SINTESIS DAN UJI AKTIVITAS ANTIBAKTERI SENYAWA PIRAZOLINA BERBAHAN DASAR 3-METOKSI-4-HIDROKSIBENZALDEHIDA (VANILIN) DAN 4-METOKSIBENZALDEHIDA (p-ANISALDEHIDA)

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INTISARI

Telah dilakukan sintesis turunan senyawa pirazolina serta uji aktivitasnya sebagai antibakteri. Senyawa pirazolina pada penelitian ini terdiri dari N-fenil-3-(4-klorofenil)-5-(4-hidroksi-3-metoksi-5-nitrofenil)-2-pirazolina (pirazolina **1**), N-fenil-3-(4-hidroksifenil)-5-(4-hidroksi-3-metoksi-5-nitrofenil)-2-pirazolina (pirazolina **2**), dan N-fenil-3-(2,4-dihidroksifenil)-5-(4-metoksifenil)-2-pirazolina (pirazolina **3**). Pirazolina **1**, **2**, dan **3** disintesis menggunakan metode refluks dengan asam asetat glasial sebagai katalis.

Pirazolina **1** dan **2** masing-masing disintesis melalui reaksi siklokondensasi 1-(4-klorofenil)-3-(4-hidroksi-3-metoksi-5-nitrofenil)-2-propen-1-on (kalkon **1**) dan 1-(4-hidroksifenil)-3-(4-hidroksi-3-metoksi-5-nitrofenil)-2-propen-1-on (kalkon **2**) dengan fenilhidrazin sedangkan pirazolina **3** disintesis dengan metode siklokondensasi antara 1-(2,4-dihidroksifenil)-3-(4-metoksifenil)-2-propen-1-on (kalkon **3**) dan hidrazin monohidrat. Senyawa kalkon **1** dan **2** masing-masing diperoleh dari reaksi kondensasi Claisen Schmidt antara 4-hidroksi-3-metoksi-5-nitrobenzaldehida (nitrovanilin) dengan 4-kloroasetofenon dan 4-hidroksiasetofenon menggunakan katalis NaOH 40% (b/v) sedangkan kalkon **3** merupakan hasil dari reaksi 4-metoksibenzaldehida (p-anisaldehida) dengan 2,4-dihidroksiasetofenon menggunakan katalis KOH 60% (b/v). Senyawa nitrovanilin diperoleh dari reaksi nitrasi vanillin menggunakan kalsium nitrat ($Ca(NO_3)_2$). Produk hasil sintesis dianalisis menggunakan spektrometer FTIR, GC-MS, ^{1}H- dan^{13}C-NMR. Uji aktivitas antibakteri hanya dilakukan pada pirazolina **3** karena pirazolina **3** mempunyai kemurnian yang paling tinggi daripada pirazolina **1** dan **2**. Uji aktivitas antibakteri menggunakan metode "difusi sumuran" menggunakan bakteri Gram positif (*S. aureus, B. cereus,* dan *B. subtillis*) dan Gram negatif (*E. coli* dan *S. flexneri*) serta DMSO 99% sebagai control negatif dan tetrasiklin (100 ppm) sebagai control positif.

Hasil reaksi nitrasi terhadap vanilin yaitu senyawa nitrovanilin dengan rendemen 95,95%. Hasil reaksi kondensasi Claisen-Schmidt berupa senyawa kalkon **1**, **2**, dan **3** dengan rendemen masing-masing 94,60%; 47,17%; dan 30,34%. Senyawa target berupa pirazolina **2** dan **3** berhasil disintesis dengan rendemen masing-masing 42,86% dan 71,43%. Senyawa pirazolina **3** menunjukkan adanya aktivitas antibakteri baik pada bakteri Gram positif maupun Gram negatif. Aktivitas tertinggi terjadi pada konsentrasi 500 ppm pada bakteri *S. aureus* dan *B. cereus* dan 1000 ppm pada bakteri *B. subtillis, E. coli* dan *S. flexneri*.

Kata kunci : pirazolina, kalkon, vanilin, p-anisaldehida, aktivitas antibakteri.

SYNTHESES AND ANTIBACTERIAL ACTIVITIES OF PYRAZOLINES FROM 3-METHOXY-4-HYDROXYBENZALDEHYDE (VANILLIN) AND 4-METHOXYBENZALDEHYDE (p-ANISALDEHYDE)

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ABSTRACT

Syntheses of pyrazoline derivatives and their antibacterial activities have been done. The pyrazolines that have been synthesized were N-phenyl-3-(4-chlorophenyl)-5-(4-hydroxy-3-methoxy-5-nitrophenyl)-2-pyrazoline (pyrazoline **1**), N-phenyl-3-(4-hydroxyphenyl)-5-(4-hydroxy-3-methoxy-5-nitrophenyl)-2-pyrazoline (pyrazoline **2**), and N-phenyl-3-(2,4-dihydroxyphenyl)-5-(4-methoxyphenyl)-2-pyrazoline (pyrazoline **3**). Pyrazolines **1**, **2**, and **3** were synthesized by reflux method with glacial acetic acid as a catalyst.

Both pyrazoline **1** or **2** were synthesized through cyclocondensation reaction between 1-(4-chlorophenyl)-3-(4-hydroxy-3-methoxy-5-nitrophenyl)-2-propen-1-on (chalcone **1**) and 1-(4-hydroxyphenyl)-3-(4-hydroxy-3-methoxy-5-nitrophenyl)-2-propen-1-on (chalcone **2**) with phenyl hydrazine, whereas pyrazoline **3** was synthesized through the cyclocondensation method, between 1-(2,4-dihydroxyphenil)-3-(4-methoxyphenyl)-2-propen-1-on (chalcone **3**) and hydrazine monohydrate. Chalcones **1** and **2** were synthesized through Claisen Schmidt condensation method of 4-hydroxy-3-methoxy-5-nitrobenzaldehyde (nitrovanillin) with 4-chloroacetophenone and with 4-hydroxyacetophenone using catalyst of NaOH 40% (w/v), whereas chalcone **3** was synthesized from 4-methoxybenzaldehyde (p-anisaldehyde) and 2,4-dihydroxyacetophenone using catalyst of KOH 60% (w/v). Nitrovanillin was obtained by nitration of vanillin using calcium nitrate ($Ca(NO_3)_2$). The products of syntheses were analyzed by FTIR, GC-MS, ^{1}H- and ^{13}C-NMR. The antibacterial activity test was only performed on pyrazoline **3** because pyrazoline **3** has the highest purity than pyrazolines **1** and **2**. The antibacterial activities test has been done with "wells diffusion method" using Gram positive bacteria (*S. aureus, B. cereus,* and *B. subtillis*) and Gram negative bacteria (*E. coli* and *S. flexneri*), also DMSO 99% as a negative control and tetracycline (100 ppm) as a positive control.

The result from nitration of vanillin showed that nitrovanillin was obtained at 95.95% yield. On the other hand, Claisen Schmidt condensation has produced chalcones **1**, **2**, and **3** with the yield of 94.60%; 47.17%; and 30.34%, whereas products of pyrazolines **2** and **3** were 42.86% and 71.43%. Pyrazoline **3** showed good antibacterial activity both in Gram positive and Gram negative bacteria. The highest activity showed at 500 ppm for *S. aureus* and *B. cereus*, also 1000 ppm for *B. subtillis, E. coli* and *S. flexneri*.

Keywords: pyrazoline, chalcone, vanillin, p-anisaldehyde, antibacterial activity.