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Structure Determination of 2,2-Diallyl-3-(3-methylureido)-1-propanol, an Unusual Product of Sodium Borohydride Reduction of Barbituric Acids

Marjatta Rautio**), Antti Hesso^{b)} and Erkki Rahkamaa^{c)}

^{a)} Department of Pharmaceutical Chemistry, University of Helsinki, Fabianink. 35, SF-00170 Helsinki 17, ^{b)} Institute of Occupational Health, Haartmanink. 1, SF-00290 Helsinki 29 and ^{c)} Department of Chemistry, University of Helsinki, Vuorikatu 20, SF-00100 Helsinki 10. Eingegangen am 13. Oktober 1980

Sodium borohydride reduces the imide carbonyl groups of 5,5-diallyl-1-methyl-barbituric acid (1) at position 4 to a methylene group and at position 6 to a primary hydroxy group which has been verified by analysis of the high resolution ¹H-NMR and mass spectra of the product 3.

Strukturaufklärung von 2,2-Diallyl-3-(3-methylureido)-1-propanol, einem ungewöhnlichen Produkt der Natriumborhydridreduktion der Barbitursäuren

Natriumborhydrid reduziert die Imidocarbonylgruppe der 5,5-Diallyl-1-methyl-barbitursäure (1) in 4-Stellung zur Methylengruppe und in 6-Stellung zu einer primären Hydroxylgruppe. Die Struktur des Reduktionsproduktes 3 wurde durch Auswertung der ¹H-NMR und Massenspektren sichergestellt.

Reduction of 5,5-diallyl-1-methyl-2,4,6-(1H,3H,5H)-pyrimidinetrione (1) with sodium borohydride in absol. methanol or dioxane-water was found to lead to the formation of four different closed-ring hydroxy compounds, a propanediol derivative, methylurea and one minor product (1%)¹). The IR spectrum of the minor product showed characteristics of an open-chain amide (1670–1650 and 1590–1570 cm⁻¹) with an alcoholic hydroxyl group (3480–3380 and 1080–1050 cm⁻¹). In this report we present results from high resolution mass spectrometry and 100 MHz ¹H-NMR spectrometry which establish structure 3, 2,2-diallyl-3-(3-methylureido)-1-propanol, for the minor product.



The hydrogenolytic formation of primary alcohols from cyclic imides has been explained to be the result of a tautomeric equilibrium between the hydroxylactam and the ring-opened aldehyde. In the presence of sodium borohydride the aldehyde will subsequently be reduced to a primary $alcohol^{2}$.

Reduction of amides to amines with sodium borohydride has previously been found to be successful only in refluxing pyridine³⁾. However, compound **3** was found to be formed in absol. methanol and in dioxane-water. In the present reduction the imide carbonyl group has already been reduced to the hydroxyl group. Further reduction of the latter may take place through 1,2 elimination of water and subsequent reduction of the imine bond thus formed.

Compound 2, with the hydroxyl groups in *trans* position, was isolated in pure form and used for further reduction. After 4 h (TLC) all of 2 had been consumed. In addition to the reduction to 3 (approximately 25% yield), 2,2-diallyl-1,3-propanediol and methylurea, isomerization to the *cis*-dihydroxy compound also occurred⁴).

Interpretation of the ¹H-NMR spectra was complicated by the existence of three labile protons in the molecule, whose chemical shifts were strongly dependent on solvent, temperature and concentration (cf. Table 1).



Table 1: ¹*H* chemical shifts (in ppm relative to TMS) and *H*-*H* coupling constants of **3** in $CDCl_3$ at room temp. and $(CD_3)_2SO$ at 58°C.

	δ (ppm)			J (Hz)	
	CDCl ₃	(CD ₃) ₂ SO		CDCI 3	(CD ₃) ₂ SO
H1	3.266	3.064	H10H	7.0	5.4
ОН	4.286	5.97	H3H4	6.7	6.2
H3	3.097	2.928	H6H7	4.9	5.0
H4	4.46	4.625	AB	2.1	2.1
H6	4.49	3.857	AC	16.0	17.0
H7	2.782	2.587	AD	1.0	1.4
H8D	1.892	1.906	AE	1.0	
H8E	2.075	1.906	BC	11.0	10.0
H9C	5.846	5.822	BD	0.8	1.0
H10A	5.088	5.025	BE	0.8	
H10B	5.103	5.034	CD	7.7	7.6
			CE	7.2	7.6
			DE	13.7	-

The most characteristic spectrum in $CDCl_3$ was obtained at room temperature from a highly diluted solution. In this spectrum the resonances of the CH_2 -OH group appear as a doublet and a triplet of 7.0 Hz, whereas in a more concentrated sample the signals were merged to singlets. In dilute solution signals of the two NH protons are superimposed to a broad signal at the low field side of the OH triplet. The methylene and methyl protons adjacent to the NH groups are doublets of 6.7 and 4.9 Hz, respectively.

In $(CD_3)_2$ SO the NH protons appear as a triplet and a quartet, thereby verifying the suggested structure of the nitrogenous side chain. Additional evidence was gained from the use of D_2O , which caused the collapse of the three doublets to sharp singlets and the disappearance of the OH and NH proton resonances.

The presence of two identical allyl groups was evident from the integrals of the typical allylic resonance patterns, which agree with the spectra calculated from the parameters collected in Table 1. In CDCl₃ the methylene protons of the allyl groups show chemical nonequivalence, appearing as the AB part of an ABX spin system and having a 0.183 ppm difference in their chemical shifts. In $(CD_3)_2$ SO the allyl group appears as a doublet of 7.6 Hz, thus indicating the isochrony of these protons. In $(CD_3)_2$ SO the multiplet of the vinylic proton was superimposed on the broad resonance of the hydroxyl proton.

A complete high resolution 75 eV mass spectrum of 3 was recorded, using photoplate detection technique, in order to obtain the exact masses of the fragment ions. The molecular ion was present with low intensity at m/e 212 and showed an elemental

composition of $C_{11}H_{20}N_2O_2$ with an error of -1.6 millimass units (m.m.u.). The results of high resolution measurements of the primary fragments are collected in Scheme 1.



The molecule contains different functional groups and, accordingly, several heteroatoms. Thus the particular fragmentation pathway can be identified from fragment ions of known elemental composition even without the detection of metastable ions. The arrows in the scheme do not necessarily signify one-step reactions, since examination of normal fragment ions does not permit such a conclusion.

The molecule may lose any of the following radicals or neutral molecules in the primary fragmentation: CH_3^* , OH^* , CHO^* , CH_2O , CH_2OH^* , $NHCH_3^*$, $C_3H_6^*$, $C_3H_5^*$, CH_3NCO or CH_3NHCO^* . The base peak at m/e 87 is formed when the molecule expels the nitrogenous side chain which retains the charge. The ion at m/e 182 is formed in two different ways. The molecule may lose either CH_2O or NHCH_3, producing ions, which differ in their exact masses by only 23,8 m.m.u. The achieved resolution (5000) was not adequate to determine the exact masses of the two ions, and therefore the error is as high as 6.3 m.m.u. The ions at m/e 183 and 181 correspond to the losses of CHO^* and CH_2OH^* , respectively, with an error of 2.4 m.m.u. The ions at m/e 101, 87, 75, 60 and 58 contain two N-atoms, while the ions at m/e 108, 93, 79, 67, 41 and 39 contain only C and H. The peak at m/e 138 contains one oxygen atom as the only heteroatom, indicating the loss of the methylureido group. The peak at m/e 84 contains one nitrogen atom as the only heteroatom.

When the spectra were recorded at 16 and 20 eV electron energies the molecular ion was not found. The most abundant ions, at m/e 182 and 87, were of almost equal intensity. Therefore, chemical ionization with isobutane as the reagent gas was used to ascertain the molecular weight of 212 for 3. In this spectrum the protonated molecule appeared as the base peak at m/e 213.

The results from the ¹H-NMR and high resolution mass spectra unambiguously establish the suggested structure of **3** and signify the reduction of an imide carbonyl group to a methylene group with sodium borohydride.

Experimental

IR spectrum: Unicam SP 1000 IR spectrometer, a 20 % solution in chloroform. ¹*H-NMR spectra:* Jeol PS/PFT-100 spectrometer connected to an EC-100 computer, 5 mm o.d. tubes at room temp. in deuteriochloroform and at +58 °C in deuteriated dimethylsulfoxide. Concentrations were varied to obtain optimal separation of the lines. *16, 20 and 70 eV mass spectra:* Varian Mat 112S mass spectrometer connected to a 166 SS data system. Samples were introduced by a solid inlet probe at a source temp. of 100 °C. Cl spectra were recorded using isobutane as the reagent gas at 150 °C. *High resolution measurements and data acquisition:* Jeol JMS 01 SG-2 mass spectrometer using photoplate detection. A JEC 980 B data system with microphotodensitometer (JMA-2H) was used for reading of the photoplates.

2,2-Diallyl-3-(3-methylureido)-1-propanol (3)

1 was reduced with sodium borohydride in absol. methanol and the reduction products were separated on a silica gel column¹⁾. After repeated reductions pure **2** was reduced further in dioxane-water (4 : 1). Combined fractions of **3** were purified on preparative TLC and subsequent filtration of the methanolic solution through neutral Al₂O₃. Evaporation of the solvent left a slightly yellow residue which failed to crystallize from various solvents. IR (CHCl₃, 20 %): 3480–3380 (OH, NH), 1670–1650 and 1590–1570 (CONH) and 1080–1050 cm⁻¹ (OH). MS [IP 16 eV; m/e (% rel. int.)]:183(30), 182 (99), 181 (17), 170 (10), 150 (11), 112 (14), 108 (12), 101 (20), 93 (12), 87 (100), 75 (15). [IP 70 eV; m/e (% rel. int.)]: 212 (M, 2), 182 (65), 93 (32), 88 (30), 87 (100), 84 (52), 79 (39), 75 (75), 67 (37), 58 (60), 41 (81), 39 (39). [Cl, isobutane; m/e (% rel. int.)]: 214 (M + 2, 12), 213 (M + 1, 100), 182 (14), 101 (9), 87 (17), 79 (11), 75 (9). Mol. wt., found 212. 151, calc. for $C_{11}H_{20}N_2O_2$ 212. 152.

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