

## Formation and X-Ray Crystal Structure of Ethyl 2-Amino-1-oxo-inden-3-carboxylate

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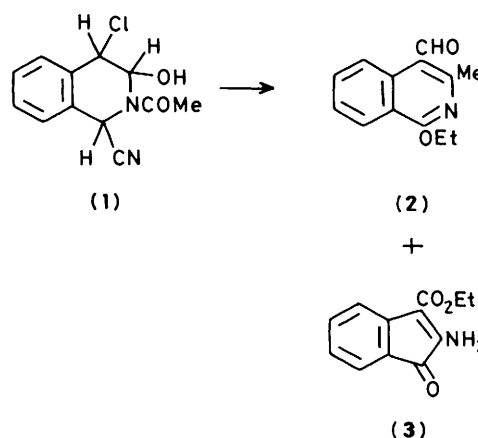
Treatment of 2-acetyl-4-chloro-1-cyano-1,2,3,4-tetrahydro-3-hydroxyisoquinoline (1) with ethanolic sodium hydroxide gave 1-ethoxy-3-methylisoquinoline-4-carbaldehyde (2) accompanied by a purple by-product identified as ethyl 2-amino-1-oxoinden-3-carboxylate (3). The structure of compound (3), the first example of a simple 1-aminoindenone, was confirmed by synthesis from the homophthalic ester (5) and by an X-ray crystallographic analysis. The mechanism of the conversion, (1)→(3), is briefly discussed.

The chlorohydrin (1) reacts with sodium hydroxide in ethanol to give the aldehyde (2) as a major product.<sup>1</sup> The chloro- and bromo-hydrins derived from other isoquinoline Reissert compounds behave similarly.<sup>2</sup> Characteristically, the crude mixtures from these reactions are deeply coloured and are seen, by thin layer chromatography (t.l.c.), to contain small amounts of orange or purple substances. We report here the isolation of a purple by-product from the transformation of compound (1) into the isoquinoline (2) and its identification as ethyl 2-amino-1-oxoinden-3-carboxylate (3).

The chlorohydrin (1) was treated with ethanolic sodium hydroxide at room temperature in the usual way.<sup>1</sup> Most of the aldehyde (2) was removed from the reaction mixture by crystallisation and the mother-liquors were subjected to repeated column and layer chromatography. The by-product (3), C<sub>12</sub>H<sub>11</sub>NO<sub>3</sub>, was obtained as deep-purple needles, λ<sub>max</sub>. 263 (ε 42 300) and 535 nm (654). The i.r. spectrum (KBr) suggested the presence of two carbonyl groups (ν<sub>max</sub>. 1 676 and 1 739 cm<sup>-1</sup>) and possibly an amino group (3 330 and 3 445 cm<sup>-1</sup>). The <sup>1</sup>H n.m.r. spectrum confirmed the presence of two protons exchangeable with D<sub>2</sub>O and showed signals for an ethoxy group and four olefinic or aromatic protons. Two alternative structures, (3) and (4), were considered for the by-product. Although isoindenones are known only as transient species,<sup>3</sup> it was possible that the amino group in the 2-ketone (4) would stabilise the structure by electron donation. However, the by-product was stable even above its melting point (127–131 °C) and its mass spectrum showed fragmentation with loss of ethanol rather than an ethoxy group. This latter observation is accommodated by the structure (3), which contains adjacent ester and amino groups.

The structure (3) was confirmed by a short, though inefficient, synthesis. The homophthalic ester (5)<sup>4</sup> was treated with thionyl chloride<sup>5</sup> in dichloromethane containing a catalytic amount of dimethylformamide and the mixture was stirred with aqueous ethanolic potassium cyanide. The purple organic layer yielded, after chromatography, a sample of compound (3) identical with the foregoing by-product. The indenone (3) was presumably formed, as planned, by base-catalysed cyclisation of an intermediate acyl cyanide. However, despite many variations of reagents and reaction conditions,<sup>5</sup> the yield of pure product did not exceed 6%. Nevertheless the structure (3) was established unambiguously by the X-ray analysis described below.

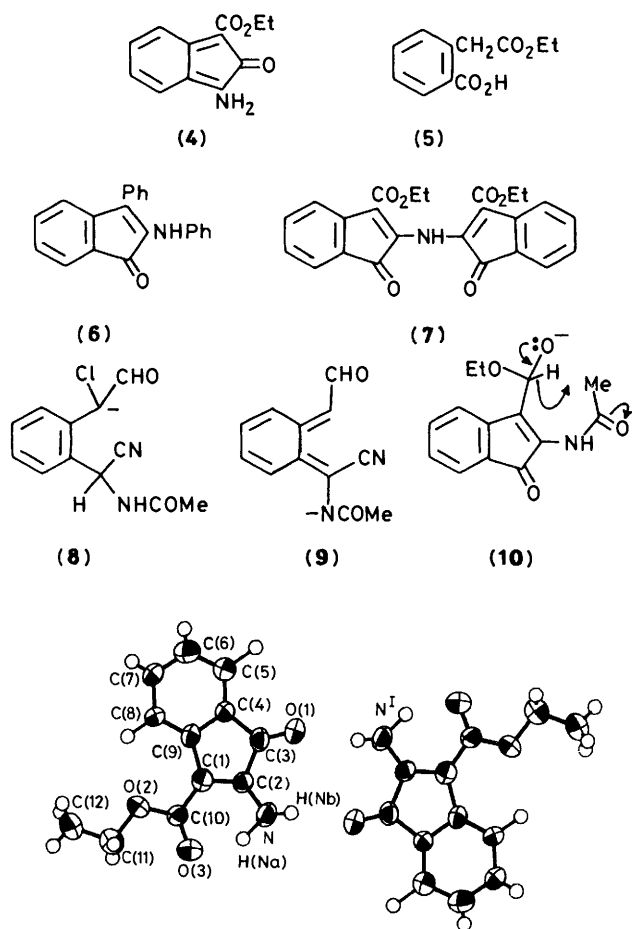
2-Aminoindenones unsubstituted on nitrogen [as in (3)] have apparently not been prepared previously. 2-Arylamino derivatives, e.g. (6), are, however, readily formed by condensation of indanones with nitrosoarenes and have been described as deep blue-violet substances.<sup>6</sup> It appears then that



the striking colour of these compounds may be attributed to the parent, 2-aminoindenone chromophore. Compound (3), a vinylogous amide, was not acetylated even in refluxing acetic anhydride containing sodium acetate. It decomposed slowly in trifluoroacetic acid at room temperature with the formation of a blue product assigned the structure (7) on the basis of its spectroscopic properties (see Experimental section).

The transformation, (1)→(3), would appear to involve the cyclisation of an anion derived from the ring-opened tautomer of compound (1) either before [as (8)] or after [as (9)] 1,4-elimination of hydrogen chloride. The acetamido group could then be detached hydrolytically. The formation of the ester (3) rather than the corresponding aldehyde is surprising, although reminiscent of a Cannizzaro reaction. One possible explanation is that acetyl group migration occurs, following the cyclisation, to give initially 2-acetamido-1-oxoinden-3-carbaldehyde. Intramolecular hydride transfer *via* the ethoxide adduct (10) would then yield a carbinolamine able to collapse to the ketone (3) and acetaldehyde.

**X-Ray Crystal Structure of Compound (3).**—The four molecules in the unit cell are arranged in pairs, each pair consisting of centrosymmetrically related molecules (Figure). The ring carbonyl group of one is hydrogen-bonded to the amino group of the other, and *vice-versa*, so that there is an eight-membered ring in which two sides are formed by hydrogen bonds. The relevant distances are O(1)·····N<sup>1</sup> 2.96(1), O(1)·····H(N<sup>1b</sup>) 2.14(7) Å. There is also an intramolecular hydrogen bond between the amino group and ester carbonyl group, the distances here being O(3)·····N 2.82(1), O(3)·····H(Na) 1.83(16) Å. The location of the amino



**Figure.** The centrosymmetric hydrogen-bonded dimeric unit. Atoms other than hydrogen are shown as 50% probability vibration ellipsoids. Hydrogen atoms are shown as spheres of arbitrary size, and have the same numbers as the atoms to which they are attached. The Roman numeral refers to the equivalent position  $-x, 2-y, -z$  with respect to the asymmetric unit at  $x, y, z$

hydrogen atoms confirms the atom type assignments of the five-membered ring substituents.

Atoms C(6), C(10), O(1), and O(3) deviate significantly from the plane of the other non-hydrogen atoms, the distances being 0.05(1), 0.08(1),  $-0.12(1)$ , and  $0.19(1)$  Å respectively. The amino and aromatic hydrogen atoms lie in the plane within experimental error.

The shortest distances between atoms in different molecules are C(aryl)····C(aryl) 3.47(1), C(aryl)····C(carboxy) 3.82(1), C(aryl)····C(ethyl) 3.74(2), C(aryl)····N 3.53(1), C(aryl)····O 3.24(1), C(ethyl)····C(ethyl) 3.68(2), C(ethyl)····O 3.66(2), N····O 2.96(1) (H-bond), 3.93(1), and O····O 3.57(1) Å.

## Experimental

**Preparation of Ethyl 2-Amino-1-oxoindene-3-carboxylate (3) from 2-Acetyl-4-chloro-1-cyano-1,2,3,4-tetrahydro-3-hydroxyisoquinoline (1).**—The chlorohydrin<sup>1</sup> (1) (2.0 g) in ethanol (250 ml) was treated with 10% aqueous sodium hydroxide (2 mol equiv.) with stirring at room temperature for 3 h. The resulting, deep red solution was dried ( $\text{MgSO}_4$ ) and evaporated to a small volume. The precipitated aldehyde (2) was filtered off and the mother-liquors were chromatographed on grade III, neutral alumina. Elution with benzene gave a purple fraction which

was purified further by chromatography successively on silica GF<sub>254</sub> plates developed with toluene–ethyl acetate (9:1) and alumina GF<sub>254</sub> type E plates developed with toluene–diethyl ether (9:1). Ethyl 2-amino-1-oxoindene-3-carboxylate (3) formed deep purple needles (8 mg), m.p. 131 °C (sintering from 127 °C) (from diethyl ether) (Found: C, 66.4; H, 6.6; N, 5.2%;  $M^+$ , 217.0737.  $\text{C}_{12}\text{H}_{11}\text{NO}_3$  requires C, 66.4; H, 6.45; N, 5.1%;  $M^+$ , 217.0739);  $\nu_{\text{max}}$  (KBr) 3 445, 3 330, 1 733, and 1 676  $\text{cm}^{-1}$ ;  $\lambda_{\text{max}}$  (EtOH) 263 ( $\epsilon$  42 300) and 535nm (654);  $\delta$  ( $\text{CDCl}_3$ ) 7.7–7.5 (m, 3 H), 6.87 (dt,  $J$  8 and 2 Hz, 1 H), ca. 6 (br s, 2 H, exchangeable with  $\text{D}_2\text{O}$ ), 4.33 (q,  $J$  8 Hz, 2 H), and 1.36 (t,  $J$  8 Hz, 3 H).

**Preparation of Ethyl 2-Amino-1-oxoindene-3-carboxylate from the Ethyl Homophthalate (5).**—The ester<sup>4</sup> (5) (260 mg) in dichloromethane (1.5 ml) containing *N,N*-dimethylformamide (27 mg) was treated with thionyl chloride (0.1 ml). The mixture was kept at room temperature for 35 min, diluted with dichloromethane (2.5 ml), then poured into a stirred, saturated aqueous solution of potassium cyanide (2.5 ml). Ethanol (2.5 ml) was added immediately to the mixture which was then stirred for 2 h. The dichloromethane layer was washed with water and dilute sulphuric acid, then dried ( $\text{MgSO}_4$ ) and evaporated. The indenone (3) (15 mg), isolated by chromatography on silica GF<sub>254</sub> plates, developed with chloroform–ethyl acetate (95:5), had spectroscopic properties identical with those of the foregoing material.

**Decomposition of Ethyl 2-Amino-1-oxoindene-3-carboxylate (3) in Trifluoroacetic Acid.**—The indenone (3) (210 mg) was kept in trifluoroacetic acid (2 ml) at room temperature for 45 min. The mixture was evaporated to dryness and the residue dissolved in a little ethanol which was then evaporated. The residue was partitioned between dichloromethane and water containing a little sodium hydrogen carbonate. The organic products were separated on silica GF<sub>254</sub> plates developed twice with chloroform. A fast-running blue component (26 mg) was identified as diethyl 1,1'-dioxo-2,2'-iminodi-indene-3,3'-dicarboxylate (7), m.p. 212–214 °C (from chloroform–ethanol) (Found: C, 69.0; H, 4.8; N, 3.15.  $\text{C}_{24}\text{H}_{19}\text{NO}_6$  requires C, 69.1; H, 4.6; N, 3.4%;  $\lambda_{\text{max}}$  ( $\text{CCl}_4$ ) 577 nm ( $\epsilon$  8 360);  $\nu_{\text{max}}$  (KBr) 1 723 and 1 675  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 10.0 (br s, 1 H, exchangeable with  $\text{D}_2\text{O}$ ), 6.94–7.73 (m, 8 H), 4.42 (q, 4 H), and 1.42 (t, 6 H);  $m/z$  417 and 371.

**Crystal Structure Analysis of the Indenone (3).**—Crystal data.  $\text{C}_{12}\text{H}_{11}\text{NO}_3$ ,  $M = 217.2$ . Monoclinic,  $a = 14.988(1)$ ,  $b = 5.133(1)$ ,  $c = 15.192(3)$  Å,  $\beta = 112.73(1)^\circ$ ,  $U = 1 078.0$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.34$   $\text{g cm}^{-3}$ .  $F(000) = 456$ . Space group  $P2_1/a$ .  $\mu = 7.2$   $\text{cm}^{-1}$  for Cu- $K_\alpha$  radiation,  $\lambda = 1.542$  Å ( $1\text{Å} \equiv 10^{-10}\text{m}$ ).

Deep purple, very thin plate-like crystals were obtained by the crystallisation of compound (3) from ether. A square plate measuring 0.1 mm along the edge was used for the measurement at room temperature (20 °C) of 2 048 independent X-ray intensities by a  $\theta$ - $\omega$  scan on a Nonius CAD4 diffractometer, by use of graphite-monochromated Cu- $K_\alpha$  radiation. These comprised all possible reflections with  $\sin \theta/\lambda < 0.61$  Å<sup>-1</sup>. 976 Reflections having  $F^2 > 2\sigma(F^2)$  were considered observed, where  $\sigma(F^2) = [C + 4(B_1 + B_2) + 0.0009I^2]^{1/2}/(t_c Lp)$ , where  $C$  is the total integrated count in time  $t_c$ ;  $B_1$  and  $B_2$  are background counts;  $I = C - 2(B_1 + B_2)$ ,  $Lp$  is the correction factor for Lorentz and polarisation effects, and  $F^2 = I/(t_c Lp)$ . Intensities were not corrected for absorption. Counting-coincidence errors were avoided by use of an attenuator on high intensities. Unit cell parameters were determined by least-squares refinement of diffractometer setting angles for 25 reflections. The sample crystal was twinned on [001] such that overlap of reflections from the two parts of the twin occurred

**Table 1.** Fractional atomic co-ordinates, with e.s.d.s in the least significant digits in parentheses. Hydrogen atoms have the suffixes of the atoms to which they are attached

	<i>x/a</i>	<i>y/b</i>	<i>z/c</i>
C(1)	0.399 5(6)	0.530 2(17)	0.263 5(6)
C(2)	0.437 4(5)	0.695 9(17)	0.339 4(6)
C(3)	0.389 6(6)	0.647 5(17)	0.408 4(7)
C(4)	0.318 4(6)	0.438 3(18)	0.365 6(6)
C(5)	0.252 6(7)	0.330 2(20)	0.399 3(7)
C(6)	0.193 3(8)	0.138 8(24)	0.341 9(8)
C(7)	0.200 8(7)	0.057 1(21)	0.259 6(7)
C(8)	0.266 4(6)	0.171 1(18)	0.227 6(6)
C(9)	0.325 3(6)	0.364 6(17)	0.280 2(6)
C(10)	0.428 1(6)	0.530 8(19)	0.183 8(6)
C(11)	0.416 2(10)	0.321 4(30)	0.040 2(8)
C(12)	0.356 8(11)	0.127 3(32)	-0.025 2(10)
N	0.505 0(5)	0.875 1(17)	0.355 5(7)
O(1)	0.411 5(5)	0.752 4(14)	0.485 2(5)
O(2)	0.385 7(4)	0.343 1(12)	0.120 0(4)
O(3)	0.484 6(4)	0.686 0(14)	0.174 1(4)
H(5)	0.244(9)	0.405(23)	0.475(8)
H(6)	0.165(5)	0.049(14)	0.361(5)
H(7)	0.155(6)	-0.036(18)	0.224(6)
H(8)	0.272(4)	0.117(13)	0.159(5)
H(11A)	0.474(6)	0.201(17)	0.078(6)
H(11B)	0.402(8)	0.475(22)	0.000(7)
H(12A)	0.341(9)	-0.033(28)	-0.005(8)
H(12B)	0.388(7)	0.062(20)	-0.064(7)
H(12C)	0.287(8)	0.155(20)	-0.061(7)
H(NA)	0.507(11)	0.882(31)	0.281(11)
H(NB)	0.525(5)	0.964(14)	0.405(5)

**Table 2.** Bond lengths (Å) in compound (3), with e.s.d.s in the least significant digits in parentheses

C(1)-C(2)	1.367(13)	C(1)-C(9)	1.497(12)
C(1)-C(10)	1.432(13)	C(2)-C(3)	1.500(13)
C(2)-N	1.320(12)	C(3)-C(4)	1.476(13)
C(3)-O(1)	1.210(12)	C(4)-C(5)	1.391(13)
C(4)-C(9)	1.393(12)	C(5)-C(6)	1.385(16)
C(5)-H(5)	1.26(12)	C(6)-C(7)	1.363(16)
C(6)-H(6)	0.76(8)	C(7)-C(8)	1.384(13)
C(7)-H(7)	0.84(10)	C(8)-C(9)	1.364(13)
C(8)-H(8)	1.11(7)	C(10)-O(2)	1.341(11)
C(10)-O(3)	1.213(12)	C(11)-C(12)	1.45(3)
C(11)-O(2)	1.456(14)	C(11)-H(11A)	1.04(9)
C(11)-H(11B)	0.97(12)	C(12)-H(12A)	0.94(14)
C(12)-H(12B)	0.95(10)	C(12)-H(12C)	0.99(12)
N-H(NA)	1.14(16)	N-H(NB)	0.83(8)

whenever  $h = 0$ . A correction factor for the  $(0kl)$  intensities was determined by measuring a number of non-overlapping intensities from both parts of the twin. Computations were carried out on I.C.L. 2976 and Gould S.E.L. 32/27 computers at Glasgow University; the principal computer programs used are listed in ref. 7. Atomic scattering factors were taken from ref. 8.

**Structure determination.** The formula corresponds to the asymmetric unit, so that the molecule has no crystallographic symmetry, and all atoms are in general positions. The structure was solved by the MULTAN program, the hydrogen atoms being located in difference-Fourier maps calculated during the anisotropic least-squares refinement, which reduced  $R$  to a final value of 0.089 for the observed reflections, with  $R'$  0.137 [ $R' = (\sum w \Delta^2 / \sum w |F_o|^2)^{1/2}$ ]. All isotropic hydrogen parameters were included in the refinement. The function minimised was  $\sum w \Delta^2$ , where  $w = 1/\sigma^2(F_o)$ ,  $\Delta = |F_o| - |F_c|$ . A difference-Fourier map computed from the final structure factors for the observed reflections showed no peaks or holes of magnitude  $> 0.4 \text{ e } \text{Å}^{-3}$ .

**Table 3.** Selected bond angles (°) in compound (3)

C(2)-C(1)-C(9)	107.7(8)	C(2)-C(1)-C(10)	123.3(8)
C(9)-C(1)-C(10)	129.0(8)	C(1)-C(2)-C(3)	109.3(8)
C(1)-C(2)-N	129.0(9)	C(3)-C(2)-N	121.7(9)
C(2)-C(3)-C(4)	105.8(8)	C(2)-C(3)-O(1)	125.1(9)
C(4)-C(3)-O(1)	129.0(9)	C(3)-C(4)-C(5)	128.5(8)
C(3)-C(4)-C(9)	107.9(8)	C(5)-C(4)-C(9)	123.6(9)
C(4)-C(5)-C(6)	115.1(9)	C(5)-C(6)-C(7)	122.5(11)
C(6)-C(7)-C(8)	120.9(10)	C(7)-C(8)-C(9)	119.3(9)
C(1)-C(9)-C(4)	109.3(8)	C(1)-C(9)-C(8)	132.0(8)
C(4)-C(9)-C(8)	118.7(8)	C(1)-C(10)-O(2)	113.4(8)
C(1)-C(10)-O(3)	123.7(9)	O(2)-C(10)-O(3)	122.9(8)
C(12)-C(11)-O(2)	108.5(12)	C(2)-N-H(NA)	98.7(79)
C(2)-N-H(NB)	122.2(48)	H(NA)-N-H(NB)	137.8(93)
C(10)-O(2)-C(11)	116.3(9)		

**Table 4.** Some torsion angles (°) in compound (3)

C(9)-C(1)-C(2)-C(3)	-0.3(7)
C(2)-C(1)-C(9)-C(8)	179.8(14)
C(10)-C(1)-C(2)-C(3)	178.5(12)
C(2)-C(1)-C(10)-O(2)	176.6(13)
C(10)-C(1)-C(9)-C(4)	-177.4(13)
C(9)-C(1)-C(10)-O(2)	-4.9(8)
C(1)-C(2)-C(3)-C(4)	-0.7(8)
N-C(2)-C(3)-C(4)	179.3(12)
C(2)-C(3)-C(4)-C(5)	-177.0(13)
O(1)-C(3)-C(4)-C(5)	7.2(10)
C(3)-C(4)-C(5)-C(6)	178.7(15)
C(3)-C(4)-C(9)-C(8)	179.6(12)
C(9)-C(4)-C(5)-C(6)	0.5(10)
C(4)-C(5)-C(6)-C(7)	1.8(10)
C(6)-C(7)-C(8)-C(9)	1.1(10)
C(7)-C(8)-C(9)-C(4)	1.1(9)
O(3)-C(10)-O(2)-C(11)	4.3(10)
C(2)-C(1)-C(9)-C(4)	1.3(8)
C(9)-C(1)-C(2)-N	179.7(13)
C(10)-C(1)-C(2)-N	-1.5(9)
C(2)-C(1)-C(10)-O(3)	-3.8(9)
C(10)-C(1)-C(9)-C(8)	1.1(10)
C(9)-C(1)-C(10)-O(3)	174.7(15)
C(1)-C(2)-C(3)-O(1)	175.4(13)
N-C(2)-C(3)-O(1)	-4.6(10)
C(2)-C(3)-C(4)-C(9)	1.4(8)
O(1)-C(3)-C(4)-C(9)	-174.4(14)
C(3)-C(4)-C(9)-C(1)	-1.7(7)
C(5)-C(4)-C(9)-C(1)	176.9(12)
C(5)-C(4)-C(9)-C(8)	-1.9(9)
C(5)-C(6)-C(7)-C(8)	-2.6(10)
C(7)-C(8)-C(9)-C(1)	-177.3(15)
C(1)-C(10)-O(2)-C(11)	-176.1(12)
C(12)-C(11)-O(2)-C(10)	-174.6(14)

## Results

Atomic co-ordinates and their estimated standard deviations are in Table 1. Temperature factors and bond angles are available as a Supplementary Publication (SUP. No. 56120, 3pp).<sup>\*</sup> Structure factors are available from the editorial office on request. Tables 2-4 show the bond lengths, selected bond angles, and selected torsion angles. The labelling of the atoms is shown in the Figure.

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<sup>\*</sup> For details of the Supplementary Publications Scheme see Instructions for Authors (1985) in *J. Chem. Soc., Perkin Trans. 1*, 1985, Issue 1.

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