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СРАВНИТЕЛЬНАЯ ПРЯМАЯ ЭТЕРИФИКАЦИЯ ГЛИЦЕРИНА ФЕНИЛУКСУСНОЙ КИСЛОТОЙ И БЕНЗОЙНОЙ КИСЛОТОЙ

***Аннотация:** В этой статье моноэфиры глицерина были синтезированы путем прямой реакции этерификации между глицерином, фенилуксусной кислотой и бензойной кислотой, условия синтеза сравнивались в обоих случаях. Реакции проводили с использованием кислотного катализатора Amberlyst -15 при 110 ° C. Выход синтеза был выше в случае фенилуксусной кислоты, чем в случае бензойной кислоты.*

***Ключевые слова:** Этерификация, Глицерин, Амберлист-15.*

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COMPARATIVE DIRECT ESTERIFICATION OF GLYCEROL WITH PHENYL ACETIC ACID, AND BENZOIC ACID

Annotation: *In this paper, glycerol monoesters were synthesized through a direct esterification reaction between glycerol, phenylacetic acid and benzoic acid, the synthesis conditions were compared in both cases. The reactions were carried out by using acidic catalyst Amberlyst -15 ,at 110°C , The synthesis yield was higher in the case of phenylacetic acid than in the case of benzoic acid.*

Key words: *Esterification, Glycerol, Amberlyst-15.*

1. Introduction:

Glycerol is an aliphatic three-function hydroxylase, and is a very important material in organic synthesis reactions as it:

1- A relatively cheap raw material and Non-toxic.

2- It is biodegradable inside the body.

3- Glycerol can be involved in many chemical reactions to synthesize different products, as it can be a starting material for synthesis of ethers, esters, carboxylic acids, polymers, diols, and other compounds as shown in figure (1) that are used in the industrial, food, pharmaceutical, and pharmaceutical fields and others [1,2,3].

4- Glycerol can be obtained in several methods and reactions, Where it is a by-product of several chemical reactions such as: biofuels synthesis, some saponification reactions, and reactions to obtain some fatty acids, in addition to the possibility of obtaining glycerol from propylene oxide [4,5,6].

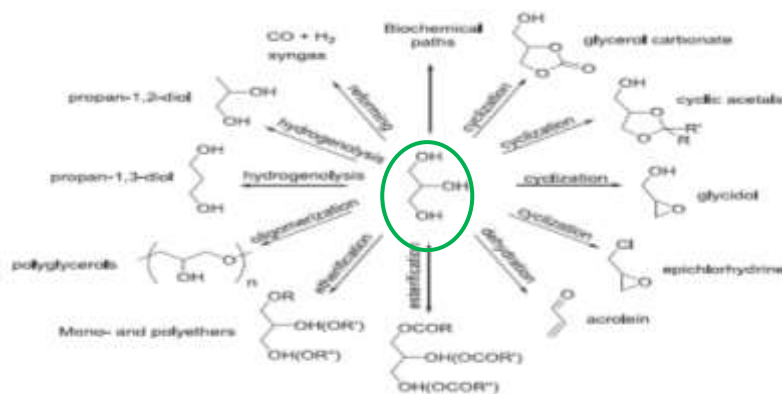


Figure 1. The most important chemical reactions to glycerol

Therefore, dozens of derivatives of glycerol were prepared such as alkyl, halide, ketone, cyclic, non-cyclic derivatives, polymers, and others, in addition to synthesizing esters, esters of saturated, unsaturated, fatty and aromatic acids. [7,8], The reaction of esterification between carboxylic acids and alcohols is one of the most important reactions in organic synthesis, because it was prepared esters and used it in many fields: such as cosmetics, perfumes, pharmaceuticals, and plastics industries, in addition to flavoring industry which are used In abundance in the food industry [9,10 ,11].

Glycerol esters were prepared with dozens of carboxylic acids: such as acetic acid, where the interaction it with glycerol by esterification reaction, it was studied to prepare the single, double and triple substitution esters, where the triple acetate of glycerol using as a solvent for dissolution and extension of many Medicines, organic compounds, as an anti-bacterial and emulsifying agent [12 ,13], the interaction of glycerol with citric and cinnamic acid was also studied: as cinnamic acid and its derivatives are important substances in the pharmaceutical and cosmetic industries, as for citric acid, it is one of the most important arteries of the food industries of all kinds, so esters of these two acids were synthesized with glycerol and the applications of the prepared esters were studied [14]

Glycerol also forms compounds called glycerides, where the esters formed by glycerol and fatty acids have carbon atoms in between (C12 - C20) with glycerides. These glycerides may be saturated or unsaturated depending on the nature of the acid used. These esters include fats, oils, animal and vegetable waxes, in addition to lipids and phospholipids, Glycerides have very great importance and applications in industries where the use of these glycerides as drug carriers (excipients) such as alginate esters is one of the most important modern applications of these compounds [15,16].

In recent years, polyesters were manufactured from glycerol and various phenyl esters. These ester polymers were used as drug carriers [17].

Esters of polymers have been used in the pharmaceutical industries as carriers of some pharmaceutical substances to reduce their hydrophilic properties, so they are able to cross the cell wall of the cell in order to deliver the drug to the desired target without changing its therapeutic efficacy [18].

2. EXPERIMENTAL:

2-1. Apparatus

- Spectra NMR proton and carbon device 400 MHz model Bruker by Switzerland company,
- spectrum infrared device model FT-IR-4100 from the Japanese company Jasco,

2-2. Reagents and materials

All chemical material and catalysts, from Sigma Aldrich and Merck

2-3. EXPERIMENTAL PROCEDURE:

Glycerol monoesters have been synthesized by using the apparatus as shown in Figure (2)

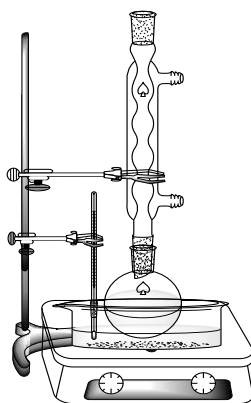


Figure 2. Box reactor for synthesis mono ester

2-3-1. Preparation (2,3-DiHydroxy Propyl Benzoate):

(0.0025mol, 0.3gr) of benzoic acid is added to a blister ball flask equipped with a magnetic stirrer, then (5% mol) of the acid medium is added. Then (1.81gr, 0.0197mol) of glycerol is added, then the reaction mixture is stirred at a temperature of 110 °C with monitoring the reaction progress by TLC aluminum thin layer chromatography using a dredging array consisting of (ethyl acetate n-hexane) (25%: 75%). The chromatogram was according by TLC aluminum thin layer chromatography of the reaction medium.

Then the mixture is left to cool down, then alkaline water saturated with: Sodium carbonate is added to the reaction medium:

To dissolve the excess glycerol used as the reactant and solvent in the reaction, In addition to converting the unreacted acid residue into a dissolved sodium salt by reacting with sodium carbonate in the aqueous phase, Then the reaction product was extracted with ethyl acetate several times.

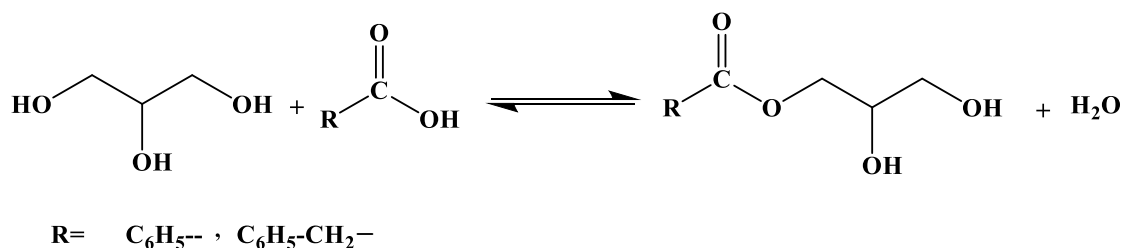
Finally, the organic phase was collected and evaporated under vacuum, dried in a disc using “P₂O₅”, then purified using glass plate chromatography to obtain an oily product with a high viscosity of yield (69%).

reaction mixture of glycerol and acid with an interactive ratio 10:1 have been put in 100 mL one neck glass flask in oil bath equipped with a magnetic stirrer and a reflux as shown in figure 2. After the acid has been completely dissolved, the acid catalyst Amberst-15 has been added for 10% mole. The reaction process has been monitored by the thin layer chromatography T.L.C mobile phase n-hexane :ethyl

acetate (6:4). The reaction ran 6 hours at 110 ° C then the catalyst has been removed by filtration. Removing the non-reactivated glycerol has been done by wash with brine. The product extract by ethyl acetate :water then the extracts have been dried over anhydrous Na₂SO₄. After removal of the solvent, the residue was purified by column chromatography using (1:1) from n-hexan: ethylacetate to give desired ester and defined its proprieties.

3. RESULTS AND DISCUSSION:

Esterification normally is a process used for preparation the esters by direct reaction between carboxylic acids and alcohols in presence of an acid catalytic, in this work we have reported a conversion of glycerol to its corresponding esters with high selectivity. Depending **direct reaction “fisher esterification”** whereas glycerol reacts with phenylacetic acid and benzoic acid.



Scheme 1. esterification of glycerol with carboxylic acid

phenyl-acetic acid is a derivative of the aromatic acetic acid, where the carboxyl group involved in the esterification reaction is linked to an aliphatic carbon atom with the SP³ hybridization pattern, In the case of benzoic acid, the carboxyl group involved in the esterification reaction is directly related to the aromatic ring, linked to a carbon atom with the SP² hybridization pattern and this difference in the attachment of the carboxyl group subject to the reaction affects the stability of the carbon carbocation formed in an intermediate period during the course of the reaction and thus affects the speed of the reaction and the yield of the prepared ester.

Whereas, according to the proposed mechanism for the conduct of the esterification reaction by the direct method, a carbon afferent is formed as an intermediate state, [19,20] and the greater the stability of this analogy formed, the faster the reaction.

while the carbonic carbocation is more stable in the case of phenylacetic acid than in the case of benzoic acid, and this explains the relatively high yield in the case of phenylacetic acid, We note that the yield when using phenylacetic acid is higher than when using benzoic acid, since the carboxylic group in the carboxylic acid is directly related to the aromatic ring.

Several factors have been studied their effect on yield: type of catalyst, quantity of catalyst, percentage of reactants and solvents.

3-1. the effect of e catalyst:

This reaction is carried out in an acidic medium, and therefore a heterogeneous acid catalyst Amberlyst-15 was used.

Table 1. effect of acid catalyst Amberlyst-15.

T = 110 °C , t = 4h , ratio : 1:acid ,10 glycerol ,	
Carboxylic Acid	Yield%
Phenylacetic acid	80%
Benzoic acid	69%

3-2. The effect of solvents:

this reaction were studied using several solvents was studied, where a wide range of proton polar solvents and proton non polar solvents can be used, as the proton solvents such as alcohols should be excluded as they compete with glycerol in the interaction with the acid, which greatly reduces the yield, and therefore, after several experiments, it is preferable to use Glycerol as a reactant and as a solvent at the same time, where it must be used in excess quantities.

table 2 . The effect of solvents.

T = 110 °C , t = 4h , ratio : 1:acid ,10 glycerol ,		
Solvets	Yield%	
	Phenylacetic acid	Benzoic acid
DMSO	41	38
Toluene	45	40
Excess glycerol	80	69

3-3. Molar ratio between (glycerol : acid) :

The change in the molar ratio of the reactants changes the yield and direction of the reaction. Sometimes this reaction can be done by changing the amount of acid or glycerol, We will explain here the effect of changing the amount of glycerol, since the synthesis of monoesters favors an excess of glycerol.

table 3. The effect of Molar ratio (glycerol : acid)

T = 110 °C , t = 4h , A-15		
Molar ratio (glycerol:acid)	Y%	
	Phenylacetic acid	Benzoic acid
3:1	40	55
5:1	50	61
8:1	76	69
10:1	76	69

4. CHARECTARIZATION:

(2,3-dihydroxypropyl 2-phenylacetate) : (80%) was obtained as a colorless oil. FT-IR, (KBr, v, cm⁻¹) : 1260 cm⁻¹: (C-O-C), 1732 cm⁻¹: (C=O , ester) 3416 cm⁻¹: (OH), 2952 cm⁻¹: (C_{SP2}-H, stretch).

¹H-NMR: (400MHz, DMSO, TMS=0ppm, δ, ppm): 7.19-7.2 (m, 5H) , 3.32-3.37 (dd, 2H, J²=11, J³=5.71Hz), 3.65-3.69 (m, 1H) , 3.923.96 (dd, 1H, J²=11.1, J³=6.5Hz) (diastereotopic protons), 4.05-4.09 (dd, 1H, J²=11.2, J³=6.5Hz), 3.63 (s, 2H),

¹³C-NMR: (100.6MHz, DMSO, TMS=0ppm, δ, ppm) : 63.4:CH₂, 70:CH, 66.8:CH₂, 171:C=O, 40:CH₂, 134.39:C, Ar , (126.75 , 129.32, 128.29):CH, Ar

(2,3-DiHydroxy Propyl Benzoate) : yeild(69%), R_f 0.58 (ethyl acetate-n.hexane) (75:25).

IR spectrum (v, cm⁻¹): 1715 (C=O), 1600, 1585, 1500 (C=C), 3100-3600 (-OH).

¹H-NMR (δ, ppm): 4.0 (2H, d, J=4Hz, CH₂OH, C-3), 4.13-4.49 (1H, m, CHOH, C-2), 4.64 (2H, d, J=4Hz,

CH₂O-CO-, C-1), 6.1 (2H, s, OH), 7.20 (3H, d, J=8Hz, Ar).

¹³C-NMR (δ, ppm): C-1 66.0 (Aδ=+3.16), C-2 70.0 (-2.2), C-3 63.0 (+0.16), aromatic. C (132.8, 129.9, 128.1),
-COO- (166.7).

5. Conclusion:

Through the previous study, some aromatic carboxylic acids were converted to their corresponding esters through a direct esterification reaction according to "Fischer reaction" with glycerol in an acidic medium and in the presence of a heterogeneous catalyst "Amberlest-15". Purification of manufactured compounds, in addition to the importance of these compounds in the fields of industrial, food, pharmaceutical and others.

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