Crystal structure of *N*-[1′,1′-(diphenyl)-hydroxymethyl]-3(*S*)-[1′(*R*)-hydroxyethyl]-4(*S*)-(*t*-butyl-oxomethyl)-azetidin-2-one, $C_{23}H_{27}NO_4$, *an unexpectedly stable intermediate in the photochemical cleavage of N-benzhydryl protecting group*

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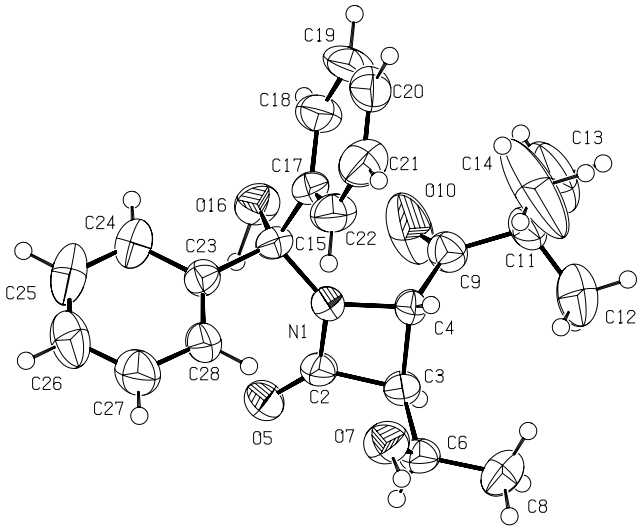

Abstract

$C_{23}H_{27}NO_4$, monoclinic, $P12_11$ (No. 4), a = 6.356(2) Å, b = 17.418(5) Å, c = 9.586(3) Å, β = 100.75(2)°, V = 1042.6 Å^3, Z = 2, $R_{gt}(F)$ = 0.055, $wR_{ref}(F^2)$ = 0.153, T = 293 K.

Source of material

Starting from *N*-(diphenyl-methyl)-3(*S*)-[1′(*R*)-hydroxyethyl]-4(*S*)-(*t*-butyl-oxomethyl)-azetidin-2-one [3], after treatment at 293 K with *N*-bromosuccinimide (1.2 equiv.) in CH_2Cl_2-H_2O mixture (5:1) under irradiation (white light) in the presence of a catalytic amount of molecular bromine (0.1 equiv.), we could isolate the titled compound (crude) as a yellowish oil. A typical signal at 87.4 ppm in ^{13}C NMR spectroscopy indicated the presence of an *O*,*N*-hemi-aminal motif (N–C–OH) [6]. The compound was crystallized by slow evaporation from a CH_2Cl_2 solution.

Experimental details

All the H atoms of the CH_2, CH_3 and aromatic groups were calculated. Those of the CH and OH were located by difference Fourier maps. The H atoms were refined with a common isotropic temperature factor (U_{iso} = 0.120(4) Å^2).

Discussion

Chiral functionalized azetidinones (β-lactams) are valuable key-intermediates in organic synthesis for the preparation of various biologically active compounds [1], particularly in the field of antibiotics related to the large family of penicillins [2]. Recently, we became interested in the synthesis of novel precursors of carbapenems [3, 4]. Our strategy involved the use of a benzhydryl moiety as *N*-protecting group of the azetidinone ring, instead of the habitual *p*-anisyl substituent [2] which requires large quantities of ceric ammonium nitrate (CAN), a highly toxic reagent, for deprotection. We found that the benzhydryl group could be readily and quantitatively cleaved by a two-step process as follows [5]: (i) photoactivated bromination and in situ hydrolysis of the resulting *N*-(1,1-diphenyl)-bromomethyl residue into *N*-(1,1-diphenyl)-hydroxymethyl residue; (ii) acid-catalyzed decomposition of the hemi-aminal intermediate into NH-azetidinone and benzophenone. Usually, hemi-acetal and hemi-aminal compounds are unstable, and rapidly decompose to regenerate their carbonyl precursors. However, *N*-[1′,1′-(diphenyl)-hydroxymethyl]-3(*S*)-[1′(*R*)-hydroxyethyl]-4(*S*)-(*t*-butyl-oxomethyl)-azetidin-2-one was surprisingly stable and required the addition of a strong acid (*p*-Tos-OH, 1 equiv.) to release benzophenone.

X-ray diffraction analysis of a monocrystal confirmed unambiguously the *O*,*N*-hemi-aminal structure of the title compound. This structure was initially proposed on the basis of ^{1}H and ^{13}C NMR data only [6]. Only 4 structures of azetidin-2-one with the *N*-hemi-aminal motif have been reported [7-10,11]. In all these molecules the C—N (mean value 1.432 Å) and C—OH (mean value 1.390 Å) bond lengths are shorter than those observed in the title compound, 1.472(5) Å and 1.418(5) Å respectively. This is probably the result of the steric constraint on the C atom resulting from the substitution by two phenyl rings. There are two intermolecular hydrogen bonds with the following geometry: O7–H7···O5(1+*x*, *y*, *z*): *d*(O—H) = 0.86 Å; *d*(H···O) = 2.13 Å; *d*(O···O) = 2.959 Å; ∠O–H···O = 161°. O16–H16···O7(*x*–1, *y*, *z*): *d*(O—H) = 1.19 Å; *d*(H···O) = 1.98 Å; *d*(O···O) = 2.998 Å; ∠O–H···O = 140°. A slight intramolecular interaction is also observed between the OH and the C=O of the *N*-hemi-aminal group: O16–H16···O5: O16-H16 = 1.19 Å; H···O = 2.54 Å; O···O = 3.510 Å and O-H···O = 137°. This is rather curious as a nice intramolecular H bond involving this hydroxyl and the other carbonyl oxygen (O10) would be possible (*d*(O16···O10) = 2.91 Å but H16 is not properly oriented (*d*(H16···O10) = 3.19 Å).

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Table 1. Data collection and handling.

Crystal:	colourless parallelipiped, size 0.18 × 0.20 × 0.32 mm
Wavelength:	Mo K_α radiation (0.71069 Å)
μ:	0.83 cm^{-1}
Diffractometer, scan mode:	MAR345, 53 images, $\Delta\varphi = 3°$
$2\theta_{max}$:	46.5°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	4332, 2782
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 2285
$N(param)_{refined}$:	270
Programs:	SHELXS-97 [11], SHELXL-97 [12], PLATON [13]

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

Atom	Site	x	y	z	U_{iso}
H(8A)	2*a*	1.2414	0.1235	0.0276	0.120(4)
H(8B)	2*a*	1.1566	0.2077	0.0329	0.120
H(8C)	2*a*	1.0330	0.1490	–0.0766	0.120
H(12A)	2*a*	0.7989	0.3117	–0.1415	0.120
H(12B)	2*a*	0.9925	0.3113	–0.0134	0.120
H(12C)	2*a*	0.9549	0.3822	–0.1159	0.120
H(13A)	2*a*	0.4865	0.3968	–0.1331	0.120
H(13B)	2*a*	0.6461	0.4663	–0.1155	0.120
H(13C)	2*a*	0.4971	0.4532	–0.0044	0.120
H(14A)	2*a*	0.9570	0.4660	0.0778	0.120
H(14B)	2*a*	1.0024	0.3953	0.1800	0.120
H(14C)	2*a*	0.8110	0.4505	0.1897	0.120
H(18)	2*a*	0.4642	0.3982	0.4412	0.120
H(19)	2*a*	0.6536	0.5068	0.5299	0.120
H(20)	2*a*	1.0163	0.5002	0.6150	0.120
H(21)	2*a*	1.1917	0.3864	0.6032	0.120
H(22)	2*a*	1.0068	0.2775	0.5151	0.120
H(24)	2*a*	0.3499	0.2231	0.6097	0.120
H(25)	2*a*	0.3780	0.1317	0.7847	0.120
H(26)	2*a*	0.6527	0.0426	0.8156	0.120
H(27)	2*a*	0.9078	0.0499	0.6754	0.120
H(28)	2*a*	0.8839	0.1408	0.4987	0.120
H(3)	2*a*	0.69(1)	0.169(4)	0.028(8)	0.120
H(4)	2*a*	0.95(1)	0.277(4)	0.238(7)	0.120
H(6)	2*a*	0.95(1)	0.078(4)	0.105(7)	0.120
H(7)	2*a*	1.22(1)	0.114(4)	0.265(7)	0.120
H(16)	2*a*	0.340(7)	0.207(4)	0.335(6)	0.120

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}
N(1)	2*a*	0.6801(5)	0.2220(2)	0.2979(3)	0.054(2)	0.037(2)	0.044(2)	–0.001(1)	0.016(1)	0.002(1)
C(2)	2*a*	0.6454(6)	0.1541(2)	0.2287(4)	0.047(2)	0.037(2)	0.049(2)	–0.003(2)	0.012(2)	–0.006(2)
C(3)	2*a*	0.7761(6)	0.1769(2)	0.1173(4)	0.050(2)	0.040(2)	0.041(2)	–0.003(2)	0.010(2)	–0.005(2)
C(4)	2*a*	0.7882(6)	0.2582(2)	0.1906(4)	0.050(2)	0.039(2)	0.036(2)	–0.002(2)	0.013(2)	0.002(2)
O(5)	2*a*	0.5462(5)	0.0969(2)	0.2499(3)	0.072(2)	0.045(2)	0.071(2)	–0.015(2)	0.023(2)	–0.007(2)
C(6)	2*a*	0.9821(7)	0.1306(3)	0.1251(4)	0.057(3)	0.042(2)	0.054(2)	–0.001(2)	0.012(2)	–0.009(2)
O(7)	2*a*	1.0983(5)	0.1356(2)	0.2667(3)	0.066(2)	0.068(2)	0.059(2)	0.013(2)	0.008(2)	0.003(2)
C(8)	2*a*	1.1155(7)	0.1549(3)	0.0174(5)	0.057(3)	0.084(3)	0.065(3)	–0.002(2)	0.023(2)	–0.009(3)
C(9)	2*a*	0.6508(7)	0.3185(3)	0.1006(5)	0.053(3)	0.052(3)	0.056(2)	0.004(2)	0.008(2)	0.007(2)
O(10)	2*a*	0.4592(6)	0.3156(3)	0.0943(5)	0.057(2)	0.132(4)	0.163(4)	0.015(2)	0.015(2)	0.091(3)
C(11)	2*a*	0.7487(7)	0.3789(3)	0.0213(5)	0.080(3)	0.049(3)	0.053(3)	0.001(2)	0.012(2)	0.014(2)
C(12)	2*a*	0.886(2)	0.3428(5)	–0.071(1)	0.25(1)	0.118(7)	0.154(7)	0.033(7)	0.128(8)	0.066(6)
C(13)	2*a*	0.579(1)	0.4283(5)	–0.066(1)	0.140(7)	0.124(6)	0.179(9)	0.024(5)	0.026(6)	0.097(6)
C(14)	2*a*	0.893(2)	0.4269(6)	0.127(1)	0.30(2)	0.138(7)	0.144(8)	–0.146(9)	–0.068(8)	0.062(7)
C(15)	2*a*	0.5914(6)	0.2532(2)	0.4173(4)	0.048(2)	0.043(2)	0.048(2)	0.009(2)	0.016(2)	–0.002(2)
O(16)	2*a*	0.3720(4)	0.2716(2)	0.3714(3)	0.041(2)	0.067(2)	0.074(2)	0.009(1)	0.010(1)	0.000(2)
C(17)	2*a*	0.7152(6)	0.3266(2)	0.4705(4)	0.056(2)	0.042(2)	0.045(2)	0.000(2)	0.018(2)	–0.008(2)
C(18)	2*a*	0.6111(8)	0.3952(3)	0.4743(5)	0.076(3)	0.048(3)	0.070(3)	0.012(2)	0.014(2)	0.002(2)
C(19)	2*a*	0.725(1)	0.4604(3)	0.5279(6)	0.140(6)	0.036(3)	0.083(4)	0.004(3)	0.027(4)	–0.007(2)
C(20)	2*a*	0.941(1)	0.4568(3)	0.5775(6)	0.117(5)	0.055(3)	0.064(3)	–0.028(3)	0.035(3)	–0.017(2)
C(21)	2*a*	1.0445(8)	0.3890(3)	0.5714(6)	0.068(3)	0.082(4)	0.081(3)	–0.019(3)	0.020(3)	–0.026(3)
C(22)	2*a*	0.9338(7)	0.3235(3)	0.5184(5)	0.058(3)	0.055(3)	0.076(3)	–0.002(2)	0.018(2)	–0.014(2)
C(23)	2*a*	0.6143(6)	0.1916(2)	0.5347(4)	0.051(2)	0.046(2)	0.039(2)	–0.003(2)	0.010(2)	–0.004(2)
C(24)	2*a*	0.4626(7)	0.1882(3)	0.6219(5)	0.055(3)	0.083(3)	0.055(3)	–0.008(2)	0.018(2)	0.003(3)
C(25)	2*a*	0.4795(9)	0.1333(4)	0.7263(5)	0.080(4)	0.120(5)	0.056(3)	–0.029(4)	0.027(2)	0.003(3)
C(26)	2*a*	0.644(1)	0.0803(3)	0.7461(5)	0.097(4)	0.085(4)	0.047(3)	–0.022(3)	0.004(3)	0.015(3)
C(27)	2*a*	0.7943(9)	0.0845(3)	0.6616(5)	0.098(4)	0.066(3)	0.053(3)	0.007(3)	0.009(3)	0.007(2)
C(28)	2*a*	0.7807(7)	0.1392(2)	0.5558(4)	0.066(3)	0.048(3)	0.047(2)	0.002(2)	0.015(2)	0.008(2)

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