© 2019 IJSRSET | Volume 6 | Issue 3 | Print ISSN: 2395-1990 | Online ISSN : 2394-4099
Themed Section : Engineering and Technology
DOI : https://doi.org/10.32628/IJSRSET

Synthesis, Characterization and Biological Evaluation Of 2-Chloroquinoline-Tetramethyl-Hexahydro- 1H-xanthene-1,8-(2H) Dione Derivatives

Arun Vaghasiya[1], Chetana Rajyaguru[1], Kaushik Joshi[2], Govind Kher[3], Jatin Upadhiyay[1]

[1]Department of Chemistry, M.V.M. Science and Home Science College, Rajkot, Gujarat, India
[1]Department of Chemistry, D.K.V. Arts and Science College, Jamnagar, Gujarat, India
[1]Department of Chemistry, Tolani College of Arts and Science, Adipur, Gujarat, India

ABSTRACT

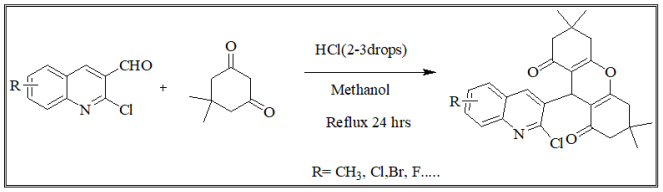
9-(2-chloro-substitutedquinolin-3-yl)-3,4,6,7-tetrahydro-3,3,6,6-tetramethyl-2H-xanthene-1,8(5H,9H)-diones (DMDMO-1 to 12) were prepared with good yield by very effective method using the basic idea with quite novel approach 2-chloro-5,8-dimethylquinoline-3-carbaldehyde and 5,5-dimethylcyclohexane-1,3-dione was refluxed for 12 to 18 hrs. in presence of HCl. Completion of reaction was checked by thin layer chromatographic (TLC) technique. All the new synthesized compounds authorized with better functional group and derivatizations were characterized by IR, ^{1}HNMR and elemental analyses. All the synthesized compounds were assessed for their antimicrobial activity.

Keywords : 2-chloro-5,8-dimethylquinoline-3-carbaldehyde, 5,5-dimethylcyclohexane-1,3-dione, HCl.

I. INTRODUCTION

Xanthenes and thioxanthenes are important class of the biologically active heterocycles.[1] xanthene moieties containing Natural and synthetic products shows a bride range of biological activities such as antitumor,[2] antibacterial,[3] antifungal,[4] analgesic and antiinammatory [5] activities. Nowadays a number of technique for the diversely functionalized xanthene derivatives have been founded, some methods particularly for the preparation of 9-substituted xanthene derivatives.[6] especially,substitution of the xanthenyl-9-position with an indolyl substituent has received much importance due to the broad range of biological and pharmacological activities of indole derivatives.[7] The synthesis of xanthene derivatives, particularly benzoxanthenes, has introduced as a powerful tool in organic synthesis due to their wide range of biological and therapeutic properties such as antibacterial [8], antiviral [9] and anti-inflammatory activities [10] as well as in photodynamic therapy [11] and for antagonism of the paralyzing action of zoxazolamine [12] in addition, due to their useful spectroscopic and visual properties, they were used as dying agents [13], in laser technologies [14], and in fluorescent materials for visualization of biomolecules [15]. Many methods proposed to the synthesize xanthenes and benzoxanthenes including cyclodehydrations [16], trapping of benzynes by phenols [17], cyclocondensation between 2-hydroxyaromatic aldehydes and 2-tetralone [18], the reaction of 2-naphthol with aldehydes or acetals under acidic conditions and intramolecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones[19].

Reaction Scheme



II. MATERIAL AND METHODS

Methods

All the chemicals used in the synthesis are of analytical grade purchased from local vendors. Melting points of synthesized compounds (DMDMO-1 to 12) were determined by open capillary tubes and are uncorrected. Formation of the compounds was routinely checked by TLC on silica gel-G plates of 0.5 mm thickness and spots were located by iodine. IR spectra were recorded on IRAffinity-1S FTIR Spectrophotometer-Shimadzu using 'neat' sample. 1H NMR was determined in DMSO-d6 solution on a Bruker Ac 400 MHz spectrometer. Mass spectra were recorded on Shimadzu GC-MS-QP-2010 model using Direct Injection Probe technique. Elemental analyses of the all the synthesized compounds were carried out on Elemental Vario EL III Carlo Erba 1108 model and the results are in agreements with the structures assigned.

General methods for the Synthesis of 9-(2-chloro-6,8-dimethylquinolin-3-yl)-3,4,6,7-tetrahydro-3,3,6,6-tetramethyl-2H-xanthene-1,8(5H,9H)-dione (DMDMO-1 to 12)

Mixture of 2-chloro-(substituted)quinoline-3-carbaldehyde and 5,5-dimethylcyclohexane-1,3-dione was refluxed for 12 to 18 hrs. in presence of HCl. Completion of reaction was checked by thin layer chromatographic (TLC) technique. After cooling, reaction mixture was washed with methanol and filtered to get solid 9-(2-chloro-(substituted)quinolin-3-yl)-3,3,6,6-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8(2H)-dione product (DMDMO-1 to 12), which was recrystallized from methanol.

Table 1 : Physical parameters of compound DMDMO -1 to 12.

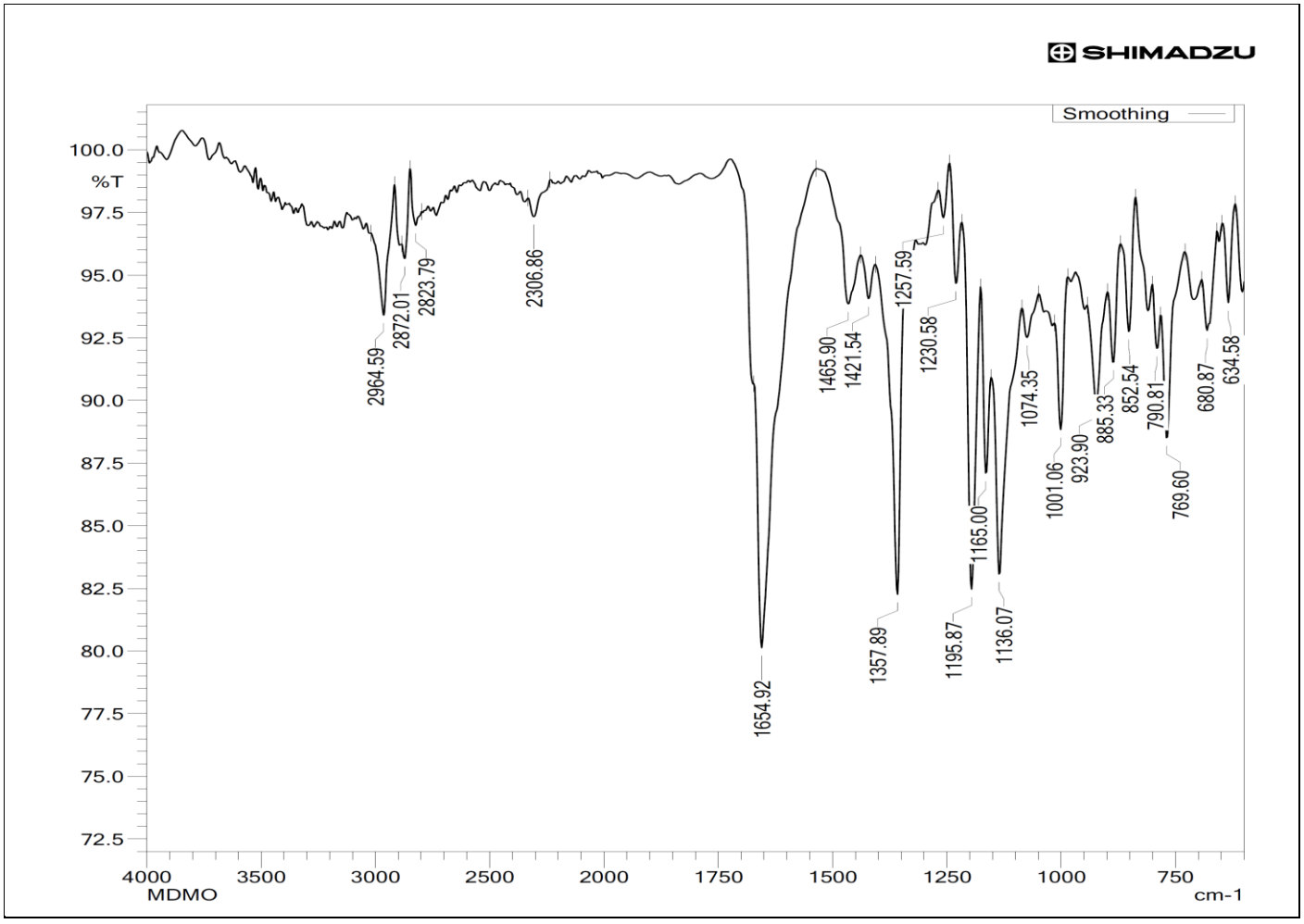
Code	R	M. F.	M. W.	M. P. °C	% Yield
1	6,8-dimethyl	$C_{12}H_{10}ClNO$	219.67	198	78
2	6-methyl	$C_{11}H_8ClNO$	205.64	189	66
3	8-bromo	$C_{10}H_5BrClNO$	270.51	191	69
4	7-nitro	$C_{10}H_5ClN_2O_3$	236.61	188	76
5	6-nitro	$C_{10}H_5ClN_2O_3$	236.61	195	71
6	8-choloro	$C_{10}H_5Cl_2NO$	226.06	186	64
7	8-flouro	$C_{10}H_5ClFNO$	209.60	182	70
8	8-methyl	$C_{11}H_8ClNO$	205.64	199	72
9	6-chloro,7-nitro	$C_{10}H_4Cl_2N_2O_3$	271.05	181	64
10	7-chloro,6-flouro	$C_{10}H_4Cl_2FNO$	244.05	189	68

11	6,8-diflouro	$C_{10}H_4Cl_3NO$	260.50	192	79
12	7,8-dimethyl	$C_{12}H_{10}ClNO$	219.67	195	63

Spectroscopy

IR spectral study

IR spectra were recorded on IRAffinity-1S FTIR Spectrophotometer-Shimadzu using 'neat' sample. Various functional groups present in molecule were identified by characteristic frequency obtained for them.



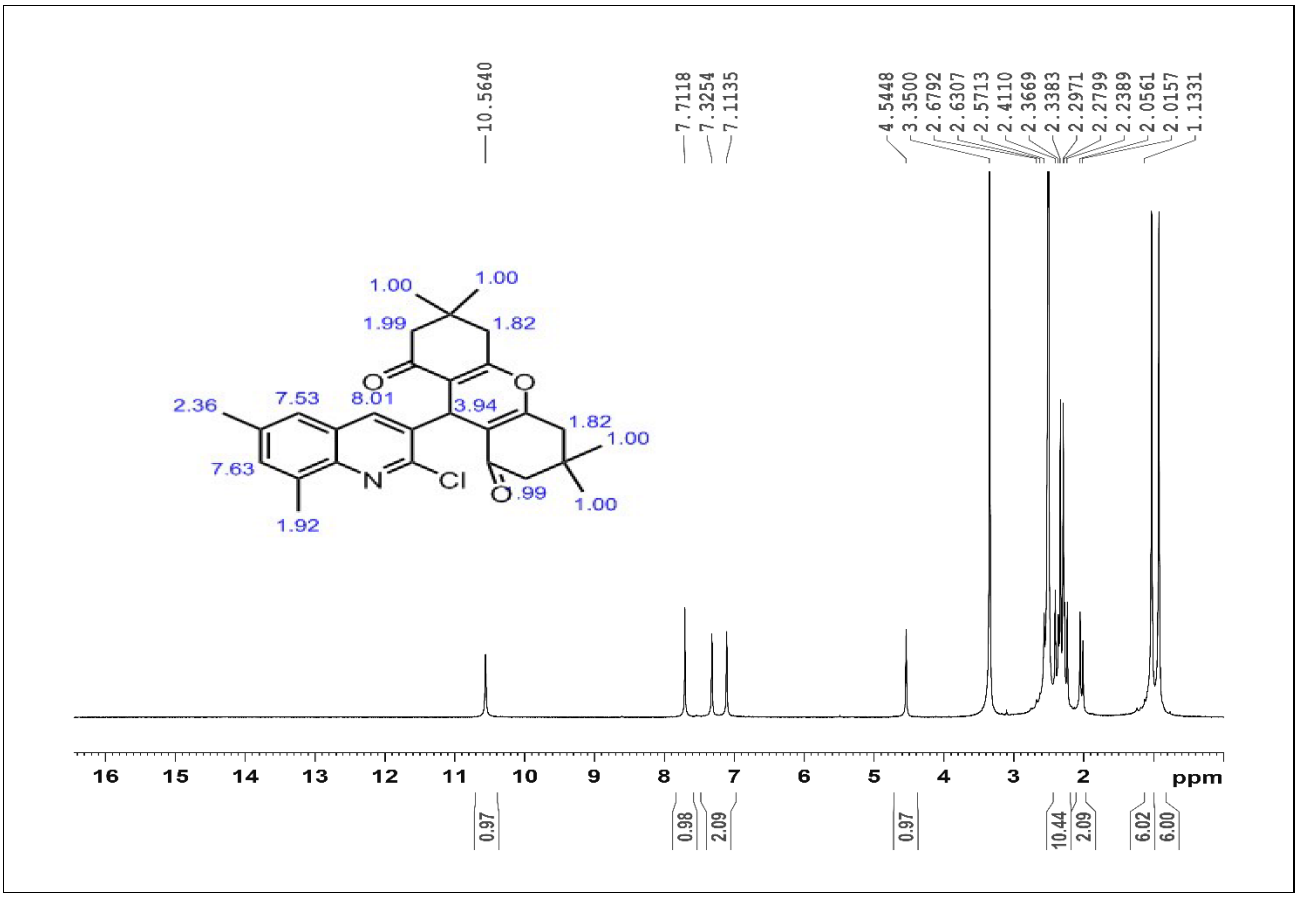
FT-IR spectrum of DMDMO-1.

^{1}H NMR spectral study

^{1}H NMR spectra were recorded in DMSO-d6 solution on a Bruker Ac 400 MHz spectrometer using TMS as an internal standard. Number of protons and their chemical shifts were found to support the structure of the synthesized compounds.

Table 2: ^{1}H NMR data of compound DMDMO -1.

Sr. No.	Signal Position	Relative No. of Proton	Multiplicity
1	1.18	12	Singlet
2	2.27	3	Singlet
3	2.29	3	Singlet
4	7.11 to 7.31	3	Singlet
5	2.33	8	Singlet



^{1}H-NMR spectrum of DMDMO-1.

Biological evaluation

Antimicrobial evaluation

All the synthesized compounds (DMDMO-1 – DMDMO-12) were tested for their antibacterial and antifungal activity (MIC) in vitro by broth dilution method with two Gram-positive bacteria Staphylococcus aureus MTCC-96, Bacillus subtilis MTCC-441, two Gram-negative bacteria Salmonella typhosa Para B MTCC-3224, Escherichia coli MTCC 442, and two fungal strains Candida albicans MTCC 227, Aspergillus niger MTCC 282, taking ampicillin, chloramphenicol, ciprofloxacin, norfloxacin, nystatin and greseofulvin as standard drugs. The standard strains were procured from the Microbial Type Culture Collection (MTCC) and Gene Bank, Institute of Microbial Technology, Chandigarh, India.

The minimal inhibitory concentration (MIC) values for all the newly synthesized compounds, defined as the lowest concentration of the compound preventing the visible growth, were determined by using microdilution broth method according to NCCLS standards. Serial dilutions of the test compounds and reference drugs were prepared in Muellere-Hinton agar. Drugs (10 mg) were dissolved in dimethylsulfoxide (DMSO, 1 mL). Further progressive dilutions with melted Muellere-Hinton agar were performed to obtain the required concentrations. In primary screening 1000 μg mL-1, 500 μg mL-1 and 250 μg mL-1 concentrations of the synthesized drugs were taken. The active synthesized drugs found in this primary screening were further tested in a second set of dilution at 125 μg mL-1, 100 μg mL-1, 50 μg mL-1, 25 μg mL-1, 12.5 μg mL-1, and 6.25 μg mL-1 concentration against all microorganisms. The tubes were inoculated with 10^8 cfu mL-1 (colony forming unit/mL) and incubated at 37 °C for 24 hours. The MIC was the lowest concentration of the tested compound that yields no visible growth (turbidity) on the plate. To ensure that the solvent had no effect on the bacterial growth, a control was performed with the test medium supplemented with DMSO at the same dilutions as used in the experiments and it was observed that DMSO had no effect on the microorganisms in the concentrations studied. The results obtained from antimicrobial susceptibility testing are depicted in Table 1.

Table 1. Antibacterial and antifungal activity of synthesized compounds (DMDMO-1 – DMDMO-12)

Code	Minimum inhibition concentration (μg mL^{-1})					
	Gram's positive		Gram's negative		Fungal species	
	S. a.	B. s.	E. c.	S. t.	C. a.	A. n.
DMDMO-1	125	62.5	125	125	250	250
DMDMO-2	125	125	62.5	62.5	250	250
DMDMO-3	250	250	125	125	250	250
DMDMO-4	500	500	250	250	500	500
DMDMO-5	500	500	250	250	500	500
DMDMO-6	250	250	125	125	500	500
DMDMO-7	250	250	250	250	250	250
DMDMO-8	500	500	250	500	250	250
DMDMO-9	125	125	62.5	62.5	125	125
DMDMO-10	250	500	125	125	500	500
DMDMO-11	125	250	125	125	250	250
DMDMO-12	250	250	125	250	500	500
Ampicillin	250	100	100	100	--	--
Chloramphenicol	50	50	50	50	--	--

Ciprofloxacin	50	50	25	25	--	--
Norfloxacin	10	10	10	10	--	--
Nystatin	--	--	--	--	100	100
Griseofulvin	--	--	--	--	100	100

III. CONCLUSION

Structural activity relationship showed that -chloro and -nitro substitution at 4th and 5th position [DMDMO-9] showed excellent activity against grams positive, grams negative and fungal species compared to other derivatives. DMDMO-2 also showed good activity against gram-positive and gram-negative bacteria.

IV. REFERENCES

[1] (a) M. R. Taghartapeh, N. N. Pesyan, H. Rashidnejad, H. R. Khavasi and A. Soltani, J. Mol. Struct., 2017, 1149, 862; (b) L. Jeyaseeli, A. D. Gupta, K. A. Kumar, K. Mazumdar, N. K. Dutta and S. G. Dastidar, Int. J. Antimicrob. Agents, 2006, 27, 58; (c) T. Yıldız and H. B. Kuc¨ uk, ¨ RSC Adv., 2017, 7, 16644.

[2] S. Y. Wu, Y. H. Fu, G. Y. Chen, X. B. Li, Q. Zhou, C. R. Han, X. P. Song, X. J. Du, M. L. Xie and G. G. Yao, Phytochem. Lett., 2015, 11, 236.

[3] (a) S. Naseem, M. Khalid, M. N. Tahir, M. A. Halim, A. A. C. Braga, M. M. Naseer and Z. Shaa, J. Mol. Struct., 2017, 1143, 235; (b) A. Barmak, K. Niknam, G. Mohebbi and H. Pournabi, Microb. Pathog., 2019, 130, 95; (c) A. Akbari and A. Hosseini-Nia, J. Saudi Chem. Soc., 2017, 21, S7.

[4] (a) J. M. Khurana, D. Magoo, K. Aggarwal, N. Aggarwal, R. Kumar and C. Srivastava, Eur. J. Med. Chem., 2012, 58, 470; (b) U. Kusampally, R. Pagadala and C. R. Kamatala, Tetrahedron Lett., 2017, 58, 3316.

[5] (a) H. N. Hafez, M. I. Hegab, I. S. Ahmed-Farag and A. B. A. ElGazzar, Bioorg. Med. Chem. Lett., 2008, 18, 4538; (b) A. G. Banerjee, L. P. Kothapalli, P. A. Sharma, A. B. Thomas, R. K. Nanda, S. K. Shrivastava and V. V. Khatanglekar, Arabian J. Chem., 2016, 9, S480.

[6] (a) C. G. Piscopo, S. Buhler, G. Sartori and R. Maggi, ¨ Catal. Sci. Technol., 2012, 2, 2449; (b) H. Jian, K. Liu, W. H. Wang, Z. J. Li, B. Dai and L. He, Tetrahedron Lett., 2017, 58, 1137; (c) Q. Chen, G. D. Yu, X. F. Wang, Y. C. Ou and Y. P. Huo, Green Chem., 2019, 21, 798; (d) Subodh, N. K. Mogha, K. Chaudhary, G. Kumar and D. T. Masram, ACS Omega, 2018, 3, 16377; (e) Q. Chen, X. F. Wang, G. D. Yu, C. X. Wen and Y. P. Huo, Org. Chem. Front., 2018, 5, 2652.

[7] (a) F. Peng, S. Y. Hou, T. Y. Zhang, Y. Y. Wu, M. Y. Zhang, X. M. Yan, M. Y. Xia and Y. X. Zhang, RSC Adv., 2019, 9, 28754; (b) A. Kumari and R. K. Singh, Bioorg. Chem., 2019, 89, 103021; (c) P. V. Thanikachalam, R. K. Maurya, V. Garg and V. Monga, Eur. J. Med. Chem., 2019, 180, 562; (d) S. Nomiyama, T. Hondo and T. Tsuchimoto, Adv. Synth. Catal., 2016, 358, 1136.

[8] Hideu T. Jpn Tokkyo Koho JP, 56005480; 1981, Chem Abstr 1981, 95, 80922b.

[9] Lambert RW, Martin JA, Merrett JH, Parkes KEB, Thomas GJ. PCT Int. Appl. WO 9706178; 1997. Chem Abstr 1997,126, P212377y.

[10] Poupelin JP, Saint-Rut G, Foussard-Blanpin O, Narcisse G, Uchida-Ernouf G, Lacroix R. Synthesis and anti-inflammatory properties of bis(2-hydroxy-1- naphthyl)methane derivatives. I. Monosubstituted derivatives. Eur J Med Chem 1978 13, 67-71.

[11] Ion RM, Frackowiak D, Wiktorowicz K. The incorporation of various porphyrins into blood cells measured via flow cytometry, absorption and emission spectroscopy. Acta Biochim Polonica 1998, 45, 833-45.

[12] Saint-Ruf G, Hieu HT, Poupelin JP. The effect of dibenzoxanthenes on the paralyzing action

of zoxazolamine. Naturwissenschaften 1975, 62(12), 584.

[13] Menchen SM, Benson SC, Lam JYL, Zhen W, Sun D, Rosenblum BB, et al. U.S. Patent, 6,583,168; 2003. Chem Abstr 2003, 139, 54287.

[14] Ahmad, M., King, T. A., Ko, D. K., Cha, B. H., & Lee, J. (2002). Performance and photostability of xanthene and pyrromethene laser dyes in sol-gel phases. Journal of Physics D: Applied Physics, 35(13), 1473-1476.

[15] Knight CG, Stephens T. Xanthene-dye-labelled phosphatidylethanolamines as probes of interfacial pH. Biochem J. 1989, 258, 683.

[16] Bekaert A, Andrieux J, Plat M. New total synthesis of bikaverin. Tetrahedron Lett 1992, 33, 2805.

[17] Knight DW, Little PB. The first high-yielding benzyne cyclisation using a phenolic nucleophile: a new route to xanthenes. Synlett 1998, 10, 1141.

[18] Jha A, Beal J. Convenient synthesis of 12H-benzo[a]xanthenes from 2-tetralone. Tetrahedron Lett 2004, 45(49), 8999-9001.

[19] Chih-Wei Kuo & Jim-Min Fang (2001) synthesis of xanthenes, indanes, and tetrahydronaphthalenes via intramolecular phenyl–carbonyl coupling reactions, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 31, 877-892

Cite this Article

Arun Vaghasiya, Chetana Rajyaguru, Kaushik Joshi, Govind Kher, Jatin Upadhiyay, "Synthesis, Characterization and Biological Evaluation Of 2-Chloroquinoline-Tetramethyl-Hexahydro- 1H-xanthene-1,8-(2H) Dione Derivatives", International Journal of Scientific Research in Science, Engineering and Technology (IJSRSET), Online ISSN : 2394-4099, Print ISSN : 2395-1990, Volume 6 Issue 3, pp. 420-426, May-June 2019. Journal URL : https://ijsrset.com/IJSRSET218239