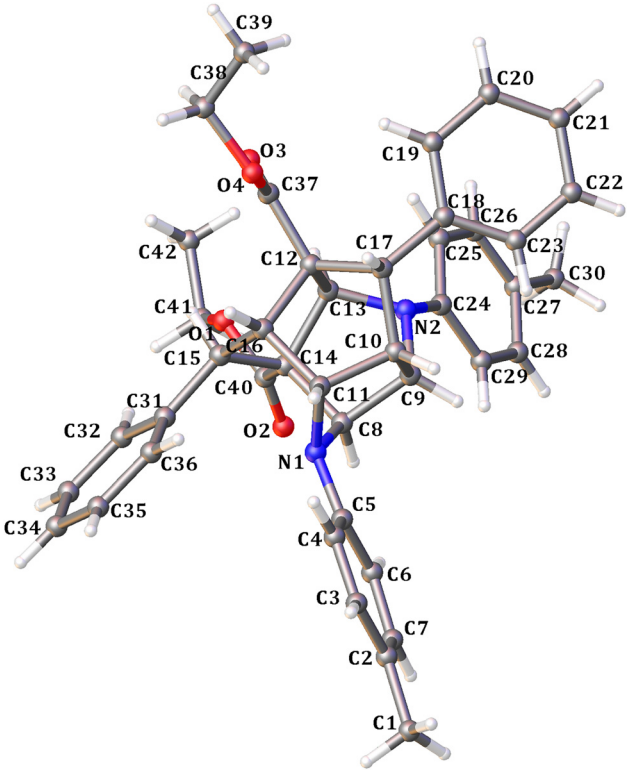
Shuai Fan, Qian Zhang, Xu-Dong Lv, Yuan-Yuan Jin and Zhao-Yong Yang*

Crystal structure of diethyl 4,6-diphenyl-1,9-di-*p*-tolylhexahydro-3*H*-2,7,3,5-(epimethanetriyliminomethanetriyl)cyclopenta[*b*]pyridine-3,5(2*H*)-dicarboxylate, $C_{42}H_{42}N_2O_4$



https://doi.org/10.1515/ncrs-2022-0029
Received January 18, 2022; accepted March 7, 2022;
published online April 4, 2022

Abstract

$C_{42}H_{42}N_2O_4$, triclinic, $P\bar{1}$ (no. 2), a = 9.309(3) Å, b = 14.191(5) Å, c = 14.918(5) Å, α = 69.221(4)°, β = 82.384(5)°, γ = 72.805(4)°, V = 1759.3(10) Å^3, Z = 2, $R_{gt}(F)$ = 0.0699, $wR_{ref}(F^2)$ = 0.1806, T = 296 K.

CCDC no.: 2142413

***Corresponding author: Zhao-Yong Yang**, Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences & Peking Union Medical College, Tiantanxili, 100050 Beijing, P. R. China,
E-mail: zhaoyongy@imb.pumc.edu.cn
Shuai Fan, Qian Zhang, Xu-Dong Lv and Yuan-Yuan Jin, Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences & Peking Union Medical College, Tiantanxili, 100050 Beijing, P. R. China

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.18 × 0.16 × 0.14 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.08 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	25.0°, 99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	13,612, 6153, 0.055
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs} > 2 σ(I_{obs}), 3035
$N(param)_{refined}$:	436
Programs:	Bruker [1], SHELX [2, 3]

The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

The preparation of 1,4-diaryl-1,4-dihydropyridine-3-carboxylic acid photoreactive raw materials was performed by a literature method [4]. Starting from aniline (0.5 mmol), ethyl propiolate (0.5 mmol) and 4-methylcinnamaldehyde (0.5 mmol); piperazine (0.25 mmol) and *p*-toluenesulfonic acid (0.02 mmol) were used as catalysts, 1,2-dichloroethane (20 mL) was used as solvent. The mixture was heated to reflux for 12 h to obtain 1-phenyl-4-(4-methyl-phenyl)-1,4-dihydroethylpyridine-3-carboxylate. The 1-phenyl-4-(4-methyl-phenyl)-1,4-dihydroethylpyridine-3-carboxylate (0.5 mmol) obtained in the first step of the reaction was placed on a blue LED (410 nm) for a photoreaction for 3 h [5]. The product was obtained by column chromatography eluting with petroleum ether and *n*-hexane 10:1. The resulting solution was evaporated to dryness to get some crystals.

Experimental details

All hydrogen atoms were placed in the calculated positions and all the non-hydrogen atoms were refined anisotropically.

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

Atom	x	y	z	U_{iso}*/U_{eq}
O1	0.1743 (3)	0.16745 (18)	0.29691 (16)	0.0652 (7)
O2	0.3072 (3)	0.0507 (2)	0.42235 (18)	0.0711 (8)
O3	0.1796 (3)	0.4520 (2)	0.14238 (17)	0.0687 (7)
O4	0.1552 (3)	0.5808 (2)	0.20067 (18)	0.0799 (8)
N1	0.3176 (3)	0.2735 (2)	0.52951 (18)	0.0493 (7)
N2	0.5155 (3)	0.2589 (2)	0.31320 (17)	0.0487 (7)
C1	0.4964 (7)	0.1597 (4)	0.9162 (3)	0.124 (2)
H1A	0.577354	0.096735	0.932153	0.186*
H1B	0.411031	0.148420	0.958220	0.186*
H1C	0.527715	0.215206	0.923377	0.186*
C2	0.4537 (5)	0.1892 (4)	0.8132 (3)	0.0767 (12)
C3	0.3774 (6)	0.2900 (4)	0.7626 (3)	0.0906 (14)
H3	0.353746	0.341019	0.791663	0.109*
C4	0.3354 (5)	0.3167 (3)	0.6701 (3)	0.0816 (13)
H4	0.282848	0.385422	0.638491	0.098*
C5	0.3687 (4)	0.2446 (3)	0.6220 (2)	0.0498 (9)
C6	0.4447 (4)	0.1445 (3)	0.6726 (2)	0.0596 (10)
H6	0.471096	0.093660	0.643180	0.072*
C7	0.4829 (5)	0.1178 (3)	0.7663 (3)	0.0745 (12)
H7	0.530535	0.048294	0.799115	0.089*
C8	0.3874 (4)	0.2111 (3)	0.4670 (2)	0.0479 (9)
H8	0.422024	0.136128	0.502876	0.057*
C9	0.5177 (4)	0.2575 (3)	0.4105 (2)	0.0491 (9)
H9	0.615509	0.219238	0.439910	0.059*
C10	0.4647 (4)	0.3726 (3)	0.4099 (2)	0.0527 (9)
H10	0.535268	0.388956	0.441691	0.063*
C11	0.3098 (4)	0.3795 (3)	0.4627 (2)	0.0525 (9)
H11	0.285327	0.431272	0.495607	0.063*
C12	0.2975 (4)	0.4145 (3)	0.2903 (2)	0.0468 (8)
C13	0.3561 (3)	0.2975 (2)	0.2937 (2)	0.0455 (8)
H13	0.333428	0.288174	0.235570	0.055*
C14	0.2766 (3)	0.2353 (2)	0.3863 (2)	0.0442 (8)
C15	0.1292 (3)	0.3177 (2)	0.3946 (2)	0.0468 (8)
H15	0.074925	0.337666	0.335826	0.056*
C16	0.1969 (4)	0.4076 (2)	0.3833 (2)	0.0472 (8)
H16	0.119324	0.473270	0.377833	0.057*
C17	0.4303 (4)	0.4507 (3)	0.3082 (2)	0.0516 (9)
H17	0.387605	0.520296	0.314144	0.062*
C18	0.5571 (4)	0.4585 (3)	0.2347 (2)	0.0517 (9)
C19	0.5300 (4)	0.5154 (3)	0.1395 (3)	0.0688 (11)
H19	0.431058	0.547224	0.120503	0.083*
C20	0.6453 (5)	0.5267 (4)	0.0711 (3)	0.0790 (13)
H20	0.622849	0.565644	0.007318	0.095*
C21	0.7907 (5)	0.4815 (4)	0.0964 (3)	0.0819 (13)
H21	0.868710	0.488925	0.050829	0.098*
C22	0.8199 (5)	0.4247 (4)	0.1907 (3)	0.0919 (15)
H22	0.919019	0.392211	0.209000	0.110*
C23	0.7059 (4)	0.4147 (3)	0.2586 (3)	0.0779 (12)
H23	0.729540	0.377389	0.322446	0.094*
C24	0.6047 (4)	0.1771 (3)	0.2812 (2)	0.0467 (8)
C25	0.6063 (4)	0.1875 (3)	0.1855 (2)	0.0646 (10)
H25	0.546384	0.247837	0.143641	0.078*
C26	0.6947 (5)	0.1106 (3)	0.1508 (3)	0.0762 (12)
H26	0.690659	0.119259	0.086344	0.091*
C27	0.7887 (4)	0.0215 (3)	0.2087 (3)	0.0730 (11)
C28	0.7883 (4)	0.0113 (3)	0.3044 (3)	0.0714 (11)
H28	0.849949	−0.048464	0.345850	0.086*
C29	0.6982 (4)	0.0878 (3)	0.3401 (2)	0.0583 (10)
H29	0.700890	0.078689	0.404744	0.070*
C30	0.8856 (5)	−0.0645 (4)	0.1719 (4)	0.1103 (17)
H30A	0.834515	−0.117846	0.184472	0.165*
H30B	0.979670	−0.094354	0.203792	0.165*
H30C	0.903803	−0.035847	0.104042	0.165*
C31	0.0198 (4)	0.2882 (3)	0.4772 (2)	0.0488 (9)
C32	−0.0508 (4)	0.2123 (3)	0.4833 (2)	0.0598 (10)
H32	−0.026867	0.178851	0.437616	0.072*
C33	−0.1563 (4)	0.1850 (3)	0.5561 (3)	0.0665 (11)
H33	−0.200474	0.132921	0.559442	0.080*
C34	−0.1948 (4)	0.2347 (3)	0.6222 (3)	0.0717 (11)
H34	−0.266248	0.217505	0.670477	0.086*
C35	−0.1275 (5)	0.3102 (3)	0.6172 (3)	0.0766 (12)
H35	−0.152676	0.343645	0.662846	0.092*
C36	−0.0228 (4)	0.3372 (3)	0.5451 (3)	0.0650 (10)
H36	0.020124	0.389617	0.542378	0.078*
C37	0.2069 (4)	0.4821 (3)	0.2022 (3)	0.0562 (10)
C38	0.0502 (7)	0.6556 (4)	0.1239 (4)	0.124 (2)
H38A	0.022017	0.618379	0.088661	0.149*
H38B	−0.040399	0.690633	0.152062	0.149*
C39	0.1196 (8)	0.7268 (6)	0.0640 (5)	0.188 (3)
H39A	0.052789	0.775482	0.014123	0.281*
H39B	0.146477	0.763653	0.099262	0.281*
H39C	0.208690	0.691633	0.036067	0.281*
C40	0.2572 (4)	0.1387 (3)	0.3739 (2)	0.0511 (9)
C41	0.1492 (5)	0.0863 (3)	0.268 (3)	0.0815 (13)
H41A	0.062347	0.064452	0.303055	0.098*
H41B	0.236245	0.025956	0.282049	0.098*
C42	0.1235 (8)	0.1309 (4)	0.1649 (3)	0.150 (2)
H42A	0.210756	0.151239	0.131389	0.225*
H42B	0.037974	0.190999	0.152275	0.225*
H42C	0.104965	0.079459	0.143257	0.225*

Comment

Cage dimers based on 4-aryl-1,4-dihydropyridines have a wide range of biological activities, such as anti-HIV drug and as an antimultidrug resistance modulator [6–8]. The caged dimeric compounds similar to the title compound has also been obtained by a dimerization by photoreaction. However, the two pyridine rings in the title compound present a special angle, which is of interest for the study of new functional caged compounds. The bond lengths and angles are in the expected ranges.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: This work was supported by the National Key Research and Development Program of China (No. 2018YFA0901800).

Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

References

1. Bruker. SAINT (version 8.23B); Bruker AXS Inc.: Madison, Wisconsin, USA, 2013.
2. Sheldrick G. M. Crystal structure refinement with SHELXL. *Acta Crystallogr.* 2015, *C71*, 3–8.
3. Sheldrick G. M. A short history of *SHELX*. *Acta Crystallogr.* 2008, *A64*, 112–122.
4. Wan J. P., Lin Y. F., Jing Y. F. Selectivity tunable divergent synthesis of 1,4-and 1,2-dihydropyridines via three-component reactions. *Tetrahedron* 2014, *70*, 7874–7880.
5. Hilgeroth A., Baumeister U., Heinemann F. W. Solution dimerization of 4-ary-1,4-dihydropyridines. *Eur. J. Org Chem.* 2000, *2000*, 245–249.
6. Hilgeroth A., Langner A. First bioanalytical evaluation of nonpeptidic cage dimeric HIV-1 protease inhibitor *N*-benzyl 4-aryl-1,4-dihydropyridine H17: biotransformation and toxicity on Hep G2 cells. *Arch. Pharm.* 2000, *333*, 32–34.
7. Hilgeroth A., Billich A. Cage dimeric 4-aryl-1,4-dihydropyridines as promising lead structures for the development of a novel class of HIV-1 protease inhibitors. *Arch. Pharm.* 1999, *332*, 3–5.
8. Coburger C., Wollmann J., Krug M., Baumert C., Seifert M., Molnar J., Lage H., Hilgeroth A. Novel structure-activity relationships and selectivity profiling of cage dimeric 1,4-dihydropyridines as multidrug resistance (MDR) modulators. *Bioorg. Med. Chem.* 2010, *18*, 4983–4990.