Synthesis of Imidazoles from Alkenes[1]

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Alkenes are converted into imidazoles through their epoxides by a sequence involving ring-opening with readily available 2-tributylstannyltetrazoles (**8**), dehydration of the resulting alcohols (**9**) using methyltriphenoxyphosphonium iodide in an improved procedure to give 1-alkenyltetrazoles (**12**), which give imidazoles (**17**) on photolysis.

The importance of imidazoles in biological processes and the successful application of imidazoles as pharmaceutical products has stimulated considerable interest in their chemistry in recent years.[2] However, there is no single, widely applicable method available for the synthesis of the imidazole ring. We now report full details of a new imidazole synthesis which starts from alkenes.

The formation of five-membered heteroaromatic compounds by electrocyclic ring closure of dienyl and heterodienyl nitrenes is well established,[3,4] and in this connection we have previously described a synthesis of 2-phenylbenzimidazoles which involves cyclisation of *N*-arylimidoyl nitrenes (**1**; R = Ph) generated by photolysis of the corresponding sulphimides.[5] Photolysis of 1,5-diphenyltetrazole also gives 2-phenylbenzimidazole presumably *via* the same nitrene intermediate.[6] Cyclisation of *N*-vinylimidoyl nitrenes (**2**) would therefore be expected to give imidazoles. We now find that nitrenes (**2**), generated from 1-alkenyltetrazoles, do indeed cyclise to give imidazoles.

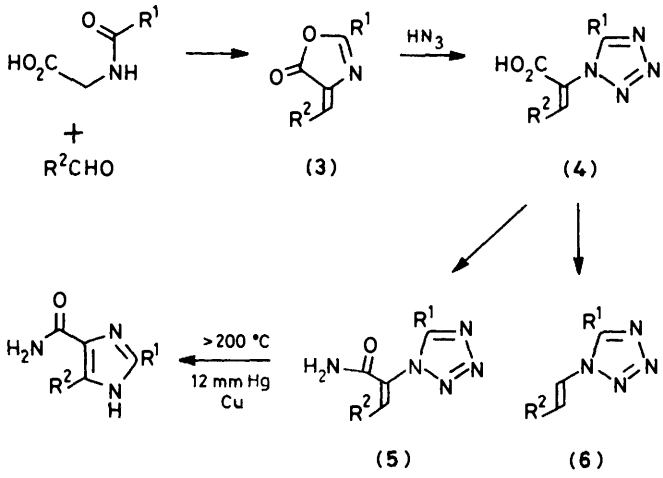
(1)

(2)

Results and Discussion

Four routes to 1-alkenyltetrazoles have been reported. The one most commonly used involves the azidolysis of azlactones (**3**) to give tetrazol-1-ylacrylic acids (**4**) (Scheme 1).[7–9] Standard transformations gave the acrylamides (**5**),[7] and copper-catalysed decarboxylation gave 1-(2-arylalk-1-enyl)tetrazoles (**6**).[8] The limitations of this route are that the condensation of the *N*-acylamino acid with the aldehyde only works well for aromatic aldehydes, and that the products necessarily bear a carboxy group on the 1-position of the alkene. Nevertheless copper-catalysed pyrolysis of the tetrazolylacrylamides (**5**) is reported to give imidazoles.[10]

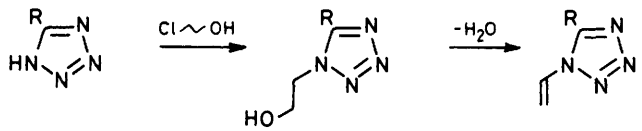
5-Aminotetrazole can be directly vinylated by treatment with vinyl acetate and mercury(II) acetate.[11] However, the conditions are somewhat harsh, and it is unlikely that the reaction would lead to selective 1-vinylation for other tetrazoles, since 5-aminotetrazole is known to show an exceptionally high preference for 1- rather than 2-alkylation.[12] 1-Vinyltetrazole itself has been prepared by reaction of ethereal hydrazoic acid with vinylisonitrile.[13] This is potentially an attractive route to



(3) (4) (5) (6)

Scheme 1.

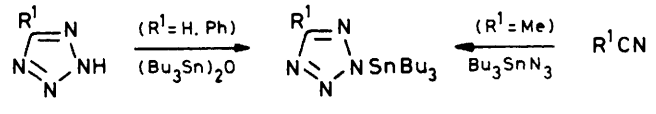
5-unsubstituted 1-alkenyltetrazoles in cases where the vinyl isonitriles are readily available. However, the preparation of such isonitriles can be tedious. The most promising route to 1-alkenyltetrazoles involved the alkylation of tetrazoles with 2-chloroethanol followed by a two-step dehydration (Scheme 2).[14] However, the route is limited by the poor regioselectivity in the alkylation step.



Scheme 2.

Alkylation of Tetrazoles using Epoxides.—Nevertheless we consider β-hydroxyalkyl tetrazoles to be attractive precursors to the required alkenyl derivatives. In principle they could be prepared by alkylation of tetrazoles with epoxides, readily available from the corresponding alkenes. However, this reaction presents two problems in that tetrazole anions are poor nucleophiles and might not react with epoxides, and are usually alkylated predominantly on N-2.[12] Both of these difficulties were overcome by using 2-tributylstannyltetrazoles,[15] rather than alkali-metal salts. The 2-tributylstannyl derivatives (**8**) of tetrazole, 5-methyltetrazole, and 5-phenyltetrazole were readily prepared by standard methods as shown in Scheme 3, and are shelf-stable materials.

Epoxides are ring opened under mild conditions by treatment with the stannyltetrazoles (**8**) in ether at room temperature, or, in some cases, in refluxing benzene. Cleavage of the stannyl

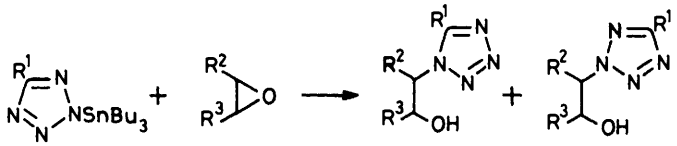


(7) (8)

a; R^1 = H
b; R^1 = Me
c; R^1 = Ph

Scheme 3.

Table 1. Ring opening of epoxides with 2-tri-n-butylstannyltetrazoles



(8) (9) (10)

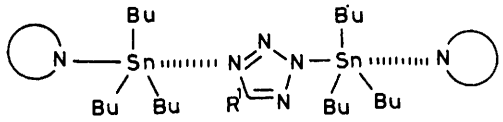
(9), (10)	R^1	R^2	R^3	Procedure[a]	Yield (9) (%)	Yield (10) (%)
a	H	H	H	A	36	28
				B	44	28
				C	43	16
b	H	H	Me	A	33	37
				B	46	42
c	Me	H	Me	C	70	20
d	Ph	H	H	A	80	8
e	Ph	H	Me	A	69	7
				B	78	18
f	Ph	$-[CH_2]_4-$		A	57	15
g	Ph	H	Ph	D	45	6
h	Ph	Ph	H	D	34	7
i	Ph	Ph	CO_2Et	D	72	10

[a] Procedure A: i, (8) + epoxide, ether, room temp.; ii, excess of HX. Procedure B: i, (7) + epoxide + 10 mol % (8), ether, room temp.; ii, HOAc. Procedure C: i, (7) + epoxide + 5 mol % $(Bu_3Sn)_2O$, ether, room temp.; ii, HOAc. Procedure D: i, (8) + epoxide, benzene, reflux; ii, HX.

ethers with hydrogen chloride or acetic acid gave 1-(2-hydroxyalkyl)tetrazoles (**9**) in moderate to good yield (Table 1). In all cases a mixture of 1- and 2-alkylated tetrazoles was formed. Chromatography gave the required 1-isomers, which in the case of the 5-phenyl and 5-methyl tetrazoles (**8c**) and (**8b**) were the major products. In most cases the ratio of 1- to 2-alkylation was greater than 4:1.

However, the 5-unsubstituted tetrazole (**8a**) gave poor regioselectivity in the alkylation reaction. The ratio and the overall yield was improved by using the stannyltetrazole catalytically (Procedure B), or generating the stannyltetrazole *in situ* by addition of catalytic amounts of $(Bu_3Sn)_2O$ (Procedure C). This last procedure is the method of choice since it is the easiest to carry out.

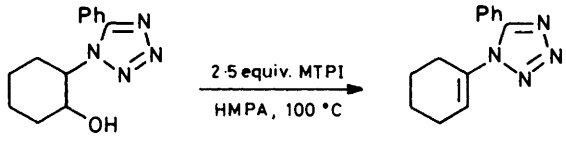
The poor regioselectivity shown by (**8a**) is puzzling since sterically the absence of a substituent at C-5 would be expected to favour 1-alkylation, and based on a consideration of their relative acidities, electronically the 5-unsubstituted derivative would be expected to be intermediate between the 5-methyl and 5-phenyl derivatives. The anomalous behaviour of the stannyl derivative (**8a**) may be related to the fact that in concentrated solution in non-polar solvents, tributylstannyltetrazoles are polymeric.[16] Evidence that the polymeric form might be involved in the alkylation with epoxides was obtained by running the reaction in methanol, a solvent which is known to disrupt this type of aggregation, which caused a pronounced reduction in the rate of reaction. The size of the substituent R^1 in the aggregated structure (**11**) would be expected to affect the strength of co-ordination of N-4 to the highly hindered tin, and leads to the prediction that the N(4)–Sn interaction would be strongest for R^1 = H. The overall effect of this strong co-ordination might be to suppress alkylation at N-1 (N-4) hence explaining the poor selectivity shown by the 5-unsubstituted tetrazole (**8a**).



(11)

The alkylation reaction proceeds well for a range of epoxides, and the ease of the reaction may result in part from the development of a strong tin–oxygen bond in the transition state. The possibility of Lewis acid type behaviour by the tin is supported by the formation, from styrene oxide, of 41% of products [(**9h**) + (**10h**)] resulting from attack of the substituted carbon, whereas exclusive attack at the unsubstituted position would be expected from a pure S_N2 reaction. Likewise, ethyl phenylglycidate underwent attack exclusively at the phenyl-bearing carbon.

Dehydration of 1-(2-Hydroxyalkyl)tetrazoles.—Initial attempts to effect the required dehydration to 1-alkenyltetrazoles were conducted on the cyclohexanol derivative (**9f**). Reaction with phosphorus oxychloride in pyridine gave no identifiable products, and a blank experiment showed that the alcohol was unstable in pyridine. The alcohol was unchanged after refluxing with toluene-4-sulphonic acid (PTSA) in xylene, and treatment with triphenylphosphine and carbon tetrachloride in refluxing acetonitrile gave only 6% of dehydrated product. An attempt to prepare the chloride by refluxing with thionyl chloride was also unsuccessful, the alcohol surviving unchanged. Dehydration was finally accomplished by treatment with methyltriphenoxyphosphonium iodide (MTPI) in hexamethylphosphoramide (HMPA) at 100 °C for 41 h, and gave a mixture of the required vinyl (**12f**) (74%) and the allyl (**13**) (14%) tetrazoles. This reagent system[17] converts alcohols into iodides, which are then dehydroiodinated by the excess of MTPI, iodide being a good base in dipolar aprotic solvents.



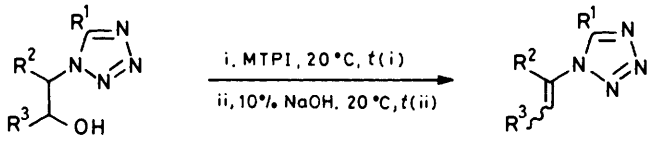
(9f) (12f)

+

(13)

It was later found that better results are obtained by using 1 equiv. of MTPI in HMPA at room temperature to form the

Table 2. Dehydration of 2-hydroxyalkyltetrazoles



(9) (12)

(9), (12)	R^1	R^2	R^3	Solvent	t(i)[a] (h)	t(ii)[b] (h)	Yield(12) (%)
a	H	H	H	DMF	4	27	69
b	H	H	Me	DMF	4	15	67
c	Me	H	Me	DMF	6	5	73
d	Ph	H	H	HMPA	3	1	93
				DMF	4	14	76
e	Ph	H	Me	HMPA	76	2	86
				DMF	22	2	83
f	Ph	$-[CH_2]_4-$		HMPA	24	3	79
g	Ph	H	Ph	HMPA	19	1	85
h	Ph	Ph	H	HMPA	19	1	89
i	Ph	Ph	CO_2Et	HMPA	10	0.75[c]	0

[a] 1—10 h sufficient; some times longer than necessary. [b] 1—2 h sufficient; some times longer than necessary. [c] NaOEt–EtOH used as base.

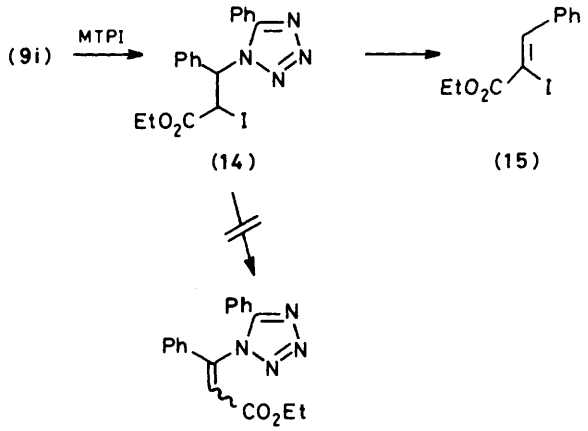
iodides, and pouring the reaction mixture into 10% aqueous sodium hydroxide to effect the elimination. This variation was successfully employed in the dehydration of the 1-(2-hydroxyalkyl)tetrazoles (**9a**—**h**) (Table 2).

The yields of 1-alkenyltetrazoles (**12**) were excellent in the 5-phenyl series, but were lower for the 5-methyl and 5-unsubstituted compounds because the product alkenes were water soluble. Extraction from the aqueous phase and separation of the alkene from HMPA which was co-extracted caused considerable loss of product. However, the use of dimethylformamide (DMF) as solvent improved the yield considerably because it could be separated without significant losses. Trial experiments using DMF in the 5-phenyl series suggested that it is marginally inferior to HMPA because on treatment with the aqueous base some reversion of the iodide to the alcohol occurred. This difference was most marked in the primary alcohol (**9d**).

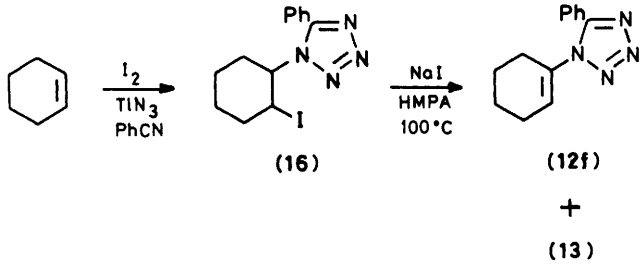
N.m.r. spectroscopy of the resulting alkenes showed them to be the *trans*-isomers, although very small amounts of the *cis*-isomers were formed in the reactions carried out in DMF. Excellent regioselectivity was observed in that the propanols (**9b**, **c**, **e**) gave the prop-1-enyltetrazoles exclusively, and in the cyclohexanol case (**9f**) the yield of the unwanted isomer (**13**) was reduced to less than 5%.

This modified dehydration procedure offers several advantages over the original method.[17] Only a slight excess of MTPI is required as opposed to over 2 equiv. used previously. Milder conditions are used, and the method which was previously only applicable to secondary alcohols, is extended to cover primary alcohols. This is because primary alkyl iodides, inert to the original procedure, are readily dehydroiodinated under the aqueous basic conditions. The work-up is also greatly facilitated since the by-product, diphenyl methylphosphonate, is hydrolysed and therefore remains in the aqueous layer. The required vinyltetrazoles are obtained in high purity.

Unfortunately the method failed completely for the β-tetrazolyl ester (**9i**) because, in the intermediate iodide (**14**), elimination of 5-phenyltetrazole to give the iodocinnamate (**15**) was favoured over loss of hydrogen iodide. This ready elimination of tetrazoles from β-tetrazolyl esters is well known,[18] and it also frustrated other attempts to dehydrate (**9i**). The synthesis of the required tetrazolylacrylates has subsequently been achieved by a different route.[19]



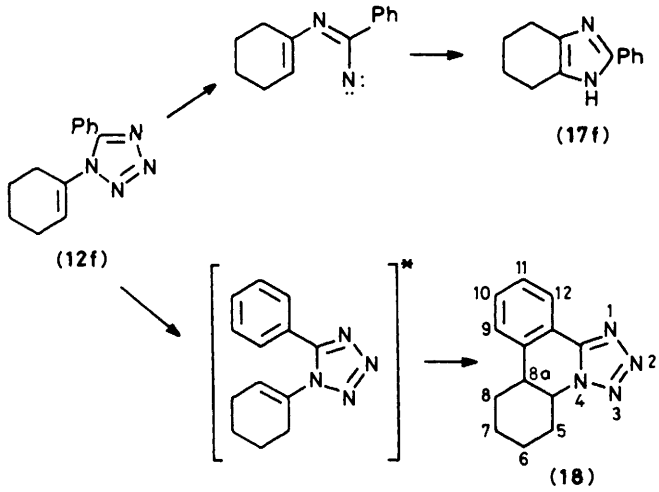
The cyclohexenyltetrazole (**12f**) was also prepared by an alternative but less satisfactory route. Reaction of cyclohexane with iodine and thallium(I) azide in benzonitrile[20] gave the iodocyclohexyltetrazole (**16**) in low yield (8%). Although dehydroiodination to the required tetrazole (**12f**) could be achieved in good yield (74%) [along with a small amount of the unwanted allyl isomer (**13**)] using sodium iodide in HMPA, the route was abandoned in favour of the epoxide method.



The alkenyltetrazoles (**12a**—**h**) show C=C stretching absorptions in the i.r. spectrum in regions expected of non-conjugated olefins indicating that the interaction between the heterocyclic ring and the C=C is not very substantial. However, the u.v. spectra show marked bathochromic shifts in going from the alcohols (**9**) to the alkenes (**12**) suggesting that there is significant conjugation of the heterocyclic nucleus with the alkene.

Preparation of Imidazoles from 1-Alkenyltetrazoles.—Irradiation of the 1-alkenyltetrazoles (**12**) in a variety of solvents did give the required imidazoles, but the initial experiments showed that other products were also formed. For example, irradiation of the cyclohexenyltetrazole (**12f**) at 254 nm in acetonitrile gave the imidazole (**17f**) in only 30% yield. The major product (**43%**), an isomer of the starting material, was assigned the structure (**18**). The imidazole probably arises *via* cyclisation of the imidoyl nitrene as expected, and the fused tetrazole is probably formed by a photocyclisation reaction[21] in an excited state, followed by a rapid aromatisation by hydrogen shift (Scheme 4).

It was found that the yields of imidazoles were highly dependent on the conditions, so the effects of solvent, wavelength, and additives were studied. By analysis of the crude photolysate by n.m.r. spectroscopy, several trends were



Scheme 4.

apparent. In the 5-phenyl series the yields of imidazole were best when the photolysis was carried out in light petroleum (b.p. 60—80 °C). Ethanol gave slightly poorer results, but addition of an acid (>2 mol) such as PTSA or trifluoroacetic acid (TFA) improved the yield, and made it competitive with petroleum as solvent. Other solvents were much inferior and in the case of the cyclohexenyltetrazole (**12f**) for example, the ratio of imidazole (**17f**) to photocyclised product (**18**) decreased from 4:1 in petroleum, through 1.5:1 in ethanol and 1:2 in acetonitrile, to 1:4 in acetone. The trend for the 5-methyl series was also quite clear, water being the best solvent for the photolysis. Photolysis of the 5-unsubstituted tetrazole (**12b**) also gave the best yields in water, but the results in petroleum and ethanol were very similar.

Butler has pointed out that in tetrazole–imidoyl azide equilibria, the azide form is favoured in non-polar solvents, in protic solvents, and in the presence of acid.[12] These are just the conditions which gave the best yields of imidazoles in our photolyses. Thus it is possible that the primary photochemical process is ring-opening of the tetrazoles and that the imidazoles are formed by subsequent photolysis of the resulting azides.

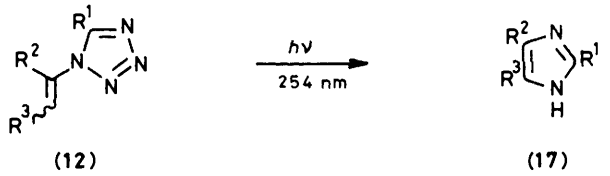
The tetrazole (**12e**) ($\lambda_{max.}$ 240 nm) gave the corresponding imidazole quite cleanly when irradiated at 254 nm but irradiation at 300 nm gave a complex mixture. However, the tetrazole (**12g**) ($\lambda_{max.}$ 284 nm) gave similar results from photolyses at 254 and 300 nm. The photolyses were apparently insensitive to the presence of acetone, a triplet sensitiser, and α-methylstyrene, a triplet quencher.

With these factors in mind, the tetrazoles were photolysed on a preparative scale, and although optimisation was not attempted in every case, the yields of imidazoles were generally quite good (Table 3), although the yield of 2-unsubstituted imidazoles were somewhat variable.

The competing photocyclisation was only a minor reaction except in the case of 1-substituted vinyltetrazoles, where under certain conditions it was the major pathway. The solvent dependence of the imidazole to photocyclisation product ratio has already been described for the cyclohexenyltetrazole (**12f**). The 1-phenylvinyltetrazole (**12h**) gave only 38% of the required imidazole on photolysis in ethanol, and was accompanied by the photocyclised tetrazole (**19**) (7%) and a 1-aminoisoquinoline (**20**) (21%) which has the skeleton of the photocyclised product. The mechanism by which (**20**) is formed is unclear, a blank experiment having ruled out the possibility that it arose by further photolysis of (**19**).

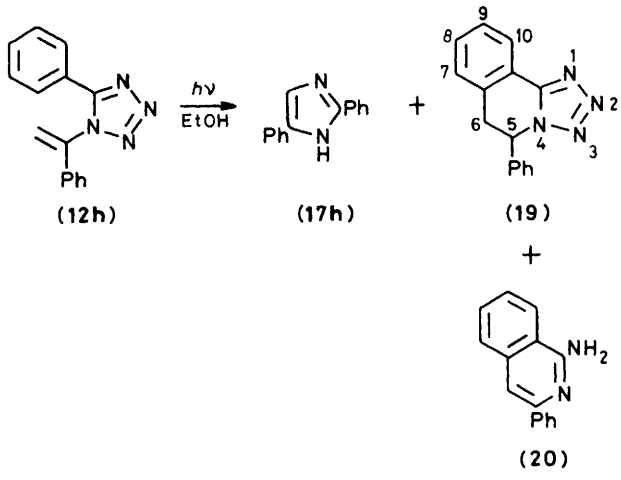
Some exploratory experiments on the thermal decomposition of the tetrazole (**12e**) were also carried out. Thermolysis in the melt at 240 °C gave a complex mixture containing only a small amount of the imidazole (**17e**), and although the use of diphenyl ether as solvent gave a much cleaner product, the yield of the imidazole was only *ca.* 25%. Addition of copper powder and bis(acetylacetonato)copper(II) to the solution thermolysis gave

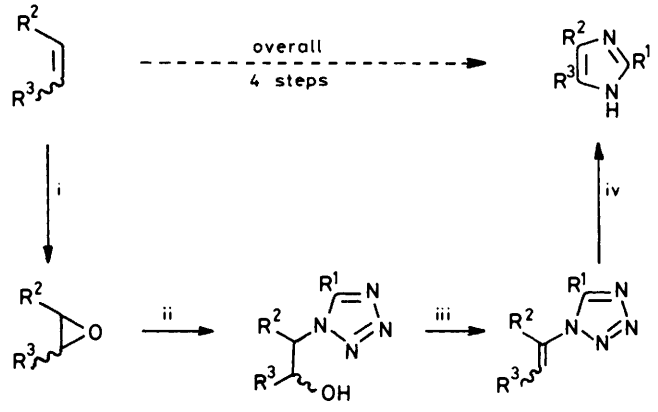
Table 3. Preparation of imidazoles



(12), (17)	R^1	R^2	R^3	Solvent	Yield (17) (%)
a	H	H	H	EtOH	32
b	H	H	Me	EtOH	62
c	Me	H	Me	H_2O	73
d	Ph	H	H	2.5 mol TFA–EtOH	61
e	Ph	H	Me	Petroleum[a]	66
f	Ph	$-[CH_2]_4-$		Petroleum[a]	64
g	Ph	H	Ph	Petroleum[a]	66
h	Ph	Ph	H	EtOH	38

[a] Light petroleum, b.p. 60—80 °C





Scheme 5. *Reagents:* i, peracid; ii, 5-R^1-2-tributylstannyltetrazole, ether, room temp., then HX; iii, MTPI, HMPA or DMF, room temp., then 10% aq. NaOH; iv, *hν*, 254 nm.

more complex product mixtures. Flash vacuum pyrolysis of the tetrazole again gave a complex mixture, containing very little of the imidazole.

Conclusions.—The route to imidazoles *via* 1-alkenyltetrazoles, which is summarised in Scheme 5, differs from the majority of imidazole syntheses.[2] Most of these are based on α-substituted ketones, which can be difficult to obtain, and harsh conditions are often necessary. The present method is based on alkenes, uses readily available reagents, and proceeds under mild conditions.

Experimental

I.r. spectra were recorded for liquids as thin films and for solids as Nujol mulls on a Perkin Elmer 298 spectrophotometer, and calibrated against polystyrene. U.v. spectra were recorded in ethanol on a Pye Unicam SP800 spectrophotometer. ^{1}H N.m.r. spectra were recorded at 90 MHz, or at 250 MHz using Perkin Elmer R32 or Bruker WM250 spectrometers. Unless otherwise stated the data given refers to the 90 MHz spectrum, with $CDCl_3$ as solvent. ^{13}C N.m.r. spectra were recorded on the Bruker instrument at 62.9 MHz. Mass spectra were recorded using a VG Micromass 7070B instrument. Column chromatography was carried out on silica gel H (type 60) or alumina 60H (basic) (type E). Photolyses were carried out in quartz vessels in a Rayonet photochemical reactor using lamps emitting at 254 or 300 nm. Petroleum refers to light petroleum, b.p. 60—80 °C unless otherwise stated. Ether refers to diethyl ether.

2-*Tri-n-butylstannyltetrazole* (**8a**).—A mixture of 1*H*-tetrazole (**7a**) (212 mg, 3.03 mmol) and tri-n-butylstannyl oxide (902 mg, 1.51 mmol) in ethanol (2.5 ml) was refluxed under nitrogen for 2 h. Removal of the solvent gave the tetrazole (**8a**), as an oil, which was used without further purification.

5-*Methyl*-2-*tri-n-butylstannyltetrazole* (**8b**).[16]—This was prepared from acetonitrile and tri-n-butylstannyl azide[22] in 83% yield after distillation, m.p. 49—55 °C (lit.,[16] 49—50 °C).

5-*Phenyl*-2-*tri-n-butylstannyltetrazole* (**8c**).—This was prepared from 5-phenyltetrazole and tri-n-butylstannyl oxide in 98% yield after recrystallisation, m.p. 66—71 °C (lit.,[16] 66—67 °C).

Ring Opening of Epoxides with 2-*Tri-n-butylstannyltetrazoles.—General procedure A.* A solution of the stannyltetrazole (**8**) and the epoxide (1.0—2.5 mol equiv.) in ether [1—2 ml per 1 mmol of (**8**)] was stirred at room temperature until no (**8**) remained (t.l.c., ^{1}H n.m.r.). Excess of hydrogen chloride or acetic acid was added and the mixture was stirred for 1—2 h. In some cases the crude products crystallised at this stage and separation of the isomeric tetrazoles was achieved by recrystallisation of the major product followed by chromatography of the residues on silica gel. Otherwise the solvent was removed and the products were isolated by chromatography, immediately, or after washing with cold petroleum to remove stannyl salts. Preparations carried out using procedure A are as follows.

1-(2-*Hydroxyethyl*)*tetrazole* (**9a**). Reaction of (**8a**) (4.60 g, 12.8 mmol) and ethylene oxide (1.6 ml, 32 mmol) in ether (10 ml) for 43 h followed by quenching with acetic acid (0.73 ml, 12.8 mmol), washing with petroleum, and chromatography on alumina gave 2-(2-hydroxyethyl)tetrazole (**10a**) (415 mg, 28%) as an oil; $\nu_{max.}$ 3 400, 2 960, 1 370, 1 290, 1 195, 1 140, 1 075, 875, and 705 cm^{-1}; δ 4.17 (2 H, t, *J* 5 Hz), 4.47 (1 H, br s), 4.83 (2 H, t, *J* 5 Hz), and 8.57 (1 H, s); *m/z* 115 (M^+), 71 and 55; which was characterised as the 3,5-*dinitrobenzoate ester*, m.p. 117—119 °C (from chloroform–petroleum) (Found: C, 39.0; H, 2.5; N, 27.0. $C_{10}H_8N_4O_6$ requires C, 39.0; H, 2.6; N, 27.3%), and 1-(2-hydroxyethyl)tetrazole (**9a**) (531 mg, 36%) as an oil; $\nu_{max.}$ 3 380, 2 960, 1 484, 1 430, 1 172, 1 104, 1 065, 972, and 869 cm^{-1}; δ[$(CD_3)_2CO$] 4.04 (2 H, t, *J* 6 Hz), 4.48 (1 H, br s), 4.68 (2 H, t, *J* 6 Hz), and 9.07 (1 H, s); *m/z* 115 (M^+ + 1), 84, 83, 71, and 55; which was characterised as the 3,5-*dinitrobenzoate ester*, m.p. 178—180 °C (from acetone–petroleum) (Found: C, 39.0; H, 2.5; N, 27.1. $C_{10}H_8N_6O_6$ requires C, 39.0; H, 2.6; N, 27.3%).

1-(2-*Hydroxypropyl*)*tetrazole* (**9b**). Reaction of (**8a**) (2.75 g, 7.66 mmol) and propylene oxide (0.804 ml, 11.5 mmol) in ether (7 ml) for 36 h, followed by quenching with acetic acid (0.44 ml, 7.66 mmol) and chromatography on alumina, gave 2-(2-hydroxypropyl)tetrazole (**10b**) (361 mg, 37%) as an oil; $\nu_{max.}$ 3 400, 2 980, 1 362, 1 283, 1 143, 1 027, 994 and 712 cm^{-1}; δ 1.29 (3 H, d, *J* 6 Hz), 3.78 (1 H, br d, *J* 5 Hz), 4.25—4.60 (1 H, m), 4.70 (2 H, d, *J* 6 Hz), and 8.54 (1 H, s); *m/z* 113, 84, 55, and 45, which was characterised as the 3,5-*dinitrobenzoate ester*, m.p. 114—116 °C (from chloroform–petroleum) (Found: C, 40.9; H, 3.0; N, 25.8. $C_{11}H_{10}N_6O_6$ requires C, 41.0; H, 3.1; N, 26.1%), and 1-(2-hydroxypropyl)tetrazole (**9b**) (325 mg, 33%) as an oil; $\nu_{max.}$ 3 380, 2 980, 1 429, 1 175, 1 108, 958, 847, 754, and 668 cm^{-1}; δ 1.28 (3 H, d, *J* 7 Hz), 4.10—4.80 (4 H, m), and 8.89 (1 H, s); *m/z* 129 (M^+ + 1), 84, 69, 55, and 45, which was characterised as the 3,5-*dinitrobenzoate ester*, m.p. 167—170 °C (from acetone–petroleum) (Found: C, 41.1; H, 3.1; N, 26.0. $C_{11}H_{10}N_6O_6$ requires C, 41.0; H, 3.1; N, 26.1%).

1-(2-*Hydroxyethyl*)-5-*phenyltetrazole* (**9d**). The tetrazole (**8c**) (4.14 g, 9.74 mol) was allowed to react with ethylene oxide (0.73 ml, 14.6 mmol) in ether (15 ml) for 3 days after which the reaction was quenched with hydrogen chloride, and the products were chromatographed on silica gel, to give 2-(2-*hydroxyethyl*)-5-*phenyltetrazole* (**10d**) (139 mg, 8%), m.p. 65 °C (from chloroform–petroleum) (Found: C, 56.8; H, 5.3; N, 29.6. $C_9H_{10}N_4O$ requires C, 56.8; H, 5.3; N, 29.5%); $\nu_{max.}$ 3 320, 1 528, 1 450, 1 149, 1 074, 862, 793, 736, 720, and 695 cm^{-1}; δ 3.55 (1 H, t, *J* 6 Hz), 4.07—4.37 (2 H, m), 4.77 (2 H, t, *J* 5 Hz), 7.35—7.63 (3 H, m), and 7.90—8.23 (2 H, m); *m/z* 190 (M^+), 162, 131, 104 (base), and 77, and 1-(2-*hydroxyethyl*)-5-*phenyltetrazole* (**9d**) (1.474 g, 80%), m.p. 79—80 °C (from chloroform–petroleum) (Found: C, 57.0; H, 5.3; N, 29.6. $C_9H_{10}N_4O$ requires C, 56.8; H, 5.3; N, 29.5%); $\nu_{max.}$ 3 290, 1 439, 1 232, 1 129, 1 080, 953, 864, 785, 742, 711, and 696 cm^{-1}; δ 4.0—4.3 (2 H, m), 4.3—4.6 (3 H, m, 1 H exch. D_2O), 7.45—7.65 (3 H, m), and 7.65—7.9 (2 H, m); *m/z* 190 (M^+), 147, 131, 118, 104, 90, 77 (base), and 45.

1-(2-*Hydroxypropyl*)-5-*phenyltetrazole* (**9e**). The tetrazole (**8c**) (10.59 g, 24.9 mmol) was allowed to react with propylene oxide (1.92 ml, 27.4 mmol) in ether (30 ml) for 90 h, after which the reaction was quenched with hydrogen chloride, and the products were purified by fractional recrystallisation from ethanol–water followed by chromatography on silica gel, to give 2-(2-*hydroxypropyl*)-5-*phenyltetrazole* (**10e**) (356 mg, 7%), m.p. 52—55 °C (from chloroform–petroleum) (Found: C, 58.6; H, 5.9; N, 27.3. $C_{10}H_{12}N_4O$ requires C, 58.8; H, 5.9; N, 27.4%); $\nu_{max.}$ 3 320, 1 533, 1 396, 1 130, 1 066, 940, 845, 782, 730, and 689 cm^{-1}; δ 1.28 (3 H, d, *J* 7 Hz), 3.52 (1 H, d, *J* 5 Hz), 4.20—4.75 (3 H, m), 7.25—7.60 (3 H, m), and 7.95—8.25 (2 H, m); *m/z* 204 (M^+), 176, 131 (base), 104, and 77, and 1-(2-*hydroxypropyl*)-5-*phenyltetrazole* (**9e**) (3.52 g, 69%), m.p. 90—92 °C (from chloroform–petroleum) (Found: C, 58.8; H, 5.9; N, 27.4. $C_{10}H_{12}N_4O$ requires C, 58.8; H, 5.9; N, 27.4%); $\nu_{max.}$ 3 340, 1 409, 1 301, 1 131, 944, 850, 785, 773, 742, and 711 cm^{-1}; $\lambda_{max.}$ 230 nm (ε 9 600); δ 1.29 (3 H, d, *J* 8 Hz), 4.15—4.70 (4 H, m), and 7.35—7.95 (5 H, m); *m/z* 205, 204, (M^+) 160, 147, 131, 118, 117, 104 (base), and 77.

1-(2-*Hydroxycyclohexyl*)-5-*phenyltetrazole* (**9f**). Tetrazole (**8c**) (17.35 g, 40.8 mmol) was allowed to react with cyclohexene oxide (4.0 g, 40.8 mmol) in ether (40 ml) for 140 h. The reaction was quenched by washing with hydrochloric acid (1M; 50 ml), the solution was washed with aqueous sodium hydroxide and

with water, dried with sodium sulphate, and concentrated; the products were isolated by fractional crystallisation from dichloromethane–petroleum followed by chromatography on silica gel, to give 2-(2-*hydroxycyclohexyl*)-5-*phenyltetrazole* (**10f**) (1.53 g, 15%), m.p. 107—108.5 °C (from dichloromethane–petroleum) (Found: C, 64.2; H, 6.6; N, 23.1. $C_{13}H_{16}N_4O$ requires C, 63.9; H, 6.6; N, 22.9%); $\nu_{max.}$ 3 375, 1 074, 962, 802, 734, and 694 cm^{-1}; δ 1.1—2.4 (8 H, m), 3.71 (1 H, d, *J* 7 Hz, exch. D_2O), 4.18 (1 H, m), 4.58 (1 H, ddd, *J* 6, 11, 12 Hz), 7.45 (3 H, m), and 8.04 (2 H, m); *m/z* 244 (M^+), 216, 104 (base), 103, 57, 56, and 43, and 1-(2-*hydroxycyclohexyl*)-5-*phenyltetrazole* (**9f**) (5.67 g, 57%), m.p. 156—158 °C (from dichloromethane–petroleum) (Found: C, 63.75; H, 6.7; N, 22.6. $C_{13}H_{16}N_4O$ requires C, 63.9; H, 6.6; N, 22.9%); $\nu_{max.}$ 3 355, 1 069, 959, 778, 740, and 700 cm^{-1}; δ 1.0—2.4 (8 H, m), 4.0—4.4 (2 H, m), 4.66 (1 H, br s, exch. D_2O), 7.56 (3 H, m), and 7.77 (2 H, m); *m/z* 244 (M^+), 216, 173 (base), 147, 118, 104, 88, 81, and 77.

General procedure B. A suspension of the 5-substituted tetrazole (**7**) in a solution of the stannyltetrazole (**8**) (0.1 mol equiv.) and the epoxide (1.5—2.5 mol equiv.) in ether [1—10 ml per 1 mmol of (**8**)] were stirred at room temperature until no (**7**) remained. As the reaction approached completion the tetrazole (**7**) was seen to disappear and in some cases the alkylated products separated from the reaction mixture as an oil. When carried out on a very small scale (< 1 mmol) no acid was added and the crude product was chromatographed directly. On a larger scale acetic acid (0.1 mol equiv.) or hydrogen chloride (excess) was added to the mixture and stirring was continued for 1 h. The solvent was removed and the products were chromatographed. Prepared according to this procedure were the following.

1-(2-*Hydroxyethyl*)*tetrazole* (**9a**). Reaction of tetrazole (316 mg, 4.51 mol) and the stannyl derivative (**8a**) (181 mg, 0.505 mmol) with ethylene oxide (0.643 ml, 12.9 mmol) in ether (2 ml) for 25 h, followed by quenching with hydrogen chloride and chromatography on alumina gave the 2-alkyltetrazole (**10a**) (28%) and the 1-alkyltetrazole (**9a**) (254 mg, 44%).

1-(2-*Hydroxypropyl*)*tetrazole* (**9b**). Reaction of tetrazole (1.00 g, 14.3 mmol) and the stannyl derivative (**8a**) (569 mg, 1.585 mmol) with propylene oxide (1.50 ml, 21.4 mmol) in ether (2 ml) for 23 h, followed by quenching with acetic acid (91 μl, 1.59 mmol) and chromatography on alumina gave the 2-alkyltetrazole (**10b**) (777 mg, 42%) and the 1-alkyltetrazole (**9b**) (849 mg, 46%).

1-(2-*Hydroxypropyl*)-5-*phenyltetrazole* (**9e**). Reaction of 5-phenyltetrazole (139 mg, 0.953 mmol) and the stannyl derivative (**8c**) (40 mg, 0.0953 mmol) with propylene oxide (100 μl, 1.43 mmol) in ether (1 ml) for 90 h, followed by chromatography on silica gel, gave the 2-alkyltetrazole (**10e**) (34 mg, 18%) and the 1-alkyltetrazole (**9e**) (153 mg, 78%).

General procedure C. A suspension of the 5-substituted tetrazole (**7**) in a solution of tri-n-butylstannyl oxide (0.05 mol equiv.) and the epoxide (1.5—2.5 mol equiv.) in ether (2—5 ml per 1 mmol of stannyl oxide) were stirred at room temperature until no (**7**) remained. Work-up and separation are as described for procedure B. Prepared according to this procedure were the following.

1-(2-*Hydroxyethyl*)*tetrazole* (**9a**). Reaction of tetrazole (360 mg, 5.14 mmol) with tri-n-butylstannyl oxide (153 mg, 0.257 mmol) and ethylene oxide (0.642 ml, 12.8 mmol) in ether (2 ml) for 25 h, followed by quenching with hydrogen chloride and chromatography on alumina, gave the 2-alkyltetrazole (**10a**) (93 mg, 16%) and the 1-alkyltetrazole (**9a**) (254 mg, 43%).

1-(2-*Hydroxypropyl*)-5-*methyltetrazole* (**9c**) Reaction of 5-methyltetrazole (705 mg, 8.38 mmol) with tri-n-butylstannyl oxide (500 mg, 0.838 mmol) and propylene oxide (0.88 ml, 12.6 mmol) in ether (2 ml) for 39 h, followed by quenching with acetic acid (96.2 μl, 1.68 mmol) and chromatography on alumina, gave 2-(2-hydroxypropyl)-5-methyltetrazole (**10c**) (242 mg, 20%) as an oil; $\nu_{max.}$ 3 420, 2 985, 1 503, 1 071, 943, 847, and 795 cm^{-1}; δ 1.27 (3 H, d, *J* 6 Hz), 2.49 (3 H, s), and 4.2—4.8 (4 H, m); *m/z* 143 (M^+ + 1), 127, 114, 98, 83, 69, 45, and 42 (base), and 1-(2-hydroxypropyl)-5-methyltetrazole (**9c**) (839 mg, 70%), as an oil; $\nu_{max.}$ 3 380, 2 985, 1 527, 1 409, 1 134, 1 057, 941, 845, and 773 cm^{-1}; δ 1.29 (3 H, d, *J* 6 Hz), 2.54 (3 H, s), and 3.83—4.83 (4 H, m); *m/z* 143 (M^+ + 1), 127, 112, 99, 98, and 69.

General procedure D. Carried out exactly as procedure A except that the reaction was conducted in refluxing benzene. The following compounds were prepared by this procedure.

1-(2-*Hydroxy*-2-*phenylethyl*)-5-*phenyltetrazole* (**9g**). The tetrazole (**8c**) (5.19 g, 12.21 mmol) was allowed to react with styrene oxide (1.67 ml, 14.65 mmol) in benzene (15 ml) at reflux for 10 h, after which the reaction was quenched with hydrogen chloride and the products were washed with petroleum and chromatographed on silica gel, to give 2-(2-*hydroxy*-2-*phenylethyl*)-5-*phenyltetrazole* (**10g**) (184 mg, 6%), m.p. 100.5—102 °C (from chloroform–petroleum) (Found: C, 67.4; H, 5.3; N, 20.9. $C_{15}H_{14}N_4O$ requires C, 67.65; H, 5.3; N, 21.0%); $\nu_{max.}$ 3 245, 3 155, 1 206, 1 062, 744, 731, and 691 cm^{-1}; δ 3.87 (1 H, d, *J* 4 Hz, exch. D_2O), 4.08—4.98 (2 H, m), 5.37 (1 H, ddd, *J* 4, 5, 6 Hz), 7.25—7.55 (8 H, m), and 7.95—8.18 (2 H, m); *m/z* 266 (M^+), 238, 210, 160, 132, 131, 107, 104, 79, and 77, and 2-(2-*hydroxy*-1-*phenylethyl*)-5-*phenyltetrazole* (**10h**) (232 mg, 7%), m.p. 92—95 °C (from chloroform–petroleum) (Found: C, 67.5; H, 5.3; N, 20.9%); $\nu_{max.}$ 3 285, 1 341, 1 070, 791, 741, 733, 701, and 693 cm^{-1}; δ 3.79 (1 H, t, *J* 6 Hz, exch. D_2O), 4.06—4.42 (1 H, m), 4.52—4.88 (1 H, m), 6.12 (1 H, dd, *J* 4, 9 Hz), 7.25—7.65 (8 H, m), and 8.0—8.23 (2 H, m); *m/z* 266 (M^+), 238, 207, 131, 104, 103, 91, and 77, and 1-(2-*hydroxy*-2-*phenylethyl*)-5-*phenyltetrazole* (**9g**) (1.465 g, 45%), m.p. 108—118 °C (from chloroform–petroleum) (Found: C, 67.9; H, 5.3; N, 21.1. $C_{15}H_{14}N_4O$ requires C, 67.65; H, 5.3; N, 21.0%); $\nu_{max.}$ 3 240, 1 413, 1 304, 1 068, 941, 781, 746, 735, 706, and 700 cm^{-1}; δ 4.33—4.70 (2 H, m), 4.74 (1 H, d, *J* 4 Hz), 5.21—5.54 (1 H, m), 7.28 (5 H, br s), and 7.35—7.75 (5 H, m); *m/z* 267, 266 (M^+), 160 (base), 159, 107, 104, 79, and 77, and 1-(2-*hydroxy*-1-*phenylethyl*)-5-*phenyltetrazole* (**9h**) (1.107 g, 34%), m.p. 130—132 °C (from chloroform–petroleum) (Found: C, 67.4; H, 5.3; N, 20.9. $C_{15}H_{14}N_4O$ requires C, 67.65; H, 5.3; N, 21.0%); $\nu_{max.}$ 3 370, 1 543, 1 068, 864, 774, 735, 722, 712, and 701 cm^{-1}; δ 3.3—3.65 (1 H, br, exch. D_2O), 3.95—4.25 (1 H, m), 4.50—4.90 (1 H, m), 5.72 (1 H, dd, *J* 4, 10 Hz), and 7.2—7.75 (10 H, m); *m/z* 267, 266 (M^+), 236 (base), 207, 193, 160, 105, 104, 103, and 77.

1-(2-*Ethoxycarbonyl*-2-*hydroxy*-1-*phenylethyl*)-5-*phenyltetrazole* (**9i**). The tetrazole (**8c**) (2.02 g, 4.75 mmol) was allowed to react with ethyl 3-phenylglycidate (1.10 g, 5.70 mmol) in benzene (5 ml) at reflux for 22 h, after which the reaction was quenched with hydrogen chloride; the products were then washed with petroleum and chromatographed on silica gel, to give 2-(2-*ethoxycarbonyl*-2-*hydroxy*-1-*phenylethyl*)-5-*phenyltetrazole* (**10i**) (164 mg, 10%), m.p. 103—105 °C (from chloroform–petroleum) (Found: C, 63.9; H, 5.3; N, 16.6. $C_{18}H_{18}N_4O_3$ requires C, 63.9; H, 5.4; N, 16.6%); $\nu_{max.}$ 3 490, 1 722, 1 238, 1 162, 1 105, 842, 733, 727, 706, and 688 cm^{-1}; δ 1.07 (3 H, t, *J* 7.5 Hz), 3.68 (1 H, br d, *J* 4.5 Hz), 4.14 (2 H, q, *J* 7.5 Hz), 5.14—5.36 (1 H, m), 6.30 (1 H, d, *J* 6 Hz), 7.25—7.67 (8 H, m), and 8.0—8.3 (2 H, m); *m/z* 338 (M^+), 236, 207, 146, 118, 104, 91, and 77; and 1-(2-*ethoxycarbonyl*-2-*hydroxy*-1-*phenylethyl*)-5-*phenyltetrazole* (**9i**) (1.162 g, 72%), m.p. 119—123 °C (from chloroform–petroleum) (Found: C, 63.6; H, 5.3; N, 16.6. $C_{18}H_{18}N_4O_3$ requires C, 63.9; H, 5.4; N, 16.6%); $\nu_{max.}$ 3 370, 1 744, 1 293, 1 240, 1 217, 1 111, 796, 746, 711, 700, and 692 cm^{-1}; δ 1.06 (3 H, t, *J* 7 Hz), 4.09 (2 H, q, *J* 7 Hz), 4.75 (1 H, br s), 5.16 (1 H, d, *J* 7 Hz), 5.89 (1 H, d, *J* 7 Hz), 7.36 (5 H, s), and 7.53 (5 H, s); *m/z* 338 (M^+), 236, 207, 146, 118, 104, 91, and 77.

Dehydration of the 2-Hydroxyalkyltetrazoles.—Attempted dehydrations of 1-(2-*hydroxycyclohexyl*)-5-*phenyltetrazole* (**9f**). (a) *Phosphorus oxychloride in pyridine.* A solution of phosphorus oxychloride (0.5 ml) in dry pyridine (2 ml) was added dropwise to a stirred solution of the alcohol (**9f**) (100 mg, 0.409 mmol) in pyridine (2 ml). The solution was stirred for 5.5 h and refluxed for 0.5 h, after which it was cooled and poured carefully into water (30 ml). It was extracted with ether, and the extract was washed with hydrochloric acid (1M), sodium hydrogencarbonate (1M), and water, and then dried over sodium sulphate and concentrated. T.l.c. showed three products in very small amounts.

(b) *PTSA.* A solution of the alcohol (**9f**) (100 mg) and PTSA monohydrate (50 mg) in toluene (5 ml) was refluxed in a Dean and Stark apparatus for 5 days. T.l.c. showed the product to consist predominantly of starting material and baseline products. A similar result was obtained after refluxing under nitrogen in xylene for 3 days.

(c) *Triphenylphosphine–carbon tetrachloride.* A solution of the alcohol (**9f**) (100 mg, 0.409 mmol), triphenylphosphine (129 mg, 0.491 mmol), and carbon tetrachloride (86.4 μl, 0.818 mmol) in dry acetonitrile (10 ml) was refluxed under nitrogen for 75 h. The solution was concentrated and chromatographed on silica gel to give the alcohol (**9f**) (82 mg, 82%) and 1-(cyclohex-2-enyl)-5-phenyltetrazole (**13**) (6 mg, 6%).

(d) *Thionyl chloride.* A solution of the alcohol (**9f**) (100 mg) in thionyl chloride (2 ml) was refluxed for 20 h. T.l.c. showed that only starting material was present.

(e) *Methyltriphenoxyphosphonium iodide in HMPA.*[17] A solution of the alcohol (**9f**) (142 mg, 0.581 mmol) and MTPI (0.656 g, 1.45 mmol) in HMPA (4 ml) was stirred at 100 °C for 41 h. Water (40 ml) was added and the solution was extracted with ether (3 × 30 ml). The extracts were washed with saturated aqueous sodium chloride (2 × 40 ml) and dried over sodium sulphate. The solvent was removed and the residue chromatographed on silica gel, to give 1-(*cyclohex*-1-*enyl*)-5-*phenyltetrazole* (**12f**) (96 mg, 74%), m.p. 102.5—104.5 °C (from chloroform–petroleum) (Found: C, 69.3; H, 6.2; N, 24.5. $C_{13}H_{14}N_4$ requires C, 69.0; H, 6.2; N, 24.8%); $\nu_{max.}$(CCl_4) 2 945, 1 675, 1 458, 1 402, 1 124, 922, and 693 cm^{-1}; $\lambda_{max.}$ 236 nm (ε 10 900); δ 1.4—2.5 (8 H, m), 6.06 (1 H, m), 7.06 (3 H, m), and 7.78 (2 H, m); *m/z* 227, 226 (M^+), 198, 197, 144, 130 (base), 117, and 103, and 1-(*cyclohex*-2-*enyl*)-5-*phenyltetrazole* (**13**) (19 mg, 14%), m.p. 95—98 °C (from chloroform–petroleum) (Found: C, 68.9; H, 6.3; N, 24.7. $C_{13}H_{14}N_4$ requires C, 69.0; H, 6.2; N, 24.8%); $\nu_{max.}$ 1 390, 1 152, 939, 836, 784, and 701 cm^{-1}; δ 1.5—2.4 (6 H, m), 5.05—5.35 (1 H, m), 5.62—5.85 (1 H, m), 5.98—6.30 (1 H, m), and 7.50—7.80 (5 H, m); *m/z* 226 (M^+), 169, 155, 142, 129, 103, 91, 90, 81 (base), and 79.

General Procedure for Dehydrations using MTPI.—A solution of the tetrazolyl alcohol (**9**) and MTPI (1.2—2.0 mol equiv.) in dry HMPA or dry DMF (2—4 ml per 1 g of MTPI) was stirred at room temperature until t.l.c. indicated that no alcohol remained. The solution was poured into 10% aqueous sodium hydroxide (10 ml per 1 ml of HMPA–DMF) and stirred at room temperature until t.l.c. showed that no iodide or phosphonate remained. The products were then isolated by filtration or by extraction with ether, and purified by recrystallisation or chromatography. Prepared according to this procedure were the following.

1-*Vinyltetrazole* (**12a**). 1-(2-Hydroxyethyl)tetrazole (**9a**) (690 mg, 6.05 mmol) was allowed to react with MTPI (3.42 g, 7.56 mmol) in DMF (10 ml) for 4 h and with aqueous hydroxide for 27 h, and the product was isolated by continuous extraction with ether and chromatography on silica gel, to give the alkenyltetrazole (**12a**) (400 mg, 69%); $\nu_{max.}$ 3 117, 1 648, 1 473, 1 094, 958, 920, and 668 cm^{-1}; $\lambda_{max.}$ 224 nm (ε 6 100); δ 5.60 (1 H, dd, *J* 2.9 Hz), 6.22 (1 H, dd, *J* 2, 18 Hz), 7.65 (1 H, dd, *J* 9, 18 Hz), and 9.52 (1 H, s); *m/z* 96 (M^+), 68, 67, 53, 42, 41, 40, and 39.

trans-1-(*Prop*-1-*enyl*)*tetrazole* (**12b**). 1-(2-Hydroxypropyl)-tetrazole (**9b**) (723 mg, 5.64 mmol) was allowed to react with MTPI (3.19 g, 7.05 mmol) in DMF (10 ml) for 4 h and with aqueous hydroxide for 15 h, after which the product was isolated by continuous extraction with ether followed by chromatography on silica gel, to give the *alkenyltetrazole* (**12b**) (418 mg, 67%), m.p. 57—58 °C (from chloroform–petroleum) (Found: C, 43.9; H, 5.5; N, 50.9. $C_4H_6N_4$ requires C, 43.6; H, 5.45; N, 50.9%); $\nu_{max.}$ 3 125, 1 674, 1 664, 1 549, 1 406, 1 200, 1 173, 1 106, 949, and 770 cm^{-1}; $\lambda_{max.}$ 229 nm (ε 7 350); δ 1.98 (3 H, dd, *J* 2, 7 Hz), 6.66 (1 H, dq, *J* 7, 14 Hz), 7.32 (1 H, dq, *J* 2, 14 Hz), and 9.2 (1 H, s); *m/z* 111, 110 (M^+), 81, 55, 54, 41, 39, and 28.

trans-5-*Methyl*-1-(*prop*-1-*enyl*)*tetrazole* (**12c**). 1-(2-Hydroxypropyl)-5-methyltetrazole (**9c**) (1.953 g, 13.74 mmol) was treated with MTPI (7.82 g, 17.29 mmol) in DMF (25 ml) for 6 h and aqueous hydroxide for 5 h, and the product was isolated by continuous extraction with ether followed by chromatography on silica gel, to give the alkenyltetrazole (**12c**) (1.240 g, 73%), m.p. 40—42 °C (from benzene–petroleum) (Found: C, 48.5; H, 6.5; N, 45.2. $C_5H_8N_4$ requires C, 48.4; H, 6.5; N, 45.1%); $\nu_{max.}$ 1 680, 1 516, 1 408, 1 258, 1 123, 1 074, 947, 806, and 672 cm^{-1}; $\lambda_{max.}$ 226 nm (ε 7 100); δ 1.97 (3 H, dq, *J* 1, 7 Hz), 2.62 (3 H, s), 6.55 (1 H, dq, *J* 7, 14 Hz), and 6.88 (1 H, dq, *J* 1, 14 Hz), *m/z* 125, 124 (M^+), 95, 81, 69, 68, 55, 54, 42, 41, and 28.

5-*Phenyl*-1-*vinyl-tetrazole* (**12d**). (i) *In HMPA.* 1-(2-Hydroxyethyl)-5-phenyltetrazole (**9d**) (660 mg, 3.47 mmol) was treated with MTPI (2.51 g, 5.55 mmol) in HMPA (10 ml) for 3 h and with aqueous hydroxide for 1 h, and the product was isolated by filtration, to give pure *alkenyltetrazole* (**12d**) (554 mg, 93%), m.p. 104—106 °C (from chloroform–petroleum) (Found: C, 62.8; H, 4.7; N, 32.3. $C_9H_8N_4$ requires C, 62.8; H, 4.7; N, 32.5%); $\nu_{max.}$ 1 641, 1 413, 1 162, 959, 919, 781, 751, 700, and 663 cm^{-1}; $\lambda_{max.}$ 239 nm (ε 11 800), δ 5.50 (1 H, dd, *J* 2, 9 Hz), 6.22 (1 H, dd, *J* 2, 16 Hz), 7.14 (1 H, dd, *J* 9, 16 Hz), and 7.52—7.87 (5 H, m); *m/z* 173, 172 (M^+), 177 (base), and 77.

(ii) *In DMF.* The alcohol (**9d**) (186 mg, 0.978 mmol) was treated with MTPI (550 mg, 1.22 mmol) in DMF (1 ml) for 4 h and with aqueous hydroxide for 1.4 h, and the product was isolated by filtration to give the alkenyltetrazole (128 mg, 76%), m.p. 103—105 °C.

trans-5-*Phenyl*-1-(*prop*-1-*enyl*)*tetrazole* (**12e**). (i) *In HMPA.* 1-(2-Hydroxypropyl)-5-phenyltetrazole (**9e**) (3.44 g, 16.86 mmol) was treated with MTPI (10.15 g, 22.4 mmol) in HMPA (40 ml) at room temperature for 20 h and at 50 °C for 6 h and with aqueous hydroxide for 2 h, and the product was isolated by extraction with ether and Kugelrohr distillation at 125 °C/0.05 mbar, to give the pure *alkenyltetrazole* (**12e**) (2.70 g, 86%), m.p. 60—63 °C (from chloroform–petroleum) (Found: C, 64.8; H, 5.4; N, 30.3. $C_{10}H_{10}N_4$ requires C, 64.5; H, 5.4; N, 30.1%); $\nu_{max.}$ 1 412, 942, 785, 739, 708, and 689 cm^{-1}; $\lambda_{max.}$ 240 nm (ε 12 000); δ 1.96 (3 H, d, *J* 5 Hz), 6.50—7.05 (2 H, m), and 7.05—7.9 (5 H, m); *m/z* 187, 186 (M^+), 158, 157, 131, 130, 104, 103, and 77.

(ii) *In DMF.* The alcohol (**9e**) (145 mg, 0.712 mmol) was treated with MTPI (550 mg, 1.22 mmol) in DMF (2 ml) for 22 h and with aqueous hydroxide for 2 h, and the product was isolated by extraction with chloroform to give the alkenyltetrazole (**12e**) (110 mg, 83%).

1-(*Cyclohex*-1-*enyl*)-5-*phenyltetrazole* (**12f**). A solution of the cyclohexanol (**9f**) (74 mg, 0.30 mmol) was treated with MTPI (250 mg, 0.553 mmol) in HMPA (1 ml) for 24 h and with aqueous hydroxide for 3 h, and the product was isolated by filtration, to give the alkenyltetrazole (**12f**) (54 mg, 79%), m.p. 94—100 °C; data already given.

trans-1-(2-*Phenylvinyl*)-5-*phenyltetrazole* (**12g**). The phenylethanol (**9g**) (1.272 g, 4.78 mmol) was treated with MTPI (3.78 g, 8.36 mmol) in HMPA (25 ml) for 19 h and with aqueous

hydroxide for 1 h, after which the product was isolated by extraction with ether and recrystallisation from chloroform–petroleum, to give the *alkenyltetrazole* (**12g**) (1.015 g, 85%), m.p. 147—149 °C (from chloroform–petroleum) (lit.,[8] m.p. 75—77 °C) (Found: C, 72.4; H, 5.0; N, 22.6. $C_{15}H_{12}N_4$ requires C, 72.6; H, 4.9; N, 22.6%); $\nu_{max.}$ 1 407, 1 133, 947, 775, 759, 733, and 699 cm^{-1}; $\lambda_{max.}$ 284 nm (ε 17 700) and 243 (13 100); δ 7.4—8.0 (m); *m/z* 249, 248 (M^+), 219, 193, 117, 90, and 87.

1-(1-*Phenylvinyl*)-5-*phenyltetrazole* (**12h**). The phenylethanol (**9h**) (780 mg, 2.93 mmol) was treated with MTPI (2.65 g, 5.86 mmol) in HMPA (10 ml) for 19 h and with aqueous hydroxide for 2 h, after which the product was isolated by extraction with ether and recrystallisation from chloroform–petroleum, to give the *alkenyltetrazole* (**12h**) (647 mg, 89%), m.p. 89.5—90.5 °C (from chloroform–petroleum) (Found: C, 72.3; H, 4.9; N, 22.5. $C_{15}H_{12}N_4$ requires C, 72.6; H, 4.9; N, 22.6%); $\nu_{max.}$ 1 643, 1 465, 1 405, 914, 781, 776, 737, 702, 696, and 632 cm^{-1}; $\lambda_{max.}$ 243 nm (ε 20 300); δ 5.63 (1 H, d, *J* 1 Hz), 6.09 (1 H, d, *J* 1 Hz), 7.05—7.77 (8 H, m), and 7.7—7.95 (2 H, m); *m/z* 249, 248 (M^+), 220, 219, 180, 129, 118, 117 (base), 103, 85, and 77.

Attempted dehydration of 1-(2-*ethoxycarbonyl*-2-*hydroxy*-1-*phenylethyl*)-5-*phenyltetrazole* (**9i**). A solution of the alcohol (**9i**) (157 mg, 0.464 mmol) and MTPI (440 mg, 0.973 mmol) in HMPA (2 ml) was stirred for 10 h, and poured into water (25 ml). After 12 h the precipitated crystals were filtered off, to give 1-(2-*ethoxycarbonyl*-2-*iodo*-1-*phenylethyl*)-5-*phenyltetrazole* (**14**) (55 mg, 26%), m.p. 170—172 °C (from chloroform–petroleum) (Found: C, 48.0; H, 3.8; N, 12.2. $C_{18}H_{17}IN_4O_2$ requires C, 48.2; H, 3.8; N, 12.5%); $\nu_{max.}$ 1 723, 1 265, 1 182, 1 138, 782, 755, 725, and 702 cm^{-1}; δ 1.02 (3 H, t, *J* 7 Hz), 4.02 (2 H, q, *J* 7 Hz), 5.54 (1 H, d, *J* 12 Hz), 5.89 (1 H, d, *J* 12 Hz), 7.27—7.75 (5 H, m), and 7.64 (5 H, s); *m/z* 448 (M^+), 247, 219, 207, 176, 148, 147, 132, 131, 104, 103, 77, and 76. Extraction of the aqueous phase with ether and concentration yielded a further crop of the iodoalkyltetrazole (26 mg, 13%). A solution of sodium ethoxide (33 mg, 0.48 mmol) in ethanol (0.5 ml) was added dropwise to a stirred suspension of the iodoalkyltetrazole (**14**) (40 mg, 0.0892 mmol) in ethanol (1 ml) and stirring was continued for 45 min. The mixture was poured into hydrochloric acid (1M; 10 ml) and extracted with ether (3 × 5 ml). The extract was washed with water, dried, and concentrated, to give a mixture of ethyl 2-iodocinnamate (**15**) and 5-phenyltetrazole (**7c**).

Preparation of 1-(*Cyclohex*-1-*enyl*)-5-*phenyltetrazole* (**12f**) *from Cyclohexene*.—(a) Cyclohexene (2.09 g, 25.5 mmol) was treated with iodine (8.10 g, 31.9 mmol) and thallium(I) azide[23] (15.72 g, 63.8 mmol) in benzonitrile (215 ml) according to a literature method,[20] to give 1-(2-*iodocyclohexyl*)-5-*phenyltetrazole* (**16**) (0.757 g, 8%), m.p. 154—155 °C (from ethanol) (Found: C, 43.85; H, 4.2; N, 15.7. $C_{13}H_{15}IN_4$ required C, 44.1; H, 4.3; N, 15.8%); $\nu_{max.}$ 1 174, 971, 782, 773, 727, 686, and 661 cm^{-1}; δ 1.2—2.9 (8 H, m), 4.3—4.9 (2 H, m), and 7.5—7.8 (5 H, m); *m/z* 354 (M^+), 227, 199, 147, 131, and 81 (base).

(b) A solution of the iodide (**16**) (100 mg, 0.284 mmol) and sodium iodide (43 mg, 0.284 mmol) in HMPA (2.5 ml) was heated at 100 °C for 24 h. Water (20 ml) was added and the solution was extracted with ether (3 × 20 ml). The extracts were washed with water (30 ml), dried with sodium sulphate, and concentrated to give 1-(cyclohex-1-enyl)-5-phenyltetrazole (**12f**) (64 mg, 74%).

Preparation of Imidazoles by Photolysis of 1-*Alkenyltetrazoles*.—*General procedure*. Solutions of the tetrazoles in the solvents specified (75—150 ml per 1 mmol of tetrazole) were irradiated with light of 254 nm wavelength, in quartz vessels, with nitrogen passing through the solution. Irradiation was continued until no tetrazole remained (t.l.c.) (the durations are given for comparison purposes) and the imidazoles were isolated as described below. No attempts were made to identify minor (< 5%) by-products.

1-*Vinyltetrazole* (**12a**). A solution of (**12a**) (191 mg, 1.99 mmol) in ethanol (150 ml) was irradiated for 40 min. The solvent was removed and the residue was distilled at 75 °C at 0.33 mmHg to give imidazole (**17a**) (43.6 mg, 32%), m.p. 86—89 °C (lit.,[24] 88—89 °C).

trans-1-(*Prop*-1-*enyl*)*tetrazole* (**12b**). A solution of (**12b**) (222 mg, 2.02 mmol) in ethanol (150 ml) was irradiated for 1 h. The solvent was removed and the residue was chromatographed on alumina, to give 4-methylimidazole (**17b**) (103 mg, 62%), m.p. 53—55 °C (after distillation) (lit.,[25] 56 °C).

trans-1-(*Prop*-1-*enyl*)-5-*methyltetrazole* (**12c**). A solution of (**12c**) (293 mg, 2.36 mmol) in water (10 ml) was irradiated for 3.5 h. The solvent was evaporated and the residue was chromatographed on alumina, to give 2,4-dimethylimidazole (**17c**) (165.5 mg, 73%), m.p. 88—91 °C (from chloroform–petroleum) (lit.,[25] 92 °C).

5-*Phenyl*-1-*vinyltetrazole* (**12d**). A solution of (**12d**) (102 mg, 0.592 mmol) and TFA (0.114 ml, 1.48 mmol) in ethanol (40 ml) was irradiated for 2.5 h. The solvent was removed and the residue was chromatographed on alumina, to give 2-phenylimidazole (**17d**) (52 mg, 61%), m.p. 138—148 °C (lit.,[26] 148—149 °C).

trans-5-*Phenyl*-1-(*prop*-1-*enyl*)*tetrazole* (**12e**). A solution of (**12e**) (408 mg, 2.19 mmol) in petroleum (175 ml) was irradiated for 4.25 h. The precipitate was filtered off, washed with petroleum, and sublimed at 140 °C at 2 mmHg, to give 4-methyl-2-phenylimidazole (**17e**) (229 mg, 66%), m.p. 180—183 °C (lit.,[27] 181—182 °C).

1-(*Cyclohex*-1-*enyl*)-5-*phenyltetrazole* (**12f**). A solution of (**12f**) (71 mg, 0.312 mmol) in petroleum (40 ml) was irradiated for 6 h. The precipitate was filtered off and washed with petroleum to give 2-phenyl-4,5-tetramethyleneimidazole (**17f**) (40 mg, 64%), m.p. 295—297 °C (lit.,[28] 298 °C). The petroleum was evaporated and the residue was chromatographed on alumina, to give 4a,5,6,7,8,8a-*hexahydrotetrazolo*[1,5-f]*phenanthridine* (**18**) (8.5 mg, 12%), m.p. 148—150 °C (from chloroform–petroleum) (Found: C, 68.7; H, 6.3; N, 24.7. $C_{13}H_{14}N_4$ requires C, 69.0; H, 6.2; N, 24.8%); $\nu_{max.}$ 1 611, 1 544, 785, 771, 744, 724, and 700 cm^{-1}; δ (250 MHz), 1.45—1.7 (3 H, m), 1.7—1.95 (1 H, m), 1.95—2.17 (2 H, m), 2.5—2.7 (2 H, m), 2.7—2.9 (1 H, m), 2.2—3.1 (2 H, m), 2.92 (1 H, ddd, *J* 3.8, 11.3, 12.7 Hz), 7.3—7.6 (3 H, m), and 8.04—8.12 (1 H, m); δ_C 23.8 (t), 25.0 (t), 26.6 (t), 29.2 (d), 42.4 (d), 59.5 (d), 121.4 (s), 124.6 (d), 125.8 (d), 127.9 (d), 131.9 (d), 137.5 (s), and 150.6 p.p.m. (s); *m/z* 226 (M^+, base), 197, 169, 141, 129, and 115.

trans-1-(2-*Phenylvinyl*)-5-*phenyltetrazole* (**12g**). A solution of (**12g**) (256 mg, 1.03 mmol) in petroleum (350 ml) was irradiated for 3 h. The solvent was removed and the residue was chromatographed on silica gel, to give 2,4-diphenylimidazole (**17h**) (150 mg, 66%); as noted previously[29,30] the m.p. varied with the solvent of recrystallisation but a good correlation with the literature values could not be obtained. A sample was prepared according to the literature method,[29] and was identical with the photolysate by i.r.

1-(1-*Phenylvinyl*)-5-*phenyltetrazole* (**12h**). A solution of the tetrazole (**12h**) (248 mg, 1.00 mmol) in ethanol (75 ml) was irradiated for 3 h. The solvent was removed and the residue was dissolved in chloroform (20 ml) and extracted with hydrochloric acid (1M, 2 × 10 ml). The insoluble hydrochloride was filtered off and washed with water. It was suspended in water (10 ml) and the solution was basified by addition of 10% aqueous sodium hydroxide. It was extracted with chloroform (3 × 10 ml) and the extracts were washed with water (10 ml) and dried over magnesium sulphate. The solvent was removed to give 2,4-diphenylimidazole (**17g**) (83 mg, 38%). The chloroform solution was evaporated to dryness, the residue was dissolved in ether

(5 ml), and a saturated solution of hydrogen chloride in ether (5 ml) was added to give a precipitate which was filtered off and washed with ether. It was dissolved by shaking with a mixture of chloroform (10 ml) and aqueous sodium hydroxide (1M; 5 ml). The extract was washed with water (5 ml) and dried with magnesium sulphate, and the solvent was removed to give 1-amino-3-phenylisoquinoline (**20**) (47 mg, 21%), m.p. 97.5—99 °C (from chloroform–petroleum) (lit.,[31] 99.0—99.5 °C); $\nu_{max.}(CHCl_3)$ 3 520, 3 410, 2 935, 1 623, 1 612, 1 567, and 1 414 cm^{-1}; δ (250 MHz) 5.23 (1 H, br s, exch. D_2O), 7.33—7.43 (1 H, approx. t), 7.43—7.56 (3 H, approx. t), 7.51 (1 H, s), 7.58—7.69 (1 H, approx. t), 7.74—7.86 (2 H, approx. t), and 8.03—8.13 (2 H, approx. d); *m/z* 220 (M^+, base), 194, 165, 110, 109.5, and 69. The ether solution of non basic components was evaporated to give *5-phenyl-5,6-dihydrotetrazolo*[5,1-a]*isoquinoline* (**19**) (17 mg, 7%) (Found: M^+, 248.1068. $C_{15}H_{12}N_4$ requires *M*, 248.1062); δ (250 MHz) 3.52 (1 H, dd, *J* 5, 16 Hz), 3.76 (1 H, dd, *J* 5, 16 Hz), 5.98 (1 H, t, *J* 5 Hz), 7.05—7.13 (2 H, m), 7.2—7.4 (4 H, m), 7.4—7.54 (2 H, m), and 8.16—8.24 (1 H, m); *m/z* 248 (M^+), 219, 147, 122, 105 (base), 77, and 57.

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