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# SYNTHESIS AND MODIFICATION OF NEW OLENANE TYPE 2-CYANO-3,4-SECO-5-ALKYNYLDERIVATIVE*

**Keywords:** Oleanolic acid, alkyne, A-seco-triterpenoids.

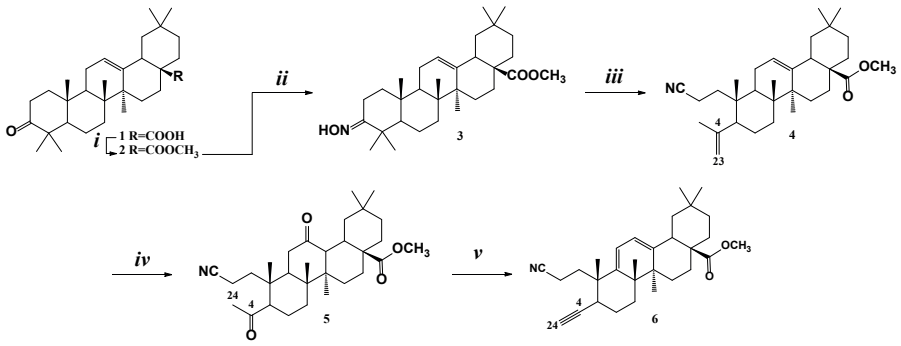
The development of pharmacological agents based on triterpenoids is an important goal of medicinal chemistry. A large number of publication on the isolation and modification of native triterpenoids indicates the importance of these compounds as promising in the synthesis of new pharmacological agents with antitumor, anti-inflammatory, antiviral, and another type of activities. Even though A-seco-triterpenoids also have a broad spectrum of biological activities significantly fewer articles are presented on the similar functionalization of the A-ring of 2-cyano-3,4-seco-4(23)-en-derivatives. These compounds were used to obtain a set of 2,3-seco-oleanane and lupane β-ketoesters with cytotoxic activity [1]. A-seco-lupanes with aldehyde function at positions C3 and C30 with the $IC_{50}$ 0.64–3.49 μM against all the tested cancer cell lines were selected as the most promising cytotoxic agents [2]. 3.30-Dicarboxy-A-seco-glycyrrhetic acid showed a marked inhibition of hepatitis B virus DNA replication with the $IC_{50}$ 12.3 μM [3].

One of the most dynamically developing areas in the chemistry of triterpenoids is the introduction of the alkynyl fragment. The most used approach to the synthesis of alkynyl-derivatives is a propargylation of C2 [4], C3 and C28 positions.

Another way to introduce alkynyl moiety is a reaction of methyl ketones with $POCl_3$. This approach was used for the synthesis of C19- [7] and 5-alkynyl-triterpenoids from betulin [8]. Examples of such modifications on oleanolic acid are not presented. In this paper, we describe the introduction of a triple bond to A-seco-ring of methyl oleanoate.

Methyl 2-cyano-3,4-seco-oleanoate **4** was obtained by standard reactions of methylation *via* acid chloride method, following oximation and Beckmann rearrangement type 2. By oxidation of **4** containing two double bonds at the C4 (ring A) and C12 (ring C) positions by ozone in $CH_2Cl_2$ 4,12-dioxo-23-nor-derivative **5** was obtained in a yield of 80 % [9].

Further reaction of **5** with $PCl_5$ led to methyl 2-cyano-3,4-seco-5-alkynyl-9(10),12(13)-dien-olean-28-oate **6** with 70 % yield after purification (Scheme).




Scheme. Reagent and conditions: *i)* a – $(COCl)_2$, $CH_2Cl_2$, 20 °C; b – MeOH, reflux; *ii)* $NH_2OH \cdot HCl$, EtONa, EtOH, reflux; *iii)* p-TsCl, Py, reflux; *iv)* $O_3$, $CH_2Cl_2$, –40 °C; *v)* $PCl_5$, Py, reflux

The structure of compounds **5** and **6** were elucidated by NMR spectroscopy. Thus, in the $^{13}C$ NMR spectrum of compound **5**, the disappearance of signals of C4(23) and C12(13) double bonds was observed. The signals of C4 and C12-oxo-groups at δ 209 and 210 ppm, respectively, were characteristic. The $^{1}H$ and $^{13}C$ spectra of compound **6** showed typical signals of the acetylene group, so the resonances of C atoms were found at δ 71.5 (C24), 83.8 (C4) ppm, while proton H24 appeared as a singlet at ~2.1 ppm. The signals of C9(11) and C12(13) double bonds were detected at δ 151.9(125.9) and δ 128.9(150.2) ppm, respectively.

Thus, the result of the research is the synthesis of methyl 2-cyano-3,4-seco-5-alkynyl-9(11),12(13)-dien-olean-28-oate with 70 % yield including steps of ozonolysis and reaction with $PCl_5$.

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