The Chemistry of Pseudomonic Acid.† Part 10.[1] Preparation of Heterocyclic Derivatives

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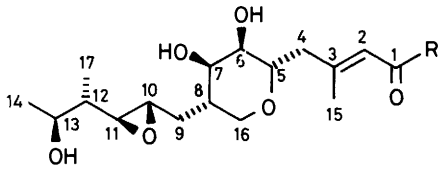
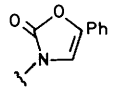
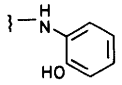
The preparation of a large variety of normonyl¶ heterocycles is described. Methods involving cyclisation of monic acid derivatives gave access to only a limited number of types of heterocycles. Olefination methods proved to be of wider applicability with phosphonate stabilised anions providing the biologically active *E*-isomer in a 3—4:1 excess. The Peterson type olefination proved to be the most useful method with the largest range of heterocycles and stereoselectivity of *E*:*Z* 4 to >10:1.

Pseudomonic acid (**1a**) and esters of monic acid (**1b**) have good antimicrobial activity *in vitro*, but when given systemically to mammalian species, including man, they are rapidly metabolised to monic acid with concomitant loss of activity.[2] In a



(**1**)

R

a; $O(CH_2)_8CO_2H$
b; OH
c; OCO_2Bu^i
d; $NHCH_2COPh$
e; 
f; 

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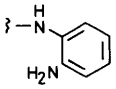
g; 
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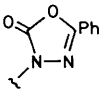
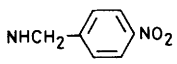
i; 
j; 
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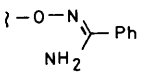
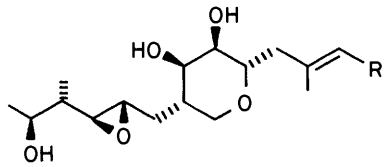
l; 

programme designed to increase the *in vivo* stability while maintaining antimicrobial potency, a series of heterocyclic replacements for the carboxy function have been synthesized. Since benzyl esters of monic acid had proved of particular interest in our earlier work[3] we sought to synthesize a range of heterocycles (**2a**—**y**). These were viewed as analogues of the



(**2**)

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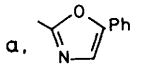
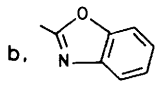
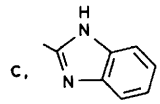
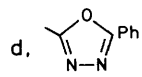
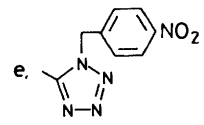
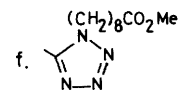
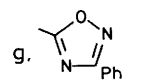
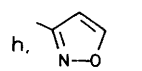
a, 
b, 
c, 
d, 
e, 
f, 
g, 
h, 

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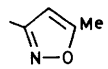
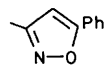
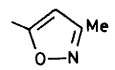
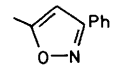
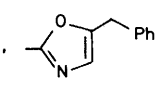
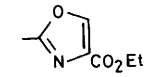
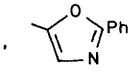
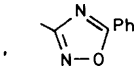
i, 
j, 
k, 
l, 
m, 
n, 
o, 
p, 

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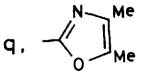
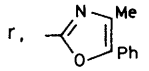
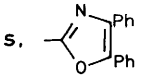
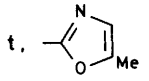
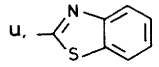
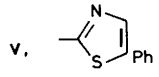
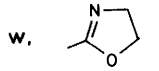
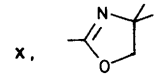
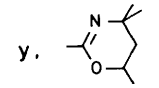
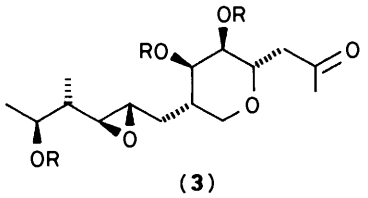
q, 
r, 
s, 
t, 
u, 
v, 
w, 
x, 
y, 

benzyl ester with much reduced conformational freedom. A wide range of phenyl heterocycles were covered including oxazoles, oxadiazoles, tetrazoles, isoxazoles, and thiazoles.

† The approved generic name for pseudomonic acid is mupirocin.
‡ *Present address:* British Biotechnology, Wallington Road, Cowley, Oxford.
§ *Present address:* Beecham Pharmaceuticals Research Division, Brockham Park, Betchworth, Surrey, RH3 7AJ.
¶ Normonyl, the trivial name for the 3-[5-(2,3-epoxy-5-hydroxy-4-methylhexyl)-3,4-dihydroxytetrahydropyran-2-yl]-2-methylprop-1(*E*)-en-1-yl radical, is used throughout for convenience.

Two strategies for the formation of these normonyl* heterocycles were investigated: (i) cyclisation of a monic acid derivative; (ii) olefination of the previously described ketone (**3a**) using Horner-Wittig or Peterson methodology.

The cyclisation route was used to prepare three types of heterocycle, the oxazole, oxadiazole, and the tetrazole. One of the classical approaches to oxazole synthesis is the Robinson–Gabriel synthesis[4] by dehydration of keto amides. Of the



(**3**)

a; R = H

b; R = TMS

examples described in the literature, most are 2,5-disubstituted and many are diaryl. These methods involve either the use of sulphuric acid, or large excesses of phosphorus pentachloride, conditions under which the monic acid nucleus tends to rearrange.[5] Recent work[6] describes the use of milder reagents to effect cyclisation including phosgene and triethylamine, conditions which we have successfully applied to our series.

In the case of oxadiazoles both the 1,3,4- and the 1,2,4- systems have been described as arising through cyclisation,[7] the former by treatment of a diacylhydrazide with phosphorus pentaoxide[8] or phosphoryl chloride[9] and the latter by dehydration of an acyl aldoxime.[10]

Tetrazoles have been prepared by a number of routes[11] but perhaps the most general of these leading to 1-monosubstituted or 1,5-disubstituted tetrazoles involves the reaction between imino chlorides and azides.

The methods presented above allow access to a limited number of heterocycles, each from a different monamide† derivative. These reactions are further restricted in the substitution patterns they can produce. Thus other methods were sought to find a more general approach and to increase the variety of heterocycles which could be produced.

The ketone (**3a**), which is readily available [12a] by ozonolysis of pseudomonic acid (**1a**) is a useful intermediate in the synthesis of acrylic acid esters *via* either the Wittig reaction or related olefination methods.[12b] The literature contains some examples where non-basic vinyl heterocycles had been made using a Wadsworth-Emmons reaction[13] but fewer examples of vinyl-substituted basic heterocycles have been described[14] and in none of these cases was systematic study of the stereochemical outcome of the reaction undertaken. Our earlier work[12] established that phosphonoacetates react with the protected ketone (**3b**) to yield α,β-unsaturated esters as a mixture of stereoisomers with a predominance of the *E*-isomer. Preparation of vinyl heterocycles by this method, would be restricted only by the availability of methyl or halogenomethyl heterocycles.

This paper describes the scope and limitations of the synthesis of a wide range of normonyl heterocycles (**2**), while the following paper[15] concentrates on the preparation of aryl substituted oxazoles and the development of the cyclisation methods.

Results and Discussion

Cyclisations.—A number of methods have been described in the literature[4] for the dehydration of amides to form oxazoles. The mildest of these methods uses phosgene and triethylamine which in our case requires protection of the hydroxy groups.[1]

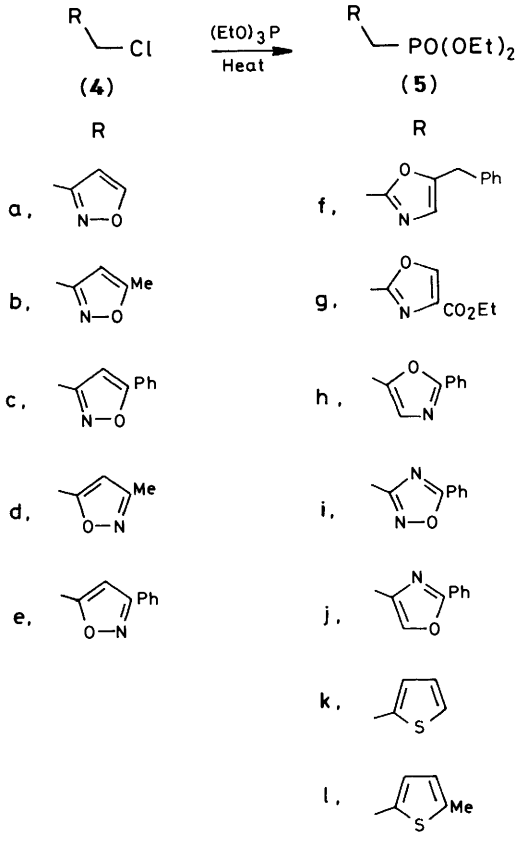
The monamide (**1d**) was prepared in 52% yield by reaction of phenacylamine (generated *in situ* from its hydrochloride) with the mixed anhydride (**1c**). This monamide, protected as its tris(trimethylsilyl) ether, was then treated with phosgene and triethylamine followed by mild acid hydrolysis to yield 11% of the oxazole (**2a**), along with varying amounts of the acyloxazolone (**1e**). In an attempt to extend the scope of the reaction to the benzo fused oxazole or imidazole (**2b, c**), the monamides (**1f, g**) were prepared. Treating these with phosgene and triethylamine failed to yield any cyclic materials, nor did the use of phosphorous pentaoxide, phosphorous pentachloride or phosphoryl chloride improve the reaction.

Similarly, the diacylhydrazide (**1h**) failed to give the expected 1,3,4-oxadiazole (**2d**) on treatment with phosgene and triethylamine, but instead produced the phosgene addition product (**1i**) in 50% yield.

This general method of cyclisation *via* the imino chloride was used to synthesize the tetrazole derivatives (**2e, f**). Reaction of the monamides (**1j, k**) with phosgene to give the imino chloride and treatment *in situ* with tetramethylguanidinium azide gave an imino azide which spontaneously cyclised to give the tetrazoles (**2e, f**) in 8 and 24% yields respectively.

Clarke[16] describes the synthesis of 1,2,4-oxadiazoles by the acylation of amidoximes followed by thermal elimination of water. This method could be used with the benzamide oxime (**1l**) and refluxing in diglyme resulted in a near quantitative yield of the oxadiazole (**2g**).

Olefinations.—(a) *Wittig reactions.* Phosphonate intermediates were prepared by Arbuzov reaction of triethyl phosphite on the appropriate halogenomethyl heterocycle (see Table 1 for references), *e.g.* treatment of 2-chloromethyl-5-methyl-isoxazole (**4b**) with triethyl phosphite at reflux gave the phosphonate (**5b**)



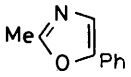
* As footnote ¶ on p. 2047.

† Monamide is the trivial name for amides of monic acid.

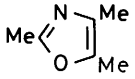
Table 1.

Halide [a]	Phosphonate	Normonyl heterocycle	$E:Z$ [b]	Yield [c] (%)
(**4a**) [d]	(**5a**)	(**2h**)	75:25	20
(**4b**) [e]	(**5b**)	(**2i**)	80:20	43
(**4c**) [e]	(**5c**)	(**2j**)	75:25	16
(**4d**) [f]	(**5d**)	(**2k**)	80:20	32
(**4e**) [g]	(**5e**)	(**2l**)	86:14	36
(**4f**) [h]	(**5f**)	(**2m**)	89:11	22
(**4g**) [i]	(**5g**)	(**2n**)		8
(**4h**) [h]	(**5h**)	(**2o**)	75:25	10
(**4i**) [j]	(**5i**)	(**2p**)	75:25	29

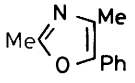
[a] All chlorides except (**4e**) and (**4g**) which were bromide. [b] From h.p.l.c. peak heights before isolation. [c] Yield of isolated materials. [d] (*a*) G. Skinner, *J. Am. Chem. Soc.*, 1924, **46**, 731; (*b*) R. G. Micetich, *Can. J. Chem.*, 1970, **48**, 467. [e] (*a*) D. Libermann, N. Rist, F. Grumbach, S. Cals, M. Moyeux, and A. Rouaix, *Bull. Soc. Chim. Fr.*, 1958, 687; (*b*) A. Angeli, *Chem. Ber.*, 1891, **23**, 2159; (*c*) H. Kano, I. Adachi, R. Kido, and K. Hirose, *J. Med. Chem.*, 1967, **10**, 411. [f] Commercially available from Aldrich Chemical Co. [g] G. A. Lee, *Synthesis*, 1982, 508. [h] M. P. Doyle, W. E. Buhro, J. G. Davidson, R. C. Elliott, J. W. Hoekstra, and M. Oppenhuizen, *J. Org. Chem.*, 1980, **45**, 3657. [i] J. W. Cornforth and R. H. Cornforth, *J. Chem. Soc.*, 1947, 96. [j] N. S. Ooi and D. Wilson, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1792; (*b*) See ref. 13.



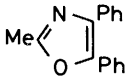
(**6**)



(**7**)



(**8**)



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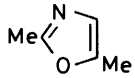

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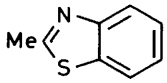
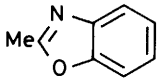
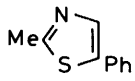


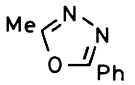
(**11**)



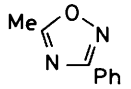
(**12**)



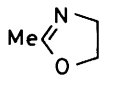
(**13**)



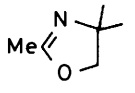
(**14**)



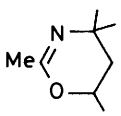
(**15**)



(**16**)



(**17**)



(**18**)

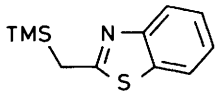
in 72% after distillation. On deprotonation of the phosphonate with sodium hydride and treatment with the protected ketone (**3b**) the desired vinylisoxazole (**2i**) was obtained as a mixture of *E* and *Z* isomers in a combined yield of 43%.

Table 2.

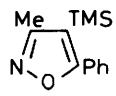
Methyl heterocycle	Normonyl heterocycle	$E:Z$ [a]	Yield [b] (%)
(**6**)[18]	(**2a**)	92:8	38
(**7**) [c]	(**2q**)	93:7	23
(**8**) [c]	(**2r**)	90:10	60
(**9**) [d]	(**2s**)	90:10	29
(**10**) [e]	(**2t**)	90:10	26
(**11**) [d]	(**2u**)	52:48	21
(**12**) [d]	(**2v**)	60:40	39
(**13**) [f]	(**2w**)	80:20	37
(**14**) [g]	(**2d**)	90:10	6
(**15**)[16]	(**2g**)	80:20	38
(**16**) [d]	(**2x**)	88:12	27
(**17**) [d]	(**2y**)	83:17	24
(**18**) [d]	(**2z**)	90:10	3

[a] From h.p.l.c. peak heights before isolation. [b] Yield of isolated material(s). [c] R. A. Jeffreys, *J. Chem. Soc.*, 1952, 4823. [d] H. Bredereck, R. Gomper, and F. Riech, *Chem. Ber.*, 1960, **93**, 1389. [e] A. Triebs and W. Sutter, *Chem. Ber.*, 1951, **84**, 96. [f] S. Scheibye, *Bull. Soc. Chim. Belg.*, 1978, **87**, 229. [g] C. Ainsworth, *J. Am. Chem. Soc.*, 1955, **77**, 1148.

The vinylisoxazole isomers were separated by chromatography and stereochemistry was assigned by ^{13}C n.m.r. Spectroscopy in (**2i**) the C-15 and C-4 carbons occur at δ 19.3 and 42.6 in the *E* isomer, and δ 26.8 and 36.8 in the *Z* isomer respectively. For monic acid esters the ^1H n.m.r. chemical shift



(**19**)



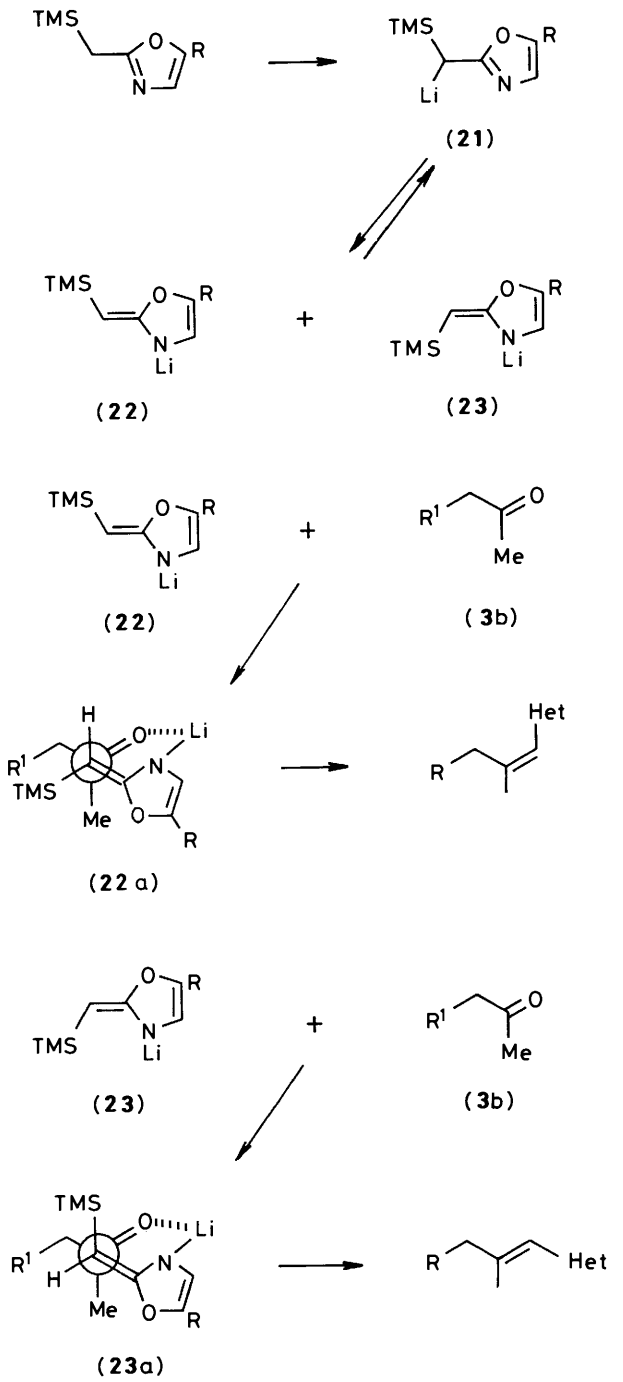
(**20**)

of the 15-H_3 could be used to assign stereochemistry but for (**2i**) both isomers exhibited a signal at *ca.* δ 2.0 for this methyl group.

The ratios of *E* and *Z* isomers and overall yields of several heterocycles prepared are shown in Table 1. As in the case of ester formation selectivity in favour of the desired *E* isomers was observed. In most cases the $E:Z$ isomer ratio was *ca.* 3—4:1. These geometrical isomers have very similar mobilities on t.l.c., resulting in difficulties in their separation.

Additional examples examined included 2-phenyl-5-diethoxyphosphonomethyloxazole[17] (**5j**) which failed to yield any product. This was believed to be due to the enhanced acidity of the heterocyclic proton leading to its abstraction and thence decomposition of the heterocycle. The failure of 2-diethylphosphonomethylthiophene (**5k**) and 2-diethylphosphonomethyl-5-methylthiophene (**5l**)[13] to react is probably due to an increased basicity of the phosphonate stabilised anion and thus to enolisation of the ketone. Further evidence for this comes from the low yields observed, in previous work, on reaction of the ketone (**3b**) with unstabilized Wittig reagents and, in particular, the anion derived from diethylphosphonomethylbenzene.

(b) *Peterson reactions.* Results obtained[12] using silyl-stabilised anions to make tetrasubstituted, α,β-unsaturated esters from the ketone indicate an increased nucleophilicity over the phophonate anions. Despite the adverse stereochemical outcome in this case a report by Corey[18] claiming that vinylbenzothiazoles could be produced by similar methodology gave impetus to explore this reaction. Corey observed that 2-methylbenzothiazole (**11**) reacts with strong bases and trimethylsilyl chloride to yield the trimethylsilylmethyl derivative (**19**). Deprotonation by a further equivalent of base yields a nucleophilic anion which reacts with ketones to form after



Scheme 1.

elimination of TMSOLi, vinylbenzothiazoles. It was further claimed that this was a superior alternative to the phosphonate.[14] When this reaction was carried out by the *in situ* generation of the derivative (**19**) and using (**3b**) as substrate a mixture of isomers was obtained in 39% yield. Disappointingly, in this case, the *E*:*Z* ratio was only 1.5:1, much in line with our previous observation using the silyl esters derivatives.[12b] The benzoxazole derivative (**12**) gave similar stereoselectivity but on examining the oxazole (**6**) or dihydro-oxazole (**16**) the *E*:*Z* ratios were higher at 12:1 and 5:1 respectively. In most of the cases studied the *E*:*Z* isomer ratios were in the range 4—> 10:1 (see Table 2). The reaction sequence was found to be applicable to a number of different heterocycles as described in Table 2. In all cases the trimethylsilylmethyl derivative was generated and used *in situ*.

The reaction using 3-methyl-5-phenylisoxazole failed to yield any olefinic products. Material was isolated whose spectral data were consistent with (**20**) indicating that the heterocyclic proton is more acidic than those of the methyl group thus leading to silylation in the ring.

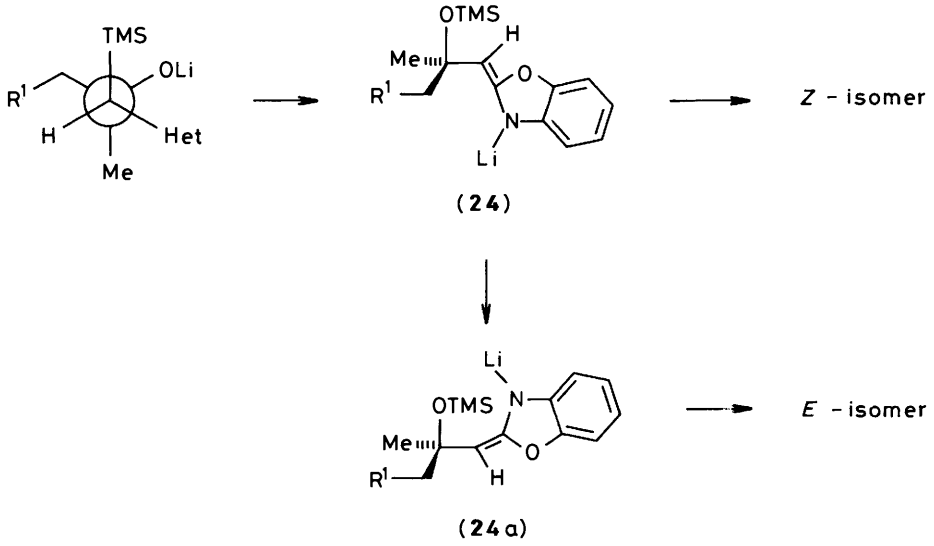
An examination of the stereospecificity of the reaction shows that while virtually no selectivity is achieved with the 2-methylbenzoxazole all of the other 4,5-disubstituted oxazole derivatives show good selectivity, with $E:Z > 10:1$. The reactive species in these Peterson reactions, the trimethylsilylmethyl anion *e.g.* (**21**), is in equilibrium with the enolate-like isomers (**22**) and (**23**) (Scheme 1). Assuming the reaction with the ketone is chelation controlled this leads to a consideration of the interactions in the two intermediates (**22a**) and (**23a**) to decide which isomer will be in excess. The intermediate (**23a**) is less sterically crowded with only the proton gauche to the two alkyl substituents on the ketone. Rapid elimination of TMSOLi will thus give the *E*-olefin. In order to explain the result with the benzo-fused systems there must either be a different steric interaction, which seems unlikely, or a mechanism for equilibrium. In the case of (**2o**) the enolate-like form is stabilised by the adjacent benzene ring and is hence more readily formed (Scheme 2). Transfer of the trimethylsilyl group to oxygen may occur to give (**24**) which can equilibrate by rotation to (**24a**). These two intermediates can eliminate TMSOLi to give the *E* and *Z* isomers respectively. A similar mechanism has been postulated by Larson[19] to explain the low selectivity observed in Peterson olefinations using α-silyl esters.

In conclusion, a number of methods of synthesizing vinyl heterocycles stereoselectively have been investigated. The most widely applicable and that with the greatest specificity has involved the use of trimethylsilylmethyl anions where a >85% excess of the *E* isomer was regularly obtained. A number of the derivatives described here do maintain good antimicrobial activity and show good pharmacokinetics with little evidence for breakdown *in vivo* details of which will be published elsewhere.

Experimental

^{1}H N.m.r. data were recorded at either 60 MHz on a Perkin-Elmer R24A or 250 MHz WM250 instrument and ^{13}C measurements were obtained using a Bruker WM250 spectrometer; all n.m.r. data were recorded at ambient temperatures with tetramethylsilane as internal standard. The numbering system used for assigning the chemical shifts is that shown in formula (**1**). Primed numbers refer to standard heterocycle numbering conventions. Mass spectra were obtained at 70 eV using a VG 70–70F instrument operating at 8eV. Column chromatography was carried out in Merck Kieselgel H (type 60). T.l.c. was performed on precoated Merck Kieselgel 60 F_{254} plates. High performance liquid chromatography (h.p.l.c.) unless otherwise stated was performed on a Waters Associates instrument using a C_{18} μ-Bondapak reverse-phase column with ammonium acetate buffer–methanol solutions as eluant. Both t.l.c. and h.p.l.c. were performed routinely on all compounds. Dimethylformamide (DMF), tetrahydrofuran (THF), pyridine, and triethylamine were dried over calcium hydride and distilled water before use.

General Method of Preparation of Monamides.—To a solution of monic acid in THF (15 ml/mmol) at −10 °C was added triethylamine (1.1 equiv.), followed by isobutyl chloroformate (1.1 equiv.) and stirred for 30 min. The amine (1 equiv.) was added and the reaction mixture stirred overnight at



Scheme 2.

room temperature then poured into brine and extracted with ethyl acetate. The extracts were washed with aqueous sodium hydrogen carbonate and brine, and then dried ($MgSO_4$) and evaporated under reduced pressure. The resulting residue was purified by chromatography (silica gel, eluting with methanol in dichloromethane) to yield pure amide.

Phenacylmonamide (**1d**). Prepared from phenacylamine (40 mmol, from phenacylammonium chloride and triethylamine) by the general method to give a white foam (10.9 g, 24 mmol, 60%); $\nu_{max.}$(film) 3 400, 1 690, 1 660, 1 630, and 1 600 cm^{-1}; $\lambda_{max.}$(EtOH) 240 nm (ε_m 22 400); δ_H ($CDCl_3$), 0.90 (3 H, d, 17-H_3), 1.20 (3 H, d, 14-H_3), 2.20 (3 H, s, 15-H_3), 4.82 (2 H, d, 1′-H_2), 5.86 (1 H, s, 2-H), 6.88 (1 H, t, NH), 7.50 (2 H, t, Aryl 3- and 5-H), 7.63 (1 H, t, Aryl 4-H), and 7.98 (2 H, d, Aryl 2- and 6-H); δ_C($CDCl_3$) 194.6 (C-2′), 167.1 (C-1), 151.9 (C-3), 134.5 (Aryl C-1), 133.8 (Aryl C-4), 128.8 (Aryl C-2 and -6), 128.7 (Aryl C-3 and 5), 119.6 (C-2), 74.9 (C-5), 70.8 (C-13), 70.3 (C-7), 68.8 (C-6), 65.2 (C-16), 60.9 (C-11), 55.4 (C-10), 46.1 (C-1′), 42.5 (C-4), 42.5 (C-12), 39.5 (C-8), 31.6 (C-9), 20.5 (C-14), 18.8 (C-15), and 12.3 (C-17); *m/z* 461 (M^+, 11%), 327 (18), 217 (96), and 136 (100) (Found: M^+, 461.2415. $C_{25}H_{35}NO_7$ requires 461.2414) (Found: C, 65.0; H, 7.5; N, 3.1. $C_{25}H_{35}NO_7$ requires: C, 65.1; H, 7.6; N, 3.0%).

o-*Hydroxyphenylmonamide* (**1f**). Prepared from *o*-aminophenol (3 mmol) by the general method to give a white foam (0.90 g, 72%); $\nu_{max.}$(film) 3 400, 1 660, 1 635, and 1 520 cm^{-1}; $\lambda_{max.}$(EtOH) 222 (ε_m 21 700), 263 (8 800), and 297 nm (8 900); δ_H($CDCl_3$) 0.86 (3H, d, 17-H_3), 1.15 (3H, d, 14-H_3), 2.21 (3 H, s, 15-H_3), 5.92 (1 H, s, 2-H), 6.8—7.0 (3 H, m, 3′- and 5′-H), 7.4 (1 H, d, 6′-H), 8.7 (1 H, s, OH), and 9.5 (1 H, br s, NH); δ_C(CD_3OD) 167.0 (C-1), 154.2 (C-3), 148.1 (C-2′), 126.7 (C-1′), 125.9 (C-6′), 122.1 (C-5′), 120.3 (C-4′), 119.8 (C-3′), 117.8 (C-2), 75.3 (C-5), 70.6 (C-7, C-13), 69.0 (C-6), 65.6 (C-16), 61.0 (C-11), 56.0 (C-10), 43.1 (C-4), 42.7 (C-12), 40.1 (C-8), 32.0 (C-9), 20.3 (C-14), 19.0 (C-15), and 12.2 (C-17); *m/z* 435 (6%, M^+), 417 (5), 309 (12), 173 (71), and 109 (100) (Found: M^+, 435.2228, $C_{23}H_{33}NO_7$ requires *M*, 435.2242).

o-*Aminophenylmonamide* (**1g**). Prepared from *o*-diaminobenzene (3 mmol) according to the general method to give the amide as a pale yellow foam (0.85 g, 68%); $\nu_{max.}$(film) 3 380, 1 660, and 1 630 cm^{-1}; $\lambda_{max.}$(EtOH) 226 (ε_m 21 400) and 299 nm (4 100); δ_H(CD_3OD) 0.95 (3 H, d, 17-H_3), 1.21 (3 H, d, 14-H_3), 2.21 (3 H, s, 15-H_3), 6.00 (1 H, s, 2-H), and 6.7—7.1 (4 H, m, Aryl); δ_C(CD_3OD) 167.9 (C-1), 154.1 (C-3), 143.0 (C-2″), 127.9 (C-4′), 126.9 (C-1′), 125.3 (C-3′), 120.8 (C-5′), 119.4 (C-3′), 118.4 (C-2), 76.2 (C-5), 71.5 (C-13), 70.7 (C-7), 70.0 (C-6), 66.3 (C-16), 61.3 (C-11), 56.8 (C-10), 43.9 (C-4), 43.6 (C-12), 41.5 (C-8), 32.9 (C-9), 20.3 (C-14), 19.0 (C-15), and 12.2 (C-17); *m/z* 434 (M^+, 13%), 172 (18), and 108 (100) (Found: M^+, 434.2393. $C_{23}H_{34}N_2O_6$ requires 434.2369).

N′-*Benzoylmonohydrazide* (**1h**). Prepared from benzohydrazide (3 mmol) by the general method to give the title compound as a white foam (0.76 g, 55%); $\nu_{max.}$(film) 3 400, 3 270, 1 690, 1 645, and 1 250 cm^{-1}; $\lambda_{max.}$(EtOH) 228 nm (ε_m 20 000); δ_H(CD_3OD) 0.93 (3 H, d, 17-H_3), 1.15 (3 H, d, 14-H_3), 2.21 (3 H, s, 15-H_3), 5.89 (1 H, s, 2-H), 7.4—7.9 (5 H, m, Aryl); δ_C(CD_3OD) 169.0 (Ph*C*O), 168.3 (C-1), 155.4 (C-3), 133.8 (Aryl C-1), 133.0 (Aryl C-4), 129.5 (Aryl C-2 and -6), 128.6 (Aryl C-3 and -5), 118.2 (C-2), 76.2 (C-5), 71.6 (C-13), 70.7 (C-7), 70.0 (C-6), 66.3 (C-16), 61.3 (C-11), 56.8 (C-10), 43.8 (C-4), 43.6 (C-12), 41.5 (C-8), 33.0 (C-9), 20.4 (C-14), 19.3 (C-15), and 12.2 (C-17); *m/z* 462 (M^+, 1%), 327 (8), 309 (8), and 105 (100) (Found: M^+, 462.2363. $C_{24}H_{34}N_2O_7$ requires 462.2361).

Benzamide O-*monyl oxime* (**1l**). Prepared from benzamidoxime (5 mmol) by the general method to give the title compound as a foam (1.51 g, 3.26 mmol, 65%); $\nu_{max.}$(film) 3 600—3 200, 2 960, 2 920, 1 720, 1 640, 1 570, 1 410, 1 220, 1 110, 1 050, 910, 780, 730, and 700 cm^{-1}; $\lambda_{max.}$(EtOH) 221 (ε_m 20 180) and 259 nm (12 000); δ_H(CD_3OD) 0.95 (3 H, d, *J* 7 Hz, 17-H_3), 1.21 (3 H, d, *J* 7 Hz, 14-H_3), 1.41 (1 H, m, 12-H), 1.70 (2 H, m, 9-H_2), 1.97 (1 H, m, 8-H), 2.26 (4 H, s + m, 15-H_3 and 4a-H), 2.70 (2 H, m, 4b- and 11-H), 2.81 (1 H, dt, *J* 2, 4 Hz, 10-H), 5.95 (1 H, s, 2-H), 7.44 (3 H, m, Phenyl), and 7.77 (2 H, m, Phenyl); δ_C(CD_3OD) 166.3 (C-1), 160.3 (C-3), 131.7, 129.5, 128.1 (Phenyl), 116.2 (C-2), 76.2 (C-5), 71.5 (C-13), 70.7 (C-7), 70.0 (C-6), 66.3 (C-16), 61.3 (C-11), 56.8 (C-10), 44.1, 43.6 (C-4 and -12), 41.5 (C-8), 32.9 (C-9), 20.4 (C-14), 19.5 (C-15), and 12.3 (C-17); *m/z* 457 (c.i., NH_3), 447 ($MH^+ - O$, 30%) 445 ($MH^+ - H_2O$, 15), 344 (22), 327 (15), 188 (28), 187 (70), and 121 (100).

2-*Normonyl*-5-*phenyloxazole* (**2a**). Phenacylmonamide (0.92 g, 2 mmol) was treated with chlorotrimethylsilane (0.76 ml, 6 mmol) and triethylamine (0.84 ml, 6 mmol) in THF (20 ml) until protection was complete by t.l.c. (6 h). The resulting solution was filtered, solvent removed under reduced pressure, and the resulting residue dissolved in dichloromethane (20 ml) and then treated with phosgene in toluene (2.3 mmol) and triethylamine (0.6 ml, 4.6 mmol) at 5 °C for 16 h. The mixture was then poured into aqueous sodium hydrogen carbonate, and this extracted with ethyl acetate; the latter was washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. The residue

was then dissolved in dioxane (40 ml) and water (10 ml). Concentrated aqueous hydrochloric acid (12 drops) was added and after 12 min the solution neutralised with aqueous sodium hydrogen carbonate and extracted with ethyl acetate. The extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure to leave a brown oil which was purified by chromatography (50 g silica, 0—10% methanol in dichloromethane). The oxazole was the second compound eluted and formed a white foam (0.11 g, 14%); $\nu_{max.}$(film) 3 400, 1 655, 1 120, and 1 050 cm^{-1}; $\lambda_{max.}$(EtOH) 301 nm (ε_m 20 800); $\delta_H(CD_3OD)$ 0.90 (3 H, d, 17-H_3), 1.21 (3 H, d, 14-H_3), 2.20 (3 H, s, 15-H_3), 6.26 (1 H, s, 2-H), and 7.3—7.8 (6 H, m, Aryl and Het-H); $\delta_C(CD_3OD)$ 161.2 (C-1), 150.0 (C-3), 146.8, 128.9, 128.1, 124.1, 122.5 (Aryl + Heteroaryl), 113.2 (C-2), 75.4 (C-5), 71.2 (C-13), 70.5 (C-7), 69.0 (C-6), 65.5 (C-16), 61.2 (C-11), 55.6 (C-10), 42.8 (C-4 and -12), 39.6 (C-8), 31.8 (C-9), 20.8 (C-14), 19.6 (C-15), and 12.6 (C-17); *m/z* 443 (M^+, 11%), and 199 (100) (Found: 443.2270. $C_{25}H_{33}NO_6$ requires 443.2305).

5-*Normonyl*-1-(p-*nitrobenzyl*)-1H-*tetrazole* (**2e**). *p*-Nitrobenzylmonamide (0.96 g, 2 mmol) in dry THF (20 ml) was treated with triethylamine (0.80 ml, 6 mmol) and trimethylchlorosilane (0.80 ml, 6 mmol) for 16 h at 20 °C. The mixture was then filtered and the filtrate evaporated under reduced pressure. The resulting residue was taken up in dichloromethane (20 ml) and then triethylamine (0.40 ml, 3 mmol) and phosgene (2 ml × 1.15M solution in toluene, 2.3 mmol) were added. After 30 min at 20 °C, tetramethylguanidinium azide (0.8 g, 5 mmol) was added and the mixture was then set aside for 16 h at 20 °C. The mixture was partitioned between aqueous sodium hydrogen carbonate and ethyl acetate and the organic layer dried ($MgSO_4$) and evaporated under reduced pressure. The resulting residue was taken up in water (20 ml) and dioxane (80 ml) and concentrated hydrochloric acid (25 drops) was added. After 12 min at 20 °C the solution was partitioned between aqueous sodium hydrogen carbonate and ethyl acetate. The organic layer was dried ($MgSO_4$) and evaporated under reduced pressure and the resulting residue purified by chromatography (20 g silica gel, 0—10% dichloromethane in methanol) to give the tetrazole as a yellow foam (60 mg, 6%); $\nu_{max.}$(film) 3 420, 1 655, 1 610, 1 425, and 1 350 cm^{-1}; $\lambda_{max.}$(EtOH) 243 nm (ε_m 14 500); $\delta_H(CDCl_3)$ 0.96 (3 H, d, 17-H_3), 1.21 (3 H, d, 14-H_3), 2.21 (3 H, s, 15-H_3), 5.60 (2 H, s, 1′-H), 6.03 (1 H, s, 2-H), 7.41 (2 H, d, 2″- and 6″-H), and 8.24 (2 H, d, 3″- and 5″-H); $\delta_C(CDCl_3)$ 153.2 (C-1), 152.0 (C-3), 148.3 (C-1″), 140.6 (C-4″), 128.7 (C-3″ and C-5″), 124.3 (C-2″ and -6″), 106.3 (C-2), 75.0 (C-5), 71.3 (C-13), 70.6 (C-7), 68.9 (C-6), 65.4 (C-16), 61.0 (C-11), 55.6 (C-10), 49.8 (C-1′), 42.8 (C-12), 42.6 (C-4), 40.1 (C-8), 31.8 (C-9), 20.9 (C-14), 20.2 (C-15), and 12.7 (C-17); *m/z* 503 (M^+, 1%) 259 (12), and 106 (100) (Found: M^+, 503.2323. $C_{24}H_{33}N_5O_7$ requires *M*, 503.2351).

1-(8-*Methoxycarbonyloctyl*)-5-*normonyl*-1H-*tetrazole* (**2f**). 8-Methoxycarbonyloctylmonamide (513 mg) in THF (30 ml) was treated with triethylamine (0.7 ml) followed by trimethylsilyl chloride (0.6 ml) and 4-*N*,*N*-dimethylaminopyridine (catalytic amount). After 1 h the solution was filtered and the filtrate evaporated to an oil which was redissolved in THF, filtered, and re-evaporated to an oil. The protected amide in THF (25 ml) was cooled to −20 °C and treated with triethylamine (0.153 ml) and phosgene in toluene (1.1M; 1 ml). The reaction was stirred at room temperature for 2 h and then treated with tetramethylguanidinium azide (395 mg, 2.5 equiv.) and stirred for 3 h at room temperature. The reaction was poured into saturated aqueous ammonium chloride and the product extracted with ethyl acetate. The combined extracts were dried ($MgSO_4$) and evaporated to an oil which was taken up in THF–water (4:1; 20 ml) and treated with 10M hydrochloric acid (10 drops). After 7 min excess of saturated aqueous sodium hydrogen carbonate was added and the product extracted with ethyl acetate. The combined extracts were washed with brine, dried ($MgSO_4$) and evaporated to an oil which was chromatographed on silica (7.5 g) eluting with 0—6% methanol in dichloromethane. Fractions containing pure product were combined and evaporated (130 mg, 24%); m.p. 80—85 °C; $\nu_{max.}(CHCl_3)$ 3 340 (br), 1 736, 1 708, and 1 646 cm^{-1}; $\lambda_{max.}$(EtOH) 235.5 nm (ε_m 13 168); $\delta_H(CDCl_3)$ 0.92 (3 H, d, 17-H_3), 1.22 (3 H, d, 14-H_3), 2.25 (3 H, s, 15-H_3), 2.30 (2 H, t, CH_2CO_2Me), 3.67 (3 H, s, OCH_3), 4.27 (2 H, t, CH_2-Tet), and 6.10 (1 H, s, 2-H); $\delta_C(CDCl_3)$ 174.4 (C-1′), 152.0 and 151.7 (C-1 and -3), 106.7 (C-2), 75.1 (C-5), 71.2 (C-13), 70.5 (C-7), 68.9 (C-6), 65.5 (C-5), 61.2 (C-11), 55.7 (C-10), 51.5 (OCH_3), 47.1 (C-9′), 42.8 (C-4 and -12), 39.9 (C-8′), 34.1 (C-2′), 31.8 (C-9), 29.5, 29.0, 28.7, 26.3 (C-4′, -5′, -6′, -7′, and -8′), 24.9 (C-3′), 20.8 (C-14), 20.1 (C-15), and 12.6 (C-17); *m/z* 538 (M^+, 4%) 507 (7), 393 (15), and 294 (100) (Found: M^+, 538.3367. $C_{27}H_{46}N_4O_7$ requires *M*, 538.3366).

Typical Procedure for Preparation of Phosphonates.—5-*Diethylphosphonomethyl*-3-*methylisoxazole* (**5d**).—5-Chloromethyl-3-methylisoxazole (1.12 g, 8.52 mmol) was dissolved in triethyl phosphite (2.0 ml, 11.6 mmol) and heated at reflux for 1 h. The residue was then distilled under reduced pressure to give the title compound (1.47 g, 6.30 mmol, 74%); b.p. 122—125 °C at 0.5 mmHg; $\nu_{max.}$(film) 2 980, 2 930, 2 910, 1 605, 1 440, 1 420, 1 390, 1 255, 1 160, 1 060—1 010, 980, and 900 cm^{-1}; $\delta_H(CDCl_3)$ 1.35 (3 H, t, *J* 7 Hz, OCH_2CH_3), 2.30 (3 H, s, CH_3-Het), 3.30 (1 H, d, $J_{H,P}$ 24 Hz, CH_2P), 4.10 (2 H, m, OCH_2CH_3), and 6.05 (1 H, d, *J* 3 Hz, CH-Het); $\delta_C(CDCl_3)$ 163.6 and 163.5 (C-2), 160.1 (C-4), 104.1 (C-3), 62.8 and 62.7 (OCH_2CH_3), 26.8 and 24.6 (C-1), 66.4 and 16.3 (OCH_2CH_3), and 11.4 (C-5); *m/z* 233 (M^+, 18%), 192 (47), 177 (41), 136 (50), 109 (100), 97 (82), 96 (35), 81 (76), and 43 (32) (Found: 233.0831. $C_9H_{16}NO_4P$ requires 233.0816).

Preparation of the Protected Ketone (**3b**).—To a solution of (2*S*,3*R*,4*R*,5*S*)-3,4-dihydroxy-5-[(2*S*,3*S*,4*S*,5*S*)-2,3-epoxy-5-hydroxy-4-methylhexyl]tetrahydropyran-2-ylacetone (604 mg, 2.0 mmol) in THF (20 ml) was added triethylamine (0.87 ml, 6.20 mmol), trimethylsilyl chloride (0.73 ml, 6.20 mmol), and a catalytic amount of 4-*N*,*N*-dimethylaminopyridine. After the mixture had been stirred at room temperature for 2 h the triethylamine hydrochloride was filtered off and the solution concentrated under reduced pressure. The resultant oil was taken up in anhydrous ether, the solution filtered, and the solvent removed under reduced pressure. The oil (the protected ketone) was then taken up in dry THF ready for the next stage of the reaction.

3-*Normonylisoxazole* (**2h**).—To a solution of lithium di-isopropylamide [from di-isopropylamine (185 μl) and butyllithium (1.60 M solution; 0.83 ml, 1.32 mmol)] in THF (10 ml) at −78 °C was added 3-diethylphosphonomethylisoxazole (**5a**), (275 mg, 1.20 mmol) in THF (5 ml). The solution was stirred for 30 min after which its temperature was allowed to rise to 0 °C when it was stirred for a further 30 min. The protected ketone (**3b**) (1.0 mmol) was added and the reaction stirred at 0 °C for 30 min then room temperature for 18 h. After this it was quenched with aqueous ammonium chloride, extracted with ethyl acetate, and dried ($MgSO_4$). Solvent removal under reduced pressure gave an oil which was taken up in THF–water (4:1; 100 ml) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time the mixture was quenched with aqueous sodium hydrogen carbonate and extracted with ethyl acetate. The extract was dried ($MgSO_4$) and solvent removal under reduced pressure to give the crude product (347 mg) which was chromatographed (0 to 5% MeOH in CH_2Cl_2, 5 g, silica) to give the title compound as an inseparable mixture with the *Z* isomer (73 mg, 0.20 mol, 20%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 930,

1 650, 1 625, 1 550, 1 450, 1 380, 1 110, 1 050, and 850 cm^{-1}; $\lambda_{max.}$(EtOH) 220 (ε_m 7 620); $\delta_H(CDCl_3)$ 0.94 (3 H, d, *J* 7 Hz, 17-H_3), 1.22 (3 H, d, *J* 7 Hz, 14-H_3), 1.35 (1 H, m, 12-H), 1.72 (2 H, m, 9-H_2), 2.00 (1 H, m, 8-H), 2.08 and 2.10 (3 H, 2 × s, 15-H_3), 2.2—2.4 (1 H, m, 4a-H), 6.25 (1 H, s, 2-H), 6.36 (1 H, d, *J* 2 Hz, 2′-H), and 8.35 (1 H, d, *J* 2 Hz, 3′-H); *m/z* (c.i., NH_3) 368 (MH^+, 47%), 124 (63), 110 (46), 58 (81), and 44 (100).

5-Methyl-3-normonylisoxazole (**2i**).—To a solution of lithium di-isopropylamide [from di-isopropylamine (0.31 ml) and butyl-lithium (1.55M solution; 1.42 ml, 2.20 mmol)] in THF (10 ml) at −78 °C was added 3-diethylphosphonomethyl-5-methylisoxazole (**5b**), (489 mg, 2.10 mmol) in THF (5 ml). The solution was stirred for 30 min after which its temperature was raised to 0 °C when it was stirred for a further 30 min. The ketone (**3b**), (2 mmol) was added and the reaction mixture stirred first at 0 °C for 30 min and then at room temperature for 3 h; it was then quenched with aqueous ammonium chloride, extracted with ethyl acetate, and the extract dried ($MgSO_4$). Evaporation of the extract under reduced pressure gave an oil which was taken up in THF–water (100 ml, 4:1) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time, the mixture was quenched with aqueous sodium hydrogen carbonate and extracted with ethyl acetate. The extract was dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product which was chromatographed (0—5% MeOH in CH_2Cl_2, 15 g SiO_2) to give the title compound (250 mg, 0.65 mmol, 33%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 930, 1 650, 1 600, 1 450, 1 380, 1 110, 1 050, 910, and 730 cm^{-1}; $\lambda_{max.}$(EtOH) 232 nm (ε_m 10 900); δ_H 0.92 (3 H, d, *J* 7 Hz, 17-H_3), 1.22 (3 H, d *J* 7 Hz, 14-H_3), 1.34 (1 H, q, *J* Hz, 12-H), 1.72 (2 H, t, *J* 6 Hz, 9-H_2), 2.03 (4 H, s + m, 15-H_3 and 8-H), 2.40 (4 H, s + m, CH_3-Het + 4a-H), 2.63 (1 H, dd, *J* 14 and 2 Hz, 4b-H), 2.70 (1 H, dd, *J* 9.2 Hz, 11-H), 2.82 (1 H, dt, *J* 2 and 5 Hz, 10-H), 6.01 (1 H, s, CH-Het), and 6.20 (1 H, s, 2-H); $\delta_C(CDCl_3)$ 168.6 (C-3′), 160.7 (C-1), 144.1 (C-3), 114.5 (C-2), 102.2 (C-2′), 75.3 (C-5), 71.0 (C-13), 70.4 (C-7), 68.9 (C-6), 65.4 (C-16), 61.1 (C-11), 55.6 (C-10), 42.7 (C-12), 42.6 (C-4), 39.5 (C-8), 31.7 (C-9), 20.7 (C-14), 19.3 (C-15), 12.5 (C-17), and 12.1 (C-4); *m/z* 381 (M^+, 1%), 227 (5), 138 (18), 137 (100), 122 (19), 69 (18), 55 (19), 45 (21), 43 (52), and 41 (31) (Found: M^+, 381.2172. $C_{20}H_{31}NO_6$ requires *M*, 381.2151) and the *Z*-isomer (60.5 mg, 0.15 mmol, 8%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 930, 1 645, 1 605, 1 405, 1 110, 1 050, 910, and 730 cm^{-1}; $\lambda_{max.}$(EtOH) 232 nm (ε_m 11 000) ;$\delta_H(CDCl_3)$ 0.94 (3 H, d *J* 7 Hz, 17-H_3), 1.21 (3 H, d, *J* 7 Hz, 14-H_3), 1.34 (1 H, q, *J* 7 Hz, 12-H), 1.59 (1 H, m, 9a-H), 1.82 (1 H, m, 9b-H), 2.04 (4 H, d, *J* 1 Hz + m, 15-H_3 and 8-H), 5.88 (1 H, s, 2′-H), and 6.05 (1 H, s, 2-H); $\delta_C(CDCl_3)$ 168.8 (C-3′), 160.1 (C-1), 146.9 (C-3), 114.2 (C-2), 103.0 (C-2′), 76.8 (C-5), 71.3 (C-13), 70.3 (C-7), 67.3 (C-6), 65.5 (C-16), 61.4 (C-11), 56.0 (C-10), 42.9 (C-12), 38.9 (C-8), 36.8 (C-4), 31.8 (C-9), 26.8 (C-15) 20.7 (C-14), 12.7 (C-17), and 12.0 (C-4′); *m/z* 382 (MH^+, 2%), 381 (M^+, 1%), 227 (7), 166 (42), 150 (54), 137 (100), 45 (50), 43 (88), and 41 (48) (Found: M^+, 381.2127. $C_{20}H_{31}NO_6$ requires *M*, 381.2151).

3-Normonyl-5-phenylisoxazole (**2j**).—To a suspension of sodium hydride (50% in oil, washed; 106 mg, 2.20 mmol) in tetrahydrofuran (THF) (10 ml) at 0 °C was added 3-diethylphosphonomethyl-5-phenylisoxazole (**5c**) (620 mg, 2.10 mmol) in THF (5 ml). The cooling bath was removed and the mixture stirred at room temperature until hydrogen evolution had ceased and the solution was homogeneous (*ca.* 2 h). The solution was cooled (0 °C) and the protected ketone (**3b**) (2.0 mmol) added; the mixture was then stirred at 0 °C for 30 min and then for 1 h at ambient temperature. The mixture was quenched with ammonium chloride and then extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give an oil which was taken up in THF–water (4:1, 100 ml) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time the mixture was quenched with sodium hydrogen carbonate and extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give the crude product which was chromatographed to give the title compound (110 mg, 0.24 mmol, 12%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 920, 1 655, 1 615, 1 590, 1 575, 1 495, 1 450, 1 420, 1 380, 1 110, 1 050, 910, 865 and 830 cm^{-1}; $\lambda_{max.}$(EtOH) 266 nm (ε_m 21 230); $\delta_H(CDCl_3)$ 0.93 (3 H, d, *J* 7 Hz, 17-H_3), 1.22 (3 H, *J* 7 H, 14-H_3), 1.33 (1 H, q, *J* 7 Hz, 12-H), 1.74 (2 H, m, 9-H_2), 2.02 (1 H, m, 8-H), 2.11 (3 H, s, 15-H_3), 2.42 (1 H, dd, *J* 12 and 9 Hz, 4a-H), 2.65 (1 H, m, 4b-H), 2.72 (1 H, dd, *J* 8 and 2 Hz, 11-H), 2.83 (1 H, dt, *J* 2 and 5 Hz, 10-H), 6.27 (1 H, s, 2-H), 6.54 (1 H, s, 2′-H), 7.44 (3 H, m, Ar), and 7.78 (2 H, m, Ar); $\delta_C(CDCl_3)$ 169.2 (C-3′), 161.1 (C-1), 144.7 (C-3), 130.1, 129.0, and 125.8 (Ar), 114.4 (C-2), 100.0 (C-2′), 75.3 (C-5), 71.1 (C-13), 70.4 (C-7), 69.0 (C-6), 65.4 (C-16), 61.2 (C-11), 55.7 (C-10), 42.7 and 42.6 (C-12 and -4), 39.5 (C-8), 31.7 (C-9), 20.8 (C-14), 19.6 (C-15), and 12.6 (C-17); *m/z* 443 (M^+, 3%), 200 (23), 199 (100), 105 (36), 94 (16), 69 (24), 57 (16), 55 (22), 43 (29), and 41 (23) (Found: 443.2286. $C_{25}H_{33}NO_6$ requires 443.2306) and the *Z* isomer (33.5 mg, 0.08 mmol, 4%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 930, 1 655, 1 615, 1 590, 1 575, 1 495, 1 450, 1 420, 1 110, 1 050, 910, 865, 830, and 790 cm^{-1}; $\lambda_{max.}$(EtOH) 266 nm; $\delta_H(CDCl_3)$ 0.94 (3 H, d, *J* 7 Hz, 17-H_3), 1.20 (3 H, d, *J* 7 Hz, 14-H_3), 1.31 (1 H, q, *J* 7 Hz, 12-H), 1.62 (1 H, m, 9a-H), 1.82 (1 H, m, 9b-H), 2.09 (4 H, m + s, 8-H + 15-H_3), 2.68 (1 H, dd, *J* 8 and 2 Hz, 11-H), 2.82 (3 H, m, 10-H + 4-H_2), 6.15 (1 H, s, 2-H), 6.43 (1 H, s, 2′-H), 7.45 (3 H, m, Ar), and 7.75 (2 H, m, Ar); $\delta_C(CDCl_3)$ 169.4 (C-3′), 160.6 (C-1), 147.5 (C-3), 130.4, 129.1, and 126.0 (Ar), 114.1 (C-2), 100.8 (C-2′), 76.8 (C-5), 71.4 (C-13), 70.3 (C-7), 67.5 (C-6), 65.5 (C-16), 61.5 (C-11), 56.0 (C-10), 43.0 (C-12), 37.0 (C-4), 31.8 (C-9), 26.8 (C-15), 20.8 (C-14), and 12.7 (C-17); *m/z* 443 (M^+, 1%), 340 (6), 228 (34), 211 (50), 199 (65), 105 (100), 77 (50), 45 (50), 43 (45), and 41 (56) (Found: M^+, 443.2303. $C_{25}H_{33}NO_6$ requires *M*, 443.2306).

3-Methyl-5-normonylisoxazole (**2k**).—To a suspension of sodium hydride (50% in oil, washed; 106 mg, 2.20 mmol) in dry dimethoxyethane (DME) (10 ml) at 0 °C was added 5-diethylphosphonomethyl-3-methylisoxazole (**5d**), (489 mg, 2.10 mmol) in DME (5 ml). The cooling bath was removed and the mixture stirred at room temperature until hydrogen evolution had ceased and the solution was homogeneous (*ca.* 2 h). The anion was cooled (0 °C), the protected ketone (3b, 2.0 mmol) added, and the mixture stirred for 30 min at 0 °C and then ambient temperature for 1 h. The mixture was quenched with ammonium chloride, extracted with ethyl acetate, and the extract dried ($MgSO_4$) and evaporated under reduced pressure to give an oil. This was taken up in THF–water (4:1; 100 ml) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time the mixture was quenched with sodium hydrogen carbonate and extracted with ethyl acetate. The extract was dried ($MgSO_4$) and evaporated under reduced pressure to give the crude product which was chromatographed to afford the title compound as an inseparable mixture with *Z* isomer (250 mg, 0.66 mmol, 32%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 930, 1 720, 1 655, 1 585, 1 570, 1 450, 1 415, 1 110, 1 050, 910, and 730 cm^{-1}; $\lambda_{max.}$(EtOH) 259 (ε_m 17 160); $\delta_H(CDCl_3)$ (*E* isomer only) 0.93 (3 H, d, *J* 7 Hz, 17-H_3), 1.21 (3 H, d, *J* 7 Hz, 14-H_3), 1.32 (1 H, q, *J* 7 Hz, 12-H), 1.75 (2 H, m, 9-H_2), 2.05 (4 H, s + m, 15-H_3 + 8-H), 2.30 (3 H, s, CH_3-Het), 2.36 (1 H, dd, *J* 14 and 10 Hz, 4a-H), 2.60 (1 H, m, 4b-H), 2.72 (1 H, dd, *J* 8 and 2 Hz, 11-H), 2.83 (1 H, m, 10-H), 5.95 (1 H, s, 2-H), and 6.25 (1 H, s, 2′-H); $\delta_C(CDCl_3)$ (*E* isomer) 168.6 (C-1), 159.6 (C-3′), 144.5 (C-3), 113.1 (C2), 102.8 (C-2′), 75.3 (C-5), 70.8 (C-13), 70.4 (C-7),

68.9 (C-6), 65.4 (C-16), 61.0 (C-11), 55.7 (C-10), 42.7 (C-4 + C-12), 39.7 (C-8), 31.8 (C-9), 20.6 (C-14), 19.5 (C-15), 12.4 (C-17), and 11.3 (*C*H$_3$-Het); *Z* isomer differs by 168.4 (C-1), 145.7 (C-3), 113.0 (C-2), 103.0 (C-2′), 39.6 (C-8), 36.2 (C-4), and 25.6 (C-15); *m/z* 381 (M^+, 1%), 279 (3), 227 (7), 149 (19), 137 (100), 97 (14), 95 (14), 69 (22), 55 (20), 43 (37), and 41 (27) (Found: 381.2166. $C_{20}H_{31}NO_6$ requires 381.2152).

5-*Normonyl*-3-*phenylisoxazole* (**21**).—To a suspension of sodium hydride (50% in oil, washed, 106 mg, 2.20 mmol) in tetrahydrofuran (THF) (10 ml) at 0 °C was added 5-diethylphosphonomethyl-3-phenylisoxazole (**5e**) (620 mg, 2.10 mmol) in THF (5 ml). The cooling bath was removed and the mixture stirred at room temperature until hydrogen evolution had ceased and the solution was homogeneous (*ca.* 1 h). The solution was cooled (0 °C), the protected ketone (**3b**) (2.00 mmol) added, and the mixture stirred at 0 °C for 30 min and then ambient temperature for 1 h. The mixture was quenched with ammonium chloride and then extracted with ethyl acetate and then dried ($MgSO_4$) extract was evaporated under reduced pressure to give an oil which was taken up in THF–water (4:1, 100 ml) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time the mixture was quenched with sodium hydrogen carbonate and extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give the crude product which was chromatographed to give the title compound (272 mg, 0.61 mmol, 31%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 920, 1 655, 1 590, 1 570, 1 465, 1 405, 1 105, 1 050, 910, 770, and 690 cm^{-1}; $\lambda_{max.}$(EtOH) 240 nm (ε_m 22 600); δ_H($CDCl_3$) 0.93 (3 H, d, *J* 7 Hz, 17-H$_3$), 1.22 (3 H, d, *J* 7 Hz, 14-H$_3$), 1.32 (1 H, m, 12-H), 1.74 (2 H, m, 9-H$_2$), 2.04 (1 H, m, 8-H), 2.13 (3 H, s, 15-H$_3$), 2.38 (1 H, dd, *J* 14 and 10 Hz, 4a-H), 2.50—2.75 (2 H, m, 11-H + 4b-H), 2.80 (1 H, dt, *J* 2 and 5 Hz, 10-H), 6.32 (1 H, s, 2-H), 6.43 (1 H, s, 2′-H), 7.46 (3 H, m, Ph), and 7.80 (2 H, m, Ph); δ_C($CDCl_3$) 169.4 (C-1), 162.4 (C-3′), 145.0 (C-3), 130.0, 129.0, and 126.8 (Ph), 113.2 (C-2), 100.1 (C-2′), 75.3 (C-5), 71.1 (C-13), 70.4 (C-7), 68.9 (C-6), 65.5 (C-16), 61.2 (C-11), 55.7 (C-10), 42.8 (C-12 and -4), 39.6 (C-8), 31.7 (C-9), 20.7 (C-14), 19.7 (C-15), and 12.6 (C-17); *m/z* 443 (M^+, 3%), 199 (100), 83 (8), 69 (14), 67 (9), 55 (11), 45 (8), 43 (15), and 41 (14) (Found: 443.2322. $C_{25}H_{33}NO_6$ requires 443.2306) and the *Z* isomer (47.4 mg, 0.11 mmol, 5%); $\nu_{max.}$ 3 600—3 200, 2 970, 2 920, 1 650, 1 590, 1 570, 1 465, 1 405, 1 105, 1 045, 770, 730, and 690 cm^{-1}; $\lambda_{max.}$(EtOH) 241 nm (ε_m 23 380); δ_H($CDCl_3$) 0.92 (3 H, d, *J* 7 Hz, 17-H$_3$), 1.22 (3 H, d, *J* 7 Hz, 14-H$_3$), 1.37 (1 H, q, *J* 7 Hz, 12-H), 1.74 (2 H, m, 9-H$_2$), 2.05 (4 H, m + s, 8-H + 15-H$_3$), 2.61 (1 H, dd, *J* 14 and 10 Hz, 4a-H), 2.73 (1 H, dd, *J* 8 and 2 Hz, 11-H), 2.82 (1 H, dt, *J* 2 and 6 Hz, 10-H), 3.03 (1 H, dd, *J* 14 and 2 Hz, 4b-H), 6.29 (1 H, s, 2-H), 6.59 (1 H, s, 2′-H), 7.45 (3 H, m, Ph), and 7.80 (2 H, m, Ph); δ_H($CDCl_3$) 169.3 (C-1), 162.5 (C-3′), 146.4 (C-3), 130.0, 129.0, and 126.8 (Ph), 113.0 (C-2), 100.4 (C-2′), 76.2 (C-5), 70.9 (C-13), 70.3 (C-7), 69.5 (C-6), 65.5 (C-16), 61.2 (C-11), 55.8 (C-10), 42.7 (C-12), 39.6 (C-8), 36.5 (C-4), 31.9 (C-9), 25.8 (C-15), 20.5 (C-14), and 12.4 (C-17); *m/z* 443 (M^+, 1%), 200 (17), 199 (100), 77 (14), 69 (17), 67 (12), 55 (22), 45 (19), 43 (26), and 41 (28) (Found: M^+, 443.2345. $C_{25}H_{33}NO_6$ requires *M*, 443.2306).

5-*Benzyl*-2-*normonyloxazole* (**2m**).—To a suspension of sodium hydride (25 mg, 1 mmol) in THF (2 ml) at 0 °C was added diethyl 2-diethylphosphonomethyl-5-benzyloxazole (**5f**), (310 mg, 1 mmol) in more THF (2 ml). The mixture was stirred at room temperature until hydrogen evolution had ceased and the solution was homogeneous (*ca.* 0.5 h). The solution was cooled (0 °C) and the protected ketone (1.0 mmol) added; the mixture was then stirred at 0 °C for 30 min and then at ambient temperature for 1 h. The mixture was quenched with ammonium chloride and extracted with ethyl acetate. The extract was dried ($MgSO_4$) and evaporated under reduced pressure to give an oil. This was taken up in THF–water (4:1; 50 ml) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time the mixture was quenched with sodium hydrogen carbonate and extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give the crude product which was purified by chromatography [silica (20 g), 0—10% methanol in dichloromethane] to give the title compound as a colourless oil (100 mg, 22%); $\nu_{max.}$(film) 3 400, 2 900, 1 655, and 730 cm^{-1}; $\lambda_{max.}$(EtOH) 266 nm (ε_m 19 800); δ_H(CD_3OD) 0.94 (3 H, d, 17-H$_3$), 1.22 (3 H, d, 14-H$_3$), 2.16 (3 H, s, 15-H$_3$), 4.05 (2 H, s, C*H*$_2$Ar), 6.13 (1 H, s, 2-H), 6.79 (1 H, s, Het-H), and 7.25 (5 H, m, Aryl); δ_C(CD_3OD) 162.6 (C-1), 152.0 (C-3), 148.0 (C-5), 138.2 (C-1″), 129.6 (C-2″, -3″, -5″, and -6″), 127.7 (C-4″), 124.1 (C-4′), 113.7 (C-2), 76.5 (C-5), 71.6 (C-13), 70.7 (C-7), 70.0 (C-6), 66.3 (C-16), 61.4 (C-11), 56.8 (C-10), 43.6 (C-4 and -12), 41.4 (C-8), 32.9 (*C*H$_2$Ar), 32.5 (C-9), 20.3 (C-14), 19.5 (C-15), and 12.2 (C-17); *m/z* 457 (M^+, 14%), 214 (23), 213 (100), 122 (14), and 45 (25) (Found: M^+, 457.2459. $C_{26}H_{35}NO_6$ requires *M*, 457.2464).

4-*Ethoxycarbonyl*-2-*normonyloxazole* (**2n**).—To a suspension of sodium hydride (50% in oil, washed; 48 mg; 1.00 mmol) in dry THF (5 ml) at 0 °C was added 2-diethylphosphonomethyl-4-ethoxycarbonyloxazole (**5g**) (275 mg, 0.95 mmol) in THF (5 ml). The cooling bath was removed and the mixture stirred at room temperature until hydrogen evolution had ceased and the solution was homogeneous (*ca.* 10 min). The anion was cooled (0 °C), the protected ketone (**3b**) (1.00 mmol) added, and the mixture stirred at 0 °C for 30 min and then ambient for 1 h. The mixture was quenched with ammonium chloride and then extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give an oil which was taken up in THF–water (4:1; 100 ml) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time the mixture was quenched with sodium hydrogen carbonate and extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give the crude product which was chromatographed to give the title compound (35 mg, 80 μmol, 8%); $\nu_{max.}$($CHCl_3$) 3 600—3 200, 1 730, 1 645, and 910 cm^{-1}; $\lambda_{max.}$(EtOH) 254 nm (ε_m 19 230); δ_H($CDCl_3$) 0.93 (3 H, d, *J* 7 Hz, 17-H$_3$), 1.21 (3 H, d, *J* 7 Hz, 14-H$_3$), 1.38 (4 H, t + m, *J*, 7 Hz, $CO_2CH_2CH_3$ and 12-H), 1.73 (2 H, t, *J* 5 Hz, 9-H$_2$), 2.00 (2 H, m, 8-H and O*H*), 2.26 (3 H, s, 15-H$_3$), 2.37 (1 H, dd, *J* 15 and 10 Hz, 4a-H), 2.81 (1 H, dt, *J* 2 and 5 Hz, 10-H), 3.15 (1 H, O*H*), 3.23 (1 H, O*H*), 4.40 (2 H, q, *J* 7 Hz, OCH_2CH_3), 6.25 (1 H, s, 2-H), and 8.13 (1 H, s, 3′-H); δ_C($CDCl_3$) 162.3 and 161.6 (C-1 and -1″), 149.5 (C-3), 142.4 (C-3′), 133.7 (C-4′), 112.3 (C-2), 75.1 (C-5), 71.3 (C-13), 70.4 (C-7), 68.9 (C-6), 65.5 (C-16), 61.4 (C-10), 61.2 (OCH_2CH_3), 55.6 (C-10), 42.8 (C-12 and -4), 39.6 (C-8), 31.7 (C-9), 20.8 (C-14), 19.7 (C-15), 14.3 (OCH_2CH_3), and 12.7 p.p.m. (C-17); *m/z* 439 (M^+, 1%), 196 (100), 195 (13), 149 (15), 69 (15), 55 (13), 45 (11), 43 (22), and 41 (16) (Found: M^+, 439.2191. $C_{22}H_{33}NO_8$ requires *M*, 439.2206).

5-*Normonyl*-2-*phenyloxazole* (**2o**).—To a suspension of sodium hydride (50% in oil, washed; 96 mg, 2.00 mmol) in THF (10 ml) at 0 °C was added 5-diethylphosphonomethyl-2-phenyloxazole (**5h**), (590 mg, 2.00 mmol) in THF (5 ml). The cooling bath was removed and the mixture stirred at room temperature until hydrogen evolution had ceased and the solution was homogeneous (*ca.* 1.5 h). The solution was cooled (0 °C) and the protected ketone (**3b**), (2.00 mmol) added; the mixture was then stirred at 0 °C for 30 min and then ambient temperature for 1 h. The mixture was quenched with ammonium chloride and extracted with ethyl acetate. The dried

($MgSO_4$) extract was evaporated under reduced pressure to give an oil which was taken up in THF–water (4:1; 100 ml) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time the mixture was quenched with sodium hydrogen carbonate and extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give the crude product which was chromatographed (0—5% MeOH in CH_2Cl_2 on silica) to give the title compound as an inseparable mixture with the *Z* isomer (91 mg, 0.21 mmol, 10%) *E*:*Z* 3:1; $\nu_{max.}$(film) (both isomers) 3 600—3 200, 2 970, 2 910, 1 640, 1 480, 1 450, 1 380, 1 110, 1 050, 905, 750, 710, and 690 cm^{-1}; $\lambda_{max.}$(EtOH) (both isomers) 306 nm (ε_m 16 170); $\delta_H(CDCl_3)$ (*E* isomer) 0.93 (3 H, d, *J* 7 Hz, 17-H_3), 1.22 (3 H, d, *J* 7 Hz, 14-H_3), 1.33 (1 H, m, 12-H), 1.76 (2 H, m, 9-H_2), 2.12 (3 H, d, *J* 15-H_3), 2.39 (1 H, dd, *J* 14 and 9 Hz, 4a-H), 6.26 (1 H, s, 2-H), 7.03 (1 H, s, 2′-H), 7.45 (3 H, m, Ph) and 8.02 (2 H, m, Ph); *m/z* 443 (M^+, 16%), 199 (100), 94 (74), 69 (41), 57 (53), 55 (48), 43 (48), and 41 (59) (Found: M^+, 443.2312. $C_{25}H_{33}NO_6$ requires *M*, 443.2308).

3-*Normonyl*-5-*phenyl*-1,2,4-*oxadiazole* (**2p**).—To a suspension of sodium hydride (50% in oil, washed; 48 mg, 1.00 mmol) in dry THF (10 ml) at 0 °C was added 3- diethylphosphonomethyl-5-phenyl-1,2,4-oxadiazole (5i, 296 mg, 1.00 mmol) in THF (5 ml). The cooling bath was removed and the mixture stirred at room temperature until hydrogen evolution had ceased and the solution was homogeneous (*ca.* 1 h). The solution was cooled (0 °C) and the protected ketone (**3b**), (1.00 mmol) added; the mixture was then stirred at 0 °C for 30 min and then at ambient temperature for 1 h. After this it was quenched with ammonium chloride and extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give an oil which was taken up in THF–water (4:1; 100 ml) and treated with concentrated hydrochloric acid (10 drops) for 5 min. After this time the mixture was quenched with sodium hydrogen carbonate and extracted with ethyl acetate. The dried ($MgSO_4$) extract was evaporated under reduced pressure to give the crude product which was chromatographed (0—5% MeOH in CH_2Cl_2, 5 g of silica) to give the title compound (98 mg, 0.22 mmol, 22%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 920, 1 660, 1 610, 1 550, 1 500, 1 450, 1 110, 1 050, 910, 730, and 690 cm^{-1}; $\lambda_{max.}$(EtOH) 244 (ε_m 27 270); $\delta_H(CDCl_3)$ 0.95 (3 H, d, *J* 7 Hz, 14-H_3), 2.30 (3 H, s, 15-H_3), 6.30 (1 H, s, 2-H), 7.50 (3 H, m, Ph), and 8.10 (2 H, m, Ph), and the *Z* isomer (31 mg, 0.97 mmol, 7%); $\nu_{max.}$(film) 3 600—3 200, 2 980, 1 660, 1 610, 1 560, 1 450, 1 380, 1 240, 1 030, 960, 730, and 695 cm^{-1}; $\lambda_{max.}$(EtOH) 243 nm (ε_m 16 120); $\delta_H(CDCl_3)$ 0.95 (3 H, d, *J* 7 Hz, 17-H_3), 1.25 (3 H, d, *J* 7 Hz, 14-H_3), 2.10 (3 H, s, 15-H_3), 6.35 (1 H, s, 2-H), 7.50 (3 H, m, Ph), and 8.10 (2 H, m, Ph); *m/z* 445 (MH^+, 8%), 227 (18), 200 (29), 171 (18), 105 (100), 77 (25), 43 (20), and 41 (18) (Found: MH^+, 445.2312. $C_{24}H_{33}N_2O_6$ requires 445.2338).

General Method in situ *Preparation and Reaction of Trimethylsilylmethyl Heterocycles.*—A solution of the methyl heteroaromatic (2.20 mmol) and butyl-lithium (2.20 mmol) in THF at −78 °C was stirred for 10—15 min. To the metalated species produced was added trimethylsilyl chloride (0.28 ml, 2.20 mmol) and this mixture was stirred for 45 min at −78 °C, followed by a further 45 min at −20 to −25 °C. The resultant solution was cooled to −78 °C and a further equivalent of butyllithium (2.04 mmol) added. Stirring was continued for 45 min after which the protected ketone (**3b**) (2.00 mmol) was added and the mixture allowed to warm to room temperature. The mixture was quenched with aqueous ammonium chloride, extracted with ethyl acetate (3 × 50 ml), and the combined extract were dried ($MgSO_4$). Evaporation of the latter under reduced pressure gave the crude product which was deprotected in the usual fashion and purified by column chromatography.

2-*Normonyl*-5-*phenyloxazole* (**2a**). The anion was prepared from 2-methyl-5-phenyl-1,3-oxazole (**6**), (350 mg, 2.20 mmol) as described and treated with the protected ketone (**3b**) (2.00 mmol) to yield a mixture of *E* and *Z* isomers of the title compounds; *Z* isomer (29 mg, 0.065 mmol, 3.3%); $\nu_{max.}$(film) 3 600—3 100, 2 970, 2 930, 1 650, 1 450, 1 110, 1 050, 950, 910, 760, and 690 cm^{-1}; $\lambda_{max.}$ 302 nm (ε_m 17 100); $\delta_H(CDCl_3)$, 0.95 (3 H, d, *J* 7 Hz, 17-H_3), 1.20 (3 H, d, *J* 7 Hz, 14-H_3), 1.29 (1 H, m, 12-H), 1.60 (1 H, dt, *J* 15 and 5 Hz, 9-H_2), 2.04 (1 H, m, 8-H), 2.13 (3 H, d *J* 0.5 Hz, 15-H_3), 2.68 (1 H, dd, *J* 10 and 2 Hz, 11-H), 2.75—3.00 (2 H, m, 10- and 4a-H), 3.06 (1 H, dd, *J* 15 and 5 Hz, 4b-H), 6.30 (1 H, s, 2-H), 7.32 (1 H, s, 1′-H), and 7.33—7.70 (5 H, m, Ph); $\delta_C(CDCl_3)$ 166.8 (C-1), 150.4 (C-3), 129.0, 128.6, 127.7, 124.3, and 121.6 (Ph + Het), 112.5 (C-2), 76.6 (C-5), 71.3 (C-13), 70.3 (C-7), 66.9 (C-6), 65.6 (C-16), 61.5 (C-11), 56.1 (C-10), 43.0 (C-12), 38.9 (C-8), 36.3 (C-4), 31.9 (C-9), 27.4 (C-15), 20.7 (C-14), and 12.7 (C-17); *m/z* 443 (M^+, 10%), 211 (32), 199 (100), 77 (32), 69 (30), 55 (39), 45 (64), 43 (63), and 41 (62) (Found: M^+, 443.2334. $C_{25}H_{33}NO_6$ requires *M*, 443.2308); *E* isomer (**2a**), (313 mg, 0.71 mmol, 35%).

4,5-*Dimethyl*-2-*normonyloxazole* (**2q**). Prepared as described from 2,4,5-trimethyloxazole (**7**) (2.2 mmol), this compound was obtained as a colourless oil (185 mg, 23%); $\nu_{max.}$(film) 3 400, 1 650, and 730 cm^{-1}; $\lambda_{max.}$ 275 nm (ε_m 14 700); $\delta_H(CDCl_3)$ 0.92 (3 H, d, 17-H_3), 1.23 (3 H, d, 14-H_3), 2.21 (3 H, s, 15-H_3), 2.09 and 2.24 (6 H, 2S, Het-CH_3), and 6.11 (1 H, s, 2-H); $\delta_C(CDCl_3)$ 159.3 (C-1), 144.9 (C-3), 142.1 (C-5′), 130.7 (C-4′), 113.2 (C-2), 75.5 (C-5), 71.0 (C-13), 70.4 (C-7), 68.9 (C-6), 65.4 (C-16), 61.1 (C-11), 55.6 (C-10), 42.7 (C-4), 42.6 (C-12), 39.5 (C-8), 31.8 (C-9), 20.7 (C-14), 19.4 (C-15), 12.5 (C-17), and 11.0, 9.9 (2 × Het-CH_3); *m/z* 395 (M^+, 9%), 151 (100), 111 (21), and 84 (27) (Found: M^+, 395.2313. $C_{21}H_{33}NO_6$ requires *M*, 395.2308).

4-*Methyl*-2-*normonyl*-5-*phenyloxazole* (**2r**). Prepared as described from 2,4-dimethyl-5-phenyloxazole (**8**) (1.1 mmol) to give a white foam (250 mg, 55%); $\nu_{max.}$ (film) 3 400, 1 655, and 910 cm^{-1}; $\lambda_{max.}$(EtOH) 225 (ε_m 15 600) and 306 nm (22 200); $\delta_H(CDCl_3)$ 0.95 (3 H, d, 17-H_3), 1.21 (3 H, d, 14-H_3), 2.31 (3 H, s, 15-H_3), 2.43 (3 H, s, Het-CH_3), 6.24 (1 H, s, 2-H), and 7.25—7.65 (5 H, m, Aryl); $\delta_C(CDCl_3)$ 159.4 (C-1), 146.6 (C-3), 144.2 (C-5′), 132.3 (C-4′), 129.2, 128.7, 127.4, and 125.1 (Ph), 113.1 (C-2), 75.4 (C-5), 71.1 (C-13), 70.4 (C-7), 68.9 (C-6) 65.5 (C-16), 61.2 (C-11), 55.6 (C-10), 42.8 (C-4 and -12), 39.5 (C-8), 31.7 (C-9), 20.8 (C-14), 19.6 (C-15), 13.3 (Het-CH_3), and 12.6 (C-17); *m/z* 457 (M^+, 6%), 213 (100), and 173 (21) (Found: M^+, 457.2448. $C_{26}H_{35}NO_6$ requires *M*, 457.2461).

2-*Normonyl*-4,5-*diphenyloxazole* (**2s**). Prepared as described from 2-methyl-4,5-diphenyloxazole (**9**) (570 mg, 2 mmol), this gave a white foam (300 mg, 29%); $\nu_{max.}$(film) 3 400, 1 655, and 910 cm^{-1}; $\lambda_{max.}$(EtOH) 229 (ε_m 20 800) and 304 nm (18 000); $\delta_H(CDCl_3)$ 0.92 (3 H, d, 17-H_3), 1.20 (3 H, d, 14-H_3), 2.34 (3 H, s, 15-H_3), 6.31 (1 H, s, 2-H), and 7.2—7.7 (10 H, m, Aryl); $\delta_C(CDCl_3)$ 160.1 (C-1), 147.3 (C-4″), 144.3 (C-3), 135—126 (Ph), 126.3 (C-5′), 113.0 (C-2), 75.5 (C-5), 71.1 (C-13), 70.4 (C-7), 68.9 (C-6), 65.4 (C-16), 61.2 (C-11), 55.6 (C-10), 42.8 (C-4 and -12), 39.5 (C-8), 31.7 (C-9), 20.8 (C-14), 19.7 (C-15), and 12.6 (C-17); *m/z* 519 (M^+, 12%), 275 (100), and 235 (34) (Found: M^+, 519.2646, $C_{31}H_{37}NO_6$ requires *M*, 519.2618).

5-*Methyl*-2-*normonyloxazole* (**2t**). Prepared as described from 2,5-dimethyloxazole (**10**) (210 mg, 2.20 mmol) to give the oxazole as a colourless oil (200 mg, 26%); $\nu_{max.}$(film) 3 400, 1 655, and 1 610 cm^{-1}; $\lambda_{max.}$(EtOH) 264 nm (ε_m 15 000); $\delta_H(CDCl_3)$ 0.94 (3 H, d, 17-H_3), 1.23 (3 H, d, 14-H_3), 2.24 (3 H, s, 15-H_3), 2.33 (3 H, s, Het-CH_3), 6.16 (1 H, s, 2-H), and 6.73 (1 H, s, 4′-H); $\delta_C(CDCl_3)$ 160.7 (C-1), 147.4 (C-5′), 145.3 (C-3), 123.1 (C-4′), 113.2 (C-2), 75.4 (C-5), 71.1 (C-13), 70.4 (C-7), 68.9 (C-6),

65.4 (C-16), 61.2 (C-11), 55.6 (C-10), 42.8 (C-4), 42.6 (C-12), 39.5 (C-8), 31.8 (C-9), 20.7 (C-14), 19.3 (C-15), 12.6 (C-17), and 10.8 (Het-CH_3); *m/z* 381 (M^+, 6%), 176 (12), and 137 (100) (Found: M^+, 381.2133. $C_{20}H_{31}NO_6$ requires *M*, 381.2116).

2-*Normonyl*-1,3-*benzoxazole* (**2b**). The anion was prepared from 2-methyl-1,3-benzoxazole (**12**) (0.26 ml, 2.20 mmol) as described and treated with the protected ketone (**3b**) (2.0 mmol) to yield a mixture of *E* and *Z* isomers of the title compound; *Z* isomer (77.5 mg, 0.19 mmol, 10%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 930, 1 655, 1 545, 1 520, 1 455, 1 250, 1 110, 1 050, and 950 cm^{-1}; $\lambda_{max.}$ 298 (ε_m 16 400); $\delta_H(CDCl_3)$ 0.94 (3 H, d, *J* 7 Hz, 17-H_3), 1.21 (3 H, d, *J* 7 Hz and 14-H_3), 1.30 (1 H, q, *J* 7 Hz, 12-H), 1.59 (1 H, dt, *J* 12 and 5 Hz, 9a-H), 1.82 (1 H, ddd, *J* 12, 5, and 6 Hz, 9b-H), 2.05 (1 H, m, 8-H), 2.19 (3 H, s, 15-H_3), 2.65 (1 H, dd, *J* 8 and 2 Hz, 11-H), 2.78 (1 H, dt, *J* 2 and 5 Hz, 10-H), 2.98 (1 H, m, 4a-H), 3.17 (1 H, dd, *J* 12 and 4 Hz, 4b-H), 6.38 (1 H, s, 2-H), 7.32 (2 H, m, Ar), and 7.50, 7.62 (2 H, m, Ar); $\delta_C(CDCl_3)$ 162.5 (C-1), 155.0 (C-3), 149.3 (C-1′), 140.7 (C-6′), 125.2, 124.7 (C-3′ and C-4′), 119.1 (C-5′), 112.6 (C-2), 110.5 (C-2′), 77.2 (C-5), 71.1 (C-13), 70.2 (C-7), 67.2 (C-6), 65.6 (C-16), 61.3 (C-11), 56.0 (C-10), 42.9 (C-12), 39.0 (C-8), 36.5 (C-4), 31.8 (C-9), 27.8 (C-15), 20.6 (C- 14), and 12.6 (C-17); *m/z* 417 (M^+, 10%), 202 (52), 187 (70), 173 (100), 133 (22), 83 (27), 45 (28), 43 (37), and 41 (33) (Found: M^+, 417.2129, $C_{23}H_{31}NO_6$ M^+, requires 417.2149); *E* isomer (87.5 mg, 0.21 mmol, 11%); $\nu_{max.}$(film) 3 600—3 100, 2 970, 1 655, 1 550, 1 455, 1 250, 1 110, 1 050, and 910 cm^{-1}; $\lambda_{max.}$ 296 nm (ε_m 20 600); $\delta_H(CDCl_3)$ 0.94 (3 H, d, *J* 7 Hz, 17-H_3), 1.22 (3 H, d, *J* 7 Hz, 14-H_3), 1.33 (1 H, q, *J* 7 Hz, 12-H), 1.73 (2 H, t, *J* 7 Hz, 9-H_2), 2.03 (1 H m, 8-H), 2.40 (3 H, s, 15-H_2), 2.42 (1 H, dd, *J* 12 and 8 Hz, 4-H_2), 2.65—2.85 (3 H, m, 10-H, 11-H, and 4-H_2), 6.38 (1 H, s, 2-H), 7.30 (2 H, m, Ar), and 7.49, 7.68 (2 H, m, Ar); $\delta_C(CDCl_3)$ 162.9 (C-1), 151.6 (C-3), 149.9 (C-1′), 141.6 (C-6′), 124.7 and 124.3 (C-3′ and -4′), 119.5 (C-5′), 113.2 (C-2), 110.3 (C-2′), 75.3 (C-5), 71.1 (C-13), 70.4 (C-7), 68.9 (C-6), 65.6 (C-16), 61.2 (C-11), 55.6 (C-10), 43.1 (C-4), 42.8 (C-12), 39.7 (C-8), 31.8 (C-9), 20.8 (C-14), 20.1 (C-15), and 12.6 (C-17); *m/z* 417 (M^+, 6%) 202 (24), 173 (100), 133 (24), 71 (28), 69 (32), 55 (38), 45 (59), 43 (63), and 41 (58), (Found: M^+, 417.2158. $C_{23}H_{31}NO_6$ requires *M*, 417.2149).

2-*Normonyl*-1,3-*benzothiazole* (**2u**). The anion was prepared from 2-methyl-1,3-benzothiazole (**11**), (0.28 ml, 2.20 mmol) as described and treated with the protected ketone (**3b**), (2.00 mmol) to yield a mixture of the *E* and *Z* isomers of the title compound. *Z* Isomer (151 mg, 0.35 mmol, 17%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 890, 1 630, 1 495, 1 435, 1 115, 1 045, 905, and 760 cm^{-1}; $\lambda_{max.}$ (EtOH) 227 nm (ε_m 19 650) and 297 (13 400); $\delta_H(CDCl_3)$ 0.93 (3 H, d, *J* 7 Hz, 17-H_3), 1.20 (3 H, d, *J* 7 Hz, 14-H_3), 1.30 (1 H, q, *J* 7 Hz, 12-H), 1.61 (1 H, dt, *J* 12 and 5 Hz, 9a-H), 1.82 (1 H, ddd, *J* 12, 6, and 5 Hz, 9b-H), 2.06 (1 H, m, 8-H), 2.14 (3 H, d, *J* 0.5 Hz, 15-H_3), 2.68 (1 H, dd, *J* 10 and 1 Hz, 11-H), 2.80 (1 H, dt, *J* 1 and 5 Hz, 10-H), 2.91 (1 H, dd, *J* 11 and 2 Hz, 4a-H), 3.20 (1 H, dd, *J* 11 and 3 Hz, 4b-H), 6.52 (1 H, s, 2-H), 7.3—7.5 (2 H, 2 × t, *J* 7 Hz, 3′- and 4′-H), and 7.8—8.0 (2 H, 2 × d, *J* 8 Hz, 2′- and 5′-H); $\delta_C(CDCl_3)$ 166.6 (C-1), 152.8 (C-6′), 149.9 (C-3), 134.0 (C-1′), 126.5 (C-2′), 125.2 (C-4′), 122.1 (C-3′), 121.4 (C-5′), 118.6 (C-2), 77.0 (C-5), 70.9 (C-13), 70.2 (C-7), 67.2 (C-6), 65.7 (C-16), 61.2 (C-11), 55.9 (C-10), 42.8 (C-12), 39.0 (C-8), 36.6 (C-4), 31.9 (C-9), 27.4 (C-15), 20.6 (C-14), and 12.5 (C-17); *m/z* 433 (M^+, 20%), 218 (64), 200 (44), 190 (25), 189 (100), 149 (37), 45 (48), 43 (32), and 41 (37) (Found: 433.1946. $C_{23}H_{31}NO_5S$ requires *M*, 433.1923); *E* isomer (186 mg, 0.43 mmol, 22%), m.p. 100—105 °C (from Et_2O); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 930, 1 640, 1 435, 1 110, 1 050, 910, and 760 cm^{-1}; $\lambda_{max.}$ (EtOH) 227 (ε_m 18 400) and 295 nm (13 600); $\delta_H(CDCl_3)$ 0.90 (3 H, d, *J* 7 Hz, 17-H_3), 1.20 (3 H, d, *J* 7 Hz, 14-H_3), 1.32 (1 H, q, *J* 7 Hz, 12-H), 1.72 (2 H, t, *J* 6 Hz, 9-H_2), 2.01 (1 H, m, 8-H), 2.26 (3 H, s, 15-H_3), 2.44 (1 H, dd, *J* 12 and 8 Hz, 4-H_2), 7.73 (1 H, s, 2-H), 7.3—7.5 (2 H, 2 × t, *J* 8 Hz, 3′- and 4′-H), and 7.8—8.0 (2 H, 2 × d, *J* 8 Hz, 2′- and 5′-H); $\delta_C(CDCl_3)$ 165.7 (C-1), 152.8 (C-6′), 147.3 (C-3), 134.7 (C-1′), 126.2 (C-2′), 124.8 (C-4), 122.6 (C-3′), 121.3 (C-5′), 121.1 (C-2), 75.6 (C-5), 71.3 (C-13), 70.5 (C-7), 68.9 (C-6), 65.5 (C-16), 61.1 (C-11), 55.6 (C-10), 43.3 (C-4), 42.7 (C-12), 31.8 (C-9), 20.8 (C-14), 20.1 (C-15), and 12.6 (C-17); *m/z* 433 (M^+, 10%), 190 (19), 189 (100), 173 (12), 149 (20), 69 (17), 55 (14), 43 (21), and 41 (20) (Found: M^+, 433.1903. $C_{23}H_{31}NO_5S$ requires *M*, 433.1923).

2-*Normonyl*-5-*phenylthiazole* (**2v**). The anion was prepared from 2-methyl-5-phenylthiazole (**13**), (1.1 mmol) as described and treated with the protected ketone (**3b**) (1.0 mmol) to yield the title compound as a white foam (170 mg, 37%); $\nu_{max.}$(film) 3 400, 1 640, 810, and 730 cm^{-1}; $\lambda_{max.}$(EtOH) 321 nm (ε_m 24 100); $\delta_H(CD_3OD)$ 0.94 (3 H, d, 17-H_3), 1.22 (3 H, d, 14-H_3), 2.21 (3 H, s, 15-H_3), 6.63 (1 H, s, 2-H), 7.3—7.7 (5 H, m, Ph), and 8.02 (1 H, s, Het-H); $\delta_C(CD_3OD)$ 166.1 (C-1), 145.5 (C-3), 139.8 (C-5′), 138.5 (C-4′), 132.5, 130.1, 129.3, and 127.5 (Ph), 121.8 (C-2), 76.6 (C-5), 71.6 (C-13), 70.7 (C-7), 70.0 (C-6), 66.3 (C-16), 66.3 (C-16), 61.3 (C-11), 56.8 (C-10), 44.1 (C-4), 43.7 (C-12), 41.5 (C-8), 33.0 (C-9), 20.3 (C-14), 20.2 (C-15), and 12.2 (C-17); *m/z* 459 (M^+, 6%), 215 (100), and 175 (21) (Found: M^+, 459.2040. $C_{25}H_{33}NO_5S$ requires *M*, 459.2077).

2-*Normonyl*-5-*phenyl*-1,3,4-*oxadiazole* (**2d**). The anion was prepared from 2-methyl-5-phenyl-1,3,4-oxadiazole (**14**), (350 mg, 2.2 mmol) as described and treated with the protected ketone (**3b**), (2.0 mmol) to give the title compound as a colourless oil (50 mg, 6%); $\nu_{max.}$(film) 3 400, 1 655, and 1 450 cm^{-1}; $\lambda_{max.}$(EtOH) 282 nm (ε_m 14 300; $\delta_H(CDCl_3)$, 0.94 (3 H, d, 17-H_3), 1.23 (3 H, d, 14-H_3), 2.33 (3 H, s, 15-H_3), 6.34 (1 H, s, 2-H), 7.45—7.6 (3 H, m, Ph), and 8.0—8.1 (2 H, m, Ph); $\delta_C(CDCl_3)$, 164.0 (C-1), 163.3 (C-5′), 151.4 (C-3), 131.5 (C-1″), 129.0 (C-4″), 126.8 (C-2″ and -6″), 124.0 (C-3″ and -5″), 109.3 (C-2), 75.2 (C-5), 71.2 (C-13), 70.5 (C-7), 68.9 (C-6), 65.6 (C-16), 61.2 (C-11), 55.6 (C-10), 43.0 (C-12), 42.8 (C-4), 39.8 (C-8), 31.8 (C-9), 20.8 (C-14), 20.2 (C-15), and 12.6 (C-17); *m/z* (rel. int.) 444 (M^+, 1%) and 200 (100) (Found: M^+, 444.2246, $C_{24}H_{32}N_2O_6$ requires *M*, 444.2260).

5-*Normonyl*-3-*phenyl*-1,2,4-*oxadiazole* (**2g**). The anion was prepared from 5-methyl-3-phenyl-1,2,4-oxadiazole (**15**) (2.2 mmol) as described and treated with the protected ketone (**3b**), (2.0 mmol) to give the title compound (264 mg, 0.59 mmol, 30%), m.p. 119—120 °C; $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 920, 1 655, 1 555, 1 535, 1 445, 1 365, 1 110, 1 050, 910, 730, and 695 cm^{-1}; $\lambda_{max.}$(EtOH) 245 nm (ε_m 31 800); $\delta_H(CD_3OD)$, 0.93 (3 H, d, *J* 7 Hz, 17-H_3), 1.20 (3 H, d, *J* 7 Hz, 14-H_3), 1.40 (1 H, m, 12-H), 1.71 (2 H, m, 9-H_2), 1.97 (1 H, m, 8-H), 2.41 (4 H, s + m, 15-H_3 and 4a-H), 2.72 (1 H, dd, *J* 2 and 8 Hz, 11-H), 2.81 (2 H, m, 10- and 4b-H), 6.41 (1 H, s, 2-H), 7.52 (3 H, m, Ph), and 8.07 (2 H, m, Ph); $\delta_C(CD_3OD)$ 176.3 (C-4′), 169.1 (C-1), 157.1 (C-3), 132.0, 129.7, and 128.2 (Ph), 110.6 (C-2), 76.1 (C-5), 71.4 (C-13), 70.6 (C-7), 69.8 (C-6), 66.3 (C-16), 61.2 (C-11), 56.7 (C-10), 44.0 and 43.5 (C-4 and -12), 41.4 (C-8), 32.8 (C-9), 20.4 (C-14 and C-15), and 12.2 (C-17); *m/z* 444 (M^+, 3%), 299 (12), 227 (28), 200 (100), 111 (28), 69 (44), 55 (34), 43 (42), and 41 (33) (Found: 444.2230. $C_{24}H_{32}N_2O_6$ requires 444.2260) and the *Z* isomer (69.7 mg, 0.16 mmol, 8%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 920, 1 650, 1 555, 1 530, 1 445, 1 350, 1 110, 1 050, 910, 730, and 695 cm^{-1}; $\lambda_{max.}$(EtOH) 243 nm (ε_m 24 770); $\delta_H(CD_3OD)$, 0.90 (3 H, d, *J* 7 Hz, 17-H_3), 1.18 (3 H, d, *J* 7 Hz, 14-H_3), 1.36 (1 H, m, 12-H), 1.5—1.8 (2 H, m, 9-H_2), 1.98 (1 H, m, 8-H), 2.15 (3 H, s, 15-H_3), 2.63 (1 H, dd, *J* 8 and 2 Hz, 11-H), 2.78 (1 H, dt, *J* 2 and 5 Hz, 10-H), 3.13 (1 H, dd, *J* 12 and 3 Hz, 4a-H), 6.42 (1 H, s, 2-H), 7.53 (3 H, m, Ph), and 8.05 (2 H, m, Ph); $\delta_C(CD_3OD)$ 176.4 (C-4′), 169.2 (C-1), 158.1 (C-3), 132.2, 129.9, 128.3 (Ph), 110.7 (C-2), 77.2 (C-5), 71.6 (C-13), 70.7 (C-6 and C-7), 66.3 (C-16), 61.3 (C-11), 56.8 (C-10), 43.6 (C-12), 41.0 (C-4), 37.0 (C-8), 33.0 (C-9), 26.0 (C-15), 20.3

(C-14), and 12.2 (C-17); *m/z* 444 (M^+, 4%) 229 (54), 200 (100), 111 (74), 82 (50), 69 (58), 55 (65), 43 (74), and 41 (68) (Found: M^+, 444.2272. $C_{24}H_{32}N_2O_6$ requires *M*, 444.2260).

2-*Normonyl*-4,5-*dihydro-oxazole* (**2w**). The anion was prepared from 2-methyl-4,5-dihydro-oxazole (**16**), (2.2 mmol) as described and treated with the protected ketone (**3b**), (2.0 mmol) to give the title compound as a white foam (200 mg, 27%); $\nu_{max.}$(film) 3 400, 1 665, 1 635, 1 600, and 730 cm^{-1}; $\lambda_{max.}$(EtOH) 225 nm (ε_m 12 000); $\delta_H(CDCl_3)$ 0.94 (3 H, d, 17-H_3), 1.22 (3 H, d, 14-H_3), 2.15 (3 H, s, 15-H_3), 3.90 (2 H, t, 5′-H_2), 4.27 (2 H, t, 4′-H_2), and 5.84 (1 H, s, 2-H); $\delta_C(CDCl_3)$ 165.1 (C-1), 151.0 (C-3), 113.7 (C-2), 75.3 (C-5), 71.0 (C-13), 70.4 (C-7), 68.7 (C-6), 67.0 (C-4′), 65.4 (C-16), 61.2 (C-11), 55.6 (C-10), 53.6 (C-5′), 42.8 (C-4 and -12), 39.5 (C-8), 31.8 (C-9), 20.8 (C-14), 19.6 (C-15), and 12.6 (C-17); *m/z* 369 (M^+, 2%), 296 (8), 154 (75) and 125 (100) (Found: M^+, 369.2144. $C_{19}H_{31}NO_6$ requires *M*, 369.2151).

4,4-*Dimethyl*-2-*normonyl*-4,5-*dihydro-oxazole* (**2x**). The anion was prepared from 2,4,4-trimethyl-4,5-dihydro-oxazole (**17**), (0.28 ml, 2.20 mmol) as described and treated with the protected ketone (**3b**), (2.00 mmol) to yield a mixture of *E* and *Z* isomers of the title compound; *Z* isomer (28 mg, 0.071 mmol, 4%); $\nu_{max.}$(film) 3 600—3 200, 2 970, 2 930, 2 890, 1 650, 1 635, 1 450, 1 380, 1 365, 1 285, 1 250, 1 110, 1 070, 1 050, 995, and 910 cm^{-1}; $\lambda_{max.}$ 223 nm (ε_m 9 800); $\delta_H(CDCl_3)$, 0.95 (3 H, d, *J* 7 Hz, 17-H_3), 1.21 (3 H, d, *J* 7 Hz, 14-H_3), 1.55 (1 H, dt, *J* 16 and 7 Hz, 9a-H), 1.80 (1 H, ddd, *J* 16, 10, and 6 Hz, 9b-H), 2.02 (3 H, d, *J* 0.5 Hz, 15-H_3), 2.6—2.7 (2 H, m, 11- and 4a-H), 2.78 (1 H, dt, *J* 1 and 5 Hz, 10-H), 3.03 (1 H, dd, *J* 15 and 4 Hz, 4b-H), and 5.81 (1 H, s, 2-H); $\delta_C(CDCl_3)$ 162.3 (C-1), 154.0 (C-3), 113.7 (C-2), 78.1 (C-1′), 76.9 (C-5), 71.3 (C-13), 70.4 (C-7), 57.3 (C-2′), 66.4 (C-6), 65.7 (C-16), 61.5 (C-11), 56.1 (C-10), 43.0 (C-12), 38.9 (C-8), 36.4 (C-4), 31.9 (C-9), 28.4 and 28.2 (C-4′ and -3′), 27.3 (C-15), 20.7 (C-14), and 12.7 (C-17); *m/z* 397 (M^+, 6%), 324 (10), 182 (100), 153 (45), 113 (25), 71 (30), 55 (62), 45 (82), 43 (68), and 41 (85) (Found: M^+, 397.2454. $C_{21}H_{35}NO_6$ requires *M*, 397.2461); *E* isomer (158 mg, 0.36 mmol, 18%); $\nu_{max.}$(film) 3 600—3 100, 2 970, 2 930, 1 665, 1 640, 1 595, 1 460, 1 365, 1 310, 1 110, 1 050, 1 000, and 910 cm^{-1}; $\lambda_{max.}$(EtOH) 226 nm (ε_m 11 600); $\delta_H(CDCl_3)$ 0.91 (3 H, d, *J* Hz, 17-H_3), 1.21 (3 H, d, *J* 7 Hz, 14-H_3), 1.29 (6 H, s, 3′-H_3 and 4′-H_3), 1.35 (1 H, m, 12-H), 1.70 (2 H, m, 9-H_2), 2.00 (1 H, m, 8-H), 2.10 (3 H, s, 15-H_3), 2.24 (1 H, dd, *J* 14 and 8 Hz, 4a- H), 2.60 (1 H, bd, *J* 14 Hz, 4b-H), 2.70 (1 H, dd, *J* 2 and 8 Hz, 11- H), 2.78 (1 H, dt, *J* 2 and 5 Hz, 10-H), 3.96 (2 H, s, 1′-H), and 5.80 (1 H, s, 2-H); $\delta_C(CDCl_3)$ 162.8 (C-1), 150.8 (C-3), 113.9 (C-2), 78.8 (C-1′), 75.3 (C-5), 70.7 (C-13), 70.3 (C-7), 68.7 (C-6), 66.1 (C- 2′), 65.5 (C-6), 61.0 (C-11), 55.6 (C-10), 42.9 and 42.7 (C-4 and 12), 39.7 (C-8), 31.8 (C-9), 28.4 (C-3′ and -4′), 20.7 (C-14), 19.6 (C-15), and 12.5 (C-17); *m/z* 397 (M^+, 4%), 324 (6), 182 (64), 154 (39), 153 (100), 113 (48), 55 (67), 45 (69), 43 (68), and 41 (85) (Found: M^+, 397.2470. $C_{21}H_{35}NO_6$ requires *M*, 397.2461).

2-*Normonyl*-4,4,6-*trimethyl*-5,6-*dihydro*-4H-1-3-*oxazine* (**2y**). The anion was prepared from 2,4,4,6-tetramethyl-5,6-dihydro-4*H*-1,3-oxazine (18, 2 mmol) as described and treated with the protected ketone (**3b**), (2.0 mmol) to give the title compound (27 mg, 3%); $\nu_{max.}(CHCl_3)$, 3 330br, 1 653, and 1 640 cm^{-1}; $\lambda_{max.}$(EtOH) 224 nm (ε_m 7 183); $\delta_H(CDCl_3)$ 0.93 (3 H, d, 17-H_3), 1.19 (3 H, d, 14-H_3), 1.25 (6 H, 2 × 4-CH_3), 1.37 (3 H, m, 6-CH_3), 1.95 (3 H, s, 15-H_3), and 5.62 (1 H, s, 2-H); *m/z* 425 (M^+, 17%), 407 (3), 352 (11), 296 (3), 238 (20), and 210 (100) (Found: M^+, 425.2756. $C_{23}H_{37}NO_6$ requires *M*, 425.2775).

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