The crystal was of extremely low diffracting power (very high R values). Scintillation detector data were collected over 30 d but the structure could not be solved because the ratio of intensity to standard deviation was too small. Data from the same crystal, measured over 12 h using an image-plate detector, solved the structure immediately by a routine input.

H atoms were refined as a riding model with fixed isotropic U values. The relatively high R values are the result of the low crystal quality. All calculations were carried out on a MicroVAX II computer using the *SHELXTL-Plus* programs (Sheldrick, 1990).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: SE1045). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Charbonneau, G.-P. & de Lugeard, Y. (1977). *Acta Cryst.* B**33**, 1586–1588.

Fleck, W. F., Strauss, D. G., Meyer, J. & Porstendorfer, G. (1978). *Z. Allg. Mikrobiol.* **18**, 389–398.

Miosga, N., Römer, W. & Hesse, G. (1985). *Z. Chem.* **25**, 146–147.

Oberhammer, H. & Bauer, S. H. (1969). *J. Am. Chem. Soc.* **91**, 10–16.

Saito, T., Ayukawa, H., Sumizawa, N., Shizuta, T., Motoki, S. & Kobayashi, K. (1991). *J. Chem. Soc. Perkin Trans.* 1, pp. 1405–1410.

Sheldrick, G. M. (1990). *SHELXTL-Plus.* Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Strauss, D. G. & Fleck, W. F. (1990). *Proceedings of the International Symposium on Advances in Bioactive Natural Product Chemistry.* Seoul, Korea.

Strauss, D., Fleck, W. F., Tresselt, D., Kochmann, W., Richter, H. P., Müller, S., Keil, A., Till, H.-J., Scharfenberg, P. & Weiher, B. (1990). Patent No. DD 285614 A5 (22-09/19-12-90).

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(–)-Norcocaine

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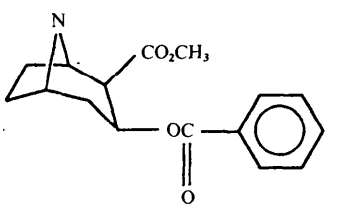
Abstract

The title compound, [2R,3S-(2β,3β)]-methyl 3-(benzoyloxy)-8-azabicyclo[3.2.1]octane-2-carboxylate, $C_{16}H_{19}NO_4$, is a metabolite of the tropane alkaloid cocaine. The molecule crystallized as the free base with the piperidine ring in a chair conformation. The tropane ring system and its methoxycarbonyl and benzoyl groups are rigid; only rotational flexibility is allowed in the conformation of the substituents.

Comment

Cocaine is a tropane alkaloid that has been widely abused as a recreational drug. It causes a variety of pharmacological effects on the central nervous, cardiovascular and sympathetic nervous systems. When inhaled through the nose or injected intravenously, cocaine causes euphoria and an increase in heart rate and blood pressure (Byke & Vandyke, 1977). The title compound (I), which is the demethylated metabolite of cocaine, shows approximately one-third the pharmacological activity of cocaine. We have begun to study the three-dimensional structures of some cocaine derivatives and report here the structure of the free-base form of norcocaine.



(I)

The title compound crystallizes as the free base with one molecule in the asymmetric unit. The fractional coordinates were defined in accordance with the known absolute configuration of (–)-norcocaine. The X-ray crystal structure of norcocaine hydrobromide has been reported (Kelly, Knox, Lazer, Nieforth & Hite, 1977) and, like the title compound, it has the piperidine ring in a chair conformation. The tropane rings show very similar internal torsion angles in all of the crystal structures reported for cocaine (Hrynchuk, Barton & Robertson, 1983) and its derivatives, cocaine hydrochloride (Gabe & Barnes, 1963), cocaine methiodide (Shen, Ruble & Hite, 1975) and norcocaine hydrobromide (Kelly *et al.*, 1977). In addition, in all four of these structures and in the free base of norcocaine reported here, the methoxycarbonyl group is bonded axially to the tropane ring at C2 and the benzoyl group is bonded equatorially to the tropane ring at C3. This substituent orientation corresponds to the stereoisomer (R)-cocaine which occurs naturally in *Erythroxylon coca* leaves and which shows the highest pharmacological activity of the eight possible stereoisomers.

The bridgehead N atom has an axial H atom that is intramolecularly hydrogen bonded to the carbonyl O atom (O3) of the methoxycarbonyl group [HN···O3 2.306 (2) Å]. This hydrogen bond is weaker than the comparable one in norcocaine hydrobromide (HN···O,

2.14 Å). Both the methoxycarbonyl group and the benzoyl group are approximately planar with very little structural flexibility. The only structural flexibility in the whole norcocaine molecule seems to be in the torsion angle around the C2—C15 (tropane–methoxycarbonyl) and C3—O1 (tropane–benzoyl) bonds. The intramolecular N—H···O3 hydrogen bond forces the conformation of the methoxycarbonyl substituent to be fixed in an orientation favorable for the formation of this bond. In each of the cocaine structures where an intramolecular hydrogen bond does not exist, there is a close intramolecular contact between the carbonyl O atom (O3) of the methoxycarbonyl group and O1 of the benzoyl group (O3···O1 = 2.85 for cocaine, 2.79 for cocaine hydrochloride and 2.82 Å for cocaine methiodide). This suggests that the conformation of the methoxycarbonyl substituent, although somewhat flexible, may depend on whether or not the carbonyl O atom is involved in an intramolecular hydrogen bond. In cocaine hydrochloride (Klein & Zhu, 1993†), the amine H atom is involved in a hydrogen bond between the N atom and the chloride ion rather than the N atom and the carbonyl O atom. This allows the methoxycarbonyl group to rotate so that the carbonyl O atom forms a close contact with the benzoyl O atom. The conformation of the benzoyl group can be described by the C2—C3—O1—C8 torsion angle; this angle is −149.3 (1) in norcocaine and −139° in the free base of cocaine, whereas in cocaine methiodide and cocaine hydrochloride it has values of −73 (2) and −77°, respectively, and in norcocaine hydrobromide it is −156°.

† Although Hrynchuk, Barton & Robertson (1983) reported the structure of cocaine previously, the H-atom positions were not located. We have redetermined the crystal structure and located the H atoms.

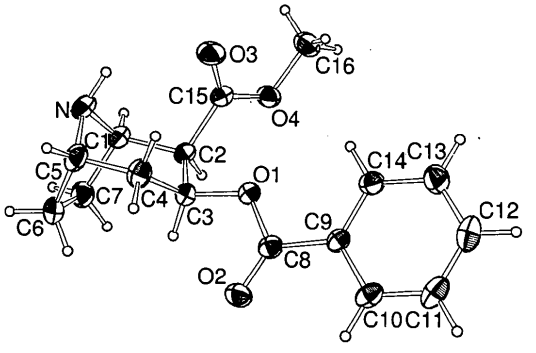


Fig. 1. Molecular structure and numbering system for (−)-norcocaine. The displacement ellipsoids are drawn at the 50% probability level.

Experimental

Crystal data

$C_{16}H_{19}NO_4$
M_r = 289.3
Orthorhombic
$P2_12_12_1$
a = 9.293 (1) Å
b = 10.189 (2) Å
c = 15.259 (2) Å
V = 1444.8 Å^3
Z = 4
D_x = 1.33 Mg m^{-3}
Mo $K\alpha$ radiation
λ = 0.7107 Å
Cell parameters from 25 reflections
θ = 13–20°
μ = 0.089 mm^{-1}
T = 105 (2) K
Prism
0.75 × 0.28 × 0.2 mm
Colorless
Crystal source: NIDA

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical
T_{min} = 0.9686, T_{max} = 0.9949
2412 measured reflections
2387 independent reflections
2111 observed reflections [$I > 3\sigma(I)$]
R_{int} = 0.02
θ_{max} = 30°
$h = 0 \rightarrow 13$
$k = 0 \rightarrow 14$
$l = 0 \rightarrow 21$
3 standard reflections
frequency: 120 min
intensity variation: 5.5%

Refinement

Refinement on F
R = 0.040
wR = 0.050
S = 1.98
2111 reflections
190 parameters
H-atom parameters not refined
$w = 1/[\sigma^2(I_{cs}) + (0.04F^2)^2]^{1/2}$
$(\Delta/\sigma)_{max} < 0.1$
$\Delta\rho_{max}$ = 0.42 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}
Extinction correction: none
Atomic scattering factors from *International Tables for X-ray Crystallography* (1974, Vol. IV)

Table 1. *Fractional atomic coordinates and equivalent isotropic displacement parameters* (Å^2)

$B_{eq} = (4/3)\Sigma_i\Sigma_j\beta_{ij}\mathbf{a}_i.\mathbf{a}_j$.

	x	y	z	B_{eq}
O1	0.3602 (1)	0.9535 (1)	0.15980 (7)	1.88 (2)
O2	0.3153 (1)	0.8279 (1)	0.04162 (7)	2.44 (2)
O3	0.4711 (2)	1.1994 (1)	0.27013 (8)	2.75 (2)
O4	0.5205 (1)	1.0139 (1)	0.34251 (7)	2.13 (2)
N	0.6792 (2)	1.2323 (1)	0.12094 (9)	2.31 (2)
C1	0.7257 (2)	1.1092 (2)	0.1625 (1)	1.95 (2)
C2	0.5985 (2)	1.0245 (1)	0.19629 (9)	1.64 (2)
C3	0.4943 (2)	0.9972 (2)	0.1206 (1)	1.76 (2)
C4	0.4661 (2)	1.1161 (2)	0.0626 (1)	2.29 (3)
C5	0.6087 (2)	1.1852 (2)	0.0410 (1)	2.35 (3)
C6	0.7223 (2)	1.0907 (2)	0.0042 (1)	2.45 (3)
C7	0.8029 (2)	1.0416 (2)	0.0863 (1)	2.41 (3)
C8	0.2810 (2)	0.8686 (1)	0.11318 (9)	1.75 (2)
C9	0.1463 (2)	0.8314 (1)	0.15947 (9)	1.64 (2)
C10	0.0565 (2)	0.7393 (2)	0.1198 (1)	2.14 (3)
C11	−0.0690 (2)	0.7009 (2)	0.1609 (1)	2.68 (3)
C12	−0.1059 (2)	0.7533 (2)	0.2416 (1)	2.83 (3)
C13	−0.0173 (2)	0.8457 (2)	0.2805 (1)	2.71 (3)
C14	0.1093 (2)	0.8845 (2)	0.2398 (1)	2.14 (3)
C15	0.5231 (2)	1.0906 (2)	0.2715 (1)	1.76 (2)
C16	0.4508 (2)	1.0678 (2)	0.4189 (1)	2.71 (3)

Table 2. *Selected geometric parameters* (Å, °)

O1—C3	1.452 (2)	C3—C4	1.524 (2)
O1—C8	1.340 (2)	C4—C5	1.537 (3)
O2—C8	1.211 (2)	C5—C6	1.536 (3)

O3—C15	1.209 (2)	C6—C7	1.544 (3)
O4—C15	1.336 (2)	C8—C9	1.487 (2)
O4—C16	1.443 (2)	C9—C10	1.394 (2)
N—C1	1.470 (2)	C9—C14	1.383 (2)
N—C5	1.465 (2)	C10—C11	1.381 (3)
C1—C2	1.551 (2)	C11—C12	1.384 (3)
C1—C7	1.530 (2)	C12—C13	1.384 (3)
C2—C3	1.533 (2)	C13—C14	1.388 (3)
C2—C15	1.504 (2)		
C3—O1—C8	116.8 (1)	C5—C6—C7	103.9 (1)
C15—O4—C16	116.1 (1)	C1—C7—C6	104.1 (1)
C1—N—C5	102.2 (1)	O1—C8—O2	123.7 (2)
N—C1—C2	113.2 (1)	O1—C8—C9	112.0 (1)
N—C1—C7	101.2 (1)	O2—C8—C9	124.3 (1)
C2—C1—C7	111.0 (1)	C8—C9—C10	118.0 (1)
C1—C2—C3	109.4 (1)	C8—C9—C14	122.0 (1)
C1—C2—C15	111.0 (1)	C10—C9—C14	120.0 (2)
C3—C2—C15	111.2 (1)	C9—C10—C11	119.9 (2)
O1—C3—C2	106.7 (1)	C10—C11—C12	120.2 (2)
O1—C3—C4	109.6 (1)	C11—C12—C13	119.8 (2)
C2—C3—C4	113.7 (1)	C12—C13—C14	120.4 (2)
C3—C4—C5	109.9 (1)	C9—C14—C13	119.7 (2)
N—C5—C4	110.9 (1)	O3—C15—O4	122.9 (2)
N—C5—C6	101.7 (1)	O3—C15—C2	125.7 (2)
C4—C5—C6	112.6 (1)	O4—C15—C2	111.4 (1)

Data were processed and refined using the *MolEN* software package (Fair, 1990). The structure was solved using the *MULTAN*11/82 series of programs (Main *et al.*, 1982).

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Lists of structure factors, anisotropic displacement parameters and H-atom coordinates have been deposited with the IUCr (Reference: LI1093). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

References

Byke, R. & Vandyke, C. (1977). *Cocaine*, edited by R. C. Peterson & R. C. Stillman, pp. 97–117. Washington, DC: US Government Printing Office.

Fair, C. K. (1990). *MolEN. An Interactive Intelligent System for Crystal Structure Analysis*. Enraf–Nonius, Delft, The Netherlands.

Gabe, E. J. & Barnes, W. H. (1963). *Acta Cryst.* **16**, 796–801.

Hrynchuk, R. J., Barton, R. J. & Robertson, B. E. (1983). *Can. J. Chem.* **61**, 481–487.

Kelly, J. A., Knox, J. R., Lazer, E. S., Nieforth, K. A. & Hite, G. (1977). *Acta Cryst.* B**33**, 3542–3545.

Klein, C. L. & Zhu, N. (1993). Unpublished results.

Main, P., Fiske, S. J., Hull, S. E., Lessinger, L., Germain, G., Declercq, J.-P. & Woolfson, M. M. (1982). *MULTAN*11/82, *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England and Louvain, Belgium.

Shen, M., Ruble, J. R. & Hite, G. (1975). *Acta Cryst.* B**31**, 2706–2709.

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A New Crystal Form of Methyl Bacteriopheophorbide *a*

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Abstract

The structure of a new crystal form of methyl bacteriopheophorbide *a*, $C_{36}H_{40}N_4O_6$, which does not contain benzene molecules of crystallization, has been determined at 200 K. The molecule is slightly ruffled with maximum displacements from planarity of ± 0.21 Å in all five rings. The crystal packing is dominated by π–π interactions between pyrrole rings I and III of adjacent molecules, which are separated by 3.58 Å.

Comment

Bacteriochlorophylls (BChls) and their demetallated analogs, bacteriopheophytins (BPheos), are prosthetic groups of antenna (Tronrud, Schmid & Matthews, 1986) and reaction-center (Allen, Feher, Yeates, Komiya & Rees, 1988; Deisenhofer & Michel, 1989; El-Kabbani, Chang, Tiede, Norris & Schiffer, 1991) proteins, whose structures have been determined by X-ray methods. The BChls in antenna complexes harvest light into reaction centers where a network of BChls and BPheos effect the primary charge separation which eventually drives the biochemistry of the organisms; for a review of this subject see Kirmaier & Holten (1987). Recently, we reported a high-precision structure (Barkigia, Gottfried, Boxer & Fajer, 1989) of methyl bacteriopheophorbide *a* (MeBPheo), a molecule lacking only the phytyl chain of BPheo, that was crystallized from CH_2Cl_2/benzene and consequently contained benzene of solvation. Since structural data clearly demonstrate that crystal packing as well as steric and protein constraints (Deisenhofer, Epp, Miki, Huber & Michel, 1984, 1985; Barkigia, Fajer, Chang & Young, 1984; Waditschatka, Kratky, Jaun, Heinzer & Eschenmoser, 1985; Tronrud *et al.*, 1986; Michel, Epp & Deisenhofer, 1986; Scheidt & Lee, 1987) cause porphyrin conformational variations which in turn modulate redox, optical and charge-transfer prop-

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