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SHORT COMMUNICATIONS

Esterification of 2,4-Dihydroxybenzoic Acid

L. G. Derkach, N. S. Novikova, and A. V. Mazepa

Bogatsky Physicochemical Institute, National Academy of Sciences of Ukraine,
Lyustdorfskaya doroga 86, Odessa, 65080 Ukraine
e-mail: nadyanovikova@rambler.ru; office.physchem@nas.gov

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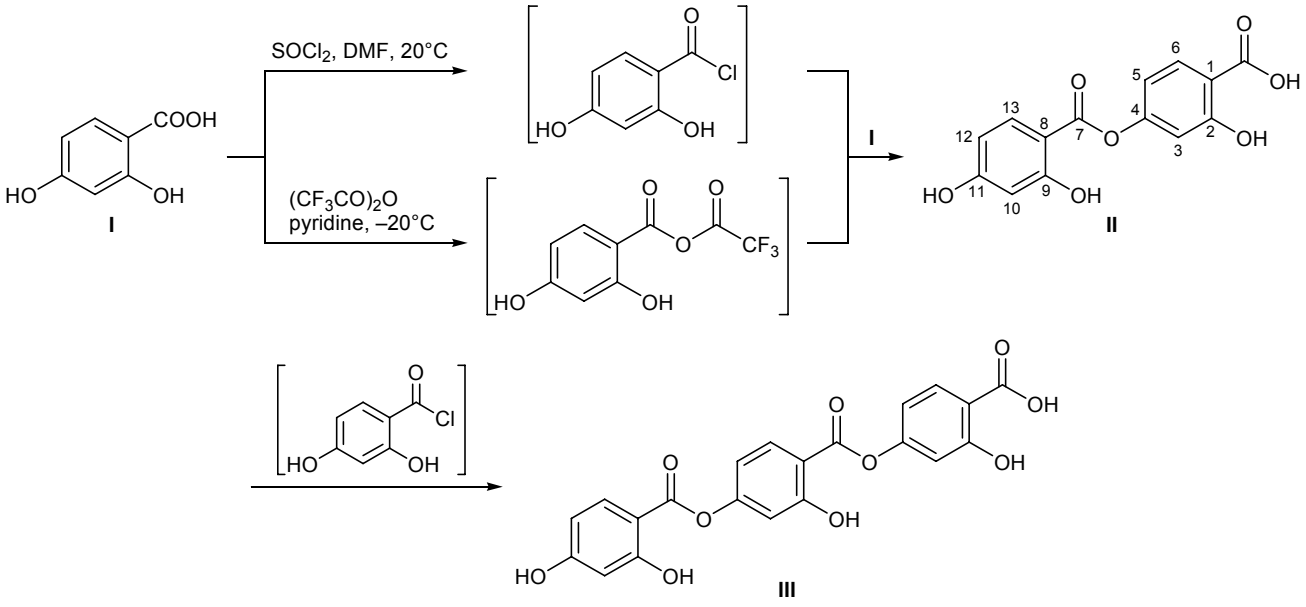
We previously synthesized methyl 4-[4-(4-hexadecyloxybenzoyloxy)benzoyloxy]-2-hydroxybenzoate whose coordination compound with terbium(III) chloride showed strong luminescence [1]. Initial methyl 2,4-dihydroxybenzoate was obtained by esterification in the presence of sulfuric acid [2]. When the reaction time was 12 h, the yield of the ester did not exceed 35% (after recrystallization). According to [3], the synthesis of ethyl and propyl 2,4-dihydroxybenzoates is even more difficult (reaction time 22 h).

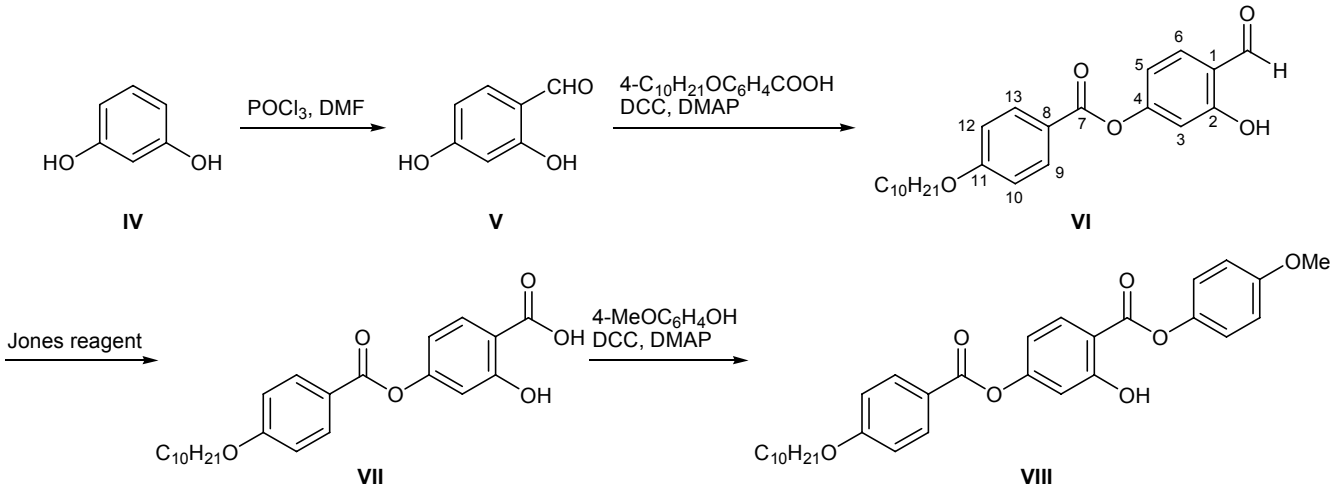
We tried to synthesize phenyl 2,4-dihydroxybenzoate through 2,4-dihydroxybenzoyl chloride which was reported in [4]. However, attempted reproduction of the procedure described in [4] resulted in the formation of a mixture of 4-(2,4-dihydroxybenzoyloxy)-2-hydroxybenzoic acid (**II**) and 4-[4-(2,4-dihydroxybenzoyloxy)-2-hydroxybenzoyloxy]-2-hydroxybenzoic acid (**III**, $[M]^+$ 425) (Scheme 1). Obviously, intermediate 2,4-dihydroxybenzoyl chloride acylates the initial acid and its acylation product **II** at the 4(4′)-hydroxy group. Variation of the reaction conditions showed that room temperature is optimum for the predominant formation of acid **II**. It was isolated, and its structure was confirmed by the 1H NMR and mass spectra.

We also tried to protect the hydroxy groups in **I** with trifluoroacetyl group to ensure carbodiimide esterification and subsequent deprotection under mild conditions. The reaction of 2,4-dihydroxybenzoic acid (**I**) with trifluoroacetic anhydride in pyridine at ~20°C produced a complex mixture of products which we failed to isolate and identify. When the reaction was

Scheme 1.



Scheme 2.



carried out at reduced temperature (–20°C), we isolated 2-hydroxy-4-(2,4-dihydroxybenzoyloxy)benzoic acid (**II**) which was identified by mass spectrometry and ^{1}H NMR. We presumed that the reaction involves intermediate formation of mixed 2,4-dihydroxybenzoic trifluoroacetic anhydride and subsequent acylation of the 4-hydroxy group (Scheme 1).

The synthesis of 4-methoxyphenyl 4-(4-decyloxybenzoyloxy)benzoate (**VIII**) by the carbodiimide method is illustrated by Scheme 2. 2,4-Dihydroxybenzaldehyde (**V**) was synthesized by the Vilsmeier formylation [5] of resorcinol (**IV**). Carbodiimide coupling of **V** with 4-decyloxybenzoic acid gave 4-(4-decyloxybenzoyloxy)-2-hydroxybenzaldehyde (**VI**) which was oxidized with the Jones reagent [6] to 2-hydroxy-4-(4-decyloxybenzoyloxy)benzoic acid (**VII**), and the subsequent carbodiimide esterification with 4-methoxyphenol afforded targeted ester **VIII**.

The structure of compounds **VI**–**VIII** was confirmed by their ^{1}H NMR and mass spectra. In the ^{1}H NMR spectrum of **VI**, the aldehyde proton signal resonated as a broadened singlet at δ 11.08 ppm, and the COOH signal of acid **VII** was a singlet at δ 11.25 ppm. Compound **VIII** displayed in the ^{1}H NMR spectrum a singlet at δ 3.86 ppm from the methoxy group, and signals from aromatic protons in the *ortho* positions with respect to the methoxy group were displaced upfield and overlapped by those belonging to other aromatic protons.

4-(2,4-Dihydroxybenzoyloxy)-2-hydroxybenzoic acid (II). *a*. Thionyl chloride, 24.8 g (0.21 mol), was added under stirring at 20°C to 3.08 g (0.02 mol) of 2,4-dihydroxybenzoic acid, 0.45 g (0.06 mol) of anhydrous dimethylformamide was then added dropwise, and the mixture was stirred for 3 h at 20°C. The yellow–green solid was filtered off, washed with anhydrous hexane (3×50 mL), and treated with boiling distilled water. After cooling, the precipitate was filtered off and dried. Yield 1.9 g (33%), mp 260°C.

b. A solution of 1.54 g (0.01 mol) of 2,4-dihydroxybenzoic acid in 20 mL of anhydrous pyridine was cooled to –20°C, 2.8 mL (0.02 mol) of trifluoroacetic anhydride cooled to 0°C was added dropwise under stirring, and the mixture was stirred for 0.5 h and poured onto crushed ice (150 mL). The precipitate was filtered off, repeatedly washed with distilled water, dried, and recrystallized from anhydrous benzene. Yield 1.56 g (54%), mp 257°C. ^{1}H NMR spectrum, δ, ppm: 6.20–7.20 m (4H, 3-H, 5-H, 10-H, 12-H), 7.70–8.40 m (2H, 6-H, 13-H), 10.10–11.86 m (4H, OH, COOH). Mass spectrum (EI), *m*/*z* (I_{rel}, %): 290 $[M]^+$, 154 (15.2), 138 (8.0), 137 (28.9), 136 (28.9), 110 (5.9), 108 (12.7), 81 (7.6), 80 (6.7), 79 (8.7), 53 (6.5), 52 (9.2), 51 (6.3). Found, %: C 57.79; H 3.59. $C_{14}H_{10}O_7$. Calculated, %: C 57.93; H 3.45.

4-(4-Decyloxybenzoyloxy)-2-hydroxybenzaldehyde (VI). 2,4-Dihydroxybenzaldehyde (**V**), 3.036 g (0.022 mol), was dissolved in 50 mL of anhydrous methylene chloride, 4.4 g (0.011 mol) of 4-decyloxybenzoic acid and 0.14 g (0.0011 mol) of 4-(dimethylamino)pyridine (DMAP) were added at room temperature, the mixture was stirred for 10 min, and 2.3 g (0.011 mol) of *N*,*N*′-dicyclohexylcarbodiimide (DCC) was added. The mixture was stirred for 25 h at room temperature, the precipitate was filtered off and washed with anhydrous methylene chloride, the solvent was removed under reduced pressure, and the residue was crystallized from ethanol–benzene (10:1).

Yield 2.0 g (46%), mp 85°C. ^{1}H NMR spectrum, δ, ppm: 0.86 t (3H, CH_3, ^3J = 6.75 Hz), 1.11–1.52 m (14H, CH_2), 1.63–1.86 m (2H, C**H**$_2$CH$_2$O), 4.09 t (2H, CH_2O, ^3J = 5.97 Hz), 6.77–7.04 m (2H, 3-H, 5-H), 7.12 d (2H, 10-H, 12-H, ^3J = 8.05 Hz), 7.75 d (1H, 6-H, ^3J = 8.30 Hz), 8.07 d (2H, 9-H, 13-H, ^3J = 8.56), 10.25 s (1H, CHO), 11.08 br.s (1H, OH). Mass spectrum (FAB), *m*/*z* (I_{rel}, %): 399 (5.0) [*M* + H]$^+$, 262 (14.7), 261 (100), 121 (47.3). Found, %: C 72.60; H 7.74. $C_{24}H_{30}O_5$. Calculated, %: C 72.36; H 7.54.

4-(4-Decyloxybenzoyloxy)-2-hydroxybenzoic acid (VII) was synthesized by oxidation of 0.4 g (1 mmol) of aldehyde **VI** with 2 mL of freshly prepared Jones reagent. The product was recrystallized from diethyl–ether–hexane (2:1). Yield 0.302 g (73%). Phase transition temperatures*: Cr→Sm 111.7, Sm→N 150.5, N→I 172.9°C. ^{1}H NMR spectrum, δ, ppm: 0.89 t (3H, CH_3, ^3J = 6.31 Hz), 1.10–1.65 m (14H, CH_2), 1.70–2.00 m (2H, C**H**$_2$CH$_2$O), 4.05 t (2H, CH_2O, ^3J = 5.49 Hz), 6.70–7.15 m (4H, 3-H, 5-H, 10-H, 12-H), 7.90–8.25 m (3H, 6-H, 9-H, 13-H), 10.57 s (1H, OH), 11.25 s (1H, COOH). Mass spectrum (FAB), *m*/*z* (I_{rel}, %): 415 (5.1) [*M* + H]$^+$, 262 (18.3), 261 (100), 259 (7.4), 123 (9.9), 122 (30.0), 121 (95.0), 109 (9.8), 108 (6.2), 107 (7.8), 106 (5.0), 97 (5.4), 93 (8.1), 92 (8.4), 91 (12.8). Found, %: C 69.78; H 7.44. $C_{24}H_{30}O_6$. Calculated, %: C 69.56; H 7.25.

4-Methoxyphenyl 4-(4-decyloxybenzoyloxy)-2-hydroxybenzoate (VIII). 4-(Dimethylamino)pyridine, 0.011 g (0.087 mmol), was added under stirring at room temperature to a mixture of 0.36 g (0.87 mmol) of acid **VII** and 0.108 g (0.87 mmol) of 4-methoxyphenol in 30 mL of anhydrous methylene chloride. The mixture was stirred for 0.25 h, 0.179 g (0.87 mmol) of *N*,*N*′-dicyclohexylcarbodiimide was added, and the mixture was stirred for 20 h at room temperature. The precipitate was filtered off, the filtrate was evaporated under reduced pressure, and the residue was washed with acetonitrile and dried. Yield 0.148 g (32%). Phase transition temperatures: Cr→N 74.8, N→I 112.0°C. ^{1}H NMR spectrum, δ, ppm: 0.91 t (3H, CH_3, ^3J = 6.31 Hz), 1.20–1.60 m (14H, CH_2), 1.76–1.95 m (2H, C**H**$_2$CH$_2$O), 3.86 s (3H, CH_3), 4.07 t (2H, CH_2O, ^3J = 5.49 Hz), 6.80–7.25 m (8H, H_{arom}), 8.05–8.25 m (3H, 6-H, 9-H, 13-H), 10.70 s (1H, OH). Mass spectrum (FAB), *m*/*z* (I_{rel}, %): 522 (6.3), 521 (18.1) [*M* + H]$^+$, 262 (12.0), 261 (67.7), 121 (100). Found, %: C 71.58; H 7.95. $C_{31}H_{36}O_7$. Calculated, %: C 71.69; H 6.92.

The electron impact (EI) mass spectra (70 eV) were recorded on an MKh-1321 spectrometer with direct sample admission into the ion source (220°C). The fast atom bombardment (FAB) mass spectra were obtained on a VG 70-70EQ instrument (xenon beam, 8 kV; *m*-nitrobenzyl alcohol and polypropylene glycol as matrix). The ^{1}H NMR spectra were measured from 5–10% solutions in $CDCl_3$ or DMSO-d_6 on a Bruker Avance DRX-500 spectrometer (500.13 MHz) using tetramethylsilane as internal reference.

* "Cr" stands for crystalline phase, "Sm" for smectic, "N" for nematic, and "I" for isotropic liquid.

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