SYNTHESIS OF ESTERS OF 3-ACETOXY-18ß-H-GLYCYRRETIC ACID WITH AMINO ALCOHOLS

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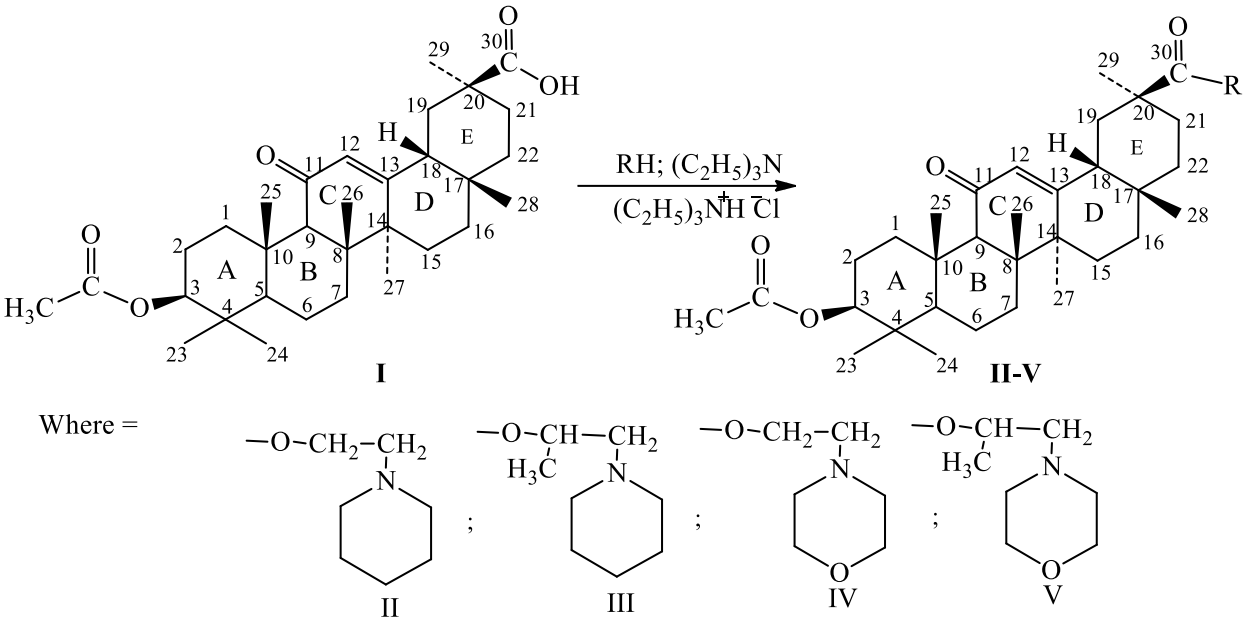
Pentacyclic triterpenoids are natural compounds that are widespread in the plant world and exhibit a variety of biological activities. One of their well-known representatives is glycyrrhetic acid of the ß-amyric type, which is an aglycone of glycyrrhizic acid, which is the main component of the root of the plant "*Glycyrriza glabra. L*"

Glycyrrhetic acid also has biological activity against viruses, inflammation, stomach ulcers and is part of a number of drugs used in medical practice [1-4].

In recent years, modified glycyrrhetic acid compounds based on hydroxyl, carboxyl groups, ketones, double bonds have been synthesized, and their biological activity has been studied [4-8]

In order to obtain new medicinal substances based on glycyrrhetic acid and study the connection between their biological activity and the structural structure and mechanism of action, esters of 3-acetoxyglycyrrhetic acid with some amino alcohols were synthesized.

The synthesis of esters was carried out according to scheme 1 given below



Where =

Glycyrrhizin-containing substances, glycyrrhetic acid, its 3-acetoxy compound and acid chloride (I), used in the experiments, were synthesized according to methods (9-11). The reaction of the corresponding amino alcohol with acid chloride(I), giving the synthesis of esters in an equimolar ratio, was carried out in a dry benzene medium. The resulting ether was purified by recrystallization from a chloroform-methanol mixture. Based on physicochemical methods (UV, IR and NMR spectroscopy), some physicochemical parameters of the obtained esters were determined and their chemical structure was confirmed. The following systems were used for thin layer chromatography: [1]- chloroform-methanol (5:1); [2]- chloroform-methanol (10:1).

β(N-morpholine)-ethyl-3-O-acetyl-18β-H-glycyrrhetate ^{1}H NMR spectrum signals of O-CH_2- protons at 3.71 ppm., signals of -H-CH_2- group protons at 2.4-2.74 ppm. observed in .

β(N-piperidine)isopropyl-3-O-acetyl-18β-H-glycyrrhetate and β(N-piperidine)isopropyl-3-O-acetyl-18β-H-glycyrrhetate ^{1}H NMR spectra of other complex esters, their due to the presence of an isopropyl residue instead of an ethyl residue, the 1.24 ppm. In the field, the doublet resonance signals characteristic of the protons of the –O-C(CH_3)-C- group differ from the presence of multiplet signals of the protons of the –O-CH- group, which resonate at 5.02-5.10 ppm.

Thus, in the complex esters of 3-O-acetyl-18β-H-glycyrrhetic acid, the protons of the C29 atom of the molecule move up to 1.11 ppm towards the strong field of resonance signals.

ß(N-piperidine)ethyl-3-O-acetyl-18ß-H-glycyrrhetate (II). White crystalline substance. The yield of the reaction is 1.04 g (83.4%), m.p= 162-164°C, Rf = 0.58(1). UV spectrum (ethanol, λ_{max}, nm) (lg ε): 258 (2.9). IR spectrum (ν, sm^{-1}): ν(CH, CH_2, CH_3)=2955,2873, ν(C=O)=1724, ν(C11=O, C=C)=1654, δ(CH_2, CH_3)=1454, δ(CH)=1380,1246, 1214, δ(C–O–C,)=1146, ν(C–N)=1090, ν(C–O–C)=1040, δ(=CH)=981

ß(N-piperidine)isopropyl-3-O-acetyl-18ß-H-glycyrrhetate(III). The reaction product was recrystallized from methanol. White yellowish crystalline substance. The yield of the reaction is 1.01 g (79.3%), m.p=210-212°C, Rf=0.73(1). UV spectrum (ethanol, λ_{max}, nm) (lg ε): 260 (2.5). IR spectrum (ν, sm^{-1}): 1732(C=O), 1284(C-O), 2872 (CH_2), 1435(CH_2) 1150-1100(C-N), 1672(C=O), 1625 (C=C), 1420(=C-H).

ß(N-morpholine)ethyl-3-O-acetyl-18ß-H-glycyrrhetate(IV). White reddish crystalline substance. The yield of the reaction is 1.05 g (84.1%), m.p =218 — 220°C, Rf =0.75(1). UV spectrum (ethanol, λ_{max}, nm) (lg ε): 260 (3.50). IR spectrum (ν, sm^{-1}): 1731(C=O)1275(C-O), 2874 (CH_2), 1455(CH_2), 1120-1050(C-N), 1220-1150(C-O-C).

ß(N-morpholine)isopropyl-3-O-acetyl-18ß-H-glycyrrhetate(V). The reaction product was recrystallized from a mixture of methanol and chloroform. . White reddish crystalline substance. The yield of the reaction is 1.04 g (81.4%), Melting point=204-206°C, Rf= 0.73(2). UV spectrum (ethanol, λ_{max}, nm) (lg ε): 259 (4.7). IR spectrum (ν, $см^{-1}$): 1732(C=O), 1284(C-O), 2872 (CH_2), 1435(CH_2) 1150-1100(C-N), 1672(C=O), 1625 (C=C), 1420(=C-H).

The membranotropic and interferon-inducing activity of these compounds is currently being studied.

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