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Two enamines derived from 1-*n*-alkyl-3-methylpyrazol-5-ones

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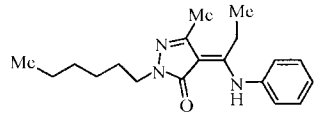
The first two crystal structures of enamines derived from 1-*n*-alkyl-3-methyl-5-pyrazolones, namely 1-(*n*-hexyl)-3-methyl-4-[1-(phenylamino)propylidene]-2-pyrazolin-5-one, $C_{19}H_{27}N_3O$, (I), and *N*,*N*′-bis{1-[1-(*n*-hexyl)-3-methyl-5-oxo-2-pyrazolin-4-ylidene]ethyl}hexane-1,6-diamine, $C_{30}H_{52}N_6O_2$, (II), are reported. The molecule of (II) lies about an inversion centre. Both (I) and (II) are stabilized by intramolecular N—H···O hydrogen bonding. This confirms previous results based on spectroscopic evidence alone.

Comment

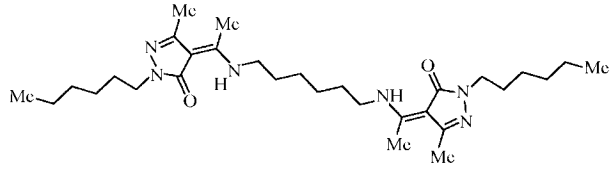
Pyrazolones constitute an important group of organic compounds (Wiley & Wiley, 1964; Elguero, 1984, 1996; Elnagdi *et al.*, 1985) for both theoretical and practical reasons (Kuznetsov *et al.*, 2001). Their application fields include analgesics and anti-inflammatory drugs (Kees *et al.*, 1996; Gürzov *et al.*, 2000), dyes (Venkataraman, 1952) and chelating extractants for several ions (Petinari *et al.*, 1999, 2000).

In addition, these compounds exhibit prototropic tautomerism, a subject that has attracted much attention (Elguero *et al.*, 1976; Wolfgang & Reiner, 1981; Nivorozhkin *et al.*, 1985; Uraev *et al.*, 1989, 2000; Gilchrist, 2001). In solution, the situation may become quite complex, since several equilibria among the different possible tautomers may be established. Such equilibria depend on the structure of the compound, its concentration, the nature of the solvent and the temperature (Kurkovskaya *et al.*, 1973). Further difficulties arise from inherent limitations in the spectroscopic techniques used in the study of these equilibria. In spite of this, ^{1}H, ^{13}C and ^{15}N NMR spectroscopies are still very powerful tools to undertake these studies in solution and are thus the most frequently used. Only in those cases where single crystals can be obtained does X-ray diffraction allow the unambiguous establishment of the structure of the tautomeric form (see, for example, O'Connell *et al.*, 1985; Uzoukwu *et al.*, 1993; Akama *et al.*, 1995; Holzer *et al.*, 2003).

Pyrazolones have been obtained by the same synthetic procedure, a condensation between an acylacetate and a hydrazine, for more than a century (Knorr, 1884; Varvouris *et al.*, 2001). In spite of the many advantages of 1-alkylpyrazolone derivatives (*e.g.* their greater solubility), most literature reports deal with 1-phenylpyrazolones or *N*-1 unsubstituted pyrazolones, and only recently has research aimed at synthesizing 1-alkylpyrazolones and derivatives been undertaken (Bartulin *et al.*, 1992, 1994; Belmar *et al.*, 1997, 1999), paying particular attention to the study of the tautomerism involved. These efforts finally led to the title enamines, (I) and (II), derived from 4-acyl-1-(*n*-hexyl)-3-methyl-5-pyrazolones (Belmar *et al.*, 2004).

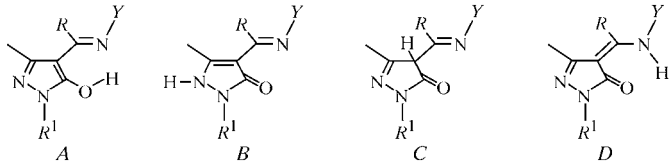


(I)



(II)

The fact that several tautomers can be envisaged for (I) and (II) left open the question of whether there was one single tautomer or a mixture of them in the solid state. Both situations have been shown to occur in related compounds (Foces-Foces *et al.*, 2000). Based upon ^{1}H, ^{13}C and ^{15}N NMR measurements, it was concluded at the time that in solution ($CDCl_3$), (I) and (II) exist mainly as enamines stabilized by an intramolecular hydrogen bond (case *D* in the scheme below). In addition, IR measurements had also suggested that the same tautomeric species was present in the solid state, though unfortunately no single crystals could be obtained to support this hypothesis. Furthermore, to our knowledge and to date, not one crystal structure of an enamine derived from an alkylpyrazolone has been reported, in contrast with the 1-aryl homologues, of which a few are known (see, for example, Singh *et al.*, 1995; Malhotra *et al.*, 1997; Wang *et al.*, 2003; Jiang *et al.*, 2004). In this paper, we present the first examples of two such enamine structures, (I) and (II).



Figs. 1 and 2 show molecular diagrams of the two structures, and Tables 1 and 3 give selected bond lengths. From an analysis of the values therein, it can be concluded that C1═O1 and C2═C5 are well defined double bonds, and that the shortest bond in the heterocycle (and, therefore, the one with

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enhanced double-bond character) is N2═C3. All these features point to the enamine character of both compounds. In addition, both structures share an intramolecular medium-strength hydrogen bond (N3—H3N···O1; Tables 2 and 4), all of which fully confirms the hypothesis previously raised on spectroscopic grounds alone.

The analogies between the two compounds go even further. The group of 17 atoms constituted by the heterocyclic ring, the alkyl substituent at N1 and the C atoms bound to atoms C3, C5 and N3 presents exactly the same conformation in both structures, with a least-squares fit (*SHELXTL*/*PC*; Sheldrick, 1994) of both moieties giving a mean deviation of 0.08 (1) Å (Fig. 3). Regarding their differences, the largest arises from the sustituents at N3, *viz*. a phenyl group in (I) and an *n*-hexyl chain in (II).

In fact, the alkyl chain lies on a symmetry centre in (II), thus defining a dimeric unit, in contrast with the monomeric character of (I). But even here, there is a striking similarity to be found. In (I), the terminal phenyl groups related by the symmetry operation $(1-x, 1-y, 1-z)$ appear connected by a π–π bond, with an interplanar distance of 3.60 (1) Å, a centre-to-centre distance of 3.78 (1) Å and a slippage angle of 17.7 (1)° (Fig. 1; for details, see Janiak, 2000). This second-order interaction also has the effect of defining some sort of dimer in (I), which thus becomes a structural unit fully comparable with that in (II): both are centrosymmetric, and present the terminal alkyl chains in a position *trans* to each other, at right angles to the line connecting their bases [the angle of the lateral chain to the N1···N1′ line is 90.2 (2)° in (I) and 92.9 (2)° in (II)].

Both 'dimers', however, have different shapes, which also promote different packing interactions. In (I), the two almost-perpendicular aromatic rings [dihedral angle = 80.1 (2)°] develop π–π interactions with their respective centrosymmetric counterparts, the first with that at $(\frac{1}{2}, \frac{1}{2}, \frac{1}{2})$ (the above-mentioned interaction between the phenyl groups which define the 'elementary dimers') and the second with that at $(0, 0, \frac{1}{2})$, connecting the aromatic system composed of the heterocyclic ring plus C1═O1 and C2═C5 with its $(-x, -y, 1-z)$ image, 3.50 (3) Å apart and with 4.20 (3) Å between centres, linking the former units together (Fig. 4). Structure (II) instead lacks any particular intermolecular contacts shorter than the usual van der Waals interactions. In spite of these dissimilar interactions, in both structures the terminal alkyl groups arrange in space in a similar way, as centrosymmetric pairs parallel to one another and at a nearest C···C distance of *ca* 4.20 Å.

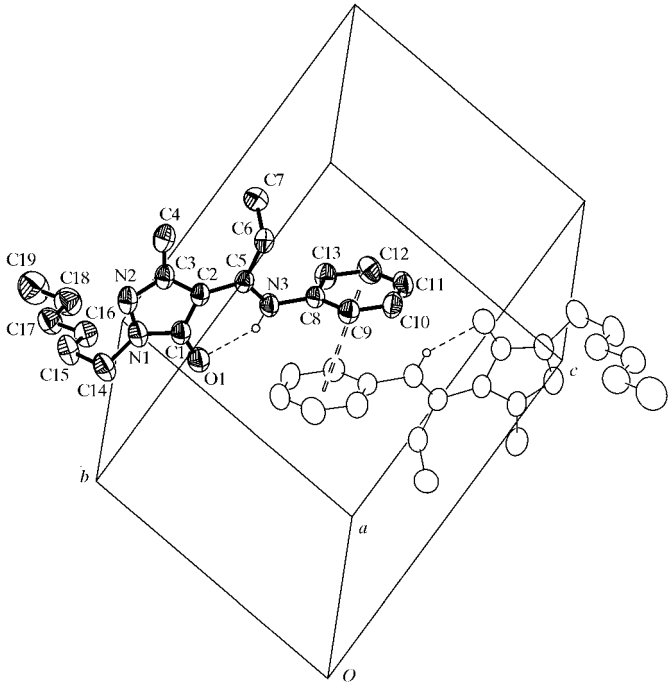

Figure 1
A molecular diagram for (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms have been omitted, apart from those involved in hydrogen bonds, which are shown as small spheres of arbitrary radii. Full ellipsoids denote the independent molecule and open ones the symmetry-related moiety at $(1-x, 1-y, 1-z)$, and double broken lines denote the π–π intaraction linking them. Single dashed lines denote the hydrogen bonds.

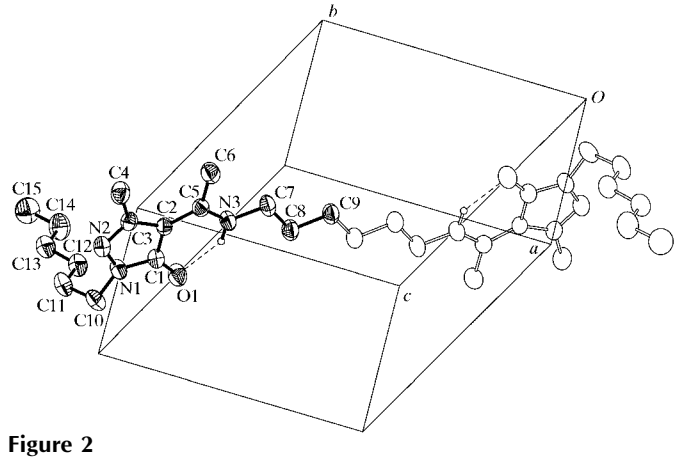

Figure 2
A molecular diagram for (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level and H atoms have been omitted, apart from those involved in hydrogen bonds, which are shown as small spheres of arbitrary radii. Full ellipsoids denote the independent half of the molecule and open ones the symmetry-related half generated by $(1-x, 1-y, 1-z)$. Single dashed lines denote the hydrogen bonds.

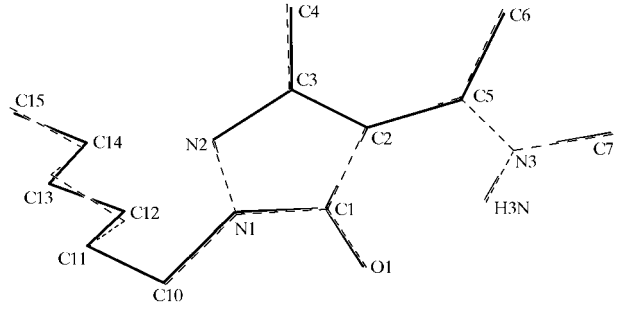

Figure 3
A superposition showing the similarities between the two nuclei of (I) and (II). All H atoms except H3N have been omitted for clarity.

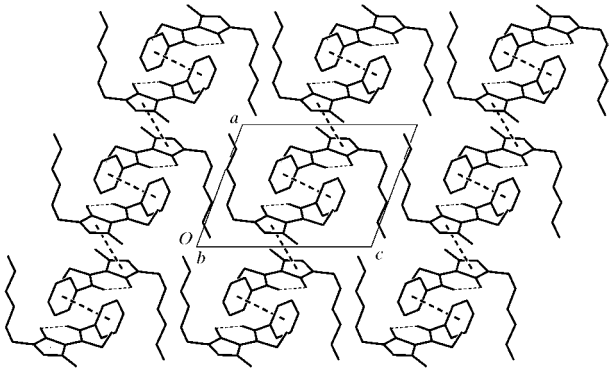

Figure 4
A packing diagram for (I), showing the leading interactions. For clarity, only H atoms involved in hydrogen bonding have been included.

Experimental

4-Acetyl-1-(*n*-hexyl)-3-methylpyrazol-5-ol and 1-(*n*-hexyl)-3-methyl-4-propionylpyrazol-5-ol were prepared using the usual methods of Jensen (1959) and Belmar *et al.* (1997). Each reaction was carried out using a magnetic stirrer in a flask provided with a Dean–Stark separator to separate the water produced during the reaction. Acylpyrazolone and the corresponding amine were dissolved in toluene and heated to reflux. The solution was then washed with brine until a neutral pH was achieved and then dried over Na_2SO_4. After filtration, the solution was concentrated in a rotary evaporator to obtain the crude enamine product. For the preparation of (I), 1-(*n*-hexyl)-3-methyl-4-propionylpyrazol-5-ol (1.00 g, 4.2 mmol) and aniline (0.4 ml, 4.2 mmol) in toluene (10 ml) were heated to reflux for 8 h. The crude product of (I) was crystallized from a heptane solution (yield 0.79 g, 60%; m.p. 367 K). Elemental analysis calculated: C 72.81, H 8.68, N 13.41%; found: C 72.70, H 8.70, N 13.50%. For the preparation of (II), 4-acetyl-1-(*n*-hexyl)-3-methylpyrazol-5-ol (3.00 g, 13.4 mmol) and 1,6-diaminohexane (0.93 g, 8.0 mmol) in toluene (20 ml) were heated to reflux for 10 h. The crude product of (II) was crystallized from a hexane–ethyl acetate mixture (9:1) (yield 1.42 g, 40%; m.p. 389 K). Elemental analysis calculated: C 68.14, H 9.91, N 15.89%; found: C 68.00, H 10.00, N 16.20%.

Compound (I)

Crystal data

$C_{19}H_{27}N_3O$
M_r = 313.44
Triclinic, $P\overline{1}$
a = 9.0221 (14) Å
b = 9.1427 (14) Å
c = 11.9077 (18) Å
α = 85.111 (2)°
β = 68.812 (2)°
γ = 78.911 (2)°
V = 898.6 (2) Å^3
Z = 2
D_x = 1.158 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2388 reflections
θ = 4.5–50.1°
μ = 0.07 mm^{-1}
T = 300 (2) K
Prism, yellow
0.32 × 0.14 × 0.12 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
5601 measured reflections
3132 independent reflections
2155 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 25.0°
$h = -10 \rightarrow 10$
$k = -10 \rightarrow 10$
$l = -14 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.158
S = 1.07
3132 reflections
211 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0865P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.004
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.28 e Å^{-3}

Table 1
Selected bond lengths (Å) for (I).

O1—C1	1.253 (2)	N3—C8	1.434 (2)
N1—C1	1.355 (2)	C1—C2	1.438 (3)
N1—N2	1.385 (2)	C2—C5	1.394 (2)
N1—C14	1.452 (3)	C2—C3	1.439 (2)
N2—C3	1.312 (2)	C3—C4	1.477 (3)
N3—C5	1.330 (2)		

Table 2
Hydrogen-bonding geometry (Å, °) for (I).

D—H···A	D—H	H···A	D···A	D—H···A
N3—H3N···O1	0.86	1.99	2.712 (2)	141

Compound (II)

Crystal data

$C_{30}H_{52}N_6O_2$
M_r = 528.78
Triclinic, $P\overline{1}$
a = 8.0168 (13) Å
b = 9.5029 (15) Å
c = 10.7032 (17) Å
α = 71.357 (2)°
β = 86.811 (2)°
γ = 85.112 (3)°
V = 769.5 (2) Å^3
Z = 1
D_x = 1.141 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1755 reflections
θ = 5.0–47.1°
μ = 0.07 mm^{-1}
T = 293 (2) K
Prism, yellow
0.28 × 0.16 × 0.10 mm

Data collection

Bruker SMART CCD area-detector diffractometer
φ and ω scans
5582 measured reflections
2689 independent reflections
1477 reflections with $I > 2\sigma(I)$
R_{int} = 0.056
θ_{max} = 25.0°
$h = -9 \rightarrow 9$
$k = -11 \rightarrow 11$
$l = -12 \rightarrow 12$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.048
$wR(F^2)$ = 0.152
S = 0.93
2689 reflections
174 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0659P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.007
$\Delta\rho_{max}$ = 0.25 e Å^{-3}
$\Delta\rho_{min}$ = −0.27 e Å^{-3}

Table 3
Selected bond lengths (Å) for (II).

O1—C1	1.248 (3)	N3—C5	1.313 (3)
N1—C1	1.360 (3)	N3—C7	1.456 (3)
N1—N2	1.385 (3)	C1—C2	1.435 (3)
N1—C10	1.447 (3)	C2—C5	1.399 (3)
N2—C3	1.312 (3)	C2—C3	1.433 (3)

Table 4
Hydrogen-bonding geometry (Å, °) for (II).

D—H···A	D—H	H···A	D···A	D—H···A
N3—H3N···O1	0.86	1.96	2.691 (3)	142

Even though all H atoms were clearly visible in difference Fourier maps (in particular those involved in intramolecular N—H···O bonds), for simplicity they were placed at their theoretical positions (C—H = 0.93–0.97 Å and N—H = 0.86 Å) and allowed to ride on their parent atoms, with U_{iso}(H) = 1.2U_{eq}(C,N) or 1.5U_{eq}(C) for methyl groups. The latter were allowed to rotate also. Full use of the CCDC package was made for searching in the Cambridge Structural Database (Allen, 2002).

For both compounds, data collection: *SMART* (Bruker, 2001); cell refinement: *SMART*; data reduction: *SAINT* (Bruker, 2000); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL*/*PC* (Sheldrick, 1994); software used to prepare material for publication: *SHELXTL*/*PC*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: OB1196). Services for accessing these data are described at the back of the journal.

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