

Short Communication

X-Ray Structure Determination of a Saturated Methylene-bridged Diphenylimidazo[2,1-*a*]isoindolone

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To achieve a favourable pharmacological effect, a great number of potential anorexic agents have been prepared.¹ The reactions of stereoisomeric 2-arylcyclohexanecarboxylic acids² with cyclic and acyclic difunctional reagents have yielded condensed isoindolones. ¹H and ¹³C NMR methods have been applied to establish the orientations of the terminal and hetero ring(s) in the products in respect of the aryl substituent on the quaternary carbon. In addition, the configuration of the bifunctional starting material can be altered, depending on the reaction conditions.^{2–4} Complete assignment of the ¹H NMR spectra of such saturated condensed isoindolones is often difficult owing to severely overlapping signals.¹ The present work reports the preparation and X-ray analysis of a saturated methylene-bridged imidazoisoindolone.

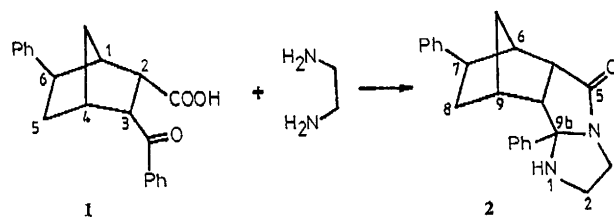
Experimental

Friedel–Crafts acylation of benzene and addition to bicyclo[2.2.1]hept-5-ene-2,3-di-*endo*-carboxylic anhydride leads to 3-*endo*-benzoyl-6-*exo*-phenylbicyclo[2.2.1]heptane-*endo*-2-carboxylic acid (**1**),⁵ which with ethylenediamine yields a mixture of 6,9-methano-7,9b-diphenyl-1,2,3,5a,6,7,8,9,9a,9b-decahydroimidazo[2,1-*a*]isoindol-5-one (**2**, m.p. 191–193°C; Scheme 1) and a *diexo* compound (**3**).⁴ After separation of the two products by elution from a silica-gel column and crystallization, **2** was isolated from the mother liquor.

Crystal data for 2. C₂₃H₂₄N₂O, *M*_r = 344.46, monoclinic, space group *P*2₁/*n*, *a* = 7.668(2), *b* = 23.038(3), *c* = 10.2654(8) Å, β = 94.65(1), *Z* = 4, *V* = 1807.5(4) Å³, *D*_c = 1.266 g cm⁻³, μ(Mo K_α) = 0.72 cm⁻¹, *F*(000) = 736,

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T = 296(1) K, colourless prisms, crystal dimensions 0.25 × 0.30 × 0.40 mm.



Scheme 1.

Data collection, analysis and refinement. A Rigaku AFC5S diffractometer was used, with graphite-monochromated Mo K_α radiation (λ = 0.71069 Å), in the ω–2θ scan mode with an ω scan rate 8.0° min⁻¹ and a scan width of (1.05 + 0.30 tanθ). The weak reflections [*F* < 10σ(*F*)] were rescanned up to two times, 3267 unique reflections measured (2θ_{max} = 50°, *R*_{int} = 0.021). The data were corrected for Lorentz and polarisation effects. An absorption (DI-FABS⁶) correction was also taken into account.

The lattice parameters were calculated by least-squares refinements of 25 reflections for **2**. The structure was solved by direct methods and refined by full-matrix least-squares techniques to an *R*-value of 0.049 (*R*_w = 0.053). The final cycle was based on 2044 independent, observed reflections [*I* > 2σ(*I*)]. The heavy atoms were refined anisotropically, and the hydrogen atoms with fixed isotropic temperature factors (1.2 times *B*_{eq} of the carrying atom). Neutral atomic scattering and dispersion factors were taken from *International Tables for X-Ray Crystallography*.⁷ All calculations were performed using the TEXSAN⁸ crystallographic software. Figures were drawn with ORTEP.⁹ The final atomic positional coordinates

Table 1. Atomic positional parameters and equivalent isotropic temperature factors for (2) with their standard deviations in parentheses.^a

Atom	x	y	z	$B_{eq}/\text{\AA}^2$
O(1)	0.6017(3)	0.7582(1)	0.9866(2)	4.3(1)
N(1)	0.3935(3)	0.9204(1)	1.0259(2)	3.3(1)
N(4)	0.4281(3)	0.8345(1)	0.9110(2)	2.7(1)
C(2)	0.5388(5)	0.9296(2)	0.9418(4)	4.2(2)
C(3)	0.5654(4)	0.8727(1)	0.8666(4)	3.7(2)
C(5)	0.4714(3)	0.7884(1)	0.9927(3)	2.9(1)
C(5A)	0.3362(4)	0.7821(1)	1.0901(3)	2.8(1)
C(6)	0.2176(4)	0.7281(1)	1.0779(3)	2.9(1)
C(7)	0.1562(4)	0.7196(1)	0.9307(3)	2.7(1)
C(8)	0.0168(4)	0.7683(1)	0.9078(3)	2.9(1)
C(9)	0.0301(4)	0.8027(1)	1.0364(3)	2.9(1)
C(9A)	0.2087(3)	0.8339(1)	1.0653(3)	2.6(1)
C(9B)	0.2930(3)	0.8716(1)	0.9632(2)	2.4(1)
C(10)	0.0529(4)	0.7527(1)	1.1349(3)	3.3(1)
C(11)	0.1683(3)	0.8972(1)	0.8548(3)	2.6(1)
C(12)	0.0500(4)	0.9397(1)	0.8854(3)	3.4(1)
C(13)	-0.0690(4)	0.9630(2)	0.7916(4)	4.3(2)
C(14)	-0.0717(4)	0.9439(2)	0.6638(3)	4.3(2)
C(15)	0.0435(4)	0.9020(2)	0.6316(3)	4.0(2)
C(16)	0.1634(4)	0.8788(1)	0.7261(3)	3.2(1)
C(17)	0.0985(4)	0.6581(1)	0.8987(3)	3.1(1)
C(18)	-0.0618(5)	0.6353(1)	0.9268(3)	4.2(2)
C(19)	-0.1024(6)	0.5773(2)	0.9042(4)	5.3(2)
C(20)	0.0149(6)	0.5409(2)	0.8535(3)	5.1(2)
C(21)	0.1731(6)	0.5622(2)	0.8215(4)	4.9(2)
C(22)	0.2152(4)	0.6204(2)	0.8439(3)	4.2(2)
H(1)	0.437(4)	0.906(1)	1.102(3)	4.1
H(2)	0.502(4)	0.959(1)	0.877(3)	5.0
H(3)	0.649(4)	0.939(1)	1.001(3)	5.0
H(4)	0.671(4)	0.853(1)	0.893(3)	4.5
H(5)	0.541(4)	0.881(1)	0.767(3)	4.5
H(6)	0.401(3)	0.784(1)	1.170(3)	3.3
H(7)	0.272(3)	0.693(1)	1.119(2)	3.6
H(8)	0.253(3)	0.728(1)	0.876(2)	3.5
H(9)	0.034(3)	0.793(1)	0.831(3)	3.5
H(10)	-0.105(3)	0.749(1)	0.894(2)	3.5
H(11)	-0.068(3)	0.829(1)	1.049(2)	3.6
H(12)	0.204(3)	0.859(1)	1.143(3)	3.3
H(13)	0.073(3)	0.767(1)	1.224(3)	4.2
H(14)	-0.051(4)	0.724(1)	1.127(3)	4.2
H(15)	0.052(4)	0.951(1)	0.975(3)	4.5
H(16)	-0.150(4)	0.991(1)	0.814(3)	5.1
H(17)	-0.161(4)	0.959(1)	0.595(3)	5.2
H(18)	0.044(4)	0.886(1)	0.539(3)	4.9
H(19)	0.241(4)	0.849(1)	0.703(3)	3.8
H(20)	-0.148(4)	0.659(1)	0.960(3)	5.3
H(21)	-0.221(4)	0.562(1)	0.926(3)	6.3
H(22)	-0.012(4)	0.498(2)	0.839(3)	6.2
H(23)	0.260(4)	0.541(1)	0.785(3)	6.0
H(24)	0.329(4)	0.638(1)	0.820(3)	5.3

^a The equivalent isotropic temperature factors for the non-hydrogen atoms are of the form $B_{eq} = 4/3 \sum_i \beta_{ij} a_i \cdot a_j$.

dinates and equivalent isotropic temperature factors are listed in Table 1.

Results and discussion

X-Ray analysis of **2** gave the solid-state structure (Fig. 1), computed from the final fractional coordinates of the

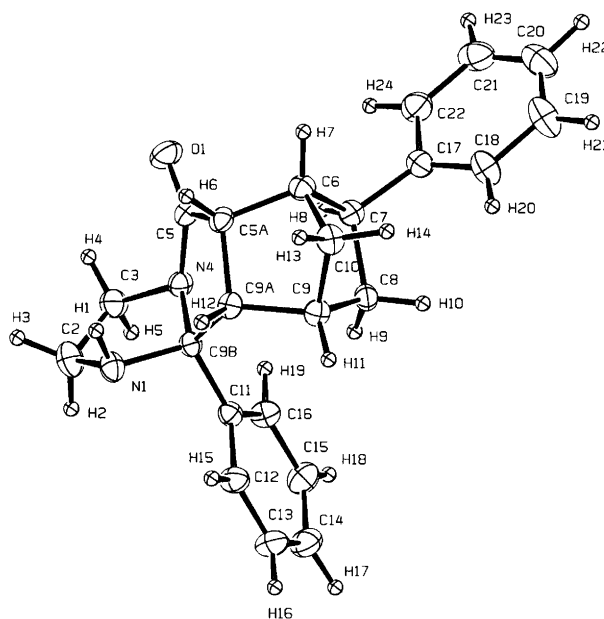


Fig. 1. ORTEP perspective view of molecule **2**, including the atomic labelling scheme.

non-hydrogen and hydrogen atoms listed in Table 1. The relevant bond lengths and bond angles are given in Table 2 and selected torsion angles in Table 3. There are no unusual values for the bonding parameters.

X-Ray analysis indicates that the phenyl substituent on the norbornane ring is 7-*exo* as in 9,11b-diphenyl-8,11-methano-7a,8,9,10,11,11a-hexahydrobenzothiazolo[2,3-*a*]isoindol-7(11b*H*)-one, the X-ray structure of which was published earlier.¹⁰ In this respect, the *exo*-phenyl group did not alter its configuration during the reaction. Since compound **1** was prepared from di-*endo*-bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic anhydride by addition and acylation of benzene in one step, it was important to establish the orientation of this phenyl group because in the starting material **1** it could be located either at position 5 or 6. The *exo* substitution is not surprising, since saturation of the norbornene double bond generally results exclusively in an *exo* substituted product.

The 9b-phenyl group is *endo* and *trans* to the di-*exo* annulation hydrogens at C-5a,9a. In the reaction of **1** and ethylenediamine, isomers can be formed that differ in the annulation of the bicyclic ring and/or the orientation of the 9b-phenyl group. The *trans*-H-5a (H6),H-9a (H12), *endo*-9b-phenyl structure agrees with that deduced from NMR results.⁵ In comparison with **1**, the di-*endo* configuration remained unaltered in **2**, a general finding in many other cyclizations.^{11,12} However, we also isolated a di-*exo* compound **3** from the reaction mixture, the structure of which was established by NMR spectroscopy (suitable crystals for the determination of its crystal structure could not be prepared). The alteration of the original di-*endo* configuration in the latter product is noteworthy, because we have, so far, found only a single example of *endo*→*exo* isomerization in the literature, i.e., the *trans*-

Table 2. Bond distances (Å) and angles (°) in the molecule (**2**)^a.

O(1)–C(5)	1.223(3)	C(9)–C(10)	1.534(4)
N(1)–C(2)	1.480(4)	C(9A)–C(9B)	1.543(4)
N(1)–C(9B)	1.481(3)	C(9B)–C(11)	1.526(4)
N(4)–C(3)	1.473(4)	C(11)–C(12)	1.389(4)
N(4)–C(5)	1.377(3)	C(11)–C(16)	1.384(4)
N(4)–C(9B)	1.477(3)	C(12)–C(13)	1.380(4)
C(2)–C(3)	1.544(5)	C(13)–C(14)	1.383(5)
C(5)–C(5A)	1.505(4)	C(14)–C(15)	1.367(5)
C(5A)–C(6)	1.541(4)	C(15)–C(16)	1.388(4)
C(5A)–C(9A)	1.550(4)	C(17)–C(18)	1.389(4)
C(6)–C(7)	1.558(4)	C(17)–C(22)	1.398(4)
C(6)–C(10)	1.542(4)	C(18)–C(19)	1.386(5)
C(7)–C(8)	1.555(4)	C(19)–C(20)	1.363(5)
C(7)–C(17)	1.512(4)	C(20)–C(21)	1.373(5)
C(8)–C(9)	1.536(4)	C(21)–C(22)	1.393(5)
C(9)–C(9A)	1.553(4)		
C(2)–N(1)–C(9B)	104.2(2)	C(9)–C(9A)–C(9B)	122.8(2)
C(3)–N(4)–C(5)	120.4(2)	N(1)–C(9B)–N(4)	104.0(2)
C(3)–N(4)–C(9B)	107.8(2)	N(1)–C(9B)–C(9A)	111.3(2)
C(5)–N(4)–C(9B)	111.6(2)	N(1)–C(9B)–C(11)	107.3(2)
N(1)–C(2)–C(3)	107.8(3)	N(4)–C(9B)–C(9A)	105.4(2)
N(4)–C(3)–C(2)	103.1(2)	N(4)–C(9B)–C(11)	112.1(2)
O(1)–C(5)–N(4)	124.4(3)	C(9A)–C(9B)–C(11)	116.2(2)
O(1)–C(5)–C(5A)	126.1(3)	C(6)–C(10)–C(9)	94.5(2)
N(4)–C(5)–C(5A)	109.5(2)	C(9B)–C(11)–C(12)	119.4(2)
C(5)–C(5A)–C(6)	117.2(2)	C(9B)–C(11)–C(16)	123.0(2)
C(5)–C(5A)–C(9A)	106.1(2)	C(12)–C(11)–C(16)	117.6(3)
C(6)–C(5A)–C(9A)	104.4(2)	C(11)–C(12)–C(13)	121.6(3)
C(5A)–C(6)–C(7)	108.1(2)	C(12)–C(13)–C(14)	119.7(3)
C(5A)–C(6)–C(10)	99.7(2)	C(13)–C(14)–C(15)	119.6(3)
C(7)–C(6)–C(10)	102.8(2)	C(14)–C(15)–C(16)	120.5(3)
C(6)–C(7)–C(8)	101.9(2)	C(11)–C(16)–C(15)	121.0(3)
C(6)–C(7)–C(17)	112.9(2)	C(7)–C(17)–C(18)	124.0(3)
C(8)–C(7)–C(17)	117.2(2)	C(7)–C(17)–C(22)	118.9(3)
C(7)–C(8)–C(9)	104.2(2)	C(18)–C(17)–C(22)	117.0(3)
C(8)–C(9)–C(9A)	113.5(2)	C(17)–C(18)–C(19)	121.4(3)
C(8)–C(9)–C(10)	100.0(2)	C(18)–C(19)–C(20)	120.6(4)
C(9A)–C(9)–C(10)	99.8(2)	C(19)–C(20)–C(21)	119.7(4)
C(5A)–C(9A)–C(9)	102.1(2)	C(20)–C(21)–C(22)	120.1(4)
C(5A)–C(9A)–C(9B)	104.5(2)	C(17)–C(22)–C(21)	121.1(3)

^a E.s.d.s are given in parentheses.

formation of bicyclo[2.2.1]hept-5-ene-2,3-di-*endo*-carboxylic anhydride to the di-*exo* anhydride on prolonged heating.¹³

Table 3. Selected torsion angles (°) for **2**^a.

C(9A)–C(9B)–N(4)–C(5)	–18.2(3)
C(9B)–N(4)–C(5)–C(5A)	14.4(3)
N(4)–C(5)–C(5A)–C(9A)	–4.3(3)
C(5)–C(5A)–C(9A)–C(9B)	–6.5(3)
C(5)–C(9A)–C(9B)–N(4)	14.3(3)
C(3)–N(4)–C(9B)–N(1)	–35.4(3)
N(4)–C(9B)–N(1)–C(2)	34.9(3)
C(9B)–N(1)–C(2)–C(3)	–22.5(3)
N(1)–C(2)–C(3)–N(4)	1.4(3)
C(2)–C(3)–N(4)–C(9B)	20.7(3)

^a E.s.d.s. are given in parentheses.

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