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LETTERS TO THE EDITOR

Synthesis of 11-Amino-9,10-dihydro-9,10-ethanoanthracen-12-ylcarboxylic Acid

N. A. Anisimova, V. M. Berestovitskaya, and G. A. Berkova

Herzen Russian State Pedagogical University, Moika emb. 48, St. Petersburg, 191186 Russia
e-mail: kohrgpu@yandex.ru

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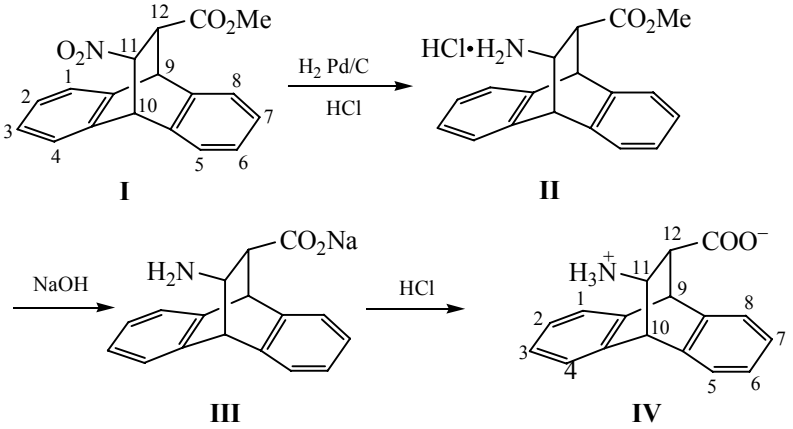
Modern organic chemistry is characterized by the successful development of scientific research aiming to obtain the synthetic analogs of the natural products with a wide range of biological activity. One among these trends is the synthesis of cyclic systems that serve as the natural compounds skeleton. For example, ethanoanthracene derivatives are parts of the toxic diterpenoids [1] and are of considerable interest for the synthesis of β-peptides [2], which can accommodate a compact conformations of the natural peptides.

According to the current literature data [3–5], β-peptides synthesized on the basis of the cyclic β-amino carboxylic acids can be considered as the potential pharmacologically active drugs. For this reason, the synthesis of β-aminocarboxylic acids containing the carbocycles is of obvious interest.

In the present work we performed the reduction of the nitro group of methyl 9,10-dihydro-11-nitro-9,10-ethanoanthracen-12-ylcarboxylate **I** [6] using an acidic palladium catalyst in methanol to produce the corresponding 11-amino-9,10-dihydro-9,10-ethano-anthracen-12-ylcarboxylate **II** followed by hydrolysis of the ester function.



I **II** **III** **IV**

The alkaline hydrolysis of hydrochloride **II** carried out by boiling in an aqueous sodium hydroxide solution for 24 h resulted in a sodium salt **III**. The acidification of the sodium salt with hydrochloric acid to pH 7 affords 11-amino-9,10-dihydro-9,10-ethano-anthracen-12-yl-carboxylic acid **IV**.

Note that in the patent literature there is a mention of the synthesis of esters of amino-9,10-dihydro-9,10-ethanoanthracenecarboxylates by the other method [7].

The composition of the obtained compounds **II**–**IV** was confirmed by the elemental analysis. Their

structures were established by the ^{1}H NMR and IR spectroscopy, and their characteristics were consistent with the relevant characteristics of the structurally similar compounds described in [6–8]. The ^{1}H NMR spectra of the obtained compounds **II**–**IV** contain the proton signals of all the structural fragments. The signals of aromatic protons H^{1-8} were observed in the range of 7.0–7.5 ppm as a broadened multiplet. The protons $H^{9,10}$ signals occur in the range of 4.70–4.94 ppm. The bridging protons $H^{11,12}$ resonate at 3.50–3.80 ppm.

It is known that amino acids have a zwitter-ionic structure [9]. In the spectrum of free amino acid **IV** the NH_3^+ group signal appears at 2.6–2.8 ppm, which is consistent with the published data [10, 11]. In our case, the zwitter-ionic structure was confirmed by the downfield shifting of the NH_3^+ proton signal to 8.30–8.40 ppm in ester hydrochloride **II**. A similar manifestation of the NH_3^+ proton in the amino acids hydrochlorides has been also noted in [12, 13].

In the IR spectrum of the resulting ester hydrochloride **II** the stretching vibrations of the NH_3^+ group are observed in the range of 3200–3350 cm^{-1}. In the spectrum of β-amino acid **IV** the stretching and bending vibrations of the NH_3^+ group give rise to broad absorption bands at 3100–3400 and 1630–1640 cm^{-1}, respectively. Characteristically, the absorption band of the carbonyl group of ester hydrochloride **II** appears at 1730 cm^{-1}. In the spectrum of acid **IV** the absorption band of the COO^- ionized group is observed at 1610 cm^{-1}. Thus, the IR and ^{1}H NMR spectral data allow a conclusion that acid **IV** has a bipolar ion structure.

Methyl 11-amino-9,10-dihydro-9,10-ethano-12-anthracenylcarboxylate acid (II). Yield 98%, R_f 0.54. ^{1}H NMR spectrum (CD_3OD), δ, ppm: 3.60 s (3H, CO_2CH_3), 3.70– 3.80 m (2H, $H^{11,12}$), 4.75–4.82 m (1H, H^9), 4.90–4.95 m (1H, H^{10}), 7.0–7.5 m (8H, H^{1-8}), 8.30–8.40 m (3H, NH_3^+). Found, %: C 68.34, 68.36; H 5.74, 5.77; N 4.56, 4.58. $C_{18}H_{18}NO_2Cl$. Calculated, %: C 68.46; H 5.71; N 4.44.

11-Amino-9,10-dihydro-9,10-ethano-12-anthracenylcarboxylic acid sodium salt (III). Yield 87%, mp > 300°C. ^{1}H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 3.50–3.62 m (2H, $H^{11,12}$), 4.70–4.80 m (1H, H^9), 4.90–4.98 m (1H, H^{10}), 7.10–7.45 m (8H, H^{1-8}). Found, %: N 4.83, 4.86. $C_{17}H_{15}NO_2Na$. Calculated, %: N 4.88.

11-Amino-9,10-dihydro-9,10-ethano-12-anthracenylcarboxylic acid (IV). Yield 95%, mp 140–142°C. ^{1}H NMR spectrum [$(CD_3)_2SO$], δ, ppm: 2.60–2.80 m (3H, NH_3), 3.50–3.60 m (2H, $H^{11,12}$), 4.70–4.80 m (1H, H^9), 4.90–4.95 m (1H, H^{10}), 7.0–7.5 m (8H, H^{1-8}). Found, %: C 76.93, 76.95; H 5.60, 5.63; N 5.34, 5.36. $C_{17}H_{16}NO_2$. Calculated, %: C 76.98; H 5.66; N 5.28.

The ^{1}H NMR spectra were taken on a Bruker AC-200 spectrometer (200 MHz) relative to external HMDS with accuracy of up to ±0.5 Hz. The IR spectra were registered on a InfraLUM FT-02 spectrometer for the samples in chloroform or mineral oil.

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