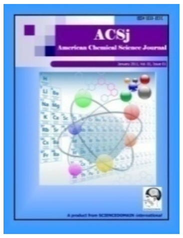

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Acylation of Grape Leaves Polyprenols

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Authors' contributions

This work was carried out in collaboration between all authors. Authors NKK and KUK designed the study and read the first draft of the manuscript. Authors UTZ and NKK performed the experiment, calculations and all the analyses of the study. Author KMS managed the literature searches and the final corrections on the manuscript. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: The study is aimed to obtain acylated derivatives of polyprenols which were isolated from leaves of grape Vitis vinifera L.
Study Design: Modification of natural compounds.
Place and Duration of Study: Department of Organic Chemistry, Institute of the Chemistry of Plant Substances (ICPS). The study was carried out between January, 2011 and December, 2012.
Methodology: Polyprenols were acylated by anhydrides of mono- and dicarboxylic acids in absolute benzene in the presence of catalytic amounts of dry pyridine within 1-2 hours (method A). Polyprenols were acylated also by anhydrides of mono- and dicarboxylic acids in the presence of catalyst (dry pyridine) in absence of solvents at 70-80°C within 1 or 2 hours (method B). For the acylation of polyprenols the microwave method has been used in absence of the solvent and the catalyst (method C). The courses of reactions were controlled by TLC, HPLC, and HPTLC. Structure of acyl-products determined by IR-, 1H NMR and mass-spectra.
Results: In the method A with decreasing of acid's strength and increasing of molecular weight the yield of acyl-products is decreased. Acylation by benzoyl anhydride yielded to acyl-products between acylation by acetic and propionic anhydrides. Decreasing of yields of acyl-products was observed at usage of anhydrides of dicarboxylic acids. In the method

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B decreasing of the yields was observed also with decreasing of acid's strength and increasing of molecular weight of the acylating agent. Thus yields were a bit high (in addition 1-6 %). In the method C (MWA) duration of acylation reaction has sharply contracted (on 20 60 times in comparison with the method A, and 10-30 times in comparison with the method B), i.e. yields of acyl-products are enlarged by 13.5-24.6 % (in comparison with a method A) and 7.5-21.6 % (with a method B) at usage of anhydrides of monocarboxylic acids. At MWA acylation by anhydrides of dicarboxylic acids duration of reaction contracts at 20-40 times in comparison with the method A and 10-30 times in comparison with the method B. The yields are increased on 8.2 - 17.5 % (in comparison with the method A) and 5.2-16.5 % (in comparison with the method B).

Conclusion: Acylation reactions of polyprenols with anhydrides of mono- and dicarboxylic acids, organic acids have been studied in various conditions. Usage MWA allows performing esterifications with high yields (from 59 % to 89.6 % in the case of monocarboxylic acids and from 56.2 to 78 % in the case of dicarboxylic acids). Duration of MWA acylation reaction was 6-10 minutes in the case of polyprenol acylation by monocarboxylic acids, and 12-14 minutes in the case of dicarboxylic acids. Therefore MWA method, undoubtedly, is a cost effective method for the acylation.

Keywords: Polyprenols; modification; esterification; acylation; anhydrides of mono- and dicarboxylic acids; organic acids; microwave; acyl-products.

1. INTRODUCTION

Plant polyprenols are one of important group of biologically active substances. They are perspective synthons for obtaining physiological active compounds also. They introduce a great interest because of possibility using as pharmaceutical drugs, agricultural preparations and biological active additions. In nature polyprenols are occupied in green parts, especially in plant leaves. In human organism they concentrated in pancreas, brain, heart and other tissues. Polyprenols differ among themselves on quantity and geometric configuration of double bonds and this difference characteristically for a various plant families.

Synthesis of long cycle polyprenols is multistage; therefore it is reasonable to discover available natural sources for their obtaining. Polyprenols are polyunsaturated allylic therpene alcohols and high chemical activity. Modification of polyprenols should give derivatives with the new biological properties. Specific properties of allylic compounds are their ability to rearrangements. Polyprenols are polyunsaturated compounds; quantity of double bonds which one equal to quantity of isoprene units, a component skeleton of the molecule. Hence, polyisopenoids enlist in modification as alkenes. Chemical structure of polyprenols guesses formation enough high reaction capability of intermediates, and it easies passing synthetic processes. At the same time availability of polyisopenoids levies special demands in a choice of reaction condition and compounds.

Modification of polyprenols for the purpose of obtaining potential biologically active substances is intensely researched [1-3]. It is known grow stimulation activity of polyprenylacetate from coniferous plants [4]. Geranyl ester of fernasylacetic acid, solanesylacetic and decaprenylacetic acids possess antiulcer activity and are applied in the capacity of medical products [5,6].

Earlier we have studied acylation of polyprenols of cotton leaves by anhydrides of monocarboxylic (acetic, propionic, butyric- and benzoic anhydrides) and dicarboxylic (succinic, maleinic and phthalic) acids without solvents and catalytic amount of a pyridine [7, 8]. The capability direct acylation of polyprenols with usage of organic acids in the literature misses. It is well known that the esterification goes only by refluxing a carboxylic acid and an alcohol in the presence of an acid catalyst.

2. EXPERIMENTAL

2.1 Materials and Methods

All reagents and solvents were used with purification. IR - spectrums are removed on spectrophotometer FTIR - System 2000 (Perkin-Elmer) in Vaseline (ν, cm^{-1}). Spectrums of ^1H NMR have been removed on Brucer (400 MHz), solvent - $CHCl_3$, dial δ, Spectrums ^{13}C NMR have obtained on spectrometer Brucer (75 MHz), the solvent: $CDCl_3$, dial δ, internal standard are HMDS and TMS.

Mass spectrums of high resolution of polyprenol acetate and phthalate are metered on the instrument micrOTOF II (Bruker Daltonics), a method of ionization electro-pulverization of positively ionized atoms (MS IERPI), a diapason of scan from m/z 50 to m/z 3000, polarity of positive ions (a strain on a capillary tube 4500 V). Spray input of substances is used. The solvent is acetonitrile (with the component HCOOH or CH_3COONH_4), a flow rate of a solution of 3 μl/min. Interface temperature is 180ºC, a gas sprayer - nitrogen (4.0 l/min).

Purity of obtained acyl-derivatives was checked out with usage TLC. For TLC plates Sorbfil (Russia), a size 10x10 cm AL SIL G/UV (Germany), a size 20x20 cm, system of solvents used benzene-ethylacetate 24:1, hexane - chloroform 1:2, developing agent $KMnO_4$ in sulfuric acid, an alcoholic solution of p-methoxybenzaldehyde and sulfuric acid or an iodine pair. Systems hexane, hexane - chloroform with gradual magnification of polarity are used for column chromatography. Condition of HPLC analysis for determining ratio of polyprenyl homologues was as in [9], eluent – mixture of methanol with acetone (1:3 volume). Polyprenols which were isolated from Cotton leaves used as standard samples [12].

2.2 Acylation of Polyprenols

In the yielded report are reduced, we compare the results gained by us acylation of polyprenols of Grape leaves in usual conditions and a microwave without solvents. Polyprenols more than 94 %-s purity from 10-12 isoprene units with a relative content of homologues 8.3 %; 42.4 %; 49.3 % are used for acylation. Homologues content of polyprenols was determined by HPLC [9]. It is necessary to point that HPLC discovered only polyprenol acetate and other acyl-derivatives did not discover by this method [10,11]. For acylation reactions following agents were used: anhydrides of acetic, propionic, iso-butiric, the benzoic, succinic, maleinic and phthalic acids.

Reactions have carried out without solvents and catalytic agents, at weight ratio of acylation agents and polyprenols 1:1 within 2-10 minutes in a microwave. Molar ratio of acylating agents a little exceed of polyprenols in these cases. A reaction course checked on TLC (each 1 minute) in solvent system: benzene – ethyl acetate 24:1, on plates Sorbfil (10x10) by comprising with standard sample of polyprenols, which was isolated from cotton leaves [12]. Corresponding spots were determined for identify. In Table 1 data on an acylation by acid anhydrides in usual conditions (method A: a solvent, a catalytic agent; method B: a catalytic agent, 70-80ºC, and microwave (method C, 65-70ºC, a strain 450W) weight ratio of polyprenol : acylation agent is 1:1.

3. RESULTS AND DISCUSSION

3.1 Acylation Polyprenols

Acylation reactions were carried by using three methods. Polyprenols were acylated by anhydrides of mono- and dicarboxylic acids in absolute benzene in the presence of catalytic amounts of dry pyridine within 1-2 hours (method A). In the case of usage of anhydrides of aliphatic acids with decreasing of acid's strength and increasing of molecular weight the yield of acyl-products is decreased. Acyl-products were formed when using benzoyl anhydride (duration of reactions are 4 hours) also. However, the yield constitutes between acylation by acetic and propionic anhydrides. Decreasing of yields of acyl-products was observed at usage of anhydrides of dicarboxylic acids.

3.1.1 Method A

To a mixture of 0.5 g polyprenol homologues (n=10-12) in 2-5 ml of dry benzene added 0.5 g of the distillated or sublimed acid anhydride (acetic, propionic, butiric, benzoic, succinic, phthalic, maleinic) and 1 drip of a dry pyridine. The mixture was intermixed by 2-6 hours depending on the nature of a used anhydride. Further a reaction mixture treated feeble solution Na_2CO_3 for deleting of excess of an acid and water before neutral reaction of washing waters. The rest terrified over anhydrous Na_2SO_4, ferried out a solvent, then filtrated through coarse grinding silica gel. It isolated by hexane at first, then system of solvents hexane-chloroform gradually enlarging polarity of system. The Yields of acyl-products are given in Table 1.

Polyprenols were acylated also by anhydrides of mono- and dicarboxylic acids in the presence of catalyst (dry pyridine) in absence of solvents at reaction mixture temperature 70-80^{o}C within 1 or 2 hours (method B). Decreasing of the yields was observed in this case also with decreasing of acid's strength and increasing of molecular weight of the acylating agent. Thus yields were a bit high (in addition 1-6 %). Decreasing of yields of acyl-products is regularly iterated at usage of anhydrides of dicarboxylic acids at an acylation without the solvent. The little increasing (additionally on 1-6%) of yields of acyl-products was obtained in the last cases.

3.1.2 Method B

To a mixture of 0.5 g polyprenol homologues (n=10-12) added 0.5 g of the distillated or sublimed acid anhydride (acetic, propionic, butiric, benzoic, succinic, phthalic, maleinic) and 1 drip of a dry pyridine. A mixture heated at temperature 70-80ºC with stirring within 6 hours. Later processing led analogously to a method A.

For an acylation of polyprenols the effective microwave method (MWA) has been used in absence of the solvent and the catalytic agent (method C). At carrying out of reaction of an acylation in microwave duration of reaction has sharply contracted (on 20 60 times in comparison with the method A, and 10-30 times in comparison with the method B), i.e. yields of acyl-products are enlarged by 13.5-24.6 % (in comparison with a method A) and 7.5-21.6 % (with a method B) at usage of anhydrides of monocarboxylic acids. At MWA acylation by anhydrides of dicarboxylic acids duration of reaction contracts at 20-40 times in comparison with the method A and 10-30 times in comparison with the method B. The yields are increased on 8.2 - 17.5 % (in comparison with the method A) and 5.2-16.5 % (in comparison with the method B).

3.1.3 Method C

To a mixture of 0.5 g polyprenol homologues (n=10-12) added 0.5 g of the distillated or sublimed acid anhydride (acetic, propionic, butiric, benzoic, succinic, phthalic, maleinic). A compound intermixed within 2-10 minutes at 450W in a microwave depending on the nature of a used anhydride. Further a reaction mixture treated feeble solution Na_2CO_3 for deleting of excess of an acid and water before neutral reaction of washing waters. The rest filtrated through coarse grinding silica gel. It isolated by hexane at first, then system of solvents hexane-chloroform gradually enlarging polarity of system. The yields acyl-products are given in Table 1.

3.2 Polyprenol Acetate (Polyprenylacetate 2)

3.2.1 Method A

To a mixture of 0.5 g polyprenol-homologues (n=10-13) in 2-5 ml of dry benzene added 0.5 g of the distillated acetic anhydride and 1 drip of a dry pyridine. The compound was intermixed to 2 hours at room temperature. Later processing was led analogously to common procedure. A product yield of 0.345 g (69 %).

3.2.2 Method B

To a mixture 0.5 g polyprenol homologues (n=10-12) added 0.5 g of the distillated anhydrides of an acetic acid and 1 drip of a dry pyridine. A compound heated at temperature 70-80^{o}C with stirring within 1 hour. Later processing was led analogously to method A. A product yield of 0.36 g (72 %). Purity checked with TLC.

3.2.3 Method C

To a mixture of 0.5 g polyprenol homologues (n=10-12) added 0.5 g of the distillated acetic anhydride. The compound was intermixed to 2 minutes at 450W in a microwave. Later processing has led to analogously common procedure. A product yield of 0.45 g (90 %).

3.3 Polyprenol Acetate (2)

Oil, it is light - yellow color. R_f - 0.75 (benzene - ethyl acetate 24:1). The formula of polyprenol homologues: $C_{52}H_{84}O_{2;}$ $C_{57}H_{92}O_{2;}$ $C_{62}H_{100}O_{2;}$ MW: 740, 808, 876. IR spectrum, ν, cm^{-1}: 850, 1030, 1240, 1380, 1450, 1666, 1740 ^{1}H NMR-spectrum, (400 MHz, δ, ppm, J/Hz): 1,19 (6H, s, 2 $C\underline{H_3}$); 1,52, 1,53, 1,6 (9H, 3 trans-CH_3); 1,68, 1,69 (27H, s, 9 cis-CH_3); 1,90, 1,89 (54H, m, 27$C\underline{H_2}$); 1,95 (3H, s, $COCH_3$) 4,40 (2H, d, J=7,2, =CH-$\underline{CH_2}$OAc); 5,00 (14H, t, =CH); 5,22 (1H, t, J=7,1 =CH an end bond). Mass spectrum of ESI, m/z: 758, 826, 894 [M^+ + nNH_4] and 763, 831, 899 [M^+ + nNa], corresponding $C_{52}H_{84}O$ (a decaprenol acetate), $C_{57}H_{92}O_2$ (an undecaprenol acetate) and $C_{62}H_{100}O_2$ (a dodecaprenol acetate).

3.4 Polyprenol Propionate (3)

3.4.1 Method A

Condition of acylation and handling were led analogously to obtaining of polyprenylacetate. From 0.5 g polyprenol homologues (n=10-13) in 2-5 ml of dry benzene and 0.5 g of the distillated propionic acid anhydride have obtained 0,26 g (52 %) buttery product.

3.4.2 Method B

To a mixture of 0.5 g polyprenols homologues (n=10-12) added 0.5 g of the distillated propionic acid anhydride and 1 drip of a dry pyridine and a reaction mixture heated at temperature 70-80ºC with stirring within 2 hours. Later processing was led analogously to method A. A product yield was 0.265 g (53 %).

3.4.3 Method C

Condition and handling were led analogously to obtaining polyprenylacetate. From 0.5 g polyprenol homologues (n=10-12) and 0.5 g of the distillated propionic acid anhydride have obtained 0.26 g (52 %) buttery product. Polyprenol propionate (3) is light - yellow color oil. R_f – 0.72 (benzene - ethyl acetate 24:1). The formula of polyprenol propionate homologues: $C_{53}H_{86}O_{2;}$ $C_{58}H_{94}O_{2;}$ $C_{63}H_{102}O_{2;}$

MW: 822, 890, 958.

IR spectrum:ν, cm^{-1}: 1085, 1180 (C-O-C), 1449 (1668 (C=C), 1739 (CO), 2962 (CH of CH_3), 2925 (CH of CH_2).

3.5 Polyprenol Iso-Butyrate (4)

3.5.1 Method A

Analogically to above mentioned methods from 0.5 g polyprenol homologues (n=10-13), 2-5 ml of dry benzene and 0.5 g of the distillated iso- butyric acid anhydride have obtained 0.20 g (40 %), a buttery product.

3.5.2 Method B

Procedure was led analogously to polyprenol propionate on method B. A product yield was 0.21 g (42 %).

3.5.3 Method C

Procedure was led analogously to polyprenol propionate on method B. A product yield was 0.30 g (60 %).

Polyprenol iso-butyrate (4) is yellow color oil. R_f – 0.70 (benzene - ethyl acetate 24:1). The butyrate formula of polyprenol homologues: $C_{54}H_{88}O_{2;}$ $C_{59}H_{96}O_{2;}$ $C_{64}H_{104}O_{2;}$ MW: 700, 836, 904.

IR-spectrum: ν, cm^{-1}: 1733 (CO), 1270 (-C-O-C), 1450, 1382 (CH_3-CH_2), 1668 cm^{-1} (C=C in isoprenoid unite).

3.6 Polyprenol Benzoate (5)

3.6.1 Method A

Condition of acylation and handling are analogous to obtaining polyprenol acetate. From 0.5 g polyprenol homologues (n=10-12), 2-5 ml of dry benzene and 0.5 g of a benzoyl anhydride at stirring within 4 hours have obtained 0.29 g (59 %), a buttery product.

3.6.2 Method B

To a mixture of 0.5 g polyprenol homologues (n=10-12) added 0.5 g of the distillated benzoic acid anhydride, 1 drip of a dry pyridine, which intermixed at temperature 70-80°C within 2 hours. Later processing was led analogously to method A. A product yield was 0.33 g (65 %).

3.6.3 Method C

Procedure was led analogously to polyprenol propionate on method B. A product yield was 0.36 g (72,5 %). Compound 5 is light - yellow color oil. R_f - 0.77 (benzene - ethyl acetate 24:1). The formula of Benzoate polyprenol homologues: $C_{57}H_{86}O_2$; $C_{62}H_{94}O_2$; $C_{67}H_{102}O_2$; MW: 802, 870, 938.

IR spectrum: ν, cm^{-1}: 1726 (CO), 1270 (-C-O-C), 1451, 2960 (CH of CH_3), 1666 cm^{-1}, (C=C). Mass-spectrum of ESI: 820; 888; 956 [M^++ nNH_4]; 825; 893, 961 [M^+ + nNa], corresponding to $C_{57}H_{86}O_2$; $C_{62}H_{94}O_2$ and $C_{67}H_{102}O_2$.

3.7 Monopolyprenyl Succinate 6

3.7.1 Method A

Analogically to mentioned methods from 0.5 g polyprenol homologues (n=10-13) in 2-5 ml of dry benzene and 0.5 g of sublimed succinic anhydride was obtained 0.40 g (80 %), a buttery product.

3.7.2 Method B

To a mixture of 0.5 g polyprenol homologues (n=10-12) added 0.5 g of sublimed succinic anhydride and 1 drip of a dry pyridine. A reaction mixture heated at temperature 70-80°C with stirring within 4 hours. Later processing was led analogously to method A. A product yield was 0.42 g (83 %).

3.7.3 Method C

Procedure is analogically to polyprenol acetate on method C. A product yield was 0.44 g (88.2 %).

Monopolyprenyl succinate (6) is light yellow color oil. R_f – 0.85 (benzene - ethyl acetate 24:1). The formula of polyprenol homologues: $C_{59}H_{94}O_4$; $C_{64}H_{102}O_4$; $C_{69}H_{110}O_4$; MW: 866, 934, 1002.

IR spectrum: ν, cm^{-1}: 1739 (COO ester), 1715 (CO acid) 1270 (-C-O-C-), 1451, 2960 (CH of CH_3), 1666 (C=C) cm^{-1}.

^{1}H NMR -spectrum, (100 MHz, $CDCl_3$, δ, ppm., J/Hz): 1,65 and 1,56 (Cis- and trans - $-CH_2$-C($\underline{CH_3}$)-CH-); 1,72 (s,-C(CH_3) =C$\underline{H}$-CH_2OAc), 1.90-2.05 with centre of 1.96 (m, -CH_2-CH_2-), 4.58 (d, J=7,5 Hz)-CH-$\underline{CH_2}$-OAc); the widened singlet at 5.06 ppm is olefinic protons of the midpoint of a circuit and 5,33 (t, J-7,5 Hz) - to an olefinic proton of an end unite.

3.8 Monopolyprenyl Maleic Acid Ester (7)

3.8.1 Method A

Condition of acylation and handling are led analogically to obtaining polyprenylacetate. From 0.5 g polyprenol homologues (n=10-12), 2-5 ml of dry benzene and 0.5 g of sublimed maleinic acid anhydride have obtained 0.26 g (52 %) buttery product 7. 0.265g - 53% (B), 0. 35 g - 69.5% (C).

Compounds 7 and 8 are obtained analogically above described at heating up of a reaction mixture within 6 hours. The yields were Compounds 8 -0.245 g -49 % (A), 0.27 g -53 % (B), 0.30g -60.0% (C). Formation samples obtained on a method A, B and C were identical under the physicochemical characteristics.

Monopolyprenyl maleic acid ester (7) is light - yellow color oil. R_f – 0.87 (benzene-ethyl acetate 24:1). The formula of polyprenol homologues: $C_{59}H_{92}O_4$; $C_{64}H_{100}O_4$; $C_{69}H_{108}O_4$; MW: 864, 932, 1000.

IR spectrum: ν, cm^{-1}: 1732 (CO ester), 1700 (CO acid), 1166 (-C-O-C-), 1448, 2962 (CH of CH_3), 1668 (C=C) cm^{-1}.

^{1}H NMR -spectrum, (100 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.65 and 1.56 (cis- and trans - $-CH_2$-C($\underline{CH_3}$)-CH-); 1.72 (s,-C(CH_3) =C$\underline{H}$-CH_2OAc), 1.90-2.05 with the centre of 1.96 (m, -CH_2-CH_2-), 4.67 (d, J=7,5 Hz) –CH-$\underline{CH_2}$OAc); the widened singlet at 5.06 of olefinic protons of the midpoint of a chain and 5.33 (t, J-7,5 Hz) - to an olefinic proton of an end unite.

3.9 Monopolyprenyl Phthalic Ester (8)

3.9.1 Method A

Analogically to the mentioned above from 0.5 g polyprenol homologues (n=10-12), 2-5 ml of dry benzene and 0.5 g of a sublimed phthalic anhydride have obtained 0.25 g (49 %), a buttery product. Purity checked by TLC. Identified according to an IR - H^1 NMR - and mass-spectrums.

Compound 8 is light - yellow color oil. R_f – 0.88 (benzene - ethyl acetate 24:1). The formula of monoesters of polyprenol homologues: $C_{63}H_{94}O_4$; $C_{68}H_{102}O_4$; $C_{73}H_{110}O_4$; MW: 914, 982, 1050.
IR-spectrum: ν, cm^{-1}: 1739 (COO ester), 1715 (CO acid) 1270 (-C-O-C-), 1451, 2962 (CH of CH_3), 1666 (C=C) cm^{-1}.

^{1}H NMR-spectrum, (100 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.65 and 1.56 (cis- and a trans - $-CH_2$-C($\underline{CH_3}$)-CH-); 1.72 (s, -C(CH_3)=C$\underline{H}$-CH_2OAc), 1.90-2.05 with the centre of 1.96 (m, -CH_2-CH_2-

), 4.87 (d, J=7,5 Hz) –CH-$\underline{CH}_2$OAc); the widened singlet at 5.06 of olefinic protons of the midpoint of a chain and 5.33 (t, J=7,5 Hz) - to an olefinic proton of an end unite.

^{1}H NMR-spectrums, (400 MHz, $CDCl_3$, δ, ppm, J/Hz): 1.07, 1.19, 1.37 (15H, s, $5C\underline{H}_3$); 1.52-1.53 (5H, 2 trans-CH_3); 1.60 (21H, s, 7 cis-CH_3); 1.96 (42H, m, $21C\underline{H}_2$); 1.95 (3H, s, COAc); 4.67 (2H, d, J=6.8, =CH-$\underline{CH}_2$OAc); 5.00 (10H, t, =CH); 5.38 (1H, t, J=6,0 =CH an end unite), 7.3-7.4 (4H, m, H_{Ar}).

Mass spectrum of ESI: 864; 932; 1000 [M^++ nNH_4]; 820; 888; 956 [M $^+$+ nNH_4 - COOH]; and 869, 937; 1005 [M^+ +nNa], 825; 893, 961 [M^+ +nNa - COOH], corresponding $C_{63}H_{94}O_4$; $C_{68}H_{102}O_4$; $C_{73}H_{110}O_4$;

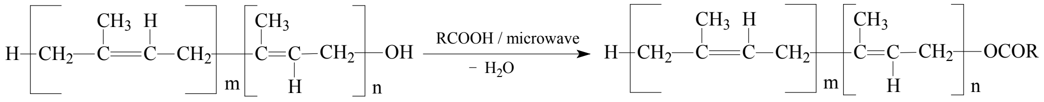
The obtained results presented in Table 1 shows that acylation of polyprenols by anhydrides of aliphatic monocarboxylic acids goes lighter (within 2-8 minutes), in comparison with benzene carboxylic acid within 10 minutes. It is necessary to note that direct of acylation of polyprenols usual conditions without involvement of catalytic agents does not go.

Table 1. The yields of acyl-products obtained in various conditions (%)

Acylation agent	Method	Temperature, ºC	Duration, min	The yield
Acetic anhydride	A	20-25	120	69.0
	B	70-80	60	72.0
	C	65-70*	2	93.6
Acetic acid*	A	-	-	0
	B	-	-	0
	C	65-70*	6	89.6
Propionic anhydride	A	20-25	120	52.0
	B	70-80	60	53.0
	C	65-70*	4	69.5
Propionic acid*	A	-	-	0
	B	-	-	0
	C	65-70*	6	66.7
Butiric anhydride	A	20-25	120	40.0
	B	70-80	60	42.0
	C	65-70*	6	60.6
Iso-butiric acid*	A	-	-	0
	B	-	-	0
	C	65-70*	8	59.0
Benzoic anhydride	A	20-25	240	59.0
	B	70-80	120	65.0
	C	65-70*	10	72.5
Benzoic acid*	A	-	-	0
	B	-	-	0
	C	65-70*	10	70.0

P.S. a) ratio of polyprenol: acylation agent 1:1(weight);
**condition of microwave, strain (450W)*

The cited data demonstrate that maximum yields of acyl-products gained in the conditions of microwave constitute 93.6 % (for polyprenol acetates), 69.5 % (for polyprenol propionates), 60 % (polyprenol butyrates) and 72.5 % (for polyprenol benzoates) accordingly. It is necessary to note that acylation process begins in the core within 2 minutes. The increasing of reaction duration (it is more than 10 minutes) leads to decreasing of the yield of acyl-products; thus there is a polymerization of starting polyprenols. As an acylation of polyprenols by acid anhydrides in microwave reaction goes promptly we have solved to lead possibility of using of acids as acylation agents in these requirements. It has appeared that reaction goes to a ratio of compounds 1:1 without solvents and the catalytic agent within 6-10 minutes and yields to corresponding acyl-products from 89.6 % (for an acetate), 66.7 % (for propionate), 59.0 % (for isobutyrate and 70 % (for Benzoate) (Table 1). It is possible to point also that aliphatic acids of iso-structure (iso-butyric acid) give rather short yields of acyl-products. Acylation of polyprenols by organic acids happens under the following scheme:

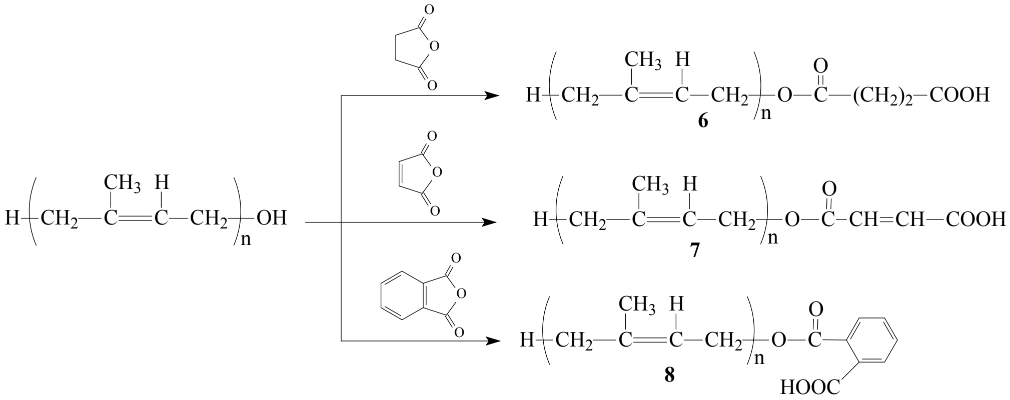


m = 3, n = 7-10, R = CH_3 (2); CH_3CH_2 (3); $(CH_3)_2$-CH_2 (4); C_6H_5 (5)

Scheme 1. Acylation of polyprenols with organic acid by using microwave

The Physicochemical characteristics and IR-spectral data obtained acyl-products correspond with the datum obtained earlier by us. Further concern reaction study of polyprenols with cyclic anhydrides of dicarboxylic acids in the same conditions was represented. As a result of these reactions it was possible to expect formation of mono- or diprenyl ethers of dicarboxylic acids. Earlier we had been demonstrated formation of mono-esters at an acylation of polyprenols by cyclic anhydrides in benzene in the presence of catalytic amounts of a pyridine [8]. It was theoretically possible to formation mono- or diprenyl ethers of dicarboxylic acids as a result of these reactions. In the conditions carried by us formations only monoprenyl ethers are determined. It can be explain that in this case (anhydrides of diatomic acids) a considerable quantity of anhydrides of diatomic acids in comparison with polyprenols (molar ratio an anhydride: polyprenol constitutes 7.6:1 (6); 7.8:1 (7); 5:1 (8)). Therefore in this case will be formed monoprenyl ethers of diatomic acids. Succinic, maleinic and phthalic anhydrides are used as acylation agents. Interaction was performed as the same conditions pointed above in the presence of catalytic amounts of a dry pyridine, and in the conditions of microwave without solvent. Reactions of the above-stated acid anhydrides with 1 are carried out at a ratio of compounds 1:1. In usual conditions an acylation for process completion at 2-6 hours (heating at 70-80ºC) depending on the nature of a used anhydride. Reaction in a microwave for interaction of anhydrides with 1 it is required only 12-14 minutes.

Succinic anhydride reacts with polyprenols go more promptly (12 minutes) in comparison with maleinic and phthalic (Table 2) anhydrides, which was more difficultly -14 minutes.



Scheme 2. Acylation of polyprenols with acid anhydrides by using microwave

Being dielectrics polyprenols strongly absorbed microwaves and consequently are strongly heated. Therefore duration of reaction dramatically decreases due to thermal effects [13, 14]. The acylation in microwave can be radical or ion mechanism. These problems have been studied by many scientists of the world. However they have not come to a common opinion. Being based on these data, we guess probability of the ion or radical mechanism of acylation in MW. In case of methods A and B for an acylation it was used acid anhydrides, therefore as catalytic agent the pyridine was used. It is necessary to mark that in A and B conditions by using acids reactions do not go. But good yields of acyl-products were obtained by method C (MW).

Similarly acylation of polyprenols monocarboxylic their interaction with succinic acid goes in microwave, forming monoprenyl esters with yield of 88.2 % (Table 2).

Table 2. The yields of mono-prenyl esters obtained in various conditions (%)

Acylation agent	Method	Temperature, ºC	Duration, min	The yield
Succinic anhydride	A	20-25	240	80.0
	B	70-80	120	83.0
	C	70-75*	12	88.2
Succinic acid*	A	-	-	0
	B	-	-	0
	C	70-75*	12	78.0
Maleinic anhydride	A	20-25	480	52.0
	B	70-80	360	53.0
	C	70-75*	12	69.5
Maleinic acid*	A	-	-	0
	B	-	-	0
	C	70-75*	12	66.7
Phthalic anhydride	A	20-25	480	49.0
	B	70-80	360	53.0
	C	70-75*	14	60.0
Phthalic acid*	A	-	-	0
	B	-	-	0
	C	70-75*	14	56.2

P.S. a) ratio of polyprenol: acylation agent 1:1(weight);
** condition of microwave, strain (450 W)*

The reaction course and purity of products were checked by TLC. Thus, acylation of polyprenols by anhydrides of aliphatic mono- and dicarboxylic acids, acids goes easily in a microwave. Thus decreasing of duration time of reaction, is eliminated necessity of usage of the solvent, excess of an anhydride and the catalytic agent which used in usual conditions of acylation. The yields target acyl-products were much more increased. The structure of the obtained compounds is affirmed by IR – and ^{1}H NMR -spectrums. In a IR-spectrum of compounds 6-8 absorption bands of two carbonyl groups are watched at 1739 (C=O), 1715 (C=O in COOH) for compound 6;. 1732, 1712 for compound 7 and 1732, 1705 for compound 8, and also the characteristic absorption bands for molecule of polyprenols. There are absorption bands at 3333 cm^{-1}, hydroxyl groups of initial polyprenols and there are absorption bands OH at COOH in the field of 3560 cm^{-1}.

In spectrum ^{1}H NMR 6-8 protons $=C\underline{H}CH_2O$, $=C\underline{H}CH_2C$, $=CC\underline{H}_2$, a trans- and cis-CH_3-groups practically coincide with those for starting polyprenol. Unlike starting polyprenols protons of the methylene groups $=C\underline{H}CH_2O$ are offset in more feeble field. So, in compound 6 they are displayed at 4.58 ppm (d, J=7 Hz), 7 - 4.67 ppm (d, J=7 Hz), in 8 - at 4.87 ppm (d, J=7 Hz). In case of the polyprenol acetates (2) these protons are marked at 4.50 ppm (d, J=7 Hz). These protons in starting polyprenols have chemical shifts in the field of 3.96 ppm (d, J=7 Hz). Similar chemical shifts are watched for moraprenol [15].

Mass spectrums ESI are removed as an example by acetate, benzoate and phthalate of polyprenols where there are appropriate pikes of molecular ions with ions of ammonium and sodium.

4. CONCLUSION

In this study, polyprenols isolated from grape leaves was successfully acylated by acid anhydrides and organic acids using microwave. It was demonstrated a capability of acylation of polyprenols by organic acids in a microwave for the first time. Usage MWA allows performing acylation reactions with high yields (from 59 % to 89.6 % in the case of monocarboxylic acids and from 56.2 to 78 % in the case of dicarboxylic acids) and in absence of the solvent and the catalyst (pyridine). Duration of MWA acylation were 6-10 minutes in the case of polyprenol acylation by monocarboxylic acids, and 12-14 minutes in the case of dicarboxylic acids. Therefore MWA method, undoubtedly, is a cost effective and friend method of an acylation.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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