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Antibacterial and antioxidant activity of *p*-quinone methide derivative synthesized from 2,6-di-*tert*-butylphenol

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Quinone methides and its derivatives have recently gained much attention as the potential building block of some important drugs in medicinal chemistry. Herein, 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone was prepared from 2,6-di-*tert*-butylphenol, which was characterized and antibacterial and antioxidant activities were evaluated. The as-synthesized compound exhibited good antioxidant and antibacterial activity against selected test organisms with zone of inhibition ranging between 7 mm to 9 mm at concentration of 2.5, 5.0, and 7.5 (mg/mL), respectively. The result shows that the compound may be a potential candidate of reducing human suffering from bacterial infections since antibacterial activity was promising.

Capsule Summary: 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone from 2,6-di-*tert*-butylphenol was synthesized and the compound shows good antibacterial and antioxidant activity.

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INTRODUCTION

Bacteria have a natural capability to pass from one person to another and fights against the drugs that are used for disease prevention (Halilu et al., 2016). During the past decades, a number of antibiotics have been produced by pharmaceutical industries, but despite these efforts, microorganisms always increased resistance to these drugs (Sreenivasa et al., 2012) hence there is always need to develop new drugs. In response to these challenges, *p*-quinone methide belongs to a class of organic compounds namely quinonoid which has a unique chemical structure that contains a conjugate of methylene group with a cyclohexadienone, which is considered to be a potential moiety presented in the naturally occurring products (Baeyer and Villiger, 1903; Barraga et al., 2004; Takao et al., 2001; Ryu et al., 2010; Miyajima et al., 2019) and photoreceptor (Tsurumi and Miyamoto, 2019; Okada, 2018; Okada, 2018; Hettie et al., 2019). Apart from its uses as an organic intermediates (Roper and Everly, 1988), *p*-quinone methide plays a very important role as potential building block of some important drugs in medicinal chemistry like DPP-IV (Patterson et al., 2009) and thrombin inhibitors (Nilsson et al., 2009), antibacterials (Thompson et al., 1993), (+)-BW37U86 (Torregrossa et al., 2005), melains (Prota, 2000) etc. Moreover, *p*-quinone methide has been used as reagent for alkylation and as an agent of effective DNA crosslinking (Wang, et al., 2003).

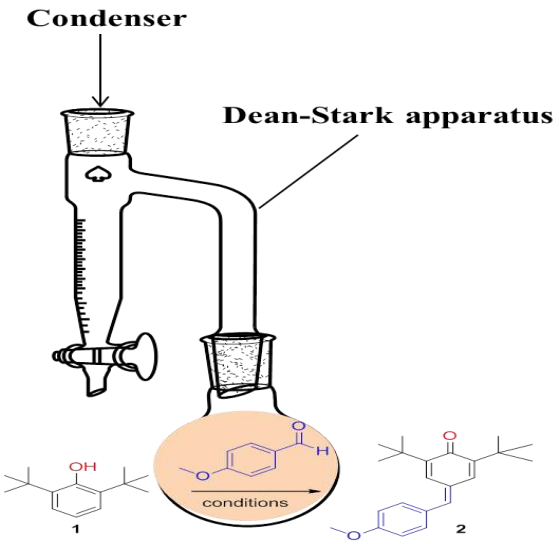

Fig. 1: Synthesis of 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone using Dean Stark apparatus

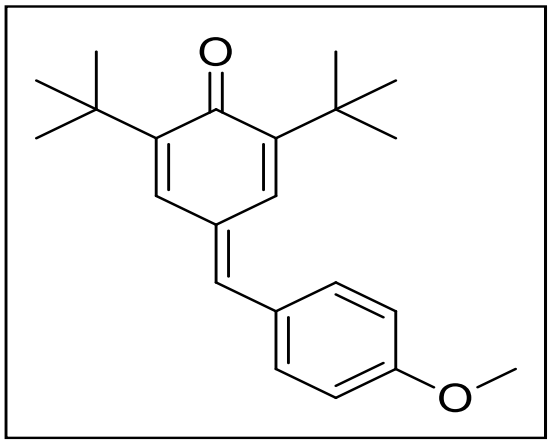

Fig. 1: ^{1}H and ^{13}C NMR data of 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone (2)

[Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J = 1.9 Hz, 1H), 7.35 (d, J = 8.6 Hz, 2H), 7.04 (s, 1H), 6.90 (dd, J = 11.8, 5.3 Hz, 3H), 3.76 (s, 3H), 1.24 (s, 9H), 1.23 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 186.52, 160.59, 148.99, 147.19, 142.73, 135.42, 132.24, 130.51, 128.67, 127.85, 114.44, 55.41, 35.45, 34.98, 29.60, 29.58, 29.55, 29.53; These data is in line with the one reported in the literature (Liu et al., 2019)]

This category of compounds are highly stable and were reported to have an excellent antioxidant and antipolymerant properties(Nesvadba, 2000; Winter and Von Ahn, 1996), which makes this research worth doing due to its potential of identifying new antibacterial and antioxidant agent that can be used to reduce human suffering from cell damage or bacterial infections. Here in, we describe the synthesis of 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone using Dean-Stark apparatus as described by (Reddy and Anand, 2015) and also the application of the as-synthesized compound as an antibacterial and antioxidant agent for the first time (Fig. 1).

MATERIAL AND METHODS

The solvents used in this research work (hexane, ethyl acetate, ethanol, and methanol) were purchased from Fisher Scientific and used without any purification. The synthesis of the compound was carried out according to the method described by (Reddy and Anand, 2015). Chromatographic technique like thin layer (TLC, using Merck 60 F254 pre-coated silica gel plate) was employed to observe and check the progress of the transformation. Column chromatographic technique was employed to isolate the compound using silica gel (100-200) mesh and a binary solvent of ethyl acetate and hexane system was utilized as the mobile phase. ^{1}H and ^{13}C NMR spectra were acquired in $CDCl_3$ on a Bruker BBFO (500 MHz) spectrometer and tetramethylsilane (TMS) served as the internal standard (δ_H =0.00 ppm). The remaining solvent signals were used for reference purposes and their chemical shifts were converted according to the TMS scale ($CDCl_3$: δ_H = 7.25-7.30 ppm). Spin multiplicities are given as s for singlet, d for doublet, t for triplet, q for quartet e.t.c. Coupling constants (*J*) are given in hertz (Hz). Test organisms were standard laboratory strains of *Staphylococcus aureus* (gram +ve), *Enterococcus faecalis* (gram +ve), and *Pseudomonas aeruginosa* (gram –ve). Antioxidant activity of 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone were evaluated using ABTS radical and DPPH radical scavenging, FRAP and peroxide value assays. The selection of these assays was due to their ease and reproducibility as well as the availability of required chemicals in the laboratory. Moreover, they are widely used assays to evaluate antioxidant activity of plant metabolites. ABTS and DPPH radical scavenging assay of the sample was performed according to the modified method described by (Kavitha and Perumal, 2018). The antioxidant capacity of test sample was estimated spectrophotometrically following the modified procedure of (Benzie et al., 1999).

2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone (2) synthesis

A mixture of *p*-Anisaldehyde (1 equiv.), 2,6-di-*tert*-butylphenol (1 equiv.), piperidine (2 equiv.) and toluene (0.25 M) was placed in a Dean-Stark apparatus and refluxed at temperature 150 °C for 12 h. The temperature of the mixture of the reaction was cooled to 100 °C and then acetic anhydride (2 equiv.) was poured and the resulting mixture was stirred for another 30 minutes at the same temperature.

Table 1: Antibacterial activity of 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone

Conc. (mg/mL)	Zone of Inhibition (mm)		
	S. aureus	*E. faecalis*	*P. aeruginosa*
2.5	-	-	7
5.0	-	-	8
7.5	8	-	9
Streptomycin (20 µg)	23	22	24

The reaction mixture was then cooled to room temperature and poured in to ice cold water (50 mL) and extracted with dichloromethane (50 mL X 2). The combined organic layer was dried over anhydrous sodium sulphate, filtered, concentrated under vacuum and subjected to column chromatography to obtain the pure2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone (Reddy and Anand, 2015).

Table 2: ABTS radical scavenging assay of 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone

Conc. (µg/mL)	Inhibition (%)
5	16.47±0.46
10	58.34± 0.32
15	98.51±0.42
20	98.95±0.25
25	99.39± 0.44

Table 3: DPPH radical scavenging assay of 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone

Conc. (µg/mL)	Inhibition (%)
5	30.72±0.46
10	57.01±0.30
15	64.55±034
20	68.64±0.26
25	87.32±0.17

Table 4: Ferric reducing antioxidant potential assay of 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone

Concentration (µg/mL)	Inhibition (%)
5	0.034
10	0.052
15	0.112
20	0.573
25	0.731

Antibacterial activity evaluation

The antibacterial activities of test samples were carried out by well diffusion method. The target microorganism were cultured in Nutrient broth and incubated for 24 hrs. The petri dishes containing Nutrient agar (NA) medium were cultured with diluted bacterial strain. Well was made of well puncture, diameter 6 mm was pre-sterilized and was maintained in aseptic chamber. The different concentration of test samples (2.5 mg, 5.0 mg and 7.5 mg) was injected to the well. Standard drug Streptomycin (20µg) was used as a positive reference standard to determine the sensitivity of microbial species tested. Then the inoculated plates were incubated at 37 ºC for 24 h. The diameter of the clear zone around the well was measured and expressed in millimeters as its anti-bacterial activity.

ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)) radical scavenging assay

ABTS radical scavenging assay of the sample was performed according to the modified method of [2]. The ABTS (7 mM, 25 ml in deionized water) stock solution was prepared with potassium persulfate ($K_2S_2O_8$) (140 mM, 440 µl). Different concentration of standard (5, 10, 20, 40, 80, and 160 µg/ml) and test samples (0.5, 1.0, 1.5, 2.0, and 2.5 mg) was mixed with the ABTS working solution (2.0 ml) and the reaction mixture was allowed to stand at room temperature for 20 min; then, the Abs was measured using an ultraviolet-visible spectrophotometer at 734 nm. The radical scavenging activity was given as ABTS radical scavenging effect and was calculated by using Eq. 1. Where: A_0 is the control; A_1 is the test.

$$\text{ABTS scavenging (\%)} = [(A_0 - A_1)/A_0]\times 100 \quad (1)$$

DPPH (2, 2-diphenyl-1-picrylhydrazyl) radical scavenging assay

DPPH radical scavenging assay of sample was modified method described by (Kavitha and Perumal, 2018). In brief, 0.135 mM DPPH was prepared in methanol. Different concentration of standard (5, 10, 20, 40, 80, and 160µg/ml) and test samples (0.5, 1.0, 1.5, 2.0, and 2.5 mg) was mixed with 2.5 ml of DPPH solution. The reaction mixture was vortexed thoroughly and kept at room temperature for 30

min. The Absorbance of the mixture was measured at 517 nm. Ascorbic acid was used as the reference standard. The ability of the test sample to scavenge DPPH radical and control was calculated using Eq. 2. Where, OD is optical density, $_C$ and $_S$ are the ODs of control and test sample, respectively.

DPPH inhibition (%) = OD_C-OD_S/OD_C ×100 (2)

Ferric reducing antioxidant potential assay (FRAP)

The antioxidant capacity of test sample was estimated spectrophotometrically following the modified procedure of (Benzie et al., 1999). The method is based on the reduction of Fe^{3+} TPTZ complex (colorless complex) to Fe^{2+}-tripyridyltriazine (blue colored complex) formed by the action of electron donating antioxidants at low pH. This reaction is monitored by measuring the change in absorbance at 593 nm. The Ferric reducing antioxidant power (FRAP) reagent was prepared by mixing 300 mM acetate buffer, 10 ml TPTZ in 40 mMHCl and 20 mM$FeCl_3.6H_2O$ in the proportion of 10:1:1 at 37°C. 2 ml of freshly prepared working FRAP reagent was pipetted and mixed with various concentrations of standard (5, 10, 20, 40, 80, and 160 µg/ml) and test samples (0.5, 1.0, 1.5, 2.0, and 2.5 mg/ml) were mixed thoroughly. An intense blue color complex was formed when ferric tripyridyltriazine (Fe^{3+} TPTZ) complex was reduced to ferrous (Fe^{2+}) form and the absorbance at 593 nm was recorded against a reagent blank after 30 min incubation at 37 °C.

RESULTS AND DISCUSSION

The ^1H NMR showed two methyl (CH_3) signals δ_H (ppm) at 1.24 and 1.23 each with 9 protons. This suggests that there are six methyl groups present in the compound. Also the presence of another signal was observed at δ_H (ppm) 3.76, this corresponds to the 3 protons of the methoxy group (OCH_3) attached to the compound. The presence of down field signals at δ_H (ppm) 6.90 suggest the presence of olefinic proton and the appearance of a signal at δ_H (ppm) between 7.04–7.47 indicates the presence of aromatic protons. These data is in line with the one reported in the literature (Liu et al., 2019) (Figs. 2-3). The 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone exhibited appreciable antibacterial activity on two of the test organisms *Staphylococcus aureus (*gram +ve) and *Pseudomonas aeruginosa* (gram –ve) with zones of inhibition ranging between 7 mm to 9 mm. The 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone proved to be more effective on gram negative bacteria than on gram positive bacteria as activity was observed on gram negative bacteria even at the lowest concentration 2.5 mg/mL, While activity was only observed at the concentration of 7.5 mg/mL on gram positive bacteria *Staphylococcus aureus (*gram +ve) and none was observed on *Enterococcus faecalis (*gram +ve) (Table 1). This may be due to the fact that the organisms have difference in cell wall compositions.

The antibacterial activity of 2, 6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone can be compared with standard antibiotic (Streptomycin, Table 1). The ABTS (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)) radical scavenging assay results shows that the compound has an IC_{50} value of 841.425 µg/ml and the standard drug (Ascorbic acid) was found to be 10.367 µg/ml when compared.

The percentage radical scavenging activity of the 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone is depicted in (Table 2). Out of five different concentrations taken for the study, 15, 20 and 25 ug/mL 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone concentrations exhibited the highest radical scavenging activity in the range (98.51±0.42), (98.95±0.251), (99.40±0.44 and 5 µg/mL of 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone showed the least activity (16.47±0.46).

The results for the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging activity of 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone is depicted in (Table 3). The results shows that out of the five different concentrations taken for the study, 25 µg/mL of 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone concentration exhibited the highest DPPH radical scavenging activity (87.32±0.17) and 5 µg/mL of the compound showed the least activity (30.72±0.46). The result reveals that as the concentration of compound increases, the degree of inhibition also increases and that is the reason why 25 µg concentration of 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone exhibited the highest radical scavenging activity in comparison to other concentrations. The formation of yellow color after the addition of the compound is an indication of stable DPPH molecule formation from free radicals (DPPH). This was measured by its absorbance. The level of inhibition increases as the sample concentration increases but absorbance and concentration of the sample are inversely proportional, when DPPH assay is considered. Thus, 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone proved to be a potential antioxidant compound.

Ferric reducing antioxidant potential assay (FRAP) of all the five different concentrations of 2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone (5, 10, 15, 20 and 25 µg/mL) was evaluated to assess the reducing power using potassium ferricyanide method. The antioxidant property of the compound causes the conversion of the Fe^{3+}/ferricyanide complex to the ferrous/Fe^{2+} forms. The reducing power measured was expressed in terms of ascorbic acid equivalent (AAE) as absorbance per specific concentration of the sample. As it is given in Table 4, all the concentrations has exhibited very low degree of inhibition, maximum reducing power was 0.7% for 25 µg /mL concentration.

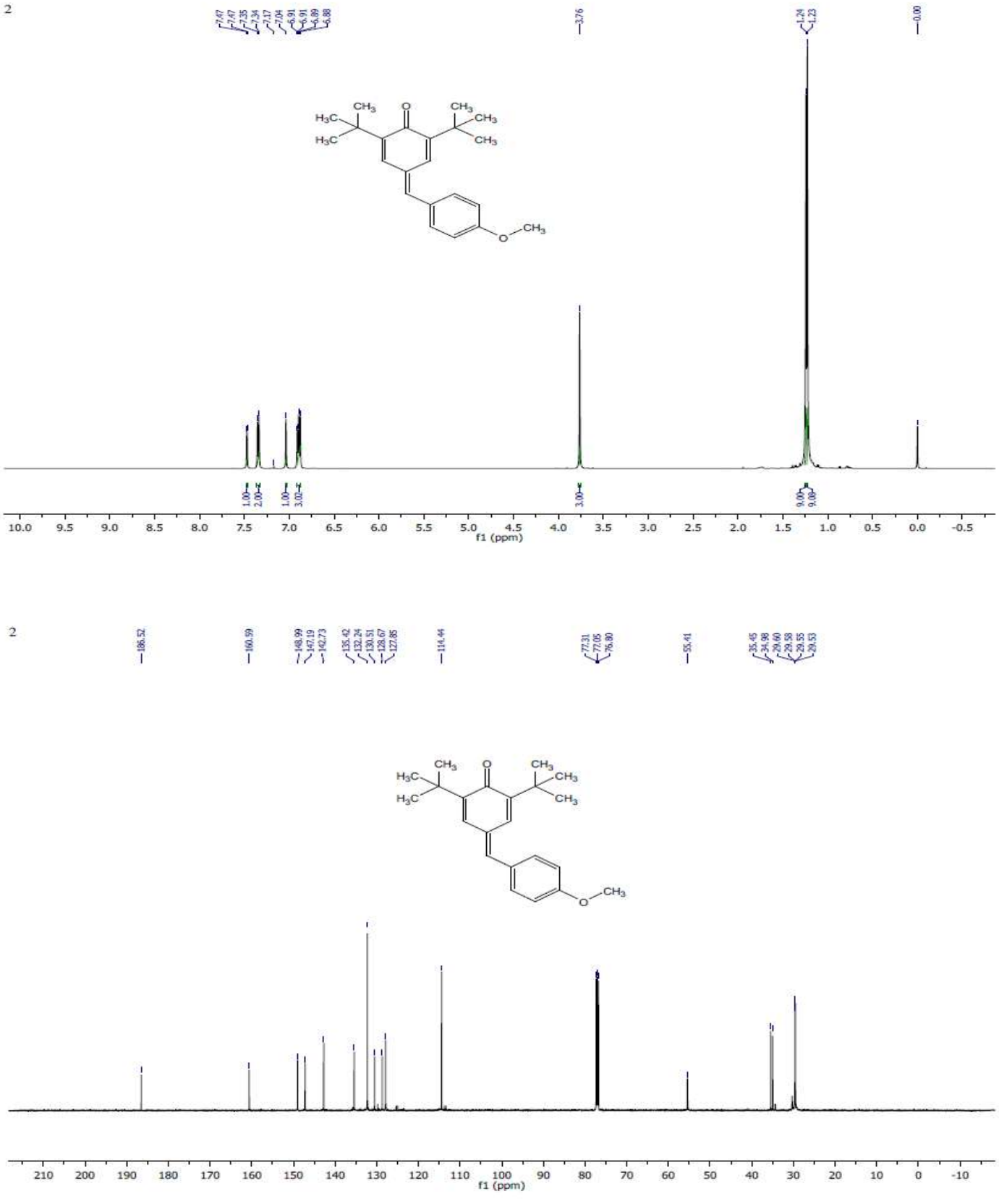

Fig. 3: ^{1}H (upper) and ^{13}C NMR (lower) of 2,6-di-tert-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone (2)

In view of promising antibacterial and antioxidant activity of p-quinone methide derivative, it could possibly be used to control the bacterial infections (Abbas et al., 2019; Bolton et al., 2018; Liu et al., 2020; Purkait and Mukherjee, 2020; Subedi et al., 2018; Swapnaja et al., 2016; Viault et al., 2018; Zhang et al., 2020), which needs toxicity studies using bioassays (He et al., 2020; Laborde et al., 2020; Matata et al., 2020; Zhang et al., 2020).

CONCLUSIONS

2,6-di-*tert*-butyl-4-(4-methoxybenzylidene)cyclohexa-2,5-dienone was synthesized from 2,6-di-*tert*-butylphenol using Dean Stark apparatus. The prepared compound was characterized and antimicrobial as well as antioxidant activity was evaluated. The results obtained proved the compound to be a good antioxidant agent and can also be useful for the treatment of bacterial infections since antimicrobial activity was promising against different microbial strains.

REFERENCES

Abbas, G., Hassan, Z., Al-Harrasi, A., khan, A., Al-Adawi, A., Ali, M., 2019. Synthesis, biological evaluation, molecular docking and structure-activity relationship studies of halogenated quinone and naphthoquinone derivatives. Journal of Molecular Structure 1195, 462-469.

Baeyer, A., Villiger, V., 1903. Dibenzalaceton und triphenylmethan, Berichte der. Deutschen Chemischen. Gesellschaft 36, 2774-2796.

Barraga, B., ´ Huerta, N., Peralta-Cruz, J., Gonza´ lez-Laredo, R., Karchesy, J., 2004. Neocandenatone, an isoflavan-cinnamylphenol quinonemethide pigment from dalbergiacongestiflora. Phytochemistry 65, 925-928.

Benzie. I., Strain. J., Ferric 1999 reducing/antioxidant power assay: Direct measure of total antioxidant activity of biological fluids and modified version for simultaneous measurement of total antioxidant power and ascorbic acid concentration. Methods in Enzymology 299, 15-27.

Bolton, J.L., Dunlap, T.L., Dietz, B.M., 2018. Formation and biological targets of botanical o-quinones. Food and Chemical Toxicology 120, 700-707.

Halilu, M., Muhammad, I., Dangoggo, S., Farouq, A., Ahmed, A., Shamsuddeen, M. Suleiman A., Yahaya, M., 2016. Phytochemical and antibacterial screening of petroleum ether and ethanol extracts of *Sidacordifolia* leaves. Journal of Chemical Society of Nigeria 41, 137-142.

He, H., Liu, Z., Wang, W., Jiang, X., 2020. Synthesis and cytotoxic evaluation of halogenated α-exo-methylene-lactones. Bioorganic and Medicinal Chemistry 28, 115281.

Hettie, K., Klockow, J., Glass, T., Chin, F., 2019. Near-infrared fluorescent rosol dye tailored toward lymphatic mapping applications. Analytical Chemistry 91, 3110.

Kavitha, S., Perumal. P., 2018. Antidiabetic and antioxidant activities of ethanolic extract of piper betle l. leaves in catfish, clarias gariepinus. Asian Journal of Pharmacy Clinical Research 11,194-8.

Laborde, M.R.R., Larramendy, M.L., Soloneski, S., 2020. Cytotoxic and genotoxic assessments of 2,4-dichlorophenoxyacetic acid (2,4-D) in in vitro mammalian cells. Toxicology *in Vitro* 65, 104783.

Liu, Z., You, P.,. Wu, C.,. Han, Y., 2019. Microwave-promoted solvent-free synthesis of *para*-quinone methides (*p*-QMs) derivatives. Journal of Saudi Chemical Society 24, 120-126.

Liu, Z.-Q., You, P.-S., Wu, C.-H., Han, Y.-H., 2020. Microwave-promoted solvent-free synthesis of para-quinone methides (p-QMs) derivatives. Journal of Saudi Chemical Society 24, 120-126.

Matata, D.Z., Moshi, M.J., Machumi, F., Ngassapa, O.D., Swanepoel, B., Oosthuizen, K., Venables, L., Koekemoer, T., Heydenreich, M., Kazyoba, P.E., van de Venter, M., 2020. Isolation of a new cytotoxic compound, 3-((Z)-heptadec-14-enyl) benzene-1-ol from Rhus natalensis root extract. Phytochemistry Letters 36, 120-126.

Miyajima, Y., Saito, Y., Takeya, M., Goto, M., Nakagawa-Goto, K., 2019. Synthesis of 4-epi-parviflorons A, C, and E: structureactivity relationship study of antiproliferativeabietane derivatives. Journal of Organic Chemistry 84, 3239-3248.

Nesvadba, P., 2000. Easy large scale syntheses of 2,6-di-t-butyl-7-cyano-, 7-carboxy-and 7-methoxycarbonyl quinonemethides. Synthetic Communications 30, 2825-2832.

Nilsson, M., Ha¨ma M., inen, l., Ivarsson, M., Gottfries, J., Xue, Y., Hansson, S., Isaksson, R., Fex, T., 2009. Compounds binding to the S2–S3 pockets of thrombin. Journal of Medicinal Chemistry 52, 2708-2715.

Okada, H., 2018. Electrophotographic photoconductor containing photosensitive layer for image forming apparatus. Patent JP2018116138A.

Okada, H., 2018. Electrophotographic photosensitive member, US Patent US20180157183A1

Patterson, D., Powers, J., LeBlanc, M., Sharkey, T., Boehler, E., Irdam, E., Osterhout, M., 2009. Development of a practical large-scale synthesis of denagliptintosylate. Organic Process Research and Development 13, 900-906.

Prota, G., 2000. Melanins, melanogenesis and melanocytes: looking at their functional significance from the chemist's viewpoint. Pigment Cell and Melanoma Research 13, 283-293.

Purkait, K., Mukherjee, A., 2020. Cytotoxicity and reactivity of a redox active 1,4-quinone-pyrazole compound and its Ru(II)-p-cymene complex. Inorganica Chimica Acta 502, 119361.

Reddy V., Anand, R., 2015. Expedient access to unsymmetrical diarylindolylmethanes through palladium-catalyzed domino electrophilic cyclization–extended conjugate addition approach. Organic Letters 17, 3390-3393.

Roper, J., Everly, C., 1988. Direct synthesis of spiro[5.5]undeca-1,4,7-trienones from phenols via a

quinonemethide intermediate. Journal of Organic Chemistry 53, 2639-2642.

Ryu, Y., Park, S., Kim, Y., Lee, J., Seo, W., Chang, J., Park, K., .Rho, M., Lee, W., 2010. SARS-CoV 3CLpro inhibitory effects of quinone-methidetriterpenes from tripterygiumregelii. Biorganic and Medicinal Chemistry Letters 20, 1873-1876.

Sreenivasa, S., Vinay, K., Mohan, N., 2012. Phytochemical analysis, antibacterial and antioxidant activity of leaf extracts of *Daturastramonium*. International Journal of Science Research 1, 83-86.

Subedi, Y.P., Alfindee, M.N., Shrestha, J.P., Becker, G., Grilley, M., Takemoto, J.Y., Chang, C.-W.T., 2018. Synthesis and biological activity investigation of azole and quinone hybridized phosphonates. Bioorganic and Medicinal Chemistry Letters 28, 3034-3037.

Swapnaja, K.J.M., Yennam, S., Chavali, M., Poornachandra, Y., Kumar, C.G., Muthusamy, K., Jayaraman, V.B., Arumugam, P., Balasubramanian, S., Sriram, K.K., 2016. Design, synthesis and biological evaluation of diaziridinyl quinone isoxazole hybrids. European Journal of Medicinal Chemistry 117, 85-98.

Takao, K., Sasaki, T., Kozaki, T., Yanagisawa, Y., Tadano, K., Kawashima, A., Shinonaga, H., 2001. Syntheses and absolute stereochemistries of UPA0043 and UPA0044, cytotoxic antibiotics having a *p*-quinone-methide structure. Organic Letters 3, 4291-4294.

Thompson, D., Thompson, J., Sugumaran, M., Molde´us, P., 1993. Biological and toxicological consequences of quinonemethide formation. Chemico-Biological Interactions 86, 129-162.

Torregrossa, M., Folk, J., Rice, K., Watson, S., Woods, J., 2005. Chronic administration of the delta opioid receptor agonist (+) BW373U86 and antidepressants on behavior in the forced swim test and BDNF mRNA expression in rats. Psychopharmacology 183, 31-40.

Tsurumi, H., Miyamoto, E., 2019. Electrophotog. Photosensitive member image forming app process cartridge. Patant JP2019078870A

Viault, G., Helesbeux, J.-J., Richomme, P., Séraphin, D., 2018. Concise semisynthesis of novel phenazine-vitamin E hybrids via regioselective tocopheryl ortho-quinone formation. Tetrahedron Letters 59, 2627-2630.

Wang, P., Liu, R., Wu, X., Ma, H., Cao, X., Zhou, P., Zhang, J., Weng, X.,. Zhang, X., Qi, J., Zhou, X., Weng, L., 2003. Water-soluble and photoinducible DNA cross-linking agent. Journal of American Chemical Society 125, 1116-1117.

Winter, R., Von Ahn, V., 1996. Method for inhibiting premature polymerization of vinyl aromatic monomers. US Patent US5545782A.

Zhang, L., Chen, P., Xu, Y., Nie, W., Zhou, Y., 2020. Enhanced photo-induced antibacterial application of graphene oxide modified by sodium anthraquinone-2-sulfonate under visible light. Applied Catalysis B: Environmental 265, 118572.

Zhang, W., Ning, B., Sun, C., Song, K., Xu, X., Fang, T., Yao, L., 2020. Dynamic nano-Ag colloids cytotoxicity to and accumulation by Escherichia coli: Effects of Fe^{3+}, ionic strength and humic acid. Journal of Environmental Sciences 89, 180-193.