Molbank **2007**, M533 http://www.mdpi.org/molbank/

Synthesis of N-acetyl-N-(3,5-dioxo-10-oxa-4-aza-tricyclo[5.2.1.0^{2,6}]dec-4-yl)-acetamide

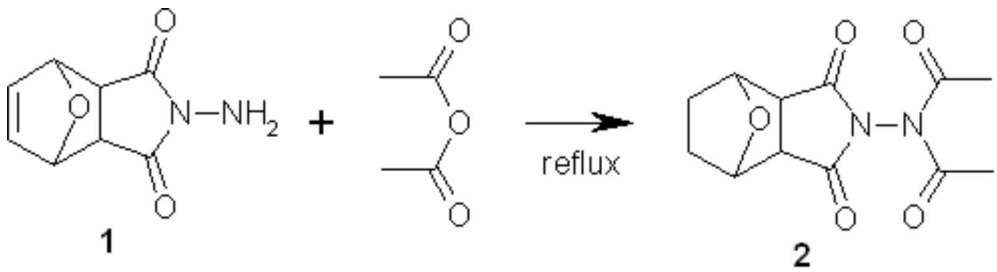
Marta Struga [1*], Jerzy Kossakowki [1], Barbara Mirosław [2], Anna E. Kozioł [2]

1 The Medical University, Department of Medical Chemistry, 3 Oczki Str., 02-007 Warsaw, Poland; Tel/Fax: (+4822)-628-06-79
2 Faculty of Chemistry, Maria Curie-Skłodowska University, 20-031 Lublin, Poland
* Author to whom correspondence should be addressed. E-mail: strugam@wp.pl

Received: 27 September 2006 / Accepted: 16 January 2007 / Published: 31 May 2007

Keywords: 4-amino-10-oxa-4-aza-tricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione, acylation

Various imide derivatives of 10-Oxa-4-aza-tricyclo[5.2.1.0^{2,6}]decane-3,5-dione have been reported and shown to exhibit a wide spectrum of biological activities including antitumor properties [1].



4-Amino-10-oxa-4-aza-tricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (1) was used as a starting material. This compound was obtained in Diels-Alder reaction of furan and furan-2,5-dione [2] and next treated with hydrazine (80% aqueous solution) [3]. Compound 2 was obtained in acylation reaction of compound 1. The reduction of compound 2 occurred during the acylation.

N-acetyl-N-(3,5-dioxo-10-oxa-4-aza-tricyclo[5.2.1.0^{2,6}]dec-4-yl)-acetamide (2).
0.01 Mole of the compound 1 and 10 ml of acetic anhydride were heated while boiling for 6h under reflux condenser. The reaction mixture was filtered off and the solvent was removed under a reduced pressure. The residue was crystallized from ethanol. Next it was purified by column chromatography (silica gel) using chloroform/methanol (19:1) as eluent.

White crystals, yield 78 %.

Melting point: 128 ºC.

^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 4.96 (s, 2H, CH-O); 3.1 (s, 2H, CH-C=O); 2.59 (s, 3H, CH_3); 2.11 (s, 3H, CH_3); 1.93 (m, 2H, CH_2); 1.68 (m, 2H, CH_2).

^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm): 174.3, 136.1, 79.8, 45.0, 38.8.

ESI MS: m/z = 289.2 $[M + Na]^+$ (100%).

Elemental Analysis: Calculated for C12H14N2O5 (266.25) calculated: C, 54.13 %; H, 5.30%; N, 10.52 %. Found: C, 54.18 %; H, 45.32 %; N, 10.72 %.

Crystal data for (2): $C_{12}H_{14}N_2O_5$, *M.W.* = 266.25, crystal system orthorhombic, space group *Pbca* with unit cell dimensions *a* = 6.977(1), *b* = 16.658(3), *c* = 21.361(4) A and *V* = 2482.6(7) A^{-3}; Z = 8, *d*(*calc*) = 1.425 g cm^{-3}, m= 0.952 mm^{-1}, F(000) = 1120.
Cis, exo configuration at the ring junction; the N,N-diacetyl fragment is planar with perpendicular orientation to the imid ring plane; the C=O bonds of acetyl groups are *anti.*

The diffraction data were collected at 275 K on a KM-4 diffractomater using the crystal of dimensions 0.22 ´ 0.15 ´ 0.11 mm and CuKa radiation. Within the q range of 5.3 to 72.2°, 2445 reflections were collected. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 (programs SHELXS97 and SHELXL97 [4, 5]). The refinement of 175 parameters converged at final *R* indices:
R_1 = 0.0311, wR_2 = 0.0889 (for 1039 observed reflections, *I* > 2s (*I*)) and R_1 = 0.1377, wR_2 = 0.1188 (all data), and Goof = 0.996. The extinction coefficient was 0.0032(3), residual electron density Dr (*max*) = 0.20 and Dr (*min*) = -0.18 e A^{-3}.

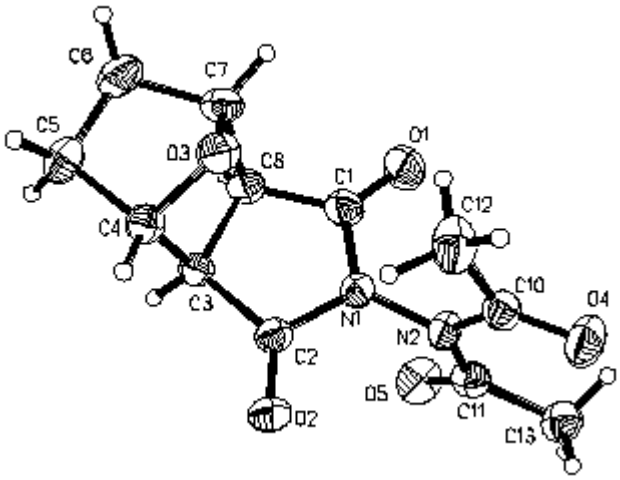


Figure 1. Perspective view of molecular structure of compound 2

N(1)-N(2)	1.383(2)	C(3)-C(4)	1.525(3)
N(1)-C(1)	1.393(3)	C(3)-C(8)	1.542(3)
N(1)-C(2)	1.396(3)	C(4)-C(5)	1.529(3)
N(2)-C(10)	1.416(2)	C(5)-C(6)	1.537(3)
N(2)-C(11)	1.420(3)	C(6)-C(7)	1.521(3)
O(1)-C(1)	1.205(3)	C(7)-C(8)	1.542(3)
O(2)-C(2)	1.201(2)	C(10)-C(12)	1.490(3)
O(3)-C(4)	1.440(2)	C(11)-C(13)	1.486(3)
O(3)-C(7)	1.442(3)	N(2)-N(1)-C(1)	122.5(2)
O(4)-C(10)	1.198(2)	N(2)-N(1)-C(2)	123.2(2)
O(5)-C(11)	1.199(2)	C(1)-N(1)-C(2)	114.0(2)
C(1)-C(8)	1.489(3)	C(1)-N(1)-N(2)-C(10)	93.2(2)
C(2)-C(3)	1.508(2)	C(2)-N(1)-N(2)-C(11)	90.6(2)

Table 1. Bond lengths (Å)

References:

1. Walter, W.G. *J. Pharm. Sci.* **1989**, *78*, 66.
2. Kwart, H.; Burchuk, J. *J. Am. Chem. Soc*. **1952**, *74*, 3094.
3. Struga, M.; Mirosław, B.; Wawrzyca-Gorczyca, I.; Kossakowski, J.; Kozioł, A.E. *Polish J. Chem.* **2007**, *81*, 51.
4. G.M. Sheldrick, SHELXS-93: Program for crystal structure solution; University of Göttingen, Germany, 1993.
5. G.M. Sheldrick, SHELXL-97: Program for the refinement of crystal structures from diffraction data; University of Göttingen, Germany, 1997.