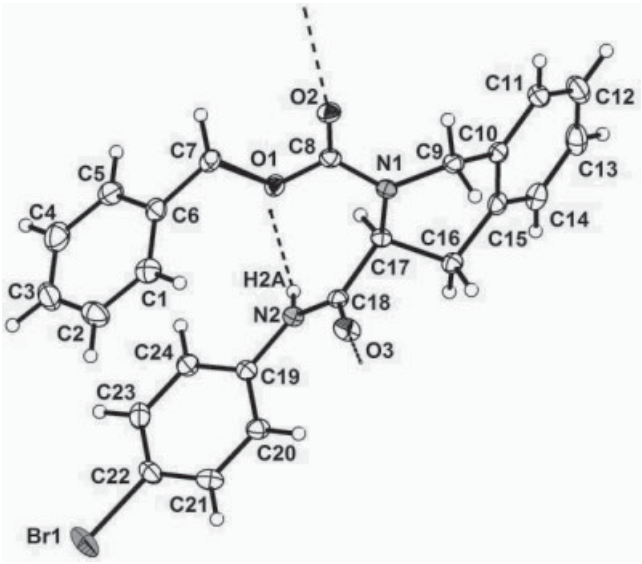
Crystal structure of (*S*)-benzyl-3-{(4-bromophenyl)carbamoyl}-3,4-dihydroisoquinoline-2(1*H*)-carboxylate, $C_{24}H_{21}BrN_2O_3$

Zamani E. D. Cele, Pralav Bhatt, Thavendran Govender, Hendrik G. Kruger and Glenn E. M. Maguire*

School of Health Sciences, University of KwaZulu Natal, Westville, Durban 4000, South Africa

Received May 30, 2013, accepted August 16, 2013, available online August 28, 2013, CCDC no. 957609



Abstract

$C_{24}H_{21}BrN_2O_3$, monoclinic, $P2_1$ (no. 4), a = 12.8659(6) Å, b = 10.6838(5) Å, c = 16.1445(8) Å, β = 104.351(2)°, V = 2149.9 Å^3, Z = 4, $R_{gt}(F)$ = 0.0228, $wR_{ref}(F^2)$ = 0.0603, T = 173 K.

Table 1. Data collection and handling.

Crystal:	colourless blocks, size 0.13×0.45×0.54 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	19.40 cm^{-1}
Diffractometer, scan mode:	Bruker Smart ApexII CCD, φ and ω scans
$2\theta_{max}$:	56.66°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	47386, 10623
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 9758
$N(param)_{refined}$:	541
Programs:	SADABS [7], OLEX2 [8], WinGX [9], SHELX [11]

Source of material

To a solution of (*S*)-2-(benzyloxycarbonyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (1.5 g, 4.8 mmol) in dry DMF (15 ml) was added *EDC*·HCl (1-ethyl-3-(dimethylamino)-carbodiimide, HCl salt, 1.1 g, 5.8 mmol), HOBt (1-hydroxybenzotriazol, 0.81 g, 5.3 mmol), 4-bromoaniline (0.91 g, 5.3 mmol) and a catalytic amount of *DMAP* (dimethylamino pyridine). The reaction mixture was then stirred at room temperature until no more starting material could be detected by thin layer chromatography (TLC) analysis (approximately 3 h). The reaction mixture was poured into 30 volumes of chilled water; the mixture was then extracted three times with ethyl acetate. The extracts were combined, washed with 10% aqueous HCl to remove latent *EDC* urea, dried over anhydrous magnesium sulfate and then concentrated to dryness affording the crude product which was purified by silica column chromatography. (hexane:ethyl acetate, 50:50) R_f = 0.6. Yield 73%. Melting point = 399-403 K. Recrystallization from ethanol at room temperature afforded colourless crystals suitable for X-ray analysis. The so-called Flack parameter (0.000(3)) was calculated by a hole-in-one method [10, 11].

* Correspondence author (e-mail: maguireg@ukzn.ac.za)

Experimental details

All H atoms were positioned geometrically and allowed to ride on their respective parent atoms. The carboxyl H atoms were located from the difference map and allowed to ride on their parent atoms.

Discussion

Tetrahydroisoquinoline (*TIQ*) and its derivatives have been extensively used as chiral catalysts including transfer hydrogenation of prochiral ketones [1,2], the Henry [3] and Michael reactions [4,5]. The title compound is a precursor in the synthesis of several chiral ligands containing the *TIQ* framework and it was derived from commercially available *S*-phenyl glycine and formaldehyde. The structure has two crystallographically independant molecules in the asymmetric unit. From the crystal structure it is evident that the *N*-containing six membered ring assumes a twisted boat conformation [(Q) = 0.6600 (15) Å, θ = 84.29 (13)°, ϕ = 246.52 (13)°] [6]. The molecules display intermolecular N–H···O hydrogen bonding via the amide and carbamate carbonyl groups. This bonding arrangement creates chains along the *b* direction.

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

Atom	Site	x	y	z	U_{iso}
H(1)	2*a*	0.0307	–0.0492	0.2647	0.028
H(2)	2*a*	–0.0119	0.0420	0.1291	0.036
H(3)	2*a*	–0.1668	0.1626	0.0855	0.041
H(4)	2*a*	–0.2747	0.2008	0.1793	0.041
H(5)	2*a*	–0.2308	0.1116	0.3166	0.031
H(7A)	2*a*	–0.1371	–0.0461	0.4118	0.025
H(7B)	2*a*	–0.0554	–0.1365	0.3796	0.025
H(9A)	2*a*	0.2849	–0.0698	0.6369	0.021
H(9B)	2*a*	0.1752	–0.1101	0.6597	0.021
H(11)	2*a*	0.1998	–0.0397	0.8089	0.028
H(12)	2*a*	0.2285	0.1242	0.9078	0.036
H(13)	2*a*	0.2732	0.3232	0.8683	0.035
H(14)	2*a*	0.2969	0.3573	0.7309	0.028
H(16A)	2*a*	0.3378	0.1466	0.5915	0.020
H(16B)	2*a*	0.2826	0.2821	0.5851	0.020
H(17)	2*a*	0.1098	0.1937	0.5373	0.018
H(20)	2*a*	0.2848	0.2034	0.3109	0.024
H(21)	2*a*	0.2744	0.2541	0.1684	0.028
H(23)	2*a*	–0.0210	0.4018	0.1444	0.027
H(24)	2*a*	–0.0118	0.3514	0.2867	0.023
H(25)	2*a*	1.0132	0.1956	–0.2855	0.028
H(26)	2*a*	1.0255	0.2355	–0.1409	0.033

Table 2. continued.

Atom	Site	*x*	*y*	*z*	U_{iso}
H(27)	2*a*	0.8822	0.1885	–0.0820	0.034
H(28)	2*a*	0.7248	0.1030	–0.1681	0.033
H(29)	2*a*	0.7119	0.0632	–0.3118	0.028
H(31A)	2*a*	0.9191	0.1235	–0.4214	0.029
H(31B)	2*a*	0.8416	0.0072	–0.4168	0.029
H(33A)	2*a*	0.4617	0.1177	–0.6124	0.024
H(33B)	2*a*	0.5522	0.0566	–0.6527	0.024
H(35)	2*a*	0.5101	0.1268	–0.8034	0.030
H(36)	2*a*	0.4858	0.2925	–0.9009	0.037
H(37)	2*a*	0.4715	0.4969	–0.8552	0.035

Table 2. continued.

Atom	Site	*x*	*y*	*z*	U_{iso}
H(38)	2*a*	0.4787	0.5385	–0.7116	0.028
H(40A)	2*a*	0.4333	0.3390	–0.5674	0.022
H(40B)	2*a*	0.5043	0.4630	–0.5640	0.022
H(41)	2*a*	0.6639	0.3557	–0.5171	0.019
H(44)	2*a*	0.7661	0.4790	–0.2548	0.025
H(45)	2*a*	0.7776	0.4882	–0.1083	0.031
H(47)	2*a*	0.5021	0.2877	–0.1450	0.028
H(48)	2*a*	0.4901	0.2805	–0.2918	0.024
H(2A)	2*a*	0.0967	0.2871	0.4221	0.019
H(4A)	2*a*	0.6611	0.4341	–0.3939	0.019

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*a*	–0.0318(1)	0.0012(2)	0.2474(1)	0.0262(8)	0.0191(8)	0.0263(8)	–0.0035(6)	0.0073(6)	–0.0032(6)
C(2)	2*a*	–0.0571(2)	0.0550(2)	0.1668(1)	0.040(1)	0.0307(9)	0.0214(8)	–0.0108(8)	0.0106(7)	–0.0054(7)
C(3)	2*a*	–0.1483(2)	0.1276(2)	0.1414(1)	0.039(1)	0.038(1)	0.0202(8)	–0.0135(8)	–0.0010(7)	0.0053(7)
C(4)	2*a*	–0.2128(1)	0.1495(2)	0.1967(1)	0.0270(9)	0.034(1)	0.037(1)	–0.0019(8)	–0.0013(7)	0.0105(8)
C(5)	2*a*	–0.1869(1)	0.0960(2)	0.2783(1)	0.0216(8)	0.0277(9)	0.0282(8)	–0.0013(6)	0.0059(6)	0.0036(7)
C(6)	2*a*	–0.0971(1)	0.0202(1)	0.30344(9)	0.0213(7)	0.0181(7)	0.0185(7)	–0.0055(6)	0.0020(6)	–0.0034(6)
C(7)	2*a*	–0.0735(1)	–0.0480(2)	0.38772(9)	0.0182(7)	0.0212(8)	0.0220(7)	–0.0063(6)	0.0017(6)	–0.0003(6)
C(8)	2*a*	0.0663(1)	–0.0519(1)	0.51557(9)	0.0158(7)	0.0186(7)	0.0172(7)	0.0022(5)	0.0075(5)	0.0002(5)
C(9)	2*a*	0.2146(1)	–0.0388(1)	0.64274(9)	0.0165(7)	0.0186(7)	0.0187(7)	0.0010(5)	0.0047(5)	0.0053(5)
C(10)	2*a*	0.2316(1)	0.0610(2)	0.71060(9)	0.0127(7)	0.0234(8)	0.0183(7)	0.0028(6)	0.0031(5)	0.0015(6)
C(11)	2*a*	0.2195(1)	0.0408(2)	0.7929(1)	0.0199(8)	0.0318(9)	0.0188(7)	0.0024(6)	0.0048(6)	0.0054(6)
C(12)	2*a*	0.2361(1)	0.1384(2)	0.8515(1)	0.0282(8)	0.044(1)	0.0176(8)	0.0077(8)	0.0053(6)	0.0012(7)
C(13)	2*a*	0.2636(1)	0.2563(2)	0.8283(1)	0.0251(8)	0.038(1)	0.0210(8)	0.0080(7)	0.0003(6)	–0.0088(7)
C(14)	2*a*	0.2771(1)	0.2767(2)	0.7466(1)	0.0183(7)	0.0252(8)	0.0252(8)	0.0017(6)	0.0009(6)	–0.0027(6)
C(15)	2*a*	0.2617(1)	0.1790(1)	0.68778(9)	0.0123(6)	0.0230(8)	0.0191(7)	0.0036(5)	0.0016(5)	0.0010(6)
C(16)	2*a*	0.2735(1)	0.1927(1)	0.59783(9)	0.0170(7)	0.0144(7)	0.0192(7)	–0.0017(5)	0.0041(5)	0.0004(5)
C(17)	2*a*	0.1729(1)	0.1401(1)	0.53518(9)	0.0160(6)	0.0136(7)	0.0164(7)	0.0004(5)	0.0053(5)	0.0007(5)
C(18)	2*a*	0.1907(1)	0.1450(1)	0.44517(9)	0.0153(6)	0.0146(7)	0.0172(7)	–0.0019(5)	0.0049(5)	0.0017(5)
C(19)	2*a*	0.1358(1)	0.2691(1)	0.31202(9)	0.0185(7)	0.0128(7)	0.0167(7)	–0.0021(5)	0.0047(5)	–0.0004(5)
C(20)	2*a*	0.2222(1)	0.2423(1)	0.27698(9)	0.0190(7)	0.0187(7)	0.0227(8)	0.0006(6)	0.0074(6)	0.0035(6)
C(21)	2*a*	0.2161(1)	0.2726(2)	0.1927(1)	0.0257(8)	0.0219(8)	0.0248(8)	0.0006(6)	0.0130(6)	0.0012(6)
C(22)	2*a*	0.1249(1)	0.3300(1)	0.14357(9)	0.0296(8)	0.0196(7)	0.0147(7)	–0.0042(6)	0.0057(6)	–0.0005(5)
C(23)	2*a*	0.0404(1)	0.3605(2)	0.17816(9)	0.0221(7)	0.0215(8)	0.0208(7)	–0.0009(7)	–0.0006(5)	0.0010(7)
C(24)	2*a*	0.0460(1)	0.3303(1)	0.26238(9)	0.0184(7)	0.0191(7)	0.0202(7)	0.0009(5)	0.0052(6)	–0.0003(5)
C(25)	2*a*	0.9544(1)	0.1767(2)	–0.2618(1)	0.0223(8)	0.0206(8)	0.0279(8)	0.0010(6)	0.0060(6)	0.0033(6)
C(26)	2*a*	0.9617(1)	0.2003(2)	–0.1758(1)	0.0292(9)	0.0242(8)	0.0250(8)	–0.0031(7)	–0.0005(6)	–0.0033(7)
C(27)	2*a*	0.8768(1)	0.1727(2)	–0.1408(1)	0.0377(9)	0.0250(8)	0.0215(8)	0.0061(7)	0.0060(7)	0.0010(6)
C(28)	2*a*	0.7835(1)	0.1217(2)	–0.1919(1)	0.0255(8)	0.0270(8)	0.0309(9)	0.0069(7)	0.0109(7)	0.0050(7)
C(29)	2*a*	0.7759(1)	0.0983(2)	–0.2772(1)	0.0185(7)	0.0226(8)	0.0278(8)	0.0030(6)	0.0027(6)	0.0027(6)
C(30)	2*a*	0.8612(1)	0.1257(1)	–0.31312(9)	0.0208(7)	0.0168(7)	0.0219(7)	0.0061(6)	0.0023(6)	0.0016(6)
C(31)	2*a*	0.8525(1)	0.0981(2)	–0.4058(1)	0.0207(8)	0.0253(8)	0.0238(8)	0.0107(6)	0.0027(6)	–0.0004(6)
C(32)	2*a*	0.6939(1)	0.1059(1)	–0.52057(9)	0.0197(7)	0.0187(7)	0.0163(7)	0.0012(6)	0.0076(6)	0.0003(5)
C(33)	2*a*	0.5283(1)	0.1351(1)	–0.63067(9)	0.0211(7)	0.0175(7)	0.0216(7)	–0.0024(6)	0.0041(6)	–0.0060(6)
C(34)	2*a*	0.5079(1)	0.2341(2)	–0.6992(1)	0.0135(7)	0.0247(8)	0.0205(7)	–0.0017(6)	0.0042(5)	–0.0026(6)
C(35)	2*a*	0.5035(1)	0.2100(2)	–0.7847(1)	0.0187(7)	0.0354(9)	0.0224(8)	0.0015(7)	0.0057(6)	–0.0058(7)
C(36)	2*a*	0.4894(1)	0.3086(2)	–0.8424(1)	0.0236(8)	0.050(1)	0.0197(8)	0.0018(7)	0.0074(7)	0.0009(7)
C(37)	2*a*	0.4805(1)	0.4300(2)	–0.8153(1)	0.0235(8)	0.041(1)	0.0255(9)	0.0008(7)	0.0087(7)	0.0115(7)
C(38)	2*a*	0.4846(1)	0.4549(2)	–0.7300(1)	0.0179(7)	0.0249(8)	0.0270(8)	0.0005(6)	0.0039(6)	0.0050(6)
C(39)	2*a*	0.4974(1)	0.3569(2)	–0.67186(9)	0.0120(6)	0.0228(8)	0.0204(6)	–0.0001(6)	0.0042(5)	0.0018(6)
C(40)	2*a*	0.5002(1)	0.3728(2)	–0.57850(8)	0.0192(6)	0.0151(6)	0.0200(6)	0.0032(6)	0.0047(5)	0.0003(6)
C(41)	2*a*	0.5978(1)	0.3041(1)	–0.52147(8)	0.0172(7)	0.0120(7)	0.0176(7)	0.0004(5)	0.0049(5)	–0.0001(5)
C(42)	2*a*	0.5798(1)	0.2849(1)	–0.43191(9)	0.0151(6)	0.0143(7)	0.0173(7)	0.0024(5)	0.0046(5)	–0.0001(5)
C(43)	2*a*	0.6285(1)	0.3764(1)	–0.28718(8)	0.0183(6)	0.0129(6)	0.0176(6)	0.0028(6)	0.0059(5)	0.0005(6)
C(44)	2*a*	0.7129(1)	0.4394(2)	–0.2324(1)	0.0219(7)	0.0192(8)	0.0224(8)	–0.0030(6)	0.0073(6)	0.0000(6)
C(45)	2*a*	0.7200(1)	0.4451(2)	–0.1456(1)	0.0265(8)	0.0277(9)	0.0214(8)	–0.0061(7)	0.0024(6)	–0.0040(6)
C(46)	2*a*	0.6414(1)	0.3867(2)	–0.11389(9)	0.0353(8)	0.0264(9)	0.0147(6)	–0.0035(7)	0.0058(6)	–0.0004(7)
C(47)	2*a*	0.5559(1)	0.3260(2)	–0.1675(1)	0.0261(8)	0.0248(8)	0.0228(8)	–0.0025(6)	0.0108(6)	0.0011(6)
C(48)	2*a*	0.5490(1)	0.3213(2)	–0.2545(1)	0.0193(7)	0.0203(7)	0.0215(7)	–0.0012(6)	0.0060(6)	–0.0013(6)
N(1)	2*a*	0.15299(9)	0.0117(1)	0.56013(7)	0.0175(6)	0.0151(6)	0.0164(6)	–0.0012(5)	0.0048(5)	0.0031(5)
N(2)	2*a*	0.13608(9)	0.2394(1)	0.39740(7)	0.0167(6)	0.0141(6)	0.0167(6)	0.0025(4)	0.0062(5)	0.0001(4)
N(3)	2*a*	0.6119(1)	0.1821(1)	–0.55830(8)	0.0200(6)	0.0135(6)	0.0175(6)	0.0006(5)	0.0028(5)	–0.0016(5)
N(4)	2*a*	0.62754(9)	0.3731(1)	–0.37461(7)	0.0189(5)	0.0131(5)	0.0173(5)	–0.0025(5)	0.0072(4)	0.0003(5)
O(1)	2*a*	0.01653(8)	0.0140(1)	0.44542(6)	0.0170(5)	0.0177(5)	0.0190(5)	–0.0030(4)	0.0016(4)	0.0014(4)
O(2)	2*a*	0.03630(8)	–0.15360(9)	0.53454(6)	0.0197(5)	0.0188(6)	0.0230(5)	–0.0038(4)	0.0059(4)	0.0034(4)

Table 3. continued.

Atom	Site	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O(3)	2*a*	0.25267(9)	0.0738(1)	0.42229(7)	0.0260(6)	0.0197(5)	0.0244(6)	0.0084(4)	0.0113(4)	0.0039(4)
O(4)	2*a*	0.76187(8)	0.1675(1)	–0.45620(7)	0.0198(5)	0.0173(5)	0.0216(5)	0.0052(4)	0.0004(4)	–0.0004(4)
O(5)	2*a*	0.70632(9)	–0.0011(1)	–0.54184(7)	0.0292(6)	0.0177(6)	0.0265(6)	0.0058(4)	0.0056(5)	–0.0032(4)
O(6)	2*a*	0.52573(8)	0.1975(1)	–0.41699(6)	0.0229(5)	0.0167(5)	0.0224(5)	–0.0049(4)	0.0079(4)	–0.0009(4)
Br(1)	2*a*	0.11789(2)	0.36877(2)	0.027727(9)	0.0535(1)	0.0369(1)	0.01450(7)	0.00020(9)	0.00882(6)	0.00157(7)
Br(2)	2*a*	0.65133(2)	0.38968(2)	0.00510(1)	0.0621(1)	0.0679(2)	0.01645(8)	–0.0231(1)	0.01104(8)	–0.00429(9)

Acknowledgments. The authors wish to thank Bernard Owaga of the School of Chemistry and Physics of the University of KwaZulu-Natal for his assistance with the crystallographic data collection.

References

1. Chakka, S. K.; Andersson, P. G.; Maguire, G. E. M.; Kruger, H. G.; Govender, T.: Synthesis and Screening of Novel C1 Substituted Tetrahydroisoquinoline Derivatives for Asymmetric Transfer Hydrogenation Reactions. Eur. J. Org. Chem. (2010) 972-980.
2. Peters, B. K.; Chakka, S. K.; Naicker, T.; Maguire, G. E. M.; Kruger, H. G.; Andersson, P. G.; Govender, T.: Synthesis of tetrahydroisoquinoline-diamine ligands and their application in asymmetric transfer hydrogenation. Tetrahedron: Asymmetry. **21** (2010) 679-687.
3. Kawthekar, R. B.; Chakka, S. K.; Francis, V.; Andersson, P. G.; Kruger, H. G.; Maguire, G. E. M.; Govender, T.: Synthesis of tetrahydroisoquinoline (*TIQ*)-oxazoline ligands and their application in enantioselective Henry reactions. Tetrahedron: Asymmetry. **21** (2010) 846-852.
4. Chakka, S. K.; Cele, Z. E. D.; Sosibo, S. C.; Francis, V.; Arvidsson, P. I.; Kruger, H. G.; Maguire, G. E. M; Govender, T.: Asymmetric conjugate addition of thioglycolate to a range of chalcones using tetrahydroisoquinoline (*TIQ*) *N*,*N*′-dioxide ligands. Tetrahedron: Asymmetry. **23** (2012) 616-622.
5. Cele, Z. E. D.; Sosibo, S. C.; Andersson, P. G.; Kruger, H. G.; Maguire, G. E. M; Govender, T.: Catalytic asymmetric carbon-carbon forming reactions catalyzed by tetrahydroisoquinoline (*TIQ*) *N*,*N*′-dioxide ligands. Tetrahedron: Asymmetry. **24** (2013) 191-195.
6. Naicker, T.; Govender, T.; Kruger, H. G.; Maguire, G. E. M.: (*S*)-*N*-Benzyl-2-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxamide. Acta Crystallogr. **E67** (2011) o67.
7. APEX2, SAINT and SADABS, Bruker AXS Inc., (2006) Madison, Wisconsin, USA.
8. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K; Puschmann, H.: OLEX2: A complete structure solution, refinement and analysis program. J. Appl. Crystallogr. **42** (2009) 339-341.
9. L.J. Farrugia.: WinGX suite for small-molecule single-crystal crystallography. J. Appl. Crystallogr. **32** (1999) 837-838.
10. Flack, H. D.: On enantiomorph-polarity estimation. Acta Crystallogr. **A39** (1983) 876-881.
11. Sheldrick, G. M.: A short history of SHELX. Acta Crystallogr. **A64** (2008) 112-122.