# The cyanocarbonyl group: synthesis and crystal structure of an imidazole carbonyl cyanide, $C_{12}N_5OH_{17}$

D. W. Jones,<sup>(1)</sup>\* M. Motevalli,<sup>(2)</sup> G. Shaw,<sup>(1)</sup> and J. D. Shaw<sup>(1)</sup>

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1-t-Butyl-5-N-(dimethylaminomethylene)aminoimidazole-4-carbonyl cyanide (BUNDAMIC) is the first acyl cyanide to be synthesized from an imidazole-4-carboxylic acid, diethylphosphorocyanidate, and triethylamine and its structure determined by x-ray crystallography. It crystallizes with four molecules in the monoclinic space group C2/m with a = 17.824(2), b = 6.784(2), c = 11.039(2) Å, and  $\beta = 96.17(1)^\circ$ ;  $\underline{R} = 0.036$  over 1086 unique x-ray reflections. The cyanocarbonyl group is nearly linear,  $C-C \equiv N$  angle  $174.4(3)^\circ$ , with dimensions  $C \equiv N$ , 1.137(3); C-C, 1.493(3); and C = O, 1.224(3) Å. The imidazole ring, in the mirror plane, has a lengthened C4 = C5 bond of 1.421(3) Å, and there is a short ring-closing approach,  $H \cdots O6 = 2.07$  Å, between the methyleneamino hydrogen and the carbonyl oxygen.

**KEY WORDS:** Acylcyanide; cyanocarbonyl; imidazole; carbonyl cyanide.

## Introduction

X-ray crystallographic determinations of the structures of compounds containing the cyanocarbonyl (or acylcyanide) group are uncommon and few purely organic carbonyl cyanides have been prepared.<sup>1-4</sup> A crystalline imidazole-4-carbonyl cyanide is of particular interest as a model in a route for the synthesis of Coformycin-like antibiotics and as an intermediate in the preparation of potential enzymatic inhibitors of carcinogenic pathways. 1-t-Butyl-5-N-(dimethylaminomethylene) amino imidazole-4-carbonyl cyanide (BUNDAMIC), as briefly reported earlier,<sup>2</sup> also has a surprisingly strong yellow color. Accordingly, its preparation and the analytical data for intermediates are given in some detail. A single-crystal x-ray analysis has been carried out to confirm the presence of the acylcyanide moeity and to observe any effect on the dimensions of the imidazole ring.

### Experimental

## **Preparations**

The ester benzyl 5-amino-1-t-butylimidazole-4carboxylate (1), prepared from benzyl-2-amino-2-cyanoacetate, triethyl orthoformate, and t-butylamine, crystallized from ethylacetate as needles, m.p. 161°C, with the following analytical and spectroscopic data: Found: C, 65.5; H, 7.05; N, 15.15%; M<sup>+</sup> 243. C<sub>15</sub>H<sub>19</sub>N<sub>3</sub>O<sub>2</sub> requires C, 65.95; H, 7.0; N, 15.35%; M, 243.  $\delta_{\rm H}$  (CDCl<sub>3</sub>), 1.65  $(9H,s,CMe_3),$ 5.15 (2H,brs,NH<sub>2</sub>), 5.45 (2H,s,OCH<sub>2</sub>), 7.25 (s,1H,2-H), 7.45 (5H,m,Ar). A 0.1 M solution of 1 in toluene was refluxed with 0.11 M dimethylformamide dimethylacetal and the filtered solution evaporated to yield a solid, m.p. 87°C, benzyl 1-t-butyl-5-N-(dimethylaminomethylene) imidazole (2): (Found: C, 66.0; H, 7.55; N, 16.85%; M<sup>+</sup> 328.  $C_{18}H_{24}N_4O_2$  requires C, 65.85; H, 7.35; N, 17.05%, M, 328);  $\delta_{H}$  (d<sub>6</sub> dmso) 1.56  $(9H,s,CMe_3),$ 2.86-2.92 (6H,2s,NMe<sub>2</sub>), 5.15 (2H,s,OCH<sub>2</sub>), 7.39 (5H,s,Ar), 7.42 (1H,s,H-2), 7.81 (1H,s,CH:N). 31g (94.5 mM) of 2 in dry ethyl acetate (180 ml) solution was shaken with 10% Pd-C (2.4 g) in a hydrogen atmosphere for 16 h, filtered and

<sup>&</sup>lt;sup>(1)</sup> Chemistry & Chemical Technology, University of Bradford, Richmond Road, West Yorks, BD7 1DP, United Kingdom.

<sup>&</sup>lt;sup>(2)</sup> Department of Chemistry, Queen Mary College, London, E1 4NS, United Kingdom.

<sup>\*</sup> To whom correspondence should be addressed.

evaporated to dryness at 30°C to give the carboxylic acid (3) as a gum (22.5 g, 100% yield) (Found: C, 55.6; H, 7.8; N, 23.2%; M<sup>+</sup> 238. C<sub>11</sub>H<sub>18</sub>N<sub>4</sub>O<sub>2</sub> requires C, 55.45, H, 7.6; N, 23.5%; M, 238);  $\delta_{\rm H}$  (d<sub>6</sub> dmso) 1.6 (9H,s,CMe<sub>3</sub>), 2.9–3.0 (6H,d,NMe<sub>2</sub>), 7.4 (1H,s, H-2).

To a stirred solution of 3 (2.38 g, 10 mM) in ethyl acetate (25 ml) was added 1.8 g (11 mM) of diethyl phosphorocyanidate (DEPC) and triethylamine (1.5 ml, 15 mM). The mixture, set aside at 0°C for 2 h, then at room temperature for 40 h, turned bright yellow. After chromatography the acylcyanide (BUNDAMIC) (1.53 g, 62%) crystallized from ethyl acetate-light petroleum: m.p. 149°C. Found: C, 58.3; H, 7.0; N, 28.2%; M<sup>+</sup> 247. C<sub>12</sub>H<sub>17</sub>N<sub>5</sub>O requires C, 58.3; H, 6.95; Ν, 28.35%; Μ<sup>+</sup> 247; λ max 248 (ε 18450), 392 (ε 5970) nM in methanol.  $\delta_{\rm H}$  (CDCl<sub>3</sub>) 1.7 (9H,s,CMe<sub>3</sub>), 3.1 - 3.3 $(6H,d,NMe_2)$  7.4 (1H,s,2-H), 8.65. (1H,s,N:CH), δ<sub>C</sub> (CDCl<sub>3</sub>) 160 (CO), 158 (N:CH), 154 (C-4), 134 (C-2), 127 (C-5), 115.5 (CN), 58 (C:), 41,35 (NMe<sub>2</sub>), 29 (Me<sub>3</sub>). <sup>1</sup>H NMR spectra were recorded at 360 MHz and <sup>13</sup>C spectra at 90.56 MHz on a Brüker Spectrospin instrument.

## X-ray measurements and structure solution

Systematic absences derived from rotation and Weissenberg photographs indicated one of the three monoclinic space groups, C2, C2/m, or Cm. A total of 1415 reflections (excluding standards, checked hourly), collected diffractometrically, reduced to 1086 unique reflections with  $|Fo| > 3\sigma$  |Fo|; crystal data are in Table 1.

Structure solution for the nonhydrogen atoms was achieved by direct methods (MULTAN 80<sup>5</sup> and SHELX 97)<sup>7</sup>. Although refinement in C2 went down to R = 0.046, it became evident that the centrosymmetric space group C2/m was more appropriate.<sup>6</sup> H atoms were inserted (riding model) and anisotropic refinement,<sup>7</sup> in C2/m, ultimately reached R = 0.036. Table 2 gives the refined positional parameters together with their  $U_{eq}$  values. Figure 1 shows the crystallographic atom numbering and thermal motion ellipsoids.

#### **Results and discussion**

The molecule is essentially planar in the (x z) plane (020 is an intense reflection). An intramolecular hydrogen bond links the N=CH-NMe<sub>2</sub> hydrogen with the carbonyl oxygen (C7-H7  $\cdots$  O12 = 157°; C7  $\cdots$ 

O12 = 2.95 Å) so as to close the O=C-C4=C5-N=C ring. The imidazole ring in BUNDAMIC is even more planar than in imidazole itself.<sup>8</sup> By contrast with the ring in a nucleoside such as 5-amino-1-(2,3-*O*-isopropylidene- $\beta$ -D-ribofurano-syl) imidazole-4-carboxylate(BARIC),<sup>1</sup> substituents C, C=O and N at positions 1,4, and 5 also all lie in the plane.

Table 3 lists the bond lengths and apparent esd's for nonhydrogen atoms in BUNDAMIC, together with the corresponding bond angles (apparent esd's  $\leq 0.2^{\circ}$ ). Bond lengths for the imidazole nucleus closely mirror those in imidazole and imidazole nucleosides except for the C4 = C5 which, at 1.421(3) Å, is 0.04 Å longer than in either benzyl  $(BARIC)^{1}$  or ethyl (EARIC) 5amino-1,2,3-O-isopropylidene-B-D-ribosylimidazole 4-carboxylate,<sup>9</sup> presumably as a consequence of conjugation with the carbonyl cyanide group. Also, the proximity (2.07 Å) of the carbonyl oxygen O6 to the aminomethylene hydrogen is associated with angles  $C4 - \delta C5 - N6 = 137.1 (2)^{\circ}$  and C5 - C4 - C11 =132.2(2)° in BUNDAMIC that are each several degrees larger than in BARIC and even than in EARIC (in which, unusually, the chelate hydrogen bond from a 5-amino hydrogen goes to the ethoxy oxygen, rather than (as in BARIC and ADIMIC<sup>10</sup>) the carbonyl). Angle C4-C11-O12 in BUNDAMIC is opened to  $130.0(2)^{\circ}$ , much the largest angle at this cyanocarbonyl carbon. As in most imidazole compounds, the largest interior bond angle is N3-C2-N1 (113.4 (2)°); the next is C5-C4-N3 = 109.6 (2)° and the others are close to 106°. Thus, with the enhanced stability of the almost closed ring, conjugation evidently results in lengthening of the formal double bond C4=C5 and slight shortening of the formal single bond C4-C11 by comparison with the corresponding dimensions in BARIC and EARIC and other 5-aminoimidazole compounds. This may, in turn, be associated with the intense yellow color of crystals and solution.

Most dimensions of the CO·C $\equiv$ N group in BUN-DAMIC, C11-O12 = 1.224(3), C11-C13 = 1.493(3), C13 $\equiv$ N14 = 1.137(3) Å, angle C11-C13 $\equiv$ N14 = 174.4(3)°, are closely similar to the corresponding dimensions in the few purely organic compounds containing the group that have been determined: Cyanoformamide,<sup>11</sup> Z-3-(benzoxanol-2-ylidine)-3-phenyl-2-oxo-1-propanenitrile<sup>3</sup> (WEVZIG), and 1-cyanocarbonyl-4-(4-diethylaminophenylamino) naphthalene<sup>4</sup> (ZIZNAX). BUNDAMIC's C $\equiv$ N bond of 1.137(3) Å is slightly shorter than the 1.15 Å typical of a simple organic cyanide, while its carbonyl bond

Compound	C <sub>12</sub> N <sub>5</sub> OH <sub>17</sub>	Max.crystal dimmm	$0.7 \times 0.5 \times 0.2$
Color, Shape	Bright yellow prisms	Scan width	$0.9 \pm 0.14 \tan \theta$
Formula weight	247.3	Standard reflections	806;406;514
Space group	C2/m	Decay of standards	<5%
Temp., °C	25	20 range, deg	$2 \le 2\theta \le 70$
Cell constants <sup>a</sup>		Range of h, k, l	$\pm 21, +8, +13$
<i>a</i> , Å	17.824(2)	Unique reflections obs. <sup>b</sup>	1086
<i>b</i> , Å	6.784(2)	Cell Volume, Å <sup>3</sup>	1327.1(5)
<i>c</i> , Å	11.039(2)	Structure solution	SHELXL-97
β, deg	96.17(1)	Structure refinement	SHELXL-97
Formula units	4	$D_x$ , g cm <sup>-3</sup>	1.23
$D_{\rm o}$ , g cm <sup>-3</sup>	1.23 (KI flotation)		
$\mu_{calc}$ cm <sup>-1</sup>	10.5	Scan	ω/2θ
Diffractometer	Enraf Nonius CAD4F	$R[F > 2\sigma(F)]$	0.036
		R (all data)	0.048
Radiation, graphite monochromator	$CuK\alpha(\lambda = 1.54184 \text{ Å})$	$wR(F^2)$	0.108
F(0,0,0)	528	Largest feature on final difference map	0.16 Å <sup>3</sup>

Table 1. Crystal data and summary of intensity data collection and structure refinement

<sup>*a*</sup> Least-squares refinement of  $(\sin\theta/\lambda)^2$  values for 15 reflections  $25 > 2\theta > 35^\circ$ .

<sup>b</sup> Corrections: Lorenz-polarization; extinction 0.0026(4).

of 1.224(3) Å is shorter than in WEVZIG and ZIZNAX and nearly as short as in cyanoformamide. When the CO·CN group is coordinated, as in the copper complex  $[Cu(en(bu)_2(C_2N_2)_2)]^{12}$ , where  $en(bu)_2$  is a Schiff base, the cyanoimino substituent  $C1 - C6 \equiv N2$  of the organometallic ring has lengths 1.47(1) and 1.13(1) Å for the moeity, while the corresponding lengths are 1.461(5) and 1.142(6) Å in bis (3-cyanoiminomethyl)-2,4-pentanedionato)Ni(II) or [Ni(acac  $C_2N_2)_2$ ].<sup>13</sup>

Table 2. Atomic coordinates (×10<sup>4</sup>) and equivalent isotropic displacement parameters (Å<sup>2</sup> × 10<sup>3</sup>)<sup>a</sup>

	х	у	Z	$U_{eq}$
N(6)	2765(1)	0	6935(1)	55(1)
N(3)	1051(1)	0	4815(2)	64(1)
N(1)	1443(1)	0	6802(1)	53(1)
C(7)	3395(1)	0	6457(2)	57(1)
N(8)	4056(1)	0	7134(2)	61(1)
O(12)	2903(1)	0	3817(1)	71(1)
C(4)	1834(1)	0	4970(2)	53(1)
C(11)	2225(1)	0	3909(2)	56(1)
C(15)	1388(1)	0	8154(2)	56(1)
C(13)	1713(1)	0	2747(2)	62(1)
C(5)	2091(1)	0	6234(2)	50(1)
C(2)	848(1)	0	5910(2)	64(1)
C(9)	4111(2)	0	8454(2)	72(1)
C(17)	564(2)	0	8376(2)	80(1)
C(10)	4744(2)	0	6546(2)	85(1)
N(14)	1374(2)	0	1812(2)	80(1)
C(16)	1759(2)	1864(3)	8698(1)	79(1)

<sup>*a*</sup>  $U_{eq}$  is defined as one-third of the trace of the orthogonalized  $U_{u}$  tensor.

In these, the carbonyl oxygen is coordinated to the metal atom (C=O 1.33(1) and 1.283(4) Å, respectively, both longer than the more usual 1.224(3) Å in BUNDAMIC) and in the planar cyanoformamide<sup>11</sup>, which has the cyano C-C = 1.477(8) Å. In the adduct titanium tetrachloride-ethylcyanoformate,<sup>14</sup> on the other hand, with cyano nitrogen coordinated to the metal at one end of an NCC=OOC<sub>2</sub>H<sub>5</sub> chain, the C-C=N bond lengths are 1.505 (3) and 1.112(3) Å, very close to the 1.493(3) and 1.137(3) Å in BUN-DAMIC; the short C=N bond in the adduct has been



Fig. 1. Thermal motion ellipsoids, showing crystallograhic atom numbering.

Table 3. Bond Lengths [Å] and Angles [°]

N(6) - C(7)	1 292(3)
N(6) = C(5)	1.357(3)
N(3) - C(2)	1.299(3)
N(3) = C(4)	1 387(3)
N(1) = C(2)	1.367(3)
N(1) = C(2) N(1) = C(5)	1.307(3)
N(1) = C(15)	1.572(3)
N(1) = C(13) C(7) = N(8)	1.307(2)
C(7) = N(6)	1.323(3)
N(8) = C(10)	1.448(3)
N(8) = C(9)	1.449(3)
O(12) = O(11)	1.224(3)
C(4) = C(5)	1.421(3)
C(4) = C(11)	1.425(3)
C(11) - C(13)	1.493(3)
C(15) - C(17)	1.514(3)
C(15) - C(16)	1.521(2)
C(15) - C(16) # 1	1.521(2)
C(13) - N(14)	1.137(3)
C(7) = N(6) = C(5)	121.50 (17)
C(2) = N(3) = C(4)	121.30(17) 105.21(18)
C(2) = N(3) = C(4)	105.21 (16) 107.22 (16)
C(2) = N(1) - C(15)	107.32 (10)
C(2) = N(1) = C(15)	123.01 (10)
V(3) = N(1) = U(13)	120.87 (17)
N(0) = C(7) = N(0)	121.92 (19)
C(7) = N(8) = C(10)	119,42 (19)
C(1) = N(8) = C(9)	121.82 (19)
U(10) = N(8) = U(9)	118.77 (19)
N(3) - C(4) - C(5)	109.59 (18)
N(3) = C(4) = C(11)	118.19 (18)
C(5) = C(4) = C(11)	132.2 (2)
O(12) - C(11) - C(4)	130.0 (2)
O(12) - C(11) - C(13)	116.49 (18)
C(4) = C(11) = C(13)	113.5 (2)
N(1) - C(15) - C(17)	109.14 (17)
N(1) - C(15) - C(16)	108.64 (11)
C(17) - C(15) - C(16)	108.91 (12)
N(1) - C(15) - C(16) #1	108.64 (11)
C(17) - C(15) - C(16) #1	108.91 (12)
C(16) - C(15) - C(16) #1	112.6 (2)
N(14) - C(13) - C(11)	174.4 (3)
N(6) = C(5) = N(1)	118.48 (16)
N(6) - C(5) - C(4)	137.1 (2)
N(1) = C(5) = C(4)	104.44 (18)
N(3) = C(2) = N(1)	113.4 (2)

<sup>*a*</sup> Symmetry transformations used to generate equivalent atoms: #  $1 x_1 = y_1 z_2$ .

attributed to diminished  $\pi$ -electron-lone-pair repulsion.

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**Supplementary material.** Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-1003/5384. Copies of available material can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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