

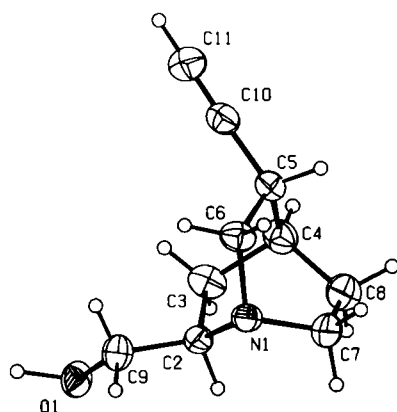
Crystal structure of (1*S*,2*R*,4*S*,5*S*)-5-ethynyl-2-hydroxymethyl-1-azabicyclo[2.2.2]octane, (HC₂)(HOCH₂)(C₇H₁₁N)

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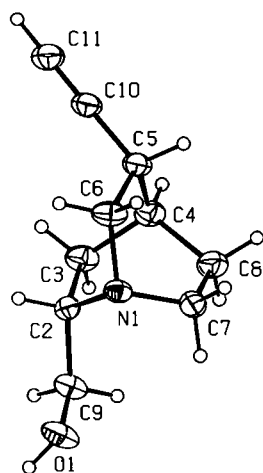
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Received September 21, 2000, CCDC-No. 1267/533



10,11-didehydro-quinicoridine (1)



10,11-didehydro-quinicorine (2)

Abstract

C₁₀H₁₅NO, orthorhombic, *P*2₁2₁2₁ (No. 19), *a* = 7.702(1) Å, *b* = 9.844(1) Å, *c* = 12.706(2) Å, *V* = 963.3 Å³, *Z* = 4, *R*_g(*F*) = 0.029, *wR*_{ref}(*F*²) = 0.045, *T* = 300 K.

Source of material

Quinicoridine[®] [1] (2.0 g, 12 mmol) was dissolved in dry CCl₄ (15 ml). Bromine (1.1 ml, 21.5 mmol) was added at 273 K. The reaction mixture was stirred for 1 h. After removal of the solvent in vacuo the resulting yellow solid was dissolved in CHCl₃ (25 ml). Et₃N (3.1 ml, 24 mmol) was added and the mixture was then stirred for 4 h at RT. After work-up (CHCl₃ and saturated

aqueous solution NaHCO₃) the vinylic bromide (0.2 g, 0.81 mmol) was dissolved in THF (10 ml), followed by addition of powdered KOH (116 mg, 2.0 mmol) and aliquat 336[®] (0.73 ml, 0.16 mmol). The reaction mixture was heated at reflux for 7 h. Work-up (CHCl₃ and saturated aqueous solution NaHCO₃) and column chromatography (ethyl acetate / methanol 6:1) furnished the title compound which crystallized after 5 h at 273 K. The compound melts at 317 K and sublimes readily.

Discussion

The title compound **1** is derived from quinicidine [2] via quinicoridine[®] (QCD) [1, 3, 4] and is to be compared to the (1*S*,2*S*,4*S*,5*S*)-diastereomer **2** which is derived from quinine [5] via quinicorine[®] (QCI) [1, 3, 4]. The transformation of QCD and QCI to compounds **1** and **2**, respectively, can formally be described as the replacement of the vinyl group by the ethynyl group (see scheme 1 in [6]). Compound **1** is called 10,11-didehydro-quinicoridine and compound **2** 10,11-didehydro-quinicorine [6]. In view of the high synthetic flexibility of alkynes we expect that **1** and **2** will become valuable homochiral building blocks, e.g. in asymmetric synthesis and in medicinal chemistry, similar to QCD and QCI [3, 4, 7]. The terminal alkynes **1** and **2** have the advantage of being solids at room temperature, while QCD and QCI are liquids. The crystal structure of **2** has already been reported in [8].

The X-ray analysis of **1** (this work) shows that its crystal packing has the higher point group symmetry (222 instead of 2) but the lower density by about 2 %. In the solid state the molecules of compound **1** are connected to helical chains by hydrogen bonds in a similar manner as found in compound **2** (see the figure in [8]) and in quinicidine [2]. The chain direction in **1** is [100] and corresponds to the [010] direction in **2**. Substituted quinuclidines are often twisted [9]. The dihedral angles C2–N1–C4–C3, C6–N1–C4–C5 and C7–N1–C4–C8 are 10.9°, 9.7° and 9.1°, respectively, with an average of 9.9° for molecule **1** and 3.7°, 6.7°

Table 1. Data collection and handling.

| | |
|---|---|
| Crystal: | colourless prism, size 0.26 × 0.28 × 0.78 mm |
| Wavelength: | Mo K _α radiation (0.71073 Å) |
| μ: | 0.73 cm ⁻¹ |
| Diffractometer, scan mode: | Stoe IPDS, 115 exposures, Δφ = 1.5° |
| 2θ _{max} : | 48.24° |
| <i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} : | 5313, 1441 |
| Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} : | <i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 988 |
| <i>N</i> (<i>param</i>) _{refined} : | 113 |
| Programs: | SHELXS-86 [10], SHELXL [11], PLATON [12] |

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and 5.8°, respectively, with an average of 5.4° for molecule **2**. Thus azabicyclo **1** is twisted almost twice as much as **2** and both are twisted clockwise. Similar large differences between the two bicyclic cages are found in the bond angles C3–C2–C9 and C2–N1–C7 being 114° and 107° in **1** and 109° and 112° in **2**. These differences are thought to arise from the differing interactions of the hydroxymethyl group in **1** and **2**. A second hydrogen bond might be possible with the ethynyl-H as donor-H atom and an O atom in the neighbouring chain as acceptor, but this hydrogen bond is very weak, because the distance H—O is larger than 2.5 Å and the angle C–H—O is only 138°.

Table 2. Atomic coordinates and displacement parameters (in Å²).

| Atom | Site | x | y | z | U _{iso} |
|-------|------|------------|-----------|-----------|------------------|
| H(1) | 4a | 0.553(3) | 0.774(2) | 0.392(2) | 0.125(8) |
| H(2) | 4a | 0.2159(2) | 0.5405(2) | 0.4584(1) | 0.056 |
| H(3) | 4a | 0.4370(3) | 0.4040(2) | 0.4711(1) | 0.074 |
| H(4) | 4a | 0.5323(3) | 0.4945(2) | 0.5552(1) | 0.074 |
| H(5) | 4a | 0.4277(3) | 0.2799(2) | 0.6269(1) | 0.075 |
| H(6) | 4a | 0.2900(3) | 0.3886(2) | 0.7783(1) | 0.064 |
| H(7) | 4a | 0.1961(3) | 0.5981(2) | 0.7671(1) | 0.066 |
| H(8) | 4a | 0.3603(3) | 0.6479(2) | 0.7050(1) | 0.066 |
| H(9) | 4a | −0.0221(3) | 0.4610(3) | 0.5523(2) | 0.100 |
| H(10) | 4a | −0.0069(3) | 0.4522(3) | 0.6753(2) | 0.100 |
| H(11) | 4a | 0.1283(3) | 0.2584(2) | 0.6492(2) | 0.106 |
| H(12) | 4a | 0.1583(3) | 0.2902(2) | 0.5292(2) | 0.106 |
| H(13) | 4a | 0.2762(3) | 0.7701(2) | 0.4798(1) | 0.070 |
| H(14) | 4a | 0.4411(3) | 0.7342(2) | 0.5474(1) | 0.070 |
| H(15) | 4a | 0.7824(3) | 0.4711(2) | 0.8386(2) | 0.095 |

Table 3. Atomic coordinates and displacement parameters (in Å²).

| Atom | Site | x | y | z | U ₁₁ | U ₂₂ | U ₃₃ | U ₁₂ | U ₁₃ | U ₂₃ |
|-------|------|-----------|-----------|------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| O(1) | 4a | 0.4658(2) | 0.6867(1) | 0.39667(9) | 0.055(1) | 0.084(1) | 0.0487(7) | −0.0152(8) | 0.0133(7) | −0.0028(7) |
| N(1) | 4a | 0.1710(2) | 0.5787(2) | 0.6106(1) | 0.037(1) | 0.075(1) | 0.0441(8) | 0.0014(8) | 0.0034(8) | 0.0116(8) |
| C(2) | 4a | 0.2879(2) | 0.5680(2) | 0.5184(1) | 0.045(1) | 0.056(1) | 0.0383(9) | −0.004(1) | 0.0000(8) | 0.0028(9) |
| C(3) | 4a | 0.4214(3) | 0.4554(2) | 0.5356(1) | 0.074(2) | 0.061(1) | 0.049(1) | 0.015(1) | 0.005(1) | −0.004(1) |
| C(4) | 4a | 0.3565(3) | 0.3622(2) | 0.6228(1) | 0.081(2) | 0.047(1) | 0.061(1) | 0.000(1) | −0.003(1) | 0.001(1) |
| C(5) | 4a | 0.3604(3) | 0.4392(2) | 0.7274(1) | 0.059(1) | 0.056(1) | 0.045(1) | −0.005(1) | −0.001(1) | 0.008(1) |
| C(6) | 4a | 0.2722(3) | 0.5776(2) | 0.7084(1) | 0.057(2) | 0.066(2) | 0.0421(9) | 0.011(1) | 0.0036(9) | −0.001(1) |
| C(7) | 4a | 0.0592(3) | 0.4558(3) | 0.6104(2) | 0.055(2) | 0.120(2) | 0.074(1) | −0.028(2) | −0.006(1) | 0.033(2) |
| C(8) | 4a | 0.1687(3) | 0.3266(2) | 0.5999(2) | 0.107(2) | 0.077(2) | 0.081(1) | −0.032(2) | −0.025(2) | 0.012(1) |
| C(9) | 4a | 0.3668(3) | 0.7031(2) | 0.4907(1) | 0.047(1) | 0.066(1) | 0.063(1) | −0.001(1) | 0.014(1) | −0.001(1) |
| C(10) | 4a | 0.5353(3) | 0.4539(2) | 0.7710(1) | 0.066(2) | 0.054(1) | 0.055(1) | 0.003(1) | −0.003(1) | 0.009(1) |
| C(11) | 4a | 0.6727(3) | 0.4635(2) | 0.8086(2) | 0.066(2) | 0.095(2) | 0.078(1) | −0.002(2) | −0.011(1) | 0.011(1) |

Acknowledgments. This work was supported by Prof. Dr. M. Binnewies, Institut für Anorganische Chemie der Universität Hannover. A DEC-ALPHA workstation was supplied by Land Niedersachsen. The help of Dr. I. Havlik and Dr. M. Dors of Institut für Technische Chemie der Universität concerning the computer operating system is gratefully acknowledged. Computing facilities of RRZN (Hannover) were also used.

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