1,3,5-Triazines. Part XII.[1] The Reaction of Trichloro-1,3,5-triazine (Cyanuric Chloride) with *N*-Phenyl-pyrrole, -indole, -carbazole, and -diphenylamine, and *N*-Ethyl-pyrrole, -carbazole, and -diphenylamine

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The reactions of trichloro-1,3,5-triazine (cyanuric chloride) with *N*-phenyl-pyrrole, -indole, and -carbazole, with *N*-ethyl-pyrrole, and -carbazole, and, for comparison purposes, with ethyldiphenylamine and triphenylamine have been investigated. The reaction with *N*-substituted pyrrole and indole yields products substituted at the 2- and 3-position respectively of the five-membered ring. *N*-Ethylcarbazole gives a ' carbon ' product substituted at the 3-position and a ' nitrogen -substituted product whilst *N*-phenylcarbazole gives two ' carbon ' derivatives substituted on the benzo and phenyl nucleus respectively. Ethyldiphenylamine gives a ' *para*-carbon '-substituted and a ' nitrogen '-substituted derivative whilst triphenylamine yields a single ' *para*-carbon '-substituted derivative.

In an earlier paper[2] we described the reactions of trichloro-1,3,5-triazine (cyanuric chloride) with a series of dialkylanilines to form, depending on steric and polar effects and the solvent media, various proportions of ' nitrogen- ' and/or ' *para*-carbon- 'substituted anilinotriazine derivatives. An extension of this work using dialkylnaphthylamines[1] showed that if the aromatic nucleus is sufficiently activated towards electrophilic attack then reaction can be forced to take place at positions other than at the carbon atom *para* to the amino-group *e.g.* with *NN*-diethyl-2-naphthylamine at the 1-position.

Our systematic study of the reactions of cyanuric chloride with tertiary arylamine derivatives has now been extended to cases where the nitrogen atom forms part of a five-membered, aromatic heterocyclic ring, *viz.* pyrrole, indole, and carbazole. *N*-Phenyl derivatives of all three, together with the *N*-ethyl derivatives of the first and of the last, were investigated. The products from these reactions again show interesting departures from the previously established pattern of substitution by cyanuric chloride, but similar to that anticipated for electrophilic attack on the species involved.[3] As the above can be considered as alkyldiaryl- and triarylamines, we have included for comparative purposes the reactions of cyanuric chloride with ethyldiphenylamine and triphenylamine.

These compounds form a series and an interesting graduation of properties is observed. The reactions fall however, into two groups. The first, the reactions of cyanuric chloride with *N*-substituted pyrroles and indoles are essentially complete within a few hours and are performed at atmospheric pressure. The second group, those involving carbazoles and di- and tri-phenylamines, is very much less reactive; these compounds require very prolonged reaction times, of the order of weeks, and/or elevated temperatures (sealed tubes). Even under these forcing conditions yields are very low (2—5%).

Over the past decade the ambident character of pyrroles,[4] indoles,[5] and carbazoles[6] has been recognised and they have been the subject of detailed studies. Papadopolous and his co-workers[7] have shown that metallic salts of pyrroles, when treated with alkyl or benzyl halides, react at the 1- and 2-positions to give alkylated products; under specified conditions dialkylated products were also obtained. A mechanism was proposed for the formation of the alternative products.[7] These reactions were shown to be influenced by similar

TABLE 1

The reactions of cyanuric chloride with *N*-phenyl-pyrrole, -indole, -carbazole, and -diphenylamine, with *N*-ethyl-pyrrole, -carbazole, and -diphenylamine, and with diethylaniline

Amine	Reaction conditions	Extent of reaction (%)	Composition of products (%)	
			C-Substituted	*N*-Substituted
N-Ethyldiphenylamine	*a*	4	60	40
N-Ethylcarbazole	*a*	2	52	48
Triphenylamine	*b*	5	100	
N-Phenylcarbazole	*b*	3	100 *	
N-Phenylpyrrole	*c*	85	100	
N-Phenylindole	*c*	70	100	
N-Ethylpyrrole	*c*	100 †		
NN-Diethylaniline	*c*	30	30	70

[a] 90° for 14 days. [b] 200° for 7 days in sealed tube. [c] 80° for 4 h.

* Two ' carbon-substituted ' derivatives obtained (see text). † Large number of products observed.

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[1] Part XI, R. A. Shaw and P. Ward, *J. Chem. Soc.* (*B*), 1969, 596.

[2] R. A. Shaw and P. Ward, *J. Chem. Soc.*, 1965, 5446.

[3] R. D. Brown and B. A. W. Coller, *Austral. J. Chem.*, 1959, **12**, 152.

[4] E. P. Papadopoulos and K. I. Y. Tabello, *J. Org. Chem.*, 1968, **33**, 1299.

[5] B. Cardillo, G. Casnati, A. Pochini, and A. Ricca, *Tetrahedron*, 1967, **23**, 3771.

[6] P. B. D. de la Mare, O. M. H. el Dusouqui, and H. E. Johnson, *J. Chem. Soc.* (*B*), 1966, 521.

[7] C. F. Hobbs, C. K. McMillin, E. P. Papadopoulos, and C. A. Vander Neuf, *J. Amer. Chem. Soc.*, 1962, **84**, 43; E. P. Papadopoulos and H. S. Habiby, *J. Org. Chem.*, 1966, **31**, 327; E. P. Papadopoulos, *ibid.*, p. 3060; E. P. Papadopoulos and N. F. Haidar, *Tetrahedron Letters*, 1968, 1721.

changes in the character of the metallic group, solvent media, *etc.* as has been exhaustively proved for ambident ions in general.

N-Phenyl-pyrrole and -indole react considerably faster than our standard of comparison, *NN*-diethylaniline. The triazine-containing products from both reactions consist to the limit of our analytical technique (*ca.* 1%), exclusively in each case, of one orange-yellow crystalline compound. The colour indicated ' carbon substitution.' As described below, this was shown to have taken place at the 2-position of the pyrrole, and at the 3-position of the indole and not in the benzo-ring of indole or in the phenyl ring of either species. This finding is reasonable since, for pyrrole, high electron-density occurs at C-2 and -5.[8] For indole the influence of the lone pair is more effective when the canonical structure is benzenoid (3-substitution) than when it is perturbed (2-substitution), an effect also displayed in the activation of the α-position of naphthalene.[9]

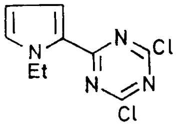
The reaction with *N*-ethylpyrrole was extremely exothermic and a complex reaction mixture containing numerous components resulted. The major component which could be isolated and purified by recrystallisation from the crude product was shown to be a ' carbon-substituted ' 2-derivative.

Because of the conjugation of the lone pair of electrons with the five-membered ring, the 3-position of carbazole (*para* to the nitrogen atom) would be expected to be activated.[3] For the reaction with *N*-ethylcarbazole this is shown to be the case and approximately equal amounts of ' carbon- ' and ' nitrogen- 'substituted compounds result. However a slightly greater proportion of ' carbon ' substitution occurred with ethyldiphenylamine. This result is analogous to those obtained by Dewar who showed that diphenylamine is mononitrated eight times faster than is carbazole.[10] With *N*-phenylcarbazole the greater proportion of substitution occurs at the *para*-carbon atom of the phenyl group, and here again triphenylamine is shown to react somewhat faster.

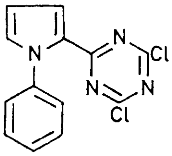
The rates of reaction of the two *N*-substituted carbazoles, and of ethyldiphenyl- and triphenyl-amines are drastically reduced, both at the ' nitrogen ' and at the ' carbon ' positions compared to the rate of the reaction between cyanuric chloride and *NN*-diethylaniline. Likely causes for this reduction in rate of ' nitrogen substitution ' are increased steric hindrance at the nitrogen atom together with the much reduced availability of the lone pair of electrons on this atom due to the partial or complete replacement of the inductively donating alkyl groups by electron-withdrawing aryl residues. The decrease in the rate of ' carbon-substitution ' is probably due to the reduced average electron density at any one *para*-position.

Determination of the Structure of the Products.—(a) ' *Nitrogen-substituted* ' *derivatives* [*compounds* (7) *and* (9)]. The evidence here rests on elemental analysis and the i.r. spectra of the compounds as described in earlier papers, *e.g.*, ref. 11.

(b) ' *Carbon-substituted* ' *derivatives.* For the ethyldiphenylamine (8) and triphenylamine derivatives (10) the evidence relies upon elemental analysis, and the i.r., u.v., and ^{1}H n.m.r. spectra of the compounds. The last technique gives spectra for both compounds (8) and (10) showing the characteristic AA'BB' four-line pattern of a 1,4-disubstituted benzene derivative, the two pairs of doublets being on either side of a complex absorption band due to the aromatic protons of the unsubstituted phenyl ring or rings. In the region of the i.r. spectrum (650—1000 cm^{-1}), where the substitution pattern of benzene gives rise to characteristic absorption, these compounds exhibit bands due to the unsubstituted



(1)



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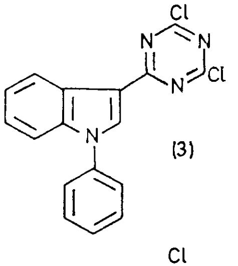

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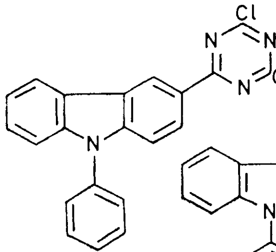

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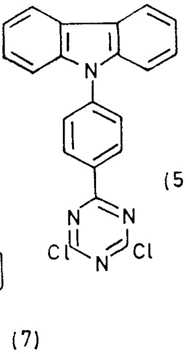

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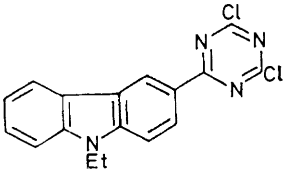

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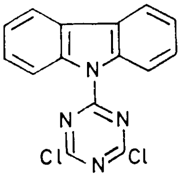

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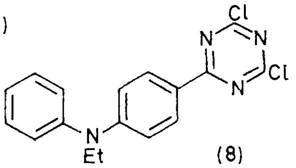

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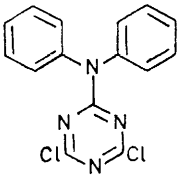

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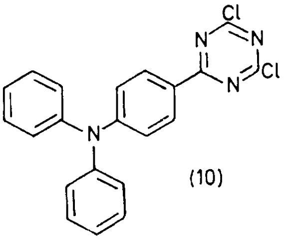

(10)

TABLE 2

Aromatic ^{1}H n.m.r. spectra of 1,4-disubstituted benzene derivatives

Compound	τ_A	τ_B	J_{AB}/Hz
$N_3C_3Cl_2C_6H_4NEt_2$	1·65	3·40	9·0
$N_3C_3Cl_2C_6H_4NEtPh$ (8)	1·70	2·90	9·0
$N_3C_3Cl_2C_6H_4NPh_2$ (10)	1·70	2·95	9·1

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[8] L. F. Fieser and M. Fieser, in ' Organic Chemistry,' Reinhold, New York, 1956, 3rd edn., p. 801.

[9] Ref. 8, p. 803.

[10] M. J. S. Dewar and D. S. Urch, *J. Chem. Soc.*, 1958, 3079.

[11] R. A. Shaw and P. Ward, *J. Chem. Soc.* (*B*), 1967, 123.

phenyl group (695 and 750 cm^{-1}) and bands in similar positions to those in 4-dichlorotriazinyl-*NN*-diethylaniline (720 and 830 cm^{-1}). In addition, there are bands associated with the triazine ring at 800 cm^{-1} and the complex carbon–chlorine band at 840 cm^{-1}. This suggests that the triazine residue has entered one of the phenyl rings *para* to the amino-group. The u.v. spectra exhibit long wavelength absorption at positions similar to that in the diethylaniline derivative, but the extinction coefficients are considerably reduced in intensity, indicative that the ethylphenyl- or diphenyl-substituents on the nitrogen atom are sterically hindering mesomerism.

TABLE 3

U.v. spectra of ' carbon-substituted ' derivatives

Compound	$\lambda_{max.}$/nm	$10^{-3}\varepsilon_{max.}$	$\lambda_{max.}$/nm	$10^{-3}\varepsilon_{max.}$	$\lambda_{max.}$/nm	$10^{-3}\varepsilon_{max.}$
$N_3C_3Cl_2C_6H_4NEt_2$	237	8·7	263	3·5	403	51·5
$N_3C_3Cl_2C_6H_4NEtPh$ (8)	263	2·1	291	2·2	398	12·6
$N_3C_3Cl_2C_6H_4NPh_2$ (10)	265	2·4	290	2·3	408	11·7
$N_3C_3Cl_2(C_4H_3NPh)$ (2)	225	6·75			340	26·6
$N_3C_3Cl_2(C_8H_5NPh)$ (3)	244	6·5	259	4·25	374	9·3
$N_3C_3Cl_2(C_4H_3NEt)$ (1)	235	5·8			347	23·7
$N_3C_3Cl_2(C_6H_4NC_{12}H_8)$ (5)	240	4·3	281	2·1	364	17·3
$N_3C_3Cl_2(C_{12}H_7NEt)$ (6)	244	3·9	276	2·5	379	16·1

TABLE 4

Analyses of triazine derivatives

		Requires (%)					Found (%)			
Compound	M.p. (°C)	C	H	Cl	N	Formula	C	H	Cl	N
$N_3C_3Cl_2(C_4H_3NPh)$ (2)	164—164·5	53·6	2·8	24·4	19·25	$C_{13}H_8Cl_2N_4$	53·7	2·8	24·5	19·1
$N_3C_3Cl_2(C_8H_5NPh)$ (3)	203—205	59·8	2·95	20·8	16·4	$C_{17}H_{10}Cl_2N_4$	59·7	3·0		16·3
$N_3C_3Cl_2(C_{12}H_7NPh)$ (4)	226—227	64·5	3·1	18·1	14·3	$C_{21}H_{12}Cl_2N_4$	64·6	3·3		
$N_3C_3Cl_2(C_6H_4NC_{12}H_8)$ (5)	235—237	64·5	3·1	18·1	14·3	$C_{21}H_{12}Cl_2N_4$	64·8	3·3		
$N_3C_3Cl_2(C_{12}H_7NEt)$ (6)	257—259	59·5	3·5	20·7	16·3	$C_{17}H_{12}Cl_2N_4$	59·9	3·8		
$N_3C_3Cl_2(NC_{12}H_8)$ (7)	195—196	57·2	2·6	22·5	17·8	$C_{15}H_8Cl_2N_4$	57·0	3·1		
$N_3C_3Cl_2(C_6H_4NEtPh)$ (8)	165—166	59·1	4·1	20·5	16·2	$C_{17}H_{14}Cl_2N_4$	58·8	4·2	20·0	15·9
$N_3C_3Cl_2(NPh_2)$ (9)	171—172	56·8	3·2	22·3	17·6	$C_{15}H_{10}Cl_2N_4$	57·0	3·5	21·8	17·6
$N_3C_3Cl_2(C_6H_4NPh_2)$ (10)	228—229	64·1	3·6	18·0	14·3	$C_{21}H_{14}Cl_2N_4$	63·9	3·6	18·3	14·3
$N_3C_3Cl_2(C_4H_3NEt)$ (1) [a]	124—125									

[a] Found: M^+ (mass spectrum), 242·0124. $C_9H_8N_4{}^{35}Cl_2$ requires 242·0126.

The characteristic four-line pattern is absent from the ^{1}H n.m.r. spectra of the *N*-phenylindole and *N*-phenylpyrrole derivatives, indicating that substitution has not taken place in the phenyl group.

Two ' carbon-substituted ' derivatives (4) and (5) were isolated from the reaction of *N*-phenylcarbazole with cyanuric chloride. By comparison of their i.r. spectra with those of the starting material, the ' carbon-substituted ' derivative from the *N*-ethylcarbazole reaction (6) and the ' carbon-substituted ' diethylaniline derivative it was shown that one was substituted in the phenyl group (90%) and the other in the carbazole ring (10%). Several authors have shown that two peaks at 760 and 725 cm^{-1} are characteristic of the four adjacent hydrogen atoms in a benzo-ring. We have found that in the major compound these absorptions are very strong whereas in the minor they are overshadowed by two peaks at 750 and 695 cm^{-1} due to an unsubstituted phenyl group, these peaks being absent in the spectrum of the former compound. The spectrum of the minor product resembles that of the ' carbon-substituted ' derivative (6) from the *N*-ethylcarbazole reaction.

The characteristic benzo and phenyl absorption bands are also present in the i.r. spectrum of the indole compound (3) indicating that substitution has taken place in the heterocyclic ring. The characteristic four-line pattern noted for compounds (8) and (10) is absent from the ^{1}H n.m.r. spectra of the *N*-phenylindole (3) and *N*-phenylpyrrole derivatives (1), whilst the phenyl signals are unchanged indicating that substitution has not taken place in the phenyl group.

For compounds (1)—(3) their ^{1}H n.m.r. spectra may be compared with the standard spectra published in the Sadtler collection and are unquestionably closely similar to a pyrrole substituted in the 2-position with an electron-withdrawing substituent, and an indole with a similar substituent in the 3-position.[12]

Perhaps the most conclusive evidence for the position of substitution of the pyrrole derivatives (1) and (2) comes from their u.v. spectra. Considerable information [13] is available concerning the effect of substituents on pyrroles. It is known that derivatives with alkyl groups on the nitrogen atom give spectra similar to that of the parent compound. However, electron-withdrawing groups, such as carboxy, on the heterocyclic ring produce a new absorption band in the region 250—330 nm. These derivatives have been extensively studied and an empirical rule states that when substitution is in the 2-position the extinction coefficient has a value >10,000 whereas 3-substitution gives rise to a band with an extinction coefficient of *ca.* 5000 or less. The triazine ring being an electron-withdrawing substituent,[11] the extinction coefficients observed suggests

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[12] Sadtler N.M.R. Spectra Catalogue, Heyden, Nos. 174, 9665.

[13] S. F. Mason, in ' Physical Methods in Heterocyclic Chemistry,' ed. A. R. Katritzky, Academic Press, London, 1963, vol. 2, p. 59.

that the pyrrole ring may well be substituted in the 2-position.

The reactions of cyanuric chloride with the tertiary arylamines described in this paper again highlight the selectivity of this electrophile.[11]

EXPERIMENTAL

The general experimental technique for the reaction of cyanuric chloride with *N*-ethylpyrrole and *N*-phenylpyrrole and -indole is similar to that described [11] for *NN*-diethylaniline; that for *N*-ethylcarbazole and ethyldiphenylamine was similar, but heating was continued under these conditions for 14 days. The reactions with *N*-phenylcarbazole and triphenylamine were carried out as follows. Cyanuric chloride (0·01 mol) and the tertiary amine (0·02 mol) were placed in a thick-walled tube which was sealed and suspended in stirred oil-bath maintained at 250° for 7 days. In all experiments the work-up procedure was carried out as described previously,[11] and separation effected by column chromatography using silica gel.

Spectra.—I.r. spectra (KBr discs) were measured using an SP 100 recording spectrophotometer operating as a double beam instrument. ^{1}H N.m.r. spectra were obtained for *ca.* 20% w/v solutions in deuteriochloroform with a Varian A60 spectrophotometer equipped with a 60 MHz radio frequency source; tetramethylsilane was used as internal standard. U.v. spectra were determined with a Unicam SP 700 recording spectrophotometer in the region 200—833 nm; analytically pure samples dissolved in ethanol (96%) were contained in 1 cm matched cells, and Beer's law was obeyed in all the cases tested.

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