

**SYNTHESIS OF CHALCONE AND PYRAZOLINE DERIVATIVES
FROM 4-METHOXYACETOPHENONE AND
2,4-DIMETHOXYACETOPHENONE AND THEIR ACTIVITIES ASSAY
AS ANTIMALARIAL AGENTS**

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ABSTRACT

The synthesis of chalcone and pyrazoline derivative from 4-methoxyacetophenone, 2,4-dimethoxyacetophenone, and antimalaria activity assay have been carried out. The objectives of this study is to synthesize (*E*)-1,3-bis(4-methoxyphenyl)prop-2-en-1-one (**chalcone A**), (*E*)-1-(2,4-dimethoxyphenyl)-3-phenylprop-2-en-1-one (**chalcone B**), 3,5-bis(4-methoxyphenyl)-4,5-dihydro-1H-pyrazole-1-carbaldehyde (**Pyrazoline A**), and 3-(2,4-dimethoxyphenyl)-5-phenyl-4,5-dihydro-1H-pyrazole-1-carbaldehyde (**Pyrazoline B**) and to discover potent antimalaria agent from the synthesized compound.

Synthesis of **chalcone A** and **B** were performed using *Claisen-Schmidt* condensation reaction. The synthesis was conducted by reacting 4-methoxyacetophenone with *p*-anisaldehyde using sonication method and 2,4-dimethoxyacetophenone with benzaldehyde using stirring method in ethanol at room temperature with the presence of KOH 10% and NaOH 20% as a catalyst. The synthesis of *N*-formylpyrazoline **A** and **B** was carried out using cyclocondensation reaction by reacting **chalcone A** or **chalcone B** with hydrazine hydrate in ethanol and 98-100% formic acid using NaOH 30% under reflux for 24 hours. All the synthesized products were characterized by using FTIR, GC-MS, ¹H-, and ¹³C-NMR spectrometers, and their antimalarial activities were tested by *in vitro* assay against *Plasmodium falciparum* 3D7.

The result showed that **chalcone A** and **B** were obtained as pale-yellow solid in 87.21 and 87.96% yield, respectively. The cyclocondensation reaction produced *N*-formylpyrazoline **A** as a white solid in 55.80% yield, while *N*-formylpyrazoline **B** was obtained as a yellow solid in 68.22% yield. The antimalaria activity test of **chalcone A**, **chalcone B**, *N*-formylpyrazoline **A**, and *N*-formylpyrazoline **B** gave IC₅₀ values of 2.89; 1.29; 24.19; dan 29.18 μM, respectively. It can be concluded that **chalcone A** and **chalcone B** were categorized as active antimalarial agents, *N*-formylpyrazoline **A** and *N*-formylpyrazoline **B** were categorized as a compound with moderate activity as antimalarial agents.

Keywords: 4-methoxyacetophenone, antimalarial, chalcone, *N*-formylpyrazoline, *Plasmodium falciparum* 3D7.

SINTESIS TURUNAN SENYAWA KALKON DAN PIRAZOLINA DARI 4-METOKSIASETOFENON DAN 2,4-DIMETOKSIASETOFENON SERTA UJI AKTIVITASNYA SEBAGAI SENYAWA ANTIMALARIA

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INTISARI

Sintesis turunan senyawa kalkon dan pirazolina dari 4-metoksiasetofenon, 2,4-dimetoksiasetofenon, dan uji antimalarianya telah dilakukan. Tujuan dari penelitian ini yaitu untuk mensintesis (E)-1,3-bis(4-metoksifenil)prop-2-en-1-on (**kalkon A**), (E)-1-(2,4-dimetoksifenil)-3-fenilprop-2-en-1-on (**kalkon B**), 3,5-bis(4-metoksifenil)-4,5-dihidro-1H-pirazole-1-karbaldehid (**Pirazolina A**), and 3-(2,4-dimetoksifenil)-5-fenil-4,5-dihidro-1H-pirazol-1-karbaldehid (**Pirazolina B**) dan senyawa yang telah disintesis diuji aktivitasnya sebagai antimalaria.

Sintesis **kalkon A** dan **B** dilakukan melalui reaksi kondensasi *Claisen-Schmidt*. Sintesis dilakukan dengan mereaksikan 4-metoksiasetofenon dengan *p*-anisaldehid menggunakan metode sonikasi dan 2,4-dimetoksiasetofenon dengan benzaldehid menggunakan metode pengadukan dalam etanol pada suhu kamar dengan adanya KOH 10% dan NaOH 20% sebagai katalis. Sintesis *N*-formilpirazolina **A** dan **B** dilakukan melalui reaksi siklokondensasi dengan mereaksikan **kalkon A** atau **kalkon B** dan hidrazin hidrat dalam etanol dan asam format 98-100% menggunakan NaOH 30% dengan metode refluks selama 24 jam. Semua produk hasil sintesis dikarakterisasi menggunakan spektrometer FTIR, GC-MS, ¹H-, dan ¹³C-NMR dan aktivitas antimalarialnya diuji secara *in vitro* terhadap *Plasmodium falciparum* 3D7.

Hasil penelitian menunjukkan bahwa **kalkon A** dan **B** menghasilkan padatan kuning pucat dengan *yield* berurutan yaitu 87,21 dan 87,96%. Reaksi siklokondensasi menghasilkan padatan putih *N*-formilpirazolina **A** dengan *yield* 55,80%, sedangkan *N*-formilpirazolina **B** diperoleh sebagai padatan kuning dengan *yield* 68,22%. Uji aktivitas antimalaria terhadap **kalkon A**, **kalkon B**, *N*-formilpirazolina **A**, dan *N*-formilpirazolina **B** memberikan nilai IC₅₀ sebesar 2,89; 1,29; 24,19; dan 29,18 µM. Dapat disimpulkan bahwa **kalkon A** dan **B** dikategorikan sebagai agen antimalaria yang aktif, sedangkan *N*-formilpirazolina **A** dan **B** dikategorikan sebagai senyawa dengan aktivitas sedang sebagai senyawa antimalaria.

Kata kunci: 4-metoksiasetofenon, antimalaria, kalkon, *N*-formilpirazolina, *Plasmodium falciparum* 3D7