 4-Cl	182	A	C <sub>11</sub> H <sub>10</sub> ClN <sub>3</sub> O <sub>2</sub>	52.0	4.3	52.4	4.0	1725	3200
70	Me	4-SCN	174	A	C <sub>13</sub> H <sub>13</sub> N <sub>3</sub> O <sub>3</sub> S	<sup>a</sup>				1720	3220
71	Et	—	118	A	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> O <sub>2</sub>	60.4	5.1	60.8	5.1	1710	3200
72	Et	3-Me	134	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	62.0	5.7	62.3	5.6	1710	3220
73	Et	2-Me	137	A	C <sub>12</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub>	62.1	5.9	62.3	5.6	1720	3220
74	Et	4-EtO	147	B	C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>3</sub>	59.1	5.6	59.8	5.8	1710	3240
75	Et	2,3-Cl <sub>2</sub>	152	B	C <sub>11</sub> H <sub>9</sub> Cl <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	46.3	3.2	46.2	3.1	1720	3240
76	Pr <sup>n</sup>	2-Me	95	B	C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	63.4	6.1	63.6	6.1		
77	Bu <sup>n</sup>	—	85	A	C <sub>13</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub>	63.4	6.2	63.6	6.1	1700	3200

\* A, Ethanol; B, Benzene-ethanol; C, Benzene-methanol; D, Dioxan-ethanol; E, Benzene.

<sup>a</sup> Literature m. p.s range from 188—192°. <sup>b</sup> Lit.,<sup>12,13</sup> m. p. 202—203°. <sup>c</sup> Lit.,<sup>12,13</sup> m. p. 154—155°.

<sup>d</sup> Lit.,<sup>13</sup> m. p. 172—173°. <sup>e</sup> Lit.,<sup>12</sup> m. p. 124—125°. <sup>f</sup> Lit.,<sup>12</sup> m. p. 176—177°. <sup>g</sup> Lit.,<sup>12</sup> m. p. 232°. <sup>h</sup> Found: N, 21.2; S, 12.9%. Required: N, 21.5; S, 12.3%. <sup>i</sup> No NH absorption observed. <sup>j</sup> Recently prepared by H. G. Garg, *J. Org. Chem.*, 1962, **27**, 1045. <sup>k</sup> M. p. recorded in patent <sup>5</sup> is erroneous.

ethyl acylarylaazoacetates thus obtained were not purified but were treated with hydroxylamine hydrochloride and an excess of sodium acetate in boiling aqueous ethanol. The alkyl-arylazoisoxazolones crystallised out on cooling (50—75%).

**2,3-Dimethyl-4-phenylazoisoxazol-5-one.**—(a) 3-Methyl-4-phenylazoisoxazol-5-one (9.6 g.) potassium carbonate (5.6 g.), and methyl iodide (6.0 g.) in acetone (125 c.c.) were refluxed for 6 hr. and the solution was filtered. The filtrate was partly evaporated and diluted with water. The pale yellow precipitate of 2,3-dimethyl-4-phenylazoisoxazol-5-one (38%), m. p. 198° (from benzene-ethanol), was collected and washed with aqueous sodium hydroxide and water (Found: C, 60.2; H, 4.8; N, 19.8; OMe, 0.0. C<sub>11</sub>H<sub>11</sub>N<sub>3</sub>O<sub>2</sub> requires C, 60.8; H, 5.1; N, 19.3; OMe, 0.0%). The compound had  $\lambda_{\text{max}}$ . (EtOH) 232, 285, and 342 m $\mu$  ( $\epsilon$  6840, 6780, and 16,140),  $\nu_{\text{max}}$ . (Nujol) 1740 cm.<sup>-1</sup> (CO).

(b) Treatment of 3-methyl-4-phenylazoisoxazol-5-one with dimethyl sulphate in boiling aqueous sodium hydroxide for 30 min. gave a 28% yield of 2,3-dimethyl-4-phenylazoisoxazol-5-one, m. p. 198° (from benzene-ethanol).

(c) Ethyl  $\alpha$ -phenylazoacetate (4.7 g.), pyridine (50 c.c.), and a 2.5% aqueous solution of *N*-methylhydroxylamine (50 c.c.) were refluxed for 1 hr. The solution was cooled and acidified with cold aqueous hydrochloric acid to give a 55% yield of the isoxazolone, m. p. 196°. The infrared spectrum was identical with those of the products prepared by methods (a) and (b).

The following compounds were prepared by method (a) described above; the first two were also made by methods (b) and (c).

**4-(2-Chlorophenylazo)-2,3-dimethylisoxazol-5-one**, (42%), m. p. 200° (from benzene-ethanol) (Found: C, 52.9; H, 4.0; N, 17.0; OMe, 0.0. C<sub>11</sub>H<sub>10</sub>ClN<sub>3</sub>O<sub>2</sub> requires C, 52.5; H, 4.0; N, 16.7; OMe, 0.0%), see Table 1 for spectral data. **4-(3-Chlorophenylazo)-2,3-dimethylisoxazol-5-one**, (35%), m. p. 190° (from benzene-methanol) (Found: C, 52.9; H, 4.0; OMe, 0.2%), **2,3-Dimethyl-4(2-tolylazo)isoxazol-5-one**, m. p. 192° (from benzene-methanol) (Found: C, 62.1; H, 5.8; N, 18.1; OMe, 0.0. C<sub>12</sub>H<sub>13</sub>N<sub>3</sub>O<sub>2</sub> requires C, 62.3; H, 5.6; N, 18.2; OMe, 0.0%),  $\nu_{\text{max}}$ . (Nujol) 1740 cm.<sup>-1</sup> (CO). **4-(2-Chlorophenylazo)-2-ethyl-3-methylisoxazol-5-one**, (10%), m. p. 124° (from benzene-petroleum) (Found: C, 53.8; H, 4.8. C<sub>12</sub>H<sub>12</sub>ClN<sub>3</sub>O<sub>2</sub> requires C, 54.2; H, 4.5%),  $\nu_{\text{max}}$ . (Nujol) 1740 cm.<sup>-1</sup> (CO).

**Reactions with Diazoalkanes.**—(a) 4-(2-Chlorophenylazo)-3-methylisoxazol-5-one (10 g.), in

<sup>13</sup> R. Schiff and G. Viciani, *Ber.*, 1897, **30**, 1159.

chloroform (200 c.c.) and ethanol (50 c.c.), was treated with an excess of diazomethane in ether (80 c.c.), and the mixture set aside for 3 days. The solvent was removed *in vacuo* and the solid residue was extracted with boiling light petroleum (200 c.c.). The solid which remained undissolved was washed repeatedly with tepid aqueous sodium hydroxide and was crystallised twice from ethanol to give 3-methyl-4-[methyl-(2-chlorophenyl)hydrazono]isoxazol-5-one, (15%), as yellow crystals, m. p. 135–136° (Found: C, 52.0; H, 4.4; N, 17.3; OMe, 0.0.  $C_{11}H_{10}ClN_3O_2$  requires C, 52.5; H, 4.0; N, 16.7; OMe, 0.0%), see Table 1 for absorption data. The petroleum extract, on evaporation, afforded a solid which was crystallised first from boiling methanol (50 c.c.) and then twice from benzene-methanol to give 4-(2-chlorophenylazo)-5-methoxy-3-methylisoxazole, (18%), as yellow crystals, m. p. 104° (Found: C, 52.6; H, 4.4; N, 16.6; OMe, 12.3.  $C_{11}H_{10}ClN_3O_2$  requires OMe, 12.3%). There was no absorption in the infrared in the region 1650–1800  $cm^{-1}$ . The mother-liquors afforded 2-(2-chlorophenyl)-4-methoxycarbonyl-5-methyl-1,2,3-triazole, (17%), as white crystals, m. p. 90° after repeated crystallisation from light petroleum (b. p. 40–60°) (Found: C, 52.0; H, 4.0; N, 16.7; OMe, 12.0%).

(b) Similar treatment of 4-(3-chlorophenylazo)-3-methylisoxazol-5-one with an excess of diazomethane gave 3-methyl-4-[methyl(3-chlorophenyl)hydrazono]isoxazol-5-one, (22%), as orange needles, m. p. 181° (from benzene) (Found: C, 52.6; H, 3.9; N, 16.9; OMe, 0.0%), 4-(3-chlorophenylazo)-5-methoxy-3-methylisoxazole, (5%), lemon crystals, m. p. 96° (from methanol) (Found: C, 52.9; H, 4.0; N, 17.2; OMe, 12.0%) no absorption 1650–1800  $cm^{-1}$ , and 2-(3-chlorophenyl)-4-methoxycarbonyl-5-methyl-1,2,3-triazole, (23%), white crystals, m. p. 104° (from petroleum) (Found: C, 52.5; H, 4.3; N, 17.2; OMe, 12.2%).

(c) Treatment of 4-(3-chlorophenylazo)-3-methylisoxazol-5-one with diazoethane gave 3-methyl-4-[ethyl(3-chlorophenyl)hydrazono]isoxazol-5-one, 26%, as lemon needles, m. p. 134° (from benzene-petroleum) (Found: C, 54.2; H, 4.5; N, 15.4; OEt, 0.0.  $C_{12}H_{12}ClN_3O_2$  requires C, 54.2; H, 4.5; N, 15.8; OEt, 0.0%),  $\lambda_{max}$  (EtOH) 249 and 384  $m\mu$  ( $\epsilon$  7200 and 17,500),  $\nu_{max}$  (KBr) 1735  $cm^{-1}$  (CO),  $\delta$  1.4 (ethyl C-Me), 4.85 (3-C-Me), 7.3–7.45 p.p.m. (aromatic protons), 4-(3-chlorophenylazo)-5-ethoxy-3-methylisoxazole, (5%), yellow needles, m. p. 78° (from petroleum) (Found: C, 53.8; H, 4.2; N, 16.3; OEt, 16.35.  $C_{12}H_{12}ClN_3O_2$  requires OEt, 16.9%),  $\lambda_{max}$  (hexane) 242 and 334  $m\mu$  ( $\epsilon$  10,000 and 12,500), no absorption 1650–1800  $cm^{-1}$ ,  $\delta$  1.56 (ethyl C-Me), 2.46 (3-C-Me), 4.73 ( $CH_2$ ), 7.28–7.6 p.p.m. (aromatic protons), and 2-(3-chlorophenyl)-4-ethoxycarbonyl-5-methyl-1,2,3-triazole, (7%), white needles, m. p. 68° (from petroleum) (Found: C, 54.1; H, 4.7; N, 15.3; OEt, 16.8%),  $\lambda_{max}$  (hexane) 278  $m\mu$  ( $\epsilon$  16,900),  $\nu_{max}$  (KBr) 1725  $cm^{-1}$  (CO),  $\delta$  1.43 (ethyl C-Me), 2.6 (5-C-Me), 4.43 ( $CH_2$ ), 7.3–7.5 p.p.m. (aromatic protons).

4-Carboxy-2-(3-chlorophenyl)-5-methyl-1,2,3-triazole was obtained as white crystals, m. p. 207° (from benzene-methanol) (Found: C, 51.0; H, 3.5; N, 17.2.  $C_{10}H_8ClN_3O_2$  requires C, 50.5; H, 3.4; N, 17.7%,  $\lambda_{max}$  (in EtOH) 278  $m\mu$  ( $\epsilon$  20,040),  $\nu_{max}$  (Nujol) 1710  $cm^{-1}$  (CO), by refluxing 2-(3-chlorophenyl)-4-methoxycarbonyl-5-methyl-1,2,3-triazole with a mixture of hydrochloric and acetic acids for 2 hr.

3-Methyl-4-phenylazoisoxazole-5-thione.—3-Methyl-4-phenylazoisoxazol-5-one (10–15 g.) and phosphorus pentasulphide (11.1 g.) were refluxed for 1 hr. in toluene (100 c.c.). The mixture was filtered and cooled to give 3-methyl-4-phenylazoisoxazole-5-thione, (71%), as red crystals, m. p. 126° (from ethanol) (Found: C, 54.3; H, 4.2; S, 14.1.  $C_{10}H_9N_3OS$  requires C, 54.8; H, 4.1; S, 14.6%).

4-(2-Chlorophenylazo)-3-methylisoxazole-5-thione was obtained, similarly (65%) as red crystals, m. p. 150° (from toluene) (Found: C, 47.9; H, 3.3; S, 12.6.  $C_{10}H_8ClN_3OS$  requires C, 47.3; H, 3.2; S, 12.6%),  $\lambda_{max}$  (EtOH) 248 and 448  $m\mu$  ( $\epsilon$  17,100 and 15,700),  $\nu_{max}$  (KBr) 3100  $cm^{-1}$  (NH),  $\delta$  2.3 (C-Me), 7.3–7.7 (aromatic protons), 15.6 p.p.m. (NH).

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