Crystal structure of 3-bromo-4,6-dibenzyloxy-2-hydroxy acetophenone, $C_{22}H_{19}BrO_4$

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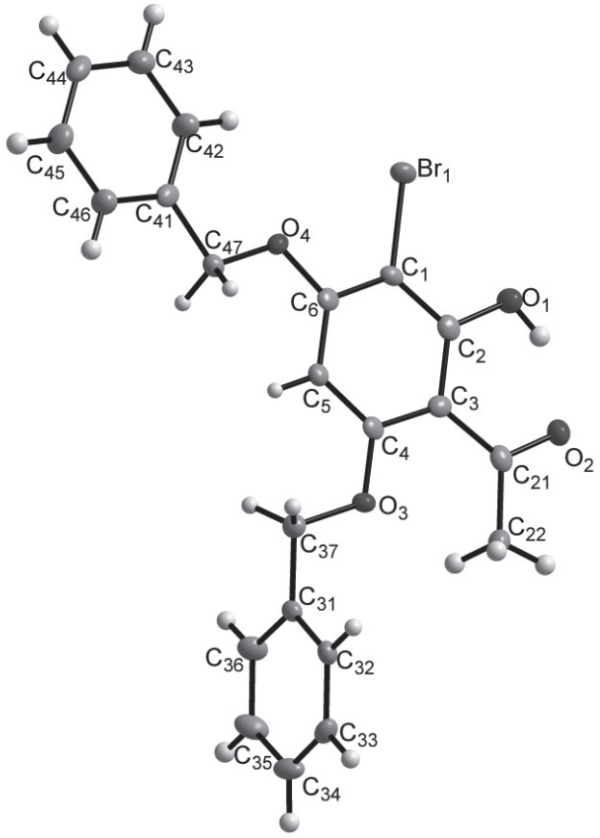

Abstract

$C_{22}H_{19}BrO_4$, triclinic, $P\bar{1}$ (no. 2), a = 8.550(2) Å, b = 11.343(2) Å, c = 11.715(2) Å, α = 102.02(3)°, β = 110.47(3)°, γ = 110.84(3)°, V = 920.2 Å^3, Z = 2, $R_{gt}(F)$ = 0.0368, $wR_{ref}(F^2)$ = 0.099, T = 100 K.

Table 1. Data collection and handling.

Crystal:	colourless cuboids, size 0.1×0.1×0.3 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	22.59 cm^{-1}
Diffractometer, scan mode:	Bruker X8 APEX-II 4K CCD, ω and φ
$2\theta_{max}$:	51.36°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	10200, 3329
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2885
$N(param)_{refined}$:	246
Programs:	SHELX, SADABS, DIAMOND, WinGX [10–13]

Source of material

To a solution of 4,6-dibenzyloxy-2-hydroxyacetophenone (0.780 g, 2.24 mmol) in glacial acetic acid (10 ml), was added drop-wise a solution of bromine (0.13 ml, 2.24 mmol) in glacial acetic acid (2 ml) at room temperature over a period of 30 min and the reaction mixture stirred for 4 h at the same temperature. The reaction was quenched by the addition of water (20 ml) and the resulting solid was filtered off. The crude product was separated by preparative thin layer chromatography (PTLC, 7:3 *n*-hexane:acetone, R_f = 0.55) to afford the title compound 4,6-dibenzyloxy-3-bromo-2-hydroxyacetophenone as a grey solid 0.58 g (94 %) and 4,6-dibenzyloxy-3,5-dibromo-2-hydroxyacetophenone as yellow needles 0.057 g (6 %). Crystals suitable for single crystal X-ray determination were grown by slow evaporation from acetone. **IR** (KBr) ν (cm^{-1}): 3069 (w), 3032 (w), 2924 (w), 1615 (s), 1582 (s), 1562 (m), 1500 (w), 1452 (w), 1413 (m), 1400 (w), 1386 (w), 1371 (w), 1357 (w), 1272 (s), 1228 (s), 1199 (m), 1166 (w), 1126 (s), 1101 (m), 1027 (w), 960 (w), 913 (w), 849 (w), 822 (w), 785 (m), 757 (m), 731 (m), 702 (m), 626 (m), 506 (w), 463 (w). **^{1}H NMR** (600 MHz, $CDCl_3$) δ : 14.58 (s, 1 H, OH); 7.42-7.34 (m, 10 H, 2×$OCH_2C_6H_5$); 6.12 (s, 1 H, H {H5}); 5.18 (s, 2 H, OCH_2Bn); 5.06 (s, 2 H, OCH_2Bn); 2.57 (s, 3 H, $COCH_3$). **^{13}C NMR** (600 MHz, acetone-d_6) δ: 205.33 (CO); 164.52 (COBn); 163.91 (COBn); 163.17 (COH); 138.16 (C_6H_6 {C31}); 137.78 (C_6H_6 {C41}); 130.58-129.23 (2×C_6H_6); 108.45 ($COCH_3$); 93.26 (C_6H_6 {C5}); 92.34 (CBr); 73.35 (CH_2 {C47}); 72.58 (CH_2 {C37}); 34.50 (CH_3).

Discussion

Phenolics are a class of compounds known for their wide range of physiological actions, ranging from anti-inflammatory, anti-bacterial, anti-oxidative, anti-allergic, anti-hypertensive, anti-ischemic, anti-arrhythmic, anti-thrombotic, anti-carcinogenic, immune-stimulating and hypocholesterolemic [1–4]. They are common plant secondary metabolites found in herbs, fruit, vegetables, grains, tea, coffee beans, propolis, red wine and flavouring agents which form an integral part of the human diet [4–7]. Bromination of 4,6-dibenzyloxy-3-bromo-2-hydroxyacetophenone with Br_2 in HOAc gave 4,6-dibenzyloxy-3-bromo-2-hydroxyacetophenone and 4,6-dibenzyloxy-3,5-dibromo-2-hydroxyacetophenone in a 90:10 ratio. As expected, bromination occurred preferentially at C1 and not at C5 of the substrate, leading to the title compound as the main product. The position of bromination was confirmed by NOESY NMR spectroscopy where a strong NOE effect was evident between the aromatic hydrogen (H5), observed at δ 6.12 ppm, and the four benzyl CH_2 protons were seen at 5.18 ppm and 5.06 ppm respectively. The molecular structure of the title compound is an example of a highly substituted acetophenone, with substituents including two benzyloxy groups, a hydroxyl and a bromine. The weak hydrogen bonding interaction between C42–H42···O4 plays a marginal role in the packing due to its resulting in the alignment of the phenyl ring creating an essentially planar molecule with an *r.m.s.* deviation of 0.0797 Å (C1-C6, C21, C22, C41-C47, O1, O2, O4, Br1), with a maximum deviation 0.153(4) Å found for atom C45. The

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intersection of this plane with the benzyl (C31-C37) group was observed at 86.63(8)° with an *r.m.s.* deviation of 0.0134 Å and a maximum deviation of –0.022(3) Å seen for atom C34, the negative sign indicates the majority of the atom density was found below the defined plane. By taking a vector though the molecule with the head of the vector being the bromine atom, one observes a head-to-tail packing for the unit cell as well as the formation of a "dimeric" unit. The "dimeric" unit is formed by two non-covalent C–H···Br interactions found between a bifurcated bromine (Br1) with the methyl (C22) and an aromatic hydrogen of the phenyl (C32) (symmetry operator [–*x*, –*y*, –*z*]) with distances of 3.999(5) Å and 3.790(5) Å respectively. The interaction of the bromine atom with the aromatic ring contributes in stabilizing the twisting of the benzyl ring from planar. Whilst two weak C–H···π interactions contribute to the stabilization of the planarity. The first being between the central ring (C1-C6) with the methylene (C47) hydrogen of the benzyloxy group with a distance of 3.560(5) Å and the second, between the phenyl of the benzyloxy group and the methyl (C22) of the aldehyde substitutent (symmetry operator [1–*x*, –*y*, –*z*]) with a distance of 3.794(5) Å. Lastly, the hydrogen bonding interaction observed between O1–H1···O2 is known to stabilize the enol form of the title compound. Compounds similar to the title compound have displayed keto-enol tautomerism [8, 9], with the enol form being predominantly found in solid state.

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	*x*	*y*	*z*	U_{iso}
H(5)	2*i*	0.1558	–0.1153	0.0665	0.020
H(22A)	2*i*	0.2676	–0.2809	–0.4121	0.034
H(22B)	2*i*	0.1076	–0.3150	–0.3651	0.034
H(22C)	2*i*	0.3123	–0.2934	–0.2719	0.034
H(32)	2*i*	0.2010	–0.5177	–0.0849	0.025
H(33)	2*i*	0.0605	–0.7481	–0.2165	0.030
H(34)	2*i*	–0.2586	–0.8616	–0.3749	0.033
H(35)	2*i*	–0.4383	–0.7455	–0.3891	0.036
H(36)	2*i*	–0.2981	–0.5163	–0.2542	0.030
H(37A)	2*i*	–0.0390	–0.3201	–0.0653	0.025
H(37B)	2*i*	0.1539	–0.3238	0.0141	0.025
H(42)	2*i*	0.3019	0.3418	0.3226	0.033
H(43)	2*i*	0.3212	0.4895	0.5058	0.037
H(44)	2*i*	0.2486	0.4085	0.6571	0.032
H(45)	2*i*	0.1533	0.1789	0.6247	0.038
H(46)	2*i*	0.1317	0.0310	0.4415	0.034
H(47A)	2*i*	0.2776	0.0287	0.2776	0.022
H(47B)	2*i*	0.0666	0.0015	0.1902	0.022
H(1)	2*i*	0.4320	0.1216	–0.2285	0.035

Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	2*i*	0.3397(4)	0.1518(3)	0.0009(2)	0.012(2)	0.013(1)	0.020(1)	0.005(1)	0.005(1)	0.005(1)
C(2)	2*i*	0.3557(4)	0.0892(3)	–0.1081(2)	0.011(2)	0.023(1)	0.019(1)	0.008(1)	0.004(1)	0.009(1)
C(3)	2*i*	0.2888(4)	–0.0549(3)	–0.1579(2)	0.012(2)	0.019(1)	0.016(1)	0.007(1)	0.002(1)	0.004(1)
C(4)	2*i*	0.2122(4)	–0.1290(3)	–0.0908(2)	0.009(2)	0.018(1)	0.021(1)	0.006(1)	0.004(1)	0.007(1)
C(5)	2*i*	0.2041(4)	–0.0640(3)	0.0212(2)	0.012(2)	0.018(1)	0.018(1)	0.005(1)	0.006(1)	0.006(1)
C(6)	2*i*	0.2671(4)	0.0758(3)	0.0654(2)	0.009(2)	0.020(1)	0.018(1)	0.006(1)	0.002(1)	0.005(1)
C(21)	2*i*	0.3078(4)	–0.1153(3)	–0.2736(2)	0.011(2)	0.024(2)	0.020(1)	0.007(1)	0.005(1)	0.010(1)
C(22)	2*i*	0.2433(4)	–0.2639(3)	–0.3360(3)	0.022(2)	0.024(2)	0.022(1)	0.008(1)	0.013(1)	0.006(1)
C(31)	2*i*	–0.0328(4)	–0.4932(3)	–0.1587(2)	0.020(2)	0.017(1)	0.017(1)	0.007(1)	0.011(1)	0.007(1)
C(32)	2*i*	0.0710(4)	–0.5636(3)	–0.1473(3)	0.018(2)	0.020(1)	0.027(1)	0.008(1)	0.014(1)	0.010(1)
C(33)	2*i*	–0.0123(4)	–0.7007(3)	–0.2260(3)	0.032(2)	0.023(2)	0.032(2)	0.018(2)	0.022(1)	0.013(1)
C(34)	2*i*	–0.2021(4)	–0.7688(3)	–0.3186(3)	0.038(2)	0.017(1)	0.021(1)	0.008(1)	0.013(1)	0.005(1)
C(35)	2*i*	–0.3078(5)	–0.6993(3)	–0.3277(3)	0.027(2)	0.022(2)	0.026(2)	0.006(1)	0.004(1)	0.008(1)
C(36)	2*i*	–0.2241(4)	–0.5626(3)	–0.2479(3)	0.024(2)	0.020(1)	0.029(1)	0.012(1)	0.009(1)	0.011(1)
C(37)	2*i*	0.0575(4)	–0.3442(2)	–0.0747(2)	0.023(2)	0.020(2)	0.019(1)	0.009(1)	0.011(1)	0.008(1)
C(41)	2*i*	0.2137(4)	0.1721(3)	0.3628(2)	0.011(2)	0.022(1)	0.019(1)	0.008(1)	0.004(1)	0.003(1)
C(42)	2*i*	0.2706(4)	0.3078(3)	0.3834(3)	0.035(2)	0.023(2)	0.030(2)	0.014(2)	0.019(1)	0.011(1)
C(43)	2*i*	0.2829(5)	0.3962(3)	0.4931(3)	0.033(2)	0.021(2)	0.038(2)	0.010(2)	0.021(2)	0.006(1)
C(44)	2*i*	0.2397(4)	0.3484(3)	0.5825(3)	0.020(2)	0.030(2)	0.022(1)	0.010(1)	0.009(1)	0.001(1)
C(45)	2*i*	0.1833(5)	0.2123(3)	0.5632(3)	0.040(2)	0.035(2)	0.028(2)	0.018(2)	0.022(1)	0.013(1)
C(46)	2*i*	0.1703(5)	0.1243(3)	0.4541(3)	0.033(2)	0.023(2)	0.031(2)	0.012(2)	0.020(1)	0.010(1)
C(47)	2*i*	0.1993(4)	0.0731(3)	0.2466(2)	0.017(2)	0.018(1)	0.022(1)	0.008(1)	0.010(1)	0.009(1)
O(1)	2*i*	0.4332(3)	0.1695(2)	–0.1627(2)	0.029(1)	0.021(1)	0.023(1)	0.011(1)	0.0149(9)	0.0104(8)
O(2)	2*i*	0.3830(3)	–0.0395(2)	–0.3232(2)	0.026(1)	0.023(1)	0.026(1)	0.0082(9)	0.0157(9)	0.0094(8)
O(3)	2*i*	0.1449(3)	–0.2662(2)	–0.1392(2)	0.021(1)	0.0141(9)	0.0205(9)	0.0061(9)	0.0107(8)	0.0053(7)
O(4)	2*i*	0.2638(3)	0.1467(2)	0.1734(2)	0.020(1)	0.017(1)	0.0200(9)	0.0076(9)	0.0107(8)	0.0040(7)
Br(1)	2*i*	0.42053(4)	0.34199(2)	0.06035(2)	0.0207(2)	0.0160(2)	0.0282(2)	0.0091(2)	0.0104(1)	0.0075(1)

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