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Crystal structure of (1*aS*,1*a*¹*S*,2*S*)-4*a*-butoxy-1*a*,1*a*¹,2,4*a*,5,6-hexahydro-1*H*-cyclobuta[*de*]naphthalen-2-yl-4-nitrobenzoate, C₂₂H₂₅NO₅

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.17 × 0.14 × 0.12 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.09 mm ⁻¹
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
$\theta_{\max}$, completeness:	28.3°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	21,787, 4985, 0.022
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3644
$N(\text{param})_{\text{refined}}$:	254
Programs:	Bruker [1], Olex2 [2]

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.53113 (10)	0.7800 (3)	0.58806 (9)	0.0644 (4)
H1	0.5182	0.9093	0.5844	0.077*
C2	0.60067 (10)	0.7077 (3)	0.56136 (8)	0.0619 (4)
C3	0.62117 (11)	0.5176 (3)	0.56502 (10)	0.0708 (5)
H3	0.6681	0.4721	0.5459	0.085*
C4	0.57076 (10)	0.3958 (3)	0.59766 (10)	0.0694 (4)
H4	0.5836	0.2664	0.6005	0.083*
C5	0.50123 (9)	0.4643 (2)	0.62621 (9)	0.0587 (4)
C6	0.48103 (9)	0.6559 (2)	0.62037 (9)	0.0621 (4)
H6	0.4333	0.7016	0.6384	0.074*
C7	0.45188 (10)	0.3257 (3)	0.66396 (10)	0.0663 (4)
C8	0.33374 (9)	0.2845 (2)	0.72671 (8)	0.0553 (3)
H8	0.3748	0.2123	0.7627	0.066*
C9	0.27728 (9)	0.1439 (2)	0.67672 (8)	0.0527 (3)
H9	0.2860	0.1484	0.6255	0.063*
C10	0.18052 (9)	0.14880 (19)	0.68438 (8)	0.0507 (3)
H10	0.1439	0.1012	0.6394	0.061*
C11	0.28185 (11)	−0.0622 (2)	0.70937 (10)	0.0667 (4)
H11A	0.2727	−0.1624	0.6726	0.080*
H11B	0.3327	−0.0867	0.7465	0.080*
C12	0.20238 (10)	−0.0100 (2)	0.74007 (9)	0.0575 (4)
C13	0.17531 (11)	−0.0233 (2)	0.80304 (10)	0.0642 (4)
H13	0.1977	−0.1173	0.8366	0.077*
C14	0.10874 (11)	0.1113 (3)	0.82123 (10)	0.0668 (4)
H14A	0.1346	0.1897	0.8626	0.080*
H14B	0.0623	0.0387	0.8361	0.080*
C15	0.07105 (10)	0.2403 (2)	0.75681 (10)	0.0645 (4)
H15A	0.0419	0.3466	0.7754	0.077*
H15B	0.0281	0.1693	0.7231	0.077*

<https://doi.org/10.1515/ncrs-2020-0496>

Received September 28, 2020; accepted October 21, 2020;
published online November 16, 2020

Abstract

C₂₂H₂₅NO₅, monoclinic, $P2_1/c$ (no. 14), $a = 15.7241(13)$ Å, $b = 7.0223(5)$ Å, $c = 18.4613(14)$ Å, $\beta = 100.329(4)^\circ$, $V = 2005.4(3)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0495$, $wR_{\text{ref}}(F^2) = 0.1564$, $T = 296(2)$ K.

CCDC no.: 2039767

The asymmetric unit of 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.

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Table 2: (continued)

Atom	x	y	z	U _{iso} */U _{eq}
C16	0.13886 (9)	0.3179 (2)	0.71436 (8)	0.0522 (3)
C17	0.20441 (11)	0.4376 (2)	0.76263 (9)	0.0576 (4)
H17	0.1840	0.5288	0.7918	0.069*
C18	0.28846 (11)	0.4244 (2)	0.76721 (9)	0.0596 (4)
H18	0.3226	0.5095	0.7983	0.072*
C19	0.13871 (11)	0.4979 (3)	0.60296 (10)	0.0674 (4)
H19A	0.1429	0.3940	0.5691	0.081*
H19B	0.1968	0.5343	0.6259	0.081*
C20	0.09433 (11)	0.6627 (2)	0.56185 (9)	0.0655 (4)
H20A	0.0912	0.7666	0.5959	0.079*
H20B	0.0357	0.6264	0.5405	0.079*
C21	0.14050 (16)	0.7310 (3)	0.50107 (11)	0.0887 (6)
H21A	0.1981	0.7732	0.5232	0.106*
H21B	0.1468	0.6242	0.4692	0.106*
C22	0.0959 (2)	0.8894 (4)	0.45509 (14)	0.1190 (9)
H22A	0.0404	0.8464	0.4300	0.178*
H22B	0.1302	0.9279	0.4196	0.178*
H22C	0.0883	0.9954	0.4862	0.178*
N1	0.65651 (10)	0.8387 (3)	0.52871 (9)	0.0807 (5)
O1	0.63772 (13)	1.0053 (3)	0.52389 (13)	0.1229 (7)
O2	0.71968 (11)	0.7727 (3)	0.50842 (10)	0.1181 (6)
O3	0.47294 (9)	0.1625 (2)	0.67558 (10)	0.0951 (5)
O4	0.38273 (6)	0.40487 (16)	0.68382 (7)	0.0630 (3)
O5	0.09169 (7)	0.43701 (16)	0.65788 (7)	0.0653 (3)

Source of material

All of these reactions were executed in argon atmosphere with dry solvents, unless otherwise noted. All the commercially chemicals were purchased and used without any further purification.

The 4-(but-3-yn-1-yl)-4-butoxycyclohexa-2,5-dien-1-one was synthesized as following: To a well-stirred mixture of 4-(but-3-yn-1-yl)phenol (10 mmol) in butan-1-ol (15 mL) was added the phenyliodine(III) diacetate (15 mmol) at 0 °C in several portions. Then the mixture was warmed to room temperature and stirred overnight followed by quenching with the saturated aqueous NaHCO₃ (40 mL) and the saturated aqueous Na₂SO₃ (20 mL) and extracted with ethyl acetate (30 mL) three times. The combined organic mixture was washed with brine (30 mL), dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by flash column chromatography using petroleum ether/ethyl acetate eluent to afford the 4-(but-3-yn-1-yl)-4-butoxycyclohexa-2,5-dien-1-one.

The 4-butoxy-4-(penta-3,4-dien-1-yl)cyclohexa-2,5-dien-1-one was synthesized: To a well-stirred solution of 4-(but-3-yn-1-yl)-4-butoxycyclohexa-2,5-dien-1-one (2 mmol) in dioxane (10 mL) was sequentially added para-formaldehyde (300 mg, 10.0 mmol) CuBr (114.8 mg,

0.8 mmol) and diisopropylamine (0.56 mL, 4.0 mmol) under argon atmosphere. The resulting mixture was stirred at 110 °C for about 1 h (traced by TLC). After cooling to room temperature, the reaction mixture was filtered through a plug of celite and followed by washing with DCM (10 mL × 3). The organic phase was concentrated under reduced pressure and the residue purified by flash column chromatography using PE/ethyl acetate eluent to afford 4-butoxy-4-(penta-3,4-dien-1-yl)cyclohexa-2,5-dien-1-one.

The (R)-4a-butoxy-1,4a,5,6-tetrahydro-2H-cyclobuta[de]naphthalen-2-one was synthesized: To a 25 mL Schlenk tube equipped with magnetic stirring bar was added the 4-butoxy-4-(penta-3,4-dien-1-yl) cyclohexa-2,5-dien-1-one (100.2 mg) and TFE (2.0 mL), The tube was sealed and the resulting mixture was stirred for 4 h at 100 °C, before being cooled down to rt, and the mixture was transferred to a round-bottom flask and followed by concentration under reduced pressure, and then the resulting sticky oil was purified by column chromatography on silica gel using the petroleum ether/ethyl acetate as the eluent to afford the (R)-4a-butoxy-1,4a,5,6-tetrahydro-2H-cyclobuta[de]naphthalen-2-one.

The (1a*S*,1a'*S*,2*R*,4a*R*)-4a-butoxy-1a,1a',2,4a,5,6-hexahydro-1H-cyclobuta[de]naphthalen-2-ol was synthesized: To a solution of (R)-4a-butoxy-1,4a,5,6-tetrahydro-2H-cyclobuta[de]naphthalen-2-one (151.8 mg, 0.474 mmol) in dry MeOH (5 mL) was added NaBH₄ (36.05 mg, 2.0 equiv). The reaction mixture was stirred for another 1 h at room temperature, then concentrated under reduced pressure. The resulting residue was purified by flash column chromatography using PE/EA eluent to afford the (1a*S*,1a'*S*,2*R*,4a*R*)-4a-butoxy-1a,1a',2,4a,5,6-hexahydro-1H-cyclobuta[de]naphthalen-2-ol.

The (1a*S*,1a'*S*,2*S*,4a*R*)-4a-butoxy-1a,1a',2,4a,5,6-hexahydro-1H-cyclobuta [de]naphthalen-2-yl 4-nitrobenzoate was synthesized: To a stirred solution of alcohol (1a*S*,1a'*S*,2*R*,4a*R*)-4a-butoxy-1a,1a',2,4a,5,6-hexahydro-1H-cyclobuta[de]naphthalen-2-ol (54 mg, 0.17 mmol), *p*-nitrobenzoic acid (142.05 mg, 0.85 mmol), and PPh₃ (248.2 mg, 0.85 mmol) in THF (5.0 mL) was added DEAD (148.02 mg, 0.13 mL, 0.85 mmol) at 0 °C. The resulting mixture was stirred at room temperature overnight before it was quenched with saturated aq. NaHCO₃ solution (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine (20 mL) and dried over anhydrous Na₂SO₄. After filtration and evaporation of the solvent, the residue so obtained was purified by flash column chromatography with petroleum ether/EtOAc (15:1 to 10:1) to give the (1a*S*,1a'*S*,2*S*,4a*R*)-4a-butoxy-1a,1a',2,4a,5,6-hexahydro-1H-cyclobuta[de]naphthalen-2-yl 4-nitrobenzoate.

Experimental details

Hydrogen atoms were placed in their geometrically idealized positions and constrained to ride on their parent atoms.

Comment

The cyclobutane and the cyclobutene derivatives containing polycyclic compounds are very common in natural products and bioactive compounds [3], and there are numerous methods for the construction of the cyclobutane and the cyclobutene derivatives *via* the photochemistry initiation [4] and the transition metal catalyzed [5] and the Lewis acid promoted [6] and the thermal promoted fashion [7]. Recently, we disclosed a powerful, distinct, and atom-economical method for the synthesis of cyclobutane-fused oxygen containing tricyclic framework *via* a thermal promoted intramolecular [2+2] cycloaddition of cyclohexadienone-tethered allenes [8]. However, the method for the dicyclobutanes containing ring system remains rather rare reported to date. As our continuing efforts on the efficient synthetic methods for cyclic compounds synthesis associate with allenes [9], we herein report a useful method and the crystal structure of the titled compound.

There is one molecule in the asymmetric unit of the title structure (see the Figure). The single crystal structure verifies that all bond lengths are in normal ranges. Furthermore, the crystal packing doesn't exhibit strong intramolecular or intermolecular hydrogen bond.

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

Research funding: This work was supported by Henan Postdoctoral Foundation and the Foundation of

Postdoctoral innovation base of Anyang Institute of Technology.

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

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