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Synthesis of Quinozoline-4-(3H)-one and Quinolone Derivatives Via Organic Clay as a Catalyst

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Abstract: *In this we have carried out Frielander synthesis (modified Niementowski reaction) and Niementowski reaction for synthesis of quinozoline 4-(3H)-one derivatives and quinoline derivatives. The reaction of anthranillic acid, amides, diketones (Cyclisation) have been performed over organic clays as the catalyst, under solvent-less conditions using microwave irradiation as the energy source, obtaining the corresponding quinozoline derivatives. Reaction of anthranilic acid with acetyl acetone and ethyl acetoacetate (1:1) yields new compounds 3-methyl-6H-benzo[c][1,5]oxazocin-6-one and 3-methyl-3H-benzo[c][1,5]oxazocine-4,6-dione respectively. These reactions represent some examples of efficient microwave irradiation promoted organic condensation and cyclisation in which the reaction can be carried out in the open vessels by using organic clay as a catalyst and provides products with satisfactory yields and simple work up as greener approach.*

Keywords: Organic Clay, Quinoline, Microwave Irradiation, Catalyst.

I. INTRODUCTION

In medicinal and pesticide chemistry, quinazolinones and their derivatives occupy an important position by presenting a wide range of bioactivities. Various quinazolin-4(3H)-ones, quinoline derivatives are well known to possess an array of physiological activities, e.g. anticancer, muscle relaxant, hypnotic, anti-inflammatory, antineoplastic, diuretic, and antihypertensive activities, and are widely used in pharmaceuticals.[1]Quinazoline and quinazolinone compounds are also used in preparation of various functional materials for synthetic chemistry and also present in various drugs molecules.
In accordance with the significance of quinazolin-4(3*H*)-ones and quinoline derivatives various synthetic methods have been developed for the construction of these kind of fused heterocycles. Many quinazolines can be prepared from 2-aminobenzaldehyde, 2-aminophenyl ketones or anthranilic acids. Typically, quinazolin-4(3*H*)-ones are prepared from an anthranilic acid or its derivative[1]. From the literature search many of synthetic methods for elaboration of this simple ring structure are, however, time consuming, tedious and often low yielding.[2-5]
In general, the most common method for the synthesis of quinozolin-4(3H)-one derivatives involve Niementowski reaction (condensation of anthranillic acid and amides) and the Niementowski modification of Friedlander synthesis by heating a mixture of anthranilic acid with a ketone.[6, 7] The rapid synthesis of variety of organic compounds under microwave irradiation has been widely demonstrated. Microwave irradiation provides enhanced reaction rate and improved product yield in chemical synthesis and application of it is quite successful in the formation of a variety of carbon-heteroatom bonds.[8] The focus has lately shifted to less cumbersome solvent-free methods[9-11] wherein solid acid catalyst like organic clay under solvent-free conditions carry a number of benefits[12,13]. Clay minerals are a class of inorganic layered compounds which are the good materials for catalysis because of their inherent features in composition and structure[14]. The structure and reactivity of the catalytic clay materials are known to preserve by microwaves[15, 16].

Table 1: Solvent-free microwave-assisted synthesis of Quinoline/Quinazolinone derivatives catalyzed by Red clay (a)

Entry	Product	Time (min)	Power (w)	M.P. (˚C)	Yield (%)
1	14a	4	400	225-229	61
2	15a	5	400	356-360	79
3	16a	5	250	265-270	88

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4	17a	2	400	300 <	51
5	18a	5	400	295-298	67
6	19a	5	400	239-244	50

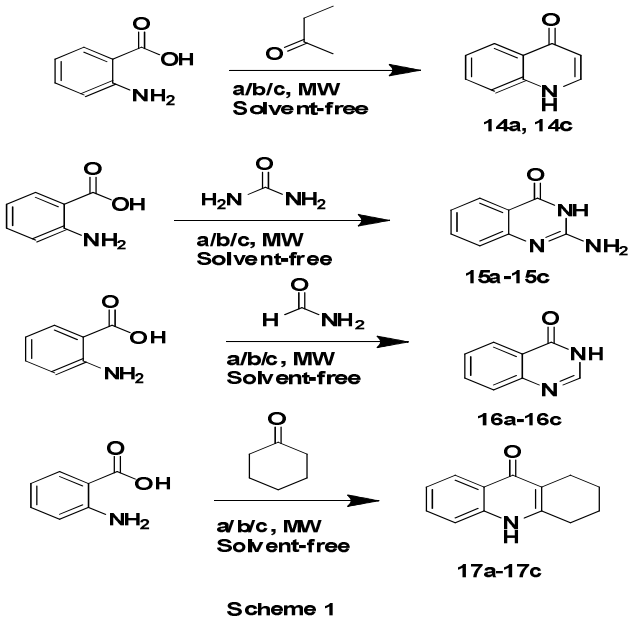
Table 2: Solvent-free microwave-assisted synthesis of Quinoline/Quinazolinone derivatives catalyzed by White clay (b)

Entry	Product	Time(min)	Power (w)	M.P. (˚C)	Yield (%)
1	14b	-	400	-	-
2	15b	6	400	357-360	71
3	16b	7	250	266-271	78
4	17b	3	400	300 <	90
5	18b	6	400	294-298	69
6	19b	6	400	237-240	57

Table 3: Solvent-free microwave-assisted synthesis of Quinoline/Quinazolinone derivatives catalyzed by Black clay (c)

Entry	Product	Time(min)	Power (w)	M.P. (˚C)	Yield (%)
1	14c	4	400	225-230	59
2	15c	5	400	356-360	75
3	16c	5	250	264-271	85
4	17c	2	400	300 <	63
5	18c	5	400	295-299	48
6	19c	5	400	238-241	82

When anthranilic acid was reacted with ethyl methyl ketone (1:1) compound **14a**, **14c** obtained in good yield with red and black clay as catalyst respectively and reaction was not worked out with white clay and it is further under investigation. Anthranilic acid was reacted with urea to produce compound **15a**, **15b** and **15c** in almost good yield with all three red, white and black clay as a catalyst respectively. When anthranilic acid reacted with formamide (1:5) compound **16a**, **16c** obtained in excellent yield with red and black clay as a catalyst as compared to white clay. Condensation of anthranilic acid with cyclohexanone (1:2) under microwave irradiation led to formation of acridone **17b** in excellent yield only with white clay as compared to red and black clay as catalyst.



Scheme 1

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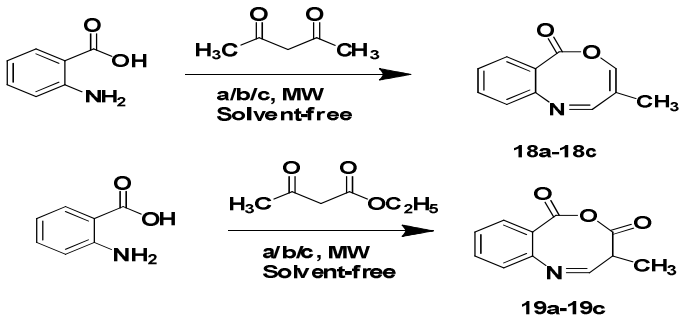

Scheme 2

a =Red clay, b= White clay, c= Black clay
MW= Microwave irradiation

When the anthranilic acid reacted with acetyl acetone (1:1) compound **18a**, **18b** obtained in good yield with red, white clay respectively as compared to **18c** with black clay as a catalyst. Also, when anthranilic acid reacted with ethyl acetoacetate (1:1) compound **19c** obtained in excellent yield with black clay as a catalyst as compared to **19a**, **19b**. (**Scheme 2**) From the spectral analysis it is clear that we got the new structures for the **18a-18c** and **19a-19c**. All the synthesized compounds were characterized by FT-IR, 1H NMR & 13C NMR spectroscopy techniques.

We present tour investigation on the use of microwave irradiation under solvent free condition by using red, white and black organic clays[17, 18] for synthesizing diverse quinazolinones and quinoline derivatives based on the Niementowski reaction. In this paper, we demonstrate that, under microwave irradiation, anthranilic acid react smoothly with an amides and ketones or urea by using organic clay as catalyst leading to quinazolinone and quinoline derivatives in moderate to excellent yields with a simple work-up[1].

II. EXPERIMENTAL

Reactions were monitored by thin layer chromatography on 0.2 mm silica gel F-252 (Merck) plates. All chemicals were obtained from Aldrich Chemicals. All solid components were employed as grained powders. Melting points were measured in open capillary tubes and are uncorrected. Analysis of organic clay used in this was done by EDX technique. Infrared spectral studies were carried out using KBr discs on a Perkin Elmer FTIR/4000 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in DMSO-d6 on Bruker Advance II 400 NMR spectrometer. All products were characterized by FT-IR, ^{1}H NMR, ^{13}C NMR and by comparison of physical characteristics with authentic samples.

General procedure for synthesis of quinozoline 4-(3H)-one and quinoline derivatives

A mixture of Anthranilic acid (0.01mol) and ethyl methyl ketone (0.01mol)/cyclohexanone (0.02mol)/acetyl acetone (0.01mol)/ethyl acetoacetate (0.01mol)/urea (0.02mol)/formamide (0.05mol) was microwave irradiated for appropriate time under solvent-free condition by using red/white/black clay as a catalyst. Completion of reaction was checked with TLC using Pet ether: Ethyl acetate (7:3). By using ethanol product was separated and spent catalyst was collected by filtration and washed with hot ethanol. Synthesized products were purified by column chromatography and characterized by spectral techniques such as IR, ^{1}H NMR, ^{13}C NMR.

Spectral analysis:

Quinolin-4(1H)-one(14a): IR (KBr, cm^{-1}): 3376, 1673, 1612, 1388, 1245, 111, 755; ^{1}H NMR (DMSO) δ (ppm): 7.67 (s, 1H), 7.47 (m, 1H), 7.24 (d, 1H), 7.19 (1H, m), 6.74 (1H, m), 6.48 (d, 1H); ^{13}C NMR (DMSO-d6) δ (ppm): 109.5, 114.51. 116.0, 131.1, 133.6, 134.9, 134.2, 151.4, 169.5

2-aminoquinazolin-4(3H)-one (15b): IR (KBr, cm^{-1}): 3214, 1719, 1679, 1624, 1451, 1407, 1297, 1143, 761; ^{1}H NMR (DMSO) δ (ppm): 7.09-7.15 (3H, m), 7.43-7.53 (1H, m), 7.99-8.01 (1H, m), 11.16 (2H, s), 11.30 (1H, s); ^{13}C NMR (DMSO-d6) δ (ppm): 114.28, 115.27, 122.29, 126.91, 134.93, 140.81, 150.28, 162.81

Quinazolin-4(3H)-one (16b): IR (KBr, cm^{-1}): 3280, 1706, 1672, 1614, 1408, 1234, 1171, 1130; ^{1}H NMR (DMSO) δ (ppm): 7.51-755 (1H, m), 7.66 (1H, d), 7.80-7.84 (1H, m), 8.09-8.14 (2H, m), 12.26 (1H, s); ^{13}C NMR (DMSO-d6) δ (ppm): 122.58, 126.74, 127.20, 134.32, 145.37, 148.72, 160.70

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1,3,4,4a,9a,10-hexahydroacridin-9(2H)-one (17b): IR (KBr, cm^{-1}): 3113, 2933, 1638, 1600, 1552, 1502, 1358, 1246, 1170; ^{1}H NMR (DMSO) δ (ppm): 8.03-8.06 (1H, q), 7.54-58 (1H, m), 7.44 (1H, d), 7.20-7.24 (1H, m), 2.68-2.71 (2H, t), 2.42-2.45 (2H, m), 1.72-1.77 (4H, m); ^{13}C NMR (DMSO- d6) δ (ppm): 21.6, 27.08, 115.49, 117.33,121.97, 123.15, 124.7, 130.94, 139.20, 146.79, 175.93

3-methyl-6H-benzo[c][1,5]oxazocin-6-one (18c): IR (KBr, cm^{-1}): 3305, 2930, 2856, 1667, 1603, 1474, 1370, 1291, 828, 773; ^{1}H NMR (DMSO-d6) (δ ppm): 8.11-8.13 (1H, m), 8.07-8.09 (1H, m), 7.79-7.81(1H, m), 7.69 (1H, d), 7.67-7.69 (1H, m), 7.49-59 (1H, m), 2.09 (3H, s); ^{13}C NMR (DMSO-d6) (δ ppm): 23.73, 120.32,126.20, 129.50, 131.58, 137.5, 147.4, 154.2, 161.3, 165.7

3-methyl-3H-benzo[c][1,5]oxazocine-4,6-dione (19c): IR (KBr, cm^{-1}): 3262, 2933, 2865, 1639, 1597, 1406, 1246, 1106, 838; ^{1}H NMR (DMSO-d6) (δ ppm): 8.19 (s, 1H), 8.06 (s, 1H), 7.13-7.95 (m, 4H), 5.76 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (DMSO-d6) (δ ppm): 98.21, 114.90, 115.09, 121.01, 122.61, 130.79, 139.13, 162.46

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REFERENCES

[1] J. P. Michael, "Quinoline, quinazoline and acridone alkaloids," Nat. Prod. Rep., vol22, pp. 627, 2005.
[2] W. L. F. Armarego, Fused Pyrimidines, Part 1: Quinazolines; Interscience: New York, 1967.
[3] K. Undheim, T. Benneche, In Comprehensive Heterocyclic Chemistry II, 6; Pergamon: Oxford, 1998.
[4] T. L. J. Gilchrist, "Synthesis of aromatic heterocycles," Chem. Soc., Perkin Trans., vol 1, pp.2491-2515, 2001.
[5] T.L. J. Gilchrist, "Synthesis of aromatic heterocycles," Chem. Soc., Perkin Trans., vol 1, pp. 2849-2866, 1999.
[6] J.E. Baldwin and P.D. Magnus, Tetrahedron organic chemistry series, pergamon press, Oxford, 1994, pp. 275, vol 11.
[7] H. Tiedtke, "The reaction of anthranilic acid with cyclohexanone under thermal activation afforded acridinone 5 in 40% yield," Chem. Ber., vol 42, pp. 621, 1909.
[8] K.R. Desai, "Green Chemistry Microwave Synthesis," First Ed., Himalaya Publication House, India, 2005.
[9] R.S. Varma and R. Dahiya, "Sodium borohydride on wet clay: Solvent-free reductive amination of carbonyl compounds using microwaves," Tetrahedron, vol 54, pp. 6293-6298, 1998.
[10] R.S. Varma and R. Dahiya, "Microwave-assisted facile synthesis of imines and enamines using envirocat EPZGTM as a catalyst,"Synlett., pp. 1245-1246, 1997.
[11] R.S. Varma and R. Dahiya, "An Expeditious and Solvent-Free Synthesis of 2-Amino-Substituted Isoflav-3-enes Using Microwave Irradiation," J. Org. Chem., vol 63, pp. 8038-8041,1998.
[12] T.S. Li, L. J. Li, B. Lu and F. Yang, "Montmorillionite clay catalysis. A facile synthesis of 2-substituted and 2,2-disubstituted 1,3-benzodioxoles," J. Chem. Soc., Perkin Trans., vol 1, pp. 3561-3564, 1998.
[13] T.S. Jin, X. Sun and T. S. Li, J. Chem. Res. (S), 2000, 128.
[14] C.H. Zhou, "An overview on strategies towards *clay*-based designer catalysts for green. and sustainable catalysis," Appl. Clay Sci., vol 53, pp. 87-96, 2011.
[15] M. Butters, "Zeolite Assisted Organic Synthesis, A Survey in Solid Supports and Catalysts in Organic Synthesis," ed. K. Smith, Ellis Horwood PTR, Prentice Hall, New York, 1992, 310.
[16] J.M. Clark and D.J. Macquarrie, "Environmentally friendly catalytic methods," Chem. Soc. Rev., vol 25, pp. 303-310, 1996.
[17] S. P Babar and V. M. Kamble, "Solvent-free one pot multi-component synthesis of 3,4-dihydropyrimidone derivatives catalyzed by organic white clay as an cheap and environmentally friendly catalyst," IJRASET, vol 9, pp. 467-472, 2021.
[18] S. P. Babar, "Oxidation of p-anisaldehyde to p-anisic acid by organic clay as novel method,"Eur. J. Mol. Clin. Med., vol 8, pp. 1358-1366, 2021.