The Structure of a By-product obtained during the Reduction of 2-Phenyl-1-cyanoacrylic Acid

By **Wilson Baker**, Lane's End, Church Road, Winscombe, Avon BS25 1BJ
   **Trevor J. King**, Department of Chemistry, University of Nottingham, Nottinham NG7 2RD
   John F. W. McOmie,* School of Chemistry, University of Bristol, Bristol BS8 1TS

The by-product, $C_{23}H_{18}N_2O$, obtained during the reduction of 2-phenyl-1-cyanoacrylic acid by sodium amalgam, has been shown by X-ray analysis to be 5-cyano-1,4,5-triphenylpyrrolidin-2-one with the two C-phenyl groups *trans* to each other. Its formation is attributed to the presence of 2-phenylaminobenzyl cyanide in the 2-phenyl-1-cyanoacrylic acid and a rational synthesis of it is described, together with details of the structure analysis.

FIFTY-SEVEN years ago one of us (W. B.) published his first paper [1] with A. Lapworth entitled 'Reduction Products of Arylidene Cyanoacetic Acids,' the reduction to β-aryl-α-cyanopropionic acids being effected in high yields by treatment with sodium amalgam in aqueous alkaline solution. During one experiment, when 120 g of 2-phenyl-1-cyanoacrylic acid (1) were stirred with water and excess of sodium amalgam, the temperature rose to 45 °C, and after several hours a heavy neutral oil was found to have separated from the aqueous alkali salt of the saturated acid. A hot alcoholic solution of this oil deposited 6.9 g of colourless needles, m.p. 171.5 °C, whose two elementary analyses and molecular-weight determination (Rast) agreed very closely with the formula $C_{23}H_{18}N_2O$. This compound was unaffected by boiling with either concentrated hydrochloric acid for 4 h or with 40% aqueous sodium hydroxide, but it yielded some ammonia when boiled with potassium hydroxide in pentanol. At the time further experiments threw no light on the structure of the compound $C_{23}H_{18}N_2O$, and because many attempts to repeat its preparation failed, its investigation was abandoned. It was manifest that it could not be derived in any simple way from 2-phenyl-1-cyanoacrylic acid, and its structure and formation have remained intriguing mysteries to the present time.

RESULTS AND DISCUSSION

In an endeavour to determine the structure of the by-product, a small specimen still available was submitted to spectroscopic analyses (see Experimental section). However, although these established the presence of certain atomic groupings, they did not lead
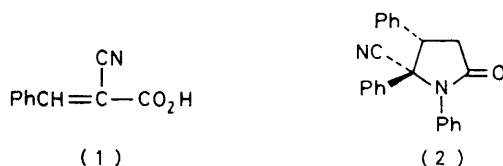
to a unique structure. An X-ray crystallographic examination was therefore undertaken, and we now report that this by-product is, unexpectedly, *trans*-5-cyano-1,4,5-triphenylpyrrolidin-2-one (2).

It is clear from structure (2) that the moiety PhCHCH₂-

CO is derived from 2-phenyl-1-cyanoacrylic acid (1) but it is very unlikely that the rest of the molecule is derived from the same acid. The most probable explanation is that a batch of crude 2-phenyl-1-cyanoacrylic acid was used for this particular reduction. The acid was made by the method of Lapworth and McRae [2] which involved the condensation of benzaldehyde with a solution of mixed sodium and potassium cyanoacetates, using aniline hydrochloride as catalyst. The mixture of cyanoacetate salts was made by heating a solution of
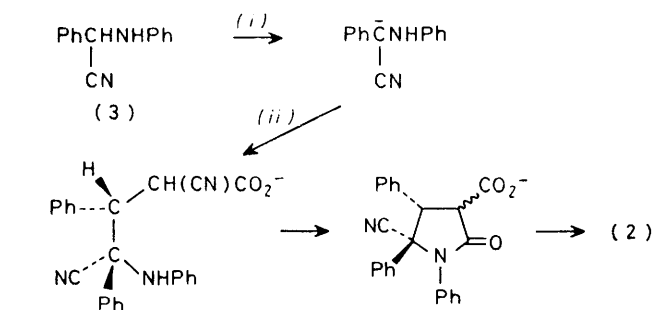

(and other diastereoisomers)

SCHEME   (i) NaOH;   (ii) PhCH=C(CN)CO₂Na

sodium chloroacetate with an excess of potassium cyanide, and finally adding enough hydrochloric acid to liberate *ca.* half the cyanoacetic acid.[3] This solution has a pH of *ca.* 3, and was used without purification for the condensation with benzaldehyde. Under these conditions some α-phenylaminobenzyl cyanide (3) could have been formed, since we have prepared it in 56% yield by mixing benzaldehyde, aniline hydrochloride, and potassium cyanide in aqueous ethanol.[4] The cyanide (3) contains a relatively acidic methine proton and, under the alkaline conditions of the sodium amalgam reduction, the sequence shown in the Scheme could occur. Michael addition of the carbanion to the C=C bond, followed by cyclisation, hydrolysis, and decarboxylation, could give the pyrrolidinone (2). Alternatively, decarboxylation might occur before, rather than after, cyclisation. The plausibility of this scheme has been confirmed by the synthesis of pyrrolidinone (2) from pure samples of cyanide (3) and acrylic acid (1) in ethanol containing sodium hydroxide. However,

the conditions for this synthesis must be critical since out of five experiments under slightly different conditions only one was successful (see Experimental section).

It is interesting that Lapworth and his co-workers studied the Michael-type addition of the cyanide (3) to αβ-unsaturated carbonyl compounds and found, for example, that with benzylideneacetophenone it gave the adduct (4) [5] and with diethyl ethylidenemalonate it

PhCH—CH₂COPh
|
PhCNHPh
|
CN

(4)

(5)
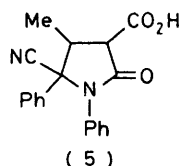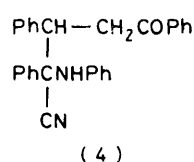
gave a variety of products including the pyrrolidinone (5) which, on boiling with hydrochloric acid, underwent decarboxylation.[6] These examples lend further support to the proposed scheme.

EXPERIMENTAL

Spectroscopic Properties.—The spectroscopic data recorded here are discussed in terms of the pyrrolidinone structure (2). The u.v. spectrum [$\lambda_{max.}$ (EtOH) 209, 218infl, 240infl, and 265infl; ε 18 400, 13 200, 3 700, and 677] is not simply equivalent to the sum of the absorptions of two benzene rings [toluene; $\lambda_{max.}$ (MeOH) 207 and 254; ε 7 000 and 160] and 1-phenylpyrrolidin-2-one [$\lambda_{max.}$ (EtOH) 246; ε 17 200].[7] In the pyrrolidine (2) the *N*-phenyl group is sterically hindered by the adjacent *C*-phenyl, and the overlap of the π-orbitals of the aromatic ring with the *p*-orbital on the sp^2-nitrogen is greatly diminished; hence the extinction coefficient also is greatly lowered. This agrees with the *X*-ray result which shows that the *N*-phenyl group is rotated *ca.* 44° out of the plane of the heterocyclic ring. A similar situation occurs in 5,5-bismethoxycarbonyl-1,4-diphenylpyrrolidin-2-one [$\lambda_{max.}$ (EtOH) 256sh; ε 842].[7]

The i.r. spectrum (Nujol) contains peaks at 1 710 (γ-lactam), 1 595, 1 500, 1 370, 1 350, 1 230, 780, 750, and 695 cm⁻¹, but no peak for C≡N in the region of 2 250 cm⁻¹. The mass spectrum showed the following ions: 338 (44%, M^+), 206 (100), 180 (17), 104 (37), and 77 (36). The molecular formulae of the parent peak (*m/e* 338.139; $C_{23}H_{18}N_2O$ requires 338.142) and the base peak (*m/e* 206.084; $C_{14}H_{10}N_2$ requires 206.084) together with a meta-stable peak at 126 (calculated 125.6) showed that the parent ion fragmented directly to the base peak with loss of C_9H_8O, most probably as PhCH₂CH=C=O, in which a hydrogen atom has migrated from the α to the β position with respect to the carbonyl group.

The ¹H n.m.r. spectrum (in CDCl₃) approximates to an AMX system and clearly corresponds to -CH-CH₂-. The computer-derived values are δ_H 3.88 (H$_A$), 3.32 (H$_B$), and 2.97 (H$_C$); J_{AB} 12.4, J_{AC} 7.5, and J_{BC} -16.8 Hz. Apart from aromatic carbons the ¹³C spectrum (in CDCl₃) showed δ_C 34.9 (CH₂), 54.4 (CH), 73.1 (*C*-CN), 117.1 (CN), and 172.6 (CO).

5-Cyano-1,4,5-triphenylpyrrolidin-2-one (2).—A mixture of α-phenylaminobenzyl cyanide [4] (5.2 g), 2-phenyl-1-cyano-acrylic acid (4.3 g), and sodium hydroxide (1 g) in ethanol (16 ml) and water (4 ml) was warmed at 60—70 °C for 2 h. It was then acidified with concentrated hydrochloric acid and warmed for 1 h. The mixture of solids was collected

and extracted with hot ethanol. The solution, after being filtered and concentrated, yielded 5-cyano-1,4,5-triphenyl-pyrrolidin-2-one (0.95 g, 11%), m.p. and mixed m.p. 182—183 °C (in a capillary tube). The i.r. spectrum was identical with that of the by-product. The mother-liquor, on concentration, gave more pyrrolidin-2-one (0.3 g), m.p. 173—174 °C. When the m.p. was determined with a hot-stage microscope the crystals melted at 170—172 °C, gradually solidified at *ca.* 175 °C, and re-melted at 179—182 °C.

Crystal Structure Determination.—Cell parameters were first found from oscillation and Weissenberg photographs, and then by least squares from the setting angles of 23 reflections on a Hilger–Watt four-circle diffractometer.

Crystal data. $C_{23}H_{18}N_2O$, $M = 338.4$. Trigonal, $a = b = 22.970(5)$, $c = 9.170(3)$ Å (hexagonal axes). $U = 4 190$ Å³, $D_m = 1.2$ g cm⁻³, $Z = 9$, $D_c = 1.207$ g cm⁻³, $F(000) = 1 602$. Space group $R3$, Mo-K_α radiation (graphite monochromator), $\lambda = 0.710 69$ Å, $\mu = 0.81$ cm⁻¹.

The crystal finally chosen for examination was a thin flake with approximate dimensions 0.2 (rotation axis, *c*) × 0.1 × 0.03 mm. A satellite crystal was present which, from photographs, comprised about 20% of the total. Reflections were scanned (ω—2θ mode) for θ < 25°,

TABLE 1

Fractional co-ordinates (× 10⁴) with estimated standard deviations in parentheses

Atom	x/a	y/b	z/c
O(1)	3 029(3)	3 312(3)	7 607
N(1)	3 907(3)	4 393(3)	7 442(11)
C(2)	3 627(4)	3 709(4)	7 545(13)
C(3)	4 192(4)	3 565(4)	7 814(13)
C(4)	4 807(4)	4 187(4)	7 199(13)
C(5)	4 649(4)	4 762(4)	7 564(13)
C(6)	4 836(4)	4 962(4)	9 101(15)
N(2)	4 962(5)	5 081(4)	10 283(15)
C(7)	3 509(4)	4 723(4)	7 256(12)
C(8)	3 659(5)	5 277(5)	8 079(14)
C(9)	3 255(6)	5 576(5)	7 876(16)
C(10)	2 740(7)	5 316(7)	6 924(18)
C(11)	2 593(6)	4 754(7)	6 114(18)
C(12)	2 990(5)	4 452(5)	6 281(14)
C(13)	5 489(4)	4 318(4)	7 693(13)
C(14)	5 573(5)	3 975(5)	8 809(17)
C(15)	6 217(7)	4 104(7)	9 150(21)
C(16)	6 756(6)	4 572(8)	8 421(21)
C(17)	6 696(6)	4 938(8)	7 341(23)
C(18)	6 051(5)	4 801(6)	6 951(17)
C(19)	4 980(4)	5 355(4)	6 493(14)
C(20)	5 467(5)	5 988(5)	7 034(15)
C(21)	5 776(6)	6 508(6)	5 997(20)
C(22)	5 602(6)	6 415(6)	4 608(21)
C(23)	5 120(6)	5 775(5)	4 056(15)
C(24)	4 811(5)	5 260(5)	5 084(14)

TABLE 2

Bond lengths (Å) with standard deviations in parentheses

N(1)–C(2)	1.37(1)	C(9)–C(10)	1.35(2)
N(1)–C(5)	1.48(1)	C(10)–C(11)	1.38(2)
N(1)–C(7)	1.46(1)	C(11)–C(12)	1.40(2)
C(2)–O(1)	1.21(1)	C(13)–C(14)	1.36(2)
C(2)–C(3)	1.51(1)	C(13)–C(18)	1.39(1)
C(3)–C(4)	1.53(1)	C(14)–C(15)	1.39(2)
C(4)–C(5)	1.57(1)	C(15)–C(16)	1.34(2)
C(4)–C(13)	1.51(1)	C(16)–C(17)	1.35(2)
C(5)–C(6)	1.48(1)	C(17)–C(18)	1.40(2)
C(5)–C(19)	1.54(1)	C(19)–C(20)	1.41(1)
C(6)–N(2)	1.12(1)	C(19)–C(24)	1.34(1)
C(7)–C(8)	1.37(1)	C(20)–C(21)	1.41(2)
C(7)–C(12)	1.37(1)	C(21)–C(22)	1.32(2)
C(8)–C(9)	1.42(2)	C(22)–C(23)	1.42(2)
		C(23)–C(24)	1.40(2)

a total of 1 642 unique planes thus being examined. Of these 1 088 had a net count $I > 3 \sigma(I)$, and were used in the refinement. The presence of 'twinning' and the weakly diffracting nature of the crystal suggested, at an early
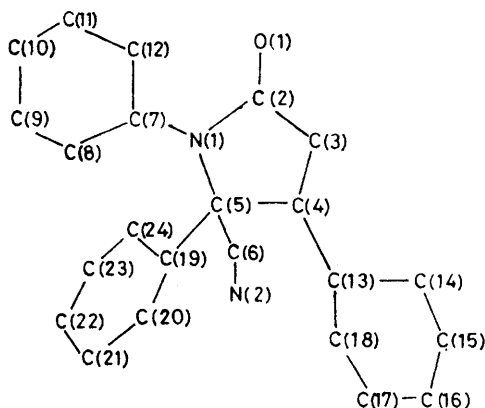

FIGURE 1 Crystallographic numbering

stage, that results of high precision were not likely to be obtained. Lorenz and polarisation corrections were made but no correction was made for absorption.

The structure was eventually solved using MULTAN 78. Final success was perhaps fortuitous and followed normalisation in which a 14-atom fragment had been included as of known structure and orientation. This fragment contained a fused 6/5 ring-system, i.e. a feature not present in the molecule. However, the solution so produced showed

TABLE 3

Bond angles (°) with standard deviations in parentheses

C(2)–N(1)–C(5)	113.4(7)	C(9)–C(10)–C(11)	120.9(10)
C(2)–N(1)–C(7)	123.1(7)	C(10)–C(11)–C(12)	119.3(11)
C(5)–N(1)–C(7)	123.6(6)	C(11)–C(12)–C(7)	118.9(10)
N(1)–C(2)–O(1)	124.9(8)	C(4)–C(13)–C(14)	122.8(8)
N(1)–C(2)–C(3)	107.4(7)	C(4)–C(13)–C(18)	118.0(9)
O(1)–C(2)–C(3)	127.0(8)	C(14)–C(13)–C(18)	119.2(9)
C(2)–C(3)–C(4)	103.3(7)	C(13)–C(14)–C(15)	119.2(12)
C(3)–C(4)–C(5)	102.2(6)	C(14)–C(15)–C(16)	121.0(14)
C(3)–C(4)–C(13)	117.3(8)	C(15)–C(16)–C(17)	121.5(11)
C(5)–C(4)–C(13)	114.9(6)	C(16)–C(17)–C(18)	118.4(13)
C(4)–C(5)–N(1)	100.8(6)	C(17)–C(18)–C(13)	120.7(13)
C(4)–C(5)–C(6)	108.1(7)	C(5)–C(19)–C(20)	118.3(9)
C(4)–C(5)–C(19)	112.9(7)	C(5)–C(19)–C(24)	119.9(7)
N(1)–C(5)–C(6)	108.8(7)	C(20)–C(19)–C(24)	121.8(9)
N(1)–C(5)–C(19)	112.1(7)	C(19)–C(20)–C(21)	116.1(11)
C(6)–C(5)–C(19)	113.3(7)	C(20)–C(21)–C(22)	122.1(11)
N(1)–C(7)–C(8)	119.1(8)	C(21)–C(22)–C(23)	121.8(12)
N(1)–C(7)–C(12)	118.1(8)	C(22)–C(23)–C(24)	116.1(12)
C(8)–C(7)–C(12)	122.7(8)	C(23)–C(24)–C(19)	122.0(9)
C(7)–C(8)–C(9)	117.3(10)	C(5)–C(6)–N(2)	176.7(9)
C(8)–C(9)–C(10)	121.0(10)		

the complete structure of the pyrrolidone; one atom only was missing in what was obviously a phenyl ring.

Refinement by full-matrix least squares proceeded routinely, the O and N atoms being identified from their temperature factors and by chemical and spectroscopic considerations.

At a late stage a difference-map revealed all the hydrogens and these were thus included thereafter in the computations in their calculated positions, which were not refined. A final weighting scheme was used of the form $w = [A(0)T(0)x + A(1)T(1)x + \ldots]^{-1}$ where the A values are the coefficients of a Chebyshev series in $T(i)x$ where $x = F_o/F_{o(max.)}$ Four terms were used with $A(0) = 40.9$, $A(1) = 39.6$, $A(2) = -7.3$, and $A(3) = -9.8$. At convergence the maximum shift/standard deviation was 0.04, and R was 7.6%.

Table 1 contains the fractional co-ordinates, and Tables 2 and 3 the bond lengths and angles (which are unremarkable). Figures 1 and 2 show, respectively, the crystallo-
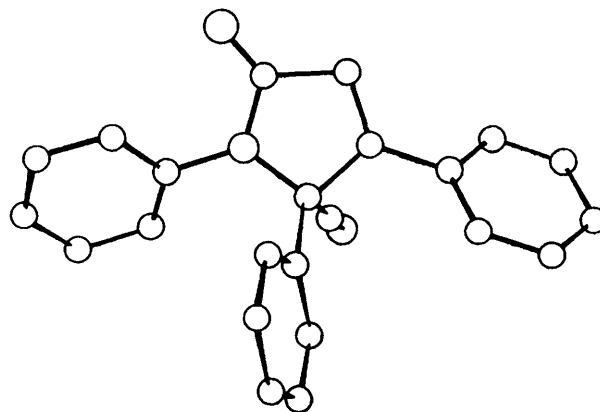

FIGURE 2 Perspective view of 5-cyano-1,4,5-triphenylpyrrolidin-2-one showing relative configuration of the molecule

graphic numbering and a perspective view of the molecule. The observed and calculated structure factors and anisotropic temperature factors are deposited as Supplementary Publication No. SUP 22910 (14 pp.).*

* For details see Notice to Authors No. 7, J.C.S. Perkin I, 1979, Index issue.

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