BIS(HYDROXYALKYLATED) DERIVATIVES OF PARABANIC ACID

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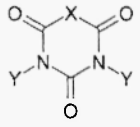
Abstract: Parabanic acid reacts with formaldehyde, ethylene oxide, and propylene oxide under mild conditions to give hydroxyalkylated derivatives. The products were isolated at high yield from the stoichiometric reaction mixtures. The N,N'-bis(hydroxymethyl)paraban-ate (**1**), N,N'-bis(hydroxyethyl)parabanate (**2**), and N,N'-bis(2-hydroxypropyl)parabanate (**3**) were identified on the basis of IR, ^{1}H , and ^{13}C NMR spectroscopy and X-ray crystallography for **3**. The isolated compounds are formed at preliminary stage of polyaddition reaction between parabanic acid and epoxides leading to parabanate-bonded polyethers.

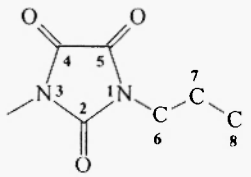
N-hydroxyalkylated derivatives of heteroaromatics like isocyanuric acid (X = N-H, Y = H) and parabanic acid (PBH_2, X = none, Y = H):



can be obtained by straight hydroxymethylation of free acids with formaldehyde or oxiranes, or by synthesis of *s*-triazene (or imidazolidine) ring from N-alkylated precursors (1,2). The polyetherols obtained in such procedures are useful substrates to obtain thermally resistant polyurethanes and polyesters (2,3). In the course of our systematic work on the subject we have focused on the synthesis of the low molecular weight products of addition of oxiranes to parabanic acid, i.e. bis(hydroxyalkylated) derivatives of parabanic acid (where X = none, Y =

Table 1. The ^{1}H, ^{13}C NMR, IR, and elemental analysis data for bis(hydroxyalkylated) derivatives of parabanic acid (N,N'-bis-YPB). Spectral assignments have been done by standard ^{1}H COSY, HMQC, and HMBC spectra obtained with Bruker Avance 500 MHz instrument. a – in DMSO-d_5, b – the posistion of $\nu_{C=O}$ [cm^{-1}] (PARAGON 1000 FT spectrophotometer, KBr), c – performed with Carlo-Erba Analyzer EA 1108. For atom numbering see the formula below Table.

Y	^{1}H NMR [a]	^{13}C NMR [a]	IR [b]	El.An.[c]	
				Calc.	Exp
$-CH_2OH$	6.67 ppm (1H, s, O*H*); 4.90 ppm (2H,s, CH_2)	154.1 ppm (C_2); 157.7 ppm ($C_{4,5}$); 62.3 ppm (C_6)	1780; 1753; 1714	C, 34.48 H, 3.45 N, 16.09	34.88 3.52 16.47
$-CH_2CH_2OH$	4.82 ppm (1H, t, C_7-O*H*, J = 6.3 Hz); 3.57 ppm (4H, m, C_6-H_2 + C_7-H_2)	155.2 ppm (C_2); 158.5 ppm ($C_{4,5}$); 42.1 ppm (C_6); 58.4 ppm (C_7)	1771; 1729	C, 41.58 H, 4.99 N, 13.86	41.47 5.02 13.64
$-CH_2CH(OH)CH_3$	4.80 ppm (1H, s, C_7-O*H*); 3.88 ppm (1H, m, C_7-*H*); 3.41 ppm (2H, C_6-H_2, AB system, J_{AB} = 13.9 Hz, ν_A = 3.38 ppm, ν_B = 3.45 ppm, J_{AC} = 4.9 Hz, J_{BC} = 7.8 Hz); 1.08 ppm (3H, d, C_8H_3, $J_{7,8}$ = 6.5 Hz)	155.3 ppm (C_2); 158.5 ppm ($C_{4,5}$); 46.0 ppm (C_6); 64.1 ppm (C_7); 21.3 ppm (C_8)	1768; 1741	C, 47,85 H, 6.00 N, 12.17	47.35 6.09 11.97



CH_2OH, CH_2CH_2OH, $CH_2CH(OH)CH_3$) (4). The N,N'-bis(hydroxymethyl)-parabanate (**1**), N,N'-bis(2-hydroxyethyl)parabanate (**2**), and N,N'-bis(2-hydroxypropyl)parabanate (**3**) have been isolated in pure form in good yields: 95%, 90%, and 80%, respectively. Whereas **1** can be obtained by simple stoichiometric reaction between formaline and PBH_2 at room temperature within 8 minutes (4), the respective oxiranes react with PBH_2 at 40° C within 12-15 hours in the presence of triethylamine (TEA) catalyst (5). The compounds have been identified by elemental analysis, the ^1H and ^{13}C NMR, and IR measurements (see Table 1). The $\nu_{(C=O)}$ stretching vibration bands of PBH_2 (1768, 1741 cm^{-1}) (6) shift slightly upon hydroxyalkylation indicating that substitution on nitrogen takes place. In the case of **3** regioselective oxirane ring opening is observed. The (*R*,*S*)-, (*S*,*S*)-, and (*R*,*R*)-**3** are formed in statistical 50% : 25% : 25% proportions, as can be estimated from X-ray crystallographic measurement performed for crystals obtained by recrystallization of crude product from butanol-heptane solvent mixture with 80% final yield. The diastereoisomers are not distinguishable by NMR. The molecular structure of **3** is presented in Figure 1.

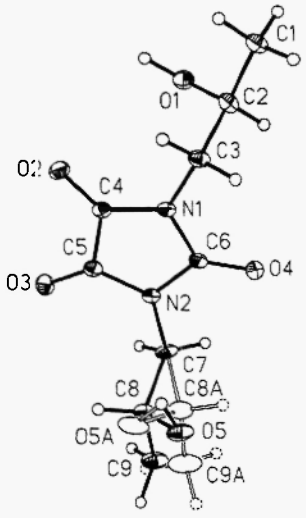


Fig.1. Molecular structure of **3** with crystallographic numbering. Selected bond lengths (Å): N(1)-C(3) 1.458(2); N(1)-C(4) 1.356(2); N(1)-C(6) 1.404(2); O(2)-C(4) 1.213(2); O(4)-C(6) 1.194(2) (for details see Table 2 and ref. 7-9).

There are four molecules of **3** in the unit cell. The hydrogen atoms attached to O5 and O5A lie at common position for both the *R* and *S* configurations at C8 (C8A). The conformations around C2-C3 and C7-C8(C8A) are antiperiplanar similarly to those found in N-propylparabanate and

Table 2. Crystal data and structure refinement for **3**.

Empirical formula	C9 H14 N2 O5
Formula weight	230.22
T /K	100(2)
λ /Å	0.71073
Crystal system	Monoclinic
Space group	$P2_1/n$
a /Å	13.448(3)
b /Å	6.0200(10)
c /Å	13.939(3)
β /°	95.38(3)
V /Å^3	1123.5(4)
Z	4
D_c /Mg·m^{-3}	1.361
μ /mm^{-1}	0.112
F(000)	488
Crystal size /mm	0.22 × 0.17 × 0.15
θ range for data collection /°	3.69 - 28.44
Ranges of *h,k,l*	-17→17, -8→5, -17→18
Reflections collected	7179
Independent reflections (R_{int})	2598 (0.0272)
Data/parameters	2598/224
GOF(F^2)	1.143
Final R_1/wR_2 indices ($I>2\sigma_I$)	0.0519/0.1056
Largest diff. peak/hole /e· Å^{-3}	0.370/-0.235

N-methyl,N'-(2-phenylethyl)parabanate (10). The N1-C3 (N2-C7) bond distances are analogous to those in other mentioned derivatives. In all cases N-alkylation resulted in elongation of N1-C6 distances from 0.008 Å (for mono-N-alkylated derivative) to 0,077 Å for **3** and shortening of C6-O4 bond (0.018 Å for **3** and 0.028 Å for N-methyl,N'-(2-phenyl)ethylparabanate) in comparison with parabanic acid (11).

From the obtained results it can be concluded that no enantioselectivity of addition of the second propylene oxide to N-(2-hydroxypropyl)parabanate occurs; the final mixture is composed of statistical (*R,R*), (*S,S*), and (*R,S*) bis(hydroxyalkylated) diastereoisomers of **3**. Identified bis(hydroxymethylated derivatives of parabanic acid are intermediates in the condensation of parabanic acid with excessive equivalents of oxiranes leading to formation of parabanate-based polymers studied by us recently (1).

Acknowledgment

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(5) The reaction has been performed in sealed ampule at the scale of 0.05 mol PBH_2, 0.1, mol oxirane, and 0.03-0.06 mol TEA. Racemic propylene oxide has been used.

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(7) Crystal data are given in Table 2, together with refinement details. All measurements of crystal were performed in low temperature using an Oxford Cryosystem device on a Kuma KM4CCD κ-axis diffractometer with graphite-monochromated MoKα radiation. The crystal was positioned at 65 mm from the CCD camera. 612 frames were measured at 0.75° intervals with a counting time of 20 sec. Accurate cell parameters were determined and refined by least-squares fit of 2700 the strongest reflections. The data were corrected for Lorentz and polarization effects. No absorption correction was applied. Data reduction and analysis were carried out with the Oxford Diffraction (Poland) Sp. z o.o (formerly Kuma Diffraction Wrocław, Poland) programs. The structure was solved by direct methods (program SHELXS97) and refined by the full-matrix least-squares method on all F^2 data using the SHELXL97 programs (8,9). Non-hydrogen atoms were refined with anisotropic displacement parameters; hydrogen atoms were included from geometry of molecules and Δρ maps. Part of hydrogen atoms were refined with isotropic displacement parameters and remaining hydrogen atoms (bonded to C7, C8A and C9A) were fixed. Molecules are partly disordered. The occupancy factor (o.f.) of the C8, C9 and O5 atoms is equal 0.55. The hydrogen atom H5O (o.f.=1) is a common for both disordered components (the O5-H5O and O5A-H5O groups).
Crystallographic data for the structure reported in this paper have been deposited with the CCDC, 12 Union Road, Cambridge 1EZ. U.K. and are available on quoting the deposition number: CCDC - 185542 for compound **3**.

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