Determination of the absolute configuration of some pharmacologically relevant molecules

A. Meents, D. Lübbert, and E. Weckert

HASYLAB-DESY, Notkestr. 85, 22607 Hamburg, Germany

The carboxamides $C_{18}H_{26}N_2O_3$ (*um1*) and $C_{32}H_{40}N_4O_4$ (*um2*) and the substance $C_{17}H_{22}N_2O_2$ (*fr384*) are of pharmacological relevance. The constitutions of the molecules and the absolute configuration of one C-atom for each molecule were known from NMR experiments. Each molecule has three asymmetric C-atoms. The aim of the investigation was to determine the absolute configuration of the remaining two asymmetric C-atoms with unknown absolute configuration. For the substance $C_{18}H_{25}NO$ (*mk023*) the configuration, which was known from NMR experiments, was to be confirmed. Intensity data were collected at different beamlines at HASYLAB. All datasets were recorded using a MAR CCD-detector. For the integration of intensities and data reduction the XDS program package [1] was used. Structure solutions were carried out with SHELXS-97 [2] and structure refinements with SHELXL-97 [3] in all four cases. For all non H-atom positions anisotropic thermal displacement parameters were refined. H-positions were refined in a riding model together with the attached C-atoms. Thermal displacement parameters for the H-atoms were refined istropically. Table 1 summarises lattice parameters, data collection parameters, structure solution and refinement parameters. For all substances the absolute configuration could be determined. ORTEP-plots of the first three molecules are shown in fig. 1-3. Results for these substances are going to be published. Results for the substance *mk023* have already been submitted [4].

Table 1: Lattice-, data collection-, structure solution-, and structure refinement parameters.

name	*um1*	*um2*	*fr384a*	*mk023*
formula	$C_{18}H_{26}N_2O_3$	$C_{32}H_{40}N_4O_4$	$C_{17}H_{22}N_2O_2$	$C_{18}H_{25}NO$
mol. weight [g/mol]	318.41	544.68	286.37	287.39
SG	P 2_1	P $2_12_12_1$	P $2_12_12_1$	P$\bar{1}$
a [Å]	12.381(5)	9.044(5)	6.163(5)	5.575(3)
b [Å]	5.333(5)	10.949(5)	15.315(5)	10.207(4)
c [Å]	12.742(5)	29.514(5)	16.054(5)	14.486(5)
$\alpha[^\circ]$	90.000(5)	90.000(5)	90.000(5)	74.687(6)
$\beta[^\circ]$	93.336(5)	90.000(5)	90.000(5)	89.945(6)
$\gamma[^\circ]$	90.000(5)	90.000(5)	90.000(5)	85.481(9)
V [Å^3]	839.9(9)	2923(2)	1515(1)	792.4(6)
Z	2	4	4	2
beamline	X11	X11	PETRA-1	PETRAI
Temperature	100K	100K	100K	100K
λ [Å]	0.8075	0.8075	0.4959	0.4959
N (obs)	16281	40638	177064	87736
N (unique)	4112	7692	9782	13034
R merged (I$\geq 2\sigma$(I))	0.021	0.025	0.014	0.021
parameters	221	365	198	290
R1	0.0305	0.0297	0.0298	0.0393
wR2	0.0869	0.0808	0.0858	0.1159
GoF	1.059	1.042	1.12	1.074

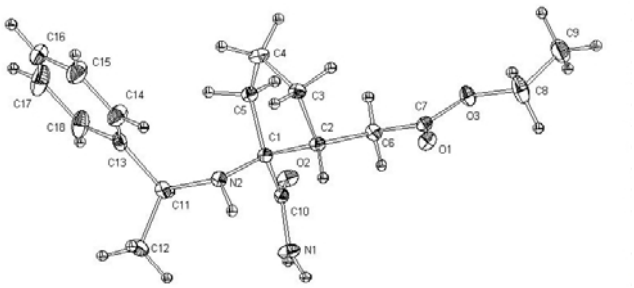

Figure 1: Configuration of molecule *um1* with thermal displacement ellipsoids (probability 50%). The absolute configuration of C-atom C11 is (S), atom C1 is (S) configurated, and atom C2 is (R) configurated.

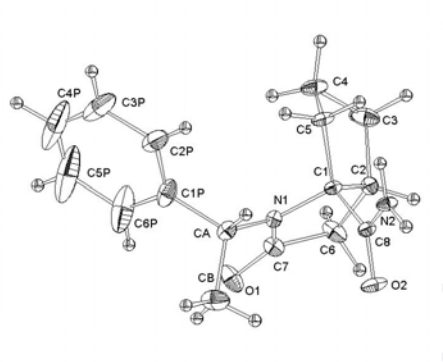

Figure 2: Configuration of molecule *um2* with thermal displacement ellipsoids (probability 50%). The absolute configuration of C-atom CA is (R), atom C1 is (R) configurated, and atom C2 is (R) configurated.

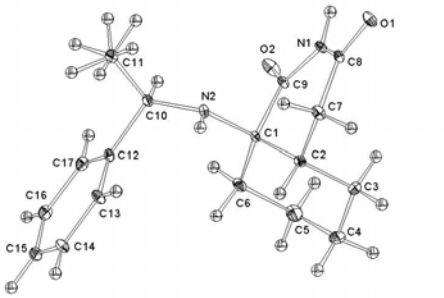

Figure 3: Configuration of molecule *fr384* with thermal displacement ellipsoids (probability 50%). The absolute configuration of C-atom C10 is (R), atom C1 is (R) configurated, and atom C2 is (S) configurated.

References

[1] W. Kabsch, J. Appl. Cryst. 21, 67-71 (1988)

[2] G. Sheldrick, SHELXS-97, University of Göttingen, Germany, (1990)

[3] G. Sheldrick, SHELXL-97, University of Göttingen, Germany, (1997)

[4] T. Lorand, E. Osz, G. Nagy, E. Weckert, D. Lübbert, A. Meents, L. Prokai, and B. Mocsis, Diastereoselective reduction of cyclic bioactive Mannich ketones. Submitted to *Tetrahedron*.