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Crystal Structure of (*E*)-3-(4-methoxyphenyl)-1-(2,3,4-tris(benzyloxy)-6-hydroxyphenyl)prop-2-en-1-one, C₃₇H₃₂O₆

Table 1: Data collection and handling.

Crystal:	Yellow cuboid
Wavelength:	Size 0.36 × 0.07 × 0.06 mm
μ :	Mo K α radiation (0.71073 Å)
Diffractometer, scan mode:	0.9 cm ⁻¹
2 θ _{max} , completeness:	Braker APEXII, φ and ω
$N(hkl)$ _{measured} , $N(hkl)$ _{unique} , R_{int} :	54°, >99%
Criterion for I_{obs} , $N(hkl)$ _{gt} :	34339, 6333, 0.127
$N(param)$ _{refined} :	$I_{obs} > 2 \sigma(I_{obs})$, 2760
Programs:	391
	SHELX [2], Bruker programs [3, 4],
	Diamond [5], WinGX [6]

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
C1	0.3365(5)	0.19617(17)	0.04830(9)	0.0319(7)
C2	0.1818(6)	0.14800(18)	0.02227(9)	0.0350(8)
C3	−0.0065(6)	0.10513(17)	0.03901(9)	0.0345(8)
H3	−0.1063	0.0737	0.0206	0.041*
C4	−0.0491(5)	0.10809(16)	0.08203(9)	0.0313(7)
C5	0.0981(5)	0.15421(16)	0.10911(8)	0.0294(7)
C6	0.2837(5)	0.19746(16)	0.09257(9)	0.0306(7)
C11	0.9718(5)	0.40883(17)	0.05245(9)	0.0325(7)
C12	0.8992(6)	0.44223(18)	0.09083(9)	0.0378(8)
H12	0.7637	0.4206	0.1047	0.045*
C13	1.0171(6)	0.50517(19)	0.10914(10)	0.0416(8)
H13	0.963	0.5265	0.1353	0.05*
C14	1.2170(6)	0.53812(18)	0.08934(9)	0.0359(8)
C15	1.2932(6)	0.5063(2)	0.05141(9)	0.0434(9)
H15	1.4291	0.5279	0.0376	0.052*
C16	1.1702(6)	0.4427(2)	0.03349(10)	0.0443(9)
H16	1.2239	0.4215	0.0072	0.053*
C17	0.5283(5)	0.24098(17)	0.02764(9)	0.0343(7)
C18	0.6636(6)	0.30294(18)	0.04987(10)	0.0391(8)
H18	0.6203	0.3158	0.0783	0.047*
C19	0.8439(5)	0.34247(18)	0.03271(9)	0.0355(8)
H19	0.8939	0.3261	0.0052	0.043*
C20	1.5052(6)	0.6436(2)	0.08900(10)	0.0526(10)
H20A	1.6466	0.6096	0.0857	0.079*
H20B	1.5511	0.6898	0.1062	0.079*
H20C	1.4448	0.6607	0.0607	0.079*
C21	−0.4912(6)	−0.04308(17)	0.10725(9)	0.0342(8)

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Abstract

C₃₇H₃₂O₆, monoclinic, $P2_1/c$ (No. 14), $a = 5.5354(7)$ Å, $b = 16.983(2)$ Å, $c = 31.211(4)$ Å, $\beta = 91.535(8)^\circ$, $V = 2932.9(7)$ Å³, $Z = 4$, $R_{gt}(F) = 0.0584$, $wR_{ref}(F^2) = 0.1738$, $T = 100$ K.

CCDC no.: 1493406

The 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

2-Hydroxy-4,5,6-tribenzyloxyacetophenone (0.152 g, 0.334 mmol, 1 eq) and 4-methoxybenzaldehyde (0.05 mL,

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Table 2 (continued)

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} */ <i>U</i> _{eq}
C22	−0.4064(6)	−0.05810(17)	0.14862(9)	0.0375(8)
H22	−0.2615	−0.0339	0.1589	0.045*
C23	−0.5322(6)	−0.10834(18)	0.17507(10)	0.0431(8)
H23	−0.4755	−0.1174	0.2036	0.052*
C24	−0.7399(6)	−0.14518(19)	0.15984(11)	0.0481(9)
H24	−0.825	−0.1799	0.178	0.058*
C25	−0.8239(6)	−0.1319(2)	0.11871(12)	0.0514(9)
H25	−0.9652	−0.1579	0.1081	0.062*
C26	−0.6993(6)	−0.08005(19)	0.09275(10)	0.0434(8)
H26	−0.7591	−0.0699	0.0645	0.052*
C27	−0.3557(6)	0.00908(17)	0.07732(9)	0.0377(8)
H27A	−0.2428	−0.0229	0.0604	0.045*
H27B	−0.4704	0.0356	0.0572	0.045*
C31	0.1461(5)	0.12346(16)	0.22402(9)	0.0298(7)
C32	−0.0655(5)	0.09905(17)	0.24331(9)	0.0346(7)
H32	−0.1802	0.0684	0.2275	0.042*
C33	−0.1096(6)	0.11924(18)	0.28543(9)	0.0371(8)
H33	−0.2545	0.1024	0.2983	0.045*
C34	0.0552(6)	0.16345(17)	0.30869(9)	0.0356(8)
H34	0.0249	0.1765	0.3377	0.043*
C35	0.2670(6)	0.18925(17)	0.28992(9)	0.0364(8)
H35	0.3806	0.2203	0.3058	0.044*
C36	0.3088(6)	0.16892(17)	0.24796(9)	0.0340(8)
H36	0.4528	0.1865	0.2351	0.041*
C37	0.1931(6)	0.10336(17)	0.17852(8)	0.0350(8)
H37A	0.3672	0.1089	0.1727	0.042*
H37B	0.1436	0.0485	0.1723	0.042*
C41	0.5116(5)	0.34166(16)	0.17096(8)	0.0294(7)
C42	0.4863(6)	0.41968(17)	0.18334(9)	0.0350(8)
H42	0.3545	0.4498	0.1722	0.042*
C43	0.6511(6)	0.45408(18)	0.21182(9)	0.0375(8)
H43	0.633	0.5077	0.2198	0.045*
C44	0.8416(6)	0.41046(18)	0.22871(9)	0.0370(8)
H44	0.9543	0.434	0.2483	0.044*
C45	0.8678(6)	0.33249(18)	0.21696(9)	0.0360(8)
H45	0.9979	0.3022	0.2287	0.043*
C46	0.7049(5)	0.29837(17)	0.18807(9)	0.0320(7)
H46	0.7253	0.245	0.1798	0.038*
C47	0.3307(5)	0.30618(17)	0.14005(9)	0.0344(8)
H47A	0.1829	0.2913	0.1553	0.041*
H47B	0.2855	0.345	0.1176	0.041*
O1	0.2128(4)	0.14140(13)	−0.02042(6)	0.0455(6)
H1	0.335	0.1673	−0.0273	0.068*
O2	−0.2233(4)	0.06683(11)	0.10220(6)	0.0372(5)
O3	0.0514(3)	0.15811(11)	0.15236(5)	0.0316(5)
O4	0.4358(3)	0.23729(11)	0.12075(6)	0.0322(5)
O10	0.5710(4)	0.22795(12)	−0.01104(6)	0.0441(6)
O11	1.3195(4)	0.60065(13)	0.11015(6)	0.0469(6)

0.401 mmol, 1.2 eq) were dissolved in ethanol:THF (5:1, 10 mL) and stirred at 0 °C. Freshly powdered KOH (0.1 g, 1.67 mmol, 5 eq) was added and stirred at room temperature overnight. Water (20 mL) was added and the reaction mixture was neutralized with 3 M HCl (1 mL). The residue was

extracted with EtOAc (3 × 30 mL); the organic layers were combined, washed with brine (20 mL), dried (Na₂SO₄) and evaporated under reduced pressure. Purification by PTLTLC (hexane:ethyl acetate:acetone; 9:0.5:0.5, *R_f* 0.21) yielded 2'-hydroxy-4',5',6'-tribenzyloxy-4-methoxychalcone as a yellow solid (0.146 g, 76.4%). ¹H NMR (600 MHz, CDCl₃) δH (ppm): 7.92 (d, 1 H, *J* 16 Hz, H-β); 7.90 (d, 1 H, *J* 16 Hz, H-α); 7.47–7.27 (m, 15 H, 3 × OCH₂C₆H₅); 7.27 (d, 2 H, *J* 8 Hz, H-2 and H-6); 6.81 (d, 2 H, *J* 8 Hz, H-3 and H-5); 6.44 (s, 1 H, H-3'); 5.16–5.04 (3 × s, 6 H, 3 × OCH₂C₆H₅); 3.87 (s, 3 H, OCH₃). ¹³C NMR (600 MHz, CDCl₃) δC (ppm): 192.8; 162.9; 161.5; 159.2; 154.3; 143.8; 137.3; 136.5; 135.7; 134.7; 130.6; 129.0–127.7; 124.3; 114.2; 109.4; 98.0; 76.0; 70.8; 55.4.

Experimental details

The crystal of the title organic compound was weakly diffracting resulting in poor quality data and a high *R*_{int} value. All hydrogen atoms were positioned geometrically and refined using a riding model, with C–H = 0.95 Å *U*_{iso}(H) = 1.2 *U*_{eq}(C) for the aromatic H, with O–H = 0.84 Å *U*_{iso}(H) = 1.5 *U*_{eq}(O) for the hydroxy H and with *U*_{iso}(H) = 1.5 *U*_{eq}(C) for methylene H atoms. The hydroxy groups were allowed to rotate with a fixed angle whilst the methylene group C–H distance was allowed to refine to best fit the experimental electron density (HFIX 147 and HFIX 24 in SHELXL [2]).

Discussion

Chalcones consist of two aromatic rings which are joined by a three carbon α,β-unsaturated carbonyl system, and are considered the precursor of flavanoids and isoflavanoids. The ease of preparation and reactivity of various chalcone analogues along with a wide spectrum of biological activity make this class of organic compounds worthy of investigation. With malaria and tuberculosis infections posing an increasing health risk to the global population, an estimated 3.4 billion people at risk for malaria alone, most of which are in Sub-Saharan Africa. The anti-malarial and anti-tubercular activity shown by a series of acetylenic chalcones as prepared and presented by Hans et al. [1]

The title compound comprises of a hydroxy (C2), methoxy (C14) and benzyloxy (C4, C5, C6) substituted chalcone and was synthesized using base mediated aldolization of 2-hydroxy-4,5,6-tribenzyloxyacetophenone with 4-methoxybenzaldehyde. The angle of interaction of the A- and B-rings was found to be 22.37(9)°, whilst the twist angles of the A-ring with the benzyloxy substituents (Rings E, D and C) were calculated at 28.06(9)°, 13.32(9)° and 88.74(8)°, respectively.

Several interactions contribute to the large twisting observed for the C-ring, the first, are two intramolecular hydrogen bonds observed between the oxygen (O4) of the benzyloxy

group with the methine hydrogen (S(6)) [7] and the second, between the methylene hydrogen and an oxygen (O3) of an adjacent benzyloxy group (S(6)). Additionally, edge-to-face π -stacking is found between the B- and C-rings with the closest distance at 3.117 Å. The chain interaction, C(8), observed between the aromatic hydrogen of ring B with the adjacent benzyloxy group oxygen (O3) (symmetry operator: $x + 1, y, z$) further re-inforcing the twisting.

Two other hydrogen bonding interactions were found, firstly, a ring $R_2^2(22)$ with a donor ketone (O10) and the acceptor methyl carbon (C20) of the methoxy group forming a tail-to-head arrangement, underpinning this is a displaced π -stacking for ring B along the a -axis with a distance of 3.927 Å. A second ring $R_2^2(14)$ was found between the hydroxy (O1) and the methylene hydrogen (H27A) of the benzyloxy group (symmetry operator: $-x, -y, -z$).

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