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2'-Deoxy-3',5'-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-2'-C-(2-trimethylsilyl-ethynyl)-D-adenosine

ROLF BUFF,^a HELEN STOECKLI-EVANS^b AND JÜRGE HUNZIKER^a

^aDepartment für Chemie und Biochemie, Universität Bern, Freiestrasse 3, CH-3012 Bern, Switzerland, and ^bInstitut de Chimie, Université de Neuchâtel, Avenue de Bellevaux 51, CH-2000 Neuchâtel, Switzerland. E-mail: hunziker@ioc.unibe.ch

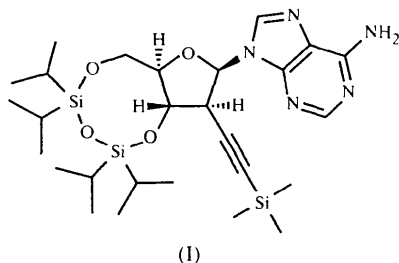
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Abstract

The structure of the title compound, C₂₇H₄₇N₅O₄Si₃, has been determined at 223 K. There are two independent molecules per asymmetric unit. The main structural characteristics are as follows: (i) the compound has a 2'S configuration and (ii) the furanose part of the molecule adopts a 3'-endo conformation [pseudorotation phase angles 27.5 (2) and 26.8 (3)°].

Comment

During studies aimed at the development of oligonucleotide analogues that display increased stability when paired with a complementary oligodeoxynucleotide and decreased stability in a duplex with an oligoribonucleotide counterpart, we synthesized 2'-deoxy-3',5'-O-(1,1,3,3-tetraisopropyl-disiloxane-1,3-diyl)-2'-C-(2-trimethylsilyl-ethynyl)-D-adenosine, (I). The preparation of (I) followed the same synthetic strategy as outlined previously for the corresponding uracil, thymine and cytidine nucleosides (Iino *et al.*, 1994). However, the assignment of the ethynyl substituent configuration in these compounds was based solely on comparison of the NMR scalar coupling constants (H1'–H2'). This structure determination confirms the desired 2'S configuration and demonstrates the influence of the ethynyl substituent on the conformation.



In the crystalline state, there are two independent molecules [labelled (1) and (2)] per asymmetric unit. The

methyl groups in both molecules undergo considerable thermal motion despite measurement at 223 K. In molecule (2), one of the isopropyl groups is disordered; there are alternate positions for C14' with occupancies of 0.581 (7) and 0.419 (7). The remainder of the bond distances and angles are normal within experimental error. The absolute configuration was predetermined from the starting material. Hence, the configuration of the (2-trimethylsilyl)ethynyl substituent could be determined as 2'S.

Unlike in other 2'-deoxynucleosides (Saenger, 1984), the sugar fragments of the two independent molecules show essentially a 3'-endo twist conformation with pseudorotation phase angles of 27.5 (2) [for molecule (1)] and 26.8 (2)° [for molecule (2)] (Rao *et al.*, 1981). By adopting a 3'-endo conformation, the sterically demanding substituents at C2', O3' and O5' all occupy a pseudo-equatorial orientation, thereby minimizing unfavourable steric interactions. In order to minimize steric clash with the (2-trimethylsilyl)ethynyl substituent and H3', the adenine base is oriented in an *anti* conformation in both independent molecules; the corresponding O4'—C1'—N9—C4 torsion angle is –157.55 (19)° in molecule (1) and –152.6 (2)° in (2). Interestingly, atom

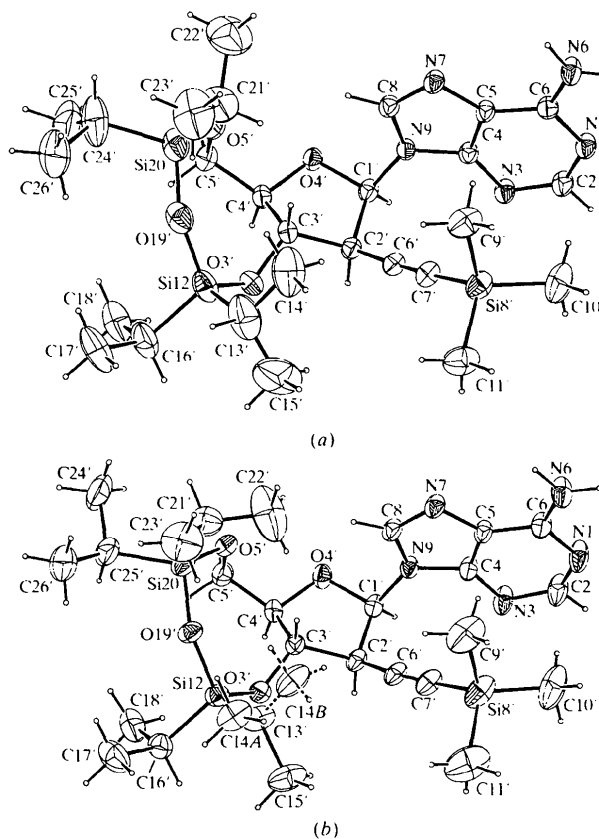


Fig. 1. Perspective views of (a) molecule (1) and (b) molecule (2), showing the numbering scheme used (displacement ellipsoids are at the 30% probability level).

N9 of the otherwise planar adenine base is considerably pyramidalized, presumably due to π - π interactions with the ethynyl substituent.

Experimental

The title compound was prepared in five steps from adenosine (Buff & Hunziker, 1998), in a sequence analogous to that used for the preparation of 2'-deoxy-3',5'-O-(1,1,3,3-tetraiso-propyldisiloxane-1,3-diyl)-2'-(2-trimethylsilylethynyl)-D-uridine from uridine (Iino *et al.*, 1994) after protection of the exocyclic amino group. Suitable crystals were grown from hot acetonitrile as colourless rods (m.p. 457 K).

Crystal data

$C_{27}H_{47}N_5O_4Si_3$
 $M_r = 589.97$
 Orthorhombic
 $P2_12_12_1$
 $a = 13.3229$ (8) Å
 $b = 15.9278$ (13) Å
 $c = 32.613$ (2) Å
 $V = 6920.6$ (8) Å³
 $Z = 8$
 $D_x = 1.132$ Mg m⁻³
 D_m not measured

Mo $K\alpha$ radiation
 $\lambda = 0.71073$ Å
 Cell parameters from 5000 reflections
 $\theta = 2.09$ – 25.96°
 $\mu = 0.173$ mm⁻¹
 $T = 223$ (2) K
 Rod
 $0.55 \times 0.40 \times 0.33$ mm
 Colourless

Data collection

Stoe image-plate diffractometer
 φ rotation scans
 Absorption correction: none
 48 944 measured reflections
 13 033 independent reflections

8180 reflections with $I > 2\sigma(I)$
 $R_{int} = 0.045$
 $\theta_{max} = 25.96^\circ$
 $h = -15 \rightarrow 15$
 $k = -19 \rightarrow 19$
 $l = -39 \rightarrow 39$

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.036$
 $wR(F^2) = 0.078$
 $S = 0.828$
 13 033 reflections
 739 parameters
 H atoms riding
 $w = 1/[\sigma^2(F_o^2) + (0.0368P)^2]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{max} = 0.052$
 $\Delta\rho_{max} = 0.262$ e Å⁻³
 $\Delta\rho_{min} = -0.210$ e Å⁻³

Extinction correction: *SHELXL97* (Sheldrick, 1997)
 Extinction coefficient: 0.00238 (13)
 Scattering factors from *International Tables for Crystallography* (Vol. C)
 Absolute structure: Flack (1983)
 Flack parameter = -0.03 (7)

N9—C4	1.389 (2)	1.381 (3)
N9—C1'	1.453 (3)	1.445 (3)
O3'—C3'	1.416 (3)	1.426 (3)
O4'—C1'	1.431 (2)	1.426 (2)
O4'—C4'	1.446 (3)	1.436 (3)
O5'—C5'	1.417 (3)	1.414 (3)
C4—C5	1.365 (3)	1.373 (4)
C5—C6	1.411 (3)	1.401 (3)
C1'—C2'	1.545 (3)	1.553 (3)
C2'—C6'	1.461 (3)	1.458 (3)
C2'—C3'	1.532 (3)	1.538 (3)
C3'—C4'	1.514 (3)	1.520 (3)
C4'—C5'	1.524 (3)	1.513 (3)
C6'—C7'	1.200 (3)	1.213 (4)
C4'—O4'—C1'—C2'	-6.8 (2)	-6.1 (3)
C4—N9—C1'—O4'	-157.55 (19)	-152.6 (2)
O4'—C1'—C2'—C3'	-19.7 (2)	-19.8 (2)
C1'—C2'—C3'—C4'	37.2 (2)	36.3 (2)
C1'—O4'—C4'—C3'	31.2 (2)	30.0 (3)
C2'—C3'—C4'—O4'	-42.4 (2)	-41.3 (2)

The majority of H atoms were included in calculated positions and treated as riding. The NH₂ H atoms were located from difference maps and refined isotropically. An initial room-temperature measurement indicated enormous thermal motion of the isopropyl and methyl groups. In an attempt to reduce this, the present data set was collected at 223 K. The thermal motion of the same atoms is still large, especially in molecule (2). Here, two positions of the methyl C14' atom could be located and were refined with final occupancies of 0.581 (7) and 0.419 (7). Attempts were made to split other atoms, for example C10' and C23', but subsequent refinement indicated further splitting of the same atoms, with worse displacement parameters and unreasonable bond distances and angles. In the final cycles of refinement, no atoms, apart from C14' in molecule (2), were split.

Data collection: *EXPOSE* (Stoe, 1997b). Cell refinement: *CELL* (Stoe, 1997a). Data reduction: *INTEGRATE* (Stoe, 1997c). Program(s) used to solve structure: *SHELXS97* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997). Molecular graphics: *PLATON* and *PLUTON* (Spek, 1990). Software used to prepare material for publication: *SHELXL97*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: HA1212). Services for accessing these data are described at the back of the journal.

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Table 1. Selected geometric parameters (Å, °)

	Molecule (1)	Molecule (2)
Si8'—C7'	1.841 (3)	1.825 (3)
N1—C2	1.329 (3)	1.336 (4)
N1—C6	1.360 (3)	1.355 (3)
N3—C2	1.339 (3)	1.339 (3)
N3—C4	1.347 (3)	1.346 (3)
N6—C6	1.329 (3)	1.338 (3)
N7—C8	1.313 (3)	1.312 (3)
N7—C5	1.398 (3)	1.394 (3)
N9—C8	1.375 (3)	1.369 (3)

Stoe (1997b). *EXPOSE. Stoe IPDS Software for Data Collection*. Version 2.79. Stoe IPDS, Darmstadt, Germany.
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2-Methoxynaphthalene at 173 K

MICHAEL BOLTE AND CHRISTIAN BAUCH

Institut für Organische Chemie, J. W. Goethe Universität Frankfurt, Marie Curie Straße 11, 60439 Frankfurt/Main, Germany. E-mail: bolte@chemie.uni-frankfurt.de

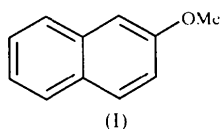
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Abstract

2-Methoxynaphthalene, C₁₁H₁₀O, crystallizes as a nearly planar molecule, with the methoxy group adopting a synperiplanar conformation with respect to the C_α atom. A search of the Cambridge Structural Database [Allen & Kennard (1993). *Chem. Des. Autom. News*, **8**, 31–37] reveals that this conformation is characteristic of the α-methoxynaphthalene moiety, because, for each of the four exceptions found, a valid explanation can be given as to why they display a different conformation.

Comment

The title compound, (I), is a common moiety in crystallographically well explored compounds, many of which have properties of potential use in medical treatment. Some of these compounds exhibit anti-inflammatory, analgesic and antipyretic activities (Ravikumar *et al.*, 1985), some display oestrogenic activity (Stora & Rerat, 1974; Cox & Sim, 1978) and others show promise in the field of cancer research (Wadhawan & Sikka, 1976; McKenna *et al.*, 1991).



We retrieved a total of 62 fragments containing a β-methoxynaphthalene moiety, with H atoms at the α and γ positions of the aromatic ring, by searching the Cambridge Structural Database (CSD, Version 5.15, April 1998; Allen & Kennard, 1993). Bond lengths and angles of the almost planar [r.m.s. deviation 0.014 (2) Å] title compound (Table 1) agree well with the mean values of the structures retrieved from the CSD: O—CH₃ 1.42 (2), O—C_{ar} 1.36 (2) Å, C—O—C 117 (1), O—C_β—C_α 124 (4), O—C_β—C_γ 124 (4)°.

A surprising aspect of almost all these reported molecules is the fact that the conformation of the methoxy group attached to the naphthalene moiety is *syn* with respect to the C_α atom. 58 of the structures from the CSD showed the 2-methoxynaphthalene moiety in the aforementioned conformation. In three of the four exceptions (Fridrichsons & Mathieson, 1955; Wadhawan & Sikka, 1976), the retrieved fragment was found to be part of a phenanthrene moiety, and in the fourth structure (Caira *et al.*, 1995) the conformation of the fragment is obviously influenced by a cyclodextrin host molecule, because the crystal structure of the guest without a host (Ravikumar *et al.*, 1985) shows the expected conformation. Therefore, these exceptions cannot really be compared with the other structures.

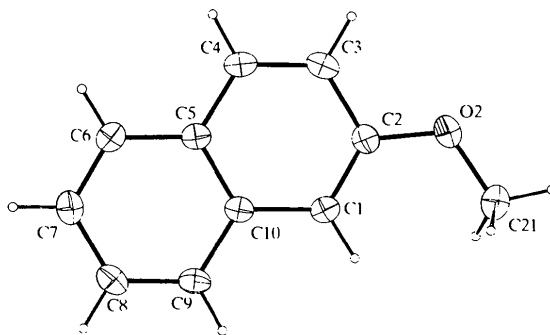


Fig. 1. A perspective view of the title compound with the atom-numbering scheme; displacement ellipsoids are at the 50% probability level.

Experimental

2-Methoxynaphthalene was first reported by Staedel (1882), who described a synthesis similar to our procedure: the only differences are that he used methyl iodide instead of dimethyl sulfate and methanol instead of water as the solvent. The procedure used here is as follows: the title compound was obtained by adding dimethyl sulfate to an aqueous solution of β-naphthol in 2 M NaOH at 313 K. The solution was then heated to 373 K and stirred continuously for 30 min at this temperature. After cooling to room temperature, the precipitated substance was isolated by filtration and purified by recrystallization from ethanol. 2-Methoxynaphthalene is a colourless compound which undergoes slow decomposition when exposed to daylight under atmospheric conditions, leaving a brown residue. This kind of chemical behaviour was observed during our attempts to obtain suitable crystals for the X-ray structure analysis. These attempts were carried out with several solvents, of which the following proved to be useful: hexane, cyclohexane, hexane/dichloromethane and 2-propanol. The crystals were formed during slow evaporation of the solvent. The main difficulty was that the title compound showed a great tendency to form thin plates. In the end, we used the crystals from the 2-propanol solution.