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A NEW SYNTHESIS AND CRYSTAL STRUCTURE OF N-(2-HYDROXYETHYL)SUCCINIMIDE

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Abstract - N-(2-Hydroxyethyl)succinimide was formed with 80 % yield in the reaction of 2-oxazolidinone with succinic anhydride at 210 °C instead of polyesteramides obtained from N-substituted 2-oxazolidinones. The identification based on the crystal structure determination.

INTRODUCTION

Several patents concerning the use and synthesis of N-(2-hydroxyethyl)succinimide have been reported during the past twenty years. N-Hydroxyalkylimides are generally important for polyesteramide manufacture.[1,2] N-(2-Hydroxyethyl)succinimide provides means for selective extraction of aromatic hydrocarbons.[3-6] It has also been patented as another starting material for polyester and cellulose acetate textile dyes.[7]

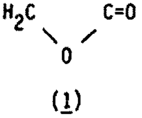
N-(2-Hydroxyethyl)succinimide may be synthesized with good yields from succinic anhydride and ethanolamine,[7,8] from succinic imide and ethylene carbonate,[9] and from succinic imide and ethylene oxide.[1] In the present paper we report, as far as we know, a new method to synthesize N-(2-hydroxyethyl)succinimide by the reaction of succinic anhydride with 2-oxazolidinone. The reaction product was identified by determining its crystal structure.

RESULTS AND DISCUSSION

Synthesis

2-Oxazolidinone (1) and its derivatives are reactive 5-membered ring compounds. The reactions of succinic and phtalic anhydrides with N-substituted 2-oxazolidinones give in the presence of a few mole per cent of LiCl polyesteramides of molecular weights up to 3500 with high yields.[10] The polymer yield corresponds to the CO_2 evolution indicating an equal consumption of oxazolidinone and anhydride.[10] 2-Oxazolidinones may be regarded as ethyleneimine derivatives due to their tendency to split off CO_2. Succinic anhydride reacts similarly with ethyleneimine giving polyamide product in acetone at 0 °C.[11]

However, as shown here, 2-oxazolidinone itself reacts with succinic anhydride in a different way. The reaction was conducted under optimum conditions for polyesteramide formation given by Burckhardt *et al.*[10] 2-Oxazolidinone and succinic anhydride were heated with 1 mol.-% of LiCl at 210 °C in an oil thermostat while nitrogen gas was conducted through the smelt to remove CO_2 liberated.[12] The evolution of CO_2 was followed by conducting the gases to a NaOH solution. Application of the method of Burckhardt *et al.* for the isolation of the expected polyesteramide (2) gave, however, no precipitate. Therefore, the following procedure was adapted: The cold reaction mixture, which was dark and viscous, was first treated with methanol (about 13 % remained unsoluble). After removal of the solvent the residue was further extracted with acetone (about 7 % remained unsoluble). Fractionation of the acetone extract gave a white product at 174-176 °C / 5 mm Hg with 80 % yield (mp. 59-50 °C after recrystallization from methanol). A molecular weight of 143 was obtained both osmometrically (benzene as a solvent) and ebulliometrically from methanol.



(1)

$$-(NH - CH_2 - CH_2 - O - CO - CH_2 - CH_2 - CO)_n-$$

(2)

In the acidic hydrolysis of this product (with 8-M HCl) succinic acid and monoethanolamine hydrochloride (mp. 81-82 °C) were isolated.[13] Ethanolamine was liberated from the salt with alkali

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*Crystal structure

and was isolated as a phenylisothiocyanate derivative (mp. 133-134 °C).[14] An alkaline hydrolysis with NaOH lead to the same products.

The minor reaction product, which was obtained with about 13 % yield on treating the crude mixture with methanol, was recrystallized from dichloroethane to a melting point of 153 °C. Ebulliometric molecular weight determination from chloroform gave 645. In the alkaline hydrolysis succinic acid was isolated, and a positive colour test with $CuSO_4$ was obtained for monoethanolamine.[15] Thus, for the minor product the polyesteramide structure (2) is possible.

The structure verification of the main product was, however, difficult with spectroscopic methods. The IR spectrum of the polyesteramide product, obtained from 3-phenyl-2-oxazolidinone and succinic anhydride, is shown in the paper of Burckhardt *et al.*, and it displays a relatively intense band ~ 1500 cm^{-1}. This band is known as the amide II band. It is a complex vibration attributed mainly to δ_{N-H} (bending in-plane) strongly coupled with ν_{C-N}. The absence of amide II band from the IR spectrum led us first consider a cyclic 8-membered lactam-lactone structure of correct atomic composition and molecular weight. The most intense peaks in the mass spectrum (see Experimental) could arise from fragmentations characteristic to lactams and lactones. Also the ^{1}H-NMR spectrum (Experimental) could be explained by this structure. A single carbonyl carbon absorption in the ^{13}C-NMR spectrum (Experimental) was, however, curious. The crystallographic analysis gave finally unambiguously the 5-ring structure of N-(2-hydroxyethyl)succinimide, which is also consistent with other experimental data.

Crystal structure

The final positional parameters and temperature factors are listed in Table 1, bond distances in Table 2, least-squares planes in Table 3 and torsional angles in Table 4. A PLUTO projection drawing of the molecule is shown in Figure 1.

Table 1. Positional and isotropic thermal parameters with their e.s.d.'s in parentheses.

Atom	x	Y	z	B(A2)
O2	-0.0576(3)	0.2759(3)	1.0833(6)	5.8(1)
O5	0.1011(3)	0.3879(4)	0.5580(7)	7.1(1)
O81	0.1192(5)	0.5084(6)	0.955(1)	4.8(2)
O82	0.0649(5)	0.4638(5)	1.184(1)	3.8(2)
N1	0.0384(3)	0.3321(3)	0.8429(6)	3.45(9)
C2	-0.0458(4)	0.3004(4)	0.9133(9)	3.9(1)
C3	-0.1156(4)	0.3007(4)	0.7497(9)	4.5(1)
C4	-0.0641(4)	0.3454(5)	0.5763(9)	4.9(1)
C5	0.0343(4)	0.3584(4)	0.6496(9)	4.5(1)
C6	0.1230(4)	0.3409(4)	0.9657(9)	4.4(1)
C7	0.1304(5)	0.4343(4)	1.0692(9)	5.4(2)
H31	-0.181(4)	0.341(5)	0.78(1)	6(2)*
H32	-0.144(5)	0.240(5)	0.72(1)	7(2)*
H41	-0.092(4)	0.415(5)	0.55(1)	6(2)*
H42	-0.058(4)	0.311(4)	0.444(9)	5(2)*
H61	0.173(4)	0.357(5)	0.860(9)	6(2)*
H62	0.119(5)	0.291(5)	1.06(1)	7(2)*
H71	0.209	0.438	1.125	4.0*
H81	0.043	0.500	0.959	4.0*
H82	0.063	0.438	1.332	4.0*

Starred atoms were refined isotropically. Anisotropically refined atoms are given in in the form of the isotropic equivalent displacement parameter defined as:
(4/3) * [a2*B(1,1) + b2*B(2,2) + c2*B(3,3) + ab(cos gamma)*B(1,2) + ac(cos beta)*B(1,3) + bc(cos alpha)*B(2,3)]

Table 2. Bond lengths (Å) and bond angles (°) with their e.s.d.'s in parentheses.

Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance	Atom 1	Atom 2	Distance
O2	C2	1.216(7)	N1	C5	1.365(7)	C4	H41	1.09(6)
O5	C5	1.217(8)	N1	C6	1.475(7)	C4	H42	1.03(6)
O81	C7	1.32(2)	C2	C3	1.493(8)	C6	C7	1.513(9)
O81	H81	1.097(8)	C3	C4	1.528(9)	C6	H61	1.04(6)
O82	C7	1.29(1)	C3	H31	1.11(7)	C6	H62	0.95(7)
O82	H82	1.074(8)	C3	H32	0.98(7)	C7	H71	1.186(8)
N1	C2	1.373(7)	C4	C5	1.504(9)			

Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle	Atom 1	Atom 2	Atom 3	Angle
C7	O81	H81	91.1(6)	C4	C3	H32	113(4)	N1	C6	H61	101(3)
C7	O82	H82	118.2(7)	H31	C3	H32	99(5)	N1	C6	H62	105(4)
C2	N1	C5	112.8(5)	C3	C4	C5	104.4(5)	C7	C6	H61	94(4)
C2	N1	C6	123.5(5)	C3	C4	H41	109(3)	C7	C6	H62	112(4)
C5	N1	C6	123.8(5)	C3	C4	H42	121(3)	H61	C6	H62	132(6)
O2	C2	N1	123.1(5)	C5	C4	H41	107(3)	O81	C7	O82	90.1(6)
O2	C2	C3	127.9(5)	C5	C4	H42	106(3)	O81	C7	C6	115.3(7)
N1	C2	C3	109.1(5)	H41	C4	H42	109(5)	O81	C7	H71	105.7(6)
C2	C3	C4	104.5(5)	O5	C5	N1	123.5(6)	O82	C7	C6	121.2(6)
C2	C3	H31	115(4)	O5	C5	C4	127.5(6)	O82	C7	H71	118.9(6)
C2	C3	H32	116(4)	N1	C5	C4	108.9(5)	C6	C7	H71	104.4(6)
C4	C3	H31	109(3)	N1	C6	C7	113.3(5)				

The 5-ring is unregular due to the presence of the heteroatom N(1) and the different surroundings of C(2) and C(5) from those of C(3) and C(4). The ring part of the molecule is nearly planar (Table 3) because of the sp^2-hybridized C(2) and C(5). However, it is possible to set a plane through N(1), C(2), C(3) and O(2) within e.s.d.'s and another through N(1), C(4), C(5) and O(5). According to the torsional angles the 5-ring has a half-chair conformation.[16] Also C(6) is in the plane N(1), C(2), C(3) and O(2) within e.s.d.'s. The ring bond lengths are slightly shorter than corresponding formal single bonds, and C(2) - O(2) and C(5) - O(5) are clearly double bonds (formal C=O 1.22 Å).[17]

Table 3. Least-squares planes
(x,y and z are ortogonal coordinates)
$0.2572x-0.9227y-0.2870z+5.8857=0$

	distance	e.s.d
	atoms in plane	
N(1)	0.004	0.004
C(2)	-0.025	0.005
C(3)	0.033	0.006
C(4)	-0.030	0.006
C(5)	0.018	0.006
	other atoms	
C(6)	-0.040	0.006
C(7)	-1.447	0.006
O(2)	-0.077	0.004
O(5)	0.052	0.005
O(81)	-2.244	0.008
O(82)	-2.301	0.007

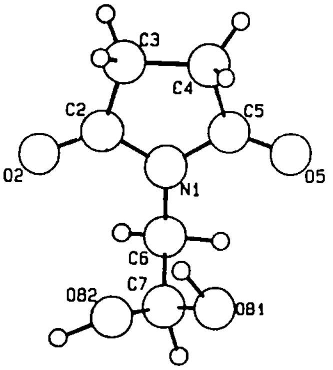

Figure 2. PLUTO plot of the molecular structure

Table 4. Torsional angles in degrees

C(5)	N(1)	C(2)	O(2)	-177.9(5)	C(5)	N(1)	C(6)	C(7)	88.9(6)
C(5)	N(1)	C(2)	C(3)	2.6(6)	O(2)	C(2)	C(3)	C(4)	175.5(5)
C(6)	N(1)	C(2)	O(2)	-0.7(8)	N(1)	C(2)	C(3)	C(4)	-5.0(6)
C(6)	N(1)	C(2)	C(3)	179.8(4)	C(2)	C(3)	C(4)	C(5)	5.4(6)
C(2)	N(1)	C(5)	O(5)	-179.5(5)	C(3)	C(4)	C(5)	O(5)	176.4(6)
C(2)	N(1)	C(5)	C(4)	1.0(6)	C(3)	C(4)	C(5)	N(1)	-4.1(6)
C(6)	N(1)	C(5)	O(5)	3.2(8)	N(1)	C(6)	C(7)	O(81)	-50.1(7)
C(6)	N(1)	C(5)	C(4)	-176.1(4)	N(1)	C(6)	C(7)	O(82)	56.6(8)
C(2)	N(1)	C(6)	C(7)	-88.0(6)					

The side-chain shows disorder in single crystals. There are two different positions for the OH-group in the molecular structure. A multiplicity of 0.5 was used for O(81) and O(82) in the refinement. The bond length O(81)-C(7) (1.32 A) or O(82)-C(7) (1.29 A) is shorter than a single C-O bond (formal C-O 1.43 A) but longer than a double bond (1.22 A). Because the thermal parameters are normal for these positions this disorder is rather static than dynamic free rotation.

The refined hydrogen atoms, H(31)...H(62), are as expected. When O(81) and O(82) were refined with the multiplicity of 0.5, H(72), H(81) and H(82) have a very low electron density. However, H(71), H(81) and H(82) were found from a difference Fourier electron density map. As C(7) is tetragonally (sp^3) hybridized C(7)-H(72) must be to the same direction with C(7)-O(81) or, alternatively, with C(7)-O(82).

There is an intermolecular hydrogen bond O(82)-H(82)···O(5) with an oxygen-oxygen distance of 2.808(8) A. The H(82)···O(5) distance is 1.776 A and the angle O(82)-H(82)···O(5) 159.7°. This hydrogen bond is, however, weak. The oxygen-oxygen distance is longer than the normal bond between ring carbonyl oxygen and alcohol oxygen (2.64 A), and also the angle differs from the right line by 20.3°.

EXPERIMENTAL

2-Oxazolidinone (mp. 88-89 °C) was prepared from dichloroethane, NH_3 and CO_2.[18] A Mechrolab Inc. Osmometer Model 301A was used for the molecular weight determination. Elementar analysis was performed with a F & M Analyzer Model 185: C 50.58 % (theor. 50.35 %), H 6.36 % (theor. 6.34 %), N 9.55 % (theor. 9.78 %).

Spectroscopic methods

The IR spectrum was recorded on a Perkin-Elmer 283 spectrometer (1 mg/188 mg KBr). ^{1}H- and ^{13}C-NMR spectra were obtained on a Perkin-Elmer R12B (60 MHz) and a JEOL FX 60 spectrometer, respectively. The ^{1}H-NMR shifts for 5 % d_6-acetone solution are: 2.69 ppm (s), 3.64 ppm (t, poorely resolved), and after the addition of 1-2 drops of d_5-pyridine the broad O-^{1}H absorption at ∿ 4.12 ppm with respect to internal TMS. The ^{13}C chemical shifts and ^{13}C-^{1}H coupling constants for 50 % solution are: C-2, C-5 178.6 ppm; C-3, C-4 28.7 ppm ($^1J_{C-H}$136.2 Hz, $^2J_{C-H}$4.1 Hz); C-6 41.5 ppm ($^1J_{C-H}$140.6 Hz), C-7 59.1 ppm ($^1J_{C-H}$144.0 Hz, $^2J_{C-H}$3.5 Hz).

The mass spectrum was taken at 70 eV on a Varian MAT-212 spectrometer connected to a Varian Model 3700 gas chromatograph (equipped with a quarz capillary column, 25 m x 0.32 I.D., with bonded SE 54 coating of 0.1 µm thickness). Mass spectral data were acquired and processed on a Spectro System MAT-188. The five most intense peaks appear at m/e values 100 (100, rel.int. %), 55 % (48.5), 113 (35), 56 (30.5) and 84 (30.5).

Crystallographic method

Colourless crystals for the X-ray structure determination were obtained by recrystallization from acetone. Data was collected on a Enraf-Nonius CAD-4 diffractometer and structure solved with computer programs MULTAN11/82[19], SDP[20] and PLUTO.[21] Conditions for data collection and crystal data are listed in Table 5.

Table 5. Crystal data and experimental parameters

crystal size	0.15x0.15x1 mm
number of reflections used for cell constants	25
space group	tetragonal; $P4_2/n$ (No.86)
cell parameters	a=14.292(2), b=14.299(1), c=6.783(3) Z=8, D_m=1.38 gcm^{-3}, D_x=1.372 gcm^{-3}, V=1386.1 A^3
radiation	MoKα (Graphit-Monochromator), λ=0.7107 A
data collection	$\theta<25^{\circ}$, ω-scan
range of hkl measured	$0\le h\le 17$ $0\le k\le 17$ $0\le l\le 8$
number of unique reflections	1212
number of refined reflections	504 $(I>3\sigma(I))$
temperature	22±1 °C
final R, R_w	0.049, 0.051
max. height of final reference map	0.2 e A^{-3}

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