The integrated intensities were obtained by a modified version (Belletti, Ugozzoli, Cantoni & Pasquinelli, 1979) of the Lehmann & Larsen (1974) peak-profile analysis procedure, and corrected for Lorentz and polarization effects, but not for absorption.

The structure was solved by direct methods and refined on F^2 by anisotropic full-matrix least squares. The H atoms were placed in calculated positions, riding on the attached atoms; four isotropic U(H) parameters, constrained to be equal for chemically equivalent H atoms, were refined, as were the orientation and C—H distance for each of the three methyl groups. H3O was found in a $\Delta\rho$ synthesis out of the plane of the parent CO_2 group and was not subsequently refined. An independent refinement on F with SHELX76 (Sheldrick, 1976) using 1223 observed $[I > 2\sigma(I)]$ reflections and 194 parameters gave results essentially equal to those reported here.

The anomalous scattering effects did not give unequivocally the absolute configuration of the molecule, the value of the Flack (1983) index being $x = 0.4\,(3)$. The configuration was assigned on the basis of the known chiralities of the menthyl C atoms in (1).

The calculations were carried out on the ENCORE91 and GOULD-POWERNODE 6040 computers of the Centro di Studio per la Strutturistica Diffrattometrica del CNR (Parma), and on a COMPAQ-486c portable computer.

Data collection: local programs. Cell refinement: LQPARM (Nardelli & Mangia, 1984). Data reduction: local programs. Program(s) used to solve structure: SHELXS86 (Sheldrick, 1985). Program(s) used to refine structure: SHELXL93 (Sheldrick, 1993); SHELX76 (Sheldrick, 1976). Molecular graphics: ORTEP (Johnson, 1965); PLUTO (Motherwell & Clegg, 1976). Geometrical calculations and preparation of the material for publication: PARST (Nardelli, 1983); PARSTCIF (Nardelli, 1991).

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5a-p-Methylphenyl-5a,5b,6,7,8,9,9a,10-octahydro-5H-isoindolo[2,1-a]benzimidazol-10-one

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Abstract

The title compound, $C_{21}H_{22}N_2O$, was prepared by the reaction of cis-2-(4-methylbenzoyl)cyclohexane-carboxylic acid and o-phenylenediamine. A mixture of two isomeric compounds was isolated and separated by column chromatography. The compounds differ in the cyclohexane–pyrrolidone annelation, which is cis in the title compound. The mutual arrangement of the aryl group and the annelation H atoms is also cis.

Comment

For the synthesis of potential anorectic compounds a great number of saturated or partly saturated isoindolone derivatives have been prepared (Stájer, Csende, Bernáth, Sohár & Szúnyog, 1994; Stájer, Csende, Bernáth &

Sohár, 1994). As the configurations of the starting aroyl-cycloalkane carboxylic acids often change, depending on the reaction conditions, the structures of the products have to be established in each case (Stájer, Sillanpää & Pihlaja, 1993; Sillanpää, Stájer & Pihlaja, 1994). Similar aromatic analogues exhibit no isomers (Aeberli, Eden, Gogerty, Houlihan & Penberthy, 1975; Houlihan, 1974), but in the saturated analogues the mutual positions of the aryl group and annelation H atoms can differ. Difficulties may arise when the signals in the NMR spectra merge; this sometimes necessitates X-ray structure elucidation.

The title compound was prepared by the reaction of cis-2-(4-methylbenzoyl)cyclohexanecarboxylic acid, (1), and o-phenylenediamine, (2). A mixture of two isomeric compounds, (3) and (4), was isolated and separated by column chromatography. Compounds (3) and (4) differ in the cyclohexane–pyrrolidone annelation, which is trans for (3) [shown by NMR (Stájer, Csende, Bernáth & Sohár, 1994)] and cis for (4), as shown by the present X-ray structure determination.
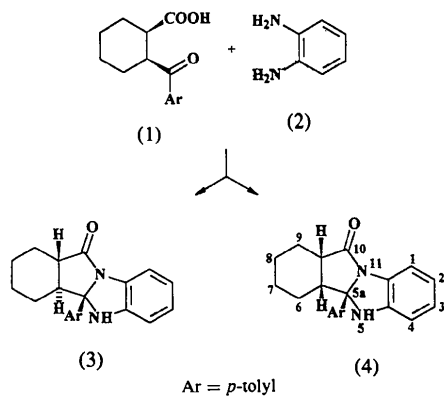
A perspective view of molecule (4) (Fig. 1) shows that the aryl group and the annelation H atoms, H5b and H9a, are cis relative to the pyrrolidone ring, which has an envelope conformation with an out-of-plane C9a atom. The geometric parameters (Table 2) do not have any unusual values. The N5—H5$\cdots$O1($\frac{1}{2}-x$, $-\frac{1}{2}+y$, $\frac{3}{2}-z$) hydrogen bond stabilizes the structure in the solid state [N5$\cdots$O1 2.937 (4) Å and N5—H5$\cdots$O1 168 (3)°].

The cyclohexane ring has a chair conformation and each five-membered ring an envelope conformation (see torsion angle values in Table 2). On comparison with compound (3), which contains a trans-condensed saturated isoindolone moiety [the cis configuration of the starting compound (1) changes during the reaction], (4) retains the original cis configuration of the starting compound (1); this is unusual because cis–trans isomerization has been found for similar reactions in many other cases (cf. Stájer, Csende, Bernáth & Sohár, 1994). Previous results show that trans-condensed pyrrolidine–
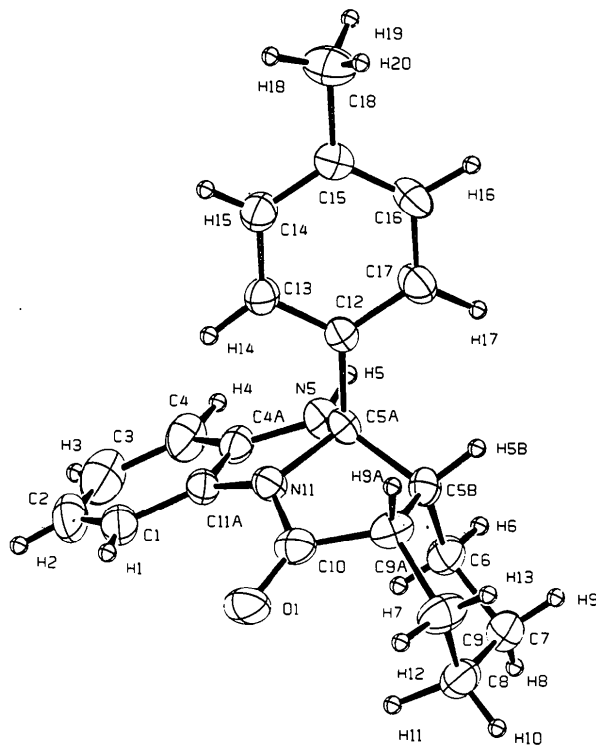

Fig. 1. Structure of compound (4) showing displacement ellipsoids at the 30% propability level, except for those of H atoms, which represent an isotropic displacement factor of 1.0 Å^2.

cyclohexane ring fusion is advantageous for analogous tetracyclic compounds.

Experimental

A mixture of (1) (6.15 g, 25 mmol), (2) (2.70 g, 25 mmol) and solid p-toluenesulfonic acid (ca 10 mg) in dry toluene (50 ml) was refluxed for 3 h using a water separator. After removal of the solvent, the residue was purified by column chromatography (silica gel, benzene, monitoring by TLC). The early fractions contained compound (4) (1.5 g, 25% yield) and the later ones compound (3) (1.76 g, 29%). Data for compound (3), together with the structure elucidation by NMR (m.p. 461–463 K), have been published elsewhere (Stájer, Csende, Bernáth & Sohár, 1994). Compound (4) (m.p. 491–492 K) was recrystallized from ethanol.

Crystal data

$C_{21}H_{22}N_2O$	Mo $K\alpha$ radiation
$M_r = 318.41$	$\lambda = 0.71069$ Å
Monoclinic	Cell parameters from 25
$P2_1/n$	reflections
$a = 9.845 (3)$ Å	$\theta = 20.0$–$23.6°$
$b = 12.445 (2)$ Å	$\mu = 0.076$ mm^{-1}
$c = 14.0154 (13)$ Å	$T = 293 (2)$ K
$\beta = 92.154 (12)°$	Prism
$V = 1716.0 (6)$ Å^3	$0.32 \times 0.26 \times 0.22$ mm
$Z = 4$	Colourless
$D_x = 1.232$ Mg m^{-3}	

Data collection

Rigaku AFC-5S diffractom-
eter
$\omega/2\theta$ scans
Absorption correction:
ψ scans (North, Phillips
& Mathews, 1968)
$T_{min} = 0.975$, $T_{max} =$
1.000
2712 measured reflections
2381 independent reflections

1401 observed reflections
$[I > 2\sigma(I)]$
$R_{int} = 0.038$
$\theta_{max} = 24.98°$
$h = 0 \rightarrow 10$
$k = 0 \rightarrow 14$
$l = -16 \rightarrow 16$
3 standard reflections
monitored every 150
reflections
intensity decay: none

Refinement

Refinement on F^2
$R(F) = 0.0441$
$wR(F^2) = 0.1164$
$S = 1.025$
2381 reflections
294 parameters
$w = 1/[\sigma^2(F_o^2) + (0.0272P)^2 + 0.3430P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = -0.001$
$\Delta\rho_{max} = 0.161$ e Å^{-3}
$\Delta\rho_{min} = -0.134$ e Å^{-3}

Extinction correction:
SHELXL93 (Sheldrick,
1993)
Extinction coefficient:
0.0078 (12)
Atomic scattering factors
from *International Tables
for Crystallography* (1992,
Vol. C, Tables 4.2.6.8 and
6.1.1.4)

Table 1. *Fractional atomic coordinates and equivalent
isotropic displacement parameters* (Å^2)

$$U_{eq} = (1/3)\Sigma_i\Sigma_jU_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
O1	0.4243 (2)	0.9631 (2)	0.8061 (2)	0.0792 (8)
N5	0.2288 (3)	0.6656 (2)	0.6983 (2)	0.0537 (8)
N11	0.3778 (2)	0.7956 (2)	0.7456 (2)	0.0479 (7)
C1	0.3813 (4)	0.8902 (4)	0.5851 (4)	0.0753 (12)
C2	0.3271 (6)	0.8844 (5)	0.4924 (4)	0.098 (2)
C3	0.2420 (6)	0.8035 (6)	0.4650 (4)	0.101 (2)
C4	0.2047 (4)	0.7236 (4)	0.5271 (3)	0.0737 (12)
C4a	0.2553 (3)	0.7282 (3)	0.6204 (2)	0.0530 (9)
C5a	0.3231 (3)	0.6917 (2)	0.7783 (3)	0.0444 (8)
C5b	0.2588 (3)	0.7249 (3)	0.8723 (2)	0.0497 (9)
C6	0.1160 (3)	0.7696 (4)	0.8577 (3)	0.0614 (10)
C7	0.0705 (4)	0.8325 (4)	0.9443 (3)	0.0720 (12)
C8	0.1648 (4)	0.9262 (3)	0.9654 (3)	0.0682 (11)
C9	0.3087 (4)	0.8862 (4)	0.9871 (3)	0.0755 (12)
C9a	0.3585 (3)	0.8125 (3)	0.9085 (3)	0.0568 (9)
C10	0.3912 (3)	0.8690 (3)	0.8167 (3)	0.0574 (9)
C11a	0.3438 (3)	0.8105 (3)	0.6474 (2)	0.0530 (9)
C12	0.4355 (3)	0.6077 (2)	0.7894 (2)	0.0432 (8)
C13	0.5488 (3)	0.6115 (3)	0.7334 (2)	0.0541 (9)
C14	0.6468 (4)	0.5321 (3)	0.7389 (3)	0.0611 (10)
C15	0.6370 (3)	0.4462 (3)	0.7994 (2)	0.0565 (9)
C16	0.5258 (4)	0.4419 (3)	0.8549 (3)	0.0679 (11)
C17	0.4262 (4)	0.5211 (3)	0.8504 (3)	0.0634 (10)
C18	0.7430 (4)	0.3580 (3)	0.8035 (3)	0.0889 (13)

Table 2. *Selected geometric parameters* (Å, °)

O1—C10	1.226 (4)	C1—C11a	1.382 (5)
N5—C4a	1.374 (4)	C4—C4a	1.382 (5)
N5—C5a	1.465 (4)	C4a—C11a	1.388 (4)
N11—C10	1.354 (4)	C5a—C12	1.527 (4)
N11—C11a	1.416 (4)	C5b—C9a	1.540 (4)
N11—C5a	1.480 (3)	C9a—C10	1.512 (5)
C4a—N5—C5a	110.4 (3)	C12—C5a—C5b	114.6 (2)
C10—N11—C11a	129.8 (3)	C6—C5b—C5a	113.0 (3)
C10—N11—C5a	112.8 (3)	C6—C5b—C9a	111.1 (3)

C11a—N11—C5a	109.9 (2)	C5a—C5b—C9a	101.2 (2)
C11a—C1—C2	116.9 (5)	C10—C9a—C9	114.8 (3)
C3—C4—C4a	118.2 (5)	C10—C9a—C5b	101.7 (3)
N5—C4a—C4	131.0 (4)	C9—C9a—C5b	116.4 (3)
N5—C4a—C11a	109.7 (3)	O1—C10—N11	125.0 (3)
C4—C4a—C11a	119.2 (4)	O1—C10—C9a	127.8 (3)
N5—C5a—N11	100.6 (2)	N11—C10—C9a	107.2 (3)
N5—C5a—C12	111.3 (2)	C1—C11a—C4a	122.5 (4)
N11—C5a—C12	111.1 (2)	C1—C11a—N11	130.5 (4)
N5—C5a—C5b	116.4 (2)	C4a—C11a—N11	106.9 (3)
N11—C5a—C5b	101.4 (2)		
C6—C5b—C9a—C10	-81.7 (3)	C9a—C5b—C6—C7	-49.6 (4)
C5a—C5b—C9a—C9	164.0 (3)	C5b—C6—C7—C8	59.7 (5)
C11a—N11—C10—O1	-28.1 (3)	C6—C7—C8—C9	-60.6 (5)
C5a—N11—C10—O1	-174.1 (3)	C7—C8—C9—C9a	53.1 (5)
C5b—C9a—C10—O1	151.8 (3)	C8—C9—C9a—C5b	-46.0 (5)
C9—C9a—C10—O1	25.2 (5)	C6—C5b—C9a—C9	43.8 (4)
C5a—N5—C4a—C11a	-12.0 (3)	N11—C5a—C5b—C9a	-34.8 (3)
C4a—N5—C5a—N11	15.6 (3)	C5a—C5b—C9a—C10	38.6 (3)
C11a—N11—C5a—N5	-14.0 (3)	C5b—C9a—C10—N11	-28.5 (3)
C5a—N11—C11a—C4a	7.9 (3)	C5a—N11—C10—C9a	6.1 (3)
N5—C4a—C11a—N11	2.4 (3)	C10—N11—C5a—C5b	18.9 (3)

H atoms were found from $\Delta\rho$ maps and were refined with isotropic displacement parameters, except for the methyl H atoms, which were included in idealized positions with fixed displacement parameters (1.2 times the displacement parameter of the host atom) and C—H distances of 0.96 Å.

Data collection: *TEXSAN* (Molecular Structure Corporation, 1989). Cell refinement: *TEXSAN* (Molecular Structure Corporation, 1989). Data reduction: *TEXSAN*. Program(s) used to solve structure: *SHELXS*86 (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *SHELXL*93.

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