

Acylation, Alkylation and Sulphonation Reactions of Ethyl 5-(4-Hydroxyphenoxy)-1*H*-*v*-triazole-4-carboxylate (1)

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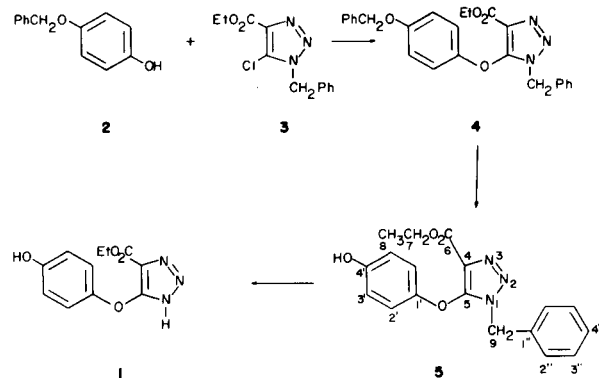
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The alkylation of 5-(4-hydroxyphenoxy)-1*H*-*v*-triazolecarboxylate (**1**) under alkaline conditions was shown to yield exclusively isomeric N-2 and N-3 alkylation products, the structures of which were assigned by ir, ¹H nmr and ¹³C nmr spectroscopy. Acylation and sulphonation under similar conditions resulted in exclusive attack at the phenolic oxygen of **1**, possibly by the migration of an initially formed *N*-derivative.

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As part of a program relating to the synthesis of novel antiallergic triazole compounds (**2,3**) we were interested in the selective protection of the triazole moiety of the intermediate **1** so that subsequent functionalisation of the hydroxyl group could be effected. Little is known of easily removable triazole protecting groups, although the benzyl (**4**), 4-toluenesulphonyl (**5**) and tropylium (**6**) groups have been used. We decided to investigate the acylation, sulphonation and alkylation of **1** in an attempt to find a procedure for reversibly blocking the triazole moiety. This work ultimately led to a study into the structural elucidation of the products formed by reaction of this system with selected electrophiles.

Scheme



Since **1** offers four potential sites for attack, three at nitrogen and one at oxygen, an initial problem was to determine at which centre attack had occurred. The location of the position of substitution of multisite nitrogen heterocycles has been a problem for many years and a variety of techniques to determine this have been used. The wider use of ¹³C nmr spectroscopy over the past few years has contributed considerably to the facility with

which isomer identification can be carried out and we have used this technique coupled with ¹H nmr and ir spectroscopy to assign the structures of our products.

Discussion.

The intermediate triazole **1** was prepared as shown in the scheme. Reaction of ethyl 1-benzyl-5-chloro-*v*-triazole-4-carboxylate (**3**) (**3,4b**) with the anion of 4-benzyloxyphenol, prepared *in situ* in *N,N*-dimethylformamide, afforded the *O,N*-dibenzyltriazole **4** in good yield. Partial hydrogenolysis of **4** at atmospheric pressure results in clean removal of the *O*-benzyl group to give **5** which on further hydrogenolysis at 1000 psi and 80-100° gave **1**. Simultaneous removal of both the *O*- and *N*-benzyl groups of **4** could be effected using the more forcing conditions.

Alkylation of the triazole **1** with either benzyl or 4-methoxybenzyl chlorides under alkaline conditions furnished a 1:1 mixture of two isomers which were readily separated by chromatographic methods. In the case of the unsubstituted benzyl derivatives direct comparison with authentic N-1 benzyl compound **5** clearly established that this was different to the two new isomers. An unambiguous assignment of each isomer was made using a combination of ir, ¹H nmr and ¹³C nmr spectroscopy, from which they were assigned the structures of the N-2 and N-3 benzyl compounds **6a** and **6b** respectively.

Similarly by direct comparison of spectral data the 4-methoxybenzyl isomers were shown to be the N-2 **7a** and N-3 **7b** derivatives.

Alkylation of **1** with 4-bromophenacyl bromide did not give a 1:1 mixture of N-2 and N-3 products but resulted instead in a preferential substitution at the N-2 position to give **8a** and **8b** in 65% and 14% yields respectively. With trityl chloride a marked steric preference for the least hindered N-2 position was observed with **9a** being formed almost exclusively. Trace amounts of the N-3 isomer **9b** were isolated however. The absence of alkylation at N-1

Table I
Ethyl 5-Aryloxy-*v*-triazole-4-carboxylates

Compound No.	Yield %	Mp °C	Recrystallisation Solvent	Formula	Analyses, %			Br/S
					C	H	N	
6a	44	95-96	ether-petroleum ether (a)	C ₁₈ H ₁₇ N ₃ O ₄	63.71	5.05	12.38	
					63.66	5.24	12.10	
6b	40	103-104	toluene-petroleum ether (a)	C ₁₈ H ₁₇ N ₃ O ₄	63.71	5.05	12.38	
					64.02	4.80	12.32	
7a	45	95-96	ether-petroleum ether (a)	C ₁₅ H ₁₅ N ₃ O ₄	61.78	5.18	11.38	
					61.76	5.17	11.35	
7b	35	114-115	toluene-petroleum ether (a)	C ₁₅ H ₁₅ N ₃ O ₄	61.78	5.18	11.38	
					61.48	5.14	11.27	
8a	65	213-214	ethanol	C ₁₉ H ₁₆ BrN ₃ O ₅	51.14	3.61	9.42	17.91
					50.88	3.61	9.32	17.60
8b	14	168-169	ethanol	C ₁₉ H ₁₆ BrN ₃ O ₅	51.14	3.61	9.42	17.91
					51.03	3.35	9.21	18.01
9a	61	177-178	ether-petroleum ether (a)	C ₃₀ H ₂₅ N ₃ O ₄	73.30	5.13	8.55	
					73.33	5.21	8.64	
9b	1	131-134	ether	C ₃₀ H ₂₅ N ₃ O ₄	M*	491.1844	(b)	
10	74	113-114	ether (c)	C ₁₃ H ₁₃ N ₃ O ₅	53.61	4.50	14.43	
					53.35	4.52	14.47	
11	80	96-98	ethanol	C ₁₂ H ₁₃ N ₃ O ₆ S	44.04	4.00	12.84	9.78
					43.98	3.89	12.65	9.76
12	79	142-143	ethanol	C ₁₈ H ₁₇ N ₃ O ₆ S	53.59	4.24	10.41	7.95
					53.39	4.38	10.48	7.84
13	33	122	ethanol	C ₂₅ H ₂₃ N ₃ O ₆ S	60.84	4.70	8.51	6.50
					60.82	4.44	8.41	6.50

(a) Fraction of bp 40-60°. (b) Insufficient material for elemental analysis. (c) Containing a little ethanol.

was a salient feature of all the alkylations carried out on this system. Further reaction of these mono-alkylated derivatives resulted, as expected, in substitution on the oxygen atom to give *O,N*-disubstituted compounds *e.g.* **13**.

Acylation and sulphonation, however, did not take place on the triazole ring under alkaline conditions. The lability of *N*-acyl or sulphonyl triazoles is well known (7) and it is probable that if attack does occur initially on nitrogen then transacylation or trans-sulphonation onto oxygen ensues under the reaction conditions. An example of a transacylation of this type has been reported (8). Thus, acetylation of **1** results exclusively in the synthesis of the *O*-acetyl derivative **10**. Similarly, mesylation and 4-toluenesulphonation of **1** resulted solely in the formation of **11** and **12** respectively.

Structural Identification.

Evidence for alkylation occurring on nitrogen was readily available from the solution ir spectra which clearly showed phenolic absorptions typical of monomeric and oligomeric hydroxyl stretching frequencies at 3590 and *ca* 3400 (broad) cm⁻¹ respectively. These absorptions were absent in the acetylated and sulphonated compounds **10-12** demonstrating unequivocally that attack in these cases occurred on oxygen.

Taking the parent *N*-benzyl derivatives **5**, **6a** and **6b** as

typical of triazole substituted compounds, the ¹H nmr spectra clearly distinguished the *N*-3 isomer **6b** by virtue of its lower field benzyl methylene signal at δ 5.74 compared with δ 5.36 in the authentic *N*-1 isomer **5**. The third, now presumed *N*-2 isomer **6a** had this signal at δ 5.42. Supportive data was available from the ¹³C nmr spectra.

In general, the ¹³C nmr spectra were obtained from solutions in deuteriochloroform. Low solubility precluded analysis of the unsubstituted compound **1** in deuteriochloroform. A change of solvent to tetradeuteriomethanol or hexadeuteriodimethylsulphoxide resulted in small chemical shift changes but these did not prevent unambiguous structural assignments.

In hexadeuteriodimethylsulphoxide the carbon signals of the triazole ring of **1** occurred at δ 123.9 C-4 and 158.9 C-5 (see Table 1) and in the *O*-substituted compounds **10-12** these signals were at δ 125.6 and 158.2 respectively. In the authentic *N*-1 compound **5** the C-5 signal α to the substituent occurred at 9.1 ppm to higher field while the C-4 (β) signal appeared at a very similar chemical shift to that observed in the unsubstituted compound.

In the *N*-3 compound **6b** the adjacent C-4 signal occurs at higher field by 12.3 ppm than in the unsubstituted compound whereas the C-5 signal is essentially unchanged. In the *N*-2 compound **6a** both C-4 and C-5 occur at slightly lower field than in the unsubstituted compound, 0.5 and

Table II

Spectroscopic Data on Ethyl 5-Aryloxy-*v*-triazole-4-carboxylates

Compound No.	Mass Spectrum	Infrared Spectrum cm ⁻¹ (a)	Ultraviolet Spectrum (ethanol) nm (b)	¹ H NMR Spectrum δ ppm (c)
6a	M ⁺ (100%), 91 (97%)	3590, 3400 (broad), 1715 (C=O)	226 (13,000), 260 (5,700)	1.31 (t, CH ₃ , 3H, J = 7.2 Hz), 4.36 (q, ester CH ₂ , 2H, J = 7.2 Hz), 5.42 (s, N-CH ₂ , 2H), 5.85 (broad exchangeable, OH, 1H), 6.82 (AB quartet, 4H, J = 8.3 Hz, Δν = 24 Hz), 7.28 (s, Ph, 5H).
6b	M ⁺ (42%), 91 (100%)	3590, 3260 (broad) 1715 (C=O)	223 (14,000), 260 (4,700)	1.25 (t, CH ₃ , 3H, J = 7.2 Hz), 4.30 (q, ester CH ₂ , 2H, J = 7.2 Hz), 5.86 (s, N-CH ₂ , 2H), 6.63 (s, exchangeable, OH, 1H), 6.83 (AB quartet, 4H, J = 8.2 Hz, Δν = 17.5 Hz), 7.30 (s, Ph, 5H).
7a	M ⁺ (98%), 121 (100%)	3590, 3400 (broad) 1720 (C=O)	226 (21,400), 262 (8,200)	1.30 (t, ester CH ₃ , 3H, J = 7 Hz), 3.72 (s, ether CH ₃ , 3H), 4.35 (q, ester CH ₂ , 2H, J = 7 Hz), 5.35 (s, N-CH ₂ , 2H), 6.65-7.30 (m, 1H exchangeable, arom + OH, 9H).
7b	M ⁺ (25%), 121 (100%)	3590, 3250 (broad) 1715 (C=O)	225 (23,800), 264 (6,300)	1.26 (t, ester CH ₃ , 3H, J = 7 Hz), 3.72 (s, ether CH ₃ , 3H), 4.30 (q, ester CH ₂ , 2H, J = 7 Hz), 5.78 (s, N-CH ₂ , 2H), 6.60-7.35 (m, 1H exchangeable, arom + OH, 9H).
8a	447 (42%), 445 (42%), 183 (98%), 181 (100%)	mull, 3380, 1720 (ester C=O), 1688 (ketone C=O)	224, (15,000), 260, (27,600)	(DMSO-d ₆), 1.23 (t, CH ₃ , 3H, J = 7.1 Hz), 4.26 (q, ester CH ₂ , 2H, J = 7.1 Hz), 6.20 (s, exchangeable, N-CH ₂ , 2H), 6.85 (AB quartet, arom, 4H, J = 8 Hz, Δν = 22 Hz), 7.84 (AB quartet, arom, 4H, J = 9 Hz, Δν = 14 Hz), 9.32 (s, exchangeable, OH, 1H).
8b	447 (57%), 445 (55%), 185 (30%), 183 (100%), 181 (70%)	mull, 3450, 1715 (ester C=O), 1700 (ketone C=O)	258 (26,200)	(DMSO-d ₆), 1.03 (t, CH ₃ , 3H, J = 7.1 Hz), 4.14 (q, ester CH ₂ , 2H, J = 7.1 Hz), 6.32 (s, exchangeable, N-CH ₂ , 2H), 6.97 (AB quartet, arom, 4H, J = 9.5 Hz, Δν = 20 Hz), 7.92 (AB quartet, 4H, J = 8 Hz, Δν = 18 Hz), 9.34 (broad s, exchangeable, OH, 1H).
9a	M ⁺ (2%), 249 (16%), 244 (40%), 243 (100%), 165 (32%)	3590, 3400 (broad) 1720 (C=O)	222 (23,800), 258 (6,800)	1.23 (t, CH ₃ , 3H, J = 7.5 Hz), 4.26 (q, ester CH ₂ , 2H, J = 7.5 Hz), 5.53 (s, exchangeable, OH, 1H), 6.72 (AB quartet, arom, 4H, J = 9 Hz, Δν = 25 Hz), 7.25 (m, Ph, 15H).
9b	M ⁺ (2%), 249 (18%), 244 (24%), 243 (100%), 165 (25%)	mull, 3350 (broad), 1735 (C=O)		(DMSO-d ₆), 0.86 (t, CH ₃ , 3H, J = 7 Hz), 6.27 (AB quartet, arom, 4H, J = 9 Hz, Δν = 31 Hz), 7.26 (m, Ph, 15H).
10	M ⁺ (9%), 250 (15%), 249 (100%), 121 (12%), 110 (25%)	3420, 3200 (broad) 1760 (acetate C=O) 1725 (ethyl ester C=O)	223 (14,100)	1.26 (t, ethyl ester CH ₃ , 3H, J = 7 Hz), 2.27 (s, acetate CH ₃ , 3H), 4.35 (q, CH ₂ , 2H, J = 7 Hz), 7.08 (m, arom, 4H), 13.00 (broad, exchangeable, NH, 1H).
11	M ⁺ (50%), 249 (40%), 248 (98%), 171 (15%), 137 (100%), 109 (90%)	3415, 3200 (broad) 1725 (C=O)	223 (15,900)	1.27 (t, ester CH ₃ , 3H, J = 7 Hz), 3.13 (s, S-CH ₃ , 3H), 4.36 (q, CH ₂ , 2H, J = 7 Hz), 7.20 (broad s, arom, 4H), 11.5 (broad exchangeable, NH, 1H).
12	M ⁺ (18%), 264 (43%), 248 (42%), 247 (30%), 202 (15%), 155 (32%), 149 (20%), 137 (32%), 110 (32%), 109 (100%), 92 (35%), 91 (95%)	3410, 3200 1720 (C=O)	226 (26,000)	1.30 (t, ester CH ₃ , 3H, J = 7.5 Hz), 2.43 (s, C-CH ₃ , 3H), 4.39 (q, CH ₂ , 2H, J = 7.5 Hz), 7.01 (AB quartet, arom, 4H, J = 10 Hz, Δν = 15 Hz), 7.52 (AB quartet, arom, 4H, J = 8.7 Hz, Δν = 24 Hz), 10.5 (broad exchangeable, NH, 1H).
13	M ⁺ (75%), 338 (80%), 137 (100%), 109 (33%), 91 (83%)	mull, 1715 (C=O)		1.25 (t, ester CH ₃ , 3H, J = 7 Hz), 2.40 (s, C-CH ₃ , 3H), 4.30 (q, ester CH ₂ , 2H, J = 7 Hz), 5.47 (s, N-CH ₂ , 2H), 6.45 (AB quartet, arom, 4H, J = 6 Hz, Δν = 6.6 Hz), 7.31 (s, Ph, 5H), 7.48 (AB quartet, arom, 4H, J = 6 Hz, Δν = 24 Hz).

(a) In chloroform unless otherwise stated. (b) Molar extinction coefficient in brackets. (c) In deuteriochloroform unless otherwise noted.

1.5 ppm respectively. In essence the presence of a substituent on the triazole nucleus at either the 1 or 3 positions causes the chemical shift of the adjacent carbon to occur at *ca* 10 ppm to higher field relative to the chemical shift in the unsubstituted compound; whereas the presence of the substituent on the 2 position has little effect on the chemical shifts of the 4 and 5 carbon signals. The chemical shifts of the benzyl methyl carbon-13 signals are also diagnostic, with a chemical shift of δ 51.2 in the N-1 compound **5**, δ 54.9 in the N-3 compound **6b** and δ 59.8 in the N-2 compound **6a**. Essentially similar observations may be made in the cases of N-2 and N-3 derivatives of the 4-methoxybenzyl compounds **7a** and **7b**, respectively.

With the phenacyl derivatives **8a** and **8b** the ^1H nmr spectra show less well defined chemical shift differences of the phenacyl methylene signals. In the N-3 isomer this signal is at δ 6.32 while it is at δ 6.20 in the N-2 isomer. These protons exchange on the addition of deuterium oxide as a result of their acidity. In the ^{13}C nmr spectra however, there is a marked difference of 4 ppm consistent with that observed between the methylene signals of the N-2 and N-3 isomers of the *N*-benzyl derivatives. Moreover, the chemical shifts of the C-4 and C-5 carbons are in good agreement with those obtained for the other *N*-substituted compounds mentioned above.

The C-5 signal in the N-2 compound **8a** was observed at δ 159.2 in hexadeuteriodimethylsulphoxide, coincident with an ester carbonyl signal. This was confirmed by obtaining the spectrum of the sample in trifluoroacetic acid whence two separate signals were observed.

The major trityl product **9a** showed the expected C-4 and C-5 chemical shifts for an N-2 derivative but insufficient of the minor isomer was isolated for a ^{13}C nmr

analysis. This was tentatively assigned the N-3 structure **9b** on the basis of the other results reported here.

The results are in general agreement with those of Townsend and others (9,10) and from their work a generalised picture is now available for imidazoles and triazoles of formula **14** in which X and Z may be C or N. These systems are generally characterised by an upfield shift of the carbon atoms α to the site of substitution (when R is alkyl or glycosyl) and a downfield shift of the carbon atoms β to the site of substitution relative to the unsubstituted heterocycle. These assignments are in agreement with recently determined long range ^{13}C nmr - ^1H nmr spin-spin coupling constants (9).

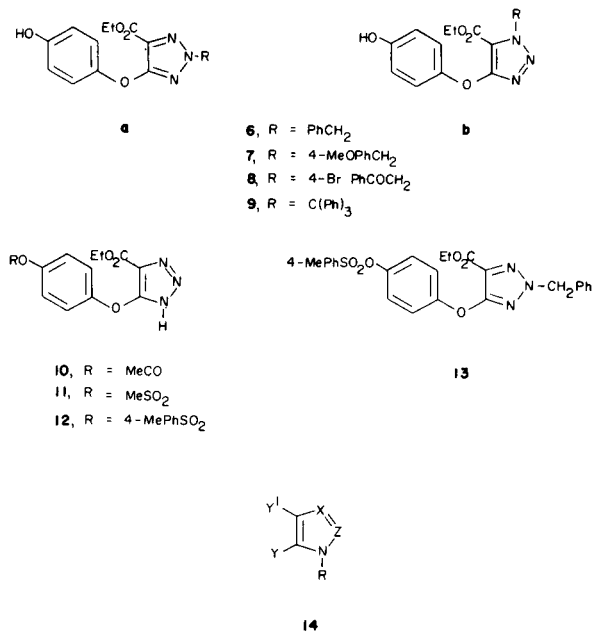


Table III

 ^{13}C NMR Chemical Shifts (δ c ppm downfield from tetramethylsilane) (a)

Compound	C-4	C-5	C-6	C-7	C-8	C-9	C-1'	C-2'	C-3'	C-4'	C-1''	C-2''	C-3''	C-4''	Others
1 (b)	123.9	158.9	159.6	60.6	14.1		154.2	119.5	116.0	148.6					
4	125.9	149.0	159.5	60.7	13.9	50.9	155.3	116.6	115.8	150.4	133.8	{128.8	128.5	128.1}	(c)
5	125.9	149.3	159.8	61.2	13.9	51.2	153.3	116.7	116.4	149.9	133.6	{129.0	128.8	128.3}	
6a	126.1	159.7	160.5	61.5	14.2	59.8	153.2	119.8	116.3	149.1	134.0	{128.8	128.7	128.1}	
6b	113.5	158.1	160.0	61.7	14.0	54.9	153.4	119.9	116.6	148.9	134.8	{128.8	128.5	128.0}	
7a	126.0	159.7	160.5	61.5	14.2	59.4	153.2	119.8	116.3	149.2	126.2	129.8	114.3	159.9	(d)
7b	113.2	158.1	160.0	61.7	14.0	54.4	153.3	119.9	116.5	148.8	126.8	129.6	114.2	159.8	(d)
8a (b)	126.1	159.2	159.2	61.7	14.0	60.7	154.3	119.5	115.9	148.1	133.9	{132.0	130.1}	128.5	(e)
8b (b)	114.7	157.3	158.5	61.3	13.6	57.8	154.0	119.1	115.8	148.4	133.0	{132.1	130.1}	128.6	(f)
9a (g)	126.5	158.3	160.9	61.6	14.1	84.3	153.6	119.2	115.9	149.5	142.0	{130.5	127.8}	128.3	
10	125.5	158.4	160.3	61.8	14.1		153.4	122.6	119.4	147.1					(h)
11	125.5	158.0	160.2	61.9	14.1		154.6	123.4	119.8	145.4					(i)
12	125.7	158.0	160.1	61.9	14.1		154.4	123.6	119.3	145.6					(j)
13	127.3	157.9	159.5	61.2	14.1	60.0	154.7	123.5	118.8	145.7	134.0	{128.7	128.5	128.2}	(k)

(a) See formula **5** for numbering sequence, spectra in deuteriochloroform unless otherwise noted. (b) In hexadeuteriodimethylsulphoxide. (c) 136.8, 127.9, 127.3 (*O*-benzyl arom), 70.4 (CH₂ of *O*-benzyl). (d) 55.2 (OCH₃). (e) 191.4 (ketone C=O). (f) 191.0 (ketone C=O). (g) In deuteriochloroform-tetra-deuteriomethanol. (h) 169.8 (acetyl C=O), 21.0 (acetyl CH₃). (i) 37.4 (S-CH₃). (j) 145.9, 132.3, 129.9, 128.6 (toluenesulphonyl arom), 21.7 (toluenesulphonyl CH₃). (k) 145.7, 132.4, 129.8, 128.9 (toluenesulphonyl arom), 21.6 (toluenesulphonyl CH₃).

Our work extends the utility of the Townsend approach to heterocycles in which Y or Y' may be an ether linkage.

The loss of nitrogen from the parent ion, frequently seen in the mass spectra of simple N-H triazoles (11), was not observed in any of the compounds studied. It is possible that alternative fragmentations precluded this loss but it is noteworthy that the abundance of the molecular ion, which is the base peak in the 2-benzyl compound **6a** was markedly reduced in the 1- and 3-benzyl compounds in which the abundances were 5% and 42% respectively. The base peak in these latter compounds was the $C_7H_7^+$ ion at m/z 91. A similar trend is seen in the 2- and 3-(4-methoxybenzyl) derivatives **7a** and **7b** respectively, but in these cases the base peak is located at m/z 121 as the $C_8H_9O^+$ ion.

The uv spectra of these compounds, while showing some differences, did not allow structural assignment.

In conclusion, we have identified the products from the acylation, sulphonation and alkylation of **1** and shown that, under alkaline conditions, the site of substitution, whether at oxygen or nitrogen, is dependent on the nature of the attacking electrophile. The exclusive attack by alkylating agents at N-2 or N-3 in 5-aryloxytriazoles containing carbonyl substituents at C-4, extending even to tricyclic derivatives (12), appears to be general.

Our final selection of the 4-methoxybenzyl moiety as a useful and general triazole protecting group is the subject of another publication (1).

EXPERIMENTAL

Melting points were determined using a Büchi melting point apparatus and are recorded uncorrected. The 1H nmr spectra were recorded on either a Perkin Elmer R32 or a Varian CFT20 at 90.0 or 79.5 MHz respectively. The ^{13}C nmr spectra were recorded on a Varian CFT20 at 20.0 MHz with proton noise decoupling. Single frequency off resonance proton decoupling was used to aid assignment. All nmr spectra were obtained at ambient temperature. Infrared spectra were obtained on a Perkin Elmer 457 instrument and ultraviolet spectra on a Perkin Elmer 554 instrument. Mass spectral data was obtained from a VG-Micromass 70-70F using electron impact ionisation techniques.

Ethyl 1-Benzyl-5-(4-benzyloxyphenoxy)-v-triazole-4-carboxylate (**4**).

To a stirred solution of 4-benzyloxyphenol (18.8 g, 0.094 mole) in dry *N,N*-dimethylformamide (200 ml) was added a 50% dispersion of sodium hydride in mineral oil (4.52 g, 0.094 mole) and the mixture was stirred at ambient temperature for 15 minutes. Ethyl 1-benzyl-5-chloro-*v*-triazole-4-carboxylate **3** (3), (25 g, 0.094 mole) was added in one portion and the mixture stirred for 20 hours at 80°. After cooling, the solvent was removed *in vacuo* and the residue partitioned between water and ethyl acetate. The organic phase was washed with dilute aqueous sodium hydroxide and water and dried (magnesium sulphate). Evaporation of the solvent gave a crystalline solid which after trituration with ether-petroleum ether (bp 60-80°) recrystallised from ethanol to give 32.18 g (81%) of **4** of mp 88-89°; ir (nujol): 1715 cm^{-1} (C=O); 1H -nmr (deuteriochloroform): δ 1.05 (t, CH_3 , 3H, J = 7.5 Hz), 4.11 (q, ester CH_2 , 2H, J = 7.5 Hz), 4.95 (s, O-benzyl CH_2 , 2H), 5.32 (s, *N*-benzyl CH_2 , 2H), 6.72 (AB quartet, O-Ph-O, 4H, J = 8 Hz, $\Delta\nu$ = 12 Hz), 7.20 (s, Ph, 5H), 7.30 (s, Ph, 5H).

Anal. Calcd. for $C_{25}H_{23}N_3O_4$: C, 69.91; H, 5.40; N, 9.79. Found: C, 69.65; H, 5.46; N, 9.81.

Ethyl 1-Benzyl-5-(4-hydroxyphenoxy)-v-triazole-4-carboxylate (**5**).

A solution of **4** (4.30 g, 0.01 mole) in *N,N*-dimethylformamide (50 ml) was hydrogenated at atmospheric pressure and room temperature over 10% palladinized charcoal (0.1 g), the course of the reaction being followed by tlc. Filtration and evaporation of the resulting solution gave an oil which crystallised on trituration with ether. Recrystallisation from aqueous acetone gave 1.85 g (55%) of **5** of mp 161-162°; ir (chloroform): 3590 (monomeric phenol), 3350 (oligomeric phenol), 1720 (C=O) cm^{-1} ; 1H nmr (deuteriochloroform): δ 1.09 (t, CH_3 , 3H, J = 7.5 Hz), 4.13 (q, ester CH_2 , 2H, J = 7.5 Hz), 5.36 (s, N- CH_2 , 2H), 6.67 (AB quartet, O-Ph-O, 4H, J = 9 Hz, $\Delta\nu$ = 16 Hz), 7.25 (s, Ph, 5H); ms: M^+ (5%), 230 (48%), 91 (100%) m/z ; uv (ethanol): 224 (14,700), 284 (2,600) nm.

Anal. Calcd. for $C_{18}H_{17}N_3O_4$: C, 63.70; H, 5.05; N, 12.38. Found: C, 63.61; H, 5.14; N, 12.21.

Ethyl 5-(4-Hydroxyphenoxy)-1*H*-v-triazole-4-carboxylate (**1**).

A suspension of **4** (17.2 g, 0.04 mole) in ethanol (400 ml) was hydrogenated at 1000 psi and 100° over 10% palladinized charcoal (1 g) for 90 minutes and the cooled solution filtered and evaporated to a brown oil. Crystallisation from aqueous ethanol afforded 8.86 g (89%) of **1** of mp 137-138°; ir (potassium bromide): 3400, 3160, 1705 (C=O) cm^{-1} ; 1H nmr (DMSO- d_6): 1.25 (t, CH_3 , 3H, J = 7.1 Hz), 4.30 (q, CH_2 , 2H, J = 7.1 Hz), 6.88 (AB quartet, aromatics, 4H, J = 9.3 Hz, $\Delta\nu$ = 14.3 Hz), two exchangeable protons not clearly seen; ms: M^+ (100%), 204 (10%), 121 (18%), 120 (9%), 110 (43%), 65 (22%) m/z ; uv (ethanol): 225 (13,000), 280 (2,600) nm.

Anal. Calcd. for $C_{11}H_{11}N_3O_4$: C, 53.01; H, 4.45; N, 16.86. Found: C, 53.14; H, 4.44; N, 16.87.

General Procedure for Alkylation, Acylation and Sulphonation of **1**.

Anhydrous potassium carbonate (4.14 g, 0.03 mole) was added to a stirred solution of **1** (2.49 g, 0.01 mole) in dry *N,N*-dimethylformamide (100 ml) and the alkyl, acyl or sulphonyl halide (0.01 mole) added. After stirring for 16-24 hours at 20-40° the solvent was evaporated *in vacuo* and water added. The products were extracted into ethyl acetate after acidification to pH 1 and the extracts dried (magnesium sulphate) and evaporated. Compounds **10-12** were isolated directly by recrystallisation from the appropriate solvent but all other compounds were chromatographed on silica gel eluting with chloroform. In the case of the bromophenacyl derivatives **8a** and **8b** the bulk of the poorly soluble **8a** was removed by recrystallisation prior to chromatography. In all instances the least polar N-2 isomers eluted first.

Compounds **6** and **8** were prepared from the corresponding alkyl bromides, but for all others the appropriate chlorides were used.

Ethyl 2-Benzyl-5-[4-(4-toluenesulphonyloxy)phenoxy]-v-triazole-4-carboxylate (**13**).

To a stirred solution of **12** (1.0 g, 2.5 mmoles) in dry *N,N*-dimethylformamide (15 ml) was added anhydrous potassium carbonate (0.523 g) and benzyl bromide (0.47 g, 2.5 mmoles) and the mixture was stirred for 4 hours at 20°. The solvent was removed *in vacuo* and the product partitioned between water and ether. The dried (magnesium sulphate) organic phase was evaporated to an oil which crystallised on standing. Recrystallisation from warm ethanol gave 0.485 g (33%) of the N-2 benzyl derivative **13** (See Table I for data). The ethanolic mother liquor contained enriched N-1 benzyl isomer but this was not isolated.

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