

Synthesis by a Novel Cyclization Reaction and Crystal and Molecular Structure of 4-Ethyl-1-isopropyl-3-[(phenylcarbamoyl)methyl]-3-pyrroline-2-one

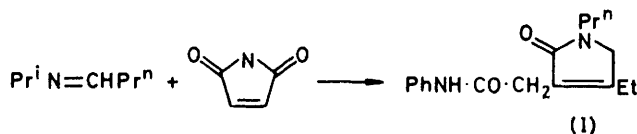
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The title compound (I) was synthesized by reaction of *N*-butylideneisopropylamine and *N*-phenylmaleimide at room temperature and without added catalysts: a reaction mechanism is suggested. The structure of (I) was unambiguously determined by X-ray diffraction analysis.

It has been previously found that Schiff bases copolymerize with acrylonitrile in the presence of radical initiators.¹ We attempted to copolymerize *N*-butylideneisopropylamine with *N*-phenylmaleimide. Unexpectedly, a novel cyclization reaction was found to occur.

Synthesis and X-Ray Characterization.—When *N*-butylideneisopropylamine and *N*-phenylmaleimide in 1:1 molar ratio were set aside in benzene solution at 60 °C for *ca.* 48 h, an addition product (I) was obtained in almost quantitative yield. Only traces of polymeric compounds were formed. By adding radical initiators, and under an inert-gas atmosphere, limited amounts of polymeric products were obtained, but were not further characterized. Large colourless crystals of the product (I) were recrystallized from benzene or ethanol, m.p. 119 °C.

Elemental analysis, molecular weight, and ¹³C and ¹H n.m.r. spectroscopy of (I) were consistent with a 1:1



addition compound. However, the molecular structure could not be completely resolved. A single-crystal X-ray diffraction analysis was therefore performed and unambiguously established (I) to be 4-ethyl-1-isopropyl-3-[(phenylcarbamoyl)methyl]-3-pyrroline-2-one.

The crystal structure consists in the packing of discrete molecules (Figure 1) linked by hydrogen bonds between N(2) and O(1) atoms belonging to pairs of molecules symmetrically related by the inversion centre at $\frac{1}{2}, \frac{1}{2}, 0$. The N...O distance [2.864(5) Å] is in agreement with those found^{2,3} in peptidic hydrogen bonds (2.85–2.95 Å). The angles N(2)–O(1')–C(9') † [130.3(7)°] and N(2)–H(N)–O(1') [172(3)°] indicate a non-strictly linear hydrogen bond.^{2,3}

Table 1 reports selected interatomic distances, together with bond and torsion angles. All observed distances are in good agreement with those found in structures containing similar groups^{3,4} except for the C–C distances involving the three methyl groups (mean

† Primed atoms belong to molecules related by a centre of inversion.

1.51 Å). The carbon atoms of these groups have thermal vibration parameters much larger than those of the atoms to which they are bonded [the largest root-mean-square displacements are C(1) 0.39, C(3) 0.33,

TABLE I

Selected interatomic distances (Å), bond angles (°), and torsion angles (°) for (I) with estimated standard deviations in parentheses

(a) Distances

O(1)–C(9)	1.243(5)	C(5)–C(6)	1.507(6)
O(2)–C(11)	1.230(5)	C(5)–C(8)	1.333(6)
N(1)–C(2)	1.465(5)	C(6)–C(7)	1.501(8)
N(1)–C(4)	1.441(5)	C(8)–C(9)	1.462(6)
N(1)–C(9)	1.359(5)	C(8)–C(10)	1.505(6)
N(2)–C(11)	1.369(5)	C(10)–C(11)	1.505(6)
N(2)–C(12)	1.405(5)	Mean C(Ph)–C(Ph)	1.387(7)
C(1)–C(2)	1.508(7)	N(2)–H(N)	1.02(6)
C(2)–C(3)	1.514(7)	Mean C–H	1.05(7)
C(4)–C(5)	1.507(6)		

(b) Angles

C(1)–C(2)–C(3)	114.1(8)	C(4)–N(1)–C(9)	111.0(6)
N(1)–C(4)–C(5)	103.3(5)	C(5)–C(6)–C(7)	113.6(8)
C(4)–C(5)–C(8)	108.9(6)	C(8)–C(10)–C(11)	111.7(6)
C(5)–C(8)–C(9)	109.5(6)	C(10)–C(11)–N(2)	114.2(7)
C(4)–N(1)–C(2)–C(1)	107.4(6)	C(11)–N(2)–C(12)	128.0(8)
Mean C–C–C(Ph ring)	120.0(9)		

(c) Torsion angles^a

N(1)–C(2)–C(1)–H(1)	61 ^b	N(2)–C(11)–C(10)–C(8)	155 ^c
N(1)–C(2)–C(3)–H(3b)	–54 ^b	C(2)–N(1)–C(9)–C(8)	–170 ^c
C(5)–C(6)–C(7)–H(7c)	–48 ^b	C(10)–C(11)–N(2)–C(12)	175 ^c
C(4)–N(1)–C(2)–C(1)	58 ^c	C(4)–C(5)–C(6)–C(7)	–78 ^c
C(9)–C(8)–C(10)–C(11)	–94 ^c		

^a The torsion angle A–B–C–D is taken to be positive if, when looking along the B–C bond, the far bond is rotated clockwise with respect to the near bond. ^b Mean σ 5°. ^c Mean σ 1.5°.

and C(7) 0.37 Å whereas for C(2) and C(6) they are 0.25 and 0.28 Å]. This indicates that the methyl groups 'ride' on adjacent carbon atoms, causing apparent shortening of the C–C bonds.⁵ The conformational non-rigidity of the ethyl and isopropyl groups makes this interpretation plausible.

The shortness of the distance between N(2) and C(12) (1.405 Å) may be explained by the partial non-saturated character of the bond between the two atoms.

In the bond angles there are moderate deviations from the canonical values which may be attributed both to ring closure and to the aforementioned conformational non-rigidity of the side-groups. Table 2 lists the princi-

pal best planes of the molecule and the atomic mean-square displacements are shown. The most relevant deviation from planarity is found in the amide groups, the ω angles⁶ being C(2)-N(1)-C(9)-C(8) 170 and C(10)-C(11)-N(2)-C(12) 175°. These deviations have been observed⁷ previously and theoretically justified.⁸

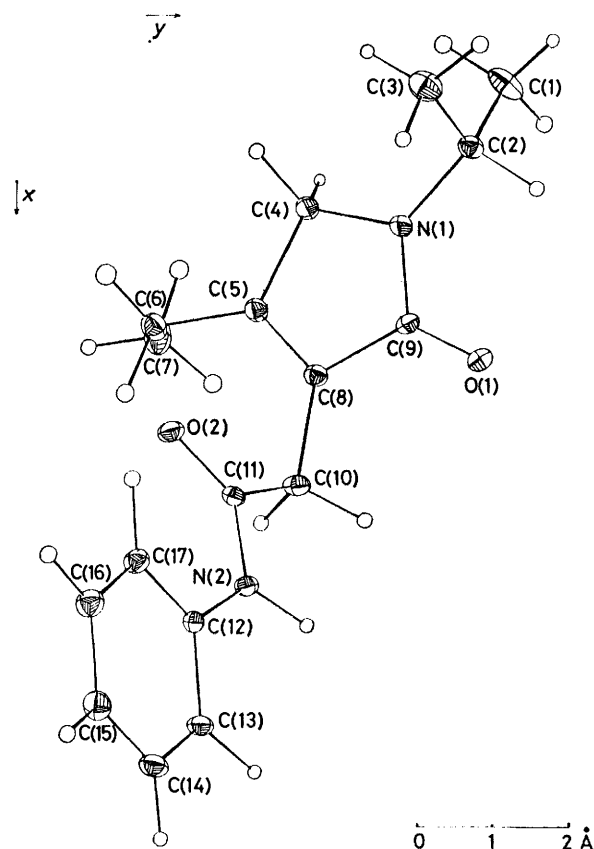


FIGURE 1 ORTEP drawing of the molecule of (I) viewed along the c axis. Hydrogen atoms are represented by open circles

The three methyl groups assume the usual staggered conformation. Figure 2 shows the crystal packing with an indication of the shortest intermolecular distances. As shown, there are only a few contacts shorter than the sum of the van der Waals radii. This indicates that in spite of the presence of hydrogen bonds, the molecular structure is scarcely influenced by the crystal packing.

N.m.r. Characterization.—The ^1H and ^{13}C n.m.r. spectra, measured for chloroform solutions, are in good agreement with the solid state structure as determined by X-ray diffraction. The ^1H n.m.r. spectrum was assigned as follows (chemical shift, relative intensity, multiplicity): isopropyl δ 1.17 (1 H, d), 4.39 (6 H, septet); ethyl 1.08 (3 H, t), 2.44 (2 H, q); phenyl ring 6.97 (1 H, t), 7.22 (2 H, t), 7.50 (2 H, d); methylene C(10) 3.35 (2 H, s); methylene C(4) 3.73 (2, s); H(N) 9.99 (1 H, s).

In order to ascertain the presence of the hydrogen bond between the amide and the carbonyl groups in

TABLE 2

Principal best planes in the molecule with relative mean-square displacements (δ) in Å. Deviations of the relevant atoms from the plane are given in square brackets

A	B	C	D	δ
Plane (1): C(12)—C(17)				
-0.172 86	0.818 87	0.547 32	5.648 00	0.005
[C(12) 0.007, C(13) -0.008, C(14) 0.006, C(15) -0.003, C(16) 0.002, C(17) -0.004, N(2) 0.041]				
Plane (2): C(12)—(17), H(13)—(17)				
-0.18132	0.821 26	0.54 098	5.575 20	0.036
[H(13) 0.06, H(14) -0.05, H(15) 0.08, H(16) -0.01, H(17) -0.00]				
Plane (3): O(1), N(1), C(2), C(4), C(8), C(9)				
-0.190 12	-0.488 74	0.851 46	-6.598 82	0.048
[O(1) -0.02, N(1) -0.07, C(2) 0.07, C(4) -0.04, C(8) 0.06, C(9) -0.02]				
Plane (4): O(2), N(2), C(10)—(12), H(N)				
-0.448 17	0.683 33	0.576 37	2.293 90	0.049
[O(2) 0.04, N(2) -0.02, C(10) -0.06, C(11) 0.02, C(12) -0.05, H(N) 0.07]				
Plane (5): N(1), C(4), C(5), C(8), C(9)				
-0.233 06	-0.449 51	0.862 34	-6.443 72	-0.002
[N(1) -0.002, C(4) 0.001, C(5) 0.000, C(8) -0.002, C(9) 0.003, O(1) 0.022, C(6) 0.011, C(10) 0.066]				
Plane (6): C(4)—(6), C(8)—(10)				
-0.249 43	-0.446 35	0.859 39	-6.484 73	0.015
[C(4) 0.02, C(5) -0.01, C(6) -0.00, C(8) -0.02, C(9) -0.01, C(10) 0.02]				

The equations are in the form $Ax + By + Cz = D$, where x , y , and z are orthogonal Å co-ordinates.

solution, the temperature coefficient of the amide proton was measured in deuteriodimethyl sulphoxide in the temperature interval 20–80 °C. The obtained value of $-5.10 \cdot 10^{-3}$ p.p.m. per °C is within the characteristic range

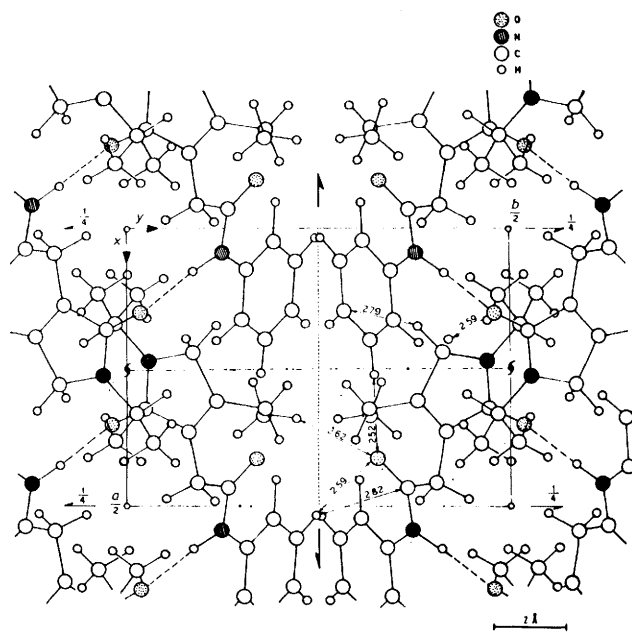


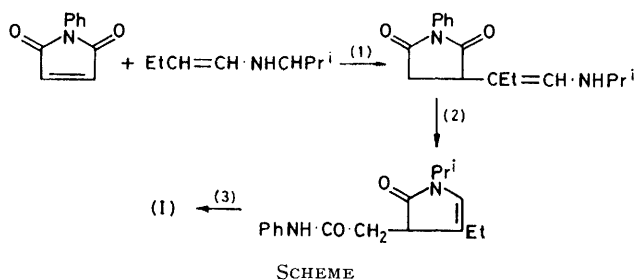
FIGURE 2 The molecular packing of (I) viewed along the c axis with the shortest contacts indicated. Dashed lines represent hydrogen bonds

of a solvated amide group, for which $\Delta\delta_{\text{NH}}/\Delta T > |3 \cdot 10^{-3}|$ p.p.m. per °C, which fact suggests that the NH proton is exposed to the solvent and free of hydrogen bonds. The molecule in dimethyl sulphoxide solution is most likely present in the monomeric form.

In the broad-band ^{13}C proton-decoupled spectrum fourteen signals were resolved of which three have double intensity, because of symmetry. The aliphatic region of the ^{13}C off-resonance decoupled spectrum consists of two quartets (δ 13.2 and 20.8) corresponding to methyl carbons C(7) and C(1)=C(3); three triplets (δ 20.9, 34.5, and 48.4) due to the methylene C(6), C(10), and C(4); and finally one doublet (δ 48.0) due to the methylene C(2).

In the aromatic region the spectrum shows one singlet (δ 138.8) due to C(12), and three doublets (δ 119.4, 123.5, and 128.7) corresponding to C(13)=C(17), C(16)=C(14), and C(15). Furthermore, the spectrum shows four singlets assigned to the olefinic carbon atoms C(8) and C(5) (δ 126.1 and 154.9) and to the two amidic carbonyls (δ 167.6 and 172.1).

Mechanism of the Reaction.—We suggest a reaction mechanism (see Scheme) which involves addition of the Schiff base, in its tautomeric enaminic form, to *N*-phenylmaleimide (step 1), followed by intramolecular *trans*-acylation (step 2) and migration (step 3) of the



double bond to the 3,4-position. It has been shown previously^{9,10} that in some cyclization reactions Schiff bases can react in the tautomeric enaminic form.

EXPERIMENTAL

The synthesis of (I) was performed as described in the text. N.m.r. spectra were recorded at 27 °C with an HFX 90 Bruker spectrometer working at 90 and 22.628 MHz for ^1H and ^{13}C . Signal positions were measured relative to tetramethylsilane as internal standard; 0.2M-solutions in deuteriochloroform and [$^2\text{H}_6$]dimethyl sulphoxide were employed. The ^1H spectrum was run in the frequency sweep mode. ^{13}C Spectra were obtained in the pulsed FT mode with broad-band and with off-resonance proton decoupling.

Single crystals suitable for X-ray measurements were obtained by slow crystallization from benzene at room temperature. X-Ray measurements were performed on crystals sealed in low-absorption glass capillaries (diam. 0.3 mm), by use of a Philips PW 1100 single-crystal automatic diffractometer. Unit-cell and crystal symmetries were determined by use of the standard control program of the PW 1100 system,¹¹ for a randomly oriented crystal. Accu-

rate unit-cell parameters were obtained by a least-squares method from the accurate positioning of the $h00$, $0k0$, and $00l$ reflections with $8^\circ < \theta < 20^\circ$.

Crystal Data.— $\text{C}_{17}\text{H}_{22}\text{N}_2\text{O}_2$, $M = 286.38$. Orthorhombic, $a = 21.411(8)$, $b = 15.678(4)$, $c = 9.653(2)$ Å, $U = 2240(2)$ Å³, $F(000) = 1232$, $D_c = 1.17$ g cm⁻³, $Z = 8$. Space group *Pbca* (No. 61). Mo- K_α radiation, $\lambda = 0.71069$ Å; $\mu(\text{Mo-}K_\alpha) = 0.83$ cm⁻¹.

Integrated intensities were measured (graphite-monochromated Mo- K_α radiation) for a crystal $0.7 \times 0.3 \times 0.3$ mm by ω - 2θ scan with a scan speed of 2.4° min⁻¹ scan width of 1 – 2° in the range θ 3 – 25° . Of 2857 reflections measured 1202 were considered observed, having $I > 3\sigma(I)$. Intensities were corrected for Lorentz and polarization effects but not for absorption. The structure was solved by direct methods by use of MULTAN.¹² The 170 reflections with $E > 1.92$ and 1079 phase relationships were used ($E^3 > 7.49$). A starting set with three origin-fixing, four arbitrary-phase, and one fixed-phase reflections (Σ_1 formula, $p > 99\%$) was employed. For each of the sixteen different solutions the tangent formula was used for attributing and refining phases. The solution with the highest figure-of-merit gave a subsequent E map with 24 peaks, 21 of which corresponded to acceptable atom positions. The structure was refined by block-diagonal least-squares methods,¹³ the

TABLE 3

Atom fractional co-ordinates ($\times 10^3$ for H, others $\times 10^4$) for (I), with estimated standard deviations in parentheses

	x/a	y/b	z/c
O(1)	3 523(2)	5 207(1)	–148(3)
O(2)	4 137(2)	3 307(1)	726(3)
N(1)	2 397(2)	4 718(2)	–1 237(4)
N(2)	5 432(2)	3 772(2)	1 037(4)
C(1)	1 197(4)	5 359(3)	–1 981(6)
C(2)	1 730(3)	5 148(2)	–768(5)
C(3)	1 218(4)	4 867(3)	408(6)
C(4)	2 249(3)	4 141(2)	–1 965(5)
C(5)	3 111(2)	3 829(2)	–1 948(4)
C(6)	3 257(3)	3 201(2)	–2 597(5)
C(7)	3 334(4)	3 224(3)	–4 147(6)
C(8)	3 661(3)	4 197(2)	–1 284(4)
C(9)	3 222(3)	4 762(2)	–818(4)
C(10)	4 582(3)	4 080(2)	–933(4)
C(11)	4 674(2)	3 690(2)	356(5)
C(12)	5 735(3)	3 448(2)	2 203(4)
C(13)	6 613(3)	3 493(2)	2 479(5)
C(14)	6 951(3)	3 205(2)	3 630(5)
C(15)	6 448(3)	2 857(3)	4 512(5)
C(16)	5 582(3)	2 811(3)	4 231(6)
C(17)	5 225(3)	3 098(2)	3 082(5)
H(N)	577(4)	414(3)	64(6)
H(1a)	153(4)	560(3)	–273(7)
H(1b)	87(4)	498(3)	–239(7)
H(1c)	83(3)	565(2)	–160(5)
H(2)	208(4)	555(3)	–38(6)
H(3a)	93(4)	451(3)	–6(6)
H(3b)	167(4)	473(3)	121(6)
H(3c)	87(4)	520(3)	92(7)
H(4a)	177(4)	383(3)	–136(6)
H(4b)	201(3)	422(2)	–296(5)
H(6a)	382(4)	302(3)	–216(7)
H(6b)	282(5)	291(4)	–228(8)
H(7a)	343(4)	280(2)	–453(6)
H(7b)	277(5)	336(3)	–450(8)
H(7c)	374(4)	356(3)	–448(7)
H(10a)	488(4)	450(3)	–85(6)
H(10b)	490(4)	386(3)	–182(6)
H(13)	700(4)	382(3)	172(6)
H(14)	757(4)	325(3)	375(6)
H(15)	669(4)	267(3)	546(7)
H(16)	517(4)	256(3)	488(7)
H(17)	453(4)	307(3)	280(6)

function minimized being $\sum_{hkl} (F_o - F_c)^2 \times w$, with the weighting scheme $w^{-1} = 1 + 0.068 F_o$.

After four cycles with isotropic and four with anisotropic thermal vibration parameters the conventional R factor decreased to 0.087. A difference electron-density map revealed peaks ranging from 0.4 to 0.2 eÅ⁻³, all corresponding to the expected hydrogen-atom positions. A further four cycles of refinement (two cycles refining hydrogen atoms only and two cycles refining only the heavy atoms) reduced R to 0.048, the mean shift being 0.3σ.

The isotropic thermal factors for the hydrogen atoms were assumed to be the same as those of the heavy atoms to which they were bonded. Table 3 lists atomic fractional co-ordinates, while the corresponding thermal vibrational parameters together with a list of observed and calculated structure factors are available in Supplementary Publication No. SUP 22510 (24 pp., 1 microfiche).*

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* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1978, Index issue.

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