On the Aromaticity of Isoindole. *X*-Ray Analysis of 2-Benzylisoindole

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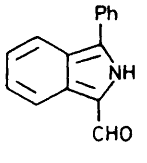
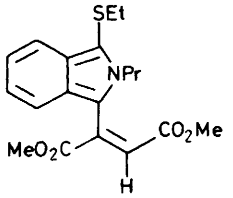
The crystal structure of an isoindole, 2-benzylisoindole, in which the heterocyclic nucleus is regarded as being minimally perturbed by the substituent, is determined by *X*-ray analysis. The isoindole shows structural characteristics indicative of an aromatic system: the carbocyclic ring shows bond alternation reminiscent of that found in naphthalene.

Recently *X*-ray crystal structures have been elucidated for 1-formyl-3-phenylisoindole (**1**)[1,2] and for 3-(*trans*-1,2-bismethoxycarbonylvinyl)-2-propyl-1-(ethylthio)isoindole (**2**).[3] These are the first structures to be arrived at in this way for the isoindole skeleton. The delay in obtaining such structural detail, in spite of its importance with respect to theoretical considerations of aromaticity, testifies to the lack of robustness of the isoindoles, a point further illustrated by the late arrival of the parent substance.[4] However, both compounds (**1**) and (**2**) are stabilised by substituents to an extent which makes them atypical representatives of the isoindole series. Compound (**1**) is stabilised by the conjugated phenyl group and (particularly) by the formyl substituent. Compound (**2**) is heavily substituted on the five-membered ring: *d* orbital overlap involving sulphur is possible, and, although the $\alpha\beta$ unsaturated ester substituent is not effectively conjugated (because it is turned out of the plane of the ring) a π–π interaction between this substituent and the heterocyclic system appears to be present and is, indeed, held to be responsible for the bright red colour of this compound.[3] We have therefore attempted to obtain a suitable crystal of an 'unperturbed' isoindole system, and report here the molecular and crystal structure of 2-benzylisoindole (**3**).



(1)



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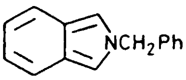


(3)

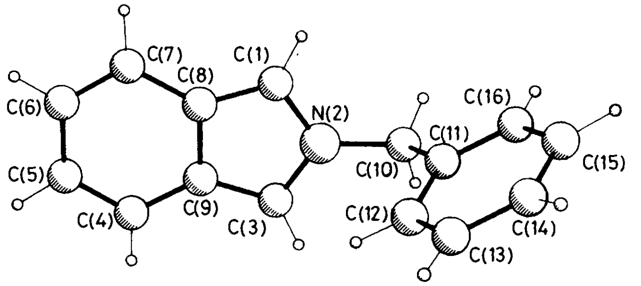


Figure 1. Molecular structure and atom numbering scheme for 2-benzylisoindole. Hydrogen atoms are given the number of the carbon atom to which they are bonded

The molecular structure and the crystallographic numbering scheme are shown in Figure 1, while Figure 2 presents bond lengths and bond angles. The isoindole ring and the phenyl ring are individually planar, the interplanar angle being 87.2°. All the hydrogen atoms are defined: the benzylic methylene group has a somewhat distorted tetrahedral geometry, the N-CH_2-C angle being opened out to 114.4 ± 0.2°. The 2-benzylisoindole molecules pack together as shown in Figure 3. There are no abnormally short intermolecular contacts, and there are no intramolecular contacts less than 3.7 Å, excluding those involving hydrogen atoms.

Within the limits of experimental error, the isoindole skeleton shows C_{2v} symmetry with the (averaged) geometry shown in Figure 4.

The bond lengths clearly show that the isoindole is a delocalised system. Thus in the carbocyclic ring the (average) lengths of the bonds C(4)–C(5) and C(4)–C(9) are 1.357 and 1.416 Å, respectively. Both these values are slightly smaller than the corresponding distances in naphthalene[5] (Table 1), although the differences are barely statistically significant. On the other hand, the C(4)–C(5) bond is slightly longer, and the C(5)–C(6) bond appreciably shorter, than the corresponding distances [*i.e.* C(1)–C(2) and C(2)–C(3), respectively] in cyclohexa-1,3-diene[6] (Table 1). In the five-membered ring the bond distances are unlike those of a pyrrole: thus the C(1)–N(2) bond of 2-benzylisoindole is 0.038 Å shorter than is the C(2)–N(1) bond of 1-methylpyrrole.[7] The isoindole system cannot, therefore, be reasonably regarded as composed of a pyrrole ring 'contiguous but virtually non-interacting'[8] with a diene system, a view that has been advanced recently.[8]

The degree of bond alternation observed in 2-benzylisoindole resembles that found in naphthalene[5] (Table 1). This accords with the view that here we are dealing with an analogous aromatic system, a conclusion in agreement with n.m.r. observations on isoindole itself.[4] A comparison with other recent *X*-ray results is also presented in Table 1. The ylide (**4**) is included to furnish a comparison with an isoindolenine structure.[9] The bond lengths of the various isoindoles indicate that the formyl

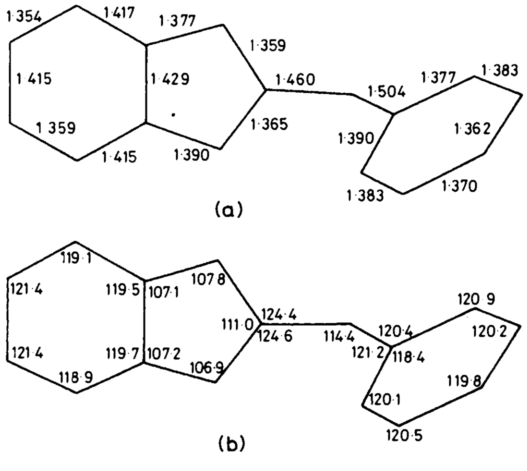


Figure 2. (a) Bond lengths (Å); e.s.d.s are 0.002—0.003 Å. (b) Bond angles (°); all e.s.d.s are 0.2°

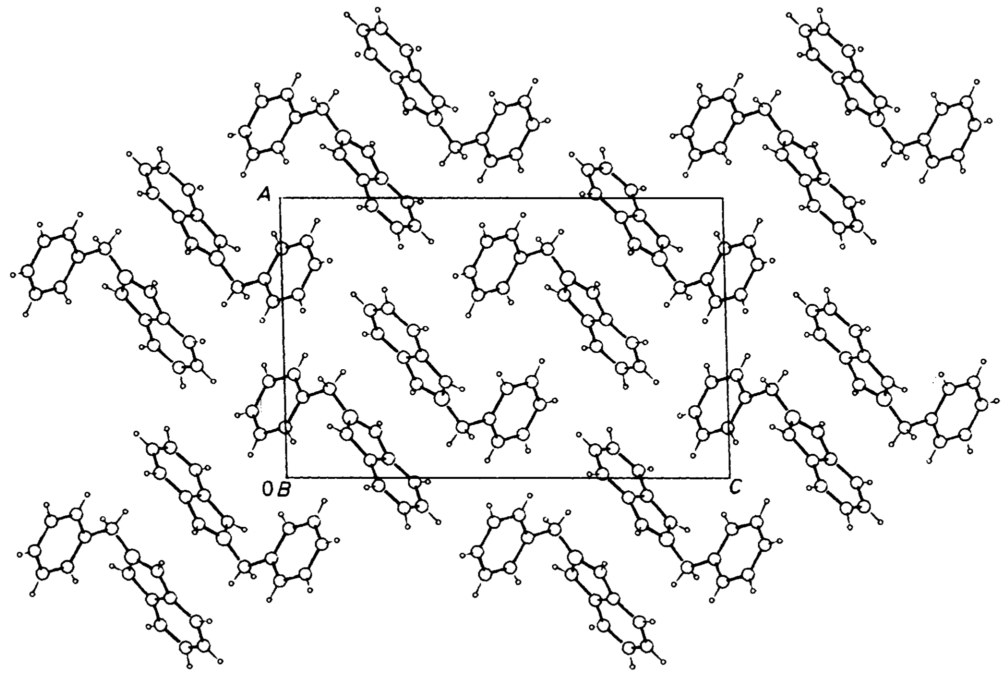
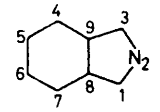


Figure 3. Packing diagram for 2-benzylisoindole

Table 1. Observed bond lengths in 2-benzylisoindole (3) and some related compounds (crystallographic numbering)

	Bond length (Å)						
	1–2 (2–3)	1–8 (3–9)	4–5 (6–7)	9–4 (7–8)	5–6	8–9	Ref.
Isoindoles							
2-Benzylisoindole (**3**)	1.359 (1.365)	1.377 (1.390)	1.359 (1.354)	1.415 (1.417)	1.415	1.429	Present work
1-Formyl-3-phenylisoindole (**1**)	1.376 (1.348)	1.412 (1.428)	1.367 (1.365)	1.414 (1.414)	1.409	1.420	2
3-(*trans*-1,2-Bismethoxycarbonylvinyl)-2-propyl-1-(ethylthio)isoindole (**2**)	1.383 (1.379)	1.387 (1.402)	1.359 (1.360)	1.417 (1.417)	1.426	1.431	3
Other compounds							
Isoindolenine ylide derivative (**4**)	1.320 (1.482)	1.458 (1.489)	1.387 (1.395)	1.384 (1.395)	1.378	1.387	9
			1–2	1–8a	2–3	4a–8a	
Cyclohexa-1,3-diene[a]			1.339		1.467		6
Naphthalene			1.377	1.424	1.411	1.421	5

[a] From electron diffraction studies. All the other results are from *X*-ray crystal data.

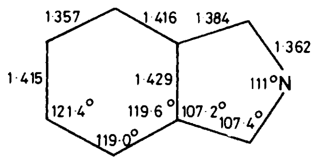
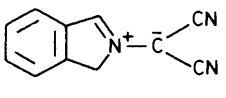


Figure 4. Averaged geometry of isoindole skeleton

derivative (**1**) is significantly distorted as predicted, but that the highly substituted compound (**2**) is much less so.

Bond lengths have also been estimated (for 2-methylisoindole) from proton n.m.r. coupling constants. Values of 1.37 Å [for C(4)–C(5)] and 1.43 Å [for C(5)–C(6)] have been obtained.[10] The agreement here is reasonable, although not so good as that obtained using the same approach in the naphthalene system.[10]



(**4**)

Because isoindole is a close relative of indole, but was unknown for many years,[1] it attracted considerable interest

Table 2. Comparison of observed and calculated bond distances for the isoindole system (crystallographic numbering)

	1–2	1–8	4–5	9–4	5–6	8–9	Ref.
Observed [average values for (3)]	1.362	1.384	1.357	1.416	1.415	1.429	Present work
Calculated (isoindole)	1.384	1.370	1.357	1.456	1.448	1.440	12

Table 3. Atom co-ordinates ($\times 10^4$) for 2-benzylisoindole (3)

	x	*y*	*z*
C(1)	1 650(2)	1 221(3)	2 017(1)
N(2)	2 158(1)	2 529(3)	1 467(1)
C(3)	1 558(2)	4 556(3)	1 371(1)
C(4)	−277(2)	6 164(4)	2 061(1)
C(5)	−1 066(2)	5 654(4)	2 619(1)
C(6)	−1 000(2)	3 549(4)	3 024(1)
C(7)	−151(2)	1 960(4)	2 872(1)
C(8)	694(2)	2 429(3)	2 299(1)
C(9)	628(2)	4 553(3)	1 889(1)
C(10)	3 182(2)	1 816(4)	1 017(1)
C(11)	2 883(2)	91(3)	399(1)
C(12)	1 803(2)	193(4)	−16(1)
C(13)	1 553(2)	−1 405(5)	−585(1)
C(14)	2 368(2)	−3 083(5)	−751(1)
C(15)	3 436(2)	−3 176(4)	−355(1)
C(16)	3 692(2)	−1 603(4)	220(1)

from theoreticians.[10–13] Some calculations included estimates of bond lengths: comparison between the observed values for (3) and the earlier, predicted, values for isoindole are given in Table 2. Clearly there is a measure of agreement here, but it is of interest to note that the Dewar calculations[12] consistently overestimate the lengths of the formal 'single' bonds [*i.e.* C(1)–C(2), C(4)–C(9), C(5)–C(6), and C(8)–C(9)] in the isoindole nucleus.

Experimental

Crystal Preparation.—2-Benzylisoindole was synthesised by the method of Garmaise and Ryan.[14] The crude viscous oil remaining after removing benzene in this preparation was kept at 4 °C overnight, when it partially crystallised. Addition of a small portion of hot ethanol removed non-crystalline material (including coloured impurities) and the needles remaining were recrystallised quickly from boiling ethanol to give large shiny needles, m.p. 110—111 °C. Attempts to obtain crystals suitable for *X*-ray diffraction studies by crystallisation of the crude compound, or by the isothermal distillation method, were unsuccessful. We have not observed the higher value for the m.p. (119—120 °C) quoted by Garmaise and Ryan.[14]

Crystal Data.—$C_{15}H_{13}N$ $M = 207.3$. Monoclinic, $a = 11.1407(14)$, $b = 5.8204(9)$, $c = 17.4414(19)$ Å, $\beta = 91.419(1)°$, $U = 1130.6$ Å^3, $Z = 4$, $D_c = 1.22$ g cm^{-3}, $F(000) = 440$. $\lambda(\text{Cu-}K_\alpha) = 1.541\,78$ Å, $\mu(\text{Cu-}K_\alpha) = 4.7$ cm^{-1}. Space group $P2_1/n$ determined unambiguously from reflection conditions $h0l = 2n$, $0k0 = 2n$.

Data Collection and Refinement.—A needle-like crystal (*ca.* 0.88 × 0.13 × 0.10 mm) was selected for data collection and sealed in a 0.3 mm Lindemann capillary. The crystal system and approximate cell dimensions were determined photographically. Accurate cell parameters were determined and reflection data collected using a Nonius CAD4 diffractometer as described previously.[15] 2 279 reflections were measured in the range $3.0 \leqslant \theta \leqslant 65.0°$ using Ni-filtered Cu-K_α radiation. The data were corrected for Lorentz and polarisation factors but not for absorption. Averaging equivalent reflections gave 1 916 unique data of which 1 506 with $F \geqslant 3\sigma(F)$ were used in the structure refinement.

The structure was solved by direct methods (SHELX EEES 1.4, 251 reflections, 2^{12} sign permutations) which gave the positions of all the non-hydrogen atoms. After four cycles of isotropic least-squares refinement R was 0.13. Anisotropic refinement (R 0.10) followed by a difference synthesis gave the positions of the hydrogen atoms as the 13 highest peaks on the difference map. These were included in subsequent refinement without constraints. The refinement converged at $R\,(=\Sigma\Delta/\Sigma F_o)$ 0.043, $R_w\,(=\Sigma\omega^{\frac{1}{2}}\Delta/\Sigma\omega^{\frac{1}{2}}F_o)$ 0.046 for 197 least-squares parameters. Reflections were weighted as $\omega = 1/[\sigma^2(F) + gF^2]$; a g value of 0.0035 gave flat analyses of variance as a function of $\sin\theta$ and $(F/F_{\max.})$. A final difference map showed maxima and minima of 0.24 and -0.20 eÅ^{-3}, respectively. The final atomic co-ordinates are given in Table 3. Tables of anisotropic thermal parameters, hydrogen atom co-ordinates and temperature factors, and observed and calculated structure factors have been deposited in Supplementary Publication No. SUP 56118 (3 pp.).[*]

All crystallographic calculations were performed on the Queen Mary College ICL2980 computer using the programs SHELX76,[16] XANADU,[17] and GEOM:[18] the diagrams were drawn using PLUTO.[19]

Acknowledgements

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