SYNTHESIS OF β-D-GLUCOPYRANOSYLEPOXYETHANE

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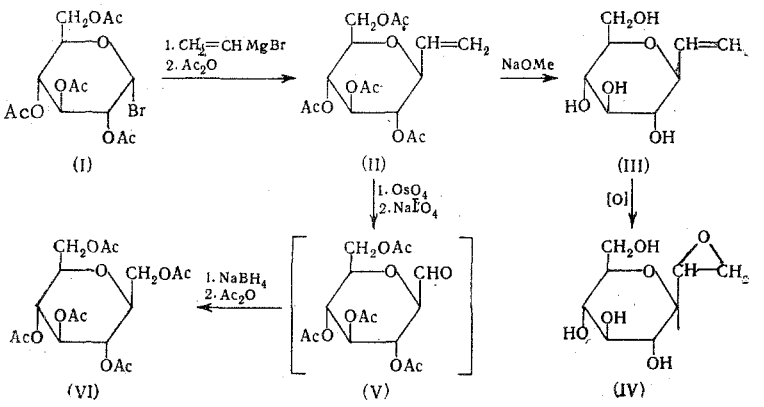
UDC 542.91:547.455

To study the catalytic groupings of glycosidase it has been proposed to use several substratelike inhibitors, which are capable of being irreversibly bound on the active center of the enzyme [1-3]. In a search for new inhibitors of this type we synthesized β-D-glucopyranosylepoxyethane (IV)



2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosylethene (II) was obtained previously by the reaction of acetobromoglucose (I) with vinylmagnesium bromide [4], but the configuration of the C-glycoside linkage in (II) was not proved. We found that a mixture of products is formed as a reaction result, from which compound (II) was isolated in 30% yield. The structure of compound (II) was proved in the following manner: the successive oxidation of (II) by treatment with OsO_4 and $NaIO_4$ led to aldehyde (V), which after reduction and acetylation gave the optically inactive acetate (VI). The latter proved to be identical with 1,3,4,-5,7-penta-O-acetyl-2,6-anhydro-D-glycero-D-guloheptitol (VI) [5].

The deacetylation of (II) led to β-D-glucopyranosylethene (III). The vinyl group in (III) exhibited a low reactivity in the epoxidation reaction; the optimum results were obtained by the oxidation of (III) with excess monoperphthalic acid in CH_3CN. The obtained β-D-glucopyranosylepoxyethane (IV) is apparently a mixture of diastereomers.

EXPERIMENTAL METHOD

The solvents were evaporated in vacuo at 45°C. The TLC (KSK silica gel, 200-250 mesh, 10% gypsum) was run in the solvent systems: ether–petroleum ether 4:1 (A), and $CHCl_3$–Me_2CO–MeOH 11:11:3 (B); the compounds were detected with concentrated H_2SO_4 at 150°. The paper chromatography on Whatman No. 1 was run in the system: Me_2CO–n-C_4H_9OH–H_2O, 14:3:2 (C); the compounds were detected with alkaline $AgNO_3$. The preparative chromatography was run on SiO_2 (100-150 mesh). The melting points (corrected) were determined on a Boetius apparatus, while the optical rotation was determined on a Perkin–Elmer 141-M polarimeter. The IR spectra were recorded on a Perkin–Elmer 257 spectrophotometer. The NMR spectrum was taken in $CDCl_3$ on a JNM-4H-100 instrument.

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Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 10, pp. 2386-2387, October, 1973. Original article submitted April 12, 1973.

2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosylethene (II). A solution of 16 g of acetobromoglucose (I) in 150 ml of absolute THF was added to a solution of Normant reagent (from 60 ml of vinyl bromide and 19 g of Mg) in 100 ml of absolute THF in 2 h at 40-50°, the mixture was stirred under gentle reflux for 5 h, cooled, and treated with 250 ml of 20% HCl solution. The aqueous layer was separated and, after extraction with ether (3 × 100 ml), was evaporated to dryness. The residue was acetylated with 250 ml of acetic anhydride and 15 g of NaOAc for 3 h at 100°, poured over ice, extracted with $CHCl_3$, washed in succession with $KHCO_3$ solution and water, evaporated, and chromatographed, using gradient elution with the mixture: petroleum ether→ether. Recrystallization of the chromatographically homogeneous sirup (ether–petroleum ether) gave 4.3 g (30% yield) of (II); mp 102.5-103°; $[\alpha]_D^{20}$ + 14° (C 1.0, $CHCl_3$); R_f 0.5 (system A); see [4]. Infrared spectrum: (ν, cm^{-1}): 908, 985 ($CH=CH_2$, def), 1650 (C=C, stretch), 1750 (OAc), 3000 ($CH_2=CH_2$ stretch). NMR spectrum: δ 5.15 ppm, multiplet of ABC type ($CH=CH_2$). The mass spectrum contains a peak that corresponds to the molecular ion (m/e 358). Found: C 53.79; H 6.06%. $C_{16}H_{22}O_9$. Calculated: C 53.59; H 6.14%.

1,3,4,5,7-Penta-O-acetyl-2,6-anhydro-D-glycero-D-guloheptitol (VI). To a solution of 270 mg of (II) in 10 ml of dioxane was added 6 ml of 1% aqueous OsO_4 solution, and after 15 min 400 mg of $NaIO_4$ was added, and the mixture was stirred for 1.5 h, extracted with $CHCl_3$ (3 × 10 ml), and the extracts were evaporated to dryness. A solution of the residue in 10 ml of alcohol was stirred for a day with 60 mg of $NaBH_4$, the filtrate was treated with Amberlite MB-6, evaporated to dryness, and the residue was acetylated with 0.5 ml of acetic anhydride in 2 ml of pyridine and then chromatographed the same as (II). The obtained sirup was recrystallized from i-C_3H_7OH to give 75 mg of (VI); mp 95.5-96.5°; $[\alpha]_D^{20}$ 0° ± 0.2° (C 1.0, $CHCl_3$); R_f 0.3 (system A). Found: C 50.70; H 6.23%. $C_{17}H_{24}O_{11}$. Calculated: C 50.49; H 5.98%.

Compound (VI), obtained as described in [5], had a double melting point: 87-88° and 96-97° (from [5]: mp 89°). The mixed melting point was 96-97°. Both specimens had identical IR spectra.

β-D-Glucopyranosylethene (III). To a solution of 2.1 g of (II) in 50 ml of absolute methanol was added 2 ml of 1 N NaOMe in MeOH, and after 2 h the mixture was treated with Dowex-50 (H^+ form) and evaporated to dryness. We obtained 1.05 g (92%) of (III) as a chromatographically homogeneous sirup; $[\alpha]_D^{20}$ + 30° (C 1.0, MeOH); R_f 0.5 (system B); R_{Glc} 2.0 (system C). Infrared spectrum (ν, cm^{-1}): 930, 1010 ($CH=CH_2$, def), 1650 (C=C, stretch), 3400 (OH). Found: C 50.24; H 7.65%. $C_8H_{14}O_5$. Calculated: C 50.52; H 7.42%.

β-D-Glucopyranosylepoxyethane (IV). To 100 mg of (III) in 5 ml of absolute CH_3CN was added 600 mg of monoperphthalic acid and the suspension was stirred for 2-3 days (checked by TLC, system B). The precipitate was filtered and washed with 20-30 ml of CH_3CN. The filtrate was stirred with 1 g of $KHCO_3$ for 4 h, filtered, evaporated, and chromatographed, using system B for elution. We obtained 54 mg (50%) of (IV) as a chromatographically homogeneous sirup; $[\alpha]_D^{20}$ −8° (C 1.0, MeOH); R_f 0.42 (system B); R_{Glc} 1.6 (system C). Infrared spectrum: 1255 cm^{-1} (α-oxide ring). Found: C 46.40; H 6.61%. $C_8H_{14}O_6$. Calculated: C 46.60; H 6.84%.

A solution of (IV) in 0.1 N $Na_2S_2O_3$ solution becomes alkaline (to phenolphthalein) after several minutes [6].

CONCLUSIONS

β-D-Glucopyranosylepoxyethane, a potential irreversible inhibitor of β-glucosidase, was synthesized.

LITERATURE CITED

1. G. Legler, Biochim. Biophys. Acta, 151, 728 (1968).
2. E. W. Thomas, Carbohydrate Res., 13, 225 (1970).
3. J. Yariv, K. J. Wilson, J. Hildesheim, and S. Blumberg, FEBS Letters, 15, 24 (1971).
4. Yu. A. Zhdanov, G. A. Korol'chenko, L. A. Kubasskaya, and R. M. Krivoruchko, Dokl. Akad. Nauk SSSR, 129, 1049 (1959).
5. B. Coxon and H. G. Fletcher, J. Am. Chem. Soc., 85, 2637 (1963).
6. W. C. J. Ross, J. Chem. Soc., 2257 (1950).