262. *Substitution of 4,5-Diphenyl-oxazoles and -imidazoles, and Some Related Compounds.*

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Substitution of the phenyl groups in 2-methyl-4,5-diphenyloxazole, as well as in some other similar oxazoles and imidazoles, is described; nitration, sulphonation, and chlorosulphonation of most of these compounds occur in the *para*-positions, in one or in both of the phenyl groups. The nitro-derivatives have been reduced to the amines which were diazotised and subjected to the usual replacement reactions.

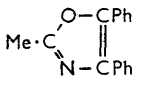
A REVIEW [1] of oxazoles shows that little work has been done on the substitution of phenyl substituents in such compounds. It has now been found that 4,5-diphenyloxazoles and their substitution products can be oxidised in high yield to the corresponding benzils (see following paper); they thus acquire interest and we report here a study of 2-methyl-4,5-diphenyloxazole (I) which is readily prepared from benzoin acetate.[2]

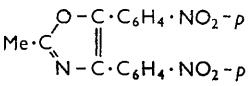
This compound (I) contains a stable ring. On nitration it forms the di-*p*-nitrophenyl derivative (II); sulphonation attacks only the 5-phenyl group; chlorosulphonation attacks both phenyl groups; and in all these reactions substitution occurs only at the *para*-position of the phenyl groups. In addition, the mononitration compound, 2-methyl-5-*p*-nitrophenyl-4-phenyl oxazole (III), is readily synthesised from 4′-nitrobenzoin acetate, $NO_2 \cdot C_6H_4 \cdot CH(OAc) \cdot COPh$; this oxazole is of value in determining the orientation of other monosubstituted diphenyloxazoles. In no case was the isomeric 4-*p*-nitrophenyl compound formed during these nitrations.

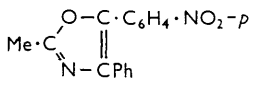
We also studied briefly the substitution of 4,5-diphenyl- and 2,4,5-triphenyl-oxazole, 2-methyl-4,5-diphenyl-, 4,5-diphenyl-, and 2,4,5-triphenyl-imidazole, 4,5-diphenyl-2-oxazolone and -imidazolone, and 2-methyl-4,5-diphenylthiazole.

[1] Wiley, *Chem. Rev.*, 1945, **37**, 401.
[2] Gompper and Rühle, *Annalen*, 1959, **626**, 88.

Chlorine and bromine oxidise the 4,5-diphenyloxazoles to the corresponding benzils in high yield and electrophilic substitution in the phenyl groups by bromine could not be effected in the presence of catalysts such as iron filings, iodine, or ferric chloride (cf. Gompper and Rühle [2]).


(I)


(II)


(III)

The nitro-compounds (II) and (III) are readily reduced to the amines without affecting the heterocyclic ring; these amines can be diazotised normally and in this way a number of substituents were introduced into the *para*-positions of the phenyl groups; further, the dinitro-compound (II) can be reduced to 5-*p*-aminophenyl-2-methyl-4-*p*-nitrophenyloxazole by sodium sulphide. From these starting materials a large number of *para*-substituted phenyl derivatives were prepared (see Tables).

That substitution in the phenyl groups takes place only in the *para*-position under the conditions used was established by oxidation with hydrogen peroxide or chromic acid; compounds (I), (II), and (III) formed benzoic acid, *p*-nitrobenzoic acid, and a mixture of these acids, respectively, in good yield, without isomers.

Since compound (III) was used as a reference substance, it was desirable to fix unambiguously the position of the nitro-group and thus of this group in 4′-nitrobenzoin acetate. This compound was first prepared by Francis and Keane [3] who formulated it as indicated; this formulation is predictable, for the nitro-group should enter the nucleus adjacent to the CH·OH group, and it was confirmed by the following synthesis:

$$p\text{-}NO_2\cdot C_6H_4\cdot CH_2\cdot COCl \longrightarrow p\text{-}NO_2\cdot C_6H_4\cdot CH_2\cdot COPh \longrightarrow$$
$$p\text{-}NO_2\cdot C_6H_4\cdot CHBr\cdot COPh \longrightarrow p\text{-}NO_2\cdot C_6H_4\cdot CH(OAc)\cdot COPh$$

The conversion of this product into the oxazole (III) by ammonium acetate in hot acetic acid [2] proves the structure of the latter.

The reactions of the compounds enumerated earlier are summarised in the annexed Table.

4,5-Diphenyl deriv. of	Reaction with HNO_3	Reaction with $Cl\cdot SO_3H$
Oxazole *	Disubstn.	Disubstn.
2-Phenyloxazole	Mono-, di-, & tri-substn.	—
Imidazole	Disubstn. & oxidn.	Disubstn.
2-Methylimidazole	,, ,,	—
2-Phenylimidazole	Trisubstn. & oxidn.	—
2-Imidazolone	Oxidn.	Disubstn.
2-Oxazolone	(Oil †)	,,
2-Methylthiazole	(Gum †)	(Gum †)

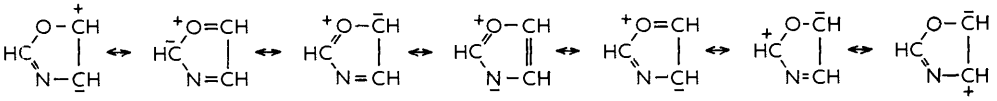
* With H_2SO_4 gives an oil. † Not studied.

The reactions studied bear on the relative reactivities of phenyl groups in the 2-, 4-, and 5-positions of oxazole towards electrophilic attack if it is assumed that these reactivities can be relayed from the ring to the *para*-positions of attached phenyl groups. The results obtained indicate that the reactivities are in the order C-5 > C-4 > C-2; for example, it had been reported [5] that the nitration of 2,5-diphenyloxazole led to substitution in the 5-phenyl group and, as found by us, in the nitration of 2,4,5-triphenyloxazole mononitration attacked the 5-phenyl group, dinitration the 4- and 5-phenyl groups, and trinitration each of the phenyl groups. Gompper *et al.* [6] found bromination of oxazoles to occur preferentially at C-5 but, if this was occupied, then at C-4, but not at C-2. Unfortunately physical measurements which could be of value in this matter do not appear to have

[3] Francis and Keane, *J.*, 1911, **99**, 344.
[4] Davidson, Weiss, and Jelling, *J. Org. Chem.*, 1937, **2**, 328.
[5] Lister and Robinson, *J.*, 1912, **101**, 1297.
[6] Gomper and Rühle, *Annalen*, 1959, **626**, 92.

been made, but Pullman and Metzger [7] determined the electron-density diagram for thiazole, showing that the 5-position has a large negative charge and the 2-position has a positive charge about one-third in magnitude of that at C-5, whereas the 4-position is neutral; it would be reasonable to assume a similar electron-density distribution in oxazole.

Consideration of the mesomeric forms of oxazole confirms the above conclusions: negative charges are at C-5 in three of the forms, at C-4 in two, and at C-2 in only one.



4,5-Diphenyloxazoles have been prepared [4] from the appropriate benzoin ester and ammonium acetate, the corresponding imidazole usually being formed as a by-product; we found that the yield of oxazole is considerably increased by substituting urea for ammonium acetate.

Experimental

M. p.s were determined in an electrically heated copper block. Known compounds were identified by mixed m. p.s. Unless otherwise stated, the quantity of starting material used in the experiments listed was 5·0 g. For analyses, etc., see the Tables.

4′-Nitrobenzoin Acetate.—(*a*) This ester was prepared in 51% yield by the method of Womack *et al.*,[8] except that they extracted the oily product with ether in order to obtain the ester whereas it is the ether-insoluble material which is required.

(*b*) 4′-Nitrodeoxybenzoin [9] was brominated [10] and the oily product refluxed with anhydrous sodium acetate (3 g.) in glacial acetic acid (30 c.c.) for 2 hr. After removal of the solvent under diminished pressure, the residue was crystallised thrice from alcohol giving the benzoin acetate (0·4 g.), m. p. and mixed m. p. 127—128°.

2-Methyl-5-p-nitrophenyl-4-phenyloxazole (III).—4′-Nitrobenzoin acetate, urea (2·3 g.), and acetic acid (30 c.c.) were refluxed for 3 hr., then poured into water; the *product* formed yellow plates (4 g., 85%) from alcohol. It (1 g.) was refluxed with 30% hydrogen peroxide (5 c.c.) in acetic acid (20 c.c.) for 1 hr.; most of the solvent was removed under diminished pressure and water was added. *p*-Nitrobenzoic acid (0·49 g.) separated and benzoic acid (0·25 g.) was extracted with ether from the aqueous filtrate.

The same condensation was repeated with ammonium acetate (5 g.) instead of urea, the product being obtained in 65% yield.

2-Methyl-5-p-nitrophenyl-4-p-sulphamoylphenyloxazole (XIV).—The oxazole (III) (10 g.) was added slowly to chlorosulphonic acid (30 c.c.) at 0° and then warmed at 50—55° for 2 hr. The solution was poured on ice, and the crude product was filtered off and left overnight in concentrated aqueous ammonia (30 c.c.); the *amide* formed yellow needles (12·4 g., 97%) from dilute pyridine. On oxidation as above, a mixture of *p*-nitro- and *p*-sulphamoyl-benzoic acid was obtained.

2-Methyl-4,5-di-p-nitrophenyloxazole (II).—The compound (I) (50 g.) was slowly added to cold fuming nitric acid (*d* 1·5, 250 c.c.), the temperature being kept at 0° during the addition; the solution was kept overnight at room temperature and then poured on ice. The yellow solid (68 g., 98%) was sparingly soluble in most organic solvents, including acetic acid and pyridine, but crystallised from nitrobenzene in yellow needles. The same product was obtained in 96% yield from the compound (III) by the above procedure. Oxidation gave *p*-nitrobenzoic acid as the sole product.

The dinitro-compound (II) was also obtained in good yield under the following conditions: (i) The compound (I) was dissolved in concentrated sulphuric acid (20 c.c.) at 0° and potassium nitrate (3 g.) was slowly added, the temperature being kept at 0—5°. After 30 min. the mixture was poured on ice (yield of pure product, 5·5 g.). (ii) The compound (I) was dissolved in concentrated sulphuric acid (20 c.c.), and nitric acid (*d* 1·4; 20 c.c.) was added gradually at room

[7] Pullman and Metzger, *Bull. Soc. chim. France*, 1948, **15**, 1021.
[8] Womack, Campbell, and Dodds, *J.*, 1938, 1405.
[9] Petrenko-Kritschenko, *Ber.*, 1892, **25**, 2242.
[10] Jenkins, *J. Amer. Chem. Soc.*, 1934, **56**, 682, 1137.

TABLE 1.

2-Methyl-4-X-phenyl-5-Y-phenyloxazoles.

				Found (%)				Required (%)		
No.	X	Y	M. p.	C	H	N	Formula	C	H	N
II	NO_2	NO_2	241—242°	59·3	3·5	13·1	$C_{16}H_{11}N_3O_5$	59·1	3·4	12·9
III	H	NO_2	95—96	68·3	4·4	10·1	$C_{16}H_{12}N_2O_3$	68·6	4·3	10·0
IV	H	NH_2	123—124			11·1	$C_{16}H_{14}N_2O$			11·2
V	H	NHAc	201—202	73·8	5·4	9·5	$C_{18}H_{16}N_2O_2$	74·0	5·5	9·6
VI	H	NHBz	183—184			7·9	$C_{23}H_{18}N_2O_2$			7·9
VII	H	Cl	40—41			5·15	$C_{16}H_{12}ClNO$			5·2
VIII	H	OH	152—153			5·55	$C_{16}H_{13}NO_2$			5·6
IX	H	CN	109—110			10·8	$C_{17}H_{12}N_2O$			10·8
X	H	CO_2H	248—249			5·0	$C_{17}H_{13}NO_3$			5·0
XI	H	CO_2Me	102—103			4·9	$C_{18}H_{15}NO_3$			4·8
XII	H	SO_3H	325 *			4·6	$C_{16}H_{13}NO_4S$			4·45
XIII	H	$SO_2{\cdot}NH_2$	170—172	61·4	4·6	8·8	$C_{16}H_{14}N_2O_3S$	61·15	4·5	8·9
XIV	$SO_2{\cdot}NH_2$	NO_2	259—260	53·8	3·8	11·7	$C_{16}H_{13}N_3O_5S$	53·5	3·6	11·7
XV	$SO_2{\cdot}NH_2$	NH_2	230—231	58·15	4·6	12·8	$C_{16}H_{15}N_3O_3S$	58·35	4·6	12·8
XVI	$SO_2{\cdot}NH_2$	CO_2Me	221—222			7·7	$C_{18}H_{16}N_2O_5S$			7·6
XVII	$SO_2{\cdot}NH_2$	H	169—170			8·95	$C_{16}H_{14}N_2O_3S$			8·9
XVIII	NH_2	NH_2	178—180	72·4	5·8	15·6	$C_{16}H_{15}N_3O$	72·4	5·7	15·85
XIX	NHAc	NHAc	124—125 †	68·6	5·6	12·0	$C_{20}H_{19}N_3O_3$	68·7	5·45	12·0
XX	NHBz	NHBz	254—255			8·9	$C_{30}H_{23}N_3O_3$			8·8
XXI	$SO_2{\cdot}NH_2$	$SO_2{\cdot}NH_2$	244—245	48·45	4·0	10·5	$C_{16}H_{15}N_3O_5S_2$	48·9	3·8	10·7
XXII	CO_2Me	CO_2Me	175—176			4·1	$C_{20}H_{17}NO_5$			4·0
XXIII	$CO{\cdot}NH_2$	$CO{\cdot}NH_2$	253—254			13·0	$C_{18}H_{15}N_3O_3$			13·1
XXIV	NO_2	NH_2	92—93	65·2	4·4	14·6	$C_{16}H_{13}N_3O_3$	65·1	4·4	14·2
XXV	NO_2	NHAc	216—217			12·7	$C_{18}H_{15}N_3O_4$			12·5
XXVI	NO_2	R ‡	211—212			10·6	$C_{18}H_{13}Cl_2N_3O_4$			10·3
XXVII	NO_2	H	134—135			10·3	$C_{16}H_{12}N_2O_3$			10·0

* Decomp. † The compound changes to a glass at this temperature without melting: if the temperature is slowly raised, the substance becomes opaque at 190—200° and melts at 204°. ‡ R = $NH{\cdot}CO{\cdot}CHCl_2$.

temperature. The solution was warmed to 50—55° for 15 min. and then poured on ice (yield of pure product, 5·5 g.).

The conditions of nitration were then moderated in an attempt to prepare a mononitro-derivative. (iii) The compound (I) (30 g.) was slowly added to cold fuming nitric acid (150 c.c.), the temperature being kept at 0—5°, and the solution was left at this temperature for a further 15 min., then poured on ice. The solid (35 g.) which separated crystallised from acetic acid and gave the dinitro-compound (II) (20 g.); a pasty solid (15 g.) separated from the mother-liquor on dilution with water and on crystallisation from alcohol gave the mononitro-compound (III) (9 g.). (iv) The compound (I) was slowly added at 0—5° to a mixture of fuming nitric acid (30 c.c.) and concentrated nitric acid (20 c.c.). The solution was left at room temperature; brown fumes were evolved, the temperature rose to 35°, and a pasty solid separated; crystallisation from alcohol gave benzil (3·5 g.). (v) The compound (I) (10 g.) was slowly added to acetic anhydride (50 c.c.), the solution cooled to 0—5°, and fuming nitric acid (30 c.c.) gradually added; the temperature rose somewhat and brown fumes were evolved. The mixture was left at room temperature for 30 min., then poured on ice. A solid (12 g.) separated. Extraction with hot alcohol gave *p*-nitrobenzoic acid (1 g.), and dilution of the mother-liquor yielded the mononitro-compound (III) (2·4 g.); the insoluble residue from the alcoholic extract was treated with hot concentrated hydrochloric acid to remove any basic material, leaving 4,4′-dinitrobenzil (0·2 g.); the acid extract yielded compound (II) (8 g.) on dilution with water. (vi) The compound (I) was left overnight in concentrated nitric acid (25 c.c.); it was recovered unchanged; if the mixture was heated on the water-bath, the oxazole dissolved completely, and after a short time a vigorous reaction set in and gave benzil quantitatively.

2-*Methyl*-4-*phenyl*-5-p-*sulphamoylphenyloxazole* (XIII).—The compound (I) (10 g.) was heated in concentrated sulphuric acid (25 c.c.) on the water-bath for 1 hr.; the *acid* (XII) which separated as the mixture was poured into water was dissolved in aqueous ammonia and reprecipitated with hydrochloric acid, yielding stout prisms (12·5 g., 93%) from dilute alcohol. The acid was dried at 100°, thionyl chloride (50 c.c.) and dimethylformamide (0·3 c.c.) were

added, and the mixture was refluxed for 30 min. The thionyl chloride was removed under diminished pressure, and cold, concentrated aqueous ammonia (25 c.c.) was added to the residue. Next morning the *sulphonamide* (12·6 g., 94%) was collected; it crystallised from dilute alcohol as pale yellow needles. Oxidation gave *p*-sulphamoylbenzoic and benzoic acid.

TABLE 2.

2-Methyl-4-X-phenyl-5-Y-phenyloxazoles (further derivatives).

X	Y	Yield (%)	Solvent for cryst.	M. p.	Found: N (%)	Formula	Reqd.: N (%)
H	Br	53	Aq.EtOH	43—44°	4·5	$C_{16}H_{12}BrNO$	4·5
$SO_2{\cdot}NH_2$	NHAc	98	,,	246—247	11·4	$C_{18}H_{17}N_3O_4S$ *	11·3
$SO_2{\cdot}NH_2$	Cl	64	,,	234—235	8·2	$C_{16}H_{13}ClN_2O_3S$	8·0
$SO_2{\cdot}NH_2$	Br	74	EtOH	219—220	7·1	$C_{16}H_{13}BrN_2O_3S$	7·1
$SO_2{\cdot}NH_2$	OH	100	Aq.EtOH	226—227	8·5	$C_{16}H_{14}N_2O_4S$	8·5
$SO_2{\cdot}NH_2$	CN	93	,,	245—246	12·2	$C_{17}H_{13}N_3O_3S$	2·4
$SO_2{\cdot}NH_2$	CO_2H	85	,,	286—287	8·0	$C_{17}H_{14}N_2O_5S$	7·9
Cl	Cl	70	EtOH	160—162	4·8	$C_{16}H_{11}Cl_2NO$	4·6
Br	Br	48	,,	168—169	3·7	$C_{16}H_{11}Br_2NO$	3·6
I	I	4	,,	157—158	3·0	$C_{16}H_{11}I_2NO$	2·9
OH	OH	75	,,	114—115	5·2	$C_{16}H_{13}NO_3$	5·2
CN	CN	74	,,	156—157	14·7	$C_{18}H_{11}N_3O$	14·7
CO_2H	CO_2H	71	,,	289—290	4·4	$C_{18}H_{13}NO_5$	4·3
NO_2	Cl	83	AcOH	196—197	8·95	$C_{16}H_{11}ClN_2O_3$	8·9
NO_2	Br	79	,,	202—203	7·9	$C_{16}H_{11}BrN_2O_3$	7·8
NO_2	OH	74	Aq.AcOH	109—110	9·6	$C_{16}H_{12}N_2O_4$	9·5
NO_2	CN	85	Aq.EtOH	192—193	13·7	$C_{17}H_{11}N_3O_3$	13·8
NO_2	CO_2H	85	AcOH	304—305	8·85	$C_{17}H_{12}N_2O_5$	8·6
NO_2	CO_2Me		Aq.AcOH	200—201	8·5	$C_{18}H_{14}N_2O_5$	8·3
NH_2	Cl	100	Aq.EtOH	158—159	9·6	$C_{16}H_{13}ClN_2O$	9·8
NHAc	Cl	100	,,	103—104	8·4	$C_{18}H_{15}ClN_2O_2$	8·6
NH_2	Br	100	,,	153—154	8·4	$C_{16}H_{13}BrN_2O$	8·5
NHAc	Br	100	,,	114—115	7·4	$C_{18}H_{15}BrN_2O_2$	7·55
NH_2	OH	100	,,	123—124	10·4	$C_{16}H_{14}N_2O_2$	10·5
Br	Cl	65	Aq.AcOH	160—161	4·2	$C_{16}H_{11}BrClNO$	4·0
Cl	Br	74	,,	161—162	4·1	$C_{16}H_{11}BrClNO$	4·0

* Found: C, 58·3; H, 4·75. Required: C, 58·2; H, 4·6%.

The same sulphonamide was prepared from 5-*p*-aminophenyl-2-methyl-4-phenyloxazole (IV). The amine (10 g.) was diazotised as described below; the cold diazonium solution was slowly added to a cold solution of cupric chloride (2 g.) in acetic acid (30 c.c.) and water (7 c.c.) previously saturated with sulphur dioxide, and passage of the gas was continued during the reaction. The mixture was set aside for 30 min., then poured into water, and the sulphonyl chloride which separated was treated as above (yield, 2·3 g., 37%).

*2-Methyl-4,5-di-*p*-sulphamoylphenyloxazole* (XXI).—The compound (I) was slowly added to cold chlorosulphonic acid (25 c.c.), and the solution was kept at 50—55° for 2 hr., then poured on ice. The sulphonyl chloride which separated was treated as above, forming pale yellow crystals (7·8 g., 93%) from alcohol. Oxidation gave *p*-sulphamoylbenzoic acid as sole product.

*5-*p*-Aminophenyl-2-methyl-4-phenyloxazole* (IV).—The compound (III), Raney nickel (*ca.* 1 g.), and alcohol (150 c.c.), were shaken with hydrogen at atmospheric pressure until no further absorption took place. The solvent was removed under diminished pressure from the filtered solution, which had an intense blue fluorescence, leaving the pale yellow *amine* (4·4 g., quantitative). After distillation (b. p. 210—211°/0·3 mm.), it formed a glass which crystallised in needles from dilute alcohol. When the reduction was carried out on a 50-g. scale in alcohol (300 c.c.) with Raney nickel (*ca.* 5 g.) at 60—70°/10 atm. the reaction was complete in 2 hr. The *acetyl* (V) and *benzoyl* (VI) *derivatives* were obtained as colourless needles from alcohol.

The amine (IV) was also prepared in quantitative yield as follows: The nitro-compound (III) was dissolved in concentrated hydrochloric acid (25 c.c.) and added to stannous chloride dihydrate (13 g.) in concentrated hydrochloric acid (25 c.c.). The mixture was heated on the water-bath for 2 hr. with occasional shaking, most of the solvent was then removed, and the amine liberated by addition of an excess of 40% sodium hydroxide.

5-p-*Chlorophenyl*-2-*methyl*-4-*phenyloxazole* (VII).—The amine (IV) was dissolved in concentrated hydrochloric acid (15 c.c.) and water (10 c.c.) and cooled. Aqueous sodium nitrite (1·5 g. in 7·5 c.c.) was slowly added through a capillary below the surface of the stirred solution which was kept at 0—5°, until a positive test was obtained with starch–iodide paper; the slight excess of nitrous acid was decomposed by sulphamic acid. The cold diazonium solution was then added with stirring to an ice-cold solution of cuprous chloride (4 g.) in concentrated hydrochloric acid (15 c.c.); the mixture was left at room temperature for 30 min., then heated to the b. p. during 30 min., next cooled and diluted with water; the solid *product* (3·1 g., 58%) crystallised from dilute alcohol as needles.

5-p-*Hydroxyphenyl*-2-*methyl*-4-*phenyloxazole* (VIII).—A diazonium solution, prepared as above but in concentrated sulphuric acid (5 c.c.) and water (15 c.c.), was slowly added to boiling 2N-sulphuric acid (150 c.c.). Then charcoal was added and boiling continued for 5 min.; the solution was filtered, diluted with water, and made alkaline with aqueous ammonia. The *phenol* (3·1 g., 62%) crystallised from dilute alcohol in needles.

5-p-*Cyanophenyl*-2-*methyl*-4-*phenyloxazole* (IX).—The diazonium chloride solution (as above) was neutralised with solid sodium hydrogen carbonate at 0—5°, then added to an ice-cold solution of cuprous cyanide (9 g.) and potassium cyanide (16 g.) in water (60 c.c.), kept at 0°, and stirred for 2 hr., after which it was allowed to reach room-temperature and stirring was continued for a further 2 hr.; warming the solution caused separation of tar. A solid which separated was extracted with boiling 25% aqueous alcohol (150 c.c.) and the extract refluxed with charcoal. The *nitrile* which separated (2·3 g., 22%) crystallised from dilute alcohol in pale brown plates.

5-p-*Carboxyphenyl*-2-*methyl*-4-*phenyloxazole* (X).—The nitrile (IX) (1 g.) was refluxed for 6 hr. with concentrated sulphuric acid (5 c.c.), acetic acid (5 c.c.), and water (5 c.c.). On dilution with water, the *carboxylic acid* (0·9 g., 84%) separated; it formed needles from alcohol and gave a *methyl ester* (XI) as plates (from alcohol).

5-p-*Aminophenyl*-2-*methyl*-4-p-*sulphamoylphenyloxazole* (XV).—The corresponding acetyl derivative (see Table 2), prepared from compound (V) and chlorosulphonic acid, in the usual way, was refluxed for 1 hr. with alcohol (50 c.c.) and concentrated hydrochloric acid (25 c.c.); most of the solvent was removed under diminished pressure and the *amine* was precipitated with concentrated aqueous ammonia; it formed pale yellow needles (4·4 g., 99%) from dilute alcohol. The same compound was prepared in quantitative yield by hydrogenating compound (XIV) (10 g.) with Raney nickel (*ca.* 2 g.) in alcohol (150 c.c.) at 60—70°/10 atm.

2-*Methyl*-5-*phenyl*-4-p-*sulphamoylphenyloxazole* (XVII).—The amine (XV) was diazotised as above in concentrated hydrochloric acid and water (15 c.c. each) by sodium nitrite (1·3 g.) in water (7·5 c.c.). 50% Hypophosphorous acid (50 c.c.) was added and the mixture was kept overnight at 0—5° and then at room temperature for 4 hr. This gave the *product* (4 g., 84%) which formed pale brown crystals from dilute alcohol.

4,5-*Di*-p-*aminophenyl*-2-*methyloxazole* (XVIII).—The compound (II) was hydrogenated as above but at 40—50°, giving a quantitative yield of the diamine, which formed colourless needles from dilute alcohol and gave a *diacetyl* (XIX) and *dibenzoyl* (XX) *derivative* (needles and plates, respectively, from dilute alcohol).

The diamine was also prepared in quantitative yield as follows: The dinitro-oxazole (II) was added to a solution of stannous chloride dihydrate (31 g.) in concentrated hydrochloric acid (230 c.c.) and refluxed until a clear solution was obtained. Most of the solvent was removed under diminished pressure and the base then liberated with an excess of 40% sodium hydroxide, when it separated as a voluminous, gelatinous precipitate; it was obtained from aqueous methanol in pale brown, dendritic crystals.

4,5-*Di*-p-*carbamoylphenyl*-2-*methyloxazole* (XXIII).—The nitrile (see Table 2) was heated with polyphosphoric acid (60 g.) for 1·5 hr. at 110—120°, then the solution was diluted with water and neutralised with concentrated aqueous ammonia. The *diamide*, obtained in quantitative yield, formed pale brown crystals from dilute alcohol.

5-p-*Aminophenyl*-2-*methyl*-4-p-*nitrophenyloxazole* (XXIV).—The dinitro-compound (II) (10 g.) and methanol (150 c.c.) were heated under reflux and a solution of sodium sulphide ($Na_2S,9H_2O$; 18 g.) and sodium hydrogen carbonate (6 g.) in water (45 c.c.) was added during 1 hr. The mixture was refluxed for a further hr., then filtered, most of the solvent was removed under diminished pressure, and water was added; the *monoamine* formed orange-red needles from dilute alcohol (yield, 6·1 g., 55%). The *acetyl derivative* (XXV) formed pale yellow needles

from dilute alcohol, and the *dichloroacetyl derivative* (XXVI) cream-coloured prisms from alcohol.

2-*Methyl*-4-p-*nitrophenyl*-5-*phenyloxazole* (XXVII).—The amine (XXIV) was deaminated to compound (XXVII), the isomer of (III); this formed yellow needles (2·5 g., 53%) from dilute alcohol. It formed the dinitro-compound (II) in 95% yield with fuming nitric acid.

Details of substances described above will be found in Table 1; the *compounds* listed in Table 2 were prepared analogously.

4,5-*Di*-p-*nitrophenyloxazole*.—4,5-Diphenyloxazole was added in portions to cold fuming nitric acid (25 c.c.), and after 15 min. at 0—5° the mixture was poured on ice. The *dinitro-derivative* (6 g., 83%) was formed; it separated as yellow needles, m. p. 222—223°, from pyridine (Found: N, 13·7. $C_{15}H_9N_3O_5$ requires N, 13·5%). The mother-liquor was concentrated under diminished pressure and then diluted with water, giving a sticky solid. Repeated crystallisation from alcohol gave 5-p-*nitrophenyl*-4-*phenyloxazole* (0·3 g., 5%), yellow crystals (from alcohol), m. p. 128—129° (Found: N, 10·4. $C_{15}H_{10}N_2O_3$ requires N, 10·5%). This nitration was repeated at —10°, then giving the mononitro-derivative (3 g., 50%).

4,5-*Di*-p-*sulphamoylphenyloxazole*.—4,5-Diphenyloxazole, by a reaction analogous to that above, gave a crude *disulphonamide* (3·9 g., 45%), that formed pale brown crystals, m. p. 156—158°, from dilute alcohol (Found: N, 10·95. $C_{15}H_{13}N_3O_5S_2$ requires N, 11·1%).

Nitration of 2,4,5-*Triphenyloxazole*.—This reaction had been investigated by Henius [11] and by Tröger and Philippson; [11] the former obtained two impure, uncharacterised products; the latter obtained a mono- (m. p. 194°) and a trinitro-derivative (m. p. 294°); by degradative oxidation they showed that the latter was 2,4,5-tri-*p*-nitrophenyloxazole, but they did not assign a structure to the former. These results have been confirmed and, in addition, we have shown that the mono-derivative is 5-*p*-nitrophenyl-2,4-diphenyloxazole; further, 4,5-di-*p*-nitrophenyl-2-phenyloxazole has been isolated. The nitration was carried out as for the 2-methyl-4,5-diphenyl analogue (first method) except that the ice-cold solution was poured into water 15 min. after addition of the base to the acid. The resulting yellow solid was extracted with boiling alcohol (100 c.c.), and the extract concentrated under diminished pressure; the residue, crystallised twice from alcohol, formed crystals (0·4 g., 7%), m. p. 191—192°, identical with the compound synthesised in 89% yield from 4′-nitrobenzoin benzoate (5 g.), urea (10 g.), and acetic acid (50 c.c.). The residue from the alcohol extraction was twice crystallised from pyridine, to give yellow 4,5-*di*-p-*nitrophenyl*-2-*phenyloxazole* (3 g.), m. p. 280° (Found: N, 10·6. $C_{21}H_{13}N_3O_5$ requires N, 10·9%). This compound was dissolved in fuming nitric acid (20 c.c.), left overnight, and poured into water; the trinitro-derivative separated, and had m. p. 306—308° after crystallisation from pyridine.

Also, 2-p-*nitrophenyl*-4,5-*diphenyloxazole* was synthesised from benzoin *p*-nitrobenzoate, urea (10 g.) and acetic acid (75 c.c.), as above, the mixture being heated for 3 hr.; it formed yellow needles (4 g., 85%), m. p. 141—142°, from alcohol (Found: N, 8·2. $C_{21}H_{14}N_2O_3$ requires N, 8·2%). Nitration of this compound gave the trinitro-derivative in 95% yield.

2-*Methyl*-4,5-*di*-p-*nitrophenylimidazole*.—2-Methyl-4,5-diphenylimidazole was nitrated as usual, giving the yellow *dinitro-compound* (4·5 g., 65%) that, crystallised from dilute alcohol, had m. p. 232—233°. When crystallised from alcohol it had m. p. 173—174° (decomp.); but on admixture of this material with the product from dilute alcohol the m. p. was 232—233° (Found: N, 17·0. $C_{16}H_{12}N_4O_4$ requires N, 17·3%). If the nitration mixture was warmed on the water-bath for 30 min. after mixing, 4,4′-dinitrobenzil (3·5 g., 55%) was obtained.

2-*Methyl*-4-p-*nitrophenyl*-5-*phenylimidazole*.—This *compound* was formed as a by-product in the preparation of the oxazole (III) and was isolated (0·6 g.) from the alcoholic mother-liquors from its crystallisation. It formed yellow crystals, m. p. 214—215°, from dilute alcohol (Found: N, 14·8. $C_{16}H_{13}N_3O_2$ requires N, 15·1%). On nitration as usual, it formed the dinitro-compound described.

4,5-*Di*-p-*nitrophenylimidazole*.—4,5-Diphenylimidazole was nitrated as usual. The *product* formed yellow needles, m. p. 181° (decomp.) (4·5 g., 64%), from acetic acid (Found: N, 18·3. $C_{15}H_{10}O_4N_4$ requires N, 18·1%). As in the case of the 2-methyl homologue, the parent base was oxidised to 4,4′-dinitrobenzil in 66% yield when heated on the water-bath with fuming nitric acid.

4,5-*Di*-p-*aminophenylimidazole*.—The preceding dinitro-compound was reduced catalytically

[11] Henius, *Annalen*, 1885, **228**, 339; Tröger and Philippson, *J. prakt. Chem.*, 1925, **110**, 65.

at 40—45°; colourless needles (from dilute alcohol), m. p. 284—285°, of the *diamine* were obtained in quantitative yield (Found: N, 22·15. $C_{15}H_{14}N_4$ requires N, 22·4%). Warming the amine (1 g.) for 30 min. on the water-bath with acetic anhydride (10 c.c.) gave 4,5-*di*-p-*acetamidophenyl*-1-*acetylimidazole* (0·7 g., 46%), m. p. 194—195° (Found: N, 14·4. $C_{21}H_{20}N_4O_3$ requires N, 14·9%). When the acidic mother-liquor was made alkaline with aqueous ammonia 4,5-*di*-p-*acetamidophenylimidazole* was obtained (0·8 g., 47%), colourless needles (from alcohol), m. p. 344—345° (Found: N, 16·2. $C_{19}H_{18}N_4O_2$ requires N, 16·8%).

4,5-*Di*-p-*sulphamoylphenylimidazole*.—4,5-Diphenylimidazole gave, as above, the *disulphonamide* (7·8 g., 94%), m. p. 307—308° (from alcohol) (Found: N, 14·7. $C_{15}H_{14}N_4O_4S_2$ requires N, 14·8%).

Nitration of 2,4,5-*Triphenylimidazole*.—The 2- and 4-*p*-nitrophenyl derivatives of this base were synthesised by Cook and Jones; [12] 2-*phenyl*-4,5-*di*-p-*nitrophenylimidazole*, similarly prepared (95%) by us from 4,4′-dinitrobenzil and benzaldehyde, formed orange-red crystals (from dilute pyridine), m. p. 342—345° (Found: N, 14·4. $C_{21}H_{14}N_4O_4$ requires N, 14·5%). Nitration of the parent base as usual gave orange-yellow 2,4,5-*tri*-p-*nitrophenylimidazole* (6·0 g., 72%), m. p. 331—334° (from dilute pyridine) (Found: N, 16·3. $C_{21}H_{13}N_5O_6$ requires N, 16·2%). This nitration was studied by Tröger and Thomas [13] who obtained a product, m. p. 147°, for which they reported analytical values in agreement with those of a trinitro-derivative, but repetition of their procedure gave only 4,4′-dinitrobenzil (1·8 g.), m. p. 211—212°. Our trinitro-compound was also obtained by nitration of 2-*p*-nitrophenyl-4,5-diphenylimidazole as usual and by the method of Cook and Jones from 4,4′-dinitrobenzil and *p*-nitrobenzaldehyde (90% yield).

4,5-*Di*-p-*sulphamoylphenyl*-2-*imidazolone*.—4,5-Diphenyl-2-imidazolone, treated as above, gave the pale-yellow *disulphonamide*, m. p. 297—298° (decomp.) from acetic acid (Found: N, 14·0. $C_{15}H_{14}N_4O_5S_2$ requires N, 14·2%).

Reaction of the parent base with nitric acid was investigated by Biltz [14] and by Chattaway and Coulson,[15] and the latter used this reaction for preparing 4,4′-dinitrobenzil, which, however, they obtained only in 20% yield.

4,5-*Di*-p-*sulphamoylophenyloxazolone*.—This *sulphonamide*, obtained as above, was precipitated from alkaline solution by acid as a powder, m. p. 320—321° (decomp.) (7·0 g., 83%) (Found: N, 10·8. $C_{15}H_{13}N_3O_6S_2$ requires N, 10·6%). Reaction of the parent base with nitric acid gave an oil which was not investigated.

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[12] Cook and Jones, *J.*, 1941, 278.
[13] Tröger and Thomas, *J. prakt. Chem.*, 1925, **110**, 48.
[14] Biltz, *Annalen*, 1909, **368**, 156; *Ber.*, 1908, **41**, 1754, 1761.
[15] Chattaway and Coulson, *J.*, 1928, 1361.