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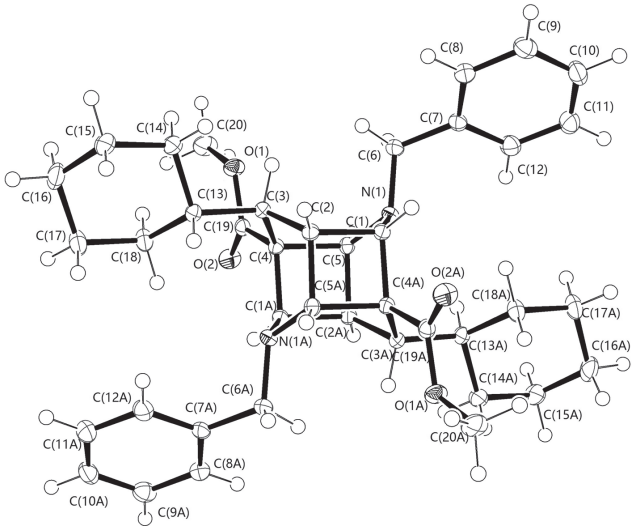
Crystal structure of dimethyl 3,9-dibenzyl-6,12-dicyclohexyl-3,9-diazahexacyclo [6.4.0.0^{2,7}.0^{4,11}.0^{5,10}]-dodecane-1,11-dicarboxylate, $C_{40}H_{50}N_2O_4$



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Abstract

$C_{40}H_{50}N_2O_4$, monoclinic, $P2_1/c$ (no. 14), $a = 10.355(2)$ Å, $b = 17.809(4)$ Å, $c = 8.9354(16)$ Å, $\beta = 97.101(4)°$, $V = 1635.2(5)$ Å^3, $Z = 2$, $R_{gt}(F) = 0.0453$, $wR_{ref}(F^2) = 0.1270$, $T = 113$ K.

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The cage centrosymmetric dimer of the title crystal structure is shown in the figure. Tables 1 and 2 contain details of the measurement method and a list of the atoms including atomic coordinates and displacement parameters.

Source of material

The title compound was synthesized by methyl 1-benzyl-1,4-dihydro-4-cyclohexylpyridine-3-carboxylate under irradiation of UV-light in methanol/THF solution. After

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Table 1: Data collection and handling.

Crystal:	Colourless prism
Size:	0.2 × 0.8 × 0.12 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.81 cm^{-1}
Diffractometer, scan mode:	Rigaku XtaLAB P200, φ and ω
$2\theta_{max}$, completeness:	55.2°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	16583, 3765, 0.0247
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3411
$N(param)_{refined}$:	209
Programs:	Rigaku [1], OLEX2 [2], ShelXL [3]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	x	y	z	U_{iso}*/U_{eq}
O1	0.15997(8)	0.08849(5)	0.86867(10)	0.0195(2)
O2	0.12979(8)	−0.03622(5)	0.88370(10)	0.0217(2)
N1	0.52972(9)	0.04945(5)	0.81502(10)	0.0134(2)
C1	0.61223(11)	0.05978(6)	0.95856(12)	0.0132(2)
H1	0.6852	0.0957	0.9504	0.016*
C2	0.53807(11)	0.07687(6)	1.09744(12)	0.0133(2)
H2	0.5786	0.1194	1.1596	0.016*
C3	0.39018(11)	0.08561(6)	1.06362(12)	0.0129(2)
H3	0.3731	0.1306	0.9972	0.016*
C4	0.33957(11)	0.01678(6)	0.97137(12)	0.0129(2)
C5	0.42058(10)	0.00086(6)	0.83221(12)	0.0132(2)
H5	0.3618	−0.0048	0.7353	0.016*
C6	0.49645(11)	0.12002(7)	0.73421(13)	0.0173(2)
H6A	0.4701	0.1578	0.8059	0.021*
H6B	0.4216	0.1114	0.6559	0.021*
C7	0.60981(11)	0.15012(7)	0.66070(13)	0.0167(2)
C8	0.66140(12)	0.22057(7)	0.69749(14)	0.0201(3)
H8	0.6258	0.2501	0.7710	0.024*
C9	0.76497(13)	0.24872(8)	0.62794(15)	0.0241(3)
H9	0.7990	0.2972	0.6535	0.029*
C10	0.81767(13)	0.20568(8)	0.52174(15)	0.0262(3)
H10	0.8881	0.2247	0.4744	0.031*
C11	0.76794(13)	0.13437(8)	0.48372(15)	0.0260(3)
H11	0.8046	0.1047	0.4114	0.031*
C12	0.66405(13)	0.10728(7)	0.55290(14)	0.0224(3)
H12	0.6294	0.0590	0.5266	0.027*
C13	0.33091(11)	0.10193(6)	1.21243(13)	0.0145(2)
H13	0.3985	0.0881	1.2978	0.017*
C14	0.30771(13)	0.18651(7)	1.22404(14)	0.0196(3)
H14A	0.3889	0.2136	1.2105	0.023*
H14B	0.2400	0.2021	1.1419	0.023*

Table 2 (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
C15	0.26481(14)	0.20837(7)	1.37554(14)	0.0237(3)
H15A	0.3365	0.1983	1.4571	0.028*
H15B	0.2453	0.2628	1.3757	0.028*
C16	0.14437(13)	0.16425(8)	1.40535(15)	0.0266(3)
H16A	0.0694	0.1801	1.3327	0.032*
H16B	0.1238	0.1757	1.5082	0.032*
C17	0.16455(13)	0.07978(8)	1.39076(15)	0.0239(3)
H17A	0.0825	0.0533	1.4031	0.029*
H17B	0.2319	0.0627	1.4719	0.029*
C18	0.20673(12)	0.05968(7)	1.23670(14)	0.0197(3)
H18A	0.2222	0.0049	1.2318	0.024*
H18B	0.1364	0.0729	1.1557	0.024*
C19	0.19836(11)	0.01828(6)	0.90829(12)	0.0147(2)
C20	0.02647(12)	0.09664(8)	0.80188(16)	0.0262(3)
H20A	0.0119	0.0666	0.7095	0.039*
H20B	0.0086	0.1496	0.7776	0.039*
H20C	−0.0317	0.0793	0.8733	0.039*

approximately 24 h. By thin-layer chromatography, the residue was purified using ethyl acetate-petroleum ether (1:40 v/v). After concentration in vacuo colorless solids were collected and dried, and recrystallized from methanol. After 1 week colorless crystals were obtained.

Experimental details

All H atoms were placed in calculated positions (C—H = 0.95–1.00 Å) and refined as riding atoms. The U_{iso} values were set to be $1.5U_{eq}$ of the carrier atom for nitrogen H atoms and $1.2U_{eq}$ for the remaining H atoms.

Discussion

Tetraasterane, cubane and homocubane have unique caged structures and lipophilic properties, which have been used in research on energy, functional materials and anti-tumor and antiviral drugs [4]. Recently, the 3,9-diazatetraasteranes possessing C_2 symmetry have been suggested to be novel inhibitors of retroviral PR on the basis of molecular modeling results [5]. As competitive inhibitors [6], they are among the most promising classes of novel inhibitors of HIV-1 PR because their bioanalytical profile of poor metabolism and protein binding suggest better oral bioavailabilities. Only a small number of 3,9-diazatetraasterane have been reported so far [7]. In order to search for new 3,9-diazatetraasterane, the title compound was synthesized and its crystal structure was determined.

The molecular structure of the title compound is shown in the figure. All bond lengths and angles are within normal ranges [8]. Crystal structure analysis revealed that the piperidine rings are in chair conformation, the apexes (prows) being the N1 and C3 atoms. In a flat cyclobutane system a significant proportion of the molecular strain comes from the eclipsed orientation of vicinal substituents around the ring. Inward methylene rocking [9] may not be possible to relieve the eclipsed-orientation strain in the present case, because of the N1 and C3 bridges connecting the two cyclobutane rings at all corners.

Because of the Csp^2 nature of the substituent at C3, the orientation of the cyclohexyl ring around the C3—C13 bond is characterized by the following torsion angles: C4—C3—C13—C14: −138.44° C2—C3—C13—C14: 98.94°. On the other hand, the torsion angle N1—C6—C7—C8 is −120.74°.

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