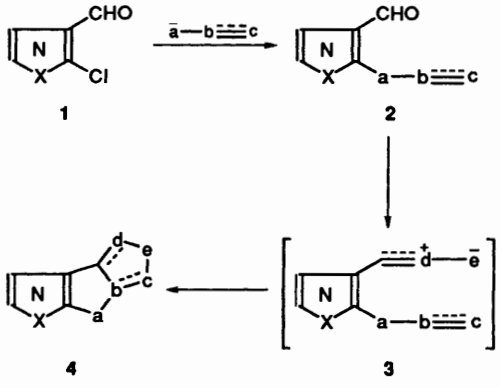
5-Chloropyrazole-4-carbaldehydes as Synthons for Intramolecular 1,3-Dipolar Cycloadditions

Gerrit L'abbé,* Sabine Emmers, Wim Dehaen and Leonard K. Dyall†
Department of Chemistry, University of Leuven, Celestijnenlaan 200F, 3001 Leuven (Heverlee), Belgium

A general method is described to transform the readily available title compounds into tri- and tetracyclic heterocycles, first by substituting the chlorine atom by an unsaturated thiolate or alkoxide, and then by modifying the aldehyde function into a 1,3-dipole. As 1,3-dipoles, nitrile oxide, nitrone, nitrile imine, azomethine ylide and azomethine imine groups were generated from the 5-allylsulfanyl-4-formylpyrazole **7**, which resulted in intramolecular cycloaddition and formation of the heterocycles shown in Scheme 2. The other pyrazoles **22**, **23**, **26**, **30** and **33** were converted *via* intramolecular nitrile oxide cycloaddition (INOC) into fused dihydroisoxazoles. A limitation to the method is the Claisen rearrangement which occurs when the allyl ether **26** or the prop-2-ynyl ether **30** is used.

The intramolecular 1,3-dipolar cycloaddition is a powerful concept for the construction of fused heterocycles and has been amply applied to benzene rings *ortho* substituted with 1,3-dipole and dipolarophile functions.[1] In the heterocyclic field, chloroformylazoles of type **1** are interesting starting materials for two reasons: firstly, the chlorine atom is easily substituted by nucleophiles (ā–b=c); and, secondly, the aldehyde function is ideally suited for conversion into a series of 1,3-dipoles. The final step is the intramolecular cyclization of dipole and dipolarophile in **3** to give the fused system **4**. Since the heterocyclic chloro aldehydes **1** are easily available,[2] the sequence **1** ⟶ **2** ⟶ **3** ⟶ **4** is a short and attractive pathway for the construction of polyheterocyclic frameworks (Scheme 1).



Scheme 1

The model compound used in this work was 5-chloro-3-methyl-1-phenylpyrazole-4-carbaldehyde **6**, which has previously been prepared by chloroformylation of commercial pyrazolone **5**.[2] Substitution with allenethiolate, generated by basic decomposition of the allylisothiourea salt, furnished the 5-(allylsulfanyl)pyrazole-4-carbaldehyde **7**. This compound could be transformed into the tricyclic heterocycles **16**–**21** by converting the aldehyde function into the 1,3-dipoles discussed below (see Scheme 2).

Thus, the aldehyde **7** was converted into the oxime **8** and then oxidized with sodium hypochlorite[3] to give the nitrile oxide **9** which cyclized spontaneously to the dihydroisoxazole **16**. The

† On sabbatical leave from the University of Newcastle, Australia.

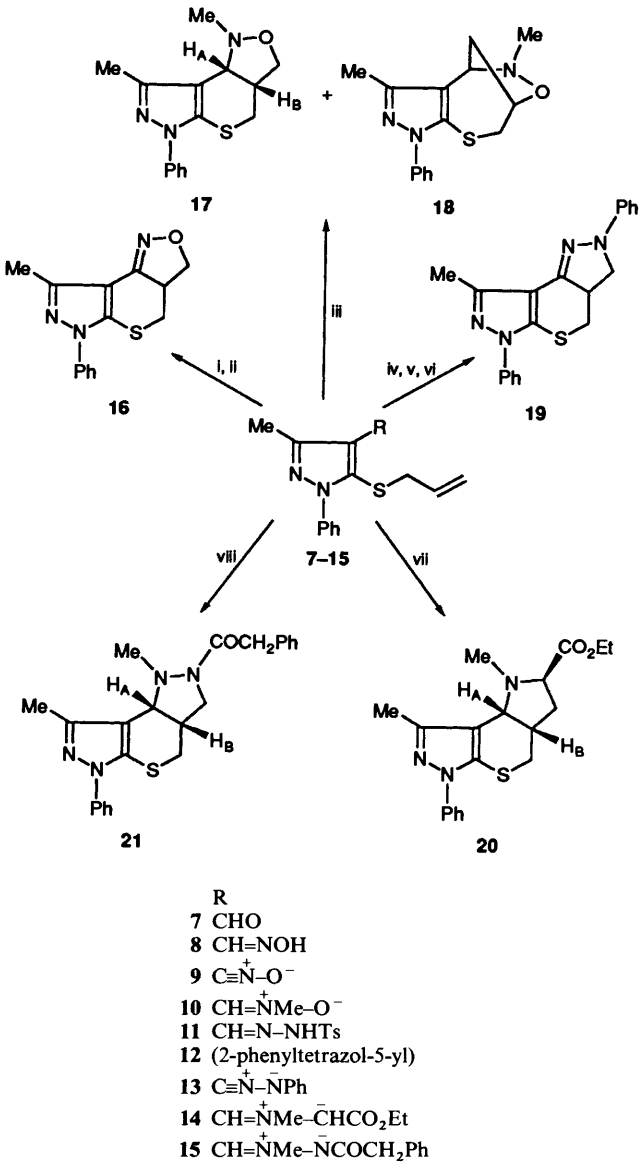
nitrone **10**, derived from aldehyde **7** and *N*-methylhydroxylamine, underwent a thermal cycloaddition to afford the regioisomers **17** and **18** in a 3:1 ratio. The formation of two regioisomeric adducts is in compliance with literature data,[4] and they are easily distinguished by NMR spectroscopy (see Experimental section). The *cis*-configuration of compound **17** follows from the coupling constant of 6 Hz between the H_A and H_B protons. At room temperature the NMR signals are broad due to conformational rigidity of the isoxazolidine ring;[5] they become sharper at 50 °C.

The aldehyde **7** was also transformed into the tetrazole **12** *via* reaction of its tosylhydrazone **11** with phenyldiazonium chloride in pyridine.[6] The tetrazole **12** is a convenient source for the nitrile imine **13** by pyrolytic extrusion of nitrogen, resulting in intramolecular cycloaddition and formation of the annulated dihydropyrazole **19**.

The condensation of *N*-alkylglycinates with unsaturated aldehydes is reported to give azomethine ylides which were trapped intramolecularly.[7] When this principle was applied to the aldehyde **7**, a diastereospecific cycloaddition of the intermediate **14** was observed, giving the *cis*-fused pyrrolidine **20**. The *cis*-relationship between H_A and H_B was deduced from the coupling constant of 6.2 Hz, and a homonuclear NOE experiment also established the *cis*-relationship between the ring-fused protons and the ester substituent.

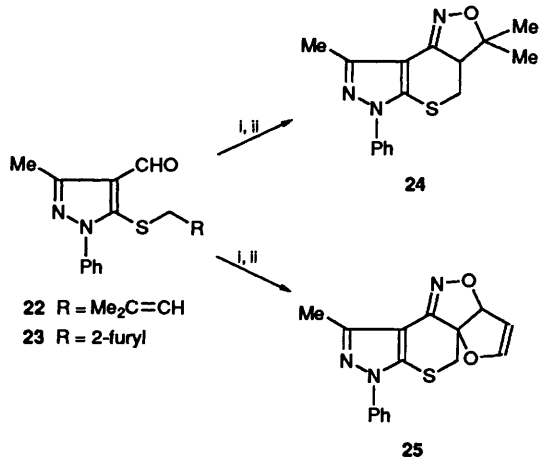
Finally, the azomethine imine **15** was produced by condensation of the aldehyde **7** with *N*-methyl-*N'*-phenylacetohydrazide in analogy with the work of Oppolzer.[8] Subsequent intramolecular cycloaddition furnished the *cis*-fused pyrazolidine **21**. Its ^{1}H NMR spectrum showed broadened signals[5] and a coupling constant J_{AB} of 7.5 Hz.

Scheme 2 is adaptable to many variations, either by changing the pyrazole N-1 and C-3 substituents, or by changing the nature of the reacting thiolate. This is exemplified by the synthesis of the pyrazoles **22** and **23**, and their conversion into the fused heterocycles **24** and **25** by the intramolecular nitrile oxide cycloaddition mode (INOC) (see Scheme 3). INOC



R
7 CHO
8 CH=NOH
9 $C\equiv\overset{+}{N}-O^{-}$
10 $CH=\overset{+}{N}Me-O^{-}$
11 CH=N–NHTs
12 (2-phenyltetrazol-5-yl)
13 $C\equiv\overset{+}{N}-\overset{-}{N}Ph$
14 $CH=\overset{+}{N}Me-\overset{-}{C}HCO_2Et$
15 $CH=\overset{+}{N}Me-\overset{-}{N}COCH_2Ph$

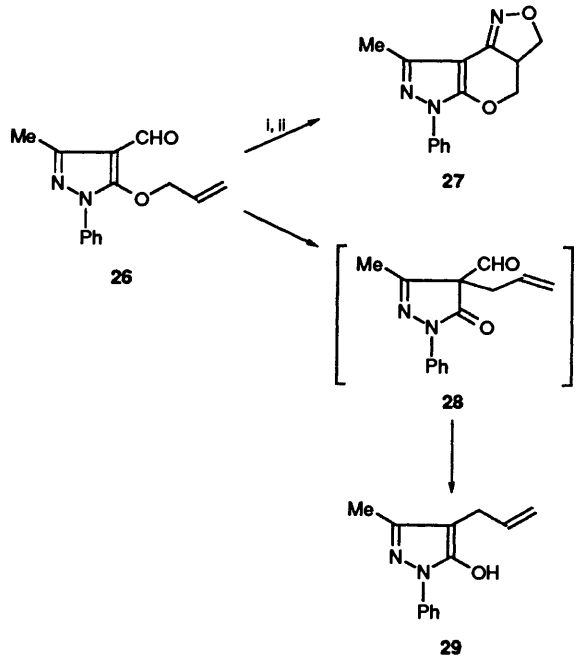
Scheme 2 *Reagents and conditions:* i, NH_2OH; ii, NaOCl; iii, MeNHOH; iv, $TsNHNH_2$; v, $PhN_2^+Cl^-$, pyridine; vi, 165 °C, low pressure; vii, $MeNHCH_2CO_2Et$; viii, $PhCH_2CONHNHMe$



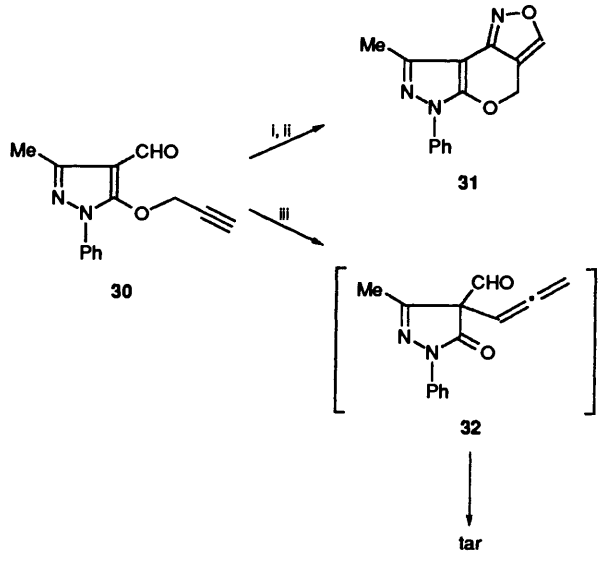
Scheme 3 *Reagents:* i, NH_2OH; ii, NaOCl

reactions with furan as the dipolarophile have already been reported.[9]

As a further extension of this work the 5-(allyloxy)pyrazole



Scheme 4 *Reagents:* i, NH_2OH; ii, NaOCl

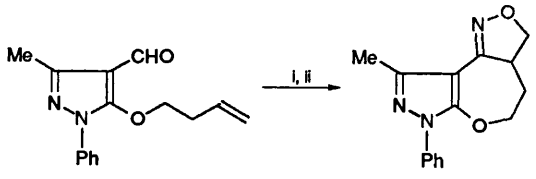


Scheme 5 *Reagents and conditions:* i, NH_2OH; ii, *N*-chlorosuccinimide, pyridine; iii, heat

26 was prepared from the chloro aldehyde **7** and subjected to the INOC reaction. This afforded the fused isoxazolopyran **27** in 69% overall yield (see Scheme 4). We found it advantageous to use the starting material **26** without extensive purification since it underwent slowly a Claisen rearrangement,[10] **26** ⟶ **28**, at room temperature. When the rearrangement was followed by ^1H NMR spectroscopy at 65 °C in deuteriated dimethyl sulfoxide solution, a clean first-order reaction was observed with a half-life of 130 min. The rearranged product **28** underwent a facile deformylation in the presence of traces of water, which precluded its isolation. After work-up the 4-allyl-5-hydroxypyrazole **29** was obtained in 66% yield and fully characterized by spectral analyses (see Experimental section).

The isoxazolopyran **31** was similarly obtained in 69% overall yield from the prop-2-ynyl ether **30** by the INOC method (see Scheme 5). Here, the Claisen rearrangement **30** ⟶ **32** was much slower; a half-life of 60 min was measured in toluene at 100 °C by IR techniques. The reaction mixture then turned into tar products.

The Claisen rearrangement of products **26** and **30** limits their potential as synthetic reagents for intramolecular 1,3-dipolar cycloadditions. These are only possible when the dipole function can be generated at or below room temperature, such as for nitrile oxides. In contrast, the allyl sulfide **7** was found unchanged when heated in xylene for 24 h. Thus, the formation of a pyrazolone is much more favoured than that of its thio analogue. The Claisen rearrangement can also be eliminated by using the homologous but-3-en-1-olate as nucleophile. The resulting pyrazole **33** was readily transformed by the INOC method into the tricyclic system **34** (see Scheme 6).



33 34

Scheme 6 *Reagents:* i, NH_2OH; ii, NaOCl

Finally, attempts to substitute the chlorine atom of compound **7** by allylamine failed since preferential condensation with the aldehyde function occurred, giving the corresponding imine.

In summary, we have demonstrated that 5-chloropyrazole-4-carbaldehydes can be used for intramolecular 1,3-dipolar cycloadditions by introducing an unsaturated nucleophile at the 5-position and converting the aldehyde function into a 1,3-dipole. Other azoles, possessing a halogen and aldehyde function in an *ortho*-relationship are also potential candidates for carrying out similar reactions. Of particular interest are the INOC reactions where dihydroisoxazoles are formed, since they are precursors for γ-amino alcohols, β-hydroxy ketones and derivatives, useful in the synthesis of natural products.[11]

Experimental

M.p.s were determined using a Reichert Thermovar apparatus. IR spectra were recorded on a Perkin-Elmer spectrometer, NMR spectra on a Bruker WM-250 or AMX-400 spectrometer, and mass spectra (EI) on a Hewlett Packard 5989A or Kratos MS50 TC (for high resolution) instrument, both operating at 70 eV.

The pyrazole **6** was prepared following a literature procedure;[2] $\delta_C(CDCl_3)$ 13.7 (Me), 117.4 (C-4, $^2J_{CH}$ 24, $^3J_{CH}$ 2), 125.1, 129.1, 129.2 and 136.9 (Ph C-atoms), 133.4 (C-5), 151.7 (C-3, $^2J_{CH}$ 5, $^3J_{CH}$ 7.5) and 183.8 (CHO).

5-Allylsulfanyl-3-methyl-1-phenylpyrazole-4-carbaldehyde **7**.—A solution of allyl bromide (12.1 g, 0.1 mol) and thiourea (7.61 g, 0.1 mol) in ethanol (150 cm^3) was first refluxed for 1 h, and then for a further 1 h after addition of ethanolic NaOH (8.0 g in 100 cm^3). The chloro aldehyde **6** (15.0 g, 68 mmol) was added to the mixture which was then refluxed for 30 min. After addition of water (150 cm^3) to the mixture it was extracted with diethyl ether (3 × 150 cm^3), dried ($MgSO_4$) and evaporated to give a crude oil which was crystallized from ethanol–water. Compound **7** was obtained as light yellow needles (11.48 g, 65%), m.p. 55 °C (Found: C, 64.9; H, 5.5. $C_{14}H_{14}N_2OS$ requires C, 65.10; H, 5.47%); ν_{max}(KBr)/cm^{-1} 1671s (CO); $\delta_H(CDCl_3$; 400 MHz) 2.55 (3 H, s, Me), 3.18 (2 H, br d, *J* 7, CH_2S), 4.80 (1 H, ddt, *J* 18, 1 and 1, vinylic H), 4.95 (1 H, ddt, *J* 10, 1 and 1, vinylic H), 5.58 (1 H, ddt, *J* 18, 10 and 7, vinylic H), 7.46, 7.51 and 7.57 (5 H, 2 t + d, *J* 8, Ph) and 10.08 (1 H, s, CHO); $\delta_C(CDCl_3)$ 13.4 (Me), 39.0 (CH_2S), 119.1 and 132.0 (CH_2=CH), 123.7 (C-4), 125.8, 128.7, 128.9 and 138.4 (Ph C-atoms), 140.0 (C-5), 151.4 (C-4) and 186.4 (CO); *m/z* 258 ($M^{\bullet+}$, 13%), 225 ($M^{\bullet+}$ − SH, 44), 217 ($M^{\bullet+}$ − C_3H_5, 13), 215 (16), 198 (19), 148 (24), 83 (39) and 77 (Ph^+, 100).

3a,4-Dihydro-8-methyl-6-phenyl-3H,6H-pyrazolo[4′,3′:5,6]*thiopyrano*[4,3-c]*isoxazole* **16**.—A solution of the aldehyde **7** (5.17 g, 20 mmol) in ethanol (100 cm^3) was treated with aqueous NH_2OH·HCl and $NaHCO_3$ (40 mmol each in 50 cm^3) and stirred overnight at room temperature. The mixture was concentrated and extracted with dichloromethane (3 × 100 cm^3), and the combined extracts were washed with water (3 × 100 cm^3), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with dichloromethane–methanol (40 : 1) as the eluent to give the oxime **8** which was crystallized from ethanol (3.77 g, 69%), m.p. 119.3 °C (Found: C, 61.4; H, 5.5. $C_{14}H_{15}N_3OS$ requires C, 61.52; H, 5.53%); $\delta_C([^2H_6]DMSO)$ 142.1 (CH=N, $^1J_{CH}$ 163, *E*-isomer).[12]

Aqueous NaOCl (13%; 8.8 mol in 5 cm^3) was added dropwise at 0 °C to a vigorously stirred solution of the oxime **8** (1.50 g, 5.5 mmol) in chloroform (30 cm^3). After the mixture had been stirred overnight at room temperature, the organic phase was separated, dried ($MgSO_4$), and evaporated, and the crude product **16** was crystallized from chloroform–hexane (1.03 g, 68%), m.p. 158 °C;* ν_{max}(KBr)/cm^{-1} 1609s and 1597s; $\delta_H(CDCl_3$; 400 MHz) 2.53 (3 H, s, Me), 3.19–3.22 (2 H, m, CH_2S), 3.82 (1 H, dd, *J* 13 and 7.5, 3-H), 3.92 (1 H, m, Σ *J* 38, 3a-H), 4.72 (1 H, dd, *J* 9 and 7.5, 3-H), 7.37, 7.48 and 7.55 (5 H, 2 t + d, *J* 8, Ph); $\delta_C(CDCl_3)$ 14.1 (Me), 31.3 (C-4), 49.0 (C-3a), 72.1 (C-3), 107.4 (C-8a), 122.9, 127.8, 129.8 and 139.0 (Ph C-atoms), 136.9 (C-5a), 149.3 (C-8) and 152.1 (C-8b); *m/z* 271 ($M^{\bullet+}$, 100%), 241 ($M^{\bullet+}$ − CH_2O, 10), 240 (11), 214 ($M^{\bullet+}$ − C_3H_5O, 11) and 77 (Ph^+, 63) ($M^{\bullet+}$, 271.0779. $C_{14}H_{13}N_3OS$ requires *M*, 271.0779).

Reaction of the Aldehyde **7** *with* N-*Methylhydroxylamine*.—A solution of the aldehyde **7** (1.6 g, 6.2 mmol) in toluene (200 cm^3) was mixed with *N*-methylhydroxylamine hydrochloride (1.5 g, 18 mmol) and sodium methoxide (0.97 g, 18 mmol) dissolved in methanol (10 cm^3), and refluxed for 3 h. The solid was filtered off and the filtrate evaporated to give the heterocycles **17** and **18** as a 77:23 mixture (1.72 g, 97%). After chromatographic purification on silica gel with chloroform–methanol (20:1) as the eluent, the pure compounds **17** (1.32 g, 74%) and **18** (0.40 g, 22%) were obtained as yellow oils.

(3aRS,8bRS)-1,3a,4,8b-Tetrahydro-1,8-dimethyl-6-phenyl-3*H*,6*H*-pyrazolo[4′,3′:5,6]thiopyrano[4,3-*c*]isoxazole **17**; ν_{max}(neat)/cm^{-1} 1627s; $\delta_H([^2H_6]DMSO$; 250 MHz; 58 °C) 2.24 (3 H, s, Me), 2.66 (3 H, br s, MeN), 3.0–3.2 (3 H, m, CH_2S + H_B), 3.84 (1 H, dd, ^2J 7 and 4, 3-H), 3.90 (1 H, d, *J* 6, H_A), 4.21 (1 H, t, *J* 7, 3-H) and 7.3–7.6 (5 H, 2 m, Ph); $\delta_C([^2H_2]DMSO)$ 12.4 (Me), 29.7 (C-4), 40.0 (C-3a), 43.6 (MeN), 61.7 (C-8b), 67.9 (C-3), 112.7 (C-8a), 122.1, 126.8, 129.2 and 139.0 (Ph C-atoms), 132.9 (C-5a) and 149.0 (C-8); *m/z* 287 ($M^{\bullet+}$, 15%), 241 ($M^{\bullet+}$ − CH_2S, 100), 227 (15) and 77 (Ph^+, 29) ($M^{\bullet+}$, 287.1108. $C_{15}H_{17}N_3OS$ requires *M*, 287.1092).

4,5,7,8-Tetrahydro-3,5-dimethyl-1-phenyl-4,7-methano-1*H*-pyrazolo[4,3-*d*][1,6,2]oxathiazocine **18**; $\delta_H(CDCl_3$; 400 MHz) 2.30 (3 H, s, Me), 2.73 (3 H, br s, NMe), 2.8–3.1 (2 H, br, methano), 2.90 (1 H, dd, *J* 14 and 4, 8-H), 3.31 (1 H, dd, *J* 14 and 3, 8-H), 4.23 (1 H, br d, *J* 7, 4-H), 5.0 (1 H, br, 7-H) and 7.35–7.44 (5 H, 2 m, Ph); $\delta_C(CDCl_3)$ 11.7 (Me), 33.1 and 39.3 (C-8 and/or methano), 45.6 (MeN), 61.2 (C-4), 76.1 (C-7), 122.6 (C-3a),

* No correct microanalysis was obtained since combustion left a residue.

125.2, 127.5, 128.4 and 139.0 (Ph C-atoms), 132.6 (C-9a) and 147.4 (C-3); *m/z* 287 ($M^{\bullet+}$, 19%), 241 ($M^{\bullet+}$ − CH_2S, 100), 227 (15) and 77 (Ph^+, 43) ($M^{\bullet+}$, 287.1105. $C_{15}H_{17}N_3OS$ requires *M*, 287.1092).

2,3,3a,4-*Tetrahydro*-2,6-*diphenyl*-8-*methyl*-6H-*thiopyrano*-[2,3-c;4,5-c']*dipyrazole* **19**.—A suspension of the aldehyde **7** (1.55 g, 6 mmol) and tosylhydrazide (1.12 g, 6 mmol) in aqueous methanol (50%, 30 cm^3), containing two drops of acetic acid, was stirred overnight at room temperature. The precipitated hydrazone **11** was filtered off (2.48 g, 97%), m.p. 136 °C (from MeOH); δ_C([$^2H_6$]DMSO) 141.7 (CH=N, $^1J_{CH}$ 162, *E*-isomer).[12]

To this compound (2.13 g, 5 mmol) in pyridine (30 cm^3) was added dropwise at −10 to −15 °C a solution of benzenediazonium chloride, prepared from aniline (0.69 g, 7.5 mmol) and sodium nitrite (0.52 g, 7.5 mmol) at 0 °C in aqueous ethanol (50%, 12 cm^3), containing hydrochloric acid (2 cm^3). After being stirred at −10 °C for 30 min, the reaction mixture was extracted with chloroform (2 × 50 cm^3), and the combined extracts were washed consecutively with 1.2 mol dm^{-3} hydrochloric acid (100 cm^3) and water (3 × 100 cm^3), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with diethyl ether–light petroleum (1:1) as the eluent to give the tetrazole **12** (1.53 g, 82%), m.p. 82.5 °C (from EtOH) (Found: C, 64.3; H, 5.0. $C_{20}H_{18}N_6S$ requires C, 64.15; H, 4.85%).

This compound (200 mg, 0.53 mmol) was heated in a sealed ampoule at 165 °C under reduced pressure (10^{-2} atm*) for 1 h. The resulting resinous product was crystallized from chloroform–hexane to give compound **19** (110 mg, 59%), m.p. 172 °C; ν_{max}(KBr)/cm^{-1} 1598s; δ_C($CDCl_3$; 250 MHz) 2.6 (3 H, s, Me), 3.16 (1 H, dd, *J* 14 and 10, 3-H), 3.19 (2 H, d, *J* 8, CH_2S), 3.76 (1 H, m, Σ *J* 40, 3a-H), 4.22 (1 H, t, *J* 10, 3-H) and 6.8–7.6 (10 H, 4 t + 2 d, *J* 8, 2 Ph); δ_C($CDCl_3$) 13.8 (Me), 31.8 (C-4), 45.2 (C-3a), 53.5 (C-3), 110.4 (C-8a), 113.3, 119.4, 122.8, 127.4, 129.1, 129.2, 139.0 and 146.7 (Ph C-atoms), 135.1 (C-5a), 145.3 (C-8b) and 148.6 (C-8); *m/z* 346 ($M^{\bullet+}$, 34%), 105 (10), 104 (16) and 77 (Ph^+, 100) ($M^{\bullet+}$, 346.1248. $C_{20}H_{18}N_4S$ requires *M*, 346.1252).

Ethyl (2RS,3aSR,8bRS)-2,3,3a,4,6,8b-*Hexahydro*-1,8-*dimethyl*-6-*phenyl*-1H-*pyrrolo*[2',3':4,5]*thiopyrano*[2,3-c]*pyrazole*-2-*carboxylate* **20**.—A solution of the aldehyde **7** (1.29 g, 5 mmol), ethyl *N*-methylglycinate hydrochloride (1.23 g, 8 mmol) and triethylamine (0.82 g, 8 mmol) in dry toluene (35 cm^3) was refluxed for 1 h with azeotropic removal of water. Then, the solvent was evaporated and the residue was crystallized from ethyl acetate to give compound **20** (0.96 g, 54%), m.p. 135 °C (Found: C, 63.95; H, 6.3. $C_{19}H_{23}N_3O_2S$ requires C, 64.02; H, 6.23%); ν_{max}(KBr)/cm^{-1} 1726s (CO); δ_H($CDCl_3$; 400 MHz) 1.28 and 4.19 (5 H, t + q, *J* 7, Et), 2.18 (1 H, ddd, *J* 13, 8 and 3, 3-H), 2.28 (1 H, ddd, *J* 13, 8 and 5, 3-H), 2.31 (3 H, s, Me), 2.41 (3 H, s, MeN), 2.72–2.90 (3 H, 2 m, CH_2S + H_B), 3.75 (1 H, dd, *J* 8 and 3, 2-H), 4.19 (1 H, br d, *J* 6.2, H_A) and 7.25, 7.40 and 7.53 (5 H, 2 t + d, *J* 8, Ph); δ_C($CDCl_3$) 12.5 and 60.3 (Et), 14.4 (Me), 32.8 (C-3), 34.3 (C-4), 35.9 (MeN), 37.7 (C-3a), 56.5 (C-8b), 64.0 (C-2), 115.3 (C-8a), 122.7, 126.9, 129.0 and 139.3 (Ph C-atoms), 133.9 (C-5a), 149.2 (C-8) and 173.8 (CO); *m/z* 357 ($M^{\bullet+}$, 1%). 284 ($M^{\bullet+}$ − CO_2Et, 100), 241 ($M^{\bullet+}$ − CO_2Et − MeN=CH_2, 10) and 77 (Ph^+, 12).

(3aSR,8bRS)-2,3,3a,4,6,8b-*Hexahydro*-1,8-*dimethyl*-6-*phenyl*-2-*phenylacetyl*-1H-*thiopyrano*[2,3-c:4,5-c']*dipyrazole* **21**.—A solution of the aldehyde **7** (0.75 g, 2.9 mmol) and *N*-methyl-*N'*-phenylacetylhydrazide (0.48 g, 2.9 mmol) in toluene (15 cm^3) was refluxed overnight with azeotropic removal of water. Then, the solvent was evaporated and the residue was chromatographed on silica gel with dichloromethane–diethyl ether (10:1) as the eluent to give compound **21** (0.98 g, 83%), m.p. 134.5 °C (from aq. MeOH) (Found: C, 68.2; H, 5.95. $C_{23}H_{24}N_4OS$ requires C, 68.29; H, 5.98%); ν_{max}(KBr)/cm^{-1} 1647s (CO); δ_H($CDCl_3$; 250 MHz) 2.39 (3 H, s, Me), 2.58 (3 H, br s, MeN), 2.90 (1 H, dd, *J* 13.5 and 5.5, 4-H), 3.21 (1 H, dd, *J* 13.5 and 2.5, 4-H), 3.35 (1 H, br, H_B), 3.58 and 3.67 (2 H, AB pattern, *J* 15, CH_2CO), 3.72 and 4.25 (2 H, 2 br, CH_2N), 4.14 (1 H, d, *J* 7.5, H_A), 7.05–7.22 (5 H, m, Ph), 7.29, 7.41 and 7.51 (5 H, 2 t + d, *J* 8, PhN); δ_C($CDCl_3$) 12.6 (Me), 30.2 (br, C-4), 34.9 (br, C-3a), 39.9 (CH_2CO), 44.2 (br, MeN and C-3), 62.1 (br, C-8b), 111.8 (br, C-8a), 122.8, 126.4, 127.1, 128.3, 129.1, 129.2, 135.7 and 139.1 (Ph C-atoms), 132.4 (br, C-5a), 149.8 (C-8) and 172.1 (CO); *m/z* 404 ($M^{\bullet+}$, 15), 285 ($M^{\bullet+}$ − $PhCH_2CO$, 100), 241 ($M^{\bullet+}$ − $PhCH_2CO$ − MeN=NH, 68), 227 (28), 95 (16), 91 ($C_7H_7^+$, 41) and 77 (Ph^+, 25).

3-*Methyl*-5-(3-*methylbut*-2-*en*-1-*ylsulfanyl*)-1-*phenylpyrazole*-4-*carbaldehyde* **22**.—A solution of dimethylallyl bromide (10 g, 67 mmol) and thiourea (5.1 g, 67 mmol) in ethanol (100 cm^3) was first refluxed for 1 h, and then for a further 1 h after addition of ethanolic NaOH (5.36 g in 65 cm^3). The chloro aldehyde **6** (13.2 g, 60 mmol) was added to the mixture which was then refluxed for 30 min. After addition of water (100 cm^3) to the mixture it was extracted with diethyl ether (3 × 100 cm^3), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give compound **22** which was crystallized from ethanol (13.6 g, 79%), m.p. 73.5 °C (Found: C, 67.0; H, 6.3. $C_{16}H_{18}N_2OS$ requires C, 67.10; H, 6.34%); ν_{max}(KBr)/cm^{-1} 1675s (CO); δ_H($CDCl_3$; 400 MHz) 1.24 (3 H, d, *J* 1, allyl Me), 1.60 (3 H, br s, allyl Me), 2.56 (3 H, s, Me), 3.18 (2 H, d, *J* 8, CH_2S), 5.03 (1 H, tm, *J* 8, vinylic H), 7.45, 7.51 and 7.58 (5 H, 2 t + d, *J* 8, Ph) and 10.02 (1 H, s, CHO); δ_C($CDCl_3$) 13.6, 17.2 and 25.6 (3 Me), 34.7 (CH_2S), 117.8 and 138.6 (CH=C), 124.1 (C-4), 125.8, 128.7, 128.9 and 138.4 (Ph C-atoms), 140.8 (C-5), 151.3 (C-3) and 186.7 (CO); *m/z* 286 ($M^{\bullet+}$, 5%), 253 ($M^{\bullet+}$ − SH, 14), 218 ($M^{\bullet+}$ − C_5H_8, 33), 77 (Ph^+, 27) and 69 ($C_5H_9^+$, 100).

5-*Furfurylsulfanyl*-3-*methyl*-1-*phenylpyrazole*-4-*carbaldehyde* **23**.—Potassium carbonate (13.8 g, 100 mmol) was added to a cooled solution of the chloro aldehyde **6** (11.03 g, 50 mmol) and 2-furylmethanethiol (5.70 g, 50 mmol) in methanol (100 cm^3). After the mixture had been refluxed for 1 h it was poured onto ice–water and extracted with chloroform (3 × 100 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated, and the crude product **23** was crystallized from ethanol (10.1 g, 67%), m.p. 66 °C (Found: C, 64.5; H, 4.6. $C_{16}H_{14}N_2O_2S$ requires C, 64.41; H, 4.73%); ν_{max}(KBr)/cm^{-1} 1669s (CO); δ_H($CDCl_3$; 250 MHz) 2.50 (3 H, s, Me), 3.80 (2 H, s, CH_2S), 5.88 (1 H, dd, *J* 3.2 and 0.7, furan 3-H), 6.19 (1 H, dd, *J* 3.2 and 1.9, furan 4-H), 7.23 (1 H, dd, *J* 1.9 and 0.7, furan 5-H), 7.4–7.55 (5 H, m, Ph) and 9.80 (1 H, s, CHO); δ_C($CDCl_3$) 13.4 (Me), 32.9 (CH_2S), 109.0, 110.6, 142.8 and 148.9 (furan C-atoms), 123.9 (C-4), 125.9, 128.8, 128.9 and 138.3 (Ph C-atoms), 139.5 (C-5), 151.5 (C-3) and 186.2 (CO); *m/z* 298 ($M^{\bullet+}$, 8%) and 81 (furfuryl$^+$, 100).

3a,4-*Dihydro*-3,3,8-*trimethyl*-6-*phenyl*-3H,6H-*pyrazolo*-[4',3':5,6]*thiopyrano*[4,3-c]*isoxazole* **24**.—A solution of the aldehyde **22** (1.43 g, 5 mmol) in ethanol (20 cm^3) was treated with aqueous NH_2OH·HCl and $NaHCO_3$ (10 mmol each in 10 cm^3) and the mixture was stirred overnight at room temperature. It was then extracted with dichloromethane (3 × 20 cm^3), and the combined extracts were washed with water

* 1 atm = 101 325 Pa.

(3 × 20 cm^3), dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel with dichloromethane–methanol (40:1) as the eluent to give the oxime which was crystallized from ethanol (1.07 g, 74%), m.p. 111 °C (Found: C, 63.7; H, 6.3. $C_{16}H_{19}N_3OS$ requires C, 63.76; H, 6.36%); $\delta_C(CDCl_3)$ 144.6 (CH=N, $^1J_{CH}$ 164, *E*-isomer).[12]

Aqueous NaOCl (13%; 5.3 mmol in 3 cm^3) was added dropwise at 0 °C to a vigorously stirred solution of the oxime (0.75 g, 2.5 mmol) in chloroform (15 cm^3). After being stirred overnight at room temperature, the mixture was extracted with diethyl ether (3 × 20 cm^3), and the combined extracts were dried ($MgSO_4$) and evaporated to give crude product **24** (0.72 g, 97%) which was crystallized from diethyl ether–light petroleum (0.40 g, 54%), m.p. 128 °C (Found: C, 64.1; H, 5.6. $C_{16}H_{17}N_3OS$ requires C, 64.19; H, 5.72%); ν_{max}(KBr)/cm^{-1} 1610s and 1595s; $\delta_H(CDCl_3$; 400 MHz) 1.20, 1.62 and 2.54 (9 H, 3 s, 3 Me), 2.93 (1 H, dd, *J* 13 and 4, 4-H), 3.16 (1 H, dd, *J* 13 and 13, 4-H), 3.43 (1 H, dd, *J* 13 and 4, 3a-H), 7.37, 7.48 and 7.55 (5 H, 2 t + d, *J* 8, Ph); $\delta_C(CDCl_3)$ 14.1, 21.8 and 26.3 (3 Me), 28.3 (C-4), 55.9 (C-3a), 85.3 (C-3), 108.7 (C-8a), 122.8, 127.7, 129.3 and 139.0 (Ph C-atoms), 136.2 (C-5a), 149.0 (C-8) and 151.9 (C-8b); *m/z* 299 ($M^{\bullet+}$, 100%), 242 ($M^{\bullet+}$ − C_3H_5O, 23), 240 (25), 214 (10), 188 (11), 118 (11) and 77 (Ph^+, 65).

10-*Methyl*-8-*phenyl*-2aH,6H,8H-*furo*[2″,3″:4′,5′]*isoxazolo*-[3′,4′:4,5]*thiopyrano*[2,3-c]*pyrazole* **25**.—A solution of the aldehyde **23** (1.43 g, 4.8 mmol) in ethanol (35 cm^3) was treated with aqueous NH_2OH·HCl and $NaHCO_3$ (10 mmol each in 15 cm^3) and stirred overnight at room temperature. After cooling of the reaction mixture, the corresponding oxime was filtered off (1.17 g, 78%), m.p. 97 °C (from EtOH) (Found: C, 61.4; H, 4.7. $C_{16}H_{15}N_3O_2S$ requires C, 61.32; H, 4.83%); $\delta_C([^2H_6]DMSO)$ 141.8 (CH=N, $^1J_{CH}$ 162, *E*-isomer).[12]

Aqueous NaOCl (13%; 2.4 mmol in 1.4 cm^3) was added dropwise at 0 °C to a vigorously stirred solution of the oxime (0.72 g, 2.3 mmol) in chloroform (200 cm^3), containing a few drops of triethylamine. After the mixture had been stirred overnight at room temperature, the organic phase was separated, dried ($MgSO_4$) and evaporated, and the residue was chromatographed on silica gel with chloroform–methanol (20:1) as the eluent to give compound **25** (0.54 g, 75%), m.p. 176.5 °C (Found: C, 61.5; H, 4.2. $C_{16}H_{13}N_3O_2S$ requires C, 61.72; H, 4.21%); ν_{max}(KBr)/cm^{-1} 1607s; $\delta_H(CDCl_3$; 400 MHz) 2.40 (3 H, s, Me), 3.12 (1 H, d, *J* 13, 6-H), 3.35 (1 H, d, *J* 13, 6-H), 5.42 (1 H, t, *J* 2.5, 3-H), 5.44 (1 H, d, *J* 2.5, 2a-H), 6.59 (1 H, d, *J* 2.5, 4-H), 7.28, 7.39 and 7.51 (5 H, 2 t + d, *J* 8, Ph); $\delta_C(CDCl_3)$ 13.6 (Me), 34.2 (C-6), 88.6 (C-2a), 94.5 (C-5a), 101.6 (C-3), 106.7 (C-10a), 122.7, 127.7, 129.2 and 138.8 (Ph C-atoms), 134.9 (C-7a), 147.6 (C-10b), 149.3 (C-10) and 149.5 (C-4); *m/z* 311 ($M^{\bullet+}$, 16%), 282 ($M^{\bullet+}$ − CHO, 21), 266 (28), 81 (furfuryl$^+$, 100) and 77 (Ph^+, 72).

5-*Allyloxy*-3-*methyl*-1-*phenylpyrazole*-4-*carbaldehyde* **26**.—To a stirred ice-cooled solution of the aldehyde **6** (5.52 g, 25 mmol) and allyl alcohol (2.9 g, 50 mmol) in tetrahydrofuran (50 cm^3) was added potassium *tert*-butoxide (3.08 g, 27 mmol), and the mixture was brought to room temperature and stirred for 1 h. After addition of diethyl ether (200 cm^3), the mixture was filtered, and the filtrate was evaporated to give compound **26** (5.08 g, 84%) as an oil of satisfactory quality (NMR) for further use; ν_{max}(neat)/cm^{-1} 1674s (CO); $\delta_H([^2H_6]DMSO$; 400 MHz) 2.40 (3 H, s, Me), 5.00 (2 H, dt, *J* 6 and 1.5, CH_2O), 5.26 (1 H, ddd, *J* 10.5, 1.5 and 1.5, vinylic H), 5.34 (1 H, ddd, *J* 17, 1.5 and 1.5, vinylic H), 5.96 (1 H, ddt, *J* 17, 10.5 and 6, vinylic H), 7.41, 7.52 and 7.68 (5 H, 2 t + d, *J* 8, Ph) and 9.90 (1 H, s, CHO); $\delta_C([^2H_6]DMSO)$ 13.7 (Me), 76.1 (CH_2O), 107.4 (C-4), 119.3 and 132.0 (CH_2=CH), 122.9, 127.5, 129.0 and 137.0 (Ph C-atoms), 150.2 (C-3), 154.5 (C-5) and 183.4 (CO); *m/z* 242 ($M^{\bullet+}$, 54%), 214 ($M^{\bullet+}$ − CO, 25), 213 ($M^{\bullet+}$ − CHO, 36), 201 ($M^{\bullet+}$ − C_3H_5, 39), 185 (13), 173 ($M^{\bullet+}$ − C_3H_5 − CO, 38), 92 (72) and 77 (Ph^+, 100) ($M^{\bullet+}$, 242.1014. $C_{14}H_{14}N_2O_2$ requires *M*, 242.1055).*

3a,4-*Dihydro*-8-*methyl*-6-*phenyl*-3H,6H-*pyrazolo*[4′,3′:5,6]-*pyrano*[4,3-c]*isoxazole* **27**.—A solution of the aldehyde **26** (5.08 g, 21 mmol) in ethanol (100 cm^3) was treated with aqueous NH_2OH·HCl and $NaHCO_3$ (41 mmol each in 50 cm^3) and stirred at room temperature for 2 h. The reaction mixture was concentrated and extracted with dichloromethane (3 × 100 cm^3). The combined extracts were dried ($MgSO_4$) and evaporated to give the corresponding oxime (4.98 g, 92%), m.p. 97 °C (from EtOH at −20 °C) (Found: C, 65.6; H, 5.95. $C_{14}H_{15}N_3O_2$ requires C, 65.37; H, 3.84%).

Aqueous NaOCl (13%, 21 mmol in 12 cm^3) was added dropwise at 0 °C to a vigorously stirred solution of the oxime (4.98 g, 19 mmol) in chloroform (250 cm^3). After the mixture had been stirred overnight at room temperature, the organic phase was separated, dried ($MgSO_4$) and evaporated and the residue was chromatographed on silica gel with chloroform–diethyl ether (2:1) as the eluent to give compound **27** (4.37 g, 88%), m.p. 155 °C (from cyclohexane) (Found: C, 65.65; H, 5.0. $C_{14}H_{13}N_3O_2$ requires C, 65.86; H, 5.14%); ν_{max}(KBr)/cm^{-1} 1642s and 1592s; $\delta_H(CDCl_3$; 400 MHz) 2.48 (3 H, s, Me), 3.75 (1 H, dd, *J* 14 and 8, 3-H), 3.93 (1 H, m, Σ *J* 40, 3a-H), 4.25 (1 H, dd, *J* 12 and 10, 4-H), 4.65 (1 H, dd, *J* 9 and 8, 3-H), 4.91 (1 H, dd, *J* 10 and 5, 4-H), 7.29, 7.42 and 7.73 (5 H, 2 t + d, *J* 8, Ph); $\delta_C(CDCl_3)$ 14.0 (Me), 46.8 (C-3a), 68.8 (C-4), 72.7 (C-3), 92.4 (C-8a), 120.6, 126.5, 129.1 and 137.7 (Ph C-atoms), 146.1 (C-8), 149.6 (C-5a) and 152.6 (C-8b); *m/z* 255 ($M^{\bullet+}$, 100%), 225 ($M^{\bullet+}$ − CH_2O, 9), 198 (27) and 77 (Ph^+, 39).

4-*Allyl*-5-*hydroxy*-3-*methyl*-1-*phenylpyrazole* **29**.—The pyrazole **26** (2.42 g, 10 mmol) was heated at 40 °C for 4 days without solvent, and the product then chromatographed on silica gel with dichloromethane as the eluent to give compound **29** (1.42 g, 66%), m.p. 79 °C (Found: C, 72.7; H, 6.5. $C_{13}H_{14}N_2O$ requires C, 72.89; H, 6.59%); ν_{max}(KBr)/cm^{-1} 2600br (OH) and 1592s; $\delta_H([^2H_6]DMSO$; 400 MHz) 2.09 (3 H, s, Me), 3.02 (2 H, br, CH_2), 4.96 (1 H, dm, *J* 10, vinylic H), 5.00 (1 H, dm, *J* 16, vinylic H), 5.84 (1 H, ddt, *J* 16, 10 and 6, vinylic H), 7.18, 7.42 and 7.73 (5 H, 2 t + d, *J* 8, Ph) and 10.75 (1 H, br, OH); $\delta_C([^2H_6]DMSO)$ 11.9 (br, Me), 25.9 (CH_2), 114.5 and 136.7 (CH_2=CH), 119.1, 124.5, 128.9 and 138.4 (Ph C-atoms, all broad except C_m) and 147.9 (br, C-3);† *m/z* 214 ($M^{\bullet+}$, 56%), 173 ($M^{\bullet+}$ − C_3H_5, 68), 106 (19), 105 (21), 91 (20) and 77 (Ph^+, 100).

3-*Methyl*-1-*phenyl*-5-(*prop*-2-*ynyloxy*)*pyrazole*-4-*carbaldehyde* **30**.—To an ice-cooled solution of the aldehyde **6** (2.21 g, 10 mmol) and prop-2-yn-1-ol (1.12 g, 20 mmol) in tetrahydrofuran (30 cm^3) was added potassium *tert*-butoxide (1.23 g, 11 mmol), and the mixture was heated at 50 °C for 15 min. It was then worked up by chromatography on silica gel with dichloromethane as the eluent to give compound **30** (2.12 g, 88.5%), m.p. 84 °C (from cyclohexane) (Found: C, 70.1; H, 5.1. $C_{14}H_{12}N_2O_2$ requires C, 69.99; H, 5.03%); ν_{max}(KBr)/cm^{-1} 3291m and 2124m (C≡CH) and 1674s (CO); $\delta_H(CDCl_3$; 400 MHz) 2.40 (3 H, s, Me), 2.48 (1 H, t, *J* 2.5, C≡CH), 5.02 (2 H, d, *J* 2.5, CH_2), 7.26, 7.36 and 7.58 (5 H, 2 t + d, *J* 8, Ph) and 9.80 (1 H, s, CHO); $\delta_C(CDCl_3)$ 13.5 (Me), 62.5 (CH_2), 76.9 and 78.0

* The kinetics of the Claisen rearrangement of compound **26** in deuteriated dimethyl sulfoxide at 65 °C were studied by following the disappearance of the methyl signals in the ^1H NMR spectra, giving a clean first-order reaction for 3 half-lives with $k_1 = 8.83 \times 10^{-5}$ s^{-1}.

† The broad signals are due to equilibration with the N-H tautomer; the C-4 and C-5 signals are not observed.

(C≡CH), 108.5 (C-4), 123.4, 127.9, 129.0 and 137.1 (Ph C-atoms), 151.4 (C-3), 153.3 (C-5) and 183.4 (CO); *m/z* 240 ($M^{\bullet+}$, 15%), 239 (18), 212 ($M^{\bullet+}$ − CO, 15), 211 ($M^{\bullet+}$ − CHO, 13), 201 ($M^{\bullet+}$ − C_3H_3, 41) 185 (15), 183 (15), 173 ($M^{\bullet+}$ − C_3H_3 − CO, 28), 145 (16), 104 (18), 92 (67) and 77 (Ph^+, 100).*

8-*Methyl*-6-*phenyl*-4H,6H-*pyrazolo*[4',3':5,6]*pyrano*[4,3-c]-*isoxazole* **31**.—A solution of the aldehyde **30** (2 g, 83 mmol) in ethanol (20 cm^3) was treated with aqueous NH_2OH·HCl and $NaHCO_3$ (91 mmol each in 10 cm^3). After 1 h the precipitated oxime was collected and dried (1.74 g, 82%), m.p. 136.5 °C (from aq. EtOH), δ_H([$^2H_6$]DMSO) 140.4 (CH=N, $^1J_{CH}$ 164, *E*-isomer).[12]

N-Chlorosuccinimide (0.15 g, 1.1 mmol) was added to a solution of the oxime (0.25 g, 1 mmol) in chloroform (10 cm^3) containing two drops of pyridine, and the mixture was stirred at room temperature for 1 h. It was worked up by chromatography on silica gel with diethyl ether–light petroleum (2:1) as the eluent to give compound **31** (213 mg, 84%), m.p. 135 °C (from $CHCl_3$–cyclohexane) (Found: C, 66.3; H, 4.5. $C_{14}H_{11}N_3O_2$ requires C, 66.40; H, 4.38%); ν_{max}(KBr)/cm^{-1} 1640s and 1590s; δ_H($CDCl_3$; 400 MHz) 2.52 (3 H, s, Me), 5.45 (2 H, s, CH_2O), 7.28, 7.44 and 7.73 (5 H, 2 t + d, *J* 8, Ph) and 8.10 (1 H, s, 3-H); δ_C($CDCl_3$) 13.9 (Me), 65.4 (C-4), 92.2 (C-8a), 107.7 (C-3a), 120.8, 126.5, 129.0 and 137.7 (Ph C-atoms), 145.2 (C-8), 149.6 (C-3) and 151.7 (C-5a and C-8b); *m/z* 253 ($M^{\bullet+}$, 100%), 225 ($M^{\bullet+}$ − CO, 10), 170 (49), 144 (15), 129 (80), 118 (14), 91 (17), 83 (32) and 77 (Ph^+, 58) ($M^{\bullet+}$, 253.0841. $C_{14}H_{11}N_3O_2$ requires *M*, 253.0851).

5-(*But*-3-*enyloxy*)-3-*methyl*-1-*phenylpyrazole*-4-*carbaldehyde* **33**.—To an ice-cooled solution of the aldehyde **6** (2.21 g, 10 mmol) and but-3-en-1-ol (0.79 g, 11 mmol) in tetrahydrofuran (25 cm^3) was added potassium *tert*-butoxide (1.23 g, 11 mmol), and the mixture was stirred overnight at room temperature. After addition of diethyl ether (80 cm^3) to the reaction mixture it was filtered and the filtrate evaporated. The residue was chromatographed on silica gel with dichloromethane as the eluent to give compound **33** as a yellow oil (2.12 g, 83%); ν_{max}(neat)/cm^{-1} 1676s (CO); δ_H($CDCl_3$; 400 MHz) 2.46 (2 H, qt, *J* 6 and 1, allyl CH_2), 2.50 (3 H, s, Me), 4.44 (2 H, t, *J* 6, CH_2O), 5.04 (1 H, dm, *J* 10, vinylic H), 5.06 (1 H, dm, *J* 17, vinylic H), 5.72 (1 H, ddt, *J* 17, 10 and 6, vinylic H), 7.35, 7.45 and 7.64 (5 H, 2 t + d, *J* 8, Ph) and 9.92 (1 H, s, CHO); δ_C($CDCl_3$) 13.8 (Me), 34.0 (allyl CH_2), 75.5 (CH_2O), 107.7 (C-4), 117.9 and 133.1 (CH_2=CH), 123.2, 127.6, 129.0 and 137.2 (Ph C-atoms), 151.3 (C-3), 155.0 (C-5) and 183.0 (CO); *m/z* 256 ($M^{\bullet+}$, 23), 202 ($M^{\bullet+}$ − CH_2=CH–CH=CH_2, 57), 185 ($M^{\bullet+}$ − C_4H_7O, 28), 92 (14), 91 (19), 77 (Ph^+, 53), 67 (17) and 55 ($C_4H_7^+$, 100) ($M^{\bullet+}$, 256.1215. $C_{15}H_{16}N_2O_2$ requires *M*, 256.1212).

3,3a,4,5-*Tetrahydro*-9-*methyl*-7-*phenyl*-7H-*pyrazolo*[3',4':2,3]*oxepino*[4,5-c]*isoxazole* **34**.—A solution of the aldehyde **33** (0.64 g, 2.5 mmol) in ethanol (20 cm^3) was treated with aqueous NH_2OH·HCl and $NaHCO_3$ (5 mmol each in 10 cm^3), and the mixture stirred overnight at room temperature. It was then concentrated, cooled and filtered to give the corresponding oxime which was crystallized from ethanol at −20 °C (0.52 g, 76%), m.p. 94 °C (Found: C, 66.3; H, 6.2. $C_{15}H_{17}N_3O_2$ requires C, 66.40; H, 6.32%); δ_C($CDCl_3$) 142.2 (CH=N, $^1J_{CH}$ 162, *E*-isomer).[12]

Aqueous NaOCl (13%; 2.1 mmol in 1.2 cm^3) was added at 0 °C to a vigorously stirred solution of the oxime (0.49 g, 1.8 mmol) in chloroform (60 cm^3). After the mixture had been stirred overnight at room temperature, the organic phase was separated and evaporated and the residue was chromatographed on silica gel with chloroform–methanol (40 : 1) as the eluent to give compound **34** (0.37 g, 76%), m.p. 175.5 °C (from $CHCl_3$–hexane) (Found: C, 66.8; H, 5.5. $C_{15}H_{15}N_3O_2$ requires C, 66.90; H, 5.61%); ν_{max}(KBr)/cm^{-1} 1598s; δ_H($CDCl_3$; 400 MHz) 2.07 (1 H, m, Σ *J* 39, 4-H), 2.30 (1 H, ddd, *J* 15, 6 and 4, 4-H), 2.46 (3 H, s, Me), 3.61 (1 H, m, Σ *J* 40, 3a-H), 3.79 (1 H, dd, *J* 13 and 8, 3-H), 4.17 (1 H, dd, *J* 12 and 10, 5-H), 4.60 (1 H, ddd, *J* 12, 6 and 2, 5-H), 4.66 (1 H, dd, *J* 10 and 8, 3-H), 7.28, 7.40 and 7.60 (5 H, 2 t + d, *J* 8, Ph); δ_C($CDCl_3$) 15.0 (Me), 29.8 (C-4), 50.9 (C-3a), 71.2 and 73.1 (C-3 and/or C-5), 94.6 (C-9a), 122.5, 126.6, 128.7 and 137.8 (Ph C-atoms), 148.0 (C-9), 152.6 (C-6a) and 153.2 (C-9b); *m/z* 269 ($M^{\bullet+}$, 100), 215 ($M^{\bullet+}$ − C_4H_7, 10), 198 (17), 118 (10), 91 (17) and 77 (Ph^+, 78).

* The kinetics of the Claisen rearrangement of compound **30** in toluene at 100 °C were studied by following the disappearance of the C≡CH and CO absorptions in the IR spectra, giving first-order plots with an averaged rate constant k_1 = 1.90 × 10^{-4} s^{-1}.

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