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Crystal structure of *N*-(diphenyl)methyl-*N*-(3′,3′-dimethyl-2′-oxo)butyl-2(*R*),3(*R*)-epoxybutyramide, $C_{23}H_{27}NO_3$

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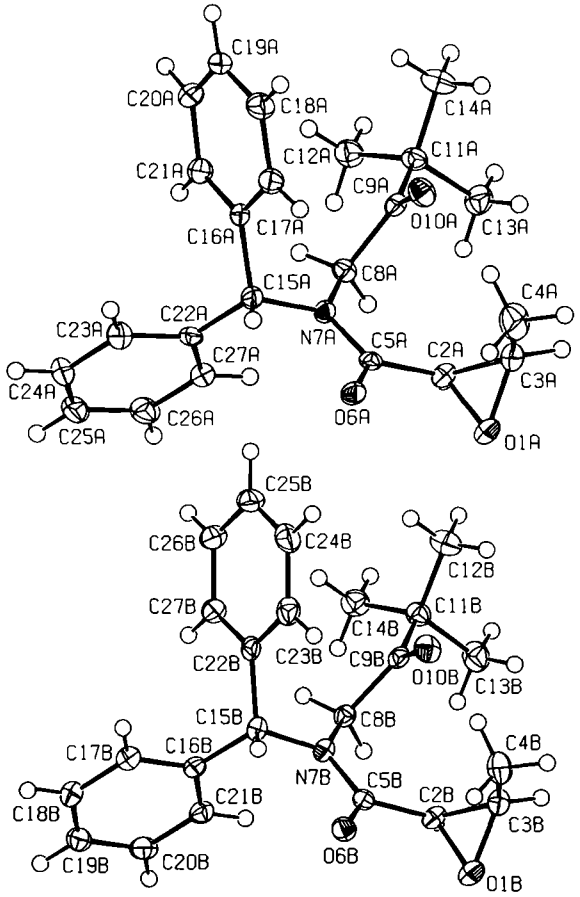

Abstract

$C_{23}H_{27}NO_3$, monoclinic, $P12_11$ (no. 4), a = 8.669(3) Å, b = 22.880(5) Å, c = 10.220(3) Å, β = 96.04(2)°, V = 2015.9 Å^3, Z = 4, $R_{gt}(F)$ = 0.039, $wR_{ref}(F^2)$ = 0.106, T = 125 K.

Source of material

The title compound was prepared from sodium 2(*R*),3(*R*)-epoxybutyrate (mixed salt with NaBr) [1] and 1-(diphenylmethyl)-amino-3,3-dimethyl-2-butanone [2] in a one-pot process. Epoxybutyrate was first activated with oxalylchloride in THF at –5 °C, then pyridine and the amino-ketone were added and reacted for 2 h at 20 °C. After work-up and column chromatography on silicagel, the epoxybutyramide was recovered in 73 % yield (R_F = 0.33; CH_2Cl_2/EtOH, *v*/*v* 10:1). Crystallization from CH_2Cl_2/MeOH/H_2O (1:1:1) gave white crystals suitable for X-ray diffraction analysis (m.p. = 157-158 °C, $[\alpha]^{20}$ = +10.8 (*c* = 1.03, $CHCl_3$), mass (EI) *m*/*e* = 365.2 [2]).

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Experimental details

The H2, H3 and H13 atoms were located from Fourier difference maps and refined freely. The other H atoms were calculated and refined with a common isotropic temperature factor of 0.041 Å^2.

Discussion

Twenty years ago, Hanessian et al. [3] described the cyclization of *N*-anisyl-*N*-(phenylcarbonylmethyl)-2(*R*),3(*R*)-epoxybutyramide into *N*-anisyl-3(*S*)-(1′(*R*)-hydroxyethyl)-4(*S*)-benzoyl-2-azetidinone under basic conditions (K_2CO_3, DMF, 60 °C, 3 h): azetidinone was the only formed product corresponding to a 4-Exo-Tet ring closure. Recently, we revisited this reaction by changing the substituents in order to make the N-deprotection step more environmentally friendly [4]. Preparing a series of *N*-benzhydryl epoxybutyramide precursors we found that, under the Hanessian's conditions, the 6-Exo-Tet and 7-Endo-Tet cyclization products were favored regarding the 4-Exo-Tet [2]. Thus, the effect of a N-bulky substituent on the conformation of the amide bond was questioned. The ^{1}H and ^{13}C NMR spectra of epoxybutyramides showed interesting features: the *N*-anisyl derivatives gave one set of signals, even at low temperature (free rotation around the N—CO amide bond), while the *N*-benzhydryl derivatives gave a splitting of all the signals, characteristic of the presence of two conformers in solution at room temperature. 2D NOESY (Nuclear Overhauser and Exchange Spectroscopy) experiments revealed that the rotamer required for cyclization into azetidinone was the minor isomer. Interestingly, this conformer has been rooted in the solid state structure of the title compound. The two independent molecules in the unit cell are very similar even when their conformation is compared. Selected bond distances are as follows: *d*(O1—C2) = 1.431(2) Å, *d*(O1—C3) = 1.435(3) Å, *d*(C2—C3) = 1.469(3) Å, *d*(C2—C5) = 1.508(3) Å, *d*(C5—N7) = 1.359(3) Å, *d*(C5—O6) = 1.227(3) Å, *d*(N7—C8) = 1.450(3) Å. There are no classical hydrogen bonds in the crystal structure.

Table 1. Data collection and handling.

Crystal:	colorless parallelepiped, size 0.20 × 0.30 × 0.32 mm
Wavelength:	Mo K_α radiation (0.71069 Å)
μ:	0.79 cm^{-1}
Diffractometer, scan mode:	MAR345 IP, φ
$2\theta_{max}$:	50.72°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	21738, 7058
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\,\sigma(I_{obs})$, 6828
$N(param)_{refined}$:	506
Programs:	SHELXS-97 [5], SHELXL-97 [6], PLATON [7]

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

Atom	Site	x	y	z	U_{iso}
H(4A1)	2*a*	0.5808	0.3305	1.2231	0.041
H(4A2)	2*a*	0.4509	0.3461	1.1099	0.041
H(4A3)	2*a*	0.5770	0.3926	1.1580	0.041
H(8A1)	2*a*	0.7712	0.4994	0.7823	0.041
H(8A2)	2*a*	0.8116	0.4333	0.8047	0.041
H(12A)	2*a*	1.0169	0.5104	0.7910	0.041
H(12B)	2*a*	1.1508	0.5416	0.8799	0.041
H(12C)	2*a*	0.9834	0.5683	0.8651	0.041
H(13A)	2*a*	1.0664	0.4171	0.9167	0.041
H(13B)	2*a*	1.0644	0.4165	1.0699	0.041
H(13C)	2*a*	1.2013	0.4468	1.0073	0.041
H(14A)	2*a*	1.1495	0.5424	1.1222	0.041
H(14B)	2*a*	1.0224	0.5081	1.1891	0.041
H(14C)	2*a*	0.9791	0.5662	1.1127	0.041
H(17A)	2*a*	0.4085	0.5289	1.0138	0.041
H(18A)	2*a*	0.4451	0.6145	1.1334	0.041
H(19A)	2*a*	0.5821	0.6908	1.0539	0.041
H(20A)	2*a*	0.6858	0.6809	0.8557	0.041
H(21A)	2*a*	0.6385	0.5972	0.7299	0.041
H(23A)	2*a*	0.2963	0.5630	0.6190	0.041
H(24A)	2*a*	0.2658	0.5734	0.3942	0.041
H(25A)	2*a*	0.4267	0.5227	0.2657	0.041
H(26A)	2*a*	0.6164	0.4614	0.3653	0.041
H(27A)	2*a*	0.6439	0.4493	0.5916	0.041
H(2A)	2*a*	0.741(4)	0.351(1)	0.865(3)	0.041
H(3A)	2*a*	0.763(3)	0.309(1)	1.085(3)	0.041
H(15A)	2*a*	0.380(4)	0.485(1)	0.799(3)	0.041

Table 2. Continued.

Atom	Site	x	y	z	U_{iso}
H(4B1)	2*a*	1.0490	0.9154	1.7045	0.041
H(4B2)	2*a*	1.1453	0.9017	1.5867	0.041
H(4B3)	2*a*	1.0338	0.8542	1.6350	0.041
H(8B1)	2*a*	0.7234	0.7516	1.2614	0.041
H(8B2)	2*a*	0.6926	0.8183	1.2803	0.041
H(12D)	2*a*	0.4392	0.7092	1.6083	0.041
H(12E)	2*a*	0.5819	0.7455	1.6703	0.041
H(12F)	2*a*	0.6081	0.6870	1.5958	0.041
H(13D)	2*a*	0.4542	0.8327	1.3930	0.041
H(13E)	2*a*	0.4972	0.8358	1.5458	0.041
H(13F)	2*a*	0.3466	0.8029	1.4877	0.041
H(14D)	2*a*	0.4756	0.7379	1.2731	0.041
H(14E)	2*a*	0.3703	0.7064	1.3670	0.041
H(14F)	2*a*	0.5355	0.6816	1.3497	0.041
H(17B)	2*a*	1.1656	0.6821	1.1132	0.041
H(18B)	2*a*	1.1611	0.6748	0.8875	0.041
H(19B)	2*a*	0.9925	0.7321	0.7503	0.041
H(20B)	2*a*	0.8282	0.7966	0.8409	0.041
H(21B)	2*a*	0.8311	0.8041	1.0677	0.041
H(23B)	2*a*	1.1116	0.7154	1.5064	0.041
H(24B)	2*a*	1.0583	0.6337	1.6259	0.041
H(25B)	2*a*	0.8911	0.5622	1.5331	0.041
H(26B)	2*a*	0.7823	0.5727	1.3167	0.041
H(27B)	2*a*	0.8390	0.6541	1.1961	0.041
H(2B)	2*a*	0.783(4)	0.901(1)	1.349(3)	0.041
H(3B)	2*a*	0.830(4)	0.937(1)	1.565(3)	0.041
H(15B)	2*a*	1.121(4)	0.763(1)	1.287(3)	0.041

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}
O(1A)	2*a*	0.5852(2)	0.29763(6)	0.9340(2)	0.0409(9)	0.0150(7)	0.0299(8)	−0.0021(6)	−0.0002(7)	0.0023(6)
C(2A)	2*a*	0.6514(2)	0.35321(8)	0.9086(2)	0.024(1)	0.0147(9)	0.023(1)	0.0008(8)	0.0042(8)	0.0006(8)
C(3A)	2*a*	0.6588(3)	0.3301(1)	1.0429(2)	0.039(1)	0.022(1)	0.023(1)	0.0001(9)	−0.003(1)	0.0047(8)
C(4A)	2*a*	0.5579(4)	0.3518(1)	1.1423(2)	0.065(2)	0.043(2)	0.020(1)	0.003(1)	0.008(1)	0.007(1)
C(5A)	2*a*	0.5351(2)	0.39972(8)	0.8633(2)	0.020(1)	0.0156(9)	0.0123(9)	−0.0018(7)	0.0015(7)	−0.0034(7)
O(6A)	2*a*	0.3953(2)	0.38979(6)	0.8565(1)	0.0196(8)	0.0179(7)	0.0251(8)	−0.0043(5)	−0.0001(6)	0.0010(6)
N(7A)	2*a*	0.5925(2)	0.45204(7)	0.8280(2)	0.0158(8)	0.0156(8)	0.0185(8)	−0.0014(6)	0.0006(6)	0.0018(6)
C(8A)	2*a*	0.7567(2)	0.46605(8)	0.8383(2)	0.017(1)	0.020(1)	0.019(1)	−0.0013(7)	0.0008(8)	−0.0005(8)
C(9A)	2*a*	0.8302(2)	0.47991(8)	0.9771(2)	0.020(1)	0.0132(9)	0.021(1)	0.0024(7)	0.0016(8)	−0.0001(7)
O(10A)	2*a*	0.7579(2)	0.47501(7)	1.0713(1)	0.0243(8)	0.0321(8)	0.0209(8)	−0.0013(6)	0.0029(6)	0.0014(6)
C(11A)	2*a*	1.0020(2)	0.49683(9)	0.9887(2)	0.0171(9)	0.021(1)	0.022(1)	−0.0013(7)	−0.0004(8)	−0.0031(8)
C(12A)	2*a*	1.0420(3)	0.5326(1)	0.8701(2)	0.020(1)	0.029(1)	0.030(1)	−0.0056(8)	−0.0001(9)	0.0010(9)
C(13A)	2*a*	1.0920(3)	0.4389(1)	0.9964(2)	0.023(1)	0.025(1)	0.037(1)	0.0043(9)	−0.0004(9)	0.000(1)
C(14A)	2*a*	1.0419(3)	0.5316(1)	1.1148(2)	0.024(1)	0.038(1)	0.029(1)	−0.0076(9)	0.0009(9)	−0.011(1)
C(15A)	2*a*	0.4820(2)	0.49808(8)	0.7795(2)	0.017(1)	0.017(1)	0.019(1)	−0.0010(7)	0.0002(8)	0.0015(7)
C(16A)	2*a*	0.5148(2)	0.55443(8)	0.8570(2)	0.020(1)	0.0144(9)	0.019(1)	0.0009(7)	−0.0036(8)	0.0018(7)
C(17A)	2*a*	0.4611(2)	0.55992(9)	0.9798(2)	0.020(1)	0.022(1)	0.023(1)	−0.0012(8)	0.0012(8)	0.0006(8)
C(18A)	2*a*	0.4848(3)	0.6110(1)	1.0527(2)	0.033(1)	0.027(1)	0.023(1)	0.0046(9)	0.0007(9)	−0.0051(9)
C(19A)	2*a*	0.5670(3)	0.65646(9)	1.0057(2)	0.045(1)	0.017(1)	0.025(1)	0.0028(9)	−0.013(1)	−0.0036(8)
C(20A)	2*a*	0.6269(3)	0.65078(9)	0.8861(2)	0.048(2)	0.018(1)	0.028(1)	−0.011(1)	−0.008(1)	0.0047(9)
C(21A)	2*a*	0.5997(3)	0.6003(1)	0.8111(2)	0.037(1)	0.022(1)	0.019(1)	−0.0070(9)	0.0007(9)	0.0035(8)
C(22A)	2*a*	0.4741(2)	0.50507(8)	0.6302(2)	0.021(1)	0.0165(9)	0.017(1)	−0.0060(7)	−0.0025(8)	−0.0016(8)
C(23A)	2*a*	0.3605(3)	0.5423(1)	0.5682(2)	0.027(1)	0.025(1)	0.027(1)	0.0023(9)	−0.0012(9)	0.0004(9)
C(24A)	2*a*	0.3423(3)	0.5487(1)	0.4337(2)	0.034(1)	0.027(1)	0.023(1)	−0.0014(9)	−0.0072(9)	0.0047(9)
C(25A)	2*a*	0.4383(3)	0.5183(1)	0.3567(2)	0.041(1)	0.031(1)	0.020(1)	−0.007(1)	−0.004(1)	0.0026(9)
C(26A)	2*a*	0.5514(3)	0.4816(1)	0.4164(2)	0.035(1)	0.030(1)	0.021(1)	−0.002(1)	0.0042(9)	−0.0035(9)
C(27A)	2*a*	0.5686(2)	0.47456(9)	0.5525(2)	0.027(1)	0.019(1)	0.022(1)	−0.0006(8)	−0.0011(8)	−0.0002(8)
O(1B)	2*a*	0.9602(2)	0.95164(6)	1.4171(2)	0.0394(9)	0.0172(7)	0.0307(9)	−0.0033(6)	0.0050(7)	−0.0018(6)
C(2B)	2*a*	0.8845(2)	0.89654(9)	1.3922(2)	0.023(1)	0.0140(9)	0.025(1)	0.0015(8)	0.0000(9)	0.0000(8)
C(3B)	2*a*	0.9186(3)	0.91830(9)	1.5276(2)	0.029(1)	0.022(1)	0.026(1)	0.0006(9)	0.0079(9)	−0.0040(8)
C(4B)	2*a*	1.0483(3)	0.8953(1)	1.6219(2)	0.037(1)	0.036(1)	0.023(1)	−0.001(1)	0.002(1)	−0.008(1)
C(5B)	2*a*	0.9850(2)	0.84945(8)	1.3412(2)	0.023(1)	0.017(1)	0.0120(9)	0.0018(7)	−0.0003(7)	0.0023(7)
O(6B)	2*a*	1.1226(2)	0.85866(6)	1.3305(1)	0.0211(8)	0.0225(7)	0.0221(7)	−0.0034(6)	0.0032(6)	−0.0013(6)
N(7B)	2*a*	0.9158(2)	0.79739(7)	1.3082(2)	0.0189(9)	0.0158(8)	0.0197(8)	0.0016(6)	0.0013(7)	−0.0012(6)
C(8B)	2*a*	0.7530(2)	0.78526(8)	1.3161(2)	0.019(1)	0.0155(9)	0.0174(9)	0.0014(7)	−0.0007(7)	−0.0002(7)
C(9B)	2*a*	0.7118(2)	0.77337(8)	1.4546(2)	0.022(1)	0.0129(9)	0.021(1)	0.0045(7)	0.0016(8)	0.0007(7)

Table 3. Continued.

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(10B)	2*a*	0.8062(2)	0.78161(7)	1.5490(1)	0.0261(8)	0.0304(8)	0.0202(8)	0.0002(6)	–0.0034(6)	–0.0004(6)
C(11B)	2*a*	0.5452(2)	0.75481(9)	1.4696(2)	0.022(1)	0.024(1)	0.020(1)	0.0016(8)	0.0019(8)	0.0027(8)
C(12B)	2*a*	0.5434(3)	0.7210(1)	1.5979(2)	0.036(1)	0.035(1)	0.028(1)	–0.001(1)	0.006(1)	0.009(1)
C(13B)	2*a*	0.4520(3)	0.8119(1)	1.4745(2)	0.026(1)	0.034(1)	0.031(1)	0.0093(9)	0.006(1)	0.001(1)
C(14B)	2*a*	0.4750(3)	0.7166(1)	1.3539(2)	0.023(1)	0.029(1)	0.031(1)	–0.0044(9)	0.0042(9)	0.0005(9)
C(15B)	2*a*	1.0135(2)	0.74965(9)	1.2649(2)	0.018(1)	0.0172(9)	0.020(1)	0.0023(7)	0.0020(8)	–0.0030(8)
C(16B)	2*a*	0.9999(2)	0.74440(8)	1.1150(2)	0.022(1)	0.0150(9)	0.020(1)	–0.0042(8)	0.0028(8)	–0.0011(8)
C(17B)	2*a*	1.0979(3)	0.70536(9)	1.0591(2)	0.029(1)	0.020(1)	0.024(1)	0.0002(8)	0.0037(9)	0.0002(8)
C(18B)	2*a*	1.0950(3)	0.70090(9)	0.9236(2)	0.036(1)	0.020(1)	0.027(1)	–0.0027(9)	0.009(1)	–0.0048(8)
C(19B)	2*a*	0.9940(3)	0.73512(9)	0.8412(2)	0.038(1)	0.024(1)	0.019(1)	–0.0102(9)	0.0051(9)	–0.0028(8)
C(20B)	2*a*	0.8960(3)	0.7736(1)	0.8955(2)	0.031(1)	0.023(1)	0.022(1)	–0.0065(9)	–0.0001(9)	0.0030(8)
C(21B)	2*a*	0.8981(2)	0.77827(9)	1.0320(2)	0.023(1)	0.018(1)	0.024(1)	–0.0025(8)	0.0033(8)	–0.0006(8)
C(22B)	2*a*	0.9810(2)	0.69341(8)	1.3375(2)	0.022(1)	0.018(1)	0.020(1)	0.0077(8)	0.0051(8)	–0.0011(8)
C(23B)	2*a*	1.0458(3)	0.6867(1)	1.4677(2)	0.027(1)	0.026(1)	0.024(1)	0.0090(8)	0.0015(9)	–0.0012(8)
C(24B)	2*a*	1.0132(3)	0.6378(1)	1.5397(2)	0.046(2)	0.034(1)	0.022(1)	0.019(1)	0.009(1)	0.007(1)
C(25B)	2*a*	0.9138(3)	0.5948(1)	1.4843(2)	0.045(2)	0.022(1)	0.038(1)	0.009(1)	0.020(1)	0.009(1)
C(26B)	2*a*	0.8488(3)	0.6012(1)	1.3550(2)	0.035(1)	0.020(1)	0.035(1)	0.0009(9)	0.011(1)	0.0028(9)
C(27B)	2*a*	0.8830(3)	0.65034(9)	1.2827(2)	0.025(1)	0.021(1)	0.024(1)	0.0033(8)	0.0042(9)	0.0018(8)

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