Metal-catalysed Highly Selective Synthesis of α-Amido-β-cyanoenaminones from Acetoacetamides and Cyanogen: Physicochemical Properties and Solid-state Conversion into Pyrroline Isomers

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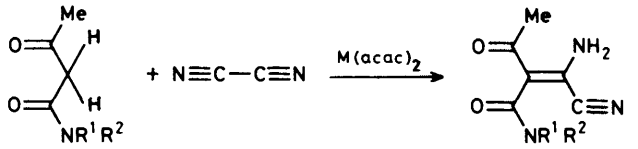
Acetoacetamides add quantitatively to cyanogen in aprotic media at ambient conditions in the presence of [M(acac)$_2$] (M = Cu or Ni; acac = acetylacetonate) complexes to give selectively 1:1 addition compounds. Products are amidic cyanoenaminones which can be converted thermally both in solution and in solid state into pyrrolinic cycloisomers. A variety of physicochemical methods including *X*-ray analysis, thermal analysis, ^{13}C n.m.r. and ^1H n.m.r. has been employed for characterizing the new compounds and monitoring the isomerization reactions.

In the last few years it has been found that the addition of various nucleophiles such as β-diketones, β-diesters, β-oxoesters, and β-oxoamides to cyanogen is effectively catalysed by metal β-carbonylenolate complexes in the homogeneous phase, under mild conditions.[1-5] The reaction of the β-oxoamides (**1**) with cyanogen to give the corresponding cyanoenaminodiones (**2**) and (**3**) is depicted in Scheme 1.



(1) (2),(3)

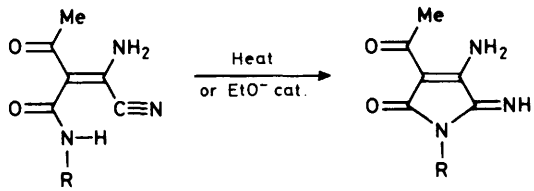
M = Zn or Cu
(**2**) R^1 = H; **a**, R^2 = CH_2Ph; **b**, R^2 = *p*-ClC_6H_4; **c**, R^2 = Ph; **d**, R^2 = Me; **e**, R^2 = H
(**3**) **a**, R^1 = R^2 = Me; **b**, R^1 = Me, R^2 = CH_2Ph; **c**, R^1 = Me, R^2 = Ph; **d**, R^1, R^2 = $(CH_2)_4$

Scheme 1.

We have previously reported the preparation of compounds (**2**) and (**3**) and briefly described the conversion of compounds (**2**) into their isomeric forms (**4**) by thermal treatment in aprotic solvents or by EtO^- catalysis (Scheme 2).[5] We report here the details of the preparation of compounds (**2**)—(**4**) and on their full physicochemical characterization. A remarkable feature of compounds (**2**), *i.e.* their thermal solid-state conversion into compounds (**4**), will also be discussed. This reaction was observed and monitored by thermal analysis (d.t.a. and d.s.c.) and a semiquantitative estimate of the relevant enthalpy data was carried out. In addition, a single-crystal *X*-ray analysis of the pyrroline derivative (**4b**) is reported.

Results and Discussion

Thermal Conversion of α-Amido-β-cyanoenaminones into their Pyrroline Isomers.—As previously reported,[5] compounds (**2**) can



(2) (4)

a, R = CH_2Ph; **b**, R = *p*-ClC_6H_4; **c**, R = Ph; **d**, R = Me; **e**, R = H

Scheme 2.

be thermally converted into (**4**) in aprotic solvents at temperatures ranging from 60—80 °C (Scheme 2). We now report that the same molecular process occurs also in the solid state. The thermal behaviour of solids (**2**) as seen on a Kofler hot-stage apparatus under polarized light reveals that the crystals of these compounds undergo a gradual crystalline modification which starts at defined temperatures [indicated as $(t_t)_{obs}$ in Table 1] and becomes rapidly complete over a temperature range of 10—20 °C (heating rate *ca.* 10 °C min^{-1}). The thermally generated species are compounds (**4**), as shown by their melting points (see Table 1); they can also be synthesised on heating of compounds (**2**) at temperatures slightly above the corresponding $(t_t)_{obs}$ or by sublimation *in vacuo* at the same temperatures.

The solid-state conversion (**2**) → (**4**) was monitored by combined t.g.–d.t.a. measurements (Figure 1, heating rate 5 °C min^{-1}) in which revealed the occurrence of an exothermic transition at temperature ranges close to those determined by visual observation in the Kofler apparatus. A semiquantitative evaluation of the ΔH values involved gave the figures reported in Table 1. Moreover, the expected endothermic peaks centred around the melting temperatures of crystals of thermally generated (**4**) were observed; their t.g.–d.t.a. curves are identical with those of authentic samples of (**4**).

The solid-state cyclization reaction was found to occur also well below $(t_t)_{obs}$, albeit at much slower rates. Thus, (**2d**) was quantitatively converted into (**4d**) at 88 °C after 3 h (see

Table 1. Melting temperatures of compounds (3) and (4) and observed transition temperatures of species (2) into (4)

Compound (R^1, R^2)	$(t_t)_{obs}$/°C [a]	M.p. (°C)	$(\Delta H_t)_{obs}$/kJ mol^{-1}
(2a) (H, CH_2Ph)	129	191	−59
(4a) (CH_2Ph)		191	
(2b) (H, *p*-ClC_6H_4)	167	192	−56
(4b) (*p*-ClC_6H_4)		192	
(2c) (H, Ph)	150	209	−56
(4c) (Ph)		209	
(2d) (H, Me)	110	185	−70 (−55 d.s.c.)
(4d) (Me)		185	
(3a) (Me, Me)		145	
(3b) (Me, CH_2Ph)		82	
(3c) (Me, Ph)		116	
(3d) $(CH_2)_4$		131	

[a] Heating rate *ca.* 10 °C min^{-1}, see text.

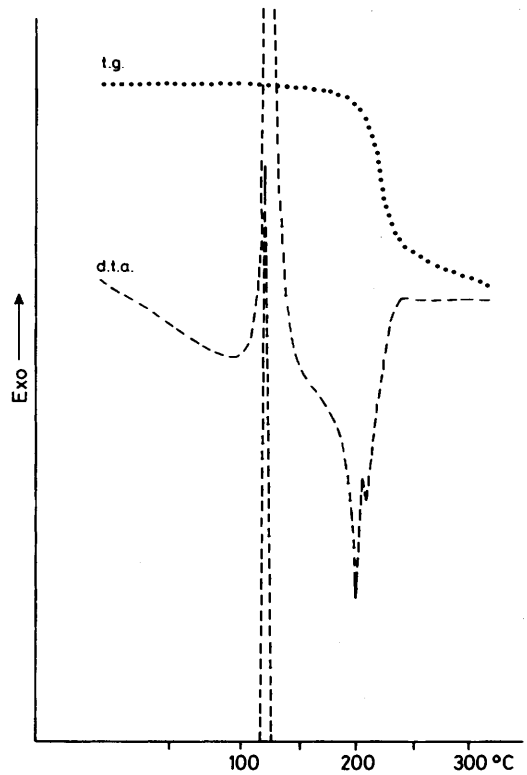


Figure 1. Thermogravimetric (t.g.) and differential thermal analysis (d.t.a.) of (**2d**). Heating rate 5 °C min^{-1}; loss of weight and ΔH on arbitrary scales.

Experimental section). This circumstance prompted the investigation of the solid-state transition (**2**) → (**4**) by the more powerful thermoanalytical technique d.s.c. We focused our attention on (**2d**). Some relevant thermograms, recorded under various conditions, are shown in Figures 2a and b.

At lower heating rates (10—20 °C min^{-1}) the d.s.c. diagrams (Figure 2a) confirm the d.t.a. findings, but they show in addition the start of the conversion at *ca.* 100 °C. At higher heating rates (100 °C min^{-1}) the exothermic peak is far more symmetrical (Figure 2b), but is considerably shifted to a higher temperature range. Finally, by heating rapidly to 105 °C (100 °C min^{-1}) and letting the system remain under isothermal conditions for 60 min, a very broad exothermic peak was observed (Figure 3).

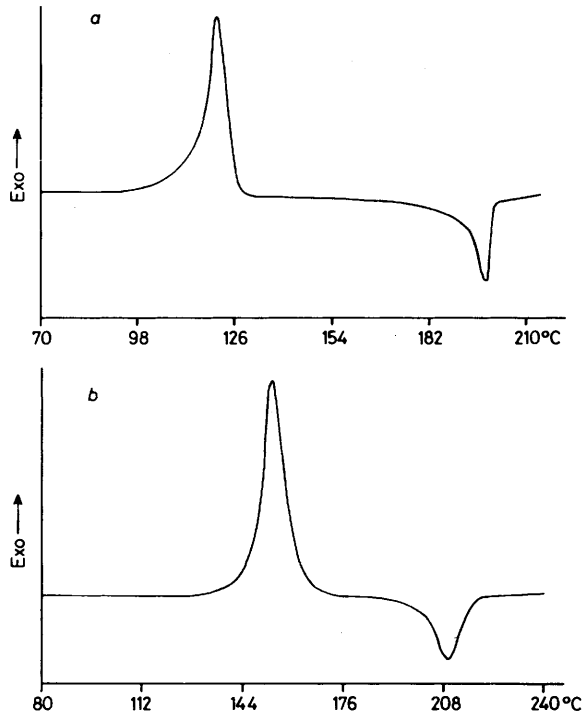


Figure 2. D.s.c. diagrams for (**2d**): *a*, heating rate 20 °C min^{-1}; *b*, heating rate 100 °C min^{-1}

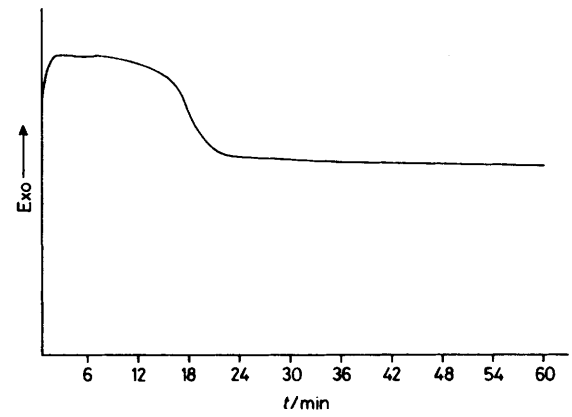


Figure 3. Heat release from a sample of (**2d**) after fast heating (100 °C min^{-1}) from room temperature up to 105 °C, under isothermal conditions

In conclusion, in spite of the various exothermal phenomena, all these observations can be rationalized on the basis of a kinetically controlled solid-state reaction.

Mass Spectra of Compounds (**2**), (**3**), *and* (**4**).—The essential data are reported in Table 2 and they appear quite consistent with the described thermal behaviour of the relevant species.

As expected from the data described above, compounds (**2**) and (**4**) have identical mass spectra which correspond to a cyclic isomer. A notable observation regarding compounds (**2**) and (**4**) is the high abundance of their molecular peaks in contrast with the lower abundance observed for compounds (**3**). For the latter species the predominant mass peak becomes, in fact, that referring to the NR^1R^2 group. Moreover, a common feature of the fragmentation patterns of (**2**)—(**4**) appears to be the easy loss of an acetyl group. The differences between the e.i. mass spectra of compounds (**3**) and (**4**) are so pronounced that they

Table 2. Significant masses observed in e.i. measurements on compounds (**2**)—(**4**) at 220 °C (injection and ionization chamber temperatures). Relative abundances are in parentheses

Compd. (R^1, R^2)	M^+	M^+ − MeCO	M^+ − NR^2	M^+ − N(R^1)(R^2)	MeCO	NR^2	N(R^1)(R^2)
(**2a**) (H, CH_2Ph) (**4a**) (CH_2Ph)	243 (100)	200 (4)	152 (1)		43 (18)	91 (87)	
(**2b**) (H, *p*-ClC_6H_4) (**4b**) (*p*-ClC_6H_4)	263 (100)	220 (6)	152 (50)		43 (30)	111 (25)	
(**2c**) (H, Ph) (**4c**) (Ph)	229 (100)	186 (12)	152 (50)		43 (65)	77 (78)	
(**2d**) (H, Me) (**4d**) (Me)	167 (96)	124 (1)	152 (100)		43 (82)	not detected	
(**3a**) (Me, Me)	181 (19)	138 (10)		137 (25)	43 (80)		44 (100)
(**3b**) (Me, CH_2Ph)	257 (15)	214 (10)		137 (7)	43 (15)		120 (100)
(**3c**) (Me, Ph)	243 (45)	200 (35)		137 (18)	43 (25)		106 (100)
(**3d**) $(CH_2)_4$	207 (30)	164 (1)		137 (10)	43 (18)		70 (100)

Table 3. ^1H Chemical shifts (δ)[a] for compounds (**2**), (**3**), and their pyrroline isomers (**4**) in $(CD_3)_2SO$ solution at *ca.* 28 °C

Compd.

(**2a**) 2.00 (s, 3 H, Ac), 4.35 (d, J_{HH} 6 Hz, 2 H, NCH_2), 7.32 (s, br, 5 H, Ph), 8.77 (br m, 3 H, NH_2 and $NHCH_2$)

(**4a**) 2.33 (s, 3 H, Ac), 4.63 (s, 2 H, NCH_2), 7.23 (br s, 5 H, Ph), 9.10 (vbr, 2 H, NH_2), 9.78 (s, 1 H, =NH)

(**4b**) 2.33 (s, 3 H, Ac), 7.30—7.50 (cm, 4 H, *p*-ClC_6H_4), 9.18 (vbr, 2 H, NH_2), 9.97 (s, 1 H, =NH)

(**4c**) 2.37 (s, 3 H, Ac), 7.37 (br s, 5 H, Ph); 8.80 (br s, 0.5 H), 9.20 (vbr s, 1.8H), and 9.97 (br s, 0.7 H, NH_2 and =NH)

(**2d**) 2.06 (s, 3 H, Ac), 2.66 (d, J_{HH} 6 Hz, 3 H, NH*Me*), 8.31 (br q, 1 H, N*H*Me), 8.77 (br s, 2 H, NH_2)

(**4d**) 2.33 (s, 3 H, Ac), 2.92 (s, 3 H, Me), 9.03 (vbr s, 2.5 H) and 9.70 (br s, 0.5 H, NH_2 and =NH)

(**4e**) 2.23 (s, 3 H, Ac), 8.03 (br s 1 H), 8.33 (br s, 1 H) and 9.23 (vbr s, 2 H, NH_2, =NH and C=NH)

(**3a**) 2.00 (s, 3 H, Ac), 2.88 s, 2.97[b] (s, 6 H, NMe_2), 7.30 (br s), 8.80[b] (br s, 2 H, NH_2)

(**3b**) 2.00 (s, 3 H, Ac), 2.87 (s, 3 H, NMe), 4.60 (br s, 2 H, NCH_2Ph), 7.33 (s, 5 H, Ph), 8.90 (br s, 2 H, NH_2)

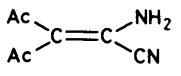
(**3d**) 1.83—2.00 (cm, 7 H, Ac and $NCH_2CH_2CH_2CH_2$), 3.33 (cm, 4 H, $NCH_2CH_2CH_2CH_2$), 8.73 (br s, 2 H, NH_2)

[a] s = singlet; d = doublet; br s = broad singlet; cm = complex multiplet; q = quartet. [b] Relative intensity 1:6, respectively.

may be considered as analytical tools for rapidly discriminating between these two classes of isomeric compounds.

^1H and ^{13}C N.m.r. Analysis of the α-Amido-β-cyanoenaminones (**2**), (**3**) *and of their Pyrroline Isomers* (**4**).—The essential spectral data are reported in Tables 3 and 4.

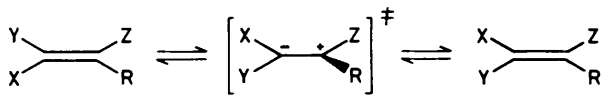
In order better to discuss the whole of the n.m.r. data for compounds (**2**) and (**3**), it seems appropriate to discuss briefly the ^1H n.m.r. behaviour of compound (**5**).



(**5**)

Compound (**5**) was described in a previous paper[6] and it can be considered as the prototype of the numerous classes of compounds prepared by us containing the cyanoenaminodione skeleton. Compound (**5**) is known to give, in $CDCl_3$ solution, two well separated resonances (δ 2.30 and 2.52) attributable to the acetyl groups, whereas in $(CD_3)_2SO$ a single resonance at δ 2.13 is detectable. These observations were accounted for by proposing the existence of a strong intramolecular hydrogen bond (N–H • • • O) between the NH_2 and the acetyl groups[7] in chloroform solution. We have now obtained more information about the structure of (**5**) in solution by examining the proton spectrum in $(CD_3)_2CO$ at various temperatures. Compound (**5**) exhibits at room temperature the methyl resonance as a broad singlet at δ 2.38 and that attributed to the NH_2 protons as a very broad signal at *ca.* δ 9.1. By decreasing the temperature, the methyl resonance shows a progressive broadening with coalescence at 15 °C. At −30 °C two sharp singlets at δ 2.53 and 2.32 are formed whereas the NH_2 resonance remains extremely broad. Finally, two broad singlets with relative intensity 1:1 at δ 10.55 and 8.98 appear at −70 °C. The temperature dependence of the acetyl signals of (**5**) indicates unambiguously that the two diastereotopic methyl groups undergo a kinetic exchange process; that is, there is rotation around the C=C double bond. A second rotational process, with a lower activation energy, is the interchange of the N–H protons through the rotation of the C–N bond. The $\Delta G^{\ddagger}$ values for the rotation around the C=C and N–C bonds are 47 and 44 kJ mol^{-1}, respectively. These values of free activation energy have been determined at the coalescence temperature of the two equal intensity signals from the maximum chemical-shift separation.[7]

It is known that olefins bearing electron-withdrawing (X, Y) and electron-releasing groups (Z) may be thermally isomerized at rates which lie on the n.m.r. timescale. The process occurs through a dipolar transition state and the isomerization is accelerated in more polar solvents.[8]



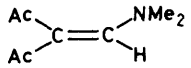
The appearance of a sharp singlet for the Me resonance in the spectrum of (**5**) in $(CD_3)_2SO$ solution at 200 MHz is therefore attributable to the high polarity of this solvent which lowers the energy of the transition state in the isomerization process so that at room temperature the interconversion is fast on the n.m.r. timescale.

The activation parameters relative to (**5**) can be compared

Table 4. ^{13}C Chemical shifts (p.p.m.) for Ac (R^1R^2NCO) $C_\alpha=C_\beta(CN)NH_2$, (**2**) or (**3**), and their pyrroline isomers (**4**), in $(CD_3)_2SO$ solution[a]

Compound	Me	CO (amide)	CO (acetyl)	C_α[b]	CN[b]	C_β	C=NH	NR^1R^2 substituents
(**2a**)	28.6	166.7	196.7	114.0	114.3	131.4		43.3 (NCH_2Ph); 127.4, 128.1, 128.7, 139
(**4a**)	28.1	169.2	193.4	97.0		153.8	156.4	40.7
		(168.8)	(193.1)			(152.5)	(159.0)	(40.2)
(**4b**)	28.2	168.3	193.7	97.6		153.6	156.0	128.5, 129.5, 129.9, 131.4, 132.6
		(167.9)	(193.4)	(97.8)		(152.1)	(158.7)	
(**4c**)	28.3	168.6	193.7	97.6		153.6	156.3	127.3, 128.4, 128.8, 129.9, 134.0
			(193.3)			(152.5)	(158.7)	
(**2d**)	28.6	166.9	196.4	114.0	114.1	131.1		26.4 (MeN)
(**4d**)	27.9	169.2	193.2	98.1		153.7	156.3	23.8 (MeN)
(**3a**)	28.2	167.2	195.9	113.9	112.4	129.8		34.7, 39.3 NMe_2
	(27.7)	(166.4)	(191.2)	(115.4)		(125.2)		

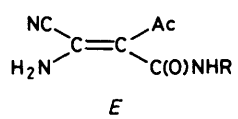
[a] Minor intensity peaks in parentheses. [b] Assignments within these groups are arbitrary.



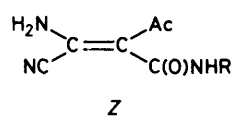
(**6**)

with those of the related enaminodione (**6**). In this case,[8a] the coalescence temperatures in CH_2Cl_2 at 60 MHz are < -40 and -11 °C for the C=C and C–N ($\Delta G^\ddagger$ 54 kJ mol^{-1}) rotations, respectively. Apparently the replacement of H by CN and of the Me groups by H at the nitrogen atom is accompanied by a raising of the energy barrier for the C=C rotation process and a decrease in the activation energy for the C–N rotation. All these results are consistent with the proposal of a dipolar transition state in which the presence of electronegative substituents at one carbon atom stabilizes the required charge separation. As expected, the electron-withdrawing nature of the CN substituent at the second carbon atom contributes to enhance the activation energy for the C=C rotation in (**5**).

In the case of the α-amido-β-cyanoenaminones (**2**) and (**3**) the presence of one amido substituent, less electron-withdrawing than the acetyl group, is expected to increase further the activation parameters for the rotation around the olefinic double bond in comparison with compound (**5**). The ^1H n.m.r. spectrum of (**2d**) (R^1 = H, R^2 = Me) in $(CD_3)_2SO$ [compounds (**2**)—(**4**) are sparingly soluble in other solvents] at room temperature shows a resonance attributable to the acetyl methyl group (at δ 2.00) as a sharp single peak (Table 3). The NH_2 protons exhibit a broad singlet at δ 8.77 whereas the amidic NH proton appears as a broad quartet due to coupling with the geminal methyl protons. The same feature is observed in the spectrum of (**2a**) (R^1 = H, R^2 = CH_2Ph). A single set of signals for each carbon atom is also observed in the ^{13}C n.m.r. spectra of these compounds. In Table 4 a complete list of the carbon-13 chemical shifts, with their attribution, is reported. The lack of multiplicity of the signals in the ^1H and ^{13}C n.m.r. spectra of (**2a**) and (**2d**) in $(CD_3)_2SO$ solution is probably attributable to a low level of one of the two isomers *E* and *Z*.



E



Z

Solubility problems prevent the investigation of a possible fast rotation around the C=C bond.

Table 5. Selected interatomic distances (Å) and angles (°) for the structure of (**4b**)

	Molecule A	Molecule B
C(4)–N(2)	1.433(20)	1.417(22)
N(2)–C(8)	1.361(16)	1.439(20)
C(8)–N(3)	1.265(16)	1.280(21)
C(8)–C(9)	1.547(21)	1.488(22)
C(9)–N(1)	1.294(20)	1.339(20)
C(9)–C(10)	1.389(18)	1.371(20)
C(10)–C(11)	1.413(20)	1.417(22)
C(11)–C(12)	1.531(20)	1.566(23)
C(11)–O(1)	1.215(21)	1.256(20)
C(10)–C(7)	1.453(22)	1.458(22)
C(7)–O(2)	1.196(17)	1.176(18)
C(7)–N(2)	1.412(17)	1.483(19)
C(7)–N(2)–C(8)	112.0(1.2)	107.9(1.2)
N(2)–C(8)–C(9)	104.7(1.1)	106.1(1.3)
C(8)–C(9)–C(10)	107.2(1.3)	109.9(1.4)
C(9)–C(10)–C(7)	107.8(1.2)	109.4(1.3)
C(10)–C(7)–N(2)	107.6(1.1)	106.5(1.2)
N(1)–O(1)	2.816(0.1)	2.777(0.1)

The presence of a mixture of isomers is detected in the case of the *N*-disubstituted derivative (**3a**) (R^1 = R^2 = Me). In fact, in $(CD_3)_2SO$ solution, this compound shows the NH_2 resonances at δ 8.80 and 7.30 with an intensity ratio of 6:1. The NMe_2 protons exhibit a broader singlet at δ 2.97 and a sharp one at δ 2.88 with an intensity ratio of *ca.* 6:1, respectively. A single sharp resonance at δ 2.00, attributable to the acetyl protons, is detectable. In the ^{13}C n.m.r. spectrum of (**3a**), in addition to the intense resonances in the range observed for compounds (**2**), this derivative shows weak absorptions at δ values which could be due to the presence of a second isomeric species, which is detectable thanks to a slow rotation rate around the olefinic double bond.

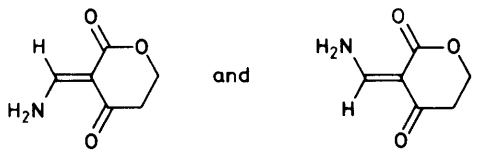
The ^{13}C n.m.r. spectra of (**2**) and (**3**) show two carbonyl resonances indicating the presence of acetyl (δ 197) and amide (δ 167) groups. Of the two resonances at *ca.* δ 114, one is due to the CN group, the second being attributable to the inter-carbonylic olefin carbon atom.

We have reported[5] that compounds (**2**) slowly convert in aprotic solvents into the corresponding pyrroline isomers (**4**) (Scheme 2). We find here that the reaction can be monitored by ^1H n.m.r. for compound (**2d**) and by ^{13}C n.m.r. spectroscopy for the corresponding benzyl derivative (**2a**), in $(CD_3)_2SO$ solution at 60 °C. In these cases conversion occurs quantitatively with $t_{\frac{1}{2}}$ *ca.* 30 min. For the phenyl derivatives (**2b**) and (**2c**) the isomerization is much faster and it is virtually instantaneous upon dissolution in $(CD_3)_2SO$ at room temperature.

Table 6. Fractional co-ordinates of (**4b**)

	Molecule A			Molecule B		
Atom	*x*	*y*	*z*	*x*	*y*	*z*
Cl(1)	0.2543(2)	0.4081(6)	0.8613(3)	0.1654(2)	0.3100(6)	1.0151(3)
C(1)	0.2808(6)	0.3735(22)	0.7492(13)	0.1241(7)	0.3326(22)	1.1043(13)
C(2)	0.2535(6)	0.4267(20)	0.6565(15)	0.0683(7)	0.3601(21)	1.0535(11)
C(3)	0.2750(7)	0.4103(20)	0.5664(12)	0.0346(6)	0.3763(20)	1.1248(13)
C(4)	0.3245(6)	0.3349(22)	0.5756(12)	0.0522(6)	0.3723(19)	1.2275(13)
C(5)	0.3506(5)	0.2743(20)	0.6699(15)	0.1064(6)	0.3440(22)	1.2756(12)
C(6)	0.3299(6)	0.2905(19)	0.7621(12)	0.1415(6)	0.3204(23)	1.2054(15)
C(7)	0.3243(6)	0.2837(20)	0.3830(11)	−0.0228(6)	0.5363(20)	1.2937(11)
C(8)	0.4002(5)	0.3858(20)	0.4933(11)	0.0067(5)	0.2548(24)	1.3708(11)
C(9)	0.4104(6)	0.3602(20)	0.3810(11)	−0.0359(5)	0.3304(22)	1.4197(11)
C(10)	0.3624(5)	0.3120(20)	0.3164(11)	−0.0534(5)	0.4918(21)	1.3728(10)
C(11)	0.3577(7)	0.2871(22)	0.2070(11)	−0.0952(6)	0.5940(21)	1.3993(12)
C(12)	0.3033(6)	0.2427(26)	0.1387(13)	−0.1116(7)	0.7803(24)	1.3446(14)
O(1)	0.3938(4)	0.3126(16)	0.1617(8)	−0.1184(4)	0.5441(14)	1.4704(8)
O(2)	0.2785(4)	0.2438(15)	0.3592(7)	−0.0242(4)	0.6571(14)	1.2342(8)
N(1)	0.4559(4)	0.3923(17)	0.3579(9)	−0.0529(5)	0.2354(17)	1.4940(9)
N(2)	0.3498(4)	0.3261(15)	0.4873(9)	0.0162(4)	0.3879(15)	1.2959(9)
N(3)	0.4370(4)	0.4505(16)	0.5636(9)	0.0296(5)	0.1026(18)	1.3958(9)

The ^{13}C n.m.r. spectra of compounds (**4**) (Table 4) are characterized by two resonances in the range δ 153—156, one of which is attributable to the imine carbon atom (C=NH), the other one to the olefinic carbon atom bearing the NH_2 substituent. The intercarbonylic carbon resonance (δ *ca.* 98) appears substantially shifted to higher field with respect to (**2**) upon cyclization. A more drastic deshielding occurs for the adjacent carbon atom (*ca.* 22 p.p.m.). Moreover, it is useful to note the strict similarity of these chemical-shift values with those of the corresponding atoms in gentiocrucine,[9] *i.e.* a lactonic enaminoketone.



I.r. Spectra.—Addition of cyanogen to compounds (**1**) causes marked changes in the overall features of their spectra. Products (**2**) and (**3**) are characterized by a complex pattern of bands in the region 3 450—3 050 cm^{-1} (ν_{NH} bands). Furthermore most of them exhibit a significant, albeit very weak, $\nu_{C\equiv N}$ absorption in the range 2 240—2 220 cm^{-1}. This band is very strong only in the case of (**2e**). While the low intensity of the $\nu_{C\equiv N}$ band is expected in view of the presence of electronegative substituents adjacent to the C≡N group,[10] the high intensity observed for compound (**2e**) cannot be explained in simple terms. At lower energy (1 710—1 500 cm^{-1}) compounds (**2**) and (**3**) exhibit a complex set of bands due to $\nu_{C=O}$ and $\nu_{C=C}$.

The cyclic isomers (**4**) are characterized by the expected sets of bands in the ranges 3 450—3 050 (ν_{NH}) and 1 710—1 500 cm^{-1} (ν_{CO}; $\nu_{C=C}$). In addition, a single or double band appears in the region 1 750—1 720 cm^{-1} attributable to the C=NH stretching vibration; this can be used as an analytical tool for monitoring the formation of compounds (**4**).

X-Ray Single-crystal Analysis of (**4b**).—Compound (**4b**) (R = *p*-ClC_6H_4) was characterized by single-crystal *X*-ray analysis (Tables 5 and 6 and Figure 4). An ORTEP drawing of the molecular structure of (**4b**) is shown in Figure 4.

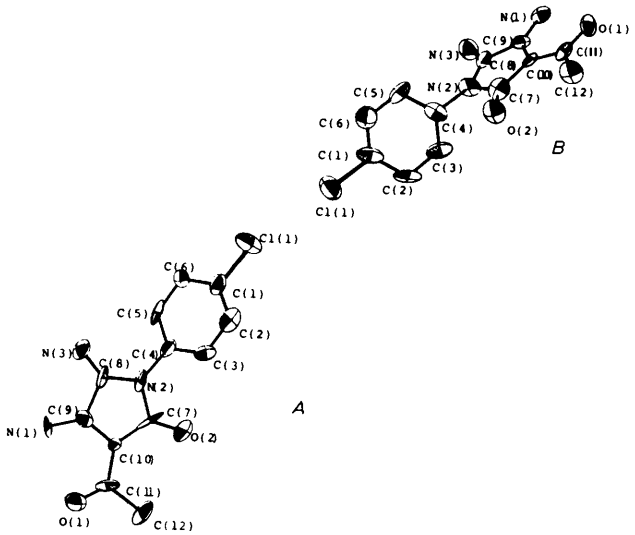


Figure 4. ORTEP view of an asymmetric unit of compound (**4b**)

The asymmetric unit consists of two independent molecules A and B (Tables 5 and 6). Bond lengths, bond angles, and observed torsional angles are not significantly different in the two molecules.

Apart from the (*p*-ClC_6H_4) moiety, all other atoms can be considered to lie in the same plane ($\sigma_{max.}$ = 0.05 Å) and the observed bond lengths are in full agreement with the occurrences of an extended resonance.

Two different types of hydrogen bonds are observed in the structure. One such bond involves the amide NH moiety of a molecule of A (or B) with the imino C=NH nitrogen of another molecule of A (or B). The other bond involves the amide NH group of a molecule A (or B) and the acetyl oxygen of another independent molecule B (or A) and *vice versa*. Atoms N(1)–O(1) are involved in an intramolecular hydrogen bond (see Table 5).

Conclusions

The i.r., m.s., and n.m.r. data discussed in this paper support the basic structures of compound (**2**)—(**4**). The ^1H n.m.r.

analysis of the model compound (**5**) has shown that cyanoenamine compounds bearing electron-withdrawing substituents at the carbon–carbon double bond can undergo rapid thermal isomerization processes. This means that compounds (**2**) and (**3**) should be expected to exhibit a fast equilibrium between the relevant *E* and *Z* configurations. The data here reported do not allow us to draw any definite conclusion in this sense and the detailed stereochemistry of compounds (**2**) and (**3**) in solution is still an open question.

For the configuration in the solid state, the results regarding the solid-state conversion of (**2d**) into (**4d**) strongly suggest an *E* configuration for (**2d**) and, probably, for all compounds (**2**) and (**3**).

It should be noted that the ^{13}C n.m.r. spectra of compounds (**4**) reveal for (**4a**)—(**4c**) the existence of small amounts either of isomeric species or of conformers of much smaller thermodynamic stabilities.

Experimental

I.r. and u.v.–visible spectra were recorded on a Perkin-Elmer 257 and Perkin-Elmer 576 spectrophotometers, respectively. I.r. data (Nujol) are given in cm^{-1} and u.v.–visible in nm. ^1H N.m.r. spectra were recorded on Varian EM 360 A instrument, and ^{13}C n.m.r. spectra were recorded on a Bruker WP 60 instrument. Mass spectra were obtained by a V.G. MM-16 F apparatus. Thermoanalyses (t.g.–d.t.a.) were carried out on a Netzsch DTA-T6 429/3/6 instrument calibrated by a calcium oxalate·$2H_2O$ dehydration process. The heating rate was 5 °C min^{-1}. A DSC-4 Perkin-Elmer apparatus was used for differential scanning calorimetric measurements.

All solvents and reagents were analytical grade. C_2N_2 was a Matheson chemical declared as technical (purity *ca.* 98%). Acetoacetamides were either commercial or prepared by literature methods.

General Procedure for Preparation of Compounds (**2**) and (**3**).—The required acetoacetamide (**1**) (10 mmol) was added to 20—30 ml of solutions containing C_2N_2 (*ca.* 1M) (the solutions were standardized according to ref. 11). After stirring for 1 min, the catalyst was added (1—5% in moles with respect to the nucleophile). The resulting solution or suspension was kept under moderate stirring in a tightly closed vessel for the required time at room temperature. Compounds (**2**) precipitated spontaneously as microcrystalline powders and were filtered off on Gooch filters without particular precautions and washed (3 × 30 ml) with the employed solvent. Details on the preparations and on the properties of adducts are reported below under specific items.

Preparation of (**2a**).—Compound (**1**) (1.9 g) was added to a solution of C_2N_2 in toluene (25 ml; 0.78M) to give a colourless suspension. [$Zn(acac)_2$] (33.6 mg) was used as a catalyst. (**2a**) precipitated after 15 min as cream crystals. The reaction was continued for 60 h, yield 2.25 g (92%) (Found: C, 63.75; H, 5.4; N, 17.2. $C_{13}H_{13}N_3O_2$ requires C, 64.2; H, 5.4; N, 17.3%); $\nu_{max.}$ 3 320, 3 260, 3 160, 3 060 (NH), 2 230 (C≡N), 1 635, 1 615, and 1 550 cm^{-1} (CO, C=C); $\lambda_{max.}$ 325 nm (ε 11 500 l mol^{-1} cm^{-1}).

Preparation of (**2b**).—Compound (**1**) (2.11 g) was added to a solution of C_2N_2 in toluene (25 ml; 0.78M) to give a colourless suspension. [$Zn(acac)_2$] (33.0 mg) was used as a catalyst. Abundant precipitation of (**2b**) occurred after 15 min, and the reaction was continued for 48 h, yield 2.48 g (94%), cream crystals (Found: C, 54.65; H, 3.9; N, 15.95. $C_{12}H_{10}ClN_3O_2$ requires C, 54.7; H, 3.8; N, 15.9%); $\nu_{max.}$ 3 340, 3 270, 3 180 (NH), 2 240 (C≡N), 1 640, 1 625, and 1 590 cm^{-1} (CO, C=C); $\lambda_{max.}$ 325 nm (ε 11 000 l mol^{-1}).

Preparation of (**2c**).—Compound (**1**) (1.77 g) was added to a solution of C_2N_2 in toluene (25 ml; 0.78M). [$Zn(acac)_2$] was used (33.5 mg) as a catalyst. The reaction pattern was identical with that of (**2b**), yield 2.25 g (96%) (Found: C, 62.9; H, 4.95; N, 18.3. $C_{12}H_{11}N_3O_2$ requires C, 62.9; H, 4.8; N, 18.3%); $\nu_{max.}$ 3 280, 3 130, 3 060 (NH), 1 660, 1 630, 1 590, and 1 550 cm^{-1} (CO; C=C); $\lambda_{max.}$ 325 nm (ε 10 700 l mol^{-1} cm^{-1}).

Preparation of (**2d**).—Compound (**1**) (1.15 g) was added to a solution of C_2N_2 in dichloroethane (25 ml; 1.03M). [$Cu(acac)_2$] (32.7 mg) was used as a catalyst. Abundant precipitation from the colourless solution began after 3 min. The crystals were brown-cream in colour. The reaction was continued for 144 h, yield 1.22 g (80%) (Found: C, 50.0; H, 5.4; N, 25.2. $C_7H_9N_3O_2$ requires C, 50.3; H, 5.4; N, 25.1%); $\nu_{max.}$ 3 350, 3 290, 3 140, 3 090 (NH), 2 240 (C≡N) 1 645, 1 610, 1 560, and 1 525 cm^{-1} (CO, C=C); $\lambda_{max.}$ 355 nm (ε 2 300 l mol^{-1} cm^{-1}).

Preparation of (**2e**).—Compound (**1**) (1.01 g) was added to a solution of C_2N_2 in toluene (25 ml; 0.78M). [$Zn(acac)_2$] (33.1 mg) was used as a catalyst. Precipitation of abundant yellow powder from the colourless solution began after 15 min. The reaction was continued for 70 h, yield 1.40 g (91%) (Found: C, 46.5; H, 4.55; N, 27.0. $C_6H_7N_3O_2$ requires C, 47.1; H, 4.6; N, 27.4%); $\nu_{max.}$ 3 370, 3 300, 3 200 (NH), 2 220 (C≡N), 1 680, and 1 630 cm^{-1} (C=C, CO); $\lambda_{max.}$ 295 (ε 9 000 l mol^{-1} cm^{-1}).

Preparation of (**3a**)—Compound (**1**) (1.62 g) was added to a solution of C_2N_2 in dichloroethane (25 ml; 1.0M). [$Cu(acac)_2$] (33.6 mg) was used as a catalyst. The resulting yellow solution was concentrated after 72 h to *ca.* 10 ml whereupon (**3a**) precipitated as a brown-yellow powder (1.75 g, 77%) (Found: C, 52.2; H, 6.05; N, 22.85. $C_8H_{11}N_3O_2$ requires C, 53.0; H, 6.1; N, 23.2%); $\nu_{max.}$ 3 320, 3 220, 3 140, 3 100 (NH), 2 240 (C≡N), 1 640, 1 610, and 1 520 cm^{-1} (C=C, CO); $\lambda_{max.}$ 330 nm (ε 9 600 l mol^{-1} cm^{-1}).

Preparation of (**3b**).—Compound (**1**) (2.62 g) was added to a solution of C_2N_2 in dichloroethane (25 ml; 1.1M). [$Cu(acac)_2$] (33.0 mg) was used as a catalyst. The mixture was a yellow solution. Solvent removal after 48 h gave an oily residue which was treated with ether (30 ml) followed by light petroleum (50 ml). After 10 days at −30 °C a greenish crystalline precipitate was obtained (1.15 g, 35%) (Found: C, 65.55, H, 5.95; N, 16.4. $C_{14}H_{15}N_3O_2$ requires C, 65.4; H, 5.9; N, 16.3%); $\nu_{max.}$ 3 310, 3 160 (NH), 2 240 (C≡N), 1 645, 1 605, and 1 515 cm^{-1} (C=C, CO); $\lambda_{max.}$ 320 (ε 9 500 l mol^{-1} cm^{-1}).

Preparation of (**3c**).—Compound (**1**) (2.45 g) was added to a solution of C_2N_2 in dichloroethane (25 ml; 1.1M). [$Cu(acac)_2$] (33.0 mg) was used as a catalyst. The mixture was a yellow solution. The procedure was as for (**3b**), after 72 h. The product was obtained as a brown powder (1.01 g, 55%) (Found: C, 63.85; H, 5,2, N, 17.35. $C_{13}H_{13}N_3O_2$ requires C, 64.2; H, 5.4; N, 17.3%); $\nu_{max.}$ 3 320 (NH), 1 710, 1 640, and 1 590 cm^{-1} (C=C, CO); $\lambda_{max.}$ 325 nm (ε 6 600 l mol^{-1} cm^{-1}).

Preparation of (**3d**).—Compound (**1**) (1.55 g) was added to a solution of C_2N_2 in dichloroethane (25 ml; 1.03M). [$Zn(acac)_2$] (32.3 mg) was used as a catalyst. The mixture was a yellow solution which turned to orange after 4 h. The solvent was removed after 48 h; addition of ether gave the product as a brown-yellow powder (1.95 g, 94%). (Found: C, 58.0; H, 6.3; N, 20.15. $C_{10}H_{13}N_3O_2$ requires C, 58.0; H, 6.3; N, 20.3%); $\nu_{max.}$ 3 320, 3 170 (NH), 2 240 (C≡N), 1 650, 1 610 and 1 525 cm^{-1} (C=C, CO); $\lambda_{max.}$ 325 nm (ε 9 600 l mol^{-1} cm^{-1}).

General Procedure for the Preparation of Compounds (**4**).—

Compounds (**4**) could be prepared *via* the four different procedures outlined below.

Method A. Cycloisomerization by base catalysis. Compound (**2b**) (0.26 g) was added to absolute ethanol (10 ml) to give a suspension. Addition of EtO^- [10% in moles with respect to (**2b**)] to ethanol under vigorous stirring caused a progressive colour change of the suspension to pink. Filtration after 60 h gave (**4b**) (0.18 g, 70%) (Found: C, 54.6; H, 3.8; N, 15.85. $C_{12}H_{10}ClN_3O_2$ requires C, 54.7; H, 3.8; N, 15.9%); $\nu_{max.}$ 3 360, 3 270, 3 180 (NH), 1 740 (C=NH), 1 640, and 1 680 cm^{-1} (C=C, CO).

Method B. Cycloisomerization in boiling dichloroethane. Compound (**2a**) (50 mg) was suspended in dichloroethane (5 ml) and refluxed for 8 h. Filtration at room temperature gave (**4a**) in 61% yield (Found: C, 64.2; H, 5.3; N, 17.25. $C_{13}H_{13}N_3O_2$ requires C 64.2; H, 5.4; N, 17.3%); $\nu_{max.}$ 3 320, 3 200 (NH), 1 725 (C=NH), 1 690, 1 650, and 1 525 cm^{-1} (C=C, CO).

Method C. Cycloisomerization by heating compounds (**2**) *as solid samples.* Compound (**2d**) (50 mg) was put at the bottom of a test tube and heated at 115 °C (see Table 1) for *ca.* 10 min. Compound (**4d**) (50 mg) was obtained upon cooling to room temperature (Found: C, 50.25; H, 5.4; N, 25.0. $C_7H_9N_3O_2$ requires C, 50.3; H, 5.4; N, 25.1%); $\nu_{max.}$ 3 320, 3 290, 3 160 (NH), 1 715 (C=NH), 1 690, 1 660, 1 640, and 1 525 cm^{-1} (C=C, CO).

Method D. Cycloisomerization by sublimation. Compound (**2c**) (20 mg) was heated at 182 °C (see Table 1) under reduced pressure (0.01 mmHg) and crystals of (**4c**) were precipitated at *ca.* 10 °C (Found: C, 62.9; H, 4.8; N, 18.3. $C_{12}H_{11}N_3O_2$ requires C, 62.9; H, 4.8; N, 18.3%); $\nu_{max.}$ 3 420, 3 350, 3 270, 3 190 (NH), 1 730, 1 720 (C=NH), 1 680, 1 645, 1 595, and 1 525 cm^{-1} (C=C, CO).

Solid-state Conversion of (**2d**) *into* (**4d**) *at* 88 °C.—A single sample of solid (**2d**) was divided into five batches of the same weight (*ca.* 50 mg) and each one was put at the bottom of a n.m.r. tube. The five tubes were kept in an oil-bath at 88 °C and each was removed from the heat source at the desired time and rapidly cooled to room temperature. Immediate dissolution of the solid material in $(CD_3)_2SO$ (0.3 ml) made possible the rapid recording of the ^1H n.m.r. spectra. The spectral patterns gradually moved from that of pure (**2d**) to that of pure (**4d**) after 3 h.

X-*Ray Analysis of* (**4b**).—Yellow crystals of $C_{12}H_{10}ClN_3O_2$ were obtained by sublimation of the crude derivative at 185 °C *in vacuo*. They are monoclinic, space group P_2 (N14) with a = 25.800(4), b = 7.385(6), c = 12.998(5) Å, β = 102.0(1.0)°; Z = 8; D = 1.44 g cm^{-3}. 2 045 unique reflections were collected on a Philips PN 1100 diffractometer using Cu-K_α monochromatized radiation, in the range 4—92° of 2θ employing θ—2θ technique. The structure was solved by SHELX direct methods and refined by blocked least-squares, $\omega = 1/0.408\ (\sigma^2F + 0.001\,47F^2)$, using anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms were found by difference Fourier map, but not refined. The final R factor of 1 183 reflections with $I > 3\sigma(I)$, was 0.092.

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