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LETTERS TO THE EDITOR

Synthetic Approach to β-Cyclodextrin Derivatives

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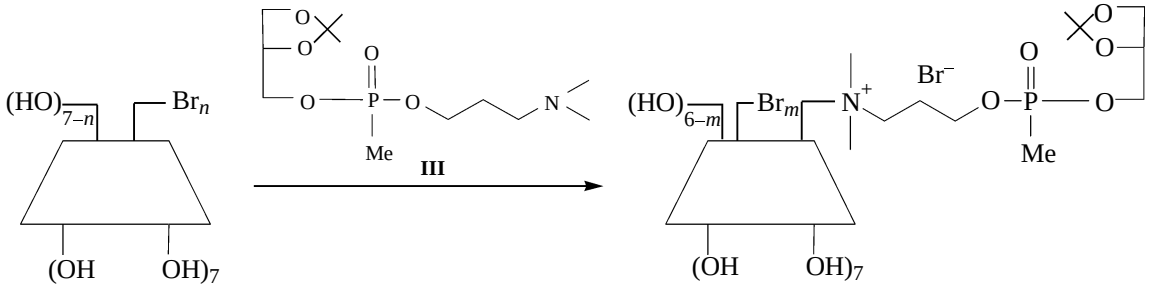
Previously we showed [1] a fundamental possibility of preparing 6-bromo-6-deoxy-β-cyclodextrins containing a preset number of bromine atoms (n = 1–7). Due to their alkylating ability toward organic amines, these derivatives attract special attention as starting materials for synthesis of alkylammonium (cationic) cyclodextrin derivatives that present some practical interest [2, 3]. Here we report on the synthesis of cationic derivatives of β-cyclodextrins containing a 1,2-*O*,*O*-isopropylideneglyceromethylphosphonate residue from 6-bromo-6-deoxy-β-cyclodextrins with an average bromine content (n) of n = 1 (compound **I**) and n = 2.9 (compound **II**). Such compounds are important intermediates for subsequent synthesis of complex glycerophospholipid analogs containing a cationic β-cyclodextrin fragment.

To this end, we reacted β-cyclodextrin bromides **I** and **II** [1] with 3 equiv of methylphosphonate **III** prepared from methylphosphonic dichloride, 1,2-*O*,*O*-isopropylideneglycerol, and 3-(*N*,*N*-dimethylamino)-propan-1-ol.



I, II **IV, V**

n = 1 (**I**), 2.9 (**II**): m = 0 (**IV**), 1.9 (**V**).

It is important that under these conditions only 1 equiv of compound **III** was alkylated to form compounds **IV** and **V**. At the same time, no reaction between equimolar amounts of bromo derivative **II** and methylphosphonate III took place under the same conditions probably because the bromine atom in derivative **II** is shielded and (or) reagent **III** is incorporated into the cyclodextrin cavity. Note that an analogous specific supramolecular effect of the cyclodextrin cavity on reaction pathway is a characteristic feature of cyclodextrin and their derivatives [2, 4].

(6-Bromo)$_m$-(6-deoxy)$_m$-6-{3-[2,3-(isopropylidenedioxy)propoxy]methylphosphoryloxy]propyl}-dimethylammonio-β-cyclodextrin bromide (IV), (m = 0). To a suspension of 0.1 g of bromodeoxy derivative **I** in 2 ml of DMF, 0.074 g of 3-(*N*,*N*-dimethylamino)propyl 2,3-(isopropylidenedioxy)propyl methylphosphonate (**III**) in 0.7 ml of DMF was added. The reaction mixture was stirred for 96 h at 20°C and then diluted with 5 ml of diethyl ether. The precipitate obtained was filtered off, washed with diethyl ether, and dried in a vacuum (1 mm) for 9 h at 50°C. Yield

0.0923 g (74%), mp 232–234°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.28 s (3H, $OCCH_3$), 1.32 s (3H, $OCCH_3$), 1.46 d (3H, PCH_3, $^2J_{PH}$ 17.26), 1.79 m (2H, CH_2CH_2N), 2.71 m (2H, CH_2N), 3.29 s (6H, NCH_3), 3.33–3.63 m (42H, C^2H–C^5H, C^6H_2), 3.98 m (2H, $CHCH_2C$), 4.00 m (2H, $POCH_2CH_2$), 4.23 m (2H, $CHCH_2OP$), 4.36 m (1H, CH_2CHCH_2), 4.42 br.s (6H, C^6OH), 4.82 br.s (7H, C^1H), 5.73 m (14H, C^2OH, C^3OH). ^{31}P NMR spectrum (DMF), δ_P, ppm: 30.5. Found, %: C 43.50; H 6.29; P 2.10. $C_{54}H_{95}BrNO_{39}P$. Calculated, %: C 43.44; H 6.41; P 2.07.

(6-Bromo)$_m$-(6-deoxy)$_m$-6-{3-[2,3-(isopropylidenedioxy)propoxy]methylphosphoryloxy]propyl}-dimethylammonio-β-cyclodextrin bromide (V) (*m* = 1.9). Compound **V** (*m* = 1.9) was prepared analogously to compound **IV** from 0.1 g of bromodeoxy derivative **II** and 0.065 g of methylphosphonate **III**. Yield 0.0876 g (72%), mp 209–210°C (decomp.). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 1.29 s (3H, $OCCH_3$), 1.34 s (3H, $OCCH_3$), 1.47 d (3H, PCH_3, $^2J_{PH}$ 17.26), 1.91 m (2H, CH_2CH_2N), 2.81 m (2H, CH_2N), 3.21 s (6H, NCH_3), 3.31–3.64 m (42H, C^2H–C^5H, C^6H_2), 3.94 m (2H, $CHCH_2C$), 4.00 m (2H, $POCH_2CH_2$), 4.23 m (2H, $CHCH_2OP$), 4.36 m (1H, CH_2CHCH_2), 4.41 br.s (4H, C^6OH), 4.85 br.s (7H, C^1H), 5.6 m (14H, C^2OH, C^3OH). ^{31}P NMR spectrum (DMF), δ_P, ppm: 30.4. Found, %: C 40.10; H 5.34; P 1.88. $C_{54}H_{93}Br_{2.9}NO_{37}P$. Calculated, %: C 40.06; H 5.79; P 1.91.

The ^{1}H NMR spectra were taken on a Bruker AC-200 spectrometer (200 MHz), internal reference TMS. The ^{31}P–{^{1}H} NMR spectra were registered on a Bruker WR-80SY spectrometer (32.4 MHz), external reference 85% phosphoric acid.

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