Pergamon

Tetrahedron, Vol. 53, No. 30, pp. 10633-10642, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00674-1

4-Substituted Protoanemonin in Intramolecular Cycloaddition Reactions of Non-stabilised Azomethine Ylides

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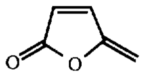
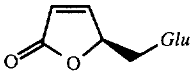
Abstract: The intramolecular cycloaddition reactions of non-stabilised azomethine ylides generated by condensation of 4-(3-propanalyl)-5-methylene-2(5H)furanone and cyclic amino acids were investigated. The reactions proceeded via highly stereoselective formation of *anti-* dipoles followed by cycloaddition reactions on either the α,β– or γ,δ– double bond to produce polycyclic cycloadducts in good yield. Both double bonds of the lactone moiety proved to be efficient dipolarophiles.

The physiological activity of many plants belonging to *Ranunculaceae* is attributed to protoanemonin (**1**).[1] It has been found that this lactone is liberated enzymically from the glucosidic precursor ranuculin (**2**).


(1)



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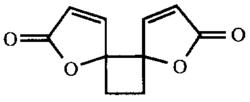
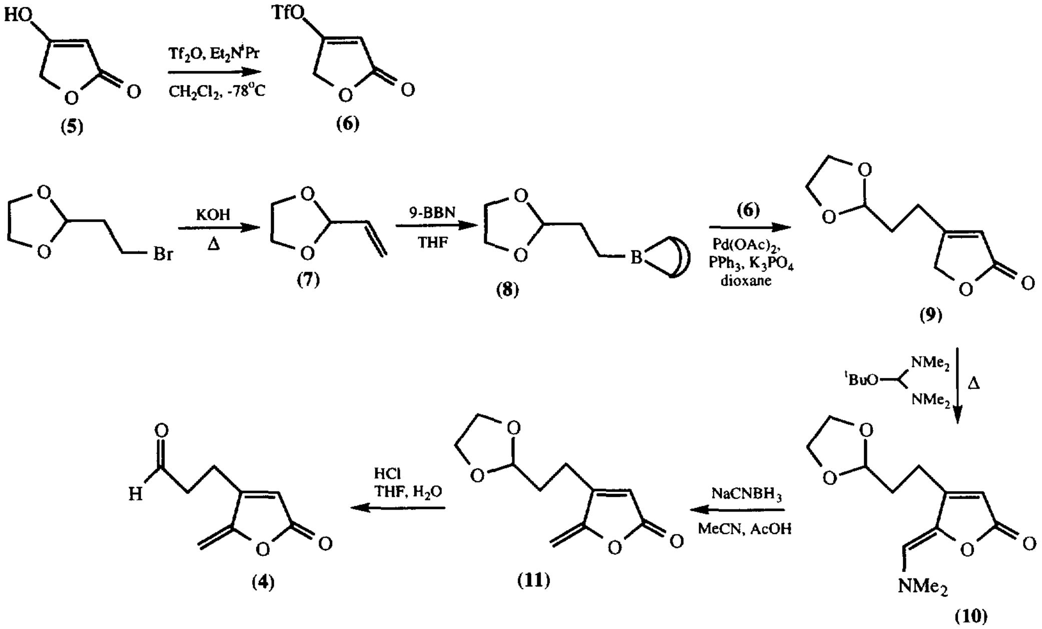

(3)

Protoanemonin (**1**) is not stable and easily dimerises producing anemonin (**3**) via a head to head [2+2]-cycloaddition reaction. The latter compound, which is also isolated from *Ranunculaceae*, shows no physiological activity.

The lactone (**1**) can be prepared from cheap starting materials and its reactivity as a C-5 synthon has been investigated.[2] The electrophilic behaviour of protoanemonin (**1**) did not prove to be synthetically useful mainly due to the complex mixture of products obtained in reactions with different kind of nucleophiles.[3] On the other hand protoanemonin showed general reactivity as a dienophile in Diels-Alder reactions reacting highly site- and regio-selectively.[4]

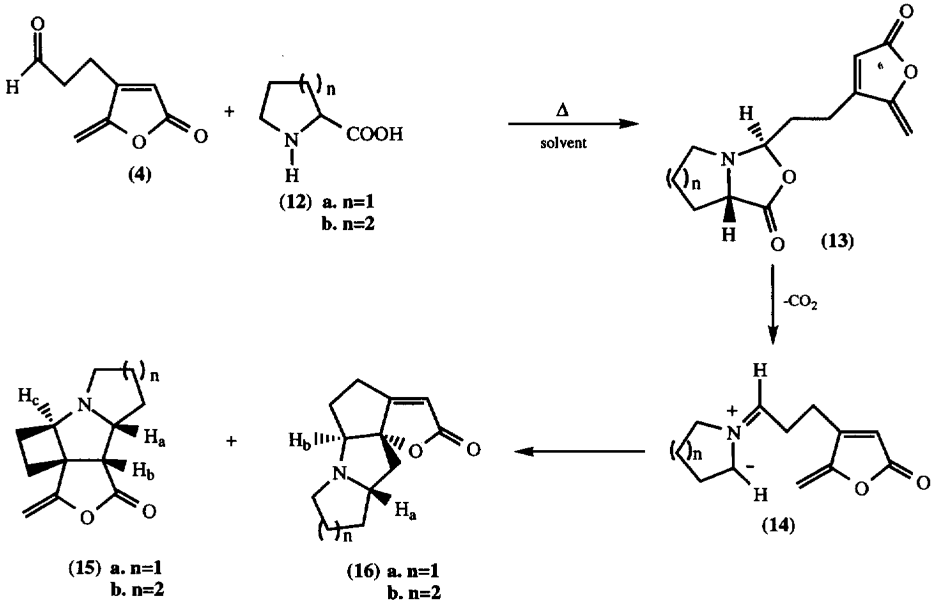
In this paper we shall discuss the utility of the 4-substituted protoanemonin (**4**) in intramolecular cycloaddition reactions to non-stabilised azomethine ylides. The required protoanemonin derivative (**4**) was synthesised as shown in **Scheme 1**. The triflate (**6**) was prepared from tetronic acid (**5**) under standard conditions in 66% yield.[5] The borate (**8**) obtained via hydroboration of alkene (**7**)[6] was not isolated but used in situ for coupling with triflate (**6**) under Suzuki's conditions to produce lactone (**9**) in 51% yield.[7] The exocyclic double bond was introduced by a two step procedure using Bredereck's reagent.[8] Heating lactone (**9**) and this reagent afforded **(10)** in 88% yield. The reduction of the enamino moiety with $NaCNBH_3$ in MeCN/AcOH produced **(11)** in 65% yield. Finally, deprotection under standard conditions afforded **(4)** in 93% yield.



Scheme 1

The aldehyde **(4)** was used as an aldehyde component in the decarboxylative generation of azomethine ylides as shown in **Scheme 2**.[9] Thus, heating **(4)** and **(12a)** in toluene produced azomethine ylide **(14)**, via the initially formed oxazolidinone **(13)**[10], which underwent intramolecular cycloaddition reactions to either the α,β– double bond to produce **(15a)** or the γ,δ– double bond to produce **(16a)** in 63% combined yield and 1:1.2 ratio respectively **(Table 1)**. The stereochemistry of these products is based on n.O.e. data. Thus for **(15a)** irradiation of H_a effected enhancement of H_b (8%). Similarly, irradiation of H_b effected enhancement of H_a (9%) and established their *cis* arrangement. The stereochemistry of H_b effectively fixes the stereochemistry of the cyclobutane. This requires a *trans*- relationship for H_a and H_c. This is supported by irradiation of H_c since no enhancement of H_a was observed. Unambiguous determination of the stereochemistry of **(16a)** based on n.O.e. data is difficult due to the presence of the quaternary C-atom in the pyrrolidine ring. However, the stereochemistry of the quaternary centre is assigned by analogy with that of **(16b)** (see below). The *trans*-relationship between H_a and H_b is sugested by the absence of any enhancement of either signal upon irradiation of the other.

Similar results were obtained when pipecolinic acid **(12b)** was used in place of proline **(12a)**, **(Scheme 2)**. The reaction of this amino acid and aldehyde **(4)**, performed under the same conditions, afforded two products **(15b)** and **(16b)** in 51% combined yield. The X-ray crystal structure of each product allowed unequivocal assignment of stereochemistry **(Figures 1** and **2)**.



Scheme 2

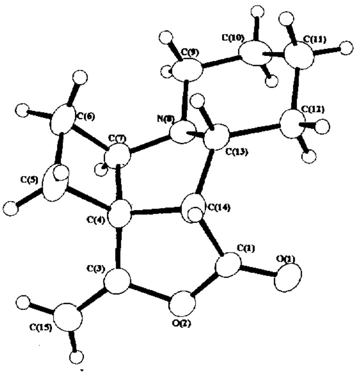


Figure 1. ORTEP[13] representation of the molecular structure of **(15b)**

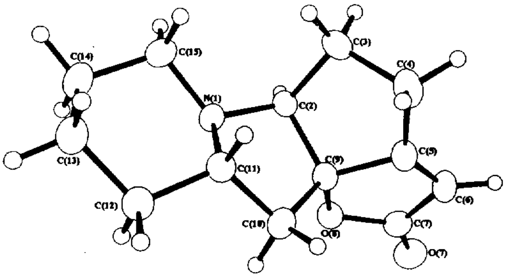


Figure 2. ORTEP[13] representation of the molecular structure of **(16b)**

The established stereochemistry of the cycloadducts shows that initial condensation of amino acid **(12)** and aldehyde **(4)** produced *anti*-dipole **(14)** followed by cycloaddition onto the α,β– or the γ,δ– double bond via *endo* transition states **(Figure 3)**.

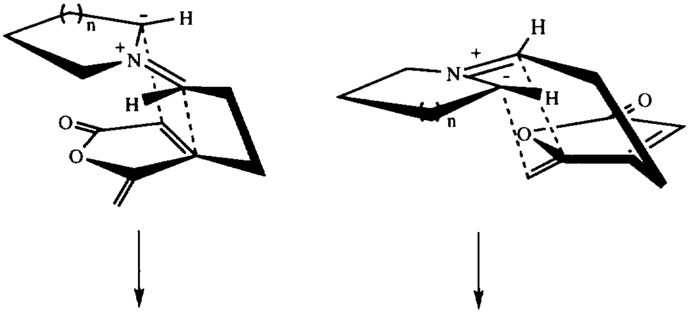
Table 1.

entry	(12)	solvent	ratio (15) : (16)^a	n	yield (%)^{b,c}
1	a	toluene	1 : 1.2	1	63
2	b	toluene	1 : 1.3	2	51
3	b	acetonitrile	1 : 2.1	2	58

[a] ratio of the isolated products, [b] yields of the isolated products, [c] reaction times: entries 1 and 2, 2h; entry 3, 11h.

The stereoselective formation of *anti*-dipole is expected, based on the mechanism proposed for the decarboxylative generation of azomethine ylid.[10] Highly stereoselective formation of *anti*-dipole is assisted by steric interaction in the *syn*-dipole **(17)**, **(Figure 4)**. Moreover *anti-syn* interconversion is prevented by both fast intramolecular cycloaddition reaction and by use of a non-polar solvent.[11]

The dipolarophilic α,β– and γ,δ– double bonds of aldehyde **(4)** exhibited similar reactivity in boiling toluene and altering the ring size of the amino acid had no effect on the product ratio **(Table 1)**. Performing the reaction at lower temperature in a polar solvent **(Table 1**, entry 3) altered the product ratio in favour of **(16b)**. This trend is in accord with higher reactivity of the γ,δ– double bond observed in Diels-Alder reactions.[4b] The two transition states **(Figure 3)** represent a balance of colombic stacking forces between dipole and dipolarophile which favour **(15)**[4b] and steric constraints which favour **(16)**. The use of more polar solvent decreases the effectiveness of the former. It has been proposed that the intermolecular Diels-Alder reactions of protoanemonin proceeds by way of biradical[4b] like transition state and such mechanistic interpretations have been championed by Firestone.[12a] Thus, a non-concerted processes could operate in the formation of **(16)**.[12b]



(15) **(16)**

Figure 3

A further unobserved regio-chemical pathway for the cycloaddition **(Figure 5)** would have provided access to the *Securinega* alkaloids.[16]

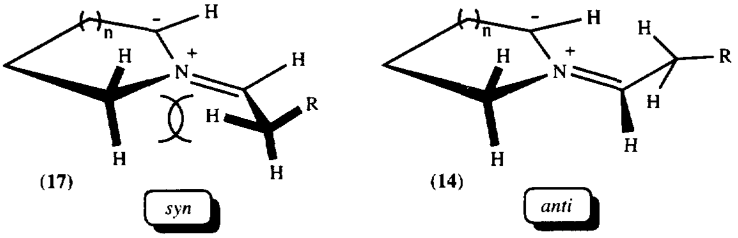


Figure 4

In summary, intramolecular cycloaddition reactions of 4-substituted protoanemonin is an efficient method for the synthesis of polycyclic heterocycles. Contrary to the results observed for the related intermolecular Diels-Alder reactions, both double bonds of the substituted proteanemonin proved to be efficient dipolarophiles in intramolecular cycloadditions to non-stabilised azomethine ylides.

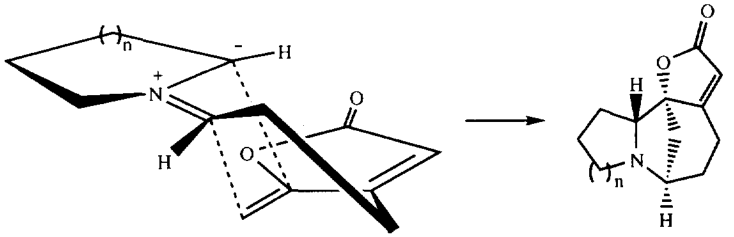


Figure 5

Experimental

Melting points were determined on a Koffler hot-stage apparatus and are uncorrected. Mass spectral data were obtained from a VG AutoSpec operating at 70eV. Nuclear magnetic resonance spectra were recorded on QE 300 and AM 400 machines operating at 300 and 400 MHz respectively. Deuterochloroform was used as a solvent with tetramethylsilane as internal standard (0.03%). Microanalyses were obtained using a Carlo Erba MOD 11016 instrument. Thin layer chromatography was carried out on Whatman PESIL G/UV polyester plates coated with 0.2mm layer of silica-gel and column chromatography was performed with silica-gel 60 (Merck 9385). THF and dioxane were sodium dried under a nitrogen atmosphere.

Triflate (6): Ethyl diisopropyl amine (0.57g, 4.4mmol) was added to a stirred solution of tetronic acid (0.44g, 4.4mmol)in dry dichloromethane (30ml) at -78C followed by triflic anhydride (1.24g, 4.4mmol). The mixture was stirred at -78C for 45min, diluted with dichloromethane (70ml) , washed with water, dried (magnesium sulfate) and the solvent evaporated under reduced pressure. Distillation of the residual oil afforded the **product** (b.p. 60-62C/0.08mmHg) as a pale yellow oil, (**Found**: C, 25.9; H, 1.25; S, 14.0. **$C_5H_3O_5F_3S$ requires**: C, 25.85; H, 1.3; S, 13.8%.); **δ:** 4.90 (s, 2H, CH_2) and 6.03 (s, 1H, =CH); **m/z(%)**: 232 (M^+, 5), 139 (54) and 69 (100).

Lactone (9): The alkene (7) (1.55g, 15.5mmol) was added under an argon atmosphere to a stirred THF solution of 9-BBN (31ml 0.5M, 15,5mmol) at 0°C. The mixture was allowed to warm to room temperature and stirred for a further 3h. Dioxan (93ml), $Pd(OAc)_2$ (0.17g, 0.76mmol), PPh_3 (0.4g, 1.5mmol), K_3PO_4 (9.85g, 46.4mmol) and triflate **(6)** (3.55g, 15.5mmol) were added to this mixture and resulting mixture was stirred and heated at 60°C for 15h. The cooled mixture was then filtered, the filtrate evaporated under reduced pressure and the residue purified by flash chromatography (SiO_2, 1:1 v/v petroleum ether-ethyl acetate) to afford the **product** (1.44g, 51%) as colourless needles (petroleum ether-dichloromethane), m.p. 41-41.5°C, (**Found**: C, 58.5; H, 6.45. **$C_9H_{12}O_4$ requires**: C, 58.7; H, 6.5%.); **d:** 2.0 (m, 2H, $CH\underline{H}_2CH_2$), 2.56 (t, 2H, J7.6Hz, $CH_2C\underline{H}_2C$=), 3.8-4.0 (m, 4H, OCH_2CH_2O), 4.77 (s, 2H, ring CH_2), 4.95 (t, 1H, J4.1Hz OCHRO) and 5.87 (s, 1H, =CH); **m/z(%)**: 183(M^+-1, 3), 149(6), 73(100), 55(9) and 45(38).

Lactone (10): Lactone **(9)** (0.37g, 2.0mmol) and Bredereck's reagent[8] (0.42g, 2.4mmol) were heated at 60°C (oil bath temperature) for 2h. The cooled reaction mixture was purified by flash chromatography (Al_2O_3, ethyl acetate) to afford the **product** (0.43g, 88%) as pale yellow rhombs (ether-dichlormethane), m.p. 54.5-55.5°C, (**Found**: C, 60.3; H, 7.2; N, 5.75. **$C_{12}H_{17}NO_4$ requires**: C, 60.25; H, 7.11; N, 5.86%.); δ: 1.96 (m, 2H, $CH\underline{H}_2CH_2$), 2.53 (t, 2H, CH_2C=), 3.16 (s, 6H, $N(CH_3)_2$), 3.86-4.02 (m, 4H, OCH_2CH_2O), 4.92 (t, 1H, J4.3Hz, $OC\underline{H}(CH_2)O$), 5.40 (s, 1H, =CHN) and 5.97 (s, 1H, =CHCOO); **m/z(%)**: 239(M^+, 53), 178(11), 166(12), 153(100), 139(10), 124(16), 96(27), 82(24), 73(61), 57(43) and 42(82).

Lactone (11): $NaCNBH_3$ (0.04g, 0.64mmol) was added to a solution of lactone **(10)** (0.075g, 0.31mmol) in acetonitrile (5ml) followed by addition of acetic acid (0.12ml). The mixture was stirred at room temperature for 18h. The solvent was then evaporated under reduced pressure, the residue carefully neutralised by the addition of 10% aqueous $NaHCO_3$ solution and then extracted (dichloromethane). The dried ($MgSO_4$) organic extract was evaporated and the residue was purified by flash chromatography (Al_2O_3, 4:1 v/v ethyl acetate-petroleum ether) to afford the **product** (0.04g, 65%) as a colourless oil which solidified upon standing, m.p. 37-39°C, (**Found**: C, 61.5; H, 6.3. **$C_{10}H_{12}O_4$ requires**: C, 61.22; H, 6.12%); δ: 2.02 (m, 2H, $CH\underline{H}_2CH_2$), 2.62 (t, 2H, J7.4Hz, CH_2C=), 3.87-4.00 (m, 4H, OCH_2CH_2O), 4.96 (d+t, 2x1H, =$C\underline{H}$(H) and OCH(R)O), 5.17 (t, 1H, J1.7Hz, =$C\underline{H}$(H)) and 6.02 (s, 1H, =CHCOO); **m/z(%)**: 196(M^+, 13), 168(12), 149(10), 136(57), 124(8), 110(30), 86(38), 73(100), 53(14) and 45(56).

Lactone (4): A solution of lactone **(11)** (0.03g, 0.16mmol) and 5% aqueous HCl solution (0.3ml) in THF (2ml) was heated at 70°C for 2h. The cooled reaction mixture was carefully neutralised with 10% $NaHCO_3$ solution and extracted (ether). The extract was dried, the solvent evaporated under reduced pressure and the residue purified by flash chromatography (SiO_2, ether) to afford the **product** (0.022g, 93%) as a colourless oil which solidified upon standing, m.p. 35-36°C, (**Found** C, 63.05; H, 5.25; **$C_8H_8O_3$ requires**: C, 63.15; H, 5.25%.); δ: 2.84 (m, 4H, CH_2CH_2), 4.96 and 5.21 (d and t, 2x1H, J2.8Hz and J2.7Hz, =CH_2), 5.98 (s, 1H, =CHCOO) and 9.85 (s, 1H, CHO); **m/z(%)**: 152(M^+, 2), 124(16), 110(100), 96(17), 81(27), 67(24), 53(19) and 39(17).

General procedure for the cycloaddition reactions of lactone (4)

A mixture of aldehyde **(4)** (0.21mmol) and amino acid (0.23mmol) in solvent (5ml) was boiled under reflux until tlc indicated the absence of starting materials. The solvent was then evaporated under reduced pressure and the residue purified by flash chromatography. Product ratios are collected in **Table 1**.

Cycloadducts (15a) and**(16a):** Flash chromatography (SiO_2, 92;8 v/v dichloromethane-methanol) afforded the **products** in 63% combined yield as colourless oils. **(15a): found** (HRMS): 205.1103, **$C_{12}H_{15}NO_2$ requires**: 205.1102; δ: 1.70-2.00 (m, 4H), 2.10-2.38 (m, 4H), 2.68 (m, 1H), 2.87 (d, 1H, J8.7Hz, H_b), 3.00 (m, 1H), 3.87 (t, 1H, J6.3Hz, H_c), 4.33 (dt, 1H, J8.5Hz and 1.9Hz, H_a) and 4.48 and 4.77 (2xd, 2x1H, J2.8Hz, $=CH_2$); **m/z(%)**: 205(M^+, 9), 96(37), 78(32), 69(17) and 43(100). **(16a): found** (HRMS): 205.1103; δ: 1.71-1.80 (m, 2H), 1.80-2.14 (m, 4H), 2.41-2.80 (m, 4H), 2.86 and 3.13 (2xm, 2x1H, NCH_2), 3.36 (dd, 1H, J9.9Hz and 5.7Hz, H_b), 3.89 (m, 1H, H_a) and 5.71 (d, 1H, J1.8Hz, =CH); **m/z(%)**: 205 (M^+, 39), 149(11), 110(9), 96(100), 70(12), 57(13) and 43(33).

Cycloadducts (15b) and **(16b)**: Flash chromatography (SiO_2, ether) afforded the **products** in 51% combined yield. Both products crystallised from petroleum ether-ether as colourless needles, m.p. 135-136°C and 109.5-110.5°C respectively. **(15b): found**: C, 71.35; H, 7.95; N, 6.3; **$C_{13}H_{17}NO_2$ requires**: C, 71.25; H, 7.75; N, 6.4%; δ: 1.19-2.41 (m, 11H), 2.78 (br d, 1H, H_b), 2.96 (m, 2H), 3.84 (t, 1H, J6.3Hz, H_c), and 4.45 and 4.77 (2xd, 2x1H, J2.4Hz and 2.7Hz, $=CH_2$); **m/z(%)**: 219 (M^+, 36), 191(13), 175(6), 163(44), 147(6), 134(23), 121(64), 110(100), 82(13), 54(13) and 41(17). **(16b): found**: C, 71.25; H, 7.85; N, 6.55%; δ: 1.25-1.38 (m, 2H), 1.57-1.65 (m, 2H), 1.77-1.88 (m, 3H), 2.03-2.19 (m, 2H), 2.25-2.72 (m, 5H), 2.84 (m, 1H), 3.54 (d, 1H, J5.7Hz) and 5.67 (s, 1H, =CH); **m/z(%)**: 219(M^+, 32), 175(8), 160(15), 134(6), 121(13), 110(100), 82(9), 67(9), 55(12) and 44(16).

*Single crystal X-ray diffraction analysis of **15b** and **16b*** - All crystallographic measurements for both complexes were carried out on a Stoe STADI4 diffractometer. In both cases data were collected in the range $4.0° < 2\theta < 130.0°$ using ω-θ scans. An empirical absorption correction using azimuthal ψ-scans was applied to **15b** (minimum and maximum transmission factors 0.999 and 0.804 respectively) but not to **16b**. Both structures were solved by direct methods using SHELXS-86[14] and were refined by full-matrix least-squares (based on F^2) using SHELXL-93.[15] The weighting scheme used in both refinements was $w = [\sigma^2(F_o^2) + (xP)^2 + yP]^{-1}$ where $P = (F_o^2 + 2F_c^2)/3$. In both cases all non-hydrogen atoms were refined with anisotropic discplacement parameters whilst hydrogen atoms were constrained to predicted positions using a riding model. Both refinements included an isotropic extinction parameter, x, so that $F_c' = kF_c[1+0.001*x*F_c^2*\lambda^3]^{-1/4}$ where k is the overall scale factor. The residuals wR_2 and R_1, given below, are defined as $wR_2 = (\Sigma[w(F_o^2-F_c^2)^2] / \Sigma w[F_o^2]^2)^{1/2}$ and $R_1 = \Sigma||F_o|-|F_c|| / \Sigma|F_o|$.

*Crystal data for **15b*** - $C_{13}H_{17}NO_2$, 0.46 x 0.23 x 0.21 mm, $M = 219.28$, orthorhombic, space group $P2_12_12_1$, $a = 8.7215(5)$, $b = 10.6943(8)$, $c = 12.4298(6)$ Å, $U = 1159.33(12)$ Å^3, $Z = 4$, $D_c = 1.26$ Mg m^{-3}, $\mu = 0.677$ mm^{-1}, $F(000) = 472$, $T = 200$K.

Data collection - Graphite monochromated Cu-K_α radiation, $\lambda = 1.54184$ Å, scan speeds 1.5 - 8.0° min^{-1}, ω scan widths 1.05° + α-doublet splitting, $4.0 < 2\theta < 130.0°$, 2184 Data collected 1797 of which were unique, $R_{int} = 0.0336$, $R_{sig} = 0.0230$. There were 1675 reflections with $F_o > 4.0\ \sigma(F_o)$.

Structure refinement - Number of parameters = 146, isotropic extinction parameter, x = 0.0085(14), goodness of fit, $s = 1.068$; weighting parameters x, y = 0.0931, 0.2714; $wR_2 = 0.1344$, $R_1 = 0.0472$.

*Crystal data for **16b*** - $C_{13}H_{17}NO_2$, 0.40 x 0.38 x 0.08 mm, $M = 219.28$, orthorhombic, space group $Pbca$, $a = 9.5520(10)$, $b = 19.952(2)$, $c = 11.8835(10)$ Å, $U = 2264.9(3)$ Å^3, $Z = 8$, $D_c = 1.29$ Mg m^{-3}, $\mu = 0.693$ mm^{-1},

$F(000) = 452$, $T = 200$ K.

Data collection - Radiation and collection range as for **15b**. 7577 Data collected, 1894 unique, R_{int}=0.0520, R_{sig} = 0.0372, 1235 reflections with $F_o > 4.0\ \sigma(F_o)$.

Structure refinement - Number of parameters = 146, goodness of fit, s = 1.086; weighting parameters x, y = 0.0555, 0.1718; wR_2 = 0.1036, R_1 = 0.0382.

Non-hydrogen atomic co-ordinates for **15b** and **16b** are listed in Tables 2 and 3 respectively whilst selected bond lengths and angles for **15b** and **16b** are listed in Tables 4 and 5 respectively. Supplementary data-sets for both structures, which include hydrogen co-ordinates, all thermal parameters and complete sets of bond lengths and angles, have been deposited at the Cambridge Crystallographic Data Centre and are available on request.

Table 2. Atomic co-ordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for (**15b**) with estimated standard deviations (e.s.d.s) in parentheses. U_{eq} is defined as $^1/_3$ of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C(1)	2790(3)	6721(2)	4333(2)	36.2(6)
O(1)	2643(2)	7184(2)	3459.8(14)	49.1(5)
O(2)	2102(2)	5601(2)	4559.7(14)	41.9(5)
C(3)	2431(3)	5228(2)	5618(2)	38.4(6)
C(4)	3155(3)	6299(2)	6193(2)	35.3(6)
C(5)	4198(3)	6081(3)	7178(2)	49.9(7)
C(6)	3329(4)	7091(3)	7809(2)	54.9(8)
C(7)	2109(3)	7171(2)	6896(2)	39.2(6)
N(8)	1934(2)	8315(2)	6278(2)	33.6(5)
C(9)	1505(3)	9424(2)	6899(2)	45.8(7)
C(10)	1321(3)	10539(3)	6145(3)	51.7(7)
C(11)	2750(4)	10734(2)	5451(2)	48.6(7)
C(12)	3166(3)	9533(2)	4860(2)	40.0(6)
C(13)	3361(3)	8488(2)	5677(2)	32.9(6)
C(14)	3707(3)	7165(2)	5287(2)	33.4(6)
C(15)	2072(4)	4091(3)	5933(2)	51.6(7)

Table 3. Atomic co-ordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for (**16b**) with e.s.d.s in parentheses. U_{eq} is defined in Table 2

	x	y	z	U_{eq}
N(1)	2860(2)	1166.5(7)	5730.1(12)	28.7(4)
C(2)	3488(2)	1656.1(9)	4963.2(14)	30.0(5)
C(3)	3995(2)	1390.5(11)	3790(2)	43.8(6)
C(4)	2973(3)	1662.8(11)	2882.2(15)	47.5(6)
C(5)	2454(2)	2276.4(10)	3452.2(15)	34.7(5)
C(6)	2425(2)	2930.8(10)	3280(2)	39.6(5)
C(7)	2239(2)	3260.5(10)	4374(2)	36.9(5)
O(7)	2152(2)	3843.7(7)	4615.4(13)	49.5(4)
O(8)	2218.9(14)	2775.9(6)	5197.9(10)	35.2(3)
C(9)	2253(2)	2123.8(9)	4671.3(15)	30.5(5)
C(10)	935(2)	1723.4(10)	5001(2)	37.1(5)
C(11)	1455(2)	1024.8(9)	5296(2)	31.7(5)
C(12)	623(2)	649.2(9)	6171(2)	37.3(5)
C(13)	1385(2)	9.0(10)	6519(2)	41.6(5)
C(14)	2878(2)	161.5(10)	6876(2)	42.2(5)
C(15)	3651(2)	558.2(10)	5980(2)	37.6(5)

Table 4. Interatomic distances (Å) and angles between interatomic vectors (°) for **(15b)** with e.s.d.s in parentheses.

C(1)-O(1)	1.200(3)	C(1)-O(2)	1.369(3)
C(1)-C(14)	1.507(3)	O(2)-C(3)	1.405(3)
C(3)-C(15)	1.315(4)	C(3)-C(4)	1.490(4)
C(4)-C(14)	1.535(3)	C(4)-C(5)	1.543(3)
C(4)-C(7)	1.571(3)	C(5)-C(6)	1.535(4)
C(6)-C(7)	1.558(4)	C(7)-N(8)	1.452(3)
N(8)-C(9)	1.463(3)	N(8)-C(13)	1.464(3)
C(9)-C(10)	1.525(4)	C(10)-C(11)	1.530(4)
C(11)-C(12)	1.524(4)	C(12)-C(13)	1.520(3)
C(13)-C(14)	1.526(3)		
O(1)-C(1)-O(2)	120.0(2)	O(1)-C(1)-C(14)	129.7(2)
O(2)-C(1)-C(14)	110.2(2)	C(1)-O(2)-C(3)	110.6(2)
C(15)-C(3)-O(2)	119.5(3)	C(15)-C(3)-C(4)	132.0(3)
O(2)-C(3)-C(4)	108.5(2)	C(3)-C(4)-C(14)	104.2(2)
C(3)-C(4)-C(5)	120.9(2)	C(14)-C(4)-C(5)	119.3(2)
C(3)-C(4)-C(7)	118.5(2)	C(14)-C(4)-C(7)	103.4(2)
C(5)-C(4)-C(7)	89.5(2)	C(6)-C(5)-C(4)	90.5(2)
C(5)-C(6)-C(7)	90.2(2)	N(8)-C(7)-C(6)	120.2(2)
N(8)-C(7)-C(4)	105.5(2)	C(6)-C(7)-C(4)	88.6(2)
C(7)-N(8)-C(9)	115.5(2)	C(7)-N(8)-C(13)	106.7(2)
C(9)-N(8)-C(13)	112.6(2)	N(8)-C(9)-C(10)	109.7(2)
C(9)-C(10)-C(11)	111.6(2)	C(12)-C(11)-C(10)	110.5(2)
C(13)-C(12)-C(11)	108.9(2)	N(8)-C(13)-C(12)	109.8(2)
N(8)-C(13)-C(14)	102.3(2)	C(12)-C(13)-C(14)	119.4(2)
C(1)-C(14)-C(13)	115.9(2)	C(1)-C(14)-C(4)	102.8(2)
C(13)-C(14)-C(4)	105.3(2)		

Table 5. Interatomic distances (Å) and angles between interatomic vectors (°) for **(16b)** with e.s.d.s in parentheses.

N(1)-C(15)	1.460(2)	N(1)-C(2)	1.465(2)
N(1)-C(11)	1.465(2)	C(2)-C(9)	1.544(3)
C(2)-C(3)	1.568(2)	C(3)-C(4)	1.553(3)
C(4)-C(5)	1.484(3)	C(5)-C(6)	1.322(3)
C(5)-C(9)	1.493(3)	C(6)-C(7)	1.468(3)
C(7)-O(7)	1.201(2)	C(7)-O(8)	1.377(2)
O(8)-C(9)	1.444(2)	C(9)-C(10)	1.542(3)
C(10)-C(11)	1.521(3)	C(11)-C(12)	1.508(3)
C(12)-C(13)	1.527(3)	C(13)-C(14)	1.519(3)
C(14)-C(15)	1.518(3)		
C(15)-N(1)-C(2)	118.0(2)	C(15)-N(1)-C(11)	112.7(2)
C(2)-N(1)-C(11)	106.58(14)	N(1)-C(2)-C(9)	103.3(2)
N(1)-C(2)-C(3)	117.0(2)	C(9)-C(2)-C(3)	103.92(14)
C(4)-C(3)-C(2)	107.8(2)	C(5)-C(4)-C(3)	100.5(2)
C(6)-C(5)-C(4)	138.6(2)	C(6)-C(5)-C(9)	110.5(2)
C(4)-C(5)-C(9)	108.5(2)	C(5)-C(6)-C(7)	107.9(2)
O(7)-C(7)-O(8)	120.6(2)	O(7)-C(7)-C(6)	130.9(2)
O(8)-C(7)-C(6)	108.5(2)	C(7)-O(8)-C(9)	108.92(14)
O(8)-C(9)-C(5)	103.87(14)	O(8)-C(9)-C(10)	109.8(2)
C(5)-C(9)-C(10)	117.2(2)	O(8)-C(9)-C(2)	117.7(2)
C(5)-C(9)-C(2)	104.1(2)	C(10)-C(9)-C(2)	104.7(2)
C(11)-C(10)-C(9)	105.5(2)	N(1)-C(11)-C(12)	109.7(2)
N(1)-C(11)-C(10)	101.7(2)	C(12)-C(11)-C(10)	116.3(2)
C(11)-C(12)-C(13)	110.6(2)	C(14)-C(13)-C(12)	110.8(2)
C(15)-C(14)-C(13)	111.4(2)	N(1)-C(15)-C(14)	108.9(2)

Acknowledgements: We thank Leeds University for support.

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(*Received in UK* 12 *May* 1997; *revised* 30 *May* 1997; *accepted* 5 *June* 1997)