Z. Kristallogr. NCS **228** (2013) 223-224 / **DOI** 10.1524/ncrs.2013.0111 

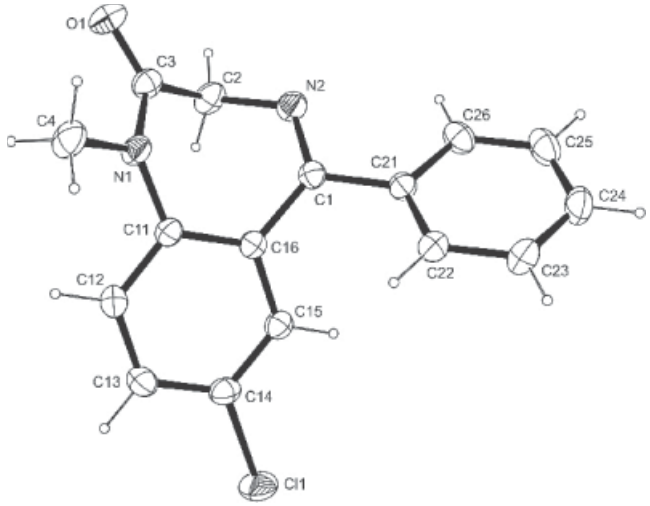


# Redetermination of the structure of 7-chloro-1,3-dihydro-1-methyl-5-phenyl-1,4-benzodiazepin-2(3*H*)-one, $C_{16}H_{13}ClN_2O$

Alaloor S. Dayananda[I], Hemmige S. Yathirajan[I], Thomas Gerber[II], Eric Hosten[II] and Richard Betz[*, II]

[I] University of Mysore, Department of Studies in Chemistry, Manasagangotri, Mysore 570 006, India
[II] Nelson Mandela Metropolitan University, Summerstrand Campus, Department of Chemistry, University Way, Summerstrand, PO Box 77000, Port Elizabeth 6031, South Africa

Received October 31, 2012, accepted February 08, 2013, available online April 26, 2013, CCDC no. 1267/3957




**Abstract**

$C_{16}H_{13}ClN_2O$, monoclinic, $P2_1/c$ (no. 14), $a$ = 7.9510(2) Å, $b$ = 13.2274(3) Å, $c$ = 12.8923(3) Å, $\beta$ = 90.172(1)°, $V$ = 1355.9 Å$^3$, $Z$ = 4, $R_{gt}(F)$ = 0.0314, $wR_{ref}(F^2)$ = 0.0834, $T$ = 200 K.

**Table 1.** Data collection and handling.

| | |
|---|---|
| Crystal: | yellow blocks, size 0.29×0.37×0.47 mm |
| Wavelength: | Mo $K_\alpha$ radiation (0.71073 Å) |
| $\mu$: | 2.78 cm$^{-1}$ |
| Diffractometer, scan mode: | Bruker APEX-II CCD, $\varphi$ and $\omega$ |
| $2\theta_{max}$: | 56.68° |
| $N(hkl)_{measured}$, $N(hkl)_{unique}$: | 23240, 3380 |
| Criterion for $I_{obs}$, $N(hkl)_{gt}$: | $I_{obs} > 2\,\sigma(I_{obs})$, 3164 |
| $N(param)_{refined}$: | 182 |
| Programs: | SHELX [5], ORTEP-3 [6], MERCURY [7], PLATON [8] |

## Source of material

Diazepam was obtained as a gift sample from R. L. Fine Chem., Bengaluru, India. X-ray quality crystals were obtained from DMSO by slow evaporation.

## Experimental details

Carbon-bound hydrogen atoms were placed in calculated positions (C–H 0.95 Å for aromatic carbon atoms and C–H 0.99 Å for the methylene group) and were included in the refinement in the riding model approximation, with $U_{iso}$(H) set to 1.2$U_{eq}$(C). The H atoms of the methyl groups were allowed to rotate with a fixed angle around the C–C bond to best fit the experimental electron density (HFIX 137 in the SHELX program suite [5]), with $U_{iso}$(H) set to 1.5$U_{eq}$(C).

## Discussion

Diazepam is mainly used to treat anxiety, insomnia, and symptoms of acute alcohol withdrawal. It is also used as a premedication for inducing sedation, anxiolysis or amnesia before certain medical procedures. In addition, it possesses anticonvulsant, hypnotic and skeletal muscle relaxant properties. The pharmacological action of diazepam enhances the effect of the neurotransmitter GABA by binding to the benzodiazepine site on the $GABA_A$ receptor (via the constituent chlorine atom) leading to central nervous system depression [1, 2]. The structure of the title compound has been reported earlier [3], however, at room temperature only. The C=N bond is *Z* configured and the length of this bond was measured at 1.2847(13) Å. Amide-type resonance slightly shortens the intracylic N–C(O) bond, the respective value is found at 1.3717(13) Å. The coordination geometry around N1 can be described as trigonal-planar, the least-squares plane defined by the non-hydrogen atoms of the amide group and the atoms immediately bonded to it –$C_{ar}$–$CH_3$–N–C(O)–$CH_2$– is essentially planar (r.m.s. of all fitted atoms = 0.0624 Å) with the aromatic carbon atom deviating most from this common plane by –0.088(1) Å. According to a puckering analysis [4], the seven-membered heterocycle adopts a boat-like conformation in which the intracyclic methylene group acts as the flagpole position. The least-squares planes defined by the respective carbon atoms of the individual aromatic moieties intersect at an angle of 54.03(5)°. In the crystal, C–H···O contacts whose range falls by up to 0.17 Å below the sum of van-der-Waals radii of the atoms participating are apparent. These are exclusively supported by hydrogen atoms on the non-halogenated phenyl moiety. The more pronounced shortening with regards to the van-der-Waals cut-off criterion is apparent for the hydrogen atom in *para*-position to the heterocyclic substituent on this phenyl group. In addition, a C–H···$\pi$ contact stemming from a hydrogen atom on the chlorinated and annealated aromatic moiety and applying the $\pi$ system of the non-substituted phenyl moiety in a neighbouring molecule as the acceptor can be detected.

* Correspondence author (e-mail: richard.betz@webmail.co.za)

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

| Atom | Site | *x* | *y* | *z* | $U_{iso}$ |
|---|---|---|---|---|---|
| H(2A) | 4*e* | –0.2655 | 0.4694 | 0.1157 | 0.033 |
| H(2B) | 4*e* | –0.4179 | 0.5424 | 0.0836 | 0.033 |
| H(4A) | 4*e* | –0.3069 | 0.6266 | 0.4222 | 0.048 |
| H(4B) | 4*e* | –0.1390 | 0.5660 | 0.4511 | 0.048 |
| H(4C) | 4*e* | –0.3143 | 0.5072 | 0.4418 | 0.048 |
| H(12) | 4*e* | –0.0607 | 0.4002 | 0.3975 | 0.033 |
| H(13) | 4*e* | 0.1897 | 0.3175 | 0.3573 | 0.034 |
| H(15) | 4*e* | 0.2376 | 0.4910 | 0.1008 | 0.026 |
| H(22) | 4*e* | 0.2739 | 0.6652 | 0.1699 | 0.032 |
| H(23) | 4*e* | 0.4599 | 0.7737 | 0.0842 | 0.043 |
| H(24) | 4*e* | 0.3856 | 0.8461 | –0.0743 | 0.043 |
| H(25) | 4*e* | 0.1219 | 0.8122 | –0.1467 | 0.041 |
| H(26) | 4*e* | –0.0656 | 0.7051 | –0.0621 | 0.032 |

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

| Atom | Site | *x* | *y* | *z* | $U_{11}$ | $U_{22}$ | $U_{33}$ | $U_{12}$ | $U_{13}$ | $U_{23}$ |
|---|---|---|---|---|---|---|---|---|---|---|
| Cl(1) | 4*e* | 0.41670(4) | 0.33320(2) | 0.19107(3) | 0.0297(2) | 0.0310(2) | 0.0515(2) | 0.0119(1) | 0.0052(1) | –0.0000(1) |
| O(1) | 4*e* | –0.48617(9) | 0.58437(7) | 0.26903(7) | 0.0200(4) | 0.0375(4) | 0.0378(4) | 0.0025(3) | 0.0028(3) | –0.0058(3) |
| N(1) | 4*e* | –0.2148(1) | 0.54469(7) | 0.30329(7) | 0.0204(4) | 0.0297(4) | 0.0207(4) | 0.0013(3) | 0.0031(3) | –0.0015(3) |
| N(2) | 4*e* | –0.1923(1) | 0.61256(7) | 0.08544(7) | 0.0220(4) | 0.0328(5) | 0.0219(4) | 0.0001(3) | –0.0012(3) | 0.0010(3) |
| C(1) | 4*e* | –0.0370(1) | 0.60258(7) | 0.11144(7) | 0.0212(4) | 0.0222(4) | 0.0175(4) | 0.0004(3) | 0.0007(3) | –0.0009(3) |
| C(2) | 4*e* | –0.3123(1) | 0.53824(9) | 0.12427(8) | 0.0197(5) | 0.0368(6) | 0.0256(5) | –0.0043(4) | –0.0024(4) | –0.0034(4) |
| C(3) | 4*e* | –0.3492(1) | 0.55732(8) | 0.23759(8) | 0.0201(4) | 0.0233(5) | 0.0277(5) | –0.0026(4) | 0.0006(4) | –0.0023(4) |
| C(4) | 4*e* | –0.2464(2) | 0.5626(1) | 0.41376(8) | 0.0305(5) | 0.0425(6) | 0.0227(5) | 0.0016(5) | 0.0057(4) | –0.0032(4) |
| C(11) | 4*e* | –0.0639(1) | 0.49539(8) | 0.27310(7) | 0.0184(4) | 0.0224(4) | 0.0219(4) | –0.0013(3) | 0.0005(3) | –0.0003(3) |
| C(12) | 4*e* | –0.0006(1) | 0.41877(8) | 0.33687(8) | 0.0256(5) | 0.0295(5) | 0.0268(5) | –0.0016(4) | 0.0029(4) | 0.0078(4) |
| C(13) | 4*e* | 0.1479(1) | 0.36946(8) | 0.31341(9) | 0.0272(5) | 0.0244(5) | 0.0338(5) | 0.0011(4) | –0.0016(4) | 0.0077(4) |
| C(14) | 4*e* | 0.2345(1) | 0.39719(8) | 0.22480(8) | 0.0207(4) | 0.0208(4) | 0.0320(5) | 0.0021(4) | 0.0004(4) | –0.0020(4) |
| C(15) | 4*e* | 0.1756(1) | 0.47284(8) | 0.16087(8) | 0.0213(4) | 0.0220(5) | 0.0226(4) | –0.0004(4) | 0.0022(3) | –0.0020(4) |
| C(16) | 4*e* | 0.0254(1) | 0.52329(7) | 0.18349(7) | 0.0193(4) | 0.0196(4) | 0.0198(4) | –0.0011(3) | –0.0002(3) | –0.0010(3) |
| C(21) | 4*e* | 0.0857(1) | 0.67279(7) | 0.06172(7) | 0.0227(5) | 0.0206(4) | 0.0199(4) | 0.0022(3) | 0.0032(3) | 0.0000(3) |
| C(22) | 4*e* | 0.2426(1) | 0.69455(9) | 0.10536(9) | 0.0222(5) | 0.0299(5) | 0.0285(5) | 0.0003(4) | 0.0013(4) | 0.0043(4) |
| C(23) | 4*e* | 0.3532(2) | 0.7592(1) | 0.0543(1) | 0.0237(5) | 0.0375(6) | 0.0455(7) | –0.0030(5) | 0.0071(5) | 0.0055(5) |
| C(24) | 4*e* | 0.3092(2) | 0.80258(9) | –0.0395(1) | 0.0365(6) | 0.0314(6) | 0.0404(6) | –0.0001(5) | 0.0184(5) | 0.0066(5) |
| C(25) | 4*e* | 0.1529(2) | 0.78220(9) | –0.08250(9) | 0.0482(7) | 0.0292(6) | 0.0240(5) | 0.0038(5) | 0.0082(5) | 0.0055(4) |
| C(26) | 4*e* | 0.0416(2) | 0.71818(8) | –0.03228(8) | 0.0349(5) | 0.0244(5) | 0.0216(5) | 0.0018(4) | –0.0011(4) | 0.0005(4) |

*Acknowledgments.* Alaloor S. Dayananda thanks the University of Mysore for research facilities.

## References

1. Mandrioli, R.; Mercolini, L.; Raggi, M. A.: Benzodiazepine metabolism: an analytical perspective. Curr. Drug Metab. **9** (2008) 827-844.
2. Riss, J.; Cloyd, J.; Gates, J.; Collins, S.: Benzodiazepines in epilepsy: pharmacology and pharmacokinetics. Acta Neurol. Scand. **118** (2008) 69-86.
3. Camerman, A.; Camerman, N.: Stereochemical Basis of Anticonvulsant Drug Action. II. Molecular Structure of Diazepam. J. Am. Chem. Soc. **94** (1972) 268-272.
4. Cremer, D.; Pople, J. A.: General definition of ring puckering coordinates.J. Am. Chem. Soc. **97** (1975) 1354-1358.
5. Sheldrick, G. M.: A short history of SHELX. Acta Crystallogr. **A64** (2008) 112-122.
6. Farrugia, L. J.: WinGX and ORTEP for Windows: an update. J. Appl. Crystallogr. **45** (2012) 849-854.
7. Macrae, C. F.; Bruno, I. J.; Chisholm, J. A.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Rodriguez-Monge, L.; Taylor, R.; van de Streek, J.; Wood, P.A.: MERCURY CSD 2.0— new features for the visualization and investigation of crystal structures. J. Appl. Crystallogr. **41** (2008) 466-470.
8. Spek, A. L.: Single-crystal structure validation with the program PLATON. J. Appl. Crystallogr. **36** (2003) 7-13.