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6,8-Dimethoxy-1,3-*trans*-dimethylisochroman-5-yl diethyl phosphate

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Key indicators

Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.005 Å
R factor = 0.074
wR factor = 0.170
Data-to-parameter ratio = 17.9

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

The title compound, $C_{17}H_{27}O_7P$, is an important intermediate in the synthesis of an oxygen analogue of the michellamines, which are bisbiaryl naphthylisoquinoline alkaloids with anti-HIV activities. The crystal structure of the title compound confirms the relative *trans* stereochemistry of the methyl substituents in the heterocycle, as well as the position of the phosphate ester at the C-5 atom of the isochromane system.

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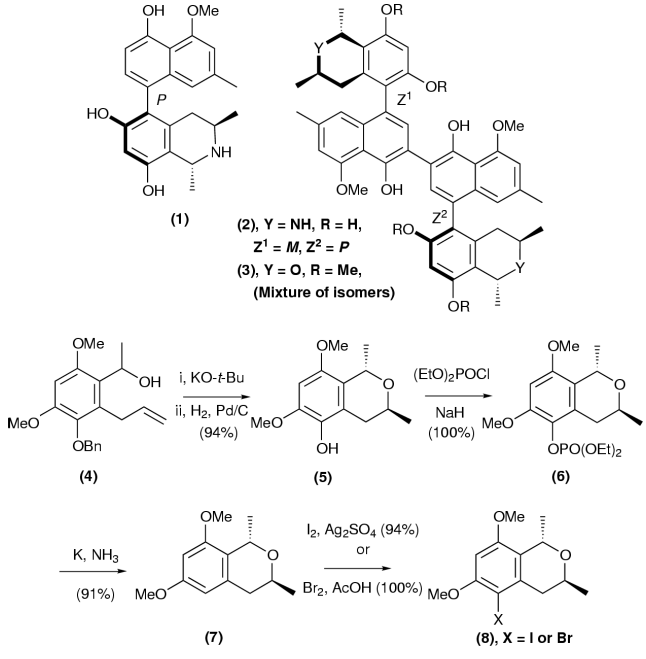
Comment

Korupensamine A, (1), and michellamine B, (2), belong to a class of biaryl naphthylisoquinoline alkaloids (Bringmann & Pokorny, 1995) which displays many interesting biological activities, including antimalarial and potent anti-HIV activity (Boyd *et al.*, 1994; Bringmann & Pokorny, 1995; Yang *et al.*, 2001). In our quest to synthesize analogues of these compounds, we succeeded in making the michellamine isochromane analogue (3) (de Koning *et al.*, 1999, 2000). One of the steps in the synthesis required deoxygenation at position C-5 of the isochromane component (5), synthesized from the open-chain alcohol (4). This was to allow for the introduction of a halogen atom [*e.g.* I or Br, as in (8)] to facilitate a Suzuki biaryl coupling reaction (Suzuki, 1999). Isochromanol (5) was thus converted into the diethyl phosphate derivative (6), which was deoxygenated to afford compound (7) in good yield, according to an established procedure (Rossi & Bunnett, 1973).



Compound (6) was found to be crystalline, and a subsequent X-ray crystal structure determination served to confirm the relative *trans* stereochemistry of the isochromane methyl groups, as well as the regiochemical position of the phosphate ester at position 5 of the isochromane system.

Experimental

Isochromanol (5) (0.18 g, 0.76 mmol) in tetrahydrofuran (2 ml) was added to sodium hydride (50% in oil, 0.044 g, 0.91 mmol) in tetrahydrofuran (5 ml), and stirred for 20 min under an argon atmosphere. Diethyl phosphorochloridate (diethylchlorophosphate) (0.12 ml, 0.14 g, 0.91 mmol, 1.2 mol equivalents) was added dropwise by syringe over 2 min and the mixture was stirred under argon for 20 h. Diethyl ether (50 ml) was added and the organic phase was washed with an aqueous sodium hydroxide solution (10% m/v, 3 × 20 ml). The organic solvent was dried and removed *in vacuo* to give a light-yellow residue. This compound was subjected to column chromatography on silica gel (50% ethyl acetate/hexane to 10% methanol/hexane) to give the product (6) (0.28 g, >99%) as a light pink semi-solid which was recrystallized by slow evaporation from toluene to afford colourless needle-like crystals (m.p. 348–349 K).

Crystal data

$C_{17}H_{27}O_7P$
$M_r = 374.36$
Monoclinic, $C2/c$
$a = 19.7987\ (11)$ Å
$b = 11.2320\ (5)$ Å
$c = 19.3329\ (11)$ Å
$\beta = 115.880\ (2)^\circ$
$V = 3868.1\ (4)$ Å^3
$Z = 8$
$D_x = 1.286$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 1024 reflections
$\theta = 2.1$–27.0°
$\mu = 0.18$ mm^{-1}
$T = 296\ (2)$ K
Needle, colourless
0.40 × 0.08 × 0.08 mm

Data collection

Bruker SMART 1K CCD diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
$T_{min} = 0.933$, $T_{max} = 0.986$
11051 measured reflections
4155 independent reflections
2976 reflections with $I > 2\sigma(I)$
$R_{int} = 0.049$
$\theta_{max} = 27.0^\circ$
$h = -24 \rightarrow 25$
$k = -11 \rightarrow 14$
$l = -24 \rightarrow 22$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.074$
$wR(F^2) = 0.170$
$S = 1.15$
4155 reflections
232 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0544P)^2 + 5.2563P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.55$ e Å^{-3}
$\Delta\rho_{min} = -0.25$ e Å^{-3}

H atoms were positioned geometrically and allowed to ride on their respective parent atoms with $U_{iso} = 1.2U_{eq}$ of the parent atom ($1.5U_{eq}$ for methyl H atoms).

Data collection: *SMART-NT* (Bruker, 1998); cell refinement: *SAINT-Plus* (Bruker, 1999); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Bruker, 1999); program(s) used to refine structure: *SHELXTL*; molecular graphics: *PLATON* (Spek, 1990); software used to prepare material for publication: *SHELXTL*.

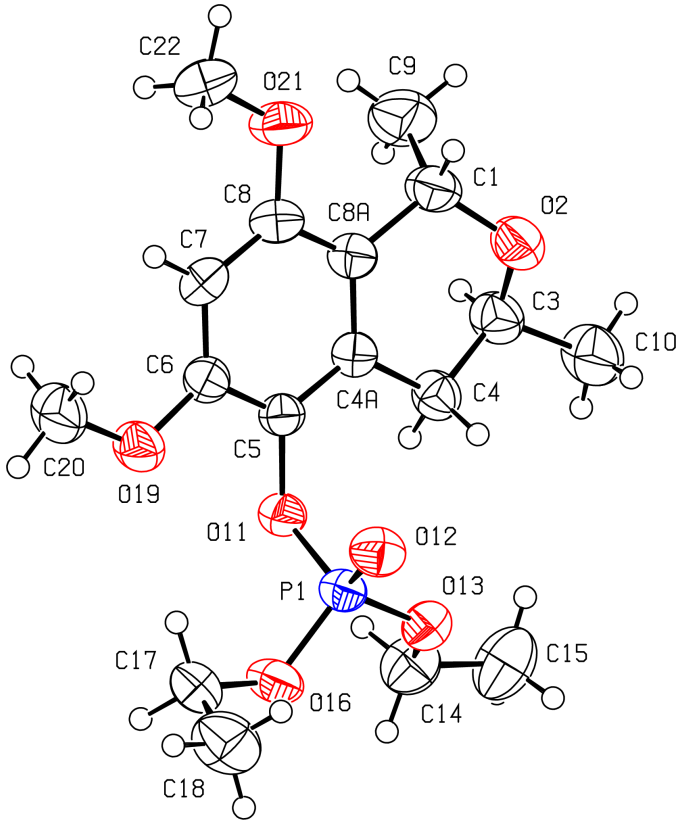


Figure 1
A view of (6), with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

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