The Chemistry of Pseudomonic Acid. Part 12.[1] Preparation of Diazole and Triazole Derivatives

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The preparations of examples of normonyl† imidazoles, pyrazoles and triazoles are described. Most derivatives were formed by treatment of monic acid amides with triphenylphosphine based dehydrating agents, resulting in cyclisation or cycloaddition of the intermediate dipolar species. One example is the novel one pot reduction–cyclisation of an α-acylamino nitrile to an imidazole.

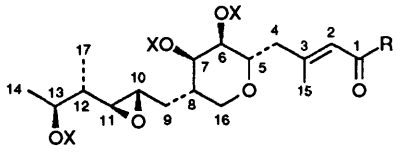
Mupirocin **1a**, is utilised by SmithKline Beecham for Bactroban‡ ointment, which is a highly effective topical antibiotic for the treatment of skin infections and for the prevention of nasal carriage of multiply resistant *Staphylococcus aureus* in the hospital environment. The replacement of the metabolically sensitive alkoxycarbonyl moiety of antibacterially active arylmethyl esters of monic acid **1b** by a variety of aryl heterocycles (including oxazoles, isoxazoles, thiazoles and oxadiazoles) has been reported previously.[1,2] These replacements were designed to be bioisosteric and yielded antibacterially active compounds for example in the case of oxazoles, but dihydrooxazole analogues were poorly active.[3] We were therefore interested in preparing further compounds with alternative isosteric replacements and selected diazoles and triazoles as key targets.

The present paper describes the preparation of imidazole, pyrazole and triazole analogues, in which there is a 1,3-disposition of substituents, mimicking the favoured *transoid* conformation of the arylmethyl ester.

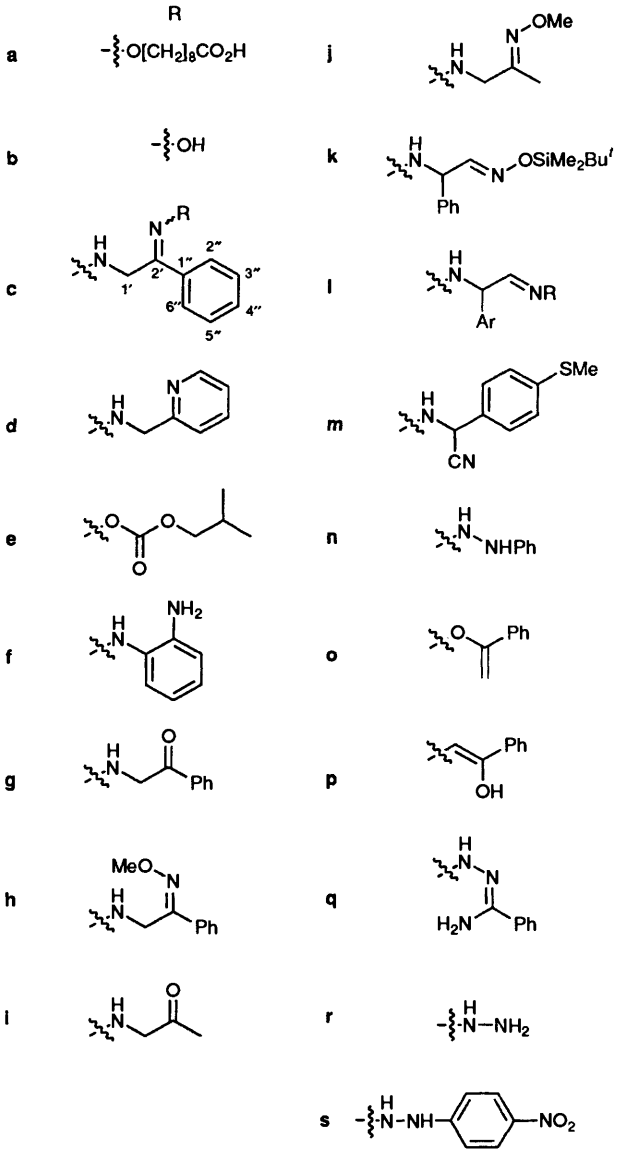
Imidazoles.—We decided initially to attempt the preparation of imidazole **3a** by the dehydrative cyclisation of a precursor of type **1c**. This approach is closely related to our successful route to oxazoles[1] and similar cyclisations have been carried out on related precursors under suitably mild conditions.[4] The feasibility of such chemistry, in our system, was first examined by attempting the preparation of the two bicyclic model systems **3b** and **3c**.

The precursor amide **1d** was prepared, as were all monic acid amides discussed in this paper, using the mixed anhydride **1e**.[2] Thus, reaction of 2-aminomethylpyridine with anhydride **1e** in tetrahydrofuran solution gave the amide **1d** in 80% yield. After trimethylsilyl (TMS) protection of the hydroxy groups, cyclisation was carried out using triphenylphosphine, tetrachloromethane and triethylamine in acetonitrile–pyridine solution,[4] to give the imidazopyridine **3b** in 22% yield after mild acid deprotection. This three step procedure was found to be widely applicable and was used for all cyclisations unless otherwise stated. The benzoimidazole **3c** was prepared similarly. The amide **1f**,[2] isolated in 74% yield accompanied by 15% of the bis-amide, was cyclised in 70% yield.

Having demonstrated the formation of fused systems, the *O*-methyloxime of keto amide **1g**[1] was prepared as a precursor to imidazole **3a**. This *O*-methyloxime was a single isomer,

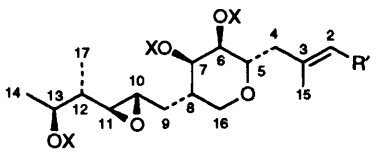


1 X = H
2 X = $SiMe_3$

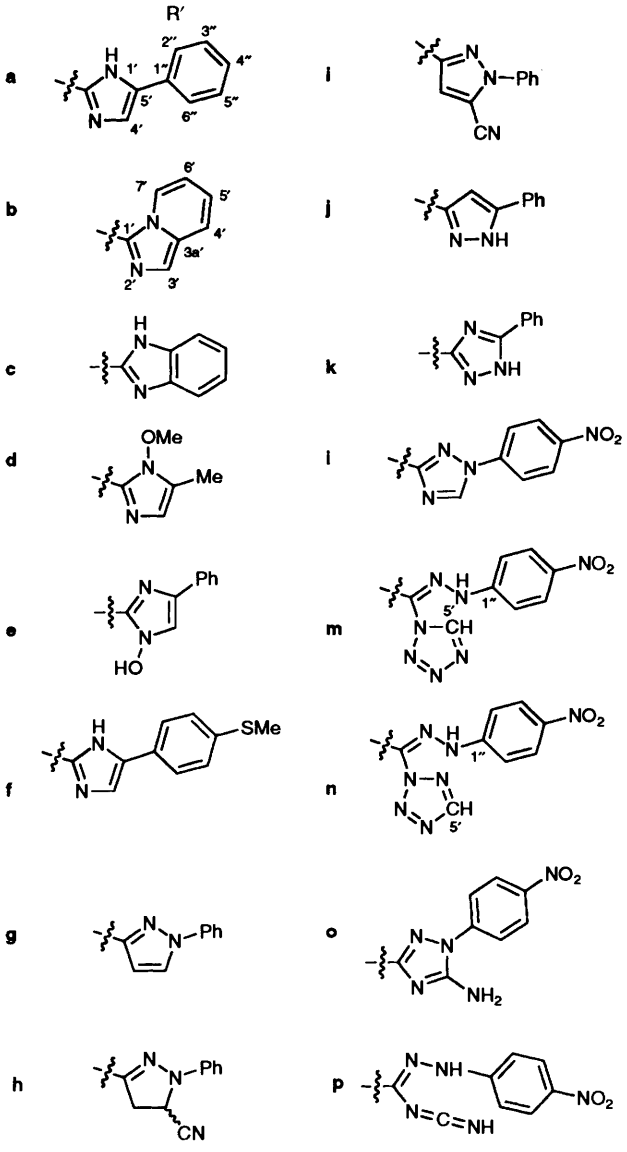


† Normonyl, the trivial name for the (1*E*)-3-[(2*S*,3*S*,4*S*,5*S*)-(2,3-epoxy-5-hydroxy-4-methylhexyl)-(2*S*,3*R*,4*R*,5*S*)-3,4-dihydroxytetrahydropyran-2-yl]-2-methylprop-1-en-1-yl radical, is used throughout for convenience.

‡ The approved generic name for pseudomonic acid is mupirocin. Bactroban is a trademark of SmithKline Beecham.



3 X = H
4 X = $SiMe_3$



presumably with the *Z*-configuration **1h** in which interaction between the methoxy and phenyl is avoided (see below).

Attempted cyclisation, however, gave none of the required methoxyimidazole. It may be that the *O*-methyloxime cannot isomerise under the conditions used to allow the nitrogen lone pair to attack the electrophilic centre formed after activation of the amide carbonyl. Therefore, in order to prepare an *O*-methyloxime with *E*-geometry, the mixed anhydride **1e** was coupled with aminoacetone[5] giving the keto amide **1i** in 54% yield. On treatment with *O*-methylhydroxylamine two *O*-methyloximes were formed, the major, less polar isomer being isolated in 49% yield. The minor isomer was only obtained contaminated with the major isomer in low yield.

The major *O*-methyloxime had ^{13}C NMR resonances at δ 43.1 and 13.1 for 1′-methylene and 3′-methyl while the mixture had additional resonances at δ 37.2 and 18.2 for the 1′ and 3′ carbons of the minor isomer. A carbon *cis* to an *O*-methyloxime is known[6] (at least in certain systems) to be shielded and thus these results are consistent with the major *O*-methyloxime being the required *E*-isomer **1j**. The analogue **1h** had its 1′ resonance at δ 34.8 in the ^{13}C NMR, which supports the assignment of *Z*-geometry.

In contrast to the unsuccessful reaction with *Z*-*O*-methyloxime **1h**, the *E*-*O*-methyl oxime **1j** was smoothly cyclised to the imidazole **3d** in 56% yield.

It would therefore appear that a correctly orientated nitrogen lone pair is required for the cyclisation and that oxime isomerisation does not occur to a significant extent under the reaction conditions used. Engel and Steglich,[4] who prepared imidazoles by similar cyclisations of imine and hydrazone derivatives, do not discuss the stereochemistry of their substrates, but all would be expected to favour the *E*-geometry which seems to be required for cyclisation.

As the required *E*-geometry should be favourable for aldoximes, the amide **1k** was judged a suitable precursor. α-Azidophenylacetaldehyde[7] was converted into a mixture of oxime isomers (3:1 *E*:*Z* respectively). After protection of the oxime as a *tert*-butyldimethylsilyl (TBDMS) ether and azide reduction, coupling to anhydride **1e** gave the required monamide **1k** in 50% yield. Treatment of **1k** under the normal cyclisation conditions indeed gave the *N*-hydroxyimidazole **3e** in 50% yield, the mild acid deprotection having also cleaved the TBDMS group. The removal of the hydroxy group to give the required imidazole **3a** was achieved in 70% yield using titanium trichloride.[8]

In the ^{13}C NMR spectrum of **3a** no resonances were observed for the imidazole ring carbons. Presumably, tautomerism of the imidazole proton resulted in broadening of these resonances.[9] Broad resonances were also noted in the ^{13}C NMR spectra of the pyrazole **3j** and the triazole **3k**. In the case of the pyrazole **3j**, the spectrum was rerun using a longer relaxation delay, resulting in a slight increase in the intensity of the ring carbon resonances.

The approach above to the 2,4-disubstituted imidazole system is lengthy; a more efficient route involves direct cyclisation of an imine **2l**. One route to such an imine is by the diisobutylaluminium hydride (DIBAL) reduction of a nitrile. DIBAL is also expected to react with the relatively acidic amide proton, so protecting the amide as its salt. Moreover, *in situ* cyclisation of the metallated intermediate avoids the necessity of isolating the sensitive aldimine **2l**, R = H. The concept was used for the preparation of the *p*-methylsulfanyl analogue **3f**. The amino nitrile **5**[10] was coupled to mixed anhydride **1e** to give amide **1m** in 54% yield. This amide was protected and treated with 2.4 equiv. of DIBAL at −78 to −40 °C followed by triethylamine and triphenylphosphine dibromide and the mixture allowed to warm to 20 °C giving a 10% yield of imidazole **3f** after deprotection.

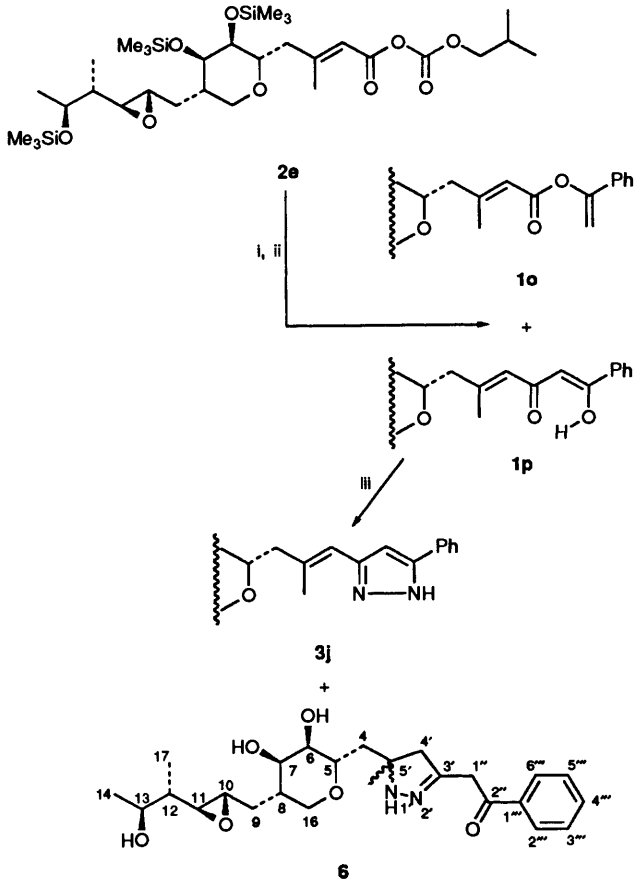
Clearly the reagents and conditions used here are not optimal, especially for a molecule containing sensitive functionality, but the method is convenient and provides a rapid entry to the imidazole system.

Pyrazoles.—The foregoing dehydrative cyclisation reactions can be formulated as proceeding *via* nitrile ylide intermediates. Nitrile imines, which can be generated in an analogous way, have been used in 1,3-dipolar cycloadditions with acetylenes[11] and cyano olefins[12] to give pyrazoles. Application of this chemistry in the present area would enable the pyrazole **3g** to be prepared.

The phenylhydrazide **2n** was treated with triphenylphosphine, tetrachloromethane and triethylamine in 1:1 pyridine–acrylonitrile to give the 1,3-dipolar cycloadduct **4h** in 52% yield as an approximately 1:1 mixture of diastereoisomers. Initial attempts to eliminate HCN from cycloadduct **4h** using DBU in

refluxing toluene were unsuccessful. Addition of CuCl to the reaction resulted in smooth elimination, presumably due to the affinity of Cu^{I} for the nitrile group.[13] In fact, CuCl alone was sufficient to effect the elimination, the required pyrazole **3g** being isolated in 42% yield after deprotection.

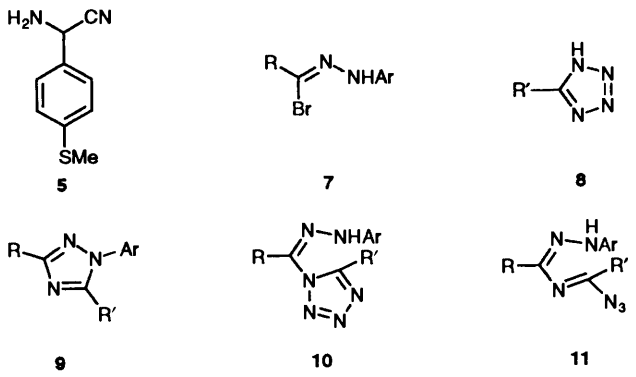
A by-product, formed especially when the reaction was not carried out under an inert atmosphere, was identified as the 5-cyanopyrazole **4i**. If $CuCl_2$ was used in place of CuCl, this oxidation product predominated. However, much polar material was also formed, presumably acid generated in the reaction caused desilylation and probably subsequent epoxide rearrangement.[14] The addition of basic copper(II) carbonate [$CuCO_3$·$Cu(OH)_2$·H_2O] allowed the cyanopyrazole **3i** to be isolated in 23% yield after deprotection. Cyanopyrazole **3i** was also observed with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone as oxidising agent.



Scheme 1 *Reagents and conditions:* i, PhCOMe, LDA, THF, −78 to −40 °C; ii, THF–0.4 mol dm^{-3} HCl (5:1) 20 °C, 2 min; iii, N_2H_4·H_2O, MeOH–H_2O, 20 °C

The pyrazole **3j** was prepared using the chemistry depicted in Scheme 1. The reaction of anhydride **2e**[15] with 2 equiv. of acetophenone enolate gave a mixture which was treated with mild acid to give an inseparable (4:1) mixture of the *C*- and *O*-acylated products **1p** and **1o** in 36% combined yield.[16] Chromatographic separation could however be achieved on silyl protected material, facilitating structure elucidation. The enolised diketone **1p** reacted rapidly with hydrazine to give three products, the required pyrazole **3j** (10%) and the two diastereoisomeric dihydropyrazoles **6** (28 and 33% yields).

Triazoles.—3,5-Disubstituted 1,2,4-triazoles are commonly prepared by the cyclisation of amidrazone derivatives.[17] The precursor **1q** to triazole **3k** was simply prepared by treating monohydrazide **1r** with *S*-methylisothiobenzamide.[18] The



amidrazone derivative **1q** could be isolated by column chromatography, but was conveniently cyclised without purification using the standard conditions to give triazole **3k** in 37% overall yield.

An alternative 1,2,4-triazole system was prepared exploiting chemistry discovered by Butler and Fitzgerald.[19] Hydrazidonoyl bromides **7**, where Ar is an electron deficient aromatic substituent, were reported to react with NH-tetrazoles **8** to give triazoles **9** *via* hydrazonoyltetrazoles **10**.

The *p*-nitrophenylhydrazide **1s** was silylated and treated with triphenylphosphine, tetrachloromethane, triethylamine and tetrazole in acetonitrile. The required triazole **4l** was obtained as the major product in 28% yield and deprotected to give **3l** in 76% yield. When the reaction was quenched before completion, 17% of the intermediate 1-hydrazonoyltetrazole **4m** and 6% of the 2-isomer **4n** could be isolated. The 1-isomer **4m** cyclised to triazole **4l** with triethylamine in acetonitrile at 20 °C, however triethylamine in refluxing toluene gave in 33% yield an additional more polar product. This material had IR absorptions at 3470 and 3380 cm^{-1}, implying a primary amine, which was confirmed by a broad, two proton resonance in the ^1H NMR at δ 5.1. No triazole ring proton resonance was observed. On the basis of the spectral data the aminotriazole structure **4o** was assigned. Deprotection to **3o** was carried out in 68% yield.

Butler and Fitzgerald hypothesised that the cyclisation of 1-hydrazonoyltetrazoles **10** proceeds *via* the imidoyl azide form **11**. The formation of aminotriazole **4o** under high temperature conditions can be rationalised as proceeding *via* a Curtius type rearrangement to the carbodiimide **4p**.[20]

The chemistry discussed above has thus resulted in the preparation of imidazole, pyrazole and triazole derivatives as potential bioisosteric equivalents of benzyl monate.

Unfortunately, all compounds here described had insufficient antibacterial activity to justify further investigation. For example, while mupirocin **1a** inhibited the growth of *S. aureus* Oxford and *Streptococcus pneumoniae* PU7 at 0.5 and 0.13 μg cm^{-3} respectively, the diazole and triazole analogues **3a**, **3g**, **3j** and **3k** only had activity in the range of 32–138 μg cm^{-3} against these organisms.

Experimental

^1H NMR data were recorded at 250 MHz on a Bruker AC-250F spectrometer using tetramethylsilane as standard, coupling constants are given in Hz. IR data were recorded on a Perkin-Elmer PE 983 machine, UV data on a Beckman DU 68 and mass spectra on a VG-ZAB spectrometer. Fast atom bombardment spectra (FAB) were run using a 3-nitrobenzyl alcohol–sodium acetate matrix. The silica gel used for both thin layer (TLC) and column chromatography was Merck type 60. Tetrahydrofuran (THF) was distilled before use from sodium–benzophenone ketyl.

General Method A: Preparation of Monamides.—To a solution of monic acid **1b** in THF (15 cm^3 $mmol^{-1}$) at −10 °C was added triethylamine (1.1 equiv.), followed by isobutyl chloroformate (1.1 equiv.) and then the mixture was stirred for 30 min. The amine (1 equiv.) was added to it and the reaction mixture was stirred overnight at room temperature and then poured into brine and extracted with ethyl acetate (30 cm^3 $mmol^{-1}$). The extracts were washed successively with saturated aqueous sodium hydrogen carbonate (2 cm^3 $mmol^{-1}$) and brine (2 cm^3 $mmol^{-1}$) and then dried ($MgSO_4$) and evaporated under reduced pressure. The resulting residue was purified by chromatography (silica gel, eluting with 0–15% methanol in dichloromethane) to yield pure amide.

General Method B: Cyclisation of Monoamides.—To the monoamide in THF (5–20 cm^3 $mmol^{-1}$) was added triethylamine (5 equiv.) and chlorotrimethylsilane (4 equiv.) followed by 4-(*N*,*N*-dimethylamino)pyridine (DMAP) (5 mol%), with ice cooling if necessary. After completion of the reaction, as judged by TLC, the mixture was diluted with diethyl ether (5–20 cm^3 $mmol^{-1}$), filtered and then concentrated by evaporation under reduced pressure.

The residue was taken up in acetonitrile–pyridine (1:1, 10 cm^3 $mmol^{-1}$) and treated with triethylamine (2 equiv.), triphenylphosphine (2 equiv.) and tetrachloromethane (4 equiv.). After completion of the reaction, as judged by TLC, saturated aqueous sodium hydrogen carbonate and ethyl acetate were added, and then the organic phase was dried and evaporated to a low volume under reduced pressure. Two portions of toluene (2 × 10 cm^3 $mmol^{-1}$) were added and then evaporated under reduced pressure to remove residual pyridine. If necessary, this material could be purified by chromatography on silica gel eluting with an appropriate gradient of ethyl acetate in hexane. The protected product was taken up in THF (20 cm^3 $mmol^{-1}$) and HCl (0.4 mol dm^{-3}; 4 cm^3 $mmol^{-1}$) was added. After 2 min at 20 °C saturated aqueous sodium hydrogen carbonate (5 cm^3 $mmol^{-1}$) and diethyl ether (20 cm^3 $mmol^{-1}$) were added. The organic phase was washed with brine and then the combined aqueous phases were extracted with ethyl acetate (20 cm^3 $mmol^{-1}$). The combined organic phases were dried, evaporated to dryness under reduced pressure and then purified by chromatography on silica gel eluting with a gradient of methanol in dichloromethane (typically from 0 to 10%).

1-*Normonylimidazo*[1,5-a]*pyridine* **3b**.—*N*-Pyridylmethyl)-monoamide **1d** was prepared in 31% yield by general method A as a white solid, m.p. 111–113 °C; ν_{max}(film)/cm^{-1} 3440, 2500, 1660, 1630 and 1450; λ_{max}(EtOH)/nm 223.5 (ε/dm^3 mol^{-1} cm^{-1} 20 000); δ_H(CD_3OD) 0.95 (3 H, d, *J* 6.9, 17-H_3), 1.2 (3 H, d, *J* 6.3, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.2 (3 H, s, 15-H_3), 2.2 (1 H, dd, *J* 9.6, 14.3, 4-H), 2.6 (1 H, br d, *J* 14.3, 4-H), 2.7 (1 H, dd, *J* 2.2, 7.6, 11-H), 2.8 (1 H, dt, *J* 2.2, 5.8, 10-H), 3.35 (1 H, dd, *J* 3.1, 9.0, 6-H), 3.6 (1 H, br d, *J* 11.5, 16-H), 3.7–3.95 (4 H, m, 6-, 7-, 13- and 16-H), 4.5 (2 H, s, 1′-H_2), 5.85 (1 H, s, 2-H), 7.3 (1 H, dd, *J* 4.6, 7.8, 5″-H), 7.4 (1 H, d, *J* 7.8, 3″-H), 7.80 (1 H, dt, *J* 1.8, 7.8, 4″-H) and 8.46 (1 H, d, *J* 4.6, 6″-H); δ_C(CD_3OD) 12.3 (C-17), 19.0 (C-15), 20.3 (C-14), 32.9 (C-9), 41.5 (C-8), 43.6 (C-12), 43.7 (C-4), 45.2 (C-1′), 56.8 (C-10), 61.2 (C-11), 66.2 (C-16), 70.0 (C-6), 70.6 (C-7), 71.5 (C-13), 76.2 (C-5), 120.7 (C-2), 122.8, 123.5 (C-3″ and -5″), 138.7 (C-4″), 149.6 (C-6″), 153.2 (C-3), 159.4 (C-2″) and 169.5 (C-1); *m*/*z* 434 (M^+, 10%), 342 (12), 324 (10), 203 (21), 189 (27), 109 (44), 107 (33) and 93 (100) (Found: M^+, 434.2378. $C_{23}H_{34}N_2O_6$ requires *M*, 434.2415) (Found: C, 63.4; H, 8.1; N, 6.3. $C_{23}H_{34}N_2O_6$ requires C, 63.59; H, 7.83; N, 6.45%).

This material (0.33 g, 0.76 mmol) was cyclised using general method B to give the *title compound* (0.07 g, 22%); λ_{max}(EtOH)/nm 227.5 (ε/dm^3 mol^{-1} cm^{-1} 20 100) and 312 (14 600); δ_H($CDCl_3$) 0.9 (3 H, d, *J* 7.0, 17-H), 1.2 (3 H, d, *J* 6.3, 14-H_3), 1.25–1.45 (1 H, m, 12-H), 1.7–1.8 (2 H, m, 9-H_2), 2.0–2.1 (1 H, m, 8-H), 2.15–2.25 (3 H, s, 15-H_3), 2.5 (1 H, dd, *J* 8.2, 14.4, 4-H), 2.7–2.9 (3 H, m, 4-, 10-, 11-H), 3.5–4.0 (6 H, m, 5-, 6-, 7-, 13-H and 16-H_2), 6.4 (1 H, s, 2-H), 6.55 (1 H, dd, *J* 6.0, 7.2, 6′-H), 6.7 (1 H, dd, *J* 6.0, 9.1, 5′-H), 7.4 (1 H, d, *J* 9.1, 4′-H), 7.45 (1 H, s, 3′-H) and 7.8 (1 H, d, *J* 7.2, 7′-H); δ_C(CD_3OD) 12.3 (C-17), 19.6 (C-15), 20.3 (C-14), 33.0 (C-9), 41.7 (C-8), 43.3 (C-4), 43.7 (C-12), 56.9 (C-10), 61.2 (C-11), 66.4 (C-16), 70.1, 70.7, 71.7 (C-6, -7 and -13), 76.6 (C-5), 113.1, 114.0 (C-2 and -6′), 119.3, 119.7, 120.2 (C-3′, -4′ and -5′), 122.7 (C-4′), 131.2 (C-3a′) 137.4 (C-1′) and 144.7 (C-3); *m*/*z* 416 (M^+, 35%), 313 (10), 183 (40) and 171 (100) (Found: M^+ 416.2312. $C_{23}H_{32}N_2O_5$ requires *M*, 416.2311).

2-*Normonylbenzo*[4,5]*imidazole* **3c**.—The *N*-(*O*-aminophenyl)monamide **1f** (0.384 g, 0.88 mmol) was cyclised using general method B to give the *title compound* (0.262 g, 71%) as a colourless foam; ν_{max}(KBr)/cm^{-1} 3382, 2970, 1656, 1619, 1449, 1275, 1052 and 744; λ_{max}(EtOH)/nm 231 (ε/dm^3 mol^{-1} cm^{-1} 18 800), 297 (20 400) and 309 (12 800); δ_H(CD_3OD) 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.5, 14-H_3), 1.25–1.45 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.25 (3 H, d, *J* 1.0, 15-H_3), 2.35 (1 H, dd, *J* 9.4, 14.5, 4-H), 2.7 (1 H, dd, *J* 2.2, 7.6, 11-H), 2.8 (1 H, br d, *J* 14.5, 4-H), 2.8 (1 H, dt, *J* 2.2, 5.7, 10-H), 3.45 (1 H, dd, *J* 3.1, 8.8, 6-H), 3.6 (1 H, dd, *J* 1.5, 11.4, 16-H), 3.7–3.9 (4 H, m, 5-, 7-, 13- and 16-H), 6.3 (1 H, br s, 2-H), 7.15–7.25 (2 H, m, 5′- and 6′-H) and 7.45–7.55 (2 H, m, 4′- and 7′-H); δ_C(CD_3OD), 12.3 (C-17), 19.8 (C-15), 20.4 (C-14), 33.1 (C-9), 41.7 (C-8), 43.8 (C-4 and -12), 57.0 (C-10), 61.3 (C-11), 66.4 (C-16), 70.1 (C-6), 70.8 (C-7), 71.7 (C-13), 76.6 (C-5), 115.6 (C-5′ and -6′), 116.4 (C-2), 123.4 (C-4′ and -7′), 140 (C-3a′ and -7a′), 147.6 (C-2′) and 152.4 (C-3); *m*/*z* 416 (M^+, 5%), 201 (30) and 172 (100) (Found: M^+, 416.2328. $C_{23}H_{32}N_2O_5$ requires *M*, 416.2311).

N-[(Z)-2-*Methoxyimino*-2-*phenylethyl*]*monamide* **1h**.—*N*-Phenacylmonamide **1g** (0.45 g, 1 mmol) in methanol (8 cm^3) was treated overnight with *O*-methylhydroxylamine hydrochloride (0.33 g, 4 mmol) and triethylamine (0.4 cm^3, 3 mmol). The solvent was removed by evaporation under reduced pressure and the residue taken up in dichloromethane (20 cm^3), any insoluble material was removed by filtration. The crude product was purified twice by chromatography on silica gel eluting first with methanol in dichloromethane (3%), then with methyl acetate, to give the *title compound* (0.068 g, 14%), ν_{max}($CHCl_3$)/cm^{-1} 3600–3200, 3001–2800, 1660, 1635, 1500, 1445 and 1045; λ_{max}(EtOH)/nm 314 (ε/dm^3 mol^{-1} cm^{-1} 30), 227 (17 000); δ_H($CDCl_3$) 0.95 (3 H, d, *J* 7, 17-H_3), 1.25 (3 H, d, *J* 6.3, 14-H_3), 1.25–1.45 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.15 (3 H, s, 15-H_3), 2.2 (1 H, dd, *J* 8.8, 14.6, 4-H), 2.4–2.6 (2 H, m, OH), 2.65–2.85 (3 H, m, 10-, 11- and 4-H), 3.4–3.9 (6 H, m, 5-, 6-, 7-, 13-H and 16-H_2), 4.05 (3 H, s, MeO), 4.5 (2 H, d, *J* 6, 1′-H), 5.6 (1 H, s, 2-H), 6.1 (1 H, t, 6, NH), 7.35–7.45 (3 H, m, 3″-, 4″- and 5″-H) and 7.5–7.85 (m, 2 H, m, 2″-and 6″-H); δ_C($CDCl_3$) 12.7 (C-17), 18.7 (C-15), 20.8 (C-14), 31.6 (C-9), 34.8 (C-1′), 39.6 (C-8), 42.6 (C-4), 42.7 (C-12), 55.6 (C-10), 61.2 (C-11), 62.4 (OMe), 65.4 (C-16), 68.8 (C-6), 70.3 (C-7), 71.2 (C-13), 74.9 (C-5), 119.7 (C-2), 128.6, 126.8 (C-2″, -3″), 129.6 (C-4″), 133.7 (C-1″), 151.4 (C-3), 155.5 (C-2′) and 166.8 (C-1); *m*/*z* 490 (M^+, 10%), 459 (15), 227 (50) and 111 (100) (Found: M^+, 490.2692. $C_{26}H_{38}N_2O_7$ requires *M*, 490.2679).

N-*Acetonylmonamide* **1i**.—To the mixed anhydride **1e** from monic acid (1.72 g, 5.0 mmol) in THF (25 cm^3) was added triethylamine (2 cm^3). Aminoacetone hydrochloride (1 g, 9 mmol) in methanol (10 cm^3) was then added dropwise to the mixture. After 30 min the solvent was removed by evaporation

under reduced pressure and the residue taken up in ethyl acetate (50 cm^3). The insoluble triethylammonium chloride was removed by filtration and the soluble material was purified by chromatography eluting with methanol in dichloromethane (0–10%) to give the *title product* **1i**, (1.07 g, 53%), ν_{max}-($CHCl_3$)/cm^{-1} 3420, 3000, 1725, 1660, 1640 and 1500; λ_{max}-(EtOH)/nm 221 (ε/dm^3 mol^{-1} cm^{-1} 15 000); δ_H($CDCl_3$) 0.9 (3 H, d, *J* 6.9, 17-H), 1.2 (3 H, d, *J* 6.2, 14-H), 1.3–1.5 (1 H, m, 12-H), 1.7 (2 H, br t, *J* 5.9, 9-H), 1.95–2.05 (1 H, m, 8-H), 2.2, 2.25 (2 × 3 H, 2 × s, 15-H_3, 3′-H_3), 2.25 (1 H, dd, *J* 8.7, 13.8, 4-H), 2.6 (1 H, br d, *J* 13.8, 4-H), 2.75 (1 H, br d, *J* 7.5, 11-H), 2.8 (1 H, br t, 10-H), 3.0–3.5 (3 H, br m, OH), 3.5–4.0 (6 H, m, 5-, 6-, 7-, 13-H and 16-H_2), 4.2 (2 H, d, *J* 4, 1′-H), 5.8 (1 H, s, 2-H) and 6.5 (1 H, br, NH); *m*/*z* 399 (M^+, 3%) and 155 (100%) (Found: M^+, 399.2283. $C_{20}H_{33}NO_7$ requires *M*, 399.2257).

N-[(E)-2-(*Methoxyimino*)*propyl*]*monamide* **1j**.—To the *N*-acetonylmonamide **1i** (0.36 g, 0.9 mmol), in methanol (8 cm^3) was added triethylamine (0.4 cm^3) and *O*-methylhydroxylamine hydrochloride (0.33 g). After 30 min at room temperature the solvent was removed by evaporation under reduced pressure and a further portion of methanol (20 cm^3) was added and evaporated under reduced pressure in an attempt to remove methylhydroxylamine. The residue was taken up in ethyl acetate (30 cm^3) and filtered to remove insoluble amine hydrochlorides. The solution was concentrated and purified by chromatography on silica gel eluting with methanol in dichloromethane (0–10%). The *title compound* was the major, less polar component (0.19 g, 49%), ν_{max}($CHCl_3$)/cm^{-1} 3600–3200, 3000–2850, 1665, 1635, 1500 and 1050; λ_{max}(EtOH)/nm 221 (ε/dm^3 mol^{-1} cm^{-1} 19 000); δ_H($CDCl_3$) 0.9 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.3, 14-H_3), 1.25–1.45 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H), 1.8 (3 H, s, 3′-H_3), 1.95–2.05 (1 H, m, 8-H), 2.2 (3 H, s, 15-H_3), 2.25 (1 H, dd, *J* 8.7, 14.6, 4-H), 2.6 (1 H, dd, *J* 2.4, 14.6, 4-H), 2.65 (1 H, br s, OH), 2.7 (1 H, dd, *J* 2.2, 7.9, 11-H), 2.8 (1 H, dt, *J* 2.2, 5.5, 10-H), 2.9–3.1 (2 H, m, OH), 3.4–4.0 (6 H, m, 5-, 6-, 7-, 13-H and 16-H_2), 4.0 (2 H, d, *J* 5, 1′-H), 3.85 (3 H, s, OMe), 5.7 (1 H, s, 2-H) and 6.2 (1 H, t, *J* 5, NH); δ_C($CDCl_3$) 12.7 (C-17), 13.1 (C-3′), 18.9 (C-15), 20.8 (C-14), 31.7 (C-9), 38.7 (C-8), 42.6 (C-4), 42.8 (C-12), 43.1 (C-1′), 55.7 (C-10), 61.2 (C-11), 61.6 (OMe), 65.4 (C-16), 68.9 (C-6), 70.4 (C-7), 71.1 (C-13), 74.9 (C-5), 118.8 (C-2), 151.6 (C-3), 153.3 (C-2′) and 167.3 (C-1); *m*/*z* 428 (M^+, 25%), 184 (50), 153 (55), 111 (60) and 43 (100) (Found: M^+, 428.2524. $C_{21}H_{36}N_2O_7$ requires *M*, 428.2523).

1-*Methoxy*-5-*methyl*-2-*normonylimidazole* **3d**.—Cyclisation of the monamide **1j** (0.16 g, 0.37 mmol) using general method B, except that methyl acetate was utilised in the final chromatography, gave the *title compound* (0.085 g, 56%), as a gum, δ_H($CDCl_3$) 0.9 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.2, 14-H_3), 1.25–1.45 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.21, 2.23 (2 × 3 H, 2 × s, 15-H_3 and 6′-H_3), 2.4 (1 H, dd, *J* 8.4, 14.3, 4-H), 2.65 (1 H, dd, *J* 3.3, 14.3, 4-H), 2.7 (1 H, dd, *J* 2.2, 7.8, 11-H), 2.8 (1 H, dt, *J* 2.2, 5.6, 10-H), 3.4–3.9 (6 H, m, 5-, 6-, 7-, 13-H and 16-H_2), 3.95 (3 H, s, OMe), 6.15 (1 H, s, 2-H) and 6.7 (1 H, q, *J* 0.6, 4′-H); δ_C($CDCl_3$) 8.1 (C-6′), 12.7 (C-17), 19.4 (C-15), 20.8 (C-14), 31.8 (C-9), 39.5 (C-8), 42.7 (C-4), 42.8 (C-12), 55.7 (C-10), 61.3 (C-11), 65.4 (C-16), 66.4 (OMe), 69.0 (C-6), 70.4 (C-7), 71.2 (C-13), 75.4 (C-5), 111.2 (C-2), 121.6 (C-4′), 123.1 (C-5′), 139.5 (C-2′) and 142.5 (C-3); *m*/*z* 410 (M^+, 3%), 379 (50), 166 (20), 147 (50) and 135 (100) (Found: M^+, 410.2397. $C_{21}H_{34}N_2O_6$ requires *M*, 410.2417).

N-[(E)-2-(tert-*Butyldimethylsiloxyimino*)-1-*phenylethyl*]-*monamide* **1k**.—α-Azidophenylacetaldehyde (1.0 g, 6.2 mmol) in methanol (10 cm^3) was treated with triethylamine (1 cm^3, 7.1 mmol) and hydroxylamine hydrochloride (1.0 g, 14.4 mmol) for 30 min at 20 °C. The solvent was then removed by evaporation under reduced pressure and the residue was triturated with THF (3 × 10 cm^3). The soluble material was purified by chromatography on silica gel eluting with dichloromethane to give α-azidophenylacetaldehyde oxime (0.62 g, 54%) as a 3:1 mixture of *E* and *Z* isomers, respectively; ν_{max}(CH_2Cl_2)/cm^{-1} 3560 and 2100; δ_H($CDCl_3$) for *Z* isomer 5.9 (1 H, d, *J* 7, 1-H), 6.9 (1 H, d, *J* 7, 2-H), 7.35 (5 H, s, 2′- to 6′-H) and 8.9 (1 H, br s, OH), for *E* isomer, 5.2 (1 H, d, *J* 7, 1-H), 7.35 (5 H, s, 2′ to 6′-H), 7.4 (1 H, d, *J* 7, 2-H) and 8.5 (1 H, s, OH).

This material (0.6 g, 3.75 mmol) in THF (5 cm^3) was treated with triethylamine (1.2 cm^3), *tert*-butyldimethylsilyl chloride (1.1 g) and a catalytic amount of DMAP. After 1 h at 20 °C, diethyl ether (10 cm^3) and saturated aqueous sodium hydrogen carbonate (10 cm^3) were added, the organic layer washed with brine (5 cm^3), dried ($MgSO_4$) and then concentrated. The crude product was purified by chromatography on silica gel eluting with hexane to give α-azidophenylacetaldehyde *O*-*tert*-butyldimethylsilyloxime as a mixture of *E* and *Z* isomers (0.93 g, 88%).

This material (0.9 g, 3.1 mmol) in ethanol (25 cm^3) was hydrogenated at room temperature and pressure over palladium on carbon (0.07 g, 5%) for 20 min. The catalyst was removed by filtration and then the solvent was evaporated to leave a residue which was treated with anhydride **1e** according to general method A to give the *title monamide* **1k** (0.7 g, 50%), ν_{max}(KBr)/cm^{-1} 3421, 2929, 1663, 1639, 1251, 939, 862 and 840; δ_H(CD_3OD) 0.15 (6 H, s, SiMe), 0.9 (9 H, s, SiBu^t), 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.4, 14-H), 1.3–1.5 (1 H, m, 12-H), 1.6–1.8 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.15 (3 H, s, 15-H_3), 2.2 (1 H, dd, *J* 9.9, 14.6, 4-H), 2.6 (1 H, d, *J* 14.6, 4-H), 2.7 (1 H, dd, *J* 2.1, 7.6, 11-H), 2.8 (1 H, dt, *J* 2.1, 5.7, 10-H), 3.4–3.9 (6 H, m, 5-, 6-, 7-, 13-H and 16-H_2), 5.7 (1 H, d, *J* 6.2, 1′-H), 5.8 (1 H, s, 2-H), 7.2–7.4 (5 H, m, Ph) and 7.6 (1 H, d, *J* 6.2, 2′-H); δ_C(CD_3OD), −5.1 (SiMe), 12.3 (C-17), 19.0 (Si*C*Me_3), 19.0 (C-15), 20.3 (C-14), 26.5 (Si*C*Me_3). 33.0 (C-9), 41.7 (C-8), 43.7 (C-12), 43.8 (C-4), 53.7 (C-1′), 56.7 (C-10), 61.2 (C-11), 66.3 (C-16), 70.0 (C-6), 70.7 (C-7), 71.6 (C-13), 76.2 (C-5), 120.6, 120.7 (C-2), 128.1, 129.8 (C-2″, -3″, -5″ and -6″), 128.8 (C-4″), 139.9 (C-1″), 153.4, 153.5 (C-3), 155.0 (C-2′) and 168.6 (C-1); *m*/*z* (FAB) 613 (MNa^+).

1-*Hydroxy*-2-*normonyl*-4-*phenylimidazole* **3e**.—The monamide **1k** (0.285 g, 0.48 mmol) was cyclised using general method B. After the acid deprotection the aqueous layer was evaporated to dryness under reduced pressure and the residue triturated with ethanol (2 × 10 cm^3). This ethanol solution was combined with the organic extracts and was purified by chromatography on silica gel eluting with methanol in dichloromethane (0–15%), to give the *title compound* **3e** (0.11 g, 50%) as a brown foam; ν_{max}(KBr)/cm^{-1} 3407, 2966, 2923, 1647, 1595, 1451, 1111 and 1048; λ_{max}(EtOH)/nm 288 (ε/dm^3 mol^{-1} cm^{-1} 16 500); δ_H(CD_3OD) 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.4, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.1 (3 H, s, 15-H_3), 2.4 (1 H, dd, *J* 8.2, 14.6, 4-H), 2.7 (1 H, dd, *J* 2.2, 6.6, 11-H), 2.75 (1 H, d, *J* 14, 4-H), 2.8 (1 H, dt, *J* 2.2, 5.7, 10-H), 3.4 (1 H, dd, *J* 3.1, 8.7, 6-H), 3.6 (1 H, br d, *J* 10.4, 16-H), 3.7–3.9 (4 H, m, 5-, 7-, 13- and 16-H), 6.25 (1 H, s, 2-H), 7.3–7.35 (1 H, m, 4″-H), 7.35–7.45 (2 H, m, 3″- and 5″-H), 7.5 (1 H, s, 5′-H) and 7.6–7.7 (2 H, m, 2″- and 6″-H); δ_C(CD_3OD) 12.3 (C-17), 19.9 (C-15), 20.4 (C-14), 33.0 (C-9), 41.6 (C-8), 43.3 (C-4), 43.7 (C-12), 57.0 (C-10), 61.3 (C-11), 66.3 (C-16), 70.0 (C-6), 70.7 (C-7), 71.7 (C-13), 76.5 (C-5), 110.6 (C-5′), 116.6 (C-2), 126.1, 130.0 (C-2″, -3″, -5″ and -6″), 129.1 (C-4″), 131.1, 132.3 (C-2′ and -4′), 138.9 (C-1″) and 147.6 (C-3); *m*/*z* 458 (M^+, 4%), 442 (20), 440 (7) and 198 (100) (Found: M^+, 458.2432. $C_{25}H_{34}N_2O_6$ requires *M*, 458.2417).

2-Normonyl-4(5)-phenylimidazole **3a**.—To the *N*-hydroxyimidazole **3e** (0.11 g, 0.24 mmol) in methanol (10 cm^3) under nitrogen was added ammonium acetate (1 g) and aqueous titanium(III) chloride (15%, 1 cm^3). After 1 h at 20 °C, the solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel eluting with methanol in dichloromethane (5–10%), to give the *title product* **3a** (74 mg, 70%); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3450, 2930, 1700, 1650, 1605 and 1050; λ_{max}(EtOH)/nm 283 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 17 600); $\delta_H(CD_3OD)$ 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.4, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.15 (3 H, s, 15-H_3) 2.3 (1 H, dd, *J* 9.4, 14.4, 4-H), 2.7 (1 H, *J* 14.4, 4-H), 2.7 (1 H, dd, *J* 2.2, 7.6, 11-H), 2.8 (1 H, dt, *J* 2.2, 5.7, 10-H), 3.4–3.9 (6 H, m, 5-, 6-, 7- and 13-H and 16-H_2), 6.2 (1 H, s, 2-H), 7.2–7.3 (1 H, m, 4″-H), 7.3–7.45 (2 H, m, 3″- and 5″-H) 7.45 (1 H, s, 5′-H) and 7.65–7.75 (2 H, d, *J* 7.4, 2″- and 6″-H); $\delta_C(CD_3OD)$ 12.2 (C-17), 19.2 (C-15), 20.3 (C-14), 33.0 (C-9), 41.6 (C-8), 43.4 (C-4), 43.7 (C-12), 56.9 (C-10), 61.3 (C-11), 66.3 (C-16), 70.1 (C-6), 70.7 (C-7), 71.7 (C-13), 76.6 (C-5), 116.2 (C-2), 125.7, 129.6 (C-2″, -3″, -5″ and -6″), 127.6 (C-4″), 142.7 (C-1″) and 147.6 (C-3); *m/z* 442 (M^+, 5%) and 198 (100) (Found: M^+ 442.2463. $C_{25}H_{34}N_2O_5$ requires *M*, 442.2468).

4(5)-(p-Methylsulfanylphenyl)-2-normonylimidazole **3f**.—*N-(α-Cyano-p-methylsulfanylbenzyl)monamide* **1m** was prepared in 54% yield by general method A as a pale yellow foam; ν_{max}(KBr)/cm^{-1} 3432, 2971, 2918, 1662, 1636, 1493, 1095 and 1051; λ_{max}(EtOH)/nm 260 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 19 000); $\delta_H(CD_3OD)$ 0.95 (3 H, d, *J* 7.2, 17-H_3), 1.2 (3 H, d, *J* 6.3, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.2 (1 H, dd, *J* 9.6, 14.6, 4-H), 2.2 (3 H, s, 15-H_3), 2.5 (3 H, s, SMe), 2.65 (1 H, d, *J* 14.6, 4-H), 2.7 (1 H, br d, *J* 7.6, 11-H), 2.8 (1 H, br, 10-H), 3.4–3.9 (6 H, m, 5-, 6-, 7- and 13-H and 16-H_2), 5.8 (1 H, s, 2-H), 6.05 (1 H, s, slow exchange, 1′-H) and 7.3–7.4 (4 H, A_2B_2q, *J* 8.6, 2″-, 3″-, 5″- and 6″-H); $\delta_C(CD_3OD)$ 12.3 (C-17), 15.3 (SMe), 19.1, 19.2 (C-15), 20.4 (C-14), 33.0 (C-4), 41.7 (C-8), 43.7 (C-12), 43.9, 44.0 (C-4), 44.4 (C-1′), 56.7 (C-10), 61.2 (C-11), 66.3 (C-16), 70.0 (C-6), 70.7 (C-7), 71.6 (C-13), 76.0, 76.1 (C-5), 119.1 (C≡N), 119.4, 119.5 (C-2), 127.6, 128.6 (C-2″, -3″, -5″ and -6″), 131.6 (C-4″), 141.6 (C-1″), 155.9 (C-3) and 168.2 (C-1); *m/z* 504 (M^+, 2%) and 178 (100) (Found: M^+, 504.2291. $C_{26}H_{36}N_2O_6S$ requires *M*, 504.2294).

Monamide **1m** (0.17 g, 0.34 mmol) in THF (5 cm^3) was treated with triethylamine (0.286 cm^3, 6 equiv.) and chlorotrimethylsilane (0.21 cm^3, 5 equiv.) and a catalytic amount of DMAP. After 1 h at 20 °C the mixture was diluted with diethyl ether, filtered, evaporated and then taken up in diethyl ether, refiltered and re-evaporated under reduced pressure. The residue was taken up in THF (6 cm^3) and cooled to −78 °C under nitrogen. A solution of diisobutylaluminium hydride (DIBAL) in toluene (1.5 mol dm^{-3}; 0.55 cm^3, 2.4 equiv.) was added and the mixture stirred for 1 h at −78 °C. Triethylamine (0.48 cm^3, 10 equiv.) and triphenylphosphine dibromide (prepared from 0.27 g triphenylphosphine and 0.147 g bromine in 4 cm^3 trichloromethane) were added to it and the mixture warmed to 0 °C. After 70 min at 0 °C, the reaction was quenched with water and extracted with diethyl ether. The organic phase was dried ($MgSO_4$) and then evaporated under reduced pressure. The residue was purified by chromatography on silica gel eluting with 10–30% ethyl acetate in hexane. The fluorescent product (0.04 g) was taken up in THF (5 cm^3) and treated with hydrochloric acid (0.4 mol dm^{-3}; 1 cm^3) for 4 min. The reaction was quenched with saturated aqueous sodium hydrogen carbonate, extracted with ethyl acetate and the organic phase dried ($MgSO_4$), evaporated under reduced pressure and then purified by chromatography on silica gel eluting with methanol in dichloromethane (0–10%) to give the *title compound* **3f** (0.017 g, 10%); ν_{max}(KBr)/cm^{-1} 3388, 2969, 2920, 1656, 1102, 1078 and 1050; λ_{max}(EtOH)/nm 301 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 26 700); $\delta_H(CD_3OD)$ 0.9 (3 H, d, *J* 7.0, 17-H_3), 1.2 (3 H, d, *J* 6.4, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.15 (3 H, s, 15-H_3), 2.3 (1 H, dd, *J* 9.4, 14.5, 4-H), 2.45 (3 H, s, SMe), 2.6–2.9 (3 H, m, 4-, 10- and 11-H), 3.4 (1 H, dd, *J* 3.0, 8.4, 6-H), 3.55 (1 H, br d, *J* 11.4, 16-H), 3.7–3.9 (4 H, m, 5-, 7-, 13- and 16-H), 6.2 (1 H, s, 2-H), 7.25 (2 H, d, *J* 8.4, 3″- and 5″-H), 7.6 (2 H, d, *J* 8.4, 2″- and 6″-H) and 7.3 (1 H, s, 5′-H); *m/z* 488 (M^+, 10%), 244 (100) and 204 (40) (Found: M^+, 488.2323. $C_{26}H_{36}N_2O_5S$ requires *M*, 488.2345).

N′-Phenylmonohydrazide **1n**.—Prepared using general method A in 58% yield as a colourless foam; ν_{max}(KBr)/cm^{-1} 3405, 2971, 1663, 1602, 1495, 1111, 1050, 754 and 694; λ_{max}(EtOH)/nm 235 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 19 200) and 276 (3550); $\delta_H(CD_3OD)$ 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.20 (3 H, d, *J* 6.5, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.15 (3 H, s, 15-H_3), 2.2 (1 H, dd, *J* 9.6, 14.5, 4-H), 2.72 (1 H, dd, *J* 2.2, 7.7, 11-H), 2.82 (1 H, dt, *J* 2.2, 5.7, 10-H), 3.3–3.9 (6 H, m, 5-, 6-, 7- and 13-H and 16-H_2) and 5.86 (1 H, s, 2-H); $\delta_C(CD_3OD)$ 12.3 (C-17), 19.1 (C-15), 20.4 (C-14), 33.0 (C-9), 41.4 (C-8), 43.7 (C-12), 43.9 (C-4), 56.9 (C-10), 61.2 (C-11), 66.3 (C-16), 70.0 (C-6), 70.7 (C-7), 71.6 (C-13), 76.1 (C-5), 114.1 (C-2′ and -6′), 118.5 (C-4′), 120.9 (C-2), 129.9 (C-3′ and -5′), 150.1 (C-1′), 154.7 (C-3) and 169.4 (C-1); *m/z* 434 (M^+, 90%) and 108 (100) (Found: M^+, 434.2397. $C_{23}H_{34}N_2O_6$ requires *M*, 434.2417).

5-Cyano-3-normonyl-1-phenyl-4,5-dihydropyrazole **3h**.—*N′*-Phenylmonohydrazide **1n** (0.35 g, 0.82 mmol) was subjected to general method B except that in the second stage acrylonitrile (4 cm^3) was used in place of acetonitrile. The *title compound* was obtained as a yellow foam (0.20 g, 52%); ν_{max}(KBr)/cm^{-1} 3427, 2969, 2921, 2235, 1640, 1598, 1499, 1111, 1050 and 751; λ_{max}(EtOH)/nm 221 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 13 200), 240 (10 800) and 323 (14 500); $\delta_H(CD_3OD)$ 0.95 (3 H, d, *J* 7.0, 17-H_3), 1.2 (3 H, d, *J* 6.3, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.1 (3 H, s, 15-H_3), 2.25 (1 H, dd, *J* 8.3, 14.3, 4-H), 2.7 (1 H, d, *J* 14.3, 4-H), 2.7 (1 H, dd, *J* 2.1, 7.3, 11-H), 2.8 (1 H, dt, *J* 2.1, 5.7, 10-H), 3.4–3.9 (8 H, m, 5-, 6-, 7- and 13-H, 4′- and 16-H_2), 5.2–5.3 (1 H, m, 5′-H), 6.05 (1 H, s, 2-H), 6.95 (1 H, t, *J* 7.3, 4″-H), 7.15 (2 H, d, *J* 7.6, 2″- and 6″-H) and 7.3 (2 H, t, *J* 7.4, 3″- and 5″-H); $\delta_C(CD_3OD)$ 12.3 (C-17), 19.76, 19.78 (C-15), 20.3 (C-14), 32.9 (C-9), 41.5 (C-8), 42.2 (C-4′), 43.7 (C-12), 44.3 (C-4), 50.9 (C-5′), 56.9 (C-10), 61.2 (C-11), 66.3 (C-16), 70.1 (C-6), 70.7 (C-7), 71.6 (C-13), 76.50, 76.52 (C-5), 115.5 (C-2), 118.6 (C≡N), 119.10, 119.13 (C-2″ and -6″), 121.9 (C-4″), 130.2 (C-3″ and -5″), 145.21, 145.24 (C-1″), 145.5 (C-3′) and 150.7 (C-3); *m/z* 442 (M^+ − HCN, 9%) and 198 (100) (Found: M^+, 442.2463. $C_{25}H_{34}N_2O_5$ requires *M*, 442.2468).

3-Normonyl-1-phenylpyrazole **3g**.—To the tristrimethylsilyl cyanodihydropyrazole **4h** (0.056 g) in toluene (3 cm^3) was added copper(I) chloride (0.021 g) and the mixture was heated to reflux under an atmosphere of nitrogen for 1.5 h. Purification by chromatography on silica gel eluting with ethyl acetate in hexane (10–40%) gave the crude protected pyrazole **4g** (0.062 g). This was treated in THF (5 cm^3) with hydrochloric acid (0.4 mol dm^{-3}; 1.5 cm^3) for 2 min. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate and extracted with ethyl acetate to give the *title compound* **3g** (9 mg, 42%) after chromatography on silica eluting with 0–4% methanol in dichloromethane; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3620, 3560, 3450, 2930, 1660, 1600, 1525 and 1050; λ_{max}(EtOH)/nm 281 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 19 200) and 207 (17 000); $\delta_H(CD_3OD)$ 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.4, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.1 (3 H, d, *J* 0.6, 15-H_3), 2.3 (1 H, dd, *J*

9.4, 14.4, 4-H), 2.7 (1 H, br d, *J* 14.4, 4-H), 2.75 (1 H, dd, *J* 2.2, 7.6, 11-H), 2.8 (1 H, dt, *J* 2.2, 5.7, 10-H), 3.4 (1 H, dd, *J* 3.1, 8.5, 6-H), 3.6 (1 H, dd, *J* 2.2, 11.4, 16-H), 3.7–3.9 (4 H, m, 5-, 7-, 13- and 16-H), 6.35 (1 H, brs, 2-H), 6.55 (1 H, d, *J* 2.5, 4′-H), 7.25–7.35 (1 H, m, 4″-H), 7.45–7.55 (2 H, m, 3″- and 5″-H), 7.7–7.75 (2 H, m, 2″- and 6″-H) and 8.15 (1 H, d, *J* 2.5, 5′-H); $\delta_C(CD_3OD)$ 12.3 (C-17), 19.3 (C-15), 20.3 (C-14), 33.1 (C-9), 41.5 (C-8), 43.7 (C-4), 43.8 (C-12), 57.0 (C-10), 61.4 (C-11), 66.4 (C-16), 70.2 (C-6), 70.8 (C-7), 71.7 (C-13), 76.9 (C-5), 108.9 (C-4′), 119.6 (C-2), 120.1 and 130.6 (C-2″, -3″, -5″ and -6″), 127.4 and 129.1 (C-4″ and -5′), 140.1 and 141.4 (C-3′ and -1″) and 153.2 (C-3); *m/z* 442 (M^+, 6%), 424 (2), 406 (4) and 198 (100) (Found: M^+, 442.2467. $C_{25}H_{34}N_2O_5$ requires *M*, 442.2468).

5-Cyano-3-normonyl-1-phenylpyrazole **3i**.—To the tris-trimethylsilyl cyanodihydropyrazole **4h** (0.12 g) in toluene (10 cm^3) was added copper(II) chloride (0.15 g) and basic copper(II) carbonate (0.10 g) and then the mixture was heated to reflux under an atmosphere of nitrogen for 30 min. The reaction mixture was cooled and purified by chromatography on silica gel eluting with ethyl acetate in hexane (10–20%) to give the protected cyanopyrazole **4i** (0.04 g). This material was dissolved in THF (4 cm^3) and HCl (0.4 mol dm^{-3}; 1 cm^3) was added to it. After 4 min at 20 °C saturated aqueous sodium hydrogen carbonate and ethyl acetate were added, the organic layer dried, evaporated under reduced pressure and then purified by chromatography on silica gel to yield the *title compound* **3i** as a white foam (0.019 g, 23% overall); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3610, 3560, 2970, 2940, 2240, 1660, 1500 and 1055; λ_{max}/nm 225 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 18 300) and 294 (6800); $\delta_H(CD_3OD)$ 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.5, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.1 (3 H, s, 15-H_3), 2.3 (1 H, dd, *J* 9.5, 14.4, 4-H), 2.65–2.75 (2 H, m, 4- and 11-H), 2.8 (1 H, dt, *J* 2.2, 5.8, 10-H), 3.4 (1 H, dd, *J* 3.0, 8.7, 6-H), 3.6 (1 H, br d, *J* 11.5, 16-H), 3.7–3.9 (4 H, m, 5-, 7-, 13- and 16-H), 6.3 (1 H, s, 2-H), 7.2 (1 H, s, 4′-H), 7.45–7.65 (3 H, m, 3″-, 4″- and 5″-H) and 7.7–7.75 (2 H, m, 2″- and 6″-H); $\delta_C(CD_3OD)$ 12.3 (C-17), 19.3 (C-15), 20.3 (C-14), 33.1 (C-9), 41.6 (C-8), 43.8 (C-4 and -12), 57.0 (C-10), 61.3 (C-11), 66.3 (C-16), 70.2 (C-6), 70.7 (C-7), 71.7 (C-13), 76.7 (C-5), 112.0 (C-5′), 115.4 (C≡N), 116.9 (C-4′), 117.8 (C-2), 124.1 and 130.7 (C-2″, -3″, -5″ and -6″), 129.9 (C-4″), 140.0 (C-1″), 142.7 (C-3′) and 152.8 (C-3); *m/z* 467 (M^+, 2%), 223 (45) and 42 (100) (Found: M^+, 467.2423. $C_{26}H_{33}N_3O_5$ requires *M*, 467.2420).

1-Phenylvinyl Monate **1o** *and 2-Hydroxy-2-phenylvinyl Normonyl Ketone* **1p**.—To lithium diisopropylamide (10 mmol) in THF (20 cm^3) at −78 °C under argon was added acetophenone (1.16 cm^3, 10 mmol). After 15 min at −78 °C isobutylcarbonic 6,7,13-tris-trimethylsilyl monic anhydride **2e** (3.0 g, 4.54 mmol) in THF (5 cm^3) was added dropwise to it over 5 min. After 45 min at −78 °C and 30 min at −30 °C the reaction was quenched by the addition of acetic acid (1.2 g) in diethyl ether (50 cm^3) followed by water (50 cm^3). The organic layer was washed with 5% aqueous citric acid (20 cm^3) and saturated aqueous sodium hydrogen carbonate, dried, concentrated by evaporation under reduced pressure and then purified by chromatography on silica gel, first with dichloromethane–hexane–diethyl ether (1:1:0 to 1:0:0 then to 97:0:3), then with diethyl ether in hexane (5–15%) to give the *C-acylated product* **2p** as a colourless gum (0.537 g, 16%); $\delta_H(CDCl_3$, *inter alia*) 0.1–0.2 (27 H, m, SiMe), 0.9 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.3, 14-H_3), 2.3 (3 H, s, 15-H_3), 5.9 (1 H, s, 2- or 1′-H), 6.1 (1 H, s, 2- or 1′-H), 7.4–7.5 (3 H, m, 3″- to 5″-H), 7.85–7.95 (2 H, m, 2″- and 6″-H) and 13.3 (1 H, br s, enol OH).

A more polar component, obtained as a colourless gum (0.30 g, 9%), was identified as the *O-acylated material* **2o**; $\delta_H(CDCl_3$, *inter alia*) 0.1–0.2 (27 H, m, SiMe), 0.9 (3 H, d, *J* 7.1, 17-H_3), 1.3 (3 H, d, *J* 6.4, 14-H_3), 2.25 (3 H, d, *J* 0.9, 15-H_3), 5.0 (1 H, d, *J* 1.9, 2′-H), 5.5 (1 H, d, *J* 1.9, 2′-H), 6.0 (1 H, br s, 2-H) and 7.3–7.6 (5 H, m, 2″- to 6″-H).

The *C*-acylated material **2p** (0.35 g, 0.53 mmol) was deprotected using general method B to give *2-hydroxy-2-phenylvinyl normonyl ketone* **1p** as a white foam (0.19 g, 81%); ν_{max}(KBr)/cm^{-1} 3468, 3311, 2960, 2922, 2871, 1720w, 1646, 1109 and 1043; λ_{max}(EtOH)/nm 351 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 21 300); $\delta_H([^2H_6]$acetone + D_2O) 0.9 (3 H, d, *J* 7.0, 17-H_3), 1.2 (3 H, d, *J* 6.4, 14-H_3), 1.4–1.6 (3 H, m, 9-H_2 and 12-H), 1.95–2.05 (1 H, m, 8-H), 2.3 (3 H, s, 15-H_3), 2.3 (1 H, dd, *J* 9.8 and 14.1, 4-H), 2.7–2.9 (3 H, m, 4-, 10- and 11-H), 3.4 (1 H, dd, *J* 3.0 and 9.1, 6-H), 3.6 (1 H, d, *J* 11.1, 16-H), 3.7–4.0 (4 H, m, 5-, 7-, 13- and 16-H), 6.05 (1 H, s, 2-H), 6.45 (1 H, s, 1′-H), 7.5–7.65 (3 H, m, 3″-, 4″-and 5″-H) and 7.95–8.05 (2 H, m, 2″- and 6″-H); $\delta_C([^2H_6]$acetone) 12.3 (C-17), 20.2 and 20.8 (C-14 and -15), 32.7 (C-9), 41.2 (C-8), 43.3 (C-12), 44.6 (C-4), 55.8 (C-10), 60.4 (C-11), 66.0 (C-16) 69.5, 70.1 and 71.1 (C-6, -7 and -13), 76.2 (C-5), 98.8 (C-1′), 124.1 (C-2), 127.7 and 129.5 (C-2″, -3″, -5″ and -6″), 133.1 (C-4″), 136.5 (C-1″), 157.0 (C-3) and 186.0 and 187.0 (C-1 and -2′); *m/z* 446 (M^+, 1%), 227 (25), 111 (80) and 69 (100) (Found: M^+, 446.2314. $C_{25}H_{34}O_7$ requires *M*, 446.2305).

The *O*-acylated material **2o** (0.17 g) was deprotected using general method B to give *1-phenylvinyl monate* **1o** (0.06 g, 53%) as a white foam; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3684, 3607, 3057, 2970, 2924, 1730, 1637, 1605 and 1208; $\delta_H([^2H_6]$acetone) 0.9 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.4, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.2 (3 H, s, 15-H_3), 2.3 (1 H, dd, *J* 9.3 and 14.7, 4-H), 2.7–2.8 (3 H, m, 4-, 10- and 11-H), 3.4–4.0 (6 H, m, 5-, 6-, 7- and 13-H and 16-H_2), 5.0 (1 H, d, *J* 1.9, 2′-H), 5.6 (1 H, d, *J* 1.9, 2′-H), 6.0 (1 H, br s, 2-H) and 7.3–7.6 (5 H, m, 2″- to 6″-H); $\delta_C(CDCl_3)$ 12.3 (C-17), 19.4 and 20.8 (C-14 and -15), 32.7 (C-9), 41.2 (C-8), 43.3 (C-12), 44.0 (C-4), 55.8 (C-10), 60.5 (C-11), 66.0 (C-16), 69.5, 70.1 and 71.1 (C-6, -7 and -13), 75.9 (C-5), 112.3 (C-2′), 116.7 (C-2), 125.6 (C-2″ and -6″), 129.3 (C-3″ and -5″), 129.5 (C-4″), 135.8 (C-1″), 153.9 (C-3) and 162.1 and 164.7 (C-1 and C-1″); *m/z* 446 (M^+, 2%), 327 (2), 277 (10), 227 (20), 111 (80) and 43 (100) (Found: M^+, 446.2310. $C_{25}H_{34}O_7$ requires *M*, 446.2305).

3-Normonyl-5-phenylpyrazole **3j** *and 5-({(2S,3R,4R,5S)-5-[(2S,3S,4S,5S)-2,3-Epoxy-5-hydroxy-4-methylhexyl]-3,4-dihydroxytetrahydropyran-2-yl}methyl)-5-methyl-3-(2-phenyl-2-oxoethyl)-4,5-dihydropyrazole* **6**.*—Using the conditions above, but omitting the separation of the two products, a 4:1 mixture of **1p** and **1o** was obtained. To this mixture (0.37 g) in methanol–water (1:1, 8 cm^3) was added hydrazine hydrate (0.15 cm^3, 3 mmol). After 3 h at 20 °C the mixture was poured into dichloromethane (50 cm^3), the layers separated and the aqueous layer extracted with more dichloromethane (50 cm^3). The combined organic layers were washed with brine (5 cm^3), dried ($MgSO_4$) and then evaporated under reduced pressure. The residue was purified by chromatography on silica gel (10 g). The first fraction was recovered enol ester **1o** (0.056 g, 75%), followed by the *pyrazole* **3j** (0.03 g, 10%); ν_{max}(KBr)/cm^{-1} 3397, 2969, 1653, 1458, 1109, 1076, 1050, 766 and 696; λ_{max}(EtOH)/nm 248 ($\varepsilon/dm^3\ mol^{-1}\ cm^{-1}$ 28 300) and 332 (685); $\delta_H(CDCl_3)$ 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.20 (3 H, d, *J* 6.5, 14-H), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.05 (3 H, s, 15-H), 2.3 (1 H, dd, *J* 8.6, 14.4, 4-H), 2.7 (1 H, br d, *J* 14.4, 4-H), 2.7 (1 H, dd, *J* 2.1, 7.5, 11-H), 2.82 (1 H, dt, *J* 2.1, 5.7, 10-H), 3.4 (1 H, dd, *J* 8.7 and 3.0, 6-H), 3.6 (1 H, br d, *J* 11.4, 16-H), 3.7–3.9 (4 H, m, 5-, 7-, 13- and 16-H), 6.25 (1 H, s, 2-H), 6.65 (1 H, s, 4′-H), 7.2–7.5 (3 H, m, 3″-, 4″- and 5″-H) and

* For the numbering scheme for compounds **6** used in the NMR assignments see Scheme 1.

7.75 (2 H, d, *J* 7.4, 2″- and 6″-H); δ_C(CD_3OD) 12.3 (C-17), 19.3 (C-15), 20.4 (C-14), 33.1 (C-9), 41.6 (C-8), 43.6 (C-4), 43.8 (C-12), 56.9 (C-10), 61.3 (C-11), 66.4 (C-16), 70.1 (C-6), 70.7 (C-7), 71.6 (C-13), 76.7 (C-5), 102.4 (C-4′), 116.5 (C-2, br), 126.7 (C-3″ and -5″), 128.7 (C-4″), 129.7 (C-2″ and -6″), 130, 134.1 and 134.7 (C-3′, -5′ and -1″, br) and 140.6 (C-3); *m*/z 442 (M^+, 7%) and 198 (100) (Found: M^+, 442.2450. $C_{25}H_{34}N_2O_5$ requires *M*, 442.2467).

The next fraction was the *less polar dihydropyrazole* **6** (0.087 g, 28%); ν_{max}/cm^{-1} 3408, 2967, 1733, 1684, 1630, 1597, 1449, 1054, 756 and 690; λ_{max}(EtOH)/nm 241 (ε/dm^3 mol^{-1} cm^{-1} 13 900) and 327 (3000); δ_H(CD_3OD) 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.20 (3 H, d, *J* 6.4, 14-H_3), 1.32 (3 H, s, 5′-CH_3), 1.3–1.5 (1 H, m, 12-H), 1.6–2.0 (5 H, m, 8-H, 4- and 9-H_2), 2.6 and 2.7 (2 H, ABq, *J* 16.8, 4′-H_2), 2.7–2.9 (2 H, m, 10- and 11-H), 3.2–3.3 (1 H, m, 6-H), 3.6 (1 H, d, *J* 11.3, 16-H), 3.7–3.9 (4 H, m, 5-, 7-, 13- and 16-H) and 7.5–8.0 (5 H, m, 2‴- to 6‴-H); δ_C($CDCl_3$) 12.4 (C-17), 20.5 (C-14), 26.1 (5′-CH_3), 31.3 (C-9), 39.0 (C-8), 40.5 (C-1″), 41.7 (C-4), 42.5 (C-12), 47.0 (C-4′), 55.5 (C-10), 60.9 (C-11), 64.2 (C-16), 65.0 (C-5′), 69.4, 69.8 and 71.0 (C-6, -7 and -13), 73.3 (C-5), 128.1 (C-2‴ and -6‴), 128.5 (C-3‴ and -5‴), 133.4 (C-4‴), 135.9 (C-1‴), 152.6 (C-3′) and 195.7 (C-2″); *m*/z 460 (M^+, 3%), 445 (3) and 201 (100) (Found: M^+, 460.2565. $C_{25}H_{36}N_2O_6$ requires *M*, 460.2573).

The final product obtained was the *more polar epimeric dihydropyrazole* **6** (0.10 g, 33%); ν_{max}(KBr)/cm^{-1} 3411, 2912, 1684, 1629, 1596, 1449, 1110 and 1057; λ_{max}(EtOH)/nm 242 (ε/dm^3 mol^{-1} cm^{-1} 12 500) and 328 (3180); δ_H(CD_3OD) 0.94 (3 H, d, *J* 7.1, 17-H_3), 1.20 (3 H, d, *J* 6.4, 14-H_3), 1.25 (3 H, s, 5′-CH_3), 1.3–1.5 (1 H, m, 12-H), 1.6–2.1 (5 H, m, 8-H and 4- and 9-H_2), 2.5 and 2.8 (ABq, *J* 17.2, 4′-H_2), 2.7 (1 H, dd, *J* 2.2 and 7.5, 11-H), 2.8 (1 H, dt, *J* 2.2 and 5.8, 10-H), 3.3–3.9 (6 H, m, 5-, 6-, 7- and 13-H and 16-H_2), 7.45–7.55 (2 H, m, 3‴- and 5‴-H), 7.6–7.7 (1 H, m, 4‴-H) and 7.95–8.05 (2 H, m, 2‴- and 6‴-H); δ_C($CDCl_3$) 12.8 (C-17), 20.9 (C-14), 26.3 (5′-CH_3), 31.7 (C-9), 39.6 (C-8), 40.8 and 43.2 (C-4 and -1″), 42.9 (C-12), 48.8 (C-4′), 55.9 (C-10), 61.3 (C-11), 64.3 (C-5′), 65.6 (C-16), 69.3, 70.4 and 71.4 (C-6, -7 and - 13), 73.9 (C-5), 128.5 and 128.9 (C-2‴, -3‴, -5‴ and -6‴), 133.8 (C-4‴), 136.3 (C-1‴), 153.7 (C-3′) and 196.0 (C-2″); *m*/z 460 (M^+, 2.5%), 445 (4) and 201 (100) (Found: M^+, 460.2551. $C_{25}H_{36}N_2O_6$ requires *M*, 460.2573).

3-*Normonyl*-5-*phenyl*-1H-1,2,4-*triazole* **3k**.—*Monohydrazide* **1r** was prepared by the general method A in 33% yield as a colourless oil; ν_{max}(film)/cm^{-1} 3320, 1660 and 1630; λ_{max}(EtOH)/nm 222 (ε/dm^3 mol^{-1} cm^{-1} 12 600); δ_H(CD_3OD) 0.95 (3 H, d, *J* 7.0, 17-H_3), 1.20 (3 H, *J* 6.4, 14-H_3), 1.35–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.9–2.0 (1 H, m, 8-H), 2.1–2.2 (1 H, m, 4-H), 2.15 (3 H, s, 15-H_3), 2.6 (1 H, br d, *J* 14.2, 4-H), 2.7 (1 H, dd, *J* 2.2, 7.6, 11-H), 2.8 (1 H, dt, *J* 2.2, 5.8, 10-H), 3.25–3.35 (1 H, m, 6-H), 3.55 (1 H, br d, *J* 11.6, 16-H), 3.65–3.9 (4 H, m, 5-, 7-, 13- and 16-H) and 5.69 (1 H, s, 2-H); δ_C(CD_3OD) 12.2 (C-17), 19.0 (C-15), 20.4 (C-14), 32.9 (C-9), 41.4 (C-8), 43.5 (C-4, C-12) 56.7 (C-10), 61.2 (C-11), 66.2 (C-16), 69.9 (C-6), 70.6 (C-7), 71.5 (C-13), 76.1 (C-5), 118.7 (C-2), 152.6 (C-3) and 169.0 (C-1); *m*/z 359 (MH^+, 1%), 327 (9), 309 (9), 227 (21) and 69 (100) (Found: MH^+, 359.2193. $C_{17}H_{31}N_2O_6$ requires *M*, 359.2187). To this material (0.22 g, 0.61 mmol) in methanol (4 cm^3) under a stream of nitrogen was added *S*-methylisothiobenzamide (0.17 g, 1 equiv.). After 30 min triethylamine (0.15 cm^3) was added to it and the mixture concentrated by evaporation under reduced pressure, to give crude product (0.45 g).

A portion of this material (0.335 g) was cyclised according to general method B to give the *title compound* **3k** as a white foam (0.075 g, 37% overall); ν_{max}(KBr)/cm^{-1} 3401, 3061, 2966, 2924 and 1661; λ_{max}(EtOH)/nm 257 (ε/dm^3 mol^{-1} cm^{-1} 18 800); δ_H(CD_3OD) 0.85 (3 H, d, *J* 6.9, 17-H_3), 1.2 (3 H, *J* 6.2, 14-H_3), 1.2–1.35 (1 H, m, 12-H), 1.5–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.25 (3 H, s, 15-H_3), 2.25–2.35 (1 H, m, 4-H), 2.55–2.75 (3 H, m, 4-, 10- and 11-H), 3.5–3.9 (6 H, m, 5-, 6-, 7-, 13-H and 16-H_2), 6.25 (1 H, s, 2-H), 7.35–7.45 (3 H, m, 3″- to 5″-H) and 8.0–8.1 (2 H, m, 2″- and 6″-H); δ_C(CD_3OD) 11.3 (C-17), 19.6 (C-15), 20.4 (C-14), 33.0 (C-9), 41.7 (C-8), 43.5 (C-4), 43.7 (C-12), 56.9 (C-10), 61.3 (C-11), 66.4 (C-16), 70.1 (C-6), 70.4 (C-7), 71.7 (C-13), 76.5 (C-5), 113.7 (br, C-2), 127.4, 129.8, 130.6, *ca.* 131 (br, C-1″ to -6″) and 147.7 (br, C-3); *m*/z 443 (M^+, 10%) and 199 (100) (Found: M^+, 443, 2422. $C_{24}H_{33}N_3O_5$ requires *M*, 443.2420).

1-(p-*Nitrophenyl*)-3-*normonyl*-1H-1,2,4-*triazole* **3l**.—N′-(p-*Nitrophenyl*)*monohydrazide* **1s** was prepared using the general method A in 67% yield as a yellow solid; ν_{max}(KBr)/cm^{-1} 3468, 3295, 2973, 2924, 2875, 1677, 1644, 1599, 1506, 1326 and 1112; λ_{max}(EtOH)/nm 356 (ε/dm^3 mol^{-1} cm^{-1} 13 900) and 200 (18 800); δ_H(CD_3OD) 0.95 (3 H, d, *J* 7.2, 17-H_3), 1.2 (3 H, d, *J* 6.3, 14-H_3), 1.35–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.2 (3 H, s, 15-H_3), 2.5–2.3 (1 H, m, 4-H), 2.5–2.75 (2 H, m, 4- and 11-H), 2.85 (1 H, dt, *J* 2.2, 5.6, 10-H), 3.45–3.55 (1 H, dd, *J* 3.1, 9.1, 6-H), 3.55–3.95 (5 H, m, 5-, 7-, 13-H and 16-H_2), 5.9 (1 H, s, 2-H), 6.8 (2 H, d, *J* 9.1, 2′- and 6′-H) and 8.1 (2 H, d, *J* 9.1, 3′- and 5′-H); δ_C(CD_3OD) 12.3 (C-17), 19.2 (C-15), 20.4 (C-14), 33.0 (C-9), 41.7 (C-8), 42.7 (C-12), 44.0 (C-4), 56.9 (C-10), 61.3 (C-11), 66.3 (C-16), 70.0 (C-6), 70.7 (C-7), 71.6 (C-13), 76.1 (C-5), 112.0 (C-2′ and -6′), 117.9 (C-2), 126.8 (C-3′ and -5′), 140.7 (C-4′), 156.0, 156.2 (C-3 and -1′) and 169.1 (C-1); *m*/z 479 (M^+, 1%), 449 (1), 429 (1), 138 (60) and 108 (100) (Found: M^+, 479.2263. $C_{23}H_{33}N_3O_8$ requires *M*, 479.2268). This material (1.0 g, 2.08 mmol) was protected as in general method B to give a yellow foam (1.23 g, 85%). To this material (0.348 g, 0.5 mmol) in acetonitrile (3 cm^3) were added triethylamine (0.5 cm^3), tetrachloromethane (0.3 cm^3), tetrazole (0.015 g) and triphenylphosphine (0.327 g). The reaction mixture rapidly became intense violet in colour. After 15 min at 20 °C the solvent was removed and the residue was purified by chromatography eluting with ethyl acetate in hexane (10–80%). The first component, a yellow gum (21 mg, 6%) was identified as 2-hydrazonoyltetrazole **4n**; ν_{max}(CH_2Cl_2)/cm^{-1} 3280, 1590, 1510 and 1335; δ_H($CDCl_3$, *inter alia*) 2.2–2.3 (4 H, m, 4-H and 15-H_3), 2.65–2.8 (3 H, m, 10-, 11- and 4-H), 6.7 (1 H, s, 2-H), 7.3 (2 H, d, *J* 9.2, 2″- and 6″-H), 8.2 (2 H, d, *J* 9.2, 3″- and 5″-H), 8.75 (1 H, s, 5′-H) and 11.5 (1 H, s, NH); *m*/z (FAB) 770 (MNa^+). The 1-hydrazonoyltetrazole **4m** was obtained as an orange gum (62 mg, 17%); ν_{max}(CH_2Cl_2)/cm^{-1} 3300, 1600, 1520 and 1335; δ_H($CDCl_3$, *inter alia*) 2.0 (3 H, s, 15-H_3), 2.15 (1 H, dd, *J* 8.9, 14.4, 4-H), 2.65–2.8 (3 H, m, 10-, 11- and 4-H), 6.0 (1 H, s, 2-H), 7.3 (2 H, d, *J* 9.3, 2″- and 6″-H), 8.25 (2 H, d, *J* 9.3, 3″- and 5″-H), 9.0 (1 H, s, 5′-H) and 10.9 (1 H, s, NH); *m*/z (FAB) 770 (MNa^+). Finally the triazole **4l** was eluted as a yellow gum (38 mg, 11%); ν_{max}(CH_2Cl_2)/cm^{-1} 1660, 1600, 1610 and 1345; δ_H($CDCl_3$, *inter alia*) 2.2 (1 H, dd, *J* 9.5, 14.8, 4-H), 2.3 (3 H, s, 15-H_3), 6.4 (1 H, s, 2-H), 7.9 (2 H, d, *J* 9.1, 2″- and 6″-H), 8.4 (2 H, d, *J* 9.1, 3″- and 5″-H) and 8.6 (1 H, s, 5′-H); *m*/z (FAB) 727 (MNa^+) and 705 (MH^+).

A similar preparation with a reaction time of 2 h gave the triazole **4l** as the only isolated product (102 mg, 28%), with ^1H NMR and TLC properties identical with those of the previous sample.

The protected triazole **4l** (36 mg) in THF (5 cm^3) was treated with hydrochloric acid (0.4 mol dm^{-3}; 1 cm^3) for 4 min at 20 °C. The reaction mixture was quenched with saturated aqueous sodium hydrogen carbonate (1 cm^3), extracted with ethyl acetate (20 cm^3), dried, evaporated under reduced pressure and then purified by chromatography on silica gel eluting with methanol in dichloromethane (0.5%) to give the *title material* **3l**

as an orange gum (19 mg, 76%); ν_{max}(KBr)/cm^{-1} 3446, 3100, 2977, 2915, 2890, 2875, 1658, 1598, 1527, 1513 and 1338; λ_{max}(EtOH)/nm 319 (ε/dm^3 mol^{-1} cm^{-1} 16 200) and 219 (15 400); δ_H(CD_3OD) 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.5, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.3 (3 H, s, 15-H_3), 2.35 (1 H, dd, *J* 9.6, 14.8, 4-H), 2.7–2.8 (2 H, m, 4- and 11-H), 2.8 (1 H, dt, *J* 2.2, 5.8, 10-H), 3.4 (1 H, dd, *J* 3.1, 8.7, 6-H), 3.6 (1 H, br d, *J* 11.4, 16-H), 3.7–3.9 (4 H, m, 5-, 7-, 13- and 16-H), 6.3 (1 H, s, 2-H), 8.1 (2 H, d, *J* 9.2, 2″- and 6″- H), 8.4 (2 H, d, *J* 9.2, 3″- and 5″-H) and 9.2 (1 H, s, 5′-H); δ_C(CD_3OD) 13.3 (C-17), 19.9 (C-15), 20.4 (C-14), 33.1 (C-9), 41.6 (C-8), 43.8 (C-12), 43.9 (C-4), 57.0 (C-10), 61.1 (C-11), 66.4 (C-16), 70.2, 70.8 and 71.1 (C-6, -7 and -13), 75.6 (C-5), 116.5 (C-2), 120.5 (C-2″ and -6″), 126.5 (C-3″ and -5″), 142.7 (C-1″), 143.3 (C-5′), 147.2 (C-3), 147.7 (C-4″) and 163.8 (C-3′); *m/z* 488 (M^+, 3%) and 244 (100) (Found: M^+, 488.2275. $C_{24}H_{32}N_4O_7$ requires *M*, 488.2271).

5-*Amino*-1-(p-*nitrophenyl*)-3-*normonyl*-1H-1,2,4-*triazole* **3o**. —The 1-hydrazonoyltetrazole **4m** (50 mg) was dissolved in toluene (8 cm^3) and triethylamine (50 mm^3) and then heated to reflux for 1 h under an atmosphere of nitrogen. The solvent was removed by evaporation under reduced pressure and the residue was purified by chromatography on silica gel (20–100% ethyl acetate in hexane) to give the previously described triazole **4l** (12 mg, 22%) and the protected aminotriazole **4o**, (18 mg, 33%); ν_{max}(CH_2Cl_2)/cm^{-1} 3470, 3380, 1730, 1620, 1600, 1520, 1345 and 850; δ_H($CDCl_3$, *inter alia*) 2.1 (1 H, dd, *J* 11.6, 15.7, 4-H), 2.25 (3 H, s, 15-H_3), 2.6 (1 H, br d, *J* 15.7, 4′-H), 5.1 (2 H, br s, NH_2), 6.1 (1 H, s, 2-H), 7.7 (2 H, d, *J* 9.1, 2″-, 6″-H) and 8.4 (2 H, d, 9.1, 3″- and 5″-H); *m/z* (FAB) 742 (MNa^+) and 720 (MH^+).

Treatment of the protected aminotriazole **4o** (21 mg) in THF (3 cm^3) with hydrochloric acid (0.4 mol dm^{-3}; 1 cm^3) at 20 °C for 3 min followed by normal work-up and purification by chromatography on silica gel (0–8% methanol in dichloromethane) gave the *title compound* **3o** (10 mg, 68%); λ_{max}(EtOH)/nm 350 (ε/dm^3 mol^{-1} cm^{-1} 6000) and 249 (10 500); δ_H(CD_3OD) 0.95 (3 H, d, *J* 7.1, 17-H_3), 1.2 (3 H, d, *J* 6.4, 14-H_3), 1.3–1.5 (1 H, m, 12-H), 1.65–1.75 (2 H, m, 9-H_2), 1.95–2.05 (1 H, m, 8-H), 2.2 (3 H, s, 15-H_3), 2.25 (1 H, dd, *J* 9.4, 14.4, 4-H), 2.6–2.8 (2 H, m, 4- and 11-H), 2.8 (1 H, dt, *J* 2.3, 5.8, 10-H), 3.4–3.9 (6 H, m, 5-, 6-, 7- and 13-H and 16-H_2), 6.1 (1 H, s, 2-H) and 7.9 and 8.4 (4 H, A_2B_2q, *J* 9.2, 2″-, 3″-, 5″- and 6″-H); *m/z* 503 (M^+, 1%) and 259 (100) (Found: M^+, 503.2388. $C_{24}H_{33}N_5O_7$ requires *M*, 503.2380).

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