Wu-Wu Li*, Yuan-Zi Gu and Lei Cao

Synthesis and crystal structure of *tert*-butyl (2'*R*,3*R*,3'*R*,4*a'**R*,9*a'**S*)-1-acetyl-5-chloro-3''-methyl-2,5'',9'-trioxo-1''-phenyl-1'',4*a'*,5'',9*a'*-tetrahydro-1'*H*,3'*H*,9'*H*-dispiro[indoline-3,4'-xanthene-2',4''-pyrazole]-3'-carboxylate, C₃₆H₃₂ClN₃O₇

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Abstract

C₃₆H₃₂ClN₃O₇, orthorhombic, *P*2₁2₁2₁ (no. 19), *a* = 11.4608(5) Å, *b* = 12.1489(5) Å, *c* = 23.1684(7) Å, *V* = 3225.9(2) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0588, *wR*_{ref}(*F*²) = 0.1546, *T* = 293 K.

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*Corresponding author: Wu-Wu Li, College of Chemistry & Chemical Engineering, Xianyang Normal University, Xianyang, 712000, PR China, e-mail: langyuan2012@126.com. <https://orcid.org/0000-0003-1644-4848>

Yuan-Zi Gu and Lei Cao, College of Chemistry & Chemical Engineering, Xianyang Normal University, Xianyang, 712000, PR China

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

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.13 × 0.11 × 0.10 mm
Wavelength:	Cu Kα radiation (1.54184 Å)
μ:	1.51 mm ⁻¹
Diffractometer, scan mode:	SuperNova, ω
θ _{max} , completeness:	74.3°, 99%
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	11,377, 5861, 0.035
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 5154
<i>N</i> (<i>param</i>) _{refined} :	429
Programs:	SHELX [1], Bruker [2]

Source of material

To a mixture of 3-methyl-4-((4-oxo-4*H*-chromen-3-yl)methyl)-1-phenyl-1*H*-pyrazol-5(4*H*)-one (0.1 mmol) and quinine-derived thiourea (20 mol%) in 1.0 mL of freshly distilled Et₂O was added *tert*-butyl 2-(1-acetyl-5-chloro-2-oxoindolin-3-ylidene)acetate. The reaction mixture was stirred at room temperature for 4 days and the progress of the reaction was monitored by TLC. Upon completion, the solvent was removed under reduced pressure and the residue was taken in water and extracted with ethyl acetate. Finally, the organic layer was washed with water and then dried over anhydrous sodium sulfate. The solvent was evaporated. The crude product was purified by column chromatography using hexane/ethylacetate (10/1, v/v) as an eluent. Crystals were obtained from slow evaporation of its ethyl acetate solution.

Experimental details

All hydrogen atoms were placed in geometrically idealized positions. The U_{iso} values of the hydrogen atoms of methyl groups were set to 1.5 $U_{\text{eq}}(\text{C})$ and the U_{iso} values of all other hydrogen atoms were set to 1.2 $U_{\text{eq}}(\text{C})$.

Comment

Oxindoles are part of many natural and biological compounds isolated from plant, marine sources [3–5] and can be converted in to advanced intermediates for complex and natural molecules [6,7]. The synthetic indolin-2-ones are reported for anticancer [8,9], antimicrobial, anticonvulsant [10], spermicidal [11] properties. Chromones are widely distributed in nature [12] and exhibit low toxicity along with a wide range of biological and pharmacological activities including antiinflammatory [13], anti-HIV [14], anticancer [15], antibacterial [16], antimalarial [17], and antitumor [18], as well as treatment of Alzheimer's disease [19]. In addition, pyrazole derivatives are reported to have various biological activities including antidiabetic [20], anaesthetic [21], antimicrobial and antioxidant [22]. Herein we combine the oxindoles, chromones and pyrazole moieties in the same molecules (hybrid drug concept) via Michael cycloaddition reaction.

As shown in the figure (cf. the figure; the hydrogen atom is omitted for clarity), there is one crystallographically independent molecule in the asymmetric unit. The structure of the title compound has one dihydrochromone skeleton, a cyclohexane ring, a indolin-2-one skeleton, one

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters ($\text{\AA}^2$).

Atom	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
C1	0.2794(5)	0.4550(5)	0.8815(2)	0.0282(12)
C2	0.2686(5)	0.5156(5)	0.9330(2)	0.0342(13)
H2	0.329590	0.560107	0.945511	0.041*
C3	0.1677(6)	0.5088(6)	0.9647(2)	0.0410(15)
H3	0.159948	0.550031	0.998264	0.049*
C4	0.0769(5)	0.4405(6)	0.9470(2)	0.0378(14)
H4	0.010625	0.433793	0.969845	0.045*
C5	0.0841(5)	0.3824(5)	0.8956(2)	0.0308(12)
H5	0.022429	0.338770	0.883084	0.037*
C6	0.1858(5)	0.3909(5)	0.8633(2)	0.0275(11)
C7	0.2816(4)	0.3646(4)	0.7739(2)	0.0226(11)
H7	0.267463	0.440940	0.762147	0.027*
C8	0.3984(4)	0.3598(4)	0.8047(2)	0.0239(11)
H8	0.403738	0.287983	0.823844	0.029*
C9	0.3928(5)	0.4472(5)	0.8516(2)	0.0278(11)
C10	0.5056(5)	0.3717(5)	0.7656(2)	0.0277(11)
H10A	0.559169	0.312081	0.774155	0.033*
H10B	0.544678	0.440105	0.775168	0.033*
C11	0.4796(4)	0.3710(4)	0.6996(2)	0.0236(11)
C12	0.3868(4)	0.2825(4)	0.6868(2)	0.0225(11)
H12	0.421713	0.212829	0.699179	0.027*
C13	0.2694(4)	0.2911(4)	0.7204(2)	0.0220(10)
C14	0.2391(5)	0.1713(5)	0.7387(2)	0.0252(11)
C15	0.0813(4)	0.2389(4)	0.6875(2)	0.0238(10)
C16	0.1621(4)	0.3225(4)	0.6870(2)	0.0244(11)
C17	0.1366(5)	0.4232(5)	0.6606(2)	0.0265(11)
H17	0.190097	0.480696	0.660424	0.032*
C18	0.0288(5)	0.4335(5)	0.6347(2)	0.0297(12)
C19	−0.0512(5)	0.3486(5)	0.6331(2)	0.0308(12)
H19	−0.122251	0.358230	0.614380	0.037*
C20	−0.0255(5)	0.2480(5)	0.6597(2)	0.0293(12)
H20	−0.077996	0.189599	0.658831	0.035*
C21	0.5894(4)	0.3482(5)	0.6662(2)	0.0263(11)
C22	0.4518(4)	0.4870(4)	0.6776(2)	0.0247(11)
C23	0.6564(5)	0.2432(5)	0.6687(3)	0.0363(14)
H23A	0.719699	0.246013	0.641559	0.055*
H23B	0.605858	0.182851	0.659173	0.055*
H23C	0.686938	0.233016	0.706900	0.055*
C24	0.5480(5)	0.6067(4)	0.6028(2)	0.0266(11)
C25	0.6561(5)	0.6313(5)	0.5790(2)	0.0319(13)
H25	0.720847	0.587944	0.587213	0.038*
C26	0.6659(6)	0.7218(5)	0.5427(2)	0.0385(15)
H26	0.737748	0.738762	0.526347	0.046*
C27	0.5705(6)	0.7866(5)	0.5306(2)	0.0402(15)
H27	0.578179	0.846566	0.505969	0.048*
C28	0.4637(6)	0.7631(5)	0.5549(3)	0.0410(15)
H28	0.399698	0.807588	0.546869	0.049*
C29	0.4512(5)	0.6716(5)	0.5917(2)	0.0338(13)
H29	0.379365	0.655189	0.608300	0.041*
C30	0.3621(5)	0.2683(4)	0.6226(2)	0.0244(11)
C31	0.2764(5)	0.1299(5)	0.5567(2)	0.0309(13)
C32	0.2283(7)	0.0171(6)	0.5721(3)	0.0450(16)
H32A	0.286159	−0.023717	0.592997	0.068*
H32B	0.208421	−0.021689	0.537332	0.068*
H32C	0.159826	0.025518	0.595537	0.068*

Table 2: (continued)

Atom	x	y	z	U_{iso}^*/U_{eq}
C33	0.1837(6)	0.2035(6)	0.5300(3)	0.0422(15)
H33A	0.117856	0.208175	0.555525	0.063*
H33B	0.159334	0.173073	0.493729	0.063*
H33C	0.215358	0.275727	0.523943	0.063*
C34	0.3847(6)	0.1202(6)	0.5199(2)	0.0441(16)
H34A	0.409591	0.192216	0.508167	0.066*
H34B	0.367734	0.076592	0.486403	0.066*
H34C	0.445624	0.085562	0.541826	0.066*
C35	0.0680(5)	0.0449(5)	0.7250(2)	0.0321(13)
C36	0.1404(6)	−0.0537(5)	0.7378(3)	0.0436(15)
H36A	0.173319	−0.046966	0.775736	0.065*
H36B	0.202048	−0.059320	0.709899	0.065*
H36C	0.092595	−0.118522	0.736037	0.065*
O1	0.4761(4)	0.5057(3)	0.86414(16)	0.0363(9)
O2	0.1892(3)	0.3315(3)	0.81252(14)	0.0257(8)
O3	0.3027(3)	0.1105(3)	0.76560(16)	0.0310(9)
O4	−0.0364(4)	0.0428(4)	0.71914(19)	0.0448(11)
O5	0.3083(3)	0.1728(3)	0.61473(14)	0.0256(8)
O6	0.3864(4)	0.3352(3)	0.58597(15)	0.0358(10)
O7	0.3726(3)	0.5478(3)	0.69324(16)	0.0310(9)
N1	0.1276(4)	0.1462(4)	0.71786(18)	0.0253(9)
N2	0.5377(4)	0.5122(4)	0.63875(18)	0.0239(9)
N3	0.6207(4)	0.4275(4)	0.63294(19)	0.0268(10)
Cl1	−0.00963(13)	0.56086(13)	0.60524(6)	0.0416(4)

1-phenyl-pyrazolone ring and one *t*-butyloxy carbonyl. Chromone skeleton and cyclohexane ring form a condensed ring structure through C7 and C8, pyrone ring adopts an envelope conformation with the C8 atom deviating from the plane of the remaining five atoms [23], cyclohexane ring exhibits a chair conformation. The spiro atom C13 connects the cyclohexane ring and the indolin-2-one ring system, indolin-2-one ring is almost planar [24] and the dihedral angle between the dihydrochromone ring and the indolin-2-one ring is 88°. The 1-phenyl-pyrazolone ring and cyclohexane ring form a spiro structure through C11, the 1-phenyl-pyrazolone ring is almost in a vertical position with the dihydrochromone ring which is evident by the dihedral angle value of 88°. The structure of the molecule is stabilized by the hydrogen bonds of the type C–H...O, adjacent molecules are connected via hydrogen bonds C3–H3...O6, C23–H23B...O1 and C34–H34C...O1 into a two-dimensional plane running along the crystallographic [100] direction.

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