

SINTESIS SENYAWA N-FENIL DAN N-ASETILPIRAZOLINA MELALUI INTERMEDIET DIBENZALASETON DAN UJI AKTIVITAS ANTIMALARIANYA

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INTISARI

Sintesis senyawa dibenzalaseton (1,5-difenilpenta-1,4-dien-3-on (**5**); 1,5-bis(3,4-dimetoksifenil)penta-1,4-dien-3-on (**6**); 1,5-bis(4-metoksifenil)-penta-1,4-dien-3-on (**7**)); dan senyawa *N*-fenilpirazolina (1,5-difenil-3-stiril-4,5-dihidro-1*H*-pirazol (**9**); 5-(3,4-dimetoksifenil)-3-(3,4-dimetoksistiril)-1-fenil-4,5-dihidro-1*H*-pirazol (**10**); 5-(4-metoksifenil)-3-(4-metoksistiril)-1-fenil-4,5-dihidro-1*H*-pirazol (**11**)); serta senyawa *N*-asetilpirazolina (1-(5-fenil-3-stiril-4,5-dihidro-1*H*-pirazol-1-il)etanon (**14**); 1-(5-(3,4-dimetoksifenil)-3-(3,4-dimetoksistiril)-4,5-dihidro-1*H*-pirazol-1-il)etanon (**15**); 1-(5-(4-metoksifenil)-3-(4-metoksistiril)-4,5-dihidro-1*H*-pirazol-1-il)etanon (**16**)) telah dilakukan. Aktivitas antimalaria senyawa 5-7, 9-11 dan 14-16 telah berhasil ditentukan melalui uji aktivitas penghambatan polinmeisasi hem.

Sintesis senyawa dibenzalaseton **5-7** dilakukan melalui kondensasi Claisen-Schmidt antara aseton (**1**) dengan turunan benzaldehida berupa benzaldehida (**2**), veratraldehida (**3**) dan *p*-anisaldehida (**4**) dengan katalis natrium hidroksida (NaOH). Senyawa turunan *N*-fenilpirazolina **9-11** diperoleh melalui reaksi siklokondensasi antara senyawa **5-7** dan fenilhidrazin (**8**) dengan asam asetat (CH₃COOH) sebagai katalis. Senyawa *N*-asetilpirazolina diperoleh dari reaksi siklokondensasi antara senyawa **5-7** dan hidrazinhidrat (**12**) dengan asam asetat (**13**) sebagai katalis dan reagen. Produk hasil sintesis dianalisis menggunakan spektrometer FTIR, *direct inlet*-MS (DI-MS), GC-MS, ¹H- dan ¹³C-NMR.

Sintesis senyawa **5, 6, 7, 9, 10, 11, 14, 15** dan **16** dihasilkan dengan persen hasil berturut-turut adalah 97,65; 90,96; 70,75; 82,17; 70,45; 88,31; 73,27; 56,10; dan 77,14 %. Uji aktivitas penghambatan polimerisasi hem senyawa tersebut menghasilkan nilai IC₅₀ masing-masing 1,23; 0,49; 1,39; 1,26; 0,79; 1,08; 3,47; 1,39; dan 3,16 mM. Nilai IC₅₀ senyawa hasil sintesis dibawah dari nilai IC₅₀ kuinin sebagai kontrol positif sehingga senyawa hasil sintesis berpotensi dikembangkan sebagai kandidat antimalaria.

Kata kunci: antimalaria, dibenzalaseton, penghambatan polimerisasi hem, *N*-asetilpirazolina, *N*-fenilpirazolina.

SYNTHESIS OF *N*-PHENYL AND *N*-ACETILPYRAZOLINE TROUGH DIBENZALACETONE INTERMEDIATES AND THEIR ANTIMALARIAL ACTIVITY ASSAYS

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ABSTRACT

Synthesis of dibenzalacetones (1,5-diphenylpenta-1,4-dien-3-one (**5**); 1,5-bis(3,4-dimetoxyphenyl)penta-1,4-dien-3-one (**6**); 1,5-bis(4-metoxyphenyl)-penta-1,4-dien-3-one (**7**)); and *N*-phenylpyrazolines (1,5-diphenyl-3-styryl-4,5-dihydro-1*H*-pyrazole (**9**); 5-(3,4-dimetoxyphenyl)-3-(3,4-dimetoxystryl)-1-phenyl-4,5-dihydro-1*H*-pyrazole (**10**); 5-(4-metoxyphenyl)-3-(4-metoxystryl)-1-phenyl-4,5-dihydro-1*H*-pyrazole(**11**)); as well as *N*-acetylpyrazolines (1-(5-phenyl-3-styryl-4,5-dihydro-1*H*-pyrazole-1-yl)etanone (**14**); 1-(5-(3,4-dimetoxyphenyl)-3-(3,4-dimetoxystryl)-4,5-dihydro-1*H*-pyrazole-1-yl)etanone (**15**); 1-(5-(4-methoxyphe-nyl)-3-(4-methoxystryl)-4,5-dihydro-1*H*-pirazole-1-yl)etanone (**16**)) have been carried out. Antimalarial activity assay of compounds **5-7**; **9-11** and **14-16** have been determined by Heme Polymerization Inhibitory Activity (HPIA) assay.

Synthesis of dibenzalacetones **5-7** have been conducted via Claisen-Schmidt condensation between acetone (**1**) and benzaldehyde derivatives, such as benzaldehyde (**2**), veratraldehyde (**3**) and *p*-anisaldehyde (**4**) with sodium hydroxide (NaOH) as catalyst. *N*-phenylpyrazolines **9-11** can be produced via cyclocondensation reaction between dibenzalacetones **5-7** and phenylhydrazine (**8**) with acetic acid (CH₃COOH) as catalyst. *N*-acetylpyrazolines of **14-16** can be obtained via cyclocondensation reaction between dibenzalacetones **5-7** and hydrazinhydrate (**12**) with acetic acid (**13**) as catalyst and reagent. Products were analyzed using FTIR spectrometry, direct inlet-MS (DI-MS), GC-MS, ¹H- and ¹³C-NMR.

The synthesis experiments afforded the expected product were the yields for **5, 6, 7, 9, 10, 11, 14, 15** and **16** were 97.65; 90.96; 70.75; 82.17; 70.45; 88.31; 73.27; 56.10; and 77.14 % respectively. The result of Heme Polymerization Inhibition Activity assay gave IC₅₀ value of 1.23; 0.49; 1.39; 1.26; 0.79; 1.08; 3.47; 1.39; and 3.16 mM respectively under IC₅₀ value of quinine as positive control. Based on the IC₅₀ value, compounds **5-7**, **9-11** and **14-16** potential as antimalarial candidates.

Keywords: antimalaria, dibenzalacetone, HPIA, *N*-acetylpirazoline, *N*-phenylpirazoline