Research Article

Synthesis of Pentagamavunon-0 (PGV-0) : An Improved Technique

Ritmaleni[1,2*]
[1]Laboratory of Medicinal Chemistry, Faculty of Pharmacy, Gadjah Mada University, Sekip Utara, Yogyakarta, Indonesia.
[2]Curcumin Research Center (CRC), Faculty of Pharmacy, Gadjah Mada University, Sekip Utara, Yogyakarta, Indonesia.
***Corresponding author's E-mail:** ritmaleni@ugm.ac.id

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ABSTRACT

Pentagamavunon-0 (PGV-0) is a very famous compound in Faculty of Pharmacy, Gadjah Mada University. This compound is a curcumin analog which has a very wide biological activities' range. So far, we adopted the published method to our organic chemistry laboratory experiment demonstration. The preparation took 14 days. In this research we were trying to improve the technique in making PGV-0 like shorten the time of reaction, more easy and clean isolation and purification technique. The result showed that the preparation now can be done in two hours' time and subsequently followed by isolation and purification. This research also confirms the right color of PGV-0.

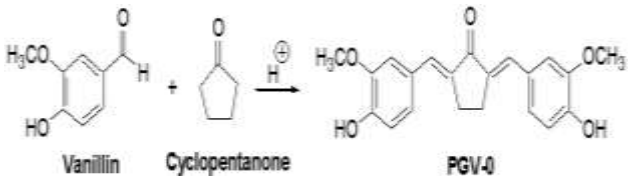
Keywords: Pentagamavunon-0, curcumin, preparation, technique, laboratory experiment.

INTRODUCTION

Pentagamavunon-0 (PGV-0) is a curcumin analog that was firstly published by Faculty of Pharmacy, Gadjah Mada University, Yogyakarta, Indonesia. Our first publication was published in 1997.[1] It has a wide range of biological activities such as antiinflammation, antioxidant and antimicrobial.[2] Its analog, pentagamavunon-1 (PGV-1) also has a good anti-cancer activity.[3] PGV-0 is a very popular compound in our department even in our country. PGV-0 has also been patented in Indonesia[4] and in the US[5]. PGV-0 and PGV-1 are two of our compounds that have enter in vivo preclinical test.[6] Not only analog of curcumin that have been successfully made. As we have Curcumin Research Center (CRC), we also made some of the analog of tetrahydrocurcumin (THC) and we evaluated its biological activities.[7-10]

There are many kinds and type of methods published in the synthesis of curcumin analogs.[11] PGV-0 is made from vanillin and cyclopentanone by using carbonyl condensation reaction. According to previous publication, it took 14 days to react both starting material.

And it needs more time for isolation and purification. So far, we implement this reaction as one topic in our organic chemistry laboratory experiment demonstration for first year undergraduate student. But this is not efficient and effective experiment so far just because we have to wait for two weeks to work on the reaction.



Scheme 1: Synthesis of PGV-0

How we are in Faculty of Pharmacy, we intended to apply our research results in the organic laboratory experiment in making some new medicines. This program is more education based research. This improved technique is aimed to shorten the reaction time and gain an easy and effective of isolation and purification processes. Among reactions that we discovered, PGV-0 is the choice because this is an easy reaction to do and in line with our organic chemistry lecture.

The techniques that been tried to be improved are whether the type of acid, solvent and particle collision could increase the rate of reaction for this PGV-0 preparation and make the whole color of PGV-0 are the same each time.

MATERIALS AND METHODS

Material

Vanillin (E-merk), vanillin (from traditional market in Yogyakarta), cyclopentanone (Aldrich), Acid Chloride (E-Merck), Phosporic acid (E-Merck), Acetic acid (E-Merck).

Experimental Technique

The experiment was designed in four parts.

One reaction was following the published method using vanillin pro analysis, followed the technique from the published method.

Four reactions were using vanillin pro analysis two reaction using different acids without solvent, two reactions using different acids with solvent, followed the technique from the published method and stirred with magnetic stirrer.

By using vanillin from Indonesian Traditional Market two reactions using different acids without solvent, two reactions using different acids with solvent, stirred with

magnetic stirrer and new technique of maceration was applied.

General procedure was carried out by mixing vanillin (3.7 g; 25 mmol) and cyclopentanone (1.1 mL : 12.5 mmol) in an erlenmeyer. Then acid (0.5 mL) was added to each flask according to the table 1. The reaction mixture of flask 0 was mixed by hand for two hours and left for 14 days. Flask 1-8 was mixed by magnetic stirrer and the reaction was followed by TLC. After that, the reaction mixture was macerated with Acetic acid and water ((1 : 1); 50 mL), filtered under vacuum and washed with hot water. Product then was allowed to dry (Table 1).

Table 1: Experimental design

No	Design	Acid	Solvent	Technique
0	I, vanillin p.a.	HCl	No	Old technique
a	II, vanillin p.a	HCl	No	Old technique
b		H_3PO_4	No	
c		HCl	Yes	
d		H_3PO_4	Yes	
1	III, vanillin from Indonesian traditional market	HCl	No	Improved technique
2		H_3PO_4	No	
3		HCl	Yes	
4		H_3PO_4	Yes	
5	IV, vanillin p.a.	HCl	No	Improved technique
6		H_3PO_4	No	
7		HCl	Yes	
8		H_3PO_4	Yes	

RESULTS AND DISCUSSION

The main reason why this small research is done is because many times each person has their own colour and texture of PGV-0. The experiment was carried out to check whether the type of acid, solvent and particle collision could increase the rate of reaction for this PGV-0 preparation. According to the results, some points can be explained like below.

Design I

This experiment was followed the published method[1]. The reaction was stirred by hand spatula for two hours and left for 14 days without any more treatment. The all techniques were followed exactly what paper said. After macerated, filtered and washed, the color and texture of PGV-0 obtained was not good like in the figure 1 below.

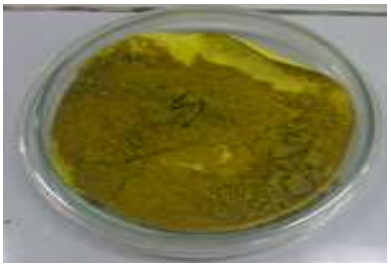


Figure 1: PGV-0 from published method

Acid, solvent and particle collision

Pro analysis vanillin and cyclopentanone were used as starting material. The experiment was followed the published method but the reaction were followed by TLC for four hours, stirred by using stirrer bar and magnetic stirrer and left for 14 days.

Reaction a and c were used HCl acid but reaction c with ethanol as solvent. Reaction b and d used H3PO4 as acid and reaction d with ethanol as solvent. Maceration and washing were also following the experiment in first design.

After drying the products, it was found that reaction a and c gave PGV-0 like product in design 1 but reaction b and c gave less PGV-0 even reaction d almost no PGV-0 collected like in figure 2 below. Here we can see that HCl is the best acid for this kind of reaction and solvent gave bad influence for the isolation processes. Stirring was important in this reaction.

Compared to stirring by hand, Stirrer bar made the particle collision much better so PGV-0 formation is more effective like shown in below figure where the texture of PGV-0 is better.

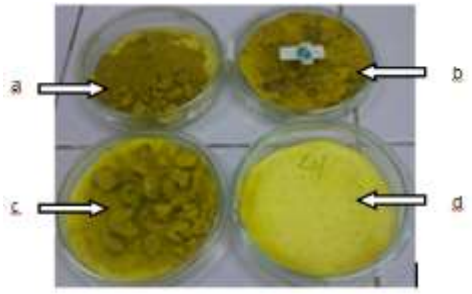


Figure 2: A series of PGV-0 from changing the acid and adding solvent.

Vanillin and maceration technique improvement

A series of preparation of PGV-0 was shown in figure 2, where vanillin from Indonesian market in Yogyakarta used as starting material. Reaction 1 used HCl with no solvent while reaction 3 used HCl with ethanol added as solvent. Reaction 2 used H3PO4 with no solvent while reaction 4 ethanol added as solvent. The reaction mixture was followed by TLC for two hours and then the product was isolated. The improved technique that used is the way of crude product macerated. Acetic acid and water ((1 : 1) (30 mL) was added to each of the reaction mixtures while mixing. Then it was transformed into a crucible. Next 20 mL of Acetic acid and water ((1 : 1) was added and stir well. This the crucial part in order to remove the acid. After filtered under vacuum and washed with hot water, the isolated PGV-0 was allowed to dry. The colour and texture of PGV-0 obtained from this technique is much better compared to previous technique like shown in figure 3 below. But because the vanillin is vanillin from one Indonesian market, that is not really pure, the appearance of PGV-0 is still not very well.

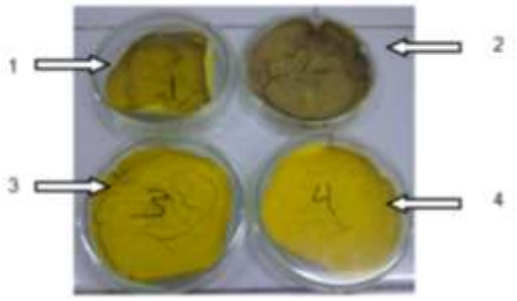


Figure 3: A series of PGV-0 from vanillin form an Indonesian traditional market and improved technique

Vanilin pro analysis

Like above experiments, this series is the same as point 3.3 but the different only on the type of vanillin used. Reaction 1 is equal to reaction 5, reaction 2 is equal to reaction 6 and etc. All the techniques are also the same. From figure below, it can be seen that that reaction 5 is much better in colour and texture compared to reaction 1. Reaction 5 also gave a higher yield among the experiments that carried out at this time.

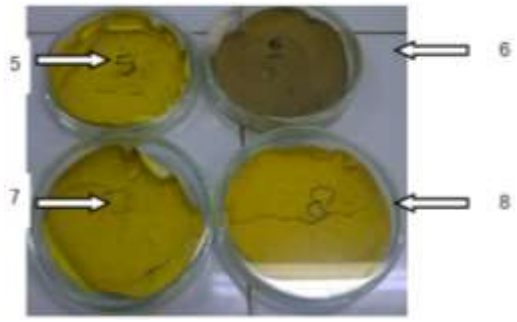


Figure 4: A series of PGV-0 from vanillin pro analysis and improved technique

Analysis

IR spectra for all samples are almost the same with ketone peak at 1667 cm^{-1}. But each has different melting point. Samples 2 -7, m. p. = 206 – 208 °C; sample 1, m. p. = 212 – 213 °C; sample 8, m. p. = 210 – 212 °C. After recrystalised from ethanol the compound is pure with m.p. 212-213 °C in orange crystalline form like figure below.

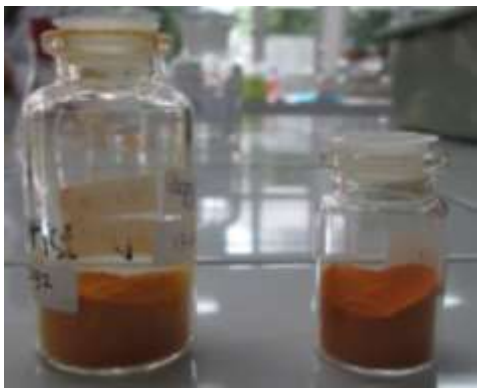


Figure 5: The best PGV-0 from improved technique

CONCLUSION

The best product found after improving some techniques is the product that used HCl as acid catalyst, no solvent, mixed with magnetic bar for two hours, macerated well in acetic acid:water (1:1) and washed with hot water. Melting Point = 212-213 °C (EtOH).

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