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# (+)-6-Benzyl-17-oxosparteine

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**Key indicators**

Single-crystal X-ray study
$T$ = 100 K
Mean $\sigma$(C–C) = 0.002 Å
$R$ factor = 0.034
$wR$ factor = 0.089
Data-to-parameter ratio = 17.6

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

The title compound, $C_{22}H_{30}N_2O$, was prepared from (−)-17-oxosparteine. The lactam N atom is essentially planar, lying 0.0150 (12) Å out of the plane of its three bonded C atoms, and the C=O distance is 1.2315 (13) Å. The conformation of the sparteine ring system is nearly identical to that of 17-oxosparteine.

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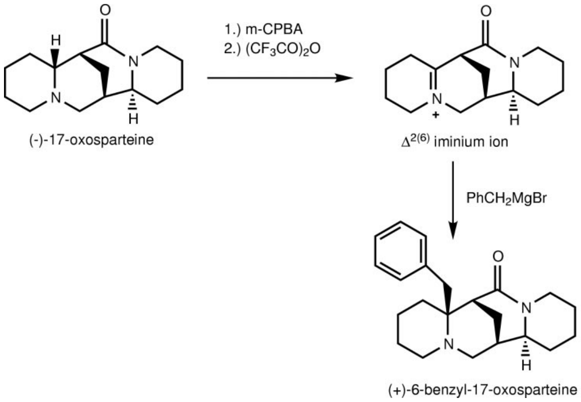
## Comment

The natural product diamine (−)-sparteine has surfaced as one of the most robust external chiral ligands for asymmetric transformations, due to its metal coordination (Li, Zn, Cu, Mg) effectiveness and commercial availability (Beak *et al.*, 1996; Gallagher *et al.*, 1995). It has been used extensively, particularly in the asymmetric deprotonation–stereoselective substitution reaction, generating enantioenriched products from achiral substrates (Resek & Beak, 1994). The development of diamine surrogates that are complementary or superior to (−)-sparteine is of current interest (Dearden *et al.*, 2002). We have developed a one-pot synthesis of 6-alkyl-substituted sparteine derivatives from 17-oxosparteine, utilizing a conventional Polonovski reaction (*m*-chloroperbenzoic acid/trifluoroacetic anhydride), followed by subsequent Grignard addition to the resulting iminium ion (see reaction scheme below). This is in contrast to alternate synthetic protocols which utilize mercuric acetate as the oxidizing agent (Majchrzak-Kuczynska *et al.*, 1995). In order to unequivocally confirm the regiochemistry and stereochemistry of the addition product, an X-ray crystal structure determination was conducted on the product obtained from reaction with benzyl magnesium bromide, namely (+)-6-benzyl-17-oxosparteine, (I). Crystallographic data are available for sparteine analogs related to (I), which include 17-oxosparteine (Katrusiak *et al.*, 1980), 17-oxosparteine *N*(1)-oxide hydrochloride (Katrusiak *et al.*, 1987), and (+)-6-benzylsparteine (Kageyama *et al.*, 1984).



The structure determination of (I) confirms that the benzyl substituent is at C6, and that it has been added with retention of configuration at that asymmetric center. The two N atoms differ in their degrees of planarity; N2 is pyramidal, with C—N—C angles in the range 111.79 (8)–114.67 (9)°, while lactam atom N1 is essentially planar, lying 0.0150 (12) Å out of the plane defined by the three C atoms bonded to it. Also, the C17═O1 is somewhat elongated *versus* normal double bonds. These features were also observed in 17-oxosparteine (Katrusiak *et al.*, 1980), which has a C═O bond length of 1.232 (5) Å. The conformation of the ring system in (I) also agrees well with that of 17-oxosparteine, with the two sets of 24 endocyclic torsion angles exhibiting an r.m.s. difference of only 2.9°. The largest differences do not involve the benzyl-substituted atom, but rather occur in the *C* ring (that containing C17), with an r.m.s. difference of 5.3° and a largest individual difference of 8.7 (5)° for C8—C9—C11—N1. The conformational difference is smallest for the *D* ring (N1 and C11–C15), where the r.m.s. difference is only 1.0°.

## Experimental

A solution of *m*-chloroperbenzoic acid (70%, 6.46 g, 37.4 mmol) in 20 ml of anhydrous $CH_2Cl_2$ was added at 273 K, to a stirred solution of 17-oxosparteine (5.8 g, 23.4 mmol; prepared according to the method of Golebiewski & Spenser, 1985) in 20 ml of anhydrous $CH_2Cl_2$. The reaction mixture was allowed to warm to room temperature and stirred for 6 h. The solution was dried over anhydrous $MgSO_4$ (essential to ensure that 17-oxosparteine $N^2$-oxide is completely free from water content, before it is subjected to the next reaction step with trifluoroacetic anhydride), filtered, and evaporated to dryness under reduced pressure. Trifluoroacetic anhydride (12.3 g, 8.2 ml, 58.5 mmol) was added dropwise over a period of 20 min to a stirred solution of 17-oxosparteine $N^2$-oxide (12.6 g crude; empirically corresponds to 17-oxosparteine, 5.8 g, 23.4 mmol) in 40 ml of anhydrous $CH_2Cl_2$ at 253 K, in the presence of a few activated molecular sieves under a blanket of argon. The reaction mixture was allowed to warm to room temperature and was stirred for an additional 4 h. The excess solvent and trifluoroacetic anhydride were removed *in vacuo* at 273 K [an NaOH solution (10%) was placed in the evaporator receiver to quench excess anhydride]. The white sticky residue was reconstituted in diethyl ether, dried over anhydrous $MgSO_4$, filtered, and evaporated to dryness under reduced pressure. The resulting sticky white solid (22 g) was found, by LC–MS analysis, to correspond exclusively to a dehydro product. To a freshly prepared 1.0 *M* solution of benzylmagnesium bromide in anhydrous diethyl ether (200 ml, 39.2 g, 200 mmol) at 253 K was added a solution of the iminium salt (16.47 g, 67 mmol) dissolved in 20 ml of anhydrous ether dropwise over a period of 20 min. The reaction was refluxed for 14 h, cooled to 263 K, and quenched with NaOH solution (15% *w*/*v*; 150 ml). The resulting solution was extracted with diethyl ether (3 × 250 ml), washed with water, dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. The resulting pale yellow oil was reconstituted in anhydrous ether and an anhydrous ethereal solution of HCl was added, producing the crude hydrochloride salt. Recrystallization from methanol/acetone yielded (+)-6-benzyl-17-oxosparteine monohydrochloride (4.8 g, 73% yield): m.p. 552.3 K. Exact mass calculated for $C_{22}H_{31}N_2O$ ($MH^+$) 339.2436, found: 339.2437; CHN analysis calcd for $C_{22}H_{31}ClN_2O$: C 70.47, H 8.33, N 7.47%; found: C 69.62, H 8.11, N 6.96%. The hydrochloride salt was treated with 10% NaOH solution to generate the free base, which was extracted with ether, washed with water, dried over anhydrous $MgSO_4$, and the solvent was evaporated under reduced pressure to yield a white solid that was recrystallized from ether, yielding translucent crystals of (+)-6-benzyl-17-oxosparteine, (I) (4.25 g, 72% yield); m.p. 464.1 K; $R_F$ = 0.79 (50% ethyl acetate–hexane); $[\alpha]_D^{25}$ = +34° ($c$ = 0.1, $CHCl_3$). CHN analysis calcd for $C_{22}H_{30}N_2O$: C 78.06, H 8.93, N 8.28%; found: C 77.79, H 8.57, N 8.20%.

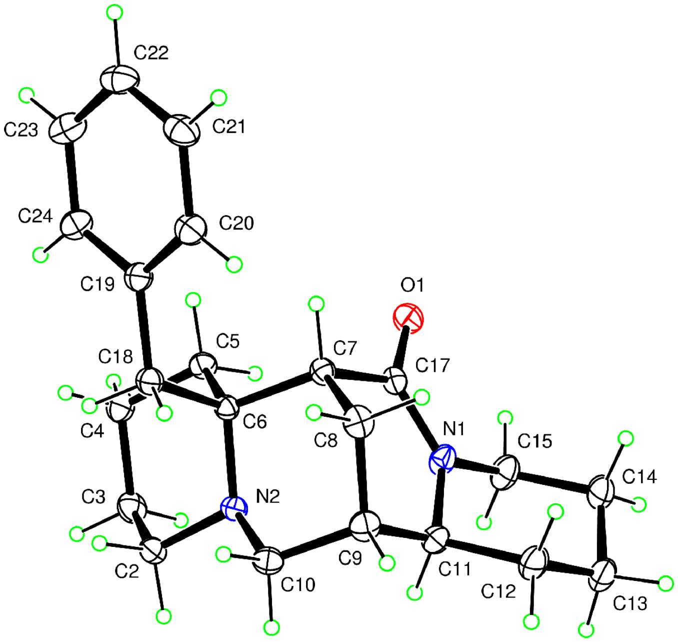


**Figure 1**
The atom-numbering scheme for (I), with displacement ellipsoids drawn at the 50% probability level.

### *Crystal data*

$C_{22}H_{30}N_2O$
$M_r$ = 338.48
Orthorhombic, $P2_12_12_1$
$a$ = 10.236 (2) Å
$b$ = 10.947 (2) Å
$c$ = 16.278 (2) Å
$V$ = 1824.0 (5) Å$^3$
$Z$ = 4
$D_x$ = 1.233 Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 3909 reflections
$\theta$ = 2.5–34.3°
$\mu$ = 0.08 mm$^{-1}$
$T$ = 100 K
Prism, colorless
0.40 × 0.40 × 0.37 mm

### *Data collection*

Nonius KappaCCD diffractometer with an Oxford Cryosystems Cryostream cooler
$\omega$ scans with $\kappa$ offsets
22 786 measured reflections
4004 independent reflections
3769 reflections with $I > 2\sigma(I)$
$R_{\rm int}$ = 0.017
$\theta_{\rm max}$ = 33.7°
$h = -15 \rightarrow 15$
$k = -17 \rightarrow 17$
$l = -24 \rightarrow 24$

### *Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)]$ = 0.034
$wR(F^2)$ = 0.089
$S$ = 1.05
4004 reflections
227 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0457P)^2 + 0.2882P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} < 0.001$
$\Delta\rho_{\rm max}$ = 0.29 e Å$^{-3}$
$\Delta\rho_{\rm min}$ = −0.20 e Å$^{-3}$
Extinction correction: *SHELXL*97
Extinction coefficient: 0.019 (2)

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**Table 1**

Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| O1—C17 | 1.2315 (13) | N2—C10 | 1.4557 (14) |
| N1—C17 | 1.3599 (14) | N2—C2 | 1.4655 (14) |
| N1—C15 | 1.4615 (14) | N2—C6 | 1.4839 (13) |
| N1—C11 | 1.4700 (14) | | |
| C17—N1—C15 | 118.69 (9) | C10—N2—C2 | 111.79 (8) |
| C17—N1—C11 | 126.74 (9) | C10—N2—C6 | 114.29 (8) |
| C15—N1—C11 | 114.54 (9) | C2—N2—C6 | 114.67 (9) |
| N2—C6—C18—C19 | 178.82 (9) | C6—C18—C19—C20 | −89.33 (12) |

The absolute configuration could not be determined from the X-ray data, but was assigned from the known configuration of (−)-sparteine (Okuda *et al.*, 1961), which has been recently confirmed by the absolute configuration determination of two polymorphs of its dibromozinc(II) complex (Lee *et al.*, 2002; Alcántara-Flores *et al.*, 2003). Friedel pairs were averaged. H atoms were placed in idealized positions, with C—H bond distances in the range 0.95–1.00 Å, and thereafter treated as riding, with displacement parameters assigned as $U_{\rm iso} = 1.2U_{\rm eq}$(C).

Data collection: *COLLECT* (Nonius, 2000); cell refinement: *HKL SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *HKL DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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## References

Alcántara-Flores, J. L., Bèrnes, S., Reyes-Ortega, Y. & Zamorano-Ulloa, R. (2003). *Acta Cryst.* C**59**, m79–m81.

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.

Beak, P., Basu, A., Gallagher, D. J., Park, Y. S. & Thayumanavan, S. (1996). *Acc. Chem. Res.* **29**, 552–560.

Dearden, M. J., Firkin, C. R., Hermet, J.-P. R. & O'Brien, P. (2002). *J. Am. Chem. Soc.* **124**, 11870–11871.

Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.

Gallagher, D. J., Wu, S., Nikolic, N. A. & Beak, P. (1995). *J. Org. Chem.* **60**, 8148–8154.

Golebiewski, W. M. & Spenser, I. D. (1985). *Can. J. Chem.* **63**, 716–719.

Kageyama, H., Miki, K., Kai, Y., Kasai, N., Okamoto, Y. & Yuki, H. (1984). *Bull. Chem. Soc. Jpn*, **57**, 1189–1196.

Katrusiak, A., Hoser, A., Grzesiak, E. & Kaluski, Z. (1980). *Acta Cryst.* B**36**, 2442–2444.

Katrusiak, A., Ratajczak-Sitarz, M. & Kaluski, Z. (1987). *Acta Cryst.* C**43**, 2386–2389.

Lee, Y.-M., Kang, S. K. & Choi, S.-N. (2002). *Acta Cryst.* C**58**, m453-m454.

Majchrzak-Kuczynska, U., Pietrzak, P. & Skolik, J. (1995). *Pol. J. Chem.* **69**, 25–32.

Nonius (2000). *COLLECT*. Nonius BV, Delft, The Netherlands.

Okuda, S., Tsuda, K. & Kataoka, H. (1961). *Chem. Ind.* pp. 1115–1116.

Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallograp*hy, Part A, edited by C. W. Carter Jr and R. M. Sweet, pp. 307–326. New York: Academic Press.

Resek, J. E. & Beak, P. (1994). *J. Am. Chem. Soc.* **116**, 405–406.

Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.

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