1,3-Dipolar Cycloadditions to Nitrogen-substituted Allenes

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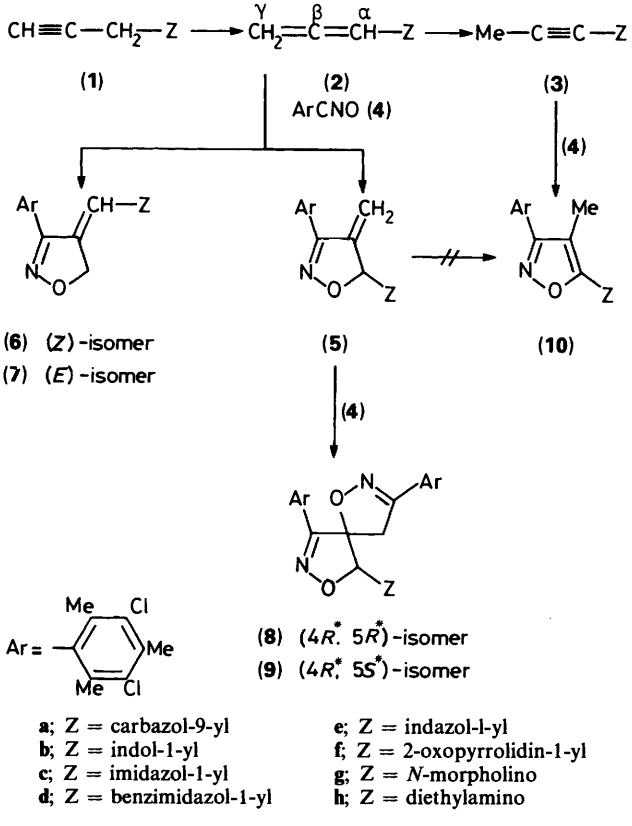
A series of nitrogen-substituted allenes (**2a–h**) was treated with 3,5-dichloro-2,4,6-trimethylbenzonitrile oxide (**4**) in boiling tetrachloromethane. The reaction occurred predominantly (or exclusively) at the α,β double bond. Regardless of the site of cycloaddition, the carbon of the nitrile oxide bonded selectively to the central carbon of the allene. 4-Methylene-4,5-dihydroisoxazole monoadducts (**5**) reacted further to form spiro-diadducts. The stereochemistry of one diadduct was determined by X-ray diffraction analysis.

Allenes are interesting dipolarophiles owing to the presence of two sites for cycloaddition, each of them potentially giving two regioisomers. Furthermore, the first-formed cycloadducts can add a second molecule of 1,3-dipole, thus providing a synthetic entry to heterospiro compounds which are not readily accessible by other routes.[1] Since nothing is known about the dipolarophilic behaviour of allenyl groups linked to nitrogen, we studied the reaction of the series of nitrogen-substituted allenes (**2a–h**) with 3,5-dichloro-2,4,6-trimethylbenzonitrile oxide (**4**) (see Scheme 1).



Scheme 1.

Results

Compounds (**2a–h**) were available upon base-promoted isomerisation of the corresponding alkyne derivatives (**1a–h**) (see Experimental section). While (**2a–f**) were quite stable, aminoallenes (**2g,h**) were found to be susceptible to further isomerisation so that they were obtained with (**3g,h**) as impurities.

The reaction of (**2a–h**) with the nitrile oxide (**4**) was carried out in boiling tetrachloromethane by using equimolar amounts of the reactants. Under these conditions, some of the starting allene was often recovered and various kinds of products were obtained, the relative proportion of which was somewhat dependent on the substituent (see Table 1). The reaction mixtures derived from (**2g,h**) also contained a small quantity of the isoxazole products (**10g,h**). It was ascertained that no isomerisation of (**5g,h**) to (**10g,h**) occurred in boiling tetrachloromethane, not even under basic or acidic catalysis. Thus, the formation of (**10g,h**) must be attributed to 1,3-dipolar cycloaddition to the acetylenic impurities (**3g,h**).

When the reaction was done with two molar equivalents of the nitrile oxide (**4**), the starting allenes disappeared completely and the diadducts (**8**) became the predominant or the exclusive products, substantially at the expense of the monoadducts (**5**). Accordingly, while compounds (**6**) and (**7**) were inert towards (**4**), the exocyclic methylene dihydroisoxazoles (**5**) reacted with it rather easily, giving the spiro compounds (**8**) and (**9**). Upon heating, compound (**9d**) underwent a slow isomerisation to (**8d**); however, on following the reaction between (**5d**) and (**4**) by NMR analysis, it was shown that (**8d**) was present as the main product even after short times, thus suggesting that (**9d**) is not the precursor of (**8d**).

Diagnostic spectral properties are reported in Tables 2 and 3. Both ^1H and ^{13}C NMR data of the diadducts are compatible only with a 4,5′-junction of the isoxazole rings, thus excluding alternative regioisomeric formulae.[2–9] However, to establish the relative stereochemistry of the two centres of chirality, we performed the X-ray crystal structure analysis of one diadduct [(**8h**)] (see Figure and Tables 4 and 5). The same (4*R**, 5*R**) stereochemistry could reasonably be extended to (**8a–g**), in the light of the close analogy of their NMR spectra. On the other hand, the conversion of (**9d**) to (**8d**) is consistent with a mutual stereoisomeric relationship. It is to be noted that crystal structure analyses of spirobi(4,5-dihydroisoxazoles) are lacking in the literature. Previous stereochemical assignments to such compounds were based on ^{13}C–H coupling constant studies.[4]

The distinction between the olefinic isomers (**6**) and (**7**) was made on the basis of proton–proton nuclear Overhauser enhancement (NOE) measurements. In fact, upon irradiation of the isoxazole protons, the intensity of the signal of the exocyclic olefinic proton was enhanced by 4–5% in the case of the (*E*)-isomers (**7a–e**), while such an effect was not discernible in the case of the (*Z*)-isomers (**6a–f**).

Table 1. Reaction of allenes (**2a–h**) with the nitrile oxide (**4**) in boiling tetrachloromethane.

Allene	mol equiv. of (**4**)	Reaction time (h)	Products (%)[a] (**5**)	(**6**)	(**7**)	(**8**)	(**9**)	Eluant
(**2a**)	1	3	28	2	25	17	—	Light petroleum–ethyl acetate (4:1)
	2	18	12	5	24	37	—	Light petroleum–ethyl acetate (4:1)
(**2b**)	1	2	39	12	—	9	—	Light petroleum–diethyl ether (1:1)
	2	16	—	10	—	56	—	Toluene–ethyl acetate (9:1)
(**2c**)	1	2[b]	—	24	—	27	—	Light petroleum–dichloromethane (1:1)
	2	6[b]	—	16[c]	—	34	—	Light petroleum–dichloromethane (1:1)
(**2d**)	1	2	16[d]	16[d]	—	14	7	Toluene–ethyl acetate (9:1)
	2	6	—	21	—	37	15	Toluene–ethyl acetate (9:1)
(**2e**)	1	2	26	4	4	31	—	Toluene–ethyl acetate (9:1)
	2	10	—	4	3	62	—	Toluene–ethyl acetate (9:1)
(**2f**)	1	2	30	5	—	18	—	Diethyl ether
	2	16	—	3	—	55	—	Diethyl ether
(**2g**)	1	4	64	—	—	11	—	Toluene–ethyl acetate (4:1)
	2	18	—	—	—	84	—	*e*
(**2h**)	1	4	54	—	—	4	—	Dichloromethane
	2	18	—	—	—	75	—	*e*

[a] Yields refer to the starting allene. [b] Some of a solid material was also isolated, whose identification was felt unnecessary as its NMR spectrum showed signals only in the region δ 2–3. [c] This compound tended to decompose upon prolonged heating. [d] Column chromatography gave a *ca.* 1:1 mixture of (**5d**) and (**6d**) in 32% overall yield; subsequent isolation of (**5d**) and (**6d**) in the pure state was performed by repeated fractional recrystallisations. [e] By recrystallisation of the crude products.

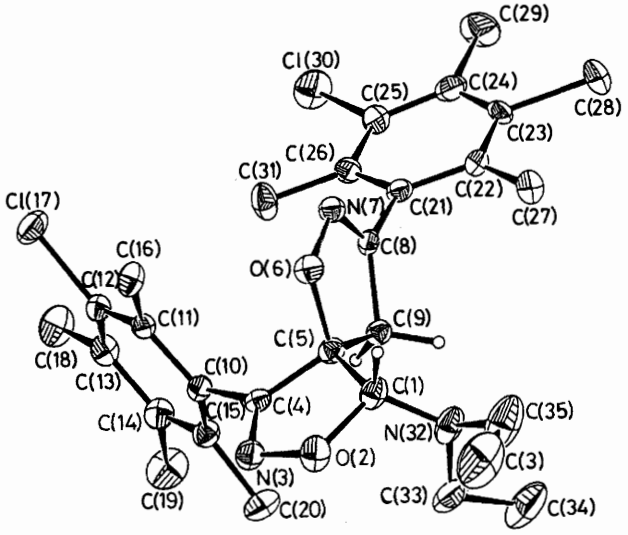


Figure. Crystal structure of diadduct (**8h**). Hydrogen atoms of methyl and ethyl groups are omitted for clarity.

Further work followed from the consideration that a stepwise, ionic cycloaddition pathway could in principle be devised in the case of strongly polarised, electron-rich allenes such as (**2g,h**). To gain information on this point, we carried out the reaction of (**2g**) with (**4**) in aprotic and protic polar solvents. In boiling acetonitrile, the products were the same as those obtained in tetrachloromethane with minor changes in yields. However, in boiling ethanol, the yield of adduct (**5g**) decreased markedly in favour of a new predominant product which was identified as (**12**) from analytical, spectral, and chemical evidence (see Scheme 2). The *trans*-configuration of (**12**) was assigned on the basis of the coupling constant of the isoxazole protons in comparison with the copious literature data for *cis* and *trans*-4,5-disubstituted 4,5-dihydroisoxazoles.[2b,10–13] Control experiments showed that: (i) compound (**5g**) was not the precursor of (**12**), being stable in boiling ethanol; (ii) allene (**2g**) was converted in ethanol into (**11**); (iii) the latter compound reacted with (**4**) to produce only (**12**). Treatment of (**2g**) with (**4**) in boiling ethanol gave also an additional product which was assigned the structure (**15**) on the basis of elemental analysis and spectral data (mass, IR, and ^{1}H and ^{13}C NMR). A tentative explanation for the formation of (**15**) would involve an 1,3-dipolar cycloaddition to the species (**14**), which could be derived from the starting allene through a dimerisation-like process. Unfortunately, no evidence was achieved to support the occurrence of this pathway.

Discussion

The results given in Table 1 reveal that, in spite of the steric hindrance due to the substituent, the α,β double bond is always more reactive than the β,γ one. This reactivity gap is particularly marked in the case of (**2g,h**), thus indicating a strong activating effect of the amino-substituent, which is in line with the pronounced dipolarophilicity of enamines.[14]

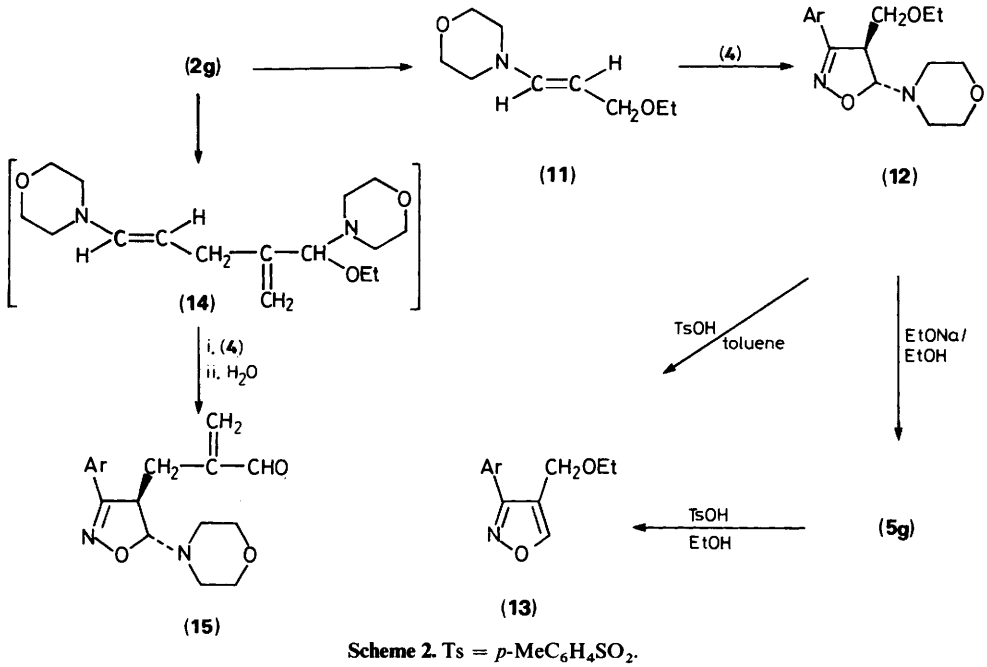
As far as regioselectivity is concerned, the present work brings to light a general pattern where the carbon of the nitrile oxide bonds exclusively to the β-carbon of the allene, regardless of the site of cycloaddition. Such a pattern corresponds to that previously observed in the reactions of (**4**) with aryl[15] and aryloxy[16] allenes, while both possible orientations were found to be operative in the case of (phenylsulphonyl)allenes.[7] This change in regioselectivity may be reasonable because the strong electron-withdrawing sulphonyl group lowers the orbital energies of the allene and locates its LUMO mainly at the β-carbon,* thus increasing the importance of the HOMO (dipole)–LUMO (dipolarophile) interaction, which drives the oxygen of (**4**) to the allenic β-carbon. However, frontier molecular orbital (FMO) considerations seem to be inadequate to justify a general regiochemical preference as pronounced as that found experimentally. Purely steric effects cannot be invoked on considering that the β,γ-cycloaddition often places the bulky substituent of (**2**) close to the aryl group of (**4**). We suggest that, for each site of cycloaddition, the transition state leading to 4-alkylidene (rather than 5-alkylidene) 4,5-dihydroisoxazoles may benefit from the incipient conjugation

* This statement finds support from MNDO calculations on (methylsulphonyl)allene.[17]

Table 2. Characterisation of 4,5-dihydroisoxazoles (**5**), (**6**), and (**7**).

Compd.	M.p.[a] (*t*/°C)	M^+ (*m*/*z*)	δ_H[b,c]	Found (%) (Required) C	H	N
(**5a**)	258–259 (Me_2SO)	434	2.40 (3 H, s), 2.52 (3 H, s), 2.60 (3 H, s), 5.23 (2 H, d, *J* 3.5), 7.1–7.9 (7 H, m), 8.1–8.3 (2 H, m)	69.1 (69.0)	4.4 (4.6)	6.6 (6.4)
(**5b**)	148–149 ($CHCl_3$)	384	2.39 (3 H, s), 2.46 (3 H, s), 2.67 (3 H, s), 5.35 (1 H, d, *J* 3.5), 5.49 (1 H, d, *J* 3.5), 6.63 (1 H, d, *J* 4), 7.0–7.7 (6 H, m)	65.7 (65.5)	4.7 (4.7)	7.2 (7.3)
(**5d**)	154–155 ($CHCl_3$–Pr^i_2O)	385	2.36 (3 H, s), 2.43 (3 H, s), 2.64 (3 H, s), 5.42 (1 H, dd, *J* 3.5 and 2), 5.60 (1 H, dd, *J* 3.5 and 2), 7.1–7.9 (5 H, m), 8.03 (1 H, s)	62.0 (62.2)	4.7 (4.4)	11.0 (10.9)
(**5e**)	151–152 (hexane-C_6H_6)	385	2.38 (3 H, s), 2.54 (3 H, s), 2.64 (3 H, s), 5.38 (1 H, d, *J* 3), 5.51 (1 H, d, *J* 3), 7.1–7.8 (5 H, m), 8.10 (1 H, s)	62.2 (62.2)	4.5 (4.4)	10.8 (10.9)
(**5f**)	162–163 (hexane-C_6H_6)	352	1.9–2.7 (13 H, overlapping), 3.2–3.6 (2 H, m), 5.18 (1 H, d, *J* 3.5), 5.38 (1 H, d, *J* 3.5), 7.01 (1 H, t, *J* 3.5)	57.8 (57.8)	3.3 (3.5)	7.8 (7.9)
(**5g**)[d]	140–141 (hexane-C_6H_6)	354	2.23 (6 H, s), 2.60 (3 H, s), 2.7–3.1 (4 H, m), 3.77 (4 H, t, *J* 5), 5.16 (1 H, d, *J* 3.5), 5.44 (1 H, d, *J* 3.5), 5.86 (1 H, t, *J* 3.5)	— —		
(**5h**)	104–105 (pentane)	340	1.18 (6 H, t, *J* 7), 2.28 (3 H, s), 2.32 (3 H, s), 2.60 (3 H, s), 2.95 (2 H, q, *J* 7), 5.05 (1 H, d, *J* 3.5), 5.35 (1 H, d, *J* 3.5), 6.05 (1 H, t, *J* 3.5)	60.0 (59.8)	6.5 (6.5)	8.1 (8.2)
(**6a**)	271–273 ($CHCl_3$)	434	2.50 (6 H, s), 2.68 (3 H, s), 5.15 (2 H, d, *J* 3.5), 6.81 (1 H, t, *J* 3.5), 6.9–7.6 (6 H, m), 7.9–8.2 (2 H, m)	69.1 (69.0)	4.7 (4.6)	6.5 (6.4)
(**6b**)	200–202 (Pr^i_2O)	384	2.38 (6 H, s), 2.68 (3 H, s), 5.55 (2 H, d, *J* 3.5), 6.73 (1 H, d, *J* 4), 6.87 (1 H, t, *J* 3.5), 7.0–7.7 (5 H, m)	65.7 (65.5)	4.7 (4.7)	7.2 (7.3)
(**6c**)	218–219 ($CHCl_3$-Pr^i_2O)	335	2.31 (6 H, s), 2.64 (3 H, s), 5.49 (2 H, d, *J* 3.5), 6.55 (1 H, t, *J* 3.5), 7.02 (1 H, br s), 7.17 (1 H, s), 7.58 (1 H, br s)	57.0 (57.0)	4.7 (4.5)	12.3 (12.5)
(**6d**)	240–241 (EtOH)	385	2.35 (6 H, s), 2.68 (3 H, s), 5.55 (2 H, d, *J* 3.5), 6.73 (1 H, t, *J* 3.5), 7.1–7.9 (4 H, m), 8.00 (1 H, s)	62.5 (62.2)	4.4 (4.4)	11.0 (10.9)
(**6e**)	195–196 (hexane-C_6H_6)	385	2.36 (6 H, s), 2.66 (3 H, s), 5.75 (2 H, d, *J* 3.5), 6.87 (1 H, t, *J* 3.5), 7.1–7.8 (4 H, m), 8.20 (1 H, s)	62.3 (62.2)	4.5 (4.4)	10.8 (10.9)
(**6f**)	124–125 (hexane-C_6H_6)	^52	1.9–2.7 (13 H, overlapping), 3.85 (2 H, t, *J* 6.5), 5.40 (2 H, d, *J* 3.5), 6.41 (1 H, t, *J* 3.5)	57.7 (57.8)	3.3 (3.5)	7.9 (7.9)
(**7a**)	192–193 ($CHCl_3$)	434	1.92 (6 H, s), 2.10 (3 H, s), 5.50 (2 H, d, *J* 3.5), 6.82 (1 H, t, *J* 3.5), 6.9–7.4 (6 H, m), 7.6–7.9 (2 H, m)	69.2 (69.0)	4.7 (4.6)	6.6 (6.4)
(**7e**)	132–133 (hexane-C_6H_6)	385	2.11 (6 H, s), 2.32 (3 H, s), 5.46 (2 H, d, *J* 3.5), 6.9–7.4 (5 H, m), 7.48 (1 H, s)	62.3 (62.2)	4.6 (4.4)	10.9 (10.9)

[a] Recrystallisation solvent in parentheses. [b] Solvent: C_2D_6SO for (**5a**), $CDCl_3$ for all other compounds. [c] *J* in Hz. [d] This compound has recently been reported (ref. 9).



Scheme 2. Ts = *p*-$MeC_6H_4SO_2$.

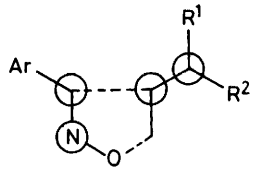
between the additional π bonds which are present in the reactants in a perpendicular plane with respect to the primary π orbitals. This is schematically depicted in formula (**16**), where the circles indicate the p orbitals not involved in the formation of the new σ bonds.

Although the configuration of the β,γ-cycloadducts has been determined, little can be said about the facial stereoselectivity of this cycloaddition process. The observed products may actually be the consequence of thermodynamic rather than kinetic factors, as suggested by the fact that, in the case of

Table 3. Characterisation of 4,5′-spirobi(4,5-dihydroisoxazoles) (**8**) and (**9**).

Compd.	M.p.[a] (*t*/°C)	M^+ (*m*/*z*)	δ_H[b,c]	$\delta_c(CDCl_3)$	Found (%) (Required) C	H	N
(**8a**)	291–293 (C_6H_6)	663	1.26 (6 H, s), 2.38 (3 H, s), 2.40 (3 H, s), 2.63 (3 H, s), 2.70 (3 H, s), 2.11, 2.61 (2 H, AB, *J* 19), 7.2–7.8 (7 H, m), 8.0–8.2 (2 H, m)	16.2–20.4, 41.3 (t), 94.5 (d), 101.4 (s), 109.5–139.2, 156.2 (s), 158.2 (s)	63.4 (63.2)	4.5 (4.4)	6.2 (6.3)
(**8b**)	298–300 ($CHCl_3$)	613	1.50 (6 H, s), 2.35 (3 H, s), 2.43 (3 H, s), 2.62 (3 H, s), 2.64 (3 H, s), 2.20, 2.62 (2 H, AB, *J* 19), 6.68 (1 H, d, *J* 4), 6.97 (1 H, s), 7.1–7.7 (5 H, m)		60.6 (60.5)	4.6 (4.4)	6.8 (6.8)
(**8c**)	274–275 (Pr^i_2O)	564	1.80 (6 H, s), 2.30 (3 H, s), 2.50 (3 H, s), 2.61 (3 H, s), 2.64 (3 H, s), 2.48, 2.82 (2 H, AB, *J* 19), 6.58 (1 H, s), 7.02 (1 H, br s), 7.24 (1 H, s), 7.72 (1 H, br s)		54.9 (55.1)	4.3 (4.3)	10.0 (9.9)
(**8d**)	277–278 ($CHCl_3$)	614	1.68 (6 H, s), 2.31 (3 H, s), 2.47 (3 H, s), 2.68 (6 H, s), 2.50, 2.72 (2 H, AB, *J* 19), 6.91 (1 H, s), 7.2–8.0 (4 H, m), 8.12 (1 H, s)	16.9–19.9, 41.2 (t), 92.0 (d), 101.7 (s), 109.8–144.0, 156.2 (s), 157.1 (s)	58.8 (58.5)	4.4 (4.3)	9.1 (9.1)
(**8e**)	210–212 (C_6H_6)	614	1.67 (6 H, s), 2.48 (3 H, s), 2.60 (3 H, s), 2.65 (6 H, s), 2.85, 3.07 (2 H, AB, *J* 19), 6.98 (1 H, s), 7.1–7.9 (4 H, m), 8.15 (1 H, s)	17.1–19.7, 42.2 (t), 92.1 (d), 100.9 (s), 108.8–141.1, 156.2 (s), 157.0 (s)	58.3 (58.5)	4.4 (4.3)	9.0 (9.1)
(**8f**)	233–235 (C_6H_6)	581	1.84 (6 H, s), 1.9–2.7 (16 H, overlapping), 2.96, 3.18 (2 H, AB, *J* 19), 3.2–3.9 (2 H, m), 6.50 (1 H, s)	17.1–19.8, 30.7 (t), 41.1 (t), 43.6 (t), 90.3 (d), 99.6 (s), 125.1–136.8, 155.9 (s), 156.1 (s), 176.2 (s)	55.9 (55.6)	4.8 (4.7)	7.1 (7.2)
(**8g**)[d]	238–239 (CCl_4)	583	1.92 (6 H, s), 2.42 (3 H, s), 2.45 (3 H, s), 2.55 (3 H, s), 2.72 (3 H, s), 2.85–3.05 (4 H, m), 3.12, 3.84 (2 H, AB, *J* 19), 3.86 (4 H, t, *J* 5), 5.85 (1 H, s)	17.2–19.9, 40.8 (t), 48.7 (t), 66.8 (t), 98.6 (s), 103.5 (d), 126.3–136.9, 155.3 (s), 156.4 (s)			
(**8h**)	212–214 (C_6H_6)	569	1.17 (6 H, t, *J* 7), 1.84 (6 H, s), 2.30 (3 H, s), 2.52 (3 H, s), 2.55 (3 H, s), 2.61 (3 H, s), 2.70 (2 H, q, *J* 7), 3.00 (2 H, q, *J* 7), 2.81, 3.53 (2 H, AB, *J* 18), 5.62 (1 H, s)	13.3–20.0, 41.1 (t), 42.9 (t), 98.8 (s), 103.6 (d), 126.9–137.0, 155.5 (s), 156.3 (s)	56.8 (56.8)	5.5 (5.5)	7.2 (7.4)
(**9d**)	185–186 ($CHCl_3$)	614	1.80 (6 H, s), 2.53 (6 H, s), 2.64 (6 H, s), 3.18, 3.90 (2 H, AB, *J* 18.5), 6.1–6.3 (1 H, m), 6.40 (1 H, s), 6.6–7.3 (3 H, m), 7.50 (1 H, s)	17.1–19.6, 42.7 (t), 95.1 (d), 100.6 (s), 106.1–138.3, 155.5 (s), 157.2 (s)	58.5 (58.5)	4.4 (4.3)	9.3 (9.1)

[a] Recrystallisation solvent in parentheses. [b] Solvent: C_5D_5N for (**8g**), $CDCl_3$ for all other compounds. [c] *J* in Hz. [d] This compound has recently been reported (ref. 9).



(**16**)

(**2a**), the major isomer (**7a**) undergoes thermal conversion to (**6a**).

Finally, a brief comment is needed about the formation of the diadducts. Steric factors reasonably account for the inertness of the monoadducts (**6**) and (**7**) towards a second molecule of nitrile oxide in contrast with the good reactivity of monoadducts (**5**). In the latter case, the preferred formation of diastereoisomers (**8**) corresponds to the approach of (**4**) to the less encumbered side of (**5**). The regiochemistry of this approach, leading to 4,5′- rather than 4,4′-spiro compounds, confirms the reported mode of cycloaddition of nitrile oxides to 4-methylene-4,5-dihydroisoxazoles.[4,9]

Experimental

M.p.s were determined on a Büchi apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer. NMR spectra were taken on Varian EM-390 (^1H) and Bruker WP80SY (^{13}C) instruments, respectively; chemical shifts are given in ppm from internal $SiMe_4$, with coupling constants in Hz. NOE measurements were performed on a Varian XL-200 instrument. Mass spectra were determined on a WG-70EQ apparatus.

Compounds (**1g**),[18] (**1h**),[18] and (**4**)[19] were prepared according to literature methods.

Preparation of Propynyl Derivatives (**1a–d**).—A solution of 3-bromopropyne (0.090 mol), unsubstituted heterocycle (0.060 mol), and tetrabutylammonium bromide (3 mmol) in benzene (180 ml) was treated with 50% NaOH (35 ml) and stirred vigorously at room temperature for the appropriate time. After addition of benzene (60 ml), the organic layer was separated, washed with water, and dried (Na_2SO_4). Evaporation of the solvent gave practically pure (**1**). Detailed data are as follows: (**1a**),[20] 4 h, 54%, m.p. 108 °C (from di-isopropyl ether); (**1b**),[21] 1 h, 86%, oil; (**1c**),[21] 1 H, 88%, oil; (**1d**),[22] 4 h, 87%, m.p. 40 °C (from di-isopropyl ether), δ ($CDCl_3$) 2.53 (1 H, t, *J* 2.5), 4.88 (2 H, d, *J* 2.5), 7.2–7.9 (4 H, m), and 8.00 (1 H, s).

Preparation of 1-(*Prop-2-ynyl*)*indazole* (**1e**).—A solution of 3-bromopropyne (0.060 mol), indazole (0.040 mol), and triethylbenzylammonium chloride (4 mmol) in benzene (120 ml) was treated with 50% NaOH (24 ml) and stirred vigorously at room temperature for 4.5 h. The organic layer was separated, washed with water, and dried (Na_2SO_4). After removal of the solvent, the residue was chromatographed on a silica gel column with toluene–ethyl acetate (9:1) as eluant to afford (**1e**)[23] (64%), m.p. 42 °C (from di-isopropyl ether); *m*/*z* 156 (M^+); δ ($CDCl_3$) 2.40 (1 H, t, *J* 2.5), 5.17 (2 H, d, *J* 2.5), 7.0–7.7 (4 H, m), and 8.00 (1 H, s).

Preparation of Allene Derivatives (**2a–c**).—A solution of (**1**) (10 mmol) in anhydrous dimethyl sulphoxide (DMSO) (5 ml) was treated with a suspension of triturated KOH (7 mmol) in anhydrous DMSO (5 mol) and stirred at room temperature for

Table 4. Fractional co-ordinates with e.s.d.s in parentheses for (**8h**).

Atom	x/a	y/b	z/c
Cl(17)	0.276 2(2)	−0.187 9(1)	0.205 14(4)
Cl(19)	−0.104 3(2)	0.078 5(1)	0.193 35(5)
Cl(28)	0.792 7(2)	0.351 5(1)	0.121 10(5)
Cl(30)	0.571 6(2)	0.194 7(1)	0.229 06(4)
O(2)	0.142 4(5)	−0.062 7(3)	0.036 80(9)
O(6)	0.413 4(4)	−0.045 5(2)	0.085 16(9)
N(3)	0.086 4(5)	−0.085 3(3)	0.068 0(1)
N(7)	0.502 6(5)	0.005 6(3)	0.105 9(1)
N(32)	0.243 8(7)	0.083 1(3)	0.023 3(1)
C(1)	0.262 0(8)	0.000 4(4)	0.040 3(1)
C(4)	0.159 8(6)	−0.047 9(3)	0.090 8(1)
C(5)	0.283 1(6)	0.005 6(3)	0.078 1(1)
C(8)	0.447 5(6)	0.082 6(4)	0.111 3(1)
C(9)	0.309 5(6)	0.097 6(4)	0.093 7(1)
C(10)	0.124 9(6)	−0.056 2(3)	0.126 9(1)
C(11)	0.197 8(6)	−0.118 2(3)	0.146 4(1)
C(12)	0.178 1(6)	−0.114 5(4)	0.180 5(1)
C(13)	0.088 0(7)	−0.054 1(4)	0.196 0(1)
C(14)	0.013 2(7)	0.003 4(4)	0.175 1(2)
C(15)	0.029 1(6)	0.003 6(4)	0.141 0(1)
C(16)	0.293 6(9)	−0.187 8(5)	0.131 9(2)
C(18)	0.074 7(8)	−0.050 5(4)	0.233 2(2)
C(20)	−0.060 6(8)	0.066 8(6)	0.120 2(2)
C(21)	0.523 8(6)	0.149 7(4)	0.132 3(1)
C(22)	0.611 0(6)	0.213 5(4)	0.117 6(2)
C(23)	0.682 8(6)	0.271 9(4)	0.139 5(2)
C(24)	0.673 8(7)	0.266 3(4)	0.173 6(2)
C(25)	0.583 4(7)	0.202 5(4)	0.186 0(2)
C(26)	0.507 7(6)	0.143 3(4)	0.166 6(1)
C(27)	0.625(1)	0.217 6(6)	0.080 5(2)
C(29)	0.762 6(8)	0.328 5(4)	0.194 9(2)
C(31)	0.412 0(7)	0.074 3(4)	0.182 1(1)
C(33)	0.111 0(9)	0.127 0(5)	0.028 8(2)
C(34)	0.119(1)	0.229 1(5)	0.025 1(2)
C(35)	0.304(1)	0.081 2(6)	−0.012 0(2)
C(36)	0.254(1)	0.018 5(7)	−0.033 3(2)

Table 5. Selected bond lengths (Å), angles (°) and torsion angles (°) with e.s.d.s in parentheses for (**8h**).

O(2)–N(3)	1.406(6)	O(2)–C(1)	1.476(8)
O(6)–N(7)	1.409(6)	O(6)–C(5)	1.476(6)
N(3)–C(4)	1.279(6)	N(7)–C(8)	1.274(7)
N(32)–C(1)	1.415(7)	C(1)–C(5)	1.539(6)
C(4)–C(5)	1.502(7)	C(4)–C(10)	1.497(6)
C(5)–C(9)	1.523(7)	C(8)–C(9)	1.504(8)
C(8)–C(21)	1.493(8)		
N(3)–O(2)–C(1)	110.8(4)	N(7)–O(6)–C(5)	109.9(3)
O(2)–N(3)–C(4)	109.6(4)	O(6)–N(7)–C(8)	109.7(4)
O(2)–C(1)–C(5)	103.1(4)	N(3)–C(4)–C(5)	114.0(4)
C(1)–C(5)–C(4)	102.1(4)	O(6)–C(5)–C(4)	108.3(4)
O(6)–C(5)–C(1)	105.9(4)	C(4)–C(5)–C(9)	117.4(4)
C(1)–C(5)–C(9)	118.4(4)	O(6)–C(5)–C(9)	104.1(4)
N(7)–C(8)–C(9)	114.1(5)	C(5)–C(9)–C(8)	101.8(4)
N(3)–O(2)–C(1)–C(5)	6.1(5)	C(1)–O(2)–N(3)–C(4)	−3.1(6)
N(7)–O(6)–C(5)–C(9)	6.0(5)	N(7)–O(6)–C(5)–C(1)	131.5(4)
N(7)–O(6)–C(5)–C(4)	−119.6(4)	C(5)–O(6)–N(7)–C(8)	−2.9(5)
O(2)–N(3)–C(4)–C(5)	−1.5(6)	O(6)–N(7)–C(8)–C(9)	−1.7(6)
O(2)–C(1)–C(5)–C(4)	−6.3(5)	N(3)–C(4)–C(5)–C(1)	5.2(6)
O(6)–C(5)–C(9)–C(8)	−6.4(5)	N(7)–C(8)–C(9)–C(5)	5.3(6)

2 h. The mixture was poured into cold water (50 ml) and extracted with ether. The organic solution was dried (Na_2SO_4) and evaporated under reduced pressure to give practically pure carbazol-9-ylallene (**2**). Yields are: (**2a**),[20] 88%; (**2b**),[21] 87%; (**2c**),[21] 52%.

Preparation of Allene Derivatives (**2d,e**).—A solution of (**1**) (14 mmol) in tetrahydrofuran (THF) (8 ml) was treated with a suspension of triturated KOH (7 mmol) in THF (8 ml) and stirred at 0 °C for 2 h. The mixture was poured into cold water (50 ml) and extracted with ether. The organic solution was dried (Na_2SO_4) and evaporated under reduced pressure to give practically pure allene (**2**). Detailed data are as follows: (**2d**),[22] 82%, δ ($CDCl_3$) 5.65 (2 H, d, *J* 6), 7.0–7.9 (5 H, overlapping signals), 7.98 (1 H, s); (**2e**),[23] 88%, δ ($CDCl_3$) 5.69 (2 H, d, *J* 6), 7.0–7.8 (5 H, overlapping signals), and 8.08 (1 H, s).

Preparation of Allene Derivative (**2f**).—A solution of pyrrolidin-2-one (0.058 mol) and 3-bromopropyne (0.070 mol) in toluene (50 ml) was treated with NaH (0.116 mol) and refluxed for 2.5 h. The undissolved material was filtered off and the solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. Distillation of the residue *in vacuo* gave the allene (**2f**),[24] 41%, b.p. 80–82 °C at 0.1 mmHg.

Preparation of Allene Derivatives (**2g,h**).—A solution of (**1**) (20 mmol) in THF (3 ml) was heated at 55 °C and treated with Bu^{t}OK (2.5 mmol). After 3 min, Bu^{t}OH (2.5 mmol) was added and the solvent was removed under reduced pressure. After addition of pentane (5 ml), the undissolved material was filtered off and the solution was submitted to fractional distillation to give the allene (**2**). Detailed data are as follows: (**2g**),[18] 39%, b.p. 75–77 °C at 10 mmHg, δ ($CDCl_3$) 2.75 (4 H, t, *J* 5), 3.77 (4 H, t, *J* 5), 5.29 (2 H, d, *J* 6), and 5.97 (1 H, t, *J* 6); (**2h**),[18] 45%, b.p. 40–45 °C at 10 mmHg, δ ($CDCl_3$) 1.08 (6 H, t, *J* 7), 2.88 (4 H, q, *J* 7), 5.23 (2 H, d, *J* 6), and 6.06 (1 H, t, *J* 6).

Reaction of Allenes (**2**) *with the Nitrile Oxide* (**4**).—A solution of the allene (**2**) (10 mmol) and nitrile oxide (**4**) (10 or 20 mmol) in tetrachloromethane (50 ml) was refluxed for the time indicated in Table 1. After evaporation of the solvent, the residue was chromatographed on a silica gel column. Eluants, products, and yields are given in Table 1. Physical, spectral, and analytical data of the products are collected in Tables 2 and 3.

In the case of the allene (**2g**), a side product was the *isoxazole* (**10g**), 6%, m.p. 192–193 °C (from benzene–hexane) (Found: C, 57.8; H, 5.8; N, 8.6. $C_{17}H_{20}Cl_2N_2O_2$ requires C, 57.5; H, 5.7; N, 8.8%); *m/z* 354 (M^+); δ ($CDCl_3$) 1.72 (3 H, s), 2.21 (6 H, s), 2.60 (3 H, s), 3.51 (4 H, t, *J* 5), and 3.89 (4 H, t, *J* 5). Similarly, the reaction of the allene (**2h**) gave, as a side product, the *isoxazole* (**10h**), 8%, m.p. 102–103 °C (from pentane) (Found: C, 59.9; H, 6.3; N, 8.2. $C_{17}H_{22}Cl_2N_2O$ requires C, 59.8; H, 6.5; N, 8.2%); *m/z* 340 (M^+); δ ($CDCl_3$) 1.26 (6 H, t, *J* 7), 1.72 (3 H, s), 2.22 (6 H, s), 2.60 (3 H, s), and 3.49 (4 H, q, *J* 7).

Reaction of Monoadducts (**5**) *with the Nitrile Oxide* (**4**).—A solution of (**5**) (1 mmol) and (**4**) (1 mmol) in tetrachloromethane (10 ml) was refluxed for 20–40 h. After evaporation of the solvent, the residue was triturated with di-isopropyl ether and collected by filtration to afford (**8**) in >90% yield. In the case of (**5d**), the reaction gave a 2:1 mixture of (**8d**) and (**9d**) (NMR analysis).

Reaction of the Allene (**2g**) *with the Nitrile Oxide* (**4**) *in Acetonitrile.*—A solution of (**2g**) (6 mmol) and (**4**) (6 mmol) in acetonitrile (30 ml) was refluxed for 2 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on a silica gel column with toluene–ethyl acetate (4:1) as eluant to give, in order of elution, diadduct (**8g**) (17%), isoxazole (**10g**) (6%), and monoadduct (**5g**) (67%).

Reaction of the Allene (**2g**) *with the Nitrile Oxide* (**4**) *in Ethanol.*—A solution of (**2g**) (14 mmol) and (**4**) (14 mmol) in ethanol (80 ml) was refluxed for 2 h. The solvent was removed

under reduced pressure and the residue was chromatographed on a silica gel column. Elution with toluene–ethyl acetate (4:1) gave (**10g**), 6%; (**5g**), 7%; and (**12**), 41%, m.p. 184–185 °C (from benzene–hexane) (Found: C, 57.0; H, 6.7; N, 7.0. $C_{19}H_{26}Cl_2N_2O_3$ requires C, 56.9; H, 6.5; N, 7.0%); *m/z* 400 (M^+); δ_H ($CDCl_3$) 1.11 (3 H, t, *J* 7), 2.35 (6 H, s), 2.56 (3 H, s), 2.6–3.1 (4 H, m), 3.2–3.6 (5 H, overlapping signals), 3.78 (4 H, t, *J* 5), and 5.30 (1 H, d, *J* 6); δ_C ($CDCl_3$) 14.7 (q), 18.7 (q), 19.0 (q), 48.0 (t), 53.1 (d), 66.6 (t), 66.8 (t), 67.5 (t), 100.4 (d), 128.7 (s), 133.8 (s), 135.3 (s), and 157.4 (s).

Further elution with toluene–ethyl acetate (1:1) gave (**15**), 10%, m.p. 153–155 °C (from benzene–hexane) (Found: C, 58.6; H, 6.0; N, 6.6. $C_{20}H_{24}Cl_2N_2O_3$ requires C, 58.4; H, 5.9; N, 6.8%); *m/z* 410 (M^+); ν_{max}(Nujol) 1 680 cm^{-1}; δ_H ($CDCl_3$) 2.30 (6 H, s), 2.3–2.5 (2 H, m), 2.53 (3 H, s), 2.6–3.0 (4 H, m), 3.5–3.8 (5 H, overlapping signals), 4.98 (1 H, d, *J* 6.5), 6.00 (1 H, s), 6.29 (1 H, s), and 9.42 (1 H, s); δ_C($CDCl_3$) 18.9 (q), 29.6 (t), 47.8 (t), 49.3 (d), 66.9 (t), 103.1 (d), 128.5 (s), 133.8 (s), 135.7 (t), 146.0 (s), 158.9 (s), and 193.5 (d).

Reaction of the Adduct (**12**) *with Sodium Ethoxide.*—A solution of (**12**) (0.10 g) in ethanol (10 ml) was treated with 0.8M sodium ethoxide in ethanol (0.32 ml) and refluxed for 2 h. The mixture was poured into water and extracted with benzene. The organic solution was dried (Na_2SO_4) and evaporated. The crude product was purified through a silica gel column with toluene–ethyl acetate (4:1) as eluant to afford (**5g**) in 53% yield.

Reaction of the Adduct (**5g**) *with Toluene*-p-*sulphonic Acid.*—A solution of (**5g**) (0.20 g) in ethanol (12 ml) was treated with toluene-*p*-sulphonic acid (60 mg) and refluxed for 4 h. The mixture was poured into water and the precipitate was collected by filtration to afford (**13**), 59%, m.p. 57–58 °C (from hexane) (Found: C, 57.3; H, 5.5; N, 4.3. $C_{15}H_{17}Cl_2NO_2$ requires C, 57.3; H, 5.4; N, 4.5%; *m/z* 313 (M^+); δ ($CDCl_3$) 1.10 (3 H, t, *J* 7), 2.13 (6 H, s), 2.59 (3 H, s), 3.39 (2 H, q, *J* 7), 4.10 (2 H, s), and 8.53 (1 H, s).

Reaction of the Adduct (**12**) *with Toluene*-p-*sulphonic Acid.*—A solution of (**12**) (0.15 g) in toluene (9 ml) was treated with toluene-*p*-sulphonic acid (45 mg) and refluxed for 4 h. The mixture was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. Chromatography of the residue on silica gel column with toluene–ethyl acetate (4:1) as eluant gave (**13**) in 45% yield.

Reaction of the Allene (**2g**) *with Ethanol.*—A solution of (**2g**) (2.6 g) in ethanol (8 ml) was refluxed for 2 h. The solvent was removed under reduced pressure and the residue was submitted to fractional distillation *in vacuo* to give (**11**) (1.2 g), b.p. 80–84 °C at 0.2 mmHg; *m/z* 171 (M^+); δ ($CDCl_3$) 1.22 (3 H, t, *J* 7), 2.90 (4 H, t, *J* 5), 3.3–4.0 (8 H, overlapping signals), 4.58 (1 H, dt, *J* 14 and 6), and 6.03 (2 H, d, *J* 14).

Reaction of Compound (**11**) *with the Nitrile Oxide* (**4**).—A solution of (**11**) (1.0 g) and (**4**) (1.4 g) in ethanol (30 ml) was refluxed for 2 h. After evaporation of the solvent, the residue was chromatographed on a silica gel column with toluene–ethyl acetate (2:1) as eluant to give (**12**) in 57% yield.

X-Ray Crystal Structure Analysis of (**8h**).—*3,3′-Bis*(3,5-*dichloro*-2,4,6-*trimethylphenyl*)-5-*diethylamino*-4,4′,5,5′-*tetrahydrospirobi*(4,5′-*isoxazole*).—Cell parameters and reflection intensities were measured with graphite-monochromated Mo-K_α radiation on an Enraf–Nonius CAD-4 diffractometer operating at room temperature in the ω scan mode for a crystal having approximate dimension 0.26 × 0.24 × 0.20 mm. The scan range was calculated from [1.00 + 0.35 tanθ]°. Reflections were scanned in the range $0 < \theta < 25°$. Three standard reflections measured every two hours showed no appreciable variation with time. The data were corrected for Lorentz and polarization effects but not for absorption. 4 969 unique reflections were collected of which 2 525 were considered to be observed [$I > 2\sigma(I)$] and used in the structure analysis.

Crystal data. $C_{27}H_{31}Cl_4N_3O_2$, M = 571.4, orthorhombic, space group *Pbca* (established from systematic absences), a = 9.471(1), b = 14.824(1), c = 40.312(4) Å, U = 5 659.7(9) Å^3, Z = 8, D_c = 1.267 g cm^{-3}, μ(Mo-K_α) = 4.5 cm^{-1}, λ(Mo-K_α) = 0.710 69 Å.

The structure was solved by direct methods;[25] the 'best' *E*-map gave all non-hydrogen atoms, excluding those of the two ethyl group that were obtained from difference Fourier maps; the last atoms have very large thermal parameters; partial disorder of the diethylamino group cannot be excluded. Hydrogen atoms of the last group together with those of C(18), C(29), C(31), and two of C(20) were included in calculated position but not refined. Final full-matrix least squares refinement for 366 parameters included atomic positions, thermal parameters (anisotropic for non-hydrogen atoms), a secondary extinction parameter, and an overall scale factor. The refinement was terminated when all shifts were less than 0.1σ with R 0.069 (R_w 0.055), GOF = 2.17. The function minimized was $\Sigma w(|F_o|-|F_c|)^2$ with weight $w = 4F_o^2/[\sigma(F_o^2) + 0.000\,4F_o^4]$. Final difference Fourier synthesis showed two residual peaks of about 0.6 e Å^{-3} near to C(35) and Cl(19). Programs used include SDP,[26] and various in-house programs for refinement and geometrical analysis running on a Gould 32/97 computer. Final atomic positional co-ordinates and equivalent isotropic thermal parameters are listed in Table 4. Selected bond lengths, bond angles, and torsion angles are given in Table 5. Tables of hydrogen atomic co-ordinates and anisotropic thermal parameters of heavy atoms have been deposited with the Cambridge Crystallographic Data Centre.*

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