# Redetermination of the crystal structure of (1*R*,2*S*)-2-((dimethylphenyl)-carbamoyl)-1-propylpiperidin-1-ium chloride monohydrate, $C_{17}H_{29}ClN_2O_2$

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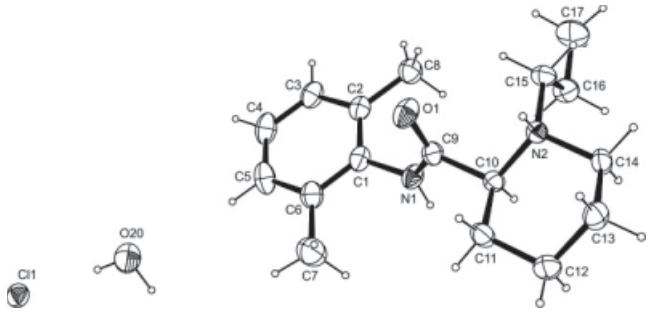


**Abstract**

$C_{17}H_{29}ClN_2O_2$, monoclinic, $P2_1$ (no. 4), $a$ = 9.5140(5) Å, $b$ = 7.2916(4) Å, $c$ = 13.0720(8) Å, $\beta$ = 97.658(2)°, $V$ = 898.8 Å$^3$, $Z$ = 2, $R_{gt}(F)$ = 0.0343, $wR_{ref}(F^2)$ = 0.0957, $T$ = 200 K.

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

| | |
|---|---|
| Crystal: | colourless blocks, size 0.15×0.28×0.46 mm |
| Wavelength: | Mo $K_\alpha$ radiation (0.71073 Å) |
| $\mu$: | 2.22 cm$^{-1}$ |
| Diffractometer, scan mode: | Bruker APEX-II CCD, $\varphi$ and $\omega$ |
| $2\theta_{max}$: | 56.64° |
| $N(hkl)_{measured}$, $N(hkl)_{unique}$: | 8394, 4295 |
| Criterion for $I_{obs}$, $N(hkl)_{gt}$: | $I_{obs} > 2\ \sigma(I_{obs})$, 3945 |
| $N(param)_{refined}$: | 218 |
| Programs: | SHELX [8], ORTEP-3 [9], MERCURY [10], PLATON [11] |

## Source of material

The title compound was obtained as a gift sample from Jubilant Life Sciences Ltd., Noida, India and was recrystallized from acetonitrle-toluene ($v$:$v$ = 1:1) by slow evaporation.

## Experimental details

Carbon-bound H atoms were placed in calculated positions (C–H 0.95 Å for aromatic carbon atoms and C–H 0.99 Å for methylene groups) 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 [8]), with $U_{iso}$(H) set to 1.5$U_{eq}$(C). Both nitrogen-bound H atoms were located on a difference Fourier map and refined freely.

## Discussion

Ropivacaine is a local anaesthetic drug belonging to the amino amide group. A review of its pharmacology and therapeutic use in regional anaesthesia has been published [1]. The crystal structures of two polymorphs of the anhydrous title compound, ropivacaine hydrochloride, are apparent in the literature [2]. Additionally, the crystal structures of the title compound itself as well as another local anaesthetic – bupivacaine – have been determined earlier [3], however, these determinations were only done at room temperature. In addition, problems with the localization of hydrogen atoms as well as twinning were reported in this study thus precluding a detailled assessment on inter- as well as possible intramolecular stabilzing contacts and forces. Protonation occurred on the intracyclic nitrogen atom. According to a puckering analysis [4, 5], the azacyclohexane ring adopts a $^4C_1$ conformation with the nitrogen atom being one of the flap atoms ($^{N2}C_{C12}$). Possibly due to the steric pretense of the two methyl groups in *ortho* position to the secondary amino group the aromatic substituent is approaching a nearly perpendicular orientation to the amido functionality, with the least-squares planes defined by the respective non-hydrogen atoms intersecting at an angle of 77.2(2)°. Both N–C bond lengths stemming from the amido group and measured at 1.336(2) Å and 1.443(2) Å, respectively, are longer than the corresponding bond lengths reported for the crystal structure determination at room temperature [3]. In the crystal, classical hydrogen bonds of the O–H···O and N–H···O type are observed next to O–H···Cl and N–H···Cl contacts. While the N–H···O contacts are supported by the hydrogen atom of the amido functionality as donor and the oxygen atom of the water molecule as acceptor, the O–H···O type hydrogen bonds apply the double bonded oxygen atom as acceptor. In total, the entities of the title compound are connected to chains along the crystallographic $b$ axis. In terms of graph-set analysis [6, 7], the graph set descriptor for the chain is $C^2_2(6)$. The chloride anion is hydrogen bonded to the water molecule and the –$NH_2$ group within the six membered ring to give a third level grapgh set descriptor $R^2_3(9)$.

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

| Atom | Site | $x$ | $y$ | $z$ | $U_{iso}$ |
|---|---|---|---|---|---|
| H(1A) | 2*a* | 0.253(2) | 0.671(3) | 0.655(2) | 0.021(4) |
| H(2A) | 2*a* | 0.183(2) | 0.255(3) | 0.882(1) | 0.022(4) |
| H(20A) | 2*a* | 0.699(3) | 0.525(4) | 0.306(2) | 0.055(7) |
| H(20B) | 2*a* | 0.714(3) | 0.427(5) | 0.223(2) | 0.074(9) |
| H(3) | 2*a* | –0.0126 | 0.4632 | 0.3236 | 0.041 |
| H(4) | 2*a* | 0.1894 | 0.4780 | 0.2409 | 0.048 |
| H(5) | 2*a* | 0.4113 | 0.5296 | 0.3350 | 0.050 |
| H(7A) | 2*a* | 0.5595 | 0.5826 | 0.4922 | 0.074 |
| H(7B) | 2*a* | 0.5105 | 0.4622 | 0.5835 | 0.074 |
| H(7C) | 2*a* | 0.4862 | 0.6794 | 0.5814 | 0.074 |
| H(8A) | 2*a* | –0.1274 | 0.4957 | 0.4696 | 0.053 |

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**Table 2.** continued.

| Atom | Site | *x* | *y* | *z* | $U_{iso}$ |
|---|---|---|---|---|---|
| H(8B) | 2*a* | –0.0457 | 0.6018 | 0.5671 | 0.053 |
| H(8C) | 2*a* | –0.0423 | 0.3825 | 0.5629 | 0.053 |
| H(10) | 2*a* | 0.2202 | 0.6183 | 0.8173 | 0.027 |
| H(11A) | 2*a* | 0.4297 | 0.3318 | 0.8554 | 0.035 |
| H(11B) | 2*a* | 0.4632 | 0.5368 | 0.8218 | 0.035 |
| H(12A) | 2*a* | 0.5242 | 0.4929 | 1.0043 | 0.038 |
| H(12B) | 2*a* | 0.4093 | 0.6532 | 0.9798 | 0.038 |
| H(13A) | 2*a* | 0.3476 | 0.2845 | 1.0358 | 0.037 |
| H(13B) | 2*a* | 0.3348 | 0.4619 | 1.1063 | 0.037 |

**Table 2.** continued.

| Atom | Site | *x* | *y* | *z* | $U_{iso}$ |
|---|---|---|---|---|---|
| H(14A) | 2*a* | 0.1072 | 0.3738 | 1.0249 | 0.032 |
| H(14B) | 2*a* | 0.1458 | 0.5743 | 0.9866 | 0.032 |
| H(15A) | 2*a* | –0.0073 | 0.3047 | 0.7617 | 0.033 |
| H(15B) | 2*a* | –0.0518 | 0.2912 | 0.8750 | 0.033 |
| H(16A) | 2*a* | –0.0302 | 0.6249 | 0.7640 | 0.039 |
| H(16B) | 2*a* | –0.0668 | 0.6171 | 0.8803 | 0.039 |
| H(17A) | 2*a* | –0.2792 | 0.6346 | 0.7600 | 0.069 |
| H(17B) | 2*a* | –0.2757 | 0.4482 | 0.8249 | 0.069 |
| H(17C) | 2*a* | –0.2380 | 0.4456 | 0.7093 | 0.069 |

**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(1) | 2*a* | 0.2137(2) | 0.2629(2) | 0.67797(9) | 0.0577(7) | 0.0235(6) | 0.0272(6) | –0.0009(5) | 0.0073(5) | 0.0003(5) |
| N(1) | 2*a* | 0.2333(2) | 0.5624(2) | 0.6341(1) | 0.0397(7) | 0.0244(7) | 0.0215(6) | –0.0009(6) | 0.0048(5) | 0.0002(5) |
| N(2) | 2*a* | 0.1541(1) | 0.3752(2) | 0.87508(9) | 0.0211(5) | 0.0203(6) | 0.0228(6) | 0.0008(5) | 0.0038(4) | 0.0004(5) |
| O(20) | 2*a* | 0.6713(2) | 0.4097(2) | 0.2754(1) | 0.0530(8) | 0.0309(7) | 0.0416(7) | –0.0021(5) | 0.0167(6) | 0.0024(5) |
| C(1) | 2*a* | 0.2215(2) | 0.5335(2) | 0.5241(1) | 0.0396(8) | 0.0221(7) | 0.0222(7) | 0.0027(6) | 0.0063(6) | 0.0017(6) |
| C(2) | 2*a* | 0.0879(2) | 0.5026(2) | 0.4695(1) | 0.0383(8) | 0.0225(7) | 0.0259(7) | 0.0030(6) | 0.0057(6) | 0.0018(5) |
| C(3) | 2*a* | 0.0775(2) | 0.4830(3) | 0.3629(1) | 0.0454(9) | 0.0316(9) | 0.0244(7) | 0.0047(7) | 0.0017(6) | 0.0006(6) |
| C(4) | 2*a* | 0.1977(2) | 0.4924(3) | 0.3137(1) | 0.057(1) | 0.043(1) | 0.0216(7) | 0.0118(8) | 0.0077(7) | 0.0021(7) |
| C(5) | 2*a* | 0.3299(2) | 0.5225(3) | 0.3697(1) | 0.049(1) | 0.049(1) | 0.0308(8) | 0.0102(8) | 0.0172(7) | 0.0051(8) |
| C(6) | 2*a* | 0.3444(2) | 0.5424(3) | 0.4765(1) | 0.0382(9) | 0.0349(9) | 0.0289(8) | 0.0037(7) | 0.0075(6) | 0.0026(7) |
| C(7) | 2*a* | 0.4876(2) | 0.5690(4) | 0.5389(2) | 0.038(1) | 0.064(2) | 0.046(1) | –0.0037(9) | 0.0059(8) | 0.001(1) |
| C(8) | 2*a* | –0.0433(2) | 0.4950(3) | 0.5218(1) | 0.0367(8) | 0.038(1) | 0.0315(8) | –0.0002(7) | 0.0045(6) | 0.0007(7) |
| C(9) | 2*a* | 0.2283(2) | 0.4250(2) | 0.7011(1) | 0.0265(6) | 0.0261(9) | 0.0233(6) | 0.0010(5) | 0.0047(5) | 0.0019(6) |
| C(10) | 2*a* | 0.2466(1) | 0.4859(2) | 0.8139(1) | 0.0227(6) | 0.0230(8) | 0.0220(6) | –0.0020(5) | 0.0039(5) | 0.0010(5) |
| C(11) | 2*a* | 0.4020(1) | 0.4619(3) | 0.8611(1) | 0.0207(6) | 0.0391(8) | 0.0277(7) | –0.0015(7) | 0.0049(5) | 0.0021(8) |
| C(12) | 2*a* | 0.4252(2) | 0.5196(3) | 0.9744(1) | 0.0251(7) | 0.0392(9) | 0.0306(8) | –0.0025(6) | –0.0008(6) | –0.0010(7) |
| C(13) | 2*a* | 0.3239(2) | 0.4168(2) | 1.0342(1) | 0.0305(7) | 0.040(1) | 0.0215(7) | 0.0017(6) | 0.0005(5) | 0.0021(6) |
| C(14) | 2*a* | 0.1714(2) | 0.4428(3) | 0.9853(1) | 0.0266(6) | 0.0335(8) | 0.0203(6) | –0.0005(7) | 0.0067(5) | 0.0002(7) |
| C(15) | 2*a* | –0.0005(2) | 0.3674(2) | 0.8294(1) | 0.0200(6) | 0.0291(8) | 0.0332(8) | –0.0032(6) | 0.0019(5) | –0.0007(6) |
| C(16) | 2*a* | –0.0748(2) | 0.5499(2) | 0.8140(1) | 0.0253(7) | 0.0324(9) | 0.0387(9) | 0.0038(6) | 0.0018(6) | –0.0018(7) |
| C(17) | 2*a* | –0.2309(2) | 0.5166(3) | 0.7734(2) | 0.0230(7) | 0.052(1) | 0.060(1) | 0.0036(7) | –0.0029(7) | 0.0018(9) |
| Cl(1) | 2*a* | 0.82264(4) | 0.45767(5) | 0.07925(3) | 0.0341(2) | 0.0246(2) | 0.0354(2) | –0.0005(2) | 0.0095(1) | –0.0015(2) |

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