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LETTERS TO THE EDITOR

Acylation of Per-6-*O*-(*tert*-butyl)(dimethyl)silyl-α-cyclodextrin with Acetylsalicylic Chloride

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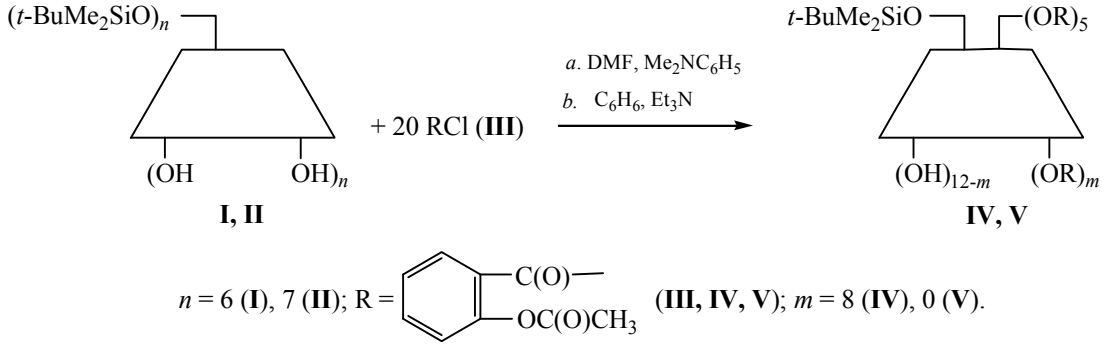
Earlier, aiming to synthesize the conjugates of α- and β-cyclodextrins containing drug residues at the cyclodextrin torus side occupied with secondary hydroxyl groups, we have performed acylation of per-6-*O*-(*tert*-butyl)(dimethyl)silyl derivatives of α- (**I**) and β-cyclodextrin (**II**) at the second hydroxyl groups with chloroanhydrides of a series of aromatic monocarpboxylic acids, followed removal of protecting silyl groups [1, 2]. Acylation of the silyl derivatives **I** and **II** occurred with good yields in pyridine as well as (in the case of compound **II)** in DMF in the presence of *N,N*-dimethylaniline (method *a*) or C_6H_6 (method *b*) in the presence of Et_3N, the amines acting as the formed hydrogen chloride scavengers (Scheme 1).

The trials to perform analogous acylation of the silyl derivative of α-cyclodextrin **I** with acetylsacicylic chloride **III** using the methods *a* and *b* unexpectedly led to the products of substitution of a substantial part of the protecting silyl groups with acetylsalicylic acid residues. From the ^{1}H NMR spectroscopy data, under the acylation conditions only one silyl group was preserved and eight (**IV**, m = 3, method *a*) or five (**V**, m = 0, method *b*) of the acetylsalicylic acid residues were attached to the cyclodextrin backbone.

Unexpected desilylation of the α-cyclodextrin derivative under the conditions of acylation with acyl chloride **III** using methods *a* and *b*, different from conventional acylation in pyridine [2], was apparently due to supramolecular effect of the inner cavity of α-cyclodextrin, as we have mentioned earlier discussing the silyl derivatives of cyclodextrins [3, 4].

Methods of acylation. *a*. A solution of 0.79 g of acyl chloride **III** in 4 mL DMF was added dropwise upon stirring at 0°C during 30 min to the solution of 0.33 g of the silyl derivative **I** and 0.53 g of *N,N*-dimethylaniline in 3 mL DMF. The mixture was incubated during 24 h at 20°C, then evaporated in vacuum (10 mmHg) to oily state; the residue was

Scheme 1.



washed with 10 mL diethyl ether, dried in vacuum, and thoroughly triturated with 10 mL of H_2O. The solid product was separated off and dried at 1 mm Hg and 80°C during 3 h. Yield of compound **IV** 0.324 g (68%), mp 144–146°C (decomp.), R_f 0.8. ^{1}H NMR ($CDCl_3$), δ, ppm: 0.03 s [6H, $Si(CH_3)_2$], 0.89 s [9H, $C(CH_3)_3$], 1.62–2.11 m [24H, $C(O)CH_3$], 2.80–4.51 m (36H, C^2H–C^6H), 4.96 m (6H, C^1H), 5.05–5.25 br.s (9H, C^2OH), 7.04–8.09 m (32H, C_6H_4). Found, %: C 57.53; H 5.10. $C_{114}H_{122}O_{54}Si$. Calculated, %: C 57.43; H 5.16.

b. The synthesis was performed as described in procedure *a*, from 0.33 g of the silyl derivative of **I**, 0.445 g Et_3N in 3 mL C_6H_6 and 0.79 g of acyl chloride **III** in 4 mL C_6H_6. The formed precipitate of triethylamine hydrochloride was filtered; the filtrate was evaporated to oil in vacuum, thoroughly triturated with 10 mL of diethyl ether, filtered off, and in vacuum. Yield of compound **V** 0.231 g (61%), mp 162–165°C (decomp.), R_f 0.7. ^{1}H NMR ($CDCl_3$), δ, ppm: 0.03 s [6H, $Si(CH_3)_2$], 0.90 s [9H, $C(CH_3)_3$], 2.11–2.30 m [15H, $C(O)CH_3$], 2.82–4.53 m (36H, C^2H–C^6H), 4.70 m (6H, C^1H), 5.01–5.21 br. s (12H, C^2OH), 7.04–7.93 m (32H, C_6H_4). Found, %: C 55.10; H 5.45. $C_{87}H_{104}O_{45}Si$. Calculated, %: C 55.06; H 5.52.

^{1}H NMR spectra were recorded using the Jeol-ECX400 spectrometer (400 MHz). TLC analysis was carried out on alumina plates Silufol UV-254 with fixed silica layer; eluent: 6% NH_3 in H_2O–BuOH–EtOH 5 : 4 : 5.

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