1,3-Cycloadditions of 3,5-Dichloro-2,4,6-trimethylbenzonitrile Oxide to 1,1-Diphenylallene

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The reaction of 3,5-dichloro-2,4,6-trimethylbenzonitrile oxide with excess of 1,1-diphenylallene in various solvents gives two isomeric monoadducts. Further reaction of one of these with the nitrile oxide gives a diadduct. Products were identified by spectroscopic properties and chemical behaviour. Kinetics were measured in CCl_4, in EtOH, and in mixtures of the two solvents, in the temperature range 40—70 °C. The solvent effect on the rates is small; activation entropies are in the range -34 to -22 cal mol^{-1} K^{-1}. A concerted mechanism of 1,3-cycloaddition is favoured for the three reactions.

ALLENES are interesting, among olefinic dipolarophiles, since they present two positions of attack. Spirobiisoxazolines were obtained by reaction of benzonitrile oxide with CH_2=C=CHR (R = H, Me, or Ph),[1] and of acetonitrile oxide with allene.[2] Both mono- and diadducts were isolated by other authors, who studied the 1,3-cycloaddition of benzonitrile and *p*-chlorobenzonitrile oxides to allenes substituted by electron-withdrawing and electron-donating groups.[3,4]

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[1] G. Stagno d'Alcontres and G. Lo Vecchio, *Gazzetta*, 1960, **90**, 1239.

[2] G. Stagno d'Alcontres, M. Gattuso, G. Lo Vecchio, M. Crisafulli, and M. C. Aversa, *Gazzetta*, 1968, **98**, 203.

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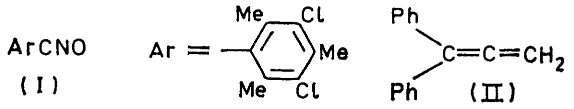
It seems advisable to use a nitrile oxide and a substituted allene of moderate reactivity if one wishes to study separately mono- and di-additions, and perform kinetic measurements. 3,5-Dichloro-2,4,6-trimethylbenzonitrile oxide (I) and 1,1-diphenylallene (II) were found suitable for such a study.



RESULTS

The 1,3-cycloaddition of nitrile oxide (I) to excess of 1,1-diphenylallene gave two products, identified as (III) and (IV). Spectroscopic properties are given in Tables 1 and 2 [mass spectral data are listed in Supplementary Publication No. SUP 20486 (2 pp.)*], while chemical behaviour is summarised in Scheme 1. Both products present the molecular peak in the mass spectrum at *m/e* 421, and ($M + 2$), ($M + 4$) peaks of the correct intensity. Hydrolytic cleavage of (III) gave the oxime (V). Its structure was deduced from its mass spectrum (molecular peak at *m/e* 439, two chlorine atoms present), i.r. spectrum (stretching of O–H, C=O, and C=N bonds, in agreement with data for similar molecules),[5] and a positive iodoform test for an acetyl group.

TABLE 1

N.m.r. spectra in $CDCl_3$ (τ values)

Compound	Ph	$>$CH	$>$CH	$=CH_2$	$>CH_2$	HO	Me in Ar	MeCO
(III)	2·62 (s)			4·78s [a]			7·44 (s, 3H) 7·83 (s, 6H)	
(IV)	2·74 (m, 5H) 3·16 (m, 5H)				4·59s [b]		7·66 (s, 3H) 7·80 (s, 6H)	
(V)	2·26—2·68 (m)					*c*	7·52 (s, 3H) 7·87 (s, 6H)	7·90 (s)
(VI)	2·62—3·08 (m)	1·82 (d) (*J* 1 Hz)	5·27 (d) (*J* 1 Hz)				7·47 (s, 3H) 8·10 (s, 6H)	
(VII)	2·20—2·75 (m)				6·41, 7·23 [d]		7·43 (s, 3H) 7·52 (s, 3H) 7·56 (s, 3H) 7·97 (s, 3H) 8·16 (s, 6H)	
(VIII)	2·63 (s)	4·03 (s)				6·74 [e]	7·44 (s, 3H) 7·82 (s, 6H)	

[a] AB system in $CD_3\cdot CO\cdot CD_3$: τ 4·59, 4·66; *J* 1·5 Hz. [b] In $CD_3\cdot CO\cdot CD_3$: τ 4·55s; in $CD_3\cdot SO\cdot CD_3$: τ 4·54s. [c] Signal not observed; for a similar case, see ref. 33. [d] AB system; *J* 19·5 Hz. [e] Broad singlet; H exchangeable with D_2O.

TABLE 2

U.v. spectra in n-hexane. Values of $\lambda_{max.}$/nm (ε in parentheses)

(III)	(IV)	(V)	(VI)	(VII)	(VIII)
268 (8700)	230 (21,200)	240sh (19,400)	*a*	279 (1150)	225sh (28,700)
	309 (13,700)			287 (1050)	257 (890)

[a] Six peaks in the region 254—286 nm (ε 420—600).

Isoxazoline (IV) rearranges to isoxazole (VI). The formula of the latter is in agreement with the molecular weight (from mass spectrum) and n.m.r. spectrum (Table 1). The position of the isoxazole proton is unequivocal, since reported τ values [3,6-9] for 5-H of variously substituted isoxazoles are in the range 0·8—2·0, while 4-H gives signals [3,6,7,10-12] of the order of τ 3—4. Among the compounds studied by n.m.r. spectroscopy, the most similar to the isomer of (VI) with inverted 4- and 5-substituents is 5-benzyl-3-phenylisoxazole,[12b] where the peak for 4-H is at τ 3·83.

Catalytic hydrogenation of (III) was incomplete. The n.m.r. spectrum of the product mixture shows the probable presence of a $CH-CH_3$ grouping.

Examination of the n.m.r. spectra of adducts (III) and (IV) confirms the structure assignment. The value τ 4·59 for 5-H_2 of (IV) is very low when compared with reported values for the corresponding protons of 3-aryl-2-isoxazolines (τ 5·38—5·78).[13,14] However in several 3-aryl-2-isoxazolines having a =CHOR group (R = Me or Ph) at C-4, the τ value of 5-H_2 was found [4] to be in the range 4·66—4·94.

U.v. spectra of compounds (III) and (IV) (Table 2) reveal the presence of a more extended conjugated system in isomer (IV), similar to those of *trans*-chalcone [$\lambda_{max.}$ 229 (ε 7250) and 309 (25,700) nm in EtOH] [15] and of β-phenylchalcone [$\lambda_{max.}$ 232·5 (ε 15,800), 250sh (13,500), and 298

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* Details of Supplementary Publications are given in Notice to Authors No. 7, *J. Chem. Soc.* (*A*), 1970, Issue No. 20 (items less than 10 pp. are supplied as full size copies).

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[7] R. G. Micetich, *Canad. J. Chem.*, 1970, **48**, 467, 3753.

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[14] M. C. Aversa, G. Cum, and M. Crisafulli, *Gazzetta*, 1966, **96**, 1046.

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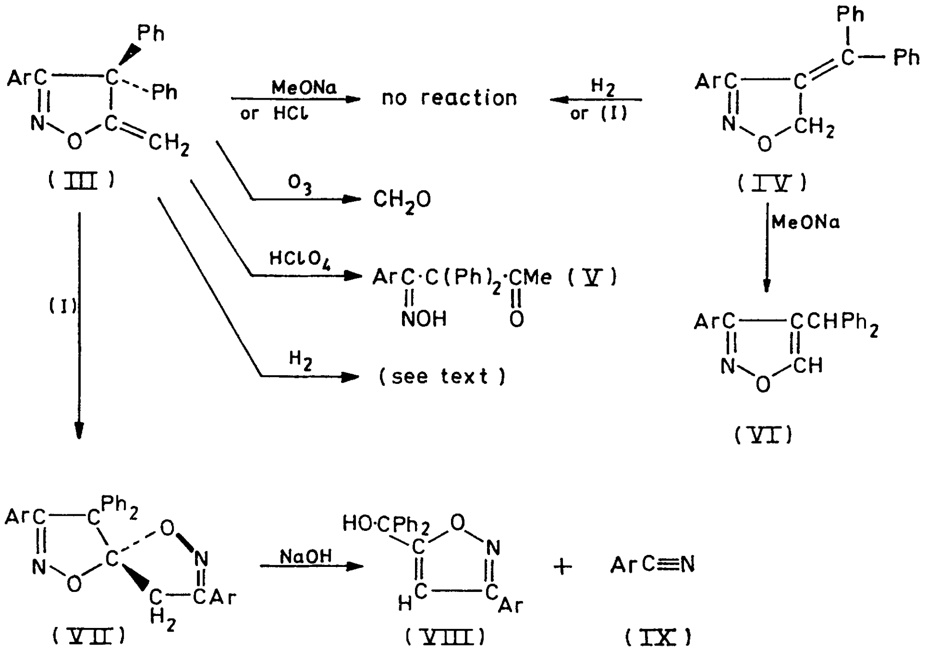
(10,000) nm in 95% EtOH].[16] Such a conjugated system is deeply altered by the rearrangement of (IV) to isoxazole (VI), which shows weak absorption at $\lambda > 250$ nm, as found for other 3-arylisoxazoles.[4,17] On the other hand, adduct (III) has an absorption maximum in a region typical for ordinary 3-aryl-2-isoxazolines [3,18] and 3-aryl-2-isoxazolin-5-ones.[19] The spectrum of oxime (V) can usefully be compared with that of acetophenone oxime [$\lambda_{max.}$ 244·5 (ε 10,840) nm in EtOH].[20]

The mass spectra show that some peaks from isomers (III), (IV), and (VI) are the same as those produced by diphenylallene fragmentation, in particular at *m/e* 115 and 165. Isoxazoline derivatives (III) and (IV) show intense peaks at *m/e* 208 and 207, attributable to $(M - \text{ArCN})^+$ and $(M - \text{ArCN} - \text{H})^+$, respectively. Isoxazole (VI) does not reveal this type of cleavage; its base peak at *m/e* 392 corresponds to the ion $(M - \text{CO} - \text{H})^+$ by analogy with the case of 3-phenylisoxazole.[21]



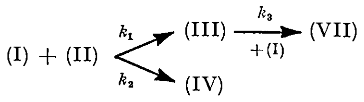
Scheme 1

When the nitrile oxide (I) reacts with the stoicheiometric amount of 1,1-diphenylallene, the product contains, besides (III) and (IV), a diadduct, identified as (VII). The same diadduct was obtained from the reaction of (III) with excess of (I). The mass spectrum of (VII) shows the correct molecular weight and the presence of four Cl atoms. τ Values and coupling constant for the methylenic protons (Table 1) indicate 4-H_2 in a 2-isoxazoline ring: reported values for similar cases are in the range 5·88—6·95 for τ and 17—19 Hz for *J*.[2,3,13,14,22,23] The reaction of the diadduct (VII) with sodium hydroxide can be explained by analogy with reported cases of base-catalysed rearrangement of spiroacetal bi-isoxazolines to α-isoxazolyl oximes,[2] and with the Beckmann fragmentation of oxime derivatives in solvolytic or basic conditions, and of oximes by thermal decomposition.[24]

In the n.m.r. spectrum of compound (VIII) (Table 1), an isoxazole 4-H and a hydroxylic proton are recognisable. The correct molecular weight and two Cl atoms were found from the mass spectrum. Also the u.v. spectrum agrees with a 3-arylisoxazole structure. Nitrile (IX) was recognised in the product by the $\nu_{C\equiv N}$ band at 2225 cm^{-1}, identical to that of an authentic sample.

The u.v. spectrum of diadduct (VII) (Table 2) is dissimilar from those of analogous spirobi-(3-aryl-2-isoxazolines) that show strong absorption maxima at *ca.* 260 nm.[1,4]

Kinetically the system under study corresponds to a set of parallel-consecutive reactions, according to Scheme 2.



Scheme 2

The rate difference between monoadditions and diaddition made possible their separate study. The former reactions were initially studied by measuring the rate of disappearance of nitrile oxide (I). The overall process ($k = k_1 + k_2$) was found to follow second-order kinetics. The main set of kinetic runs was performed by u.v. analysis at 310 nm: the variation of absorbance (*D*) with time, up to infinity, gave

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[22] G. Lo Vecchio, G. Cum, and G. Stagno d'Alcontres, *Gazzetta*, 1965, **95**, 206.

[23] A. Dondoni and F. Taddei, *Boll. sci. Fac. Chim. ind. Bologna*, 1967, **25**, 145.

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k values, while a comparison of experimental D_∞ values with those theoretically corresponding to complete conversion into adduct (IV) gave the fraction of (IV) in the mixture of (III) and (IV) (α). α Values were occasionally checked by n.m.r. spectroscopy. Rate coefficients k_1 and k_2 were obtained by the relations $k_1 = k(1 - \alpha)$ and $k_2 = k\alpha$.

TABLE 3

Kinetic results for the reaction of 1,1-diphenylallene with nitrile oxide (I) in CCl_4

t/°C	10^4k/l mol^{-1} s^{-1}	α	10^4k_1/l mol^{-1} s^{-1}	10^4k_2/l mol^{-1} s^{-1}
39·8	1·467	0·223	1·14	0·327
50·0	2·899	0·254	2·16	0·736
70·0	13·76	0·317	9·40	4·36

TABLE 4

Kinetic results for the reaction of 1,1-diphenylallene with nitrile oxide (I) in EtOH–CCl_4 (4 : 1 v/v)

t/°C	10^4k/l mol^{-1} s^{-1}	α	10^4k_1/l mol^{-1} s^{-1}	10^4k_2/l mol^{-1} s^{-1}
40·0	2·720	0·329	1·83	0·895
50·0	4·877	0·361	3·12	1·76
60·0	11·62	0·384	7·16	4·46
70·0	18·81	0·388	11·5	7·30

TABLE 5

Kinetic results for the reaction of 1,1-diphenylallene with nitrile oxide (I) in various solvent mixtures at 70·0 °C

Mixture CCl_4 : EtOH (v/v)	10^4k/l mol^{-1} s^{-1}	α	10^4k_1/l mol^{-1} s^{-1}	10^4k_2/l mol^{-1} s^{-1}
100% CCl_4	13·76	0·317	9·40	4·36
3 : 2	14·72	0·384	9·07	5·65
2 : 3	17·07	0·386	10·5	6·59
1 : 4	18·81	0·388	11·5	7·30
100% EtOH	19·17	0·420	11·1	8·05

TABLE 6

Kinetic results for the reaction of adduct (III) with nitrile oxide (I)

t/°C	40·0	50·0	60·0	70·0	70·0
10^5k_3/l mol^{-1} s^{-1}	0·781 [a]	2·10 [a]	5·66 [a]	11·2 [a]	60·4 [b]

[a] In CCl_4. [b] In EtOH–CCl_4 (3 : 2 v/v).

Kinetic measurements were for the reaction in carbon tetrachloride (Table 3) and in EtOH–CCl_4 (4 : 1 v/v) (Table 4), at different temperatures. The mixed EtOH–CCl_4 solvent was preferred to pure EtOH, because of the better solubility of (I). Rate coefficients as a function of the solvent composition were measured at 70·0 °C (Table 5).

The 1,3-cycloaddition of (I) to (III) was found to be second order in preliminary runs. Rates were measured as a function of temperature in CCl_4 only, while the solvent effect was evaluated by a run in EtOH–CCl_4 (3 : 2 v/v) at 70·0 °C (Table 6). Activation parameters for the three reactions are in Table 7.

DISCUSSION

The structures of products (III) and (IV) are incompatible with the existence of a common intermediate along the reaction path of the monoadditions. The independent parallel processes may be classified as $\alpha\beta$- and $\beta\gamma$-cycloadditions, respectively, with reference to the two reaction sites on the substituted allene.

Monoadducts (III) and (IV) both have exocyclic double bonds; only (III), which has an unsubstituted *exo*-methylene group, was found capable of adding a further molecule of nitrile oxide (I). Fully substituted double bonds are known to be scarcely reactive towards nitrile oxides,[25,26] while *exo*-methylene-cyclo-compounds were found to add benzonitrile oxide easily giving spiro-derivatives.[22,27]

Each of the three cycloadditions effected could have given two positional isomers; however all of them showed regiospecificity within the detection limits. In the reaction of (I) with (III) the orientation observed is the one expected for cycloaddition of a nitrile oxide to a 1,1-disubstituted olefin: such reactions usually give 5,5-disubstituted 2-isoxazolines.[25] In the addition of nitrile oxides to allenes, formation of a bond between oxygen and the central carbon atom of the allenic molecule was often found,[1-3] but also different directions were reported,[3] and no simple rule was stated. From an electrostatic point of view attack of oxygen at the central allenic carbon would be justified. In fact, nitrile oxides are polarised with a partial negative charge on oxygen,[10] and allenes add nucleophiles at their central carbon,[28,29] in agreement with the better reactivity of nucleophiles with sp rather than sp^2 carbon atoms.[30]

In the present case only the $\alpha\beta$-cycloaddition occurs with oxygen bonding to the central carbon of (II), while in the $\beta\gamma$-cycloaddition a bond is formed between oxygen and the terminal carbon atom. The former reaction is preferred, as is shown by the kinetic results (Tables 3—5). Values of k_1/k_2 range from 1·4 to 3·5, being larger in CCl_4 than in EtOH, and larger at 40 than

TABLE 7

Activation parameters

k	Reaction	Solvent	log A	$\Delta E^\ddagger$/kcal mol^{-1}	$\Delta S^\ddagger$/cal mol^{-1} K^{-1}
k_1	(I) + (II) $\longrightarrow$ (III)	CCl_4	6·6 ± 0·4	15·1 ± 0·6	−31 ± 2
		EtOH–CCl_4 [a]	5·7 ± 0·4	13·6 ± 0·7	−34 ± 2
k_2	(I) + (II) $\longrightarrow$ (IV)	CCl_4	8·4 ± 0·4	18·5 ± 0·6	−22 ± 2
		EtOH–CCl_4 [a]	6·7 ± 0·5	15·4 ± 0·7	−30 ± 2
k_3	(I) + (III) $\longrightarrow$ (VII)	CCl_4	8·3 ± 0·4	19·2 ± 0·6	−23 ± 2

[a] 4 : 1 (v/v).

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[30] J. Dale, ' Chemistry of Acetylenes,' ed. H. G. Viehe, Dekker, New York, 1969, ch. 1.

at 70 °C. The $\beta\gamma$-cycloaddition has a higher activation energy, not fully compensated in the temperature range of the experiments by the higher activation entropy (Table 7).

Results in Table 5 show that, while k_1 is almost insensitive to the solvent change from CCl_4 to EtOH, k_2 is increased by a factor of *ca.* 2. The greater response of the $\beta\gamma$-addition to a polar solvent indicates a more polar transition state for this reaction. This is reasonable, as the polarities of the products are in the same order: dipole moments are 3·47 D for adduct (III) and 3·77 D for (IV). The largest effect of solvent change is the one for the reaction of adduct (III), showing more than a fivefold increase in rate in passing from CCl_4 to EtOH–CCl_4 (3 : 2 v/v) (Table 6). The polarity difference between CCl_4 and EtOH is very large on any scale: dielectric constants are 2·23 and 24·3 D, and E_T values are 32·5 and 51·9, respectively.[31] All the observed solvent effects on the rates can therefore be considered as comparatively small.

Values of activation entropy (between −34 and −22 cal mol^{-1} K^{-1}), specificity in orientation, and extent of the solvent effect point to a concerted mechanism of 1,3-cycloaddition for the three reactions considered. It is common to find a slight polarity difference between transition and initial states, and in this case the reaction of adduct (III) presents such a difference to a fair degree, as judged from the solvent effect. This can be justified by the particular asymmetry of (III) which should give rise to a larger charge imbalance in the transition state of the cycloaddition.

Molecular models show that $\alpha\beta$- and $\beta\gamma$-additions must overcome steric difficulties in order to give (III) and (IV) as products, because of the close approach of the aryl group of (I) to one or both of the phenyl groups of the allene (II). Both reactions seem to choose the worse direction, from the steric point of view, by putting the Ph_2C or the $Ph_2C{=}C$ group at C-4 instead of C-5 of the product ring. The alternative direction would be contrary to electronic factors, as previously discussed, only in the case of the $\alpha\beta$-addition; for the $\beta\gamma$-addition there is no competition between steric and electronic factors, and at present there is no clear explanation of the orientation experimentally found. Tentatively, it can be suggested that the interaction between the dichlorotrimethylphenyl ring of (I) and a phenyl ring of (II) happens to be a superposition of local attractions, due to London forces, and repulsions, due to overlapping of electronic clouds, resulting in a favourable reaction path.

Among the products, adduct (III) is noteworthy because it is a rare example of a stable 5-methylene-2-isoxazoline derivative.[32] The absence of a 4-hydrogen atom inhibits its rearrangement to a 5-methylisoxazole (3-methyl-5-methylene-4,4-diprop-2-ynyl-2-isoxazoline is a similar case).[33] On the other hand, the moderate reactivity of nitrile oxide (I) keeps to a reasonable level the further reaction of the *exo*-methylene of (III). The latter cycloaddition occurs with a rate 8·4 times lower than the rate of formation of adduct (III) in CCl_4 at 70 °C (Tables 3 and 6). The diaddition is actually more similar to the formation of (IV), since in both cases the reaction site is a vinylidene group. Accordingly, the activation parameters for these two processes in CCl_4 have analogous values (Table 7).

EXPERIMENTAL

I.r., u.v., and n.m.r. spectra were taken on a Perkin-Elmer 21, a Beckmann DK-2A, and a Varian A-60 apparatus, respectively. Tetramethylsilane was used as internal standard for n.m.r. spectra. Mass spectra were measured on a Hitachi RMU6D instrument for compound (III) (all-glass inlet) and on a Perkin-Elmer 270 apparatus for other compounds (direct insertion). Dipole moments (μ) were determined by measurement of dielectric constant (Dipolmeter WTW DM 01) and of refractive index in benzene at 25 °C, following the Guggenheim method.[34]

Preparations of nitrile oxide (I) and diphenylallene (II) have been described.[10,29] 'Spectrograde' solvents and ethanol dried by standard methods were used for kinetics.

3-(3,5-*Dichloro*-2,4,6-*trimethylphenyl*)-5-*methylene*-4,4-*diphenyl*-2-*isoxazoline* (III) *and* 3-(3,5-*Dichloro*-2,4,6-*trimethylphenyl*)-4-*diphenylmethylene*-2-*isoxazoline* (IV).—A solution of (I) (0·04M) and (II) (0·12M) in EtOH–CCl_4 (1 : 1 v/v) (500 ml) was heated at 70 °C during 24 h. After removal of the solvent, the oily residue gave crystals (4·15 g) by treatment with light petroleum (b.p. 40—60 °C). The product was adsorbed on a silica gel column (270 g). Elution with benzene–light petroleum (85 : 15 v/v) afforded a small amount of a diphenylallene dimer,[29] followed by colourless crystals of *adduct* (III), m.p. 155 °C (from ethanol) (1·71 g) (Found: C, 71·2; H, 4·9; N, 3·05. $C_{25}H_{21}Cl_2NO$ requires C, 71·1; H, 5·0; N, 3·3%); μ 3·47 D. Following fractions gave colourless crystals of *adduct* (IV), m.p. 168 °C (from ethanol) (1·03 g) (Found: C, 71·3; H, 4·9; N, 3·2. $C_{25}H_{21}Cl_2NO$ requires C, 71·1; H, 5·0; N, 3·3%); μ 3·77 D.

Traces of other compounds were detected in the crude product by t.l.c. and n.m.r. The latter showed isomers (III) and (IV) in ratio 55 : 45. The same products were also obtained in CCl_4, $CHCl_3$, Et_2O, EtOH, and MeOH.

To obtain pure (III) easily, a solution of (I) (0·225 g) and (II) (1·0 g) in CCl_4 (15 ml) was left at room temperature for 9 days. After filtration and solvent removal, treatment with light petroleum followed by recrystallisation from ethanol gave adduct (III), m.p. 155 °C (0·176 g).

3,3′-*Bis*-(3,5-*dichloro*-2,4,6-*trimethylphenyl*)-4,4-*diphenyl*-5,5′-*spirobi*-2-*isoxazoline* (VII).—A solution of (I) (0·34 g) and (III) (0·32 g) in CCl_4 (3·5 ml) was left at room temperature for 10 days, and at 50 °C for 70 h. The solution was diluted with diethyl ether (1 ml) and cooled to 0 °C to give (VII) (0·19 g) as colourless *crystals*, m.p. 282 °C (from acetic acid) (Found: C, 63·8; H, 4·85; N, 4·1. $C_{50}H_{42}Cl_4N_2O_2$ requires C, 64·4; H, 4·6; N, 4·3%); $\lambda_{max.}$ (CH_2Cl_2), 279 (ε 1300) and 287 (1210) nm.

Ozonolysis of (III).—Ozonised oxygen (5%) was passed for 10 min through (III) (0·10 g) in dry ethyl acetate (20 ml) at −15 °C. A current of nitrogen was bubbled through the

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[31] C. Reichardt, *Angew. Chem. Internat. Edn.*, 1965, **4**, 29.

[32] Ch. Grundmann and P. Grünanger, 'The Nitrile Oxides,' Springer Verlag, Berlin, 1971, p. 100.

[33] D. T. Manning and H. A. Coleman, *J. Org. Chem.*, 1969, **34**, 3248.

[34] J. W. Smith, 'Electric Dipole Moments,' Butterworths, London, 1955.

mixture at 20 °C, then through a solution of chromotropic acid (50 mg) in concentrated H_2SO_4 (5 ml); after a few minutes a red-violet colour appeared, showing the presence of formaldehyde.[35]

Hydrogenation of (III).—A solution of (III) (0·10 g) in acetic acid (15 ml) was hydrogenated on 10% Pd–C during 2 h. The standard procedure gave a residue that was shown to be a mixture of unchanged (III) and other products by t.l.c. The n.m.r. spectrum ($CDCl_3$) showed, in addition to other signals, a doublet at τ 9·16 (J 7·5 Hz).

Treatment of (III) *with Sodium Methoxide in Methanol.*—A sample of (III) (50 mg) was refluxed with sodium methoxide (0·55 mmol) in methanol (21 ml) during 3 h. After the usual work-up, unchanged (III) was recovered.

Treatment of (III) *with Hydrochloric Acid.*—A sample of (III) (*ca.* 20 mg) was refluxed with concentrated HCl (1 ml), water (5 ml), and dioxan (5 ml) during 2 h. No decomposition of (III) was revealed by t.l.c.

Treatment of (III) *with Perchloric Acid in Aqueous Acetic Acid.*—A solution of (III) (0·10 g) in acetic acid (20 ml) was refluxed with 70% aqueous $HClO_4$ (5 ml) during 2 h. Ether was added, the organic layer washed with aqueous Na_2CO_3, and dried ($MgSO_4$). The solvent was removed, and a small amount of di-isopropyl ether added to give 1-(3,5-*dichloro*-2,4,6-*trimethylphenyl*)-2,2-*diphenylbutane*-1,3-*dione* 1-*oxime* (V) (35 mg) as colourless crystals, m.p. 173—174 °C (Found: C, 67·9; H, 5·1; N, 3·0. $C_{25}H_{23}Cl_2NO_2$ requires C, 68·2; H, 5·3; N, 3·1%); $\nu_{max.}$ (KBr) 3350 (OH), 1682 (C=O), and 1668 (C=N) cm^{-1}. A sample of (V) gave iodoform on treatment with NaOH and potassium iodide–iodine reagent.[36]

Attempted Hydrogenation of (IV).—A solution of (IV) (0·15 g) in 99·5% ethanol (15 ml) was stirred under hydrogen in the presence of Adams PtO_2 during 1 h. The standard procedure gave unchanged (IV) (n.m.r.).

Reaction of (IV) *with Sodium Methoxide in Methanol.*—Adduct (IV) (60 mg) was refluxed with sodium methoxide (0·65 mmol) in methanol (26 ml) during 3 h. After standing overnight at 0 °C, 3-(3,5-*dichloro*-2,4,6-*trimethylphenyl*)-4-*diphenylmethylisoxazole* (VI) separated as colourless crystals (36 mg), m.p. 174—175 °C (Found: C, 70·6; H, 4·9; N, 3·15. $C_{25}H_{21}Cl_2NO$ requires C, 71·1; H, 5·0; N, 3·3%); $\lambda_{max.}$ (n-hexane) 229sh (ε 16,400), 260 (600), 266 (565), 269 (540), 278 (430), and 286 (420) nm.

Reaction of (VII) *with Sodium Hydroxide.*—A sample of (VII) (0·15 g) in dioxan (30 ml) was refluxed with a 0·25M-NaOH solution in ethanol–water (4 : 1 v/v) (10 ml) during 2·5 h. The solution was neutralised with acetic acid. Extraction with ether gave a mixture of several compounds (t.l.c.); the i.r. spectrum (Nujol) showed the typical band of nitrile (IX) at 2225 cm^{-1}. Preparative t.l.c. on silica gel afforded 3-(3,5-*Dichloro*-2,4,6-*trimethylphenyl*)*isoxazol*-5-*yldiphenylmethanol* (VIII) (45 mg) as colourless crystals, m.p. 178—179 °C (from benzene–n-hexane) (Found: C, 67·8; H, 4·8; N, 3·1. $C_{25}H_{21}Cl_2NO_2$ requires C, 68·5; H, 4·8; N, 3·2%); $\nu_{max.}$ (Nujol) 3340 (OH) cm^{-1}. A sample previously treated with D_2O gave in the mass spectrum: m/e 442 (M + 4), 440 (M + 2), and 438 (M).

3,5-*Dichloro*-2,4,6-*trimethylbenzonitrile* (IX).—Triethyl phosphite (1 mmol) was added to a solution of (I) (1 mmol) in anhydrous benzene (15 ml). The mixture was refluxed during 10 min, diluted with benzene (10 ml), and shaken at room temperature with 5% H_2SO_4 (25 ml) for a few minutes. The benzene layer afforded (IX) (0·43 mmol) as colourless *crystals*, m.p. 192 °C (sublimes) (from n-hexane) (Found: C, 56·1; H, 4·4; N, 6·4. $C_{10}H_9NCl_2$ requires C, 56·1; H, 4·2; N, 6·5%); $\nu_{max.}$ (Nujol) 2225 (C≡N) cm^{-1}, τ ($CDCl_3$) 7·42(s).

Kinetics.—Preliminarily, the overall reaction of (I) and (II) was followed by i.r. analysis of (I) at 2296 cm^{-1} in a RIIC FH-01 0·1 mm AgCl thermostatted cell. Reaction order was investigated at 32·3 ± 0·3 °C, by working at different initial concentrations of (II) while keeping (I) at 0·06—0·08M. Concentrations of (II) and second-order rate coefficients (10^5k/l mol^{-1} s^{-1}) are: 0·24M, 9·19; 0·67M, 9·84; and 0·99M, 9·43.

Other runs involving compound (II) were carried out in sealed tubes (internal diameter 2 mm) each containing *ca.* 70 μl of solution, in a thermostat accurate to ±0·05 °C. Initial concentrations were *ca.* 0·04M for (I) and 0·12M for (II). Quenching was by cooling and dilution with n-hexane. Absorbance was measured at 310 nm; at this wavelength the ε values for (I)—(III) are less than 500 l mol^{-1} cm^{-1}. Values of α were evaluated by equation (1), where

$$D_\infty = D_0 + c_I^0[\alpha\varepsilon_{IV} + (1-\alpha)\varepsilon_{III} - \varepsilon_I - \varepsilon_{II}] \qquad (1)$$

c_I^0 is the initial concentration of (I); D_0 and D_∞ were measured at zero and 'infinity' time, respectively. The values of D_∞ were usually stable; apparently, dimerisation of 1,1-diphenylallene[29] did not interfere. The reaction degree as a function of time t [$= (D_t - D_0)/(D_\infty - D_0)$] was employed to obtain the reactant concentrations to be used in the usual second-order rate equation. Overall rate coefficients (k) were obtained by least-squares regression analysis. In a single case (run at 40·0 °C in Table 4) a stable experimental D_∞ was not obtained, and the value was used that gave the best correlation coefficient in the computation of k.

The measurement in pure EtOH (Table 5) is less accurate than the average, since nitrile oxide (I) was completely dissolved only after some heating at the reaction temperature. Samples from the initial part of the run were not considered.

U.v. analysis was also used for the reaction of nitrile oxide (I) with adduct (III); absorption at 270 nm, due mainly to the reactants, was measured, and the reaction degree calculated from it. Initial concentrations ranged from 0·1 to 0·3M for each reactant.

All kinetic runs covered 1—2 half-lives. The probable errors of rate coefficients are on the average 3—4% of measured values. Arrhenius activation energies ($\Delta E^\ddagger$), frequency factors (A), and activation entropies ($\Delta S^\ddagger$) were obtained by a standard computer programme.

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[35] F. D. Snell and C. T. Snell, 'Colorimetric Methods of Analysis,' Van Nostrand, New York, vol. III, 1953, p. 255.

[36] A. I. Vogel, 'Practical Organic Chemistry,' 3rd edn., Longmans, London, 1956, p. 1068.