

# Determination of the Absolute Configuration of $C_{12}H_{13}O_2$ by Three-Beam Diffraction

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The absolute configuration of  $C_{12}H_{13}O_2$  has been determined by three-beam interferences despite small crystals of sizes in the few 10's  $\mu m$  range.

The title compound (Fig. 1) is an intermediate compound on the way to the synthesis of monosaccharides with amino substituents in different ring positions which are of interest as substructure of aminoglycoside antibiotics, e.g. kanamycine, gentamicine, or neomycine [1]. The alcohol  $C_{12}H_{13}O_2$  was directly obtained from the corresponding tricyclic ketone (Fig. 1). Since the whole

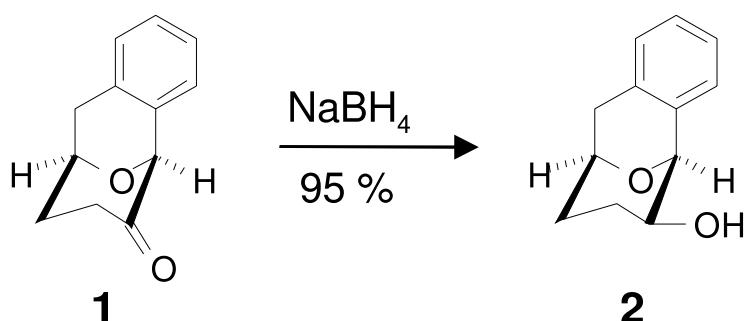


Figure 1: Reaction scheme to obtain  $C_{12}H_{13}O_2$  (2) from the tricyclic ketone (1).

reaction path aims for enantiomeric clean products the absolute conformation of the chiral center needs to be determined. If this can not be achieved by spectroscopic or other methods the usual procedure is to determine the absolute structure by X-ray crystallography provided crystals of the compound can be grown. The absolute structure can normally be determined by exploiting the violation of Friedel's law even in the case of light atom structures if the oxygen content is high enough and crystals of reasonable size are available. Both conditions were not fulfilled in this case since the available crystals were small rods of  $20\text{--}40\ \mu m$  diameter.

A more direct method to determine the absolute configuration is the direct measurement of triplet phases by three-beam diffraction [2, 3]. This method measures directly the triplet phase and is therefore independent of the presence of anomalous scattering atoms. However, the method requires a crystal or at least some mosaic blocks in a crystal of relatively high perfection. Also up to now, no measurements have been reported on crystals significantly smaller than  $100\ \mu m$  in size.

In the course of the experiments first the structure was determined in the usual way at the Petra-1 beamline. Data collection parameters are given in Tab. 1. The intensity data collection had to be carried out at room temperature since data frames at lower temperature could not be indexed indicating a phase transformation destroying the translational periodic order. Intensity data were integrated with XDS [4], the structure was solved and refined using anisotropic displacement parameters by full matrix least squares using SHELXS and SHELXL, respectively. The final difference Fourier map was featureless with  $|\Delta\rho_{\min,\max}| < 0.15\text{ e}/\text{\AA}^3$ .

The absolute structure was determined by the measurement of a number of three-beam cases se-

beamline	Petra-1	no. reflections	18477
instrument	$\psi$ -circle diffractometer	$R_{\text{int}}$	1.2 %
detector	165 mm MarCCD	no. unique reflections	939
wavelength	0.6887 Å	$d_{\text{min}}$	0.82 Å
crystal size	$0.1 \times 0.04 \times 0.04$ mm <sup>3</sup>	no. of parameters	128
space group	P3 <sub>2</sub>	R(F), wR(F <sup>2</sup> ), S	0.028, 0.082, 1.06
lattice parameters a,b	12.21 Å	lattice parameter c	5.79 Å

Table 1: Data collection and refinement parameters.

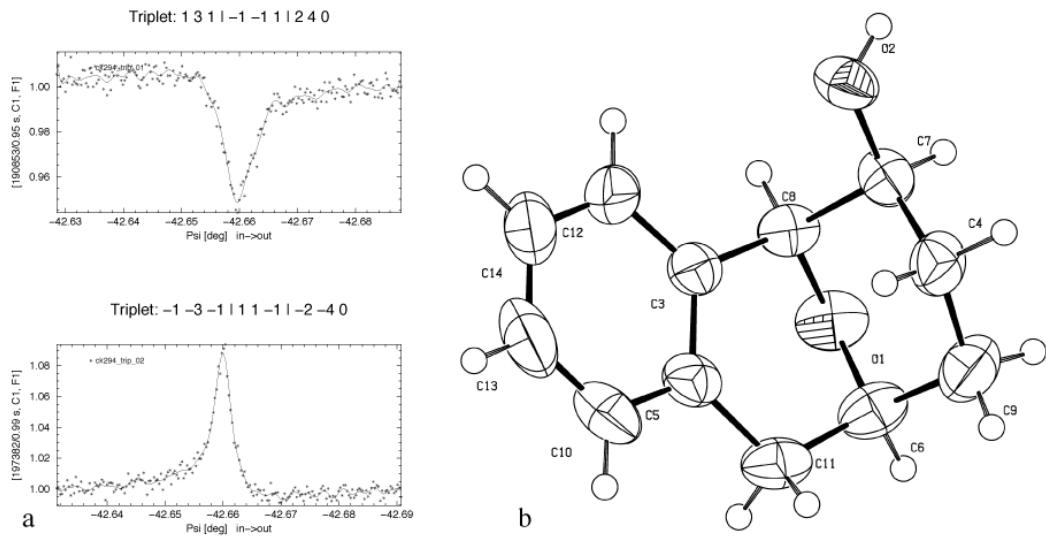


Figure 2: a: Interference profile of three-beam case  $1\ 3\ 1\ |\overline{1}\ \overline{1}\ 1\ |2\ 4\ 0$  and its centrosymmetric related one indicated a triplet phase close to  $75^\circ$  and  $-75^\circ$ , respectively. b: Representation of the molecule showing displacement ellipsoids for 50% probability.

lected appropriately. A typical interference profile is shown in Fig. 2a. The form and the slight asymmetry in the interference profile indicates a triplet phase slightly below  $|\pm 90^\circ|$  which is consistent with the calculated triplet phase of  $\pm 69^\circ$ . The results in Fig. 2a allow to assign the triplet phase  $\Phi_T=69^\circ$  unambiguously to the triplet  $1\ 3\ 1\ |\overline{1}\ \overline{1}\ 1\ |2\ 4\ 0$  thus fixing the absolute structure and the space group to P3<sub>2</sub> as compared to its enantiomorph P3<sub>1</sub>. An ORTEP-like plot of the molecule is shown in Fig. 2b. The chiral centers are at atoms C6–C8 which are all in S configuration.

## References

- [1] H.J. Roth, H. Fenner, *Arzneistoffe*, 65–72 (2000).
- [2] K. Hümmer, E. Weckert, *Acta Cryst. A* **51**, 431–438 (1995).
- [3] E. Weckert, K. Hümmer, *Acta Cryst. A* **53**, 108–143 (1997).
- [4] W. Kabsch *J.Appl.Cryst.* **26**, 795–80 (1993)