

Synthesis of hydroxylated azomethine compounds and the antioxidant activity

by Nor Basid Adiwibawa Prasetya

Submission date: 23-May-2023 03:43PM (UTC+0700)

Submission ID: 2099927481

File name: 2020_-_AIP_-_Synthesis_of_hydroxylated_azomethine_compounds.pdf (1.06M)

Word count: 4700

Character count: 27436

RESEARCH ARTICLE | JUNE 02 2020

Synthesis of hydroxylated azomethine compounds and the antioxidant activity

Nova Rifqi Rahmawati; Ngadiwiyana; Nor Basid Adiwibawa Prasetya; ... et. al

 Check for updates

AIP Conference Proceedings 2237, 020023 (2020)

<https://doi.org/10.1063/5.0005806>



View
Online



Export
Citation

CrossMark

Articles You May Be Interested In

12

Synthesis and characterization of 1,6-di-O-azomethine ester-2,4:3,5-di-O-benzylidene-D-Glucitol

AIP Conference Proceedings (February 2023)

30

Synthesis, characterization, and studying of new azo-azomethine ligand and its complexes: Analysis of their biological activity

AIP Conference Proceedings (December 2022)

Diffracting samples: Nonlinear optical properties and morphology for (2-hydroxyphenyl) [2-(2-methoxybenzylidene-amino)-5-methyl phenyl] telluride film

AIP Conference Proceedings (December 2020)

Downloaded from http://pubs.aip.org/aip/acp/article-pdf/doi/10.1063/5.0005806/1421270/020023_1_online.pdf



Time to get excited.

Lock-in Amplifiers – from DC to 8.5 GHz



Find out more



Synthesis of Hydroxylated Azomethine Compounds and the Antioxidant Activity

Nova Rifqi Rahmawati¹, Ngadiwiya¹, Nor Basid Adiwibawa Prasetya²,
Purbowatingrum Ria Sarjono³, Yosie Andriani⁴, Desy Fitriya Syamsunir⁴,
Ismiyarto^{1,a}

¹ Organic Chemistry Laboratory, Department of Chemistry, Faculty of Science and Mathematics, Diponegoro University, Semarang, Indonesia

² Analytical Chemistry Laboratory, Department of Chemistry, Faculty of Science and Mathematics, Diponegoro University, Semarang, Indonesia

³ Biochemistry Laboratory, Department of Chemistry, Faculty of Science and Mathematics, Diponegoro University
⁴ Institute of Marine Biotechnology, Universiti Malaysia Terengganu, Malaysia

^aCorresponding author: ismiyarto@live.undip.ac.id

Abstract. Azomethine compounds are one group of compounds that play a biologically important role as antioxidants. Azomethine compounds have a group ($>C=N-$) from the condensation reaction between the carbonyl group of the aldehyde or ketone and the nucleophilic primary amine through an addition-elimination reaction. The presence of a substituent such as a hydroxyl group (-OH) attached to an azomethine is reported to affect antioxidant activity. The purposes of this study were to synthesize hydroxylated azomethine derivative compounds including *N,N'*-Bis(2-hydroxybenzylidene) ethylenediamine from salicylaldehyde and ethylenediamine and *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene) ethylenediamine from vanillin and ethylenediamine, and synthesize azomethine compound *N,N'*-Bis(benzylidene) ethylenediamine as a comparison. The antioxidant activity of three azomethine derivatives was tested using DPPH method. The results were hydroxylated azomethine derivative compounds. *N,N'*-Bis(2-hydroxybenzylidene) ethylenediamine was obtained as a yellow solid with a yield of 87.04% and a melting point of 125.6-127.5 °C. *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene) ethylenediamine was obtained as a light brown solid with a yield of 70.045% and a melting point of 220.2-222.1 °C. *N,N'*-Bis(benzylidene) ethylenediamine was obtained as an orange solid with a yield of 34.83% and melting point 110.2-111.4 °C. The antioxidant activity test results show IC_{50} values for the three azomethine derivatives of *N,N'*-Bis(2-hydroxybenzylidene) ethylenediamine, *N,N'*-Bis(benzylidene) ethylenediamine and *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene) ethylenediamine were 130.573 ppm, 187.66 ppm and 235.164 ppm, respectively.

INTRODUCTION

Antioxidants are compounds that can inhibit the oxidation reaction of a substance in low concentration [1]. Antioxidants can be found from natural antioxidants or synthetic antioxidants. Natural antioxidants mostly can be found from plants containing tocopherols, carotenoids, ascorbic acid, phenols, and flavonoids [2]. One compound that can be used as a synthetic antioxidant is azomethine. Azomethine compounds are the result of a condensation reaction between carbonyl groups of aldehydes or ketones with the nucleophilic primary amine [3]. Several previous studies have reported antioxidant activity in azomethine compounds which have an imine group and are substituted with hydroxyl groups (-OH) on the benzene ring [4]. According to Nakiboglu et al. [5], DPPH free radical capture ability is influenced by hydroxyl groups (-OH). The presence of a hydroxyl group (-OH) which is bound to the benzene ring with different positions, will affect antioxidant activity.

8

The 14th Joint Conference on Chemistry 2019

AIP Conf. Proc. 2237, 020023-1-020023-11; <https://doi.org/10.1063/1.50005806>
Published by AIP Publishing, 978-0-7354-1996-4/\$30.00

020023-1

In this study, the synthesis of azomethine derivatives has two imine groups and substituted hydroxyl groups (-OH) on the benzene ring. Synthesis of hydroxylated azomethine derivatives include synthesis of *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine from salicylaldehyde and ethylenediamine substituted by hydroxyl group (-OH) at *ortho* position and *N,N'*-Bis(2-hydroxy-3-methoxybenzylidene)ethylenediamine from vanillin and ethylenediamine substituted with hydroxyl group (-OH) at *para* position and methoxy group (-OCH₃) at the *meta* position. The third synthesis of *N,N'*-Bis(benzylidene)ethylenediamine from benzaldehyde and ethylenediamine have no substituents bound to the benzene ring. Three azomethine derivatives were tested for antioxidant activity using DPPH method.

EXPERIMENTAL

Materials used include salicylaldehyde (Merck), vanillin (Sigma Aldrich), benzaldehyde (Merck), ethylenediamine (Merck), glacial acetic acid (Merck), ethanol pa (Merck), methanol pa (Merck), ethyl acetate pa (Merck), n-hexane pa (Merck), dichloromethane pa (Merck), toluene pa (Merck), chloroform pa (Merck), TLC plate, Whatman filter paper no. 42, DPPH (Sigma Aldrich), quercetin (Sigma Aldrich), DPPH (Sigma Aldrich).

The tools used include a set of laboratory glassware, a set of reflux devices, a set of Thin Layer Chromatography (TLC), Buchner funnel, magnetic stirrer and bar, analytical balance, Rotary Evaporator Buchi R-3, 254 nm UV lamp and 366 nm, Electrothermal Fuse Type Melting Point, Shimadzu UV-1280 UV-Visible (Ultra Violet-Visible) spectrophotometer, Perkin Elmer 96681 Frontier Fourier Transform Infrared (FTIR), and NMR Bruker 400 MHz.

24

Synthesis of *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine from Salicylaldehyde and Ethylenediamine

24

Ethylenediamine compound 0.67 mL (10 mmol) was dissolved in 10 mL of methanol in one neck round bottom flask. 2.12 mL (20 mmol) of salicylaldehyde compounds was dissolved into 15 mL of methanol. Salicylaldehyde solution was added drop by drop in ethylenediamine solution accompanied by stirring using a magnetic stirrer with a rotation speed of 400 rpm. The mixture was reacted at room temperature (29 °C) for 15 minutes and monitored the reaction using TLC with eluent ethyl acetate: n-hexane = 1:3. The reaction mixture was cooled in a refrigerator for 10 min and filtered and recrystallized with methanol, filtered and dried at room temperature. The solid product was weighed and analyzed for its physical properties such as melting point measurements and solubility tests. The solids of the product were analyzed using UV-Visible spectrophotometry and infrared [5].

Synthesis of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine from Vanillin and Ethylenediamine at Room Temperature (29 °C)

Ethylenediamine compounds 0.67 mL (10 mmol) was dissolved in 10 mL ethanol in a three-neck round bottom flask. 3.03 g (20 mmol) of vanillin was dissolved in 15 mL of ethanol. Vanillin solution was added dropwise to ethylenediamine solution accompanied by stirring using a magnetic stirrer with a rotation speed of 400 rpm. The mixture was reacted at room temperature for 15 minutes and monitored the reaction using TLC with eluent of ethyl acetate: n-hexane (1:3). The reaction mixture was cooled in a refrigerator for 10 min, and filtered and recrystallized with methanol, filtered and dried at room temperature. The solid product was weighed and analyzed for its physical properties in the form of melting point measurements and solubility tests. The solids of the product were analyzed using UV-Visible spectrophotometry and infrared [7].

Synthesis of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine from Vanillin and Ethylenediamine at 78 °C

Ethylenediamine compounds 0.67 mL (10 mmol) dissolved in 10 mL ethanol in a three-neck round bottom flask. 3.03 g (20 mmol) of vanillin dissolved in 15 mL of ethanol. The vanillin solution was added dropwise to the ethylenediamine solution accompanied by stirring using a magnetic stirrer with a rotation speed of 400 rpm and adding 5-10 drops of glacial acetic acid to the reaction mixture. The mixture was reacted at 78 °C for 3 hours and monitored the reaction using TLC with eluent ethyl acetate: n-hexane (1:2). Then, the reaction mixture was cooled for 10 min, filtered and recrystallized with ethanol, filtered and dried at room temperature. The product solids were

then weighed and analyzed for their physical properties such as melting point measurements and solubility tests. The solids of the product were analyzed using UV-Visible and infrared spectrophotometry [7].

Synthesis of *N,N'*-Bis(benzylidene)ethylenediamine from Benzaldehyde and Ethylenediamine

Ethylenediamine compounds 0.67 mL (10 mmol) was dissolved in 10 mL ethanol in a three-neck round bottom flask. 2.04 mL (20 mmol) of benzaldehyde compounds dissolved into 15 mL of ethanol. Benzaldehyde solution was added dropwise into ethylenediamine solution accompanied by stirring using a magnetic stirrer with a rotation speed of 400 rpm. The reaction mixture was heated at 78 °C for 3 hours and monitored using TLC with eluent ethyl acetate: n-hexane = 1:1. The reaction mixture is evaporated using a rotary evaporator to remove the solvent and dried at room temperature. The product solids are then recrystallized with ethanol, filtered, and dried at room temperature. The product solids were then weighed and analyzed for their physical properties in the form of melting point measurements and solubility tests. The solids of the product were analyzed using UV-Visible and infrared spectrophotometry [8].

Determination of Antioxidant Activity

The determination of antioxidant activity was carried out using the DPPH method qualitatively and quantitatively.

Qualitative Antioxidant Activity Test

Qualitative antioxidant activities test done with added 3.8 mL DPPH 1000 ppm solution into 0.2 mL test solution (*N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine, *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine, and *N,N'*-Bis(benzylidene)ethylenediamine) with a concentration of 1000 ppm. Quercetin solution was positive control and methanol as a negative control. The sample was kept in the darkroom for 30 min, and the color changes were observed [9].

Quantitative Antioxidant Activity Test

The quantitative antioxidant activity test was started by making a 50 µM DPPH solution. The maximum wavelength of DPPH solution was scanned using UV-Visible spectrophotometry at a wavelength range of 500 nm-560 nm [10]. Quercetin compounds as positive control and methanol as a negative control. Each of test solutions of (*N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine, *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine, and *N,N'*-Bis(benzylidene)ethylenediamine in various concentrations (10 ppm, 20 ppm, 30 ppm, 40 ppm and 50 ppm) as much as 0.2 mL was put into the dark vial added with 3.8 mL of 50 µM DPPH solution in methanol which were then homogenized in a dark vial bottle and allowed to stand for 30 minutes in a dark place. This solution is then measured for its absorbance at the wavelength obtained by scanning the 50 µM DPPH wavelength. The same treatment was carried out on quercetin. The blank used is methanol. Calculation of IC₅₀ values was obtained from the linear regression equation between sample concentration and inhibition percent, each of which was plotted as the x- and y-axis [9].

RESULTS AND DISCUSSION

Synthesis of *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine from Salicylaldehyde and Ethylenediamine

Synthesis of *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine was carried out through a condensation reaction between salicylaldehyde and ethylenediamine. This research was carried out by reacting 20 mmol salicylaldehyde and 10 mmol ethylenediamine at 29 °C for 15 minutes. The condensation reaction between salicylaldehyde and ethylenediamine is presented in Fig. 1.

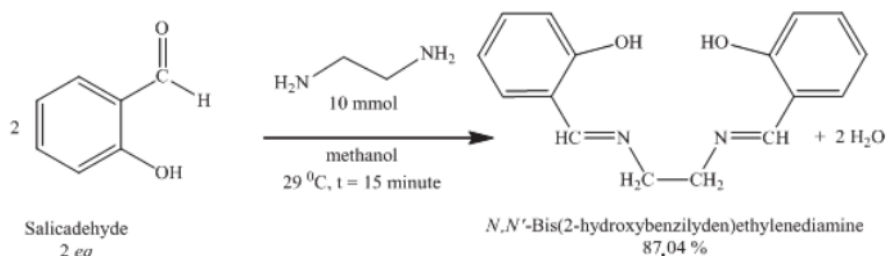


FIGURE 1. Condensation Reactions between Salicylaldehyde and Ethylenediamine

The synthesized product in the form of yellow solids was purified using a recrystallization method using methanol solvent and yield 87.04%; the physical properties were identified. Data on the physical properties of salicylaldehyde and ethylenediamine condensation reaction products are presented in Table 1.

TABLE 1. Physical Properties of Product Reaction Condensation between Salicylaldehyde and Ethylenediamine

Physical Properties	Results of Condensation Reactions between Salicylaldehyde and Ethylenediamine
Form	Solids
Color	Yellow
Melting Point	125.6 – 125.7 °C [6].
Mass	2.3356 g
Yield	87.04%
Solubility	Soluble in chloroform, dichloromethane, ethyl acetate methanol, ethanol (in heating) Not soluble in n-hexane and water.

The solid results of the synthesis were analyzed using UV-Visible spectrophotometry to ascertain the structural framework of the azomethine compound synthesized. The result obtained shows the band I at 256.0 nm of $\pi \rightarrow \pi^*$ conjugation of the benzene ring substituted by the hydroxy group (-OH) and the imine group ($>C=N-$) and the band II at 316.0 nm of $n \rightarrow \pi^*$ imine group ($>C=N-$). The UV-Visible spectrum of condensation reaction products between salicylaldehyde and ethylenediamine has two peaks with $\lambda_1 = 256$ nm and $\lambda_2 = 256$ nm respectively.

The synthesized compounds were then analyzed using infrared spectrophotometry to analyze the functional groups contained in the synthesized compounds. The results obtained are specific absorption at wavenumber 1632 cm^{-1} which is characteristic of the imine group ($>C=N-$). The infrared spectrum product of the condensation reaction product between salicylaldehyde and ethylenediamine is shown in Fig. 2.

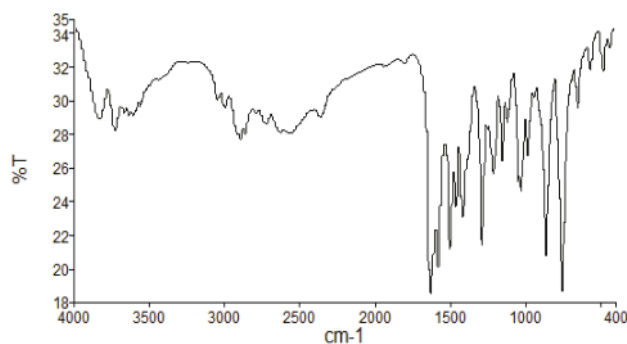


FIGURE 2. Spectrum Infrared Product Reaction Condensation between Salicylaldehyde and Ethylenediamine

The H-NMR data of condensat⁴¹ product related to the reaction between salicylaldehyde and ethylenediamine is sho⁴⁵ in Fig. 3 (H-NMR: δ 13.2 ppm (s, 2H) (-OH); δ 8.3 ppm (s, 2H) (=N-H); δ 7.25 ppm (m, 2H, Benzene); δ 7.10 ppm (dd, 2H); δ 6.9 ppm (dd, 2H); δ 6.8 ppm (m, 2H); δ 3.8 ppm (s, 4H). This data match H-NMR data from

1

Source Integrated Spectral Database System of Organic Compounds (data were obtained from the National Institute of Advanced Industrial Science and Technology (Japan)).

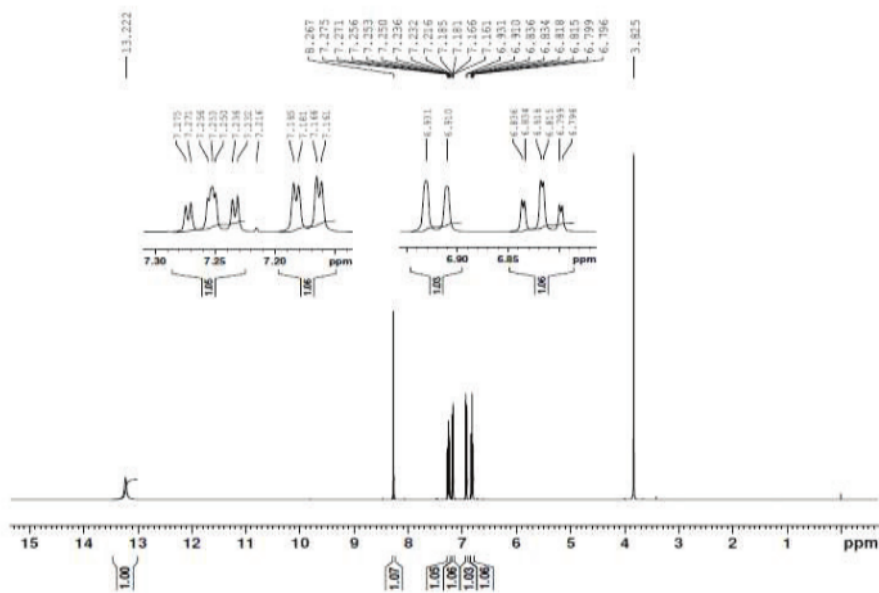


FIGURE 3. ¹H-NMR data Product Reaction Condensation between Salicylaldehyde and Ethylenediamine

The C-NMR data of condensation product related to reaction between salicylaldehyde and ethylenediamine is shown in Fig. 4 (C-NMR: δ = 166 ppm, 161 ppm, 132 ppm, 131 ppm, 131 ppm, 118.74 ppm, 118.70 ppm, 116.98 ppm and 59.70 ppm). These data match to C-NMR data from Source Integrated Spectral Database System of Organic Compounds (data were obtained from the National Institute of Advanced Industrial Science and Technology (Japan)).

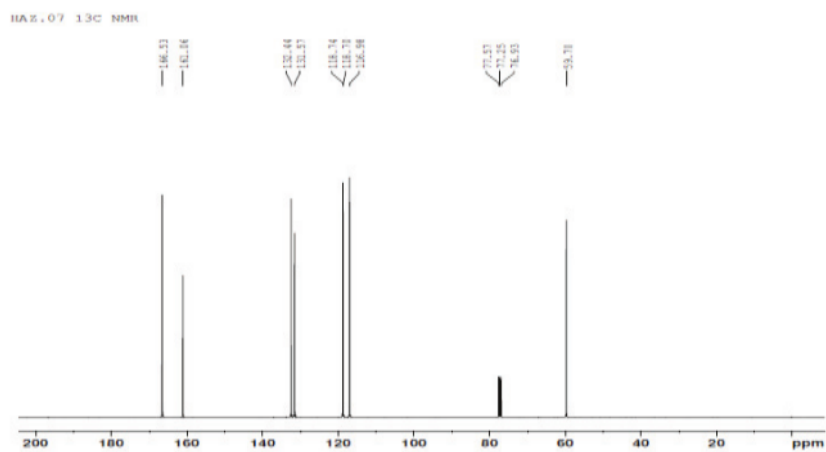


FIGURE 4. ¹³C-NMR data Product Reaction Condensation between Salicylaldehyde and Ethylenediamine

Synthesis of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine from Vanillin and Ethylenediamine

Synthesis of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine was obtained by condensation reaction between vanillin and ethylenediamine. This study was initiated by reacting 20 mmol vanillin and 10 mmol ethylenediamine with reaction conditions at room temperature for 15 minutes. Based on the TLC profile, side products are formed, namely salt. This is because the hydroxyl group (-OH) in *para* position is acidic so that the nucleophilic will attack and ammonium salt is formed, therefore, it is carried out again under the conditions of the heating reaction at 78 °C for 3 hours and the addition of a glacial acetic acid catalyst. Condensation reactions between vanillin and ethylenediamine are presented in Fig. 5.

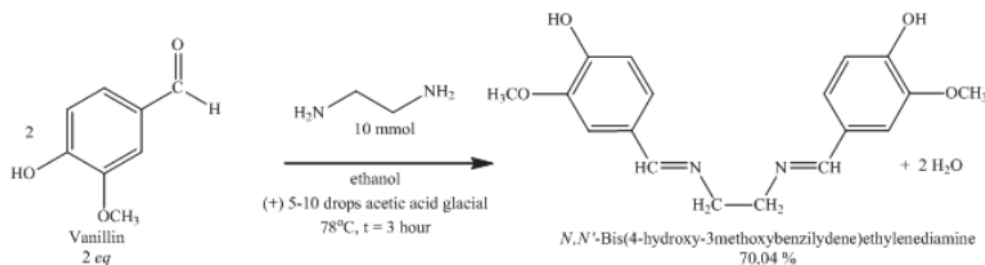


FIGURE 5. Condensation Reaction between Vanillin and Ethylenediamine

The synthesized compounds were then crystallized and purified by the recrystallization method using ethanol solvent to obtain a light brown solid with a rendering of 70.04% and identification of its physical properties was subsequently performed. Data on the physical properties of the vanillin and ethylenediamine condensation reaction products are presented in Table 2.

TABLE 2. Physical Properties of Product Reaction Condensation between Vanillin and Ethylenediamine

Physical Properties	Results of Condensation Reactions between Vanillin and Ethylenediamine
Form	Solids
Color	Young brown
Melting Point	220.2 – 221.5 °C [8]
Mass	2.3016 g
Yield	70.04%
Solubility	Soluble in chloroform, dichloromethane and ethyl acetate methanol, ethanol (with heating) Not soluble in n-hexane and water

The solid results of the synthesis were then analyzed using UV-Visible spectrophotometry to determine the structural framework of the azomethine compound synthesized. The result obtained band I at 273.4 nm of $\pi \rightarrow \pi^*$ conjugation of the benzene ring substituted by a hydroxyl group (-OH), methoxy group (-OCH₃) and imine group ($>C=N-$) and band II at 309.4 nm of $n \rightarrow \pi^*$ imine group ($>C=N-$). The UV-Visible spectrum of condensation reaction products between vanillin and ethylenediamine has two peaks with $\lambda_1 = 273$ nm and $\lambda_2 = 309$ nm respectively.

The synthesized compounds were then analyzed using infrared spectrophotometry to analyze the functional groups contained in the synthesized compounds. The results obtained are specific absorption at wavenumber 1632.74 cm⁻¹ which is characteristic of the imine group ($>C=N-$). The infrared spectrum product of the condensation reaction product between vanillin and ethylenediamine is presented in Fig. 6.

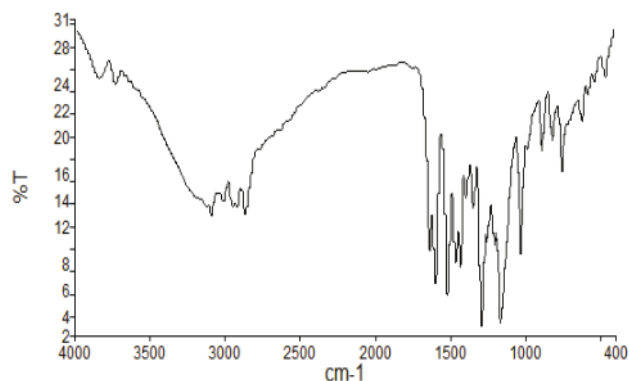


FIGURE 6. Spectrum Infrared Product Reaction Condensation between Vanillin and Ethylenediamine

47

Synthesis of *N,N'*-Bis(benzylidene)ethylenediamine from Benzaldehyde and Ethylenediamine

9

Synthesis of *N,N'*-bis-(benzylidene) ethylenediamine was carried out through a condensation reaction between benzaldehyde and ethylenediamine. This research was carried out by reacting 20 mmol benzaldehyde and 10 mmol ethylenediamine under heating reaction conditions at 78°C for 3 hours. The condensation reaction between benzaldehyde and ethylenediamine is shown in Fig.7.

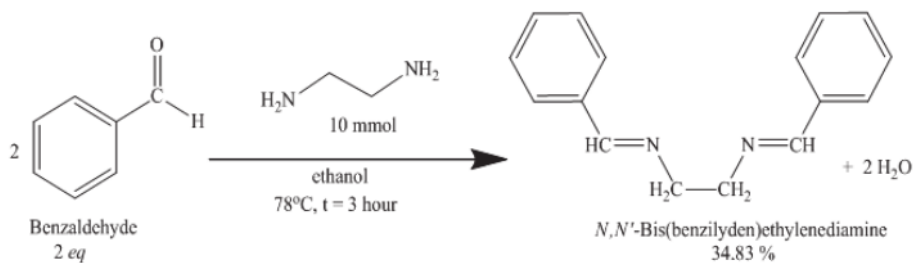


FIGURE 7. Condensation Reaction between Benzaldehyde and Ethylenediamine

The synthesized solution was evaporated using a rotary evaporator to evaporate the solvent. The reaction product was crystallized and purified by the recrystallization method using ethanol to obtain orange solids with a rendering of 34.83%. The physical properties of product solids obtained were identified. Data on the physical properties of condensation reaction products between benzaldehyde and ethylenediamine are presented in Table 3.

TABLE 3. Physical Properties of Product Reaction Condensation between Benzaldehyde and Ethylenediamine

Physical Properties	Product Reaction Condensation between Benzaldehyde and Ethylenediamine
Form	Solids
Color	Orange
Melting Point	110.2 – 111.4 °C [4]
Massa	0.8231 g
Yield	34.83%
Solubility	Soluble in dichloromethane, chloroform, and ethyl acetate ethanol, methanol (in heating) Not soluble in ether, n-hexane, water

The solids of the synthesis results were then analyzed using UV-Visible spectrophotometry to ascertain the structural framework of the azomethine compound. The results obtained absorption at 243.4 nm of $\pi \rightarrow \pi^*$ groups

>C=N- and the benzene ring conjugation. The UV-Visible spectrum of condensation reaction products between benzaldehyde and ethylenediamine has one peak at $\lambda = 243$ nm.

The synthesized compounds were then analyzed using infrared spectrophotometry to analyze the functional groups contained in the azomethine compound synthesized. The results obtained are specific absorption at wavenumber 1643.84 cm^{-1} , which is characteristic of the imine group (>C=N-). The infrared spectrum of the condensation reaction product between benzaldehyde and ethylenediamine is presented in Fig. 8.

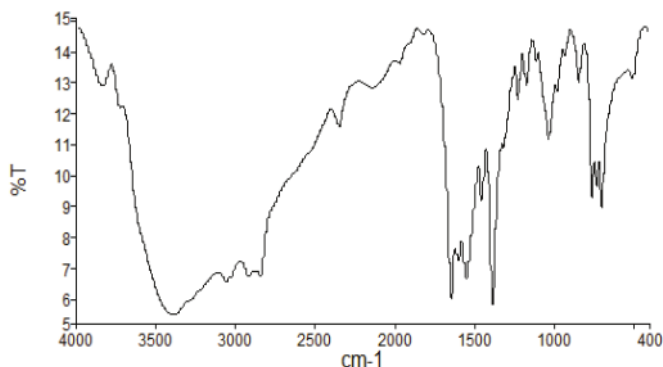


FIGURE 8. Spectrum Infrared Product Reaction Condensation between Benzaldehyde and Ethylenediamine

Effect of Hydroxyl (-OH) and Methoxy (-OCH₃) Groups in Synthesis Products

Synthesis of azomethine derivatives namely *N,N'*-Bis(benzylidene)ethylenediamine, *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine and *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine was obtained from the starting material with a hydroxyl group (-OH) substituted on different position and the formation reaction of the azomethine derivative compound was carried out under various reaction conditions. The reaction conditions of the three azomethine derivatives are presented in Table 4.

TABLE 4. Physical Properties of Product Reaction Condensation between Benzaldehyde and Ethylenediamine

No	Condition of Reaction	Synthesis Product		
		PS 1	PS 2	PS 3
1	Aldehyde aromatic	Benzaldehyde	Salicylaldehyde	Vanillin
2	Solvent	Ethanol	Methanol	Ethanol
3	Temperature (°C)	78	29	78
4	Time	3 hour	15 minute	3 hour
5	Glacial acetic acid	-	-	present
6	Massa (g)	0.8231	2.3356	2.3016
7	Yield (%)	34.83	87.04	70.04
8	Melting Point (°C)	110.2-111.4	125.6-125.7	220.2-221.5

Description =

PS 1 = *N,N'*-Bis(benzylidene)ethylenediamine

PS 2 = *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine

PS 3 = *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine

The effect of the substituents attached to the benzene ring affects the reactivity and the product obtained. The synthesis of *N,N'*-Bis(benzylidene)ethylenediamine from benzaldehyde and ethylenediamine gives the least amount of yield. Benzaldehyde has no electron driving group and no addition of an acid catalyst causes the carbonyl group to be less reactive so that the yield obtained is 34.83%. In the synthesis of *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine from salicylaldehyde and ethylenediamine was the highest content of *N,N'*-Bis(benzylidene)ethylenediamine and *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine. Product coupling on *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine is because the initial compound salicylaldehyde is known to have a hydroxyl group (-OH) in the *ortho* position which is bound to the benzene ring which can affect the reactivity of carbonyl carbon.

The presence of a hydroxyl group (-OH) substituted in the *ortho* positionable to hold an intramolecular hydrogen bond so that the hydroxyl (-OH) hydrogen atom is not easily separated and not acidic. The presence of a hydroxyl group (-OH) which is an electron pushing group, can give a positive mesomeric effect which makes the electron density of the benzene ring increase so that the carbonyl C atom (C=O) is more electropositive and susceptible to nucleophilic attack. In the synthesis, *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine can run at room temperature and in a short time. In the structure of *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine tends to be thermodynamically stable because it contains intramolecular hydrogen bonds. Structure of *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine compound is shown in Fig. 9.

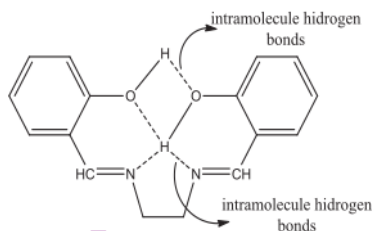


FIGURE 9. Structure of *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine

In the synthesis of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine from vanillin and ethylenediamine, the resulting yield was less than the *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine and was greater than *N,N'*-Bis(benzylidene)ethylenediamine. The product compound is *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine because the product tends to be thermodynamically unstable because it does not hold intramolecular hydrogen bonds. In the synthesis process of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine, an acid catalyst was added to increase reactivity of carbonyl carbon to be easily attacked by nucleophilic and to increase rendement. Heating was done to accelerate the rate of reaction and the formation of equilibrium. The synthesis of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine compound and obtained a rendement of 70.04%.

The melting point of a compound is the temperature at which solid phase changes into a liquid phase. The difference in the range of melting point of compounds is influenced by the strength of intermolecular hydrogen bonds. *N,N'*-Bis(benzylidene)ethylenediamine has the lowest melting point among three azomethine compounds synthesized because the structure does not have intermolecular and intramolecular hydrogen bonds. *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine has a hydroxyl group (-OH) at the *ortho* position so that it tends to be able to bind intramolecular hydrogen between the H atom on the hydroxyl group (-OH) with the N atom in the imine group (>C=N-) in the same compound; thus the melting point is lower than *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine. *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine has a methoxy group (-OCH₃) in the *meta* position and hydroxyl groups (-OH) in the *para* positions which tend to be intermolecular hydrogen-bonded. The tendency for intermolecular hydrogen bonding causes the melting point of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine to be larger.

Antioxidant Activity Test

In this study, the determination of the antioxidant activity of the azomethine compound synthesized and quercetin as a positive control was carried out using DPPH free radical reduction method. Quercetin was used as a positive control.

Qualitative Antioxidant Activity Test

Qualitative antioxidant activity test on azomethine compound was carried out by soaking the test compound with 1000 ppm concentration into 50 μ M DPPH solution. The results obtained the azomethine derivatives synthesized have antioxidant properties shown by the change in color of the solution from purple to yellow. According to Oktaviani et al. [9], antioxidant radical scavenging reaction of DPPH is shown in Fig. 10.

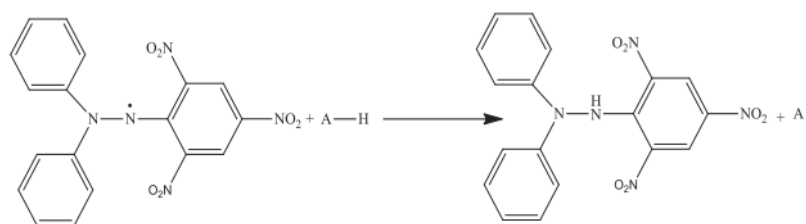


FIGURE 10. Antioxidant Radical Scavenging Reaction of DPPH

Quantitative Antioxidant Activity Test

0.2 mL of the test compound (10 ppm, 20 ppm, 30 ppm, 40 ppm, and 50 ppm) in methanol were added with 3.8 mL 50 μ M DPPH solution and incubated for 30 minutes. The antioxidant activity test of the test compound is indicated by the IC_{50} value presented in Table 5.

TABLE 5. IC_{50} values of quercetin and test compounds

Compound Test	IC_{50} (ppm)
Quercetin (positive control)	30.9
<i>N,N'</i> -Bis(benzylidene)ethylenediamine	187.66
<i>N,N'</i> -Bis(2-hydroxybenzylidene)ethylenediamine	130.573
<i>N,N'</i> -Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine	235.164

As shown in Table 5, IC_{50} values of *N,N'*-Bis(benzylidene)ethylenediamine compound antioxidant activity was affected by proton H_a to stabilize free radicals in DPPH and the structure was not steric. *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine has the greatest antioxidant activity among three azomethine derivatives synthesized and belongs to the medium antioxidant category [9]. This activity is influenced by the presence of proton H_a and hydroxyl group (-OH) at the ortho position which is capable of binding to intramolecular hydrogen so that its structure is more ordered and stable, therefore the compound is able to stabilize free radicals from DPPH. The presence of hydroxyl groups (-OH) in the ortho position will become more active in reducing free radicals [10]. The antioxidant radical scavenging reaction by *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine is shown in Fig. 11.

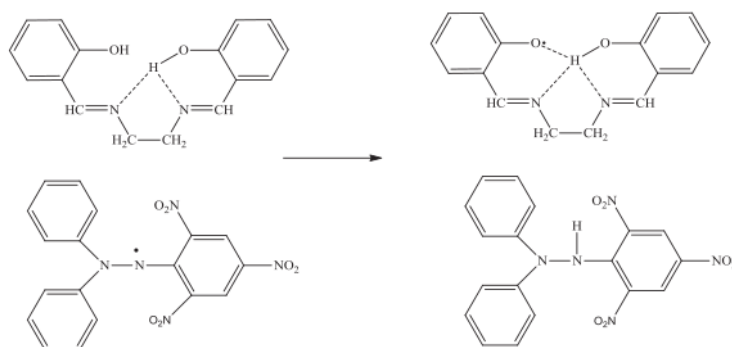


FIGURE 11. Antioxidant Radical Scavenging Reaction in *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine

Antioxidant activity of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine included in the antioxidant category is very weak and is the weakest antioxidant activity of the three azomethine derivatives synthesized [9]. Antioxidant activity of *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine is influenced by proton H_a and hydroxyl group (-OH) the structure which more unorganized and more steric than *N,N'*-Bis(benzylidene)ethylenediamine. The presence of a hydroxyl group (-OH) in the position of the para becomes less active in reducing free radicals [10].

CONCLUSION

The hydroxylated azomethine derivative compound produces compounds namely *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine in yellow color with melting point of 125.6-125.7 °C and yield 87.04%; *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine in light brown color with melting point of 220.2-221.5 °C and a yield 70.04%; *N,N'*-Bis(benzylidene)ethylenediamine in orange color with melting point of 110.2-111.4 °C and yield 34.83%. Test results of antioxidant activity on the three azomethine derivatives obtained IC_{50} values of 131 ppm, 188 ppm and 235 ppm for *N,N'*-Bis(2-hydroxybenzylidene)ethylenediamine, *N,N'*-Bis(benzylidene)ethylenediamine and *N,N'*-Bis(4-hydroxy-3-methoxybenzylidene)ethylenediamine, respectively.

ACKNOWLEDGEMENT

We are grateful to financial support from "Riset Madya Grant" Faculty of Sciences and Math, Diponegoro University No. 4838/UN7.5.8/PP/2019

REFERENCES

1. D. Pratimasari, "Uji Aktivitas Penangkap Radikal Buah Carica Papaya L. dengan Metode DPPH dan Penetapan Kadar Fenolik serta Flavonoid Totalnya", Fakultas Farmasi Universitas Muhammadiyah Surakarta, 2009.
2. Juniarti, D. Osmeli, and Yuhernita, Makara J. Sci 3(1), 50-54 (2009).
3. N. A. R. Sain, R. Shankar, R. Gupta, S. Pandey, K. Saud, R. P. Chavan, and S. T. Chavan, Int. J. Chem. 3(4), 20-41 (2015).
4. Wahab, S.S. Haider, I. Mahmood, T. Mahmood, and S.K. Sherwani, Fuuast J. Biol. 4(1), 27-32, (2014).
5. Nakiboglu, R. O. Urek, H. A. Kayali, and L. Tarhan, J. Food Chem. 104, 630-635 (2007).
6. W. Ghann, H. Sobhi, H. Kang, T. Chaves-Gill, F. Nesbit, and J. Uddin, J. Chem. Eng. 05(06), 46-66 (2017).
7. Y. Kadhum, and A. M. Abduljeel, J. De Pharma Chemica 6(5), 88-100 (2014).
8. P.P. Dholakiya, and M. N. Patel, Synth React Inorg M (4), 819-829 (2002).
9. Oktaviani, Y. Mulyani, and E. Rochima, Jurnal Perikanan Kelautan 2(1), 4 (2015).
10. E. Bendary, R. R. Francis, H. M. G. Ali, M. I. Sarwat, and S. El Hady, Ann. Agric. Sci. 58(2), 173-181 (2013).

Synthesis of hydroxylated azomethine compounds and the antioxidant activity

ORIGINALITY REPORT

18%

SIMILARITY INDEX

11%

INTERNET SOURCES

15%

PUBLICATIONS

4%

STUDENT PAPERS

PRIMARY SOURCES

- | | | |
|---|--|----|
| 1 | Submitted to University of Denver
Student Paper | 1% |
| 2 | kimia.fsm.undip.ac.id
Internet Source | 1% |
| 3 | hdl.handle.net
Internet Source | 1% |
| 4 | Dara muhammed Aziz, Sanagr Ali Hassan, Dyari Mustafa Mamand, Karzan Qurbani. "New azo-azomethine derivatives: Synthesis, characterization, computational, solvatochromic UV-Vis absorption and antibacterial studies", Journal of Molecular Structure, 2023
Publication | 1% |
| 5 | Kenji Shimizu, Toshio Nomura, Koji Takahashi. "Crystal size distribution of aluminum potassium sulfate in a batch crystallizer equipped with different types of impeller", Journal of Crystal Growth, 1998
Publication | 1% |

6	<p>Muhammad Nur, Aribat Solichin, Endang Kusdiyantini, Tri A. Winarni, Susilo, Dian Arif Rahman, Resti Maryam, Sosiowati Teke, Wuryanti, Harjum Muharam. "Ozone production by Dielectric Barrier Discharge Plasma for microbial inactivation in rice", 2013 3rd International Conference on Instrumentation, Communications, Information Technology and Biomedical Engineering (ICICI-BME), 2013</p> <p>Publication</p>	1 %
7	<p>www.ncbi.nlm.nih.gov</p> <p>Internet Source</p>	1 %
8	<p>umpir.ump.edu.my</p> <p>Internet Source</p>	1 %
9	<p>Roberto Centore, Antonio Carella, Andrea Pugliese, Augusto Sirigu, Angela Tuzi. "Double-helix pattern in a model compound of non-linear optical polymers", Acta Crystallographica Section C Crystal Structure Communications, 2006</p> <p>Publication</p>	1 %
10	<p>pubs.rsc.org</p> <p>Internet Source</p>	1 %
11	<p>Hussain A. Badran, Harith A. Hasan. "Synthesis and study dielectric properties of a</p>	1 %

new Schiff-base liquid crystal", AIP Publishing,
2020

Publication

12

S. Hotchandani, A. C. Testa. " Evidence for
Inversion of Triplet Levels in 4 -
- Dimethylaminopyridine ", The Journal of
Chemical Physics, 1971

Publication

1 %

13

Derya Kara, Mahir Alkan, Şeref Güçer. "
SELECTIVE PRECONCENTRATION AND
DETERMINATION OF COBALT(II) USING , '- (2-
HYDROXY-5-BROMO-BENZYL)-1,2-
DIAMINOPROPANE ", Analytical Letters, 2002

Publication

<1 %

14

Yani Ambari, Arlin Ocardini Saputri, Iif Hanifa
Nurrosyidah. "FORMULASI DAN UJI AKTIVITAS
ANTIOKSIDAN BODY LOTION EKSTRAK
ETANOL DAUN KEMANGI (Ocimum cannum
Sims.) DENGAN METODE DPPH (1,1 -
diphenyl-2- picrylhydrazyl)", Jurnal Ilmiah As-
Syifaa, 2022

Publication

<1 %

15

Željko Petrovski, Martyn Pillinger, Anabela A.
Valente, Isabel S. Gonçalves, Alan Hazell,
Carlos C. Romão. "Preparation and catalytic
studies of bis(halogeno)dioxomolybdenum(VI)-
diimine complexes", Journal of Molecular
Catalysis A: Chemical, 2005

Publication

<1 %

16 Malinauskas, T.. "Multifunctional emissive material based on 1-phenyl-1,2,3,4-tetrahydroquinoline", *Dyes and Pigments*, 200905
Publication <1 %

17 Submitted to Universiti Teknologi Malaysia
Student Paper <1 %

18 Mimi Golder, Samir Kumar Sadhu, Biswajit Biswas, Tannami Islam. "Comparative pharmacologic profiles of leaves and hypocotyls of a mangrove plant: *Bruguiera gymnorhiza*", *Advances in Traditional Medicine*, 2020
Publication <1 %

19 Submitted to Richard Stockton College of New Jersey
Student Paper <1 %

20 Submitted to University of Warwick
Student Paper <1 %

21 archiv.ub.uni-heidelberg.de
Internet Source <1 %

22 download.garuda.kemdikbud.go.id
Internet Source <1 %

23 Suryo Budi Santoso, Satriyo Adhy, Nurdin Bahtiar, Indra Waspada. "Development of The Smart Chicken Eggs Incubator Based on

Internet of Things Using The Object Oriented Analysis and Design Method", 2020 4th International Conference on Informatics and Computational Sciences (ICICoS), 2020

Publication

24

Mithun Kumar Ghosh, Sayantan Pathak, Tanmay Kumar Ghorai. " Synthesis of Two Mononuclear Schiff Base Metal (M = Fe, Cu) Complexes: MOF Structure, Dye Degradation, H O Sensing, and DNA Binding Property ", ACS Omega, 2019

Publication

25

Vijayakumar, S.. "@g^(^3^) measurements and optical limiting studies of 2-chloro-5-nitro-N'-[(1E)-phenylmethylidene] benzohydrazide with substituents", Optical Materials, 200909

Publication

26

eprints.unm.ac.id

Internet Source

27

van Gorkum, R.. "The oxidative drying of alkyd paint catalysed by metal complexes", Coordination Chemistry Reviews, 200509

Publication

28

A. Anjum, M. A. Sikder, M. R. Haque, C. M. Hasan, M. A. Rashid. "*In Vitro* Antioxidant and Thrombolytic Activities of *Bridelia* Species Growing in Bangladesh", Journal of Scientific Research, 2013

<1 %

<1 %

<1 %

<1 %

<1 %

29

Krishna K. Manar, Neetu, Kavita Kumari, Anamika, Chote L. Yadav, Pankaj Srivastava, Michael G. B. Drew, Nanhai Singh. "Preparation, Characterization and Photosensitizing Activities of Homoleptic Cu(II) Dithiocarbamates in TiO₂ - Based DSSC ", ChemistrySelect, 2019

Publication

<1 %

30

K. Sampath, S. J. Pradeeba, K. Kalapriya. "Photocatalytic degradation efficiency of malachite green in aqueous medium using poly(azomethine)/ZnO nanocomposite", AIP Publishing, 2019

Publication

<1 %

31

Submitted to University of Sunderland

Student Paper

<1 %

32

stdb.hnue.edu.vn

Internet Source

<1 %

33

Carolin Manuahe, Mocosuli Samuel, Ellen Adil, Orbanus Naharia. "Mosquito Larvicides of Partial and Combinations Extract of Ethnobotanical Plant from North Sulawesi, Indonesia", Pakistan Journal of Biological Sciences, 2022

Publication

<1 %

34

Submitted to University of Nottingham

Student Paper

<1 %

35

O@?sz, E.. "Preparation of 3,5-bis-(@b-d-glycopyranosyl)-1,2,4-thiadiazoles from C-(@b-d-glycopyranosyl)thioformamides",
Tetrahedron, 20010618

Publication

<1 %

36

ijpbs.net
Internet Source

<1 %

37

pdf.healthmed.ba
Internet Source

<1 %

38

Mst Serina Sultana, Mimi Golder, Biswajit Biswas, Utpal Kumar Karmakar et al.
"Antioxidative and Antidiabetic Potentials of the Pneumatophores of Heritiera fomes Buch. Ham.", Dhaka University Journal of Pharmaceutical Sciences, 2022

Publication

<1 %

39

Nevin Süleymanoğlu. "2-Propylamino-5-[4-(2-hydroxy-3,5-dichlorobenzylideneamino)phenyl]-1,3,4-thiadiazole: X-ray and DFT-calculated structures", Structural Chemistry, 10/20/2009

Publication

<1 %

40

dalspace.library.dal.ca
Internet Source

<1 %

41

Qin, Xiao-Hua, Krystyna Labuda, Jie Chen, Veronika Hruschka, Anna Khadem, Robert Liska, Heinz Redl, and Paul Slezak.

"Development of Synthetic Platelet-Activating Hydrogel Matrices to Induce Local Hemostasis", *Advanced Functional Materials*, 2015.

Publication

<1 %

42

mro.massey.ac.nz

Internet Source

<1 %

43

repositori.uin-alauddin.ac.id

Internet Source

<1 %

44

www.lifesciencesite.com

Internet Source

<1 %

45

Seibold, Sebastian. "Halogenfrei flammgeschützte Epoxidharzsysteme auf der Basis von Präformulierungen", 'American Association for Cancer Research (AACR)', 2007

Internet Source

<1 %

46

Kiviranta, Päivi H., Jukka Leppänen, Sergiy Kyrylenko, Heikki S. Salo, Maija Lahtela-Kakkonen, Anu J. Tervo, Carsten Wittekindt, Tiina Suuronen, Erkki Kuusisto, Tomi Järvinen, Antero Salminen, Antti Poso, and Erik A. A. Wallén. "*N,N'*-Bisbenzylidenebenzene-1,4-diamines and *N,N'*-Bisbenzylidenenaphthalene-1,4-diamines as

<1 %

Sirtuin Type 2 (SIRT2) Inhibitors", Journal of Medicinal Chemistry, 2006.

Publication

47

Somnath, Waris, Arif Ali, Musheer Ahmad, Kafeel Ahmad Siddiqui. "Bifunctional Self-Penetrating Co(II)-Based 3D MOF for High-Performance Environmental and Energy Storage Applications", Crystal Growth & Design, 2022

Publication

<1 %

Exclude quotes Off

Exclude matches Off

Exclude bibliography Off