Heterocyclic Letters
Vol. 6| No.1|99-104| Nov-Jan| 2016
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

MICROWAVE ASSISTED [TCT-DMF] CATALYZED FORMYLATION OF SUBSTITUTED COUMARIN

Santosh A. Jadhav[a] and *Rajendra K. Pardeshi[b]

[a]*Department of Chemistry, Vivekanand College Aurangabad, 431001 (India)*
[b]*Department of chemistry, SantRamdas College Ghansawangi Jalna, 431203 (India)*
Email : rajendrakpardeshi@gmail.com

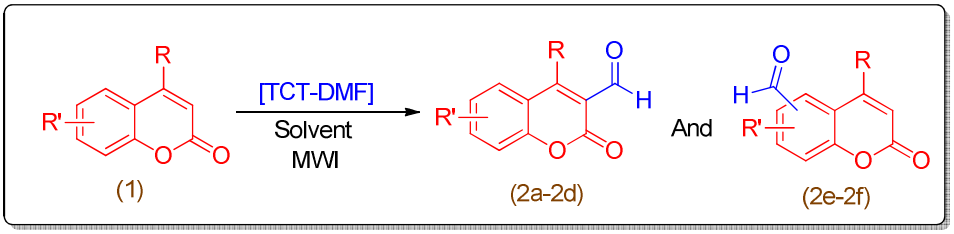
Abstract: Formylation of Coumarin derivatives by using effective an environmentally benign complex [TCT-DMF] in dichloromethane under a simple stirring and microwave condition. The structures of all synthesized compounds were confirmed by IR, NMR and Mass Spectrometry. This is a newly developed efficient method for the formylation of substituted coumarin using environmentally benign reagent under microwave irradiation method.

Keywords: Microwave irradiation method, [TCT-DMF] green reagent, Formyl coumarin.

Introduction:

Coumarins and its derivatives are more importance and useful in the field of medicinal; anti-bacterial[i], anti-cancer[ii], anti-inflammatory[iii], anti-pyretic, anti-biotic[iv], anti-fungal, anti-oxidant[v] and also reported for exhibiting photo chemical properties[vi], food and cosmetics[vii]. Various analogues of Coumarins such as formyl Coumarins[viii-x] exhibits luminescent properties[xi].

A symmetrical- 2,4,6-trichloro-1,3,5-triazine (TCT) has been found to be effective reagent for the cyclization reaction and in presence of DMF cyclization followed by formylation[xii-xvi]. Many researchers have been reported formylation of heterocyclic compound and or aromatic compounds[xvii-xx] using hazardous reagent or conditions such as hexamethylenetetramine (HMTA) in the presence of Glycero Boric acid[xxi], and in anhydrous acetic acid[xxii]. The use of microwave energy is one of the eco-friendly methods to accelerate the organic reactions and having a number of advantages such as short reaction time, easy work-up procedure, no side product and high yield. Hence, the use of microwave reaction for the synthesis of organic molecules is considered as part of green chemistry [xxiii-xxv]. In past, synthesis of some formyl Coumarin[xii-xvi]. However these suffer from some disadvantages such as hazardous reagent, catalyst or solvent. This encourage to us as a part of our research interest [xxvi-xxx], to overcome these hazardous reagent, catalyst and/or tedious process by using environmentally benign complex or reagent for the formylation of substituted coumarin. Here we first time report, formylation of hydroxy coumarin and substituted coumarin using [TCT-DMF] as reagent under microwave irradiation method.



Reaction Condition: Mixture of [cyanuric chloride (0.11 mol) and DMF (0.13 mol) 40ml of DCM]

MWI 150 W 100°C for 3 min. coumarin (**1**) (0.040 mol) was added and stirred ,microwave condition.

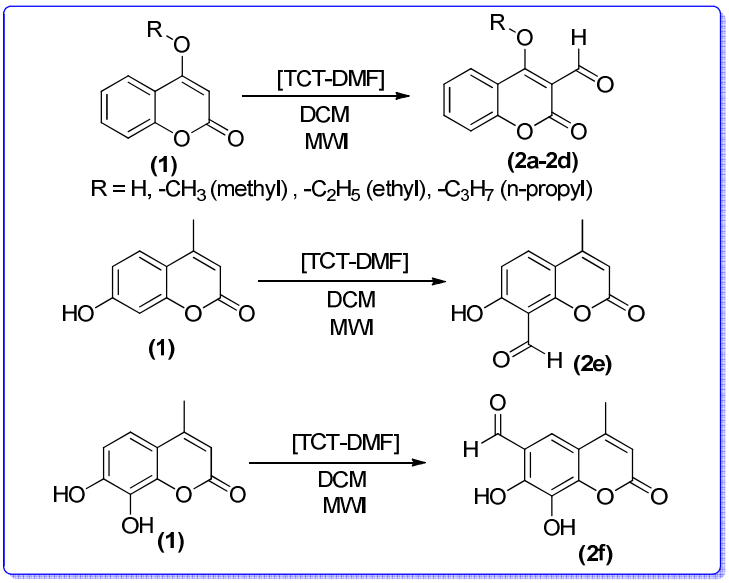


Figure 1. Synthesized formyl Coumarin and its derivative

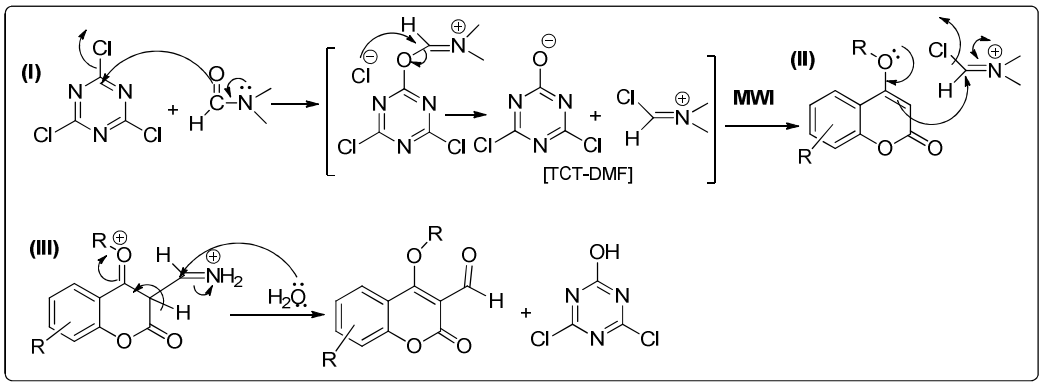


Figure 2. Plausible mechanism for the synthesis of formyl coumarins by using [TCT-DMF] Complex.

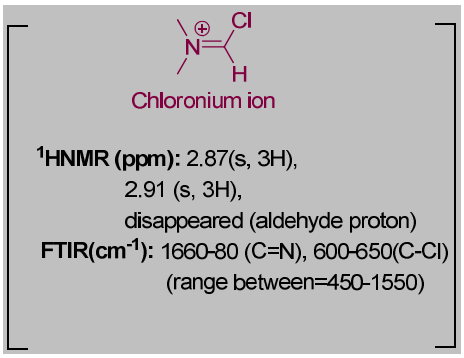


Figure 3. Prepared [TCT-DMF] Complex in DCM

Experimental section

All the compounds used in synthesis of analytical grade; the melting points of the compounds were determined in open head capillary and are uncorrected. The IR spectra of the compounds were recorded in the region of 4000-400 $^{cm-1}$ by using KBr pallet on FT-IR Perkin spectrophotometer. H^1NMR spectra were recorded on a DRX-300 Bruker FT-NMR spectrophotometer in $CDCl_3$. The values of chemical shift are expressed in δ ppm as an unit. All the compounds were checked for purity by thin layer chromatography and recrystallized from ethanol.

Results and Discussion

Initially, we prepared [TCT-DMF] as complex or reagent by optimized various solvents in different time of reaction (Table **1.,** entry 1-7) among these DCM was the best solvent not only for the preparation of reagent (Table **1.,** entry 2, figure **3**) but also formylation of coumarin and its analogue (Table **2**).

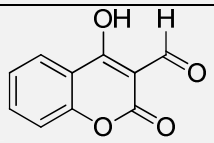
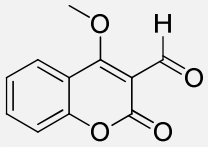
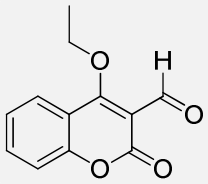
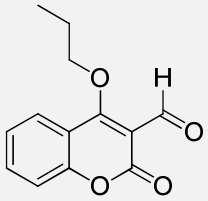
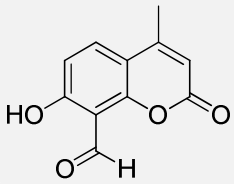
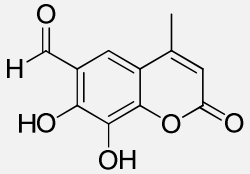
At first, we screened various solvent for the preparation of [TCT-DMF] reagent by applying different time interval in first 1-2 h there was no yield of product was obtained in each selected solvents as DMF, DCM, $CHCl_3$, Toluene, CH_3CN, Nitrobenzene. Among these DCM gave better yield of product IN 3h (Table **1**, entry **2**). If we increase the time of reaction more than 3h there is no any significant effect on the increasing the yield of product. Thus, we select DCM as solvent for the synthesis of [TCT-DMF] as complex. The prepared reagent was used for the formylation of coumarin and its derivatives under Microwave irradiation method, all example were tested reasonably good yield could be achieved in less time of reaction under MWI method (Table **2,** figure **1**). 4-alkoxy and methyl coumarin gave better yield (Table **2**, entry 2,3,4) than hydroxy and other substituent to coumarin (Table **2**). Finally structures of compound and [TCT-DMF] reagent were substantiated by FTIR, ^{1}H NMR, ^{13}CNMR and Mass Spectrometry.

Table 1 Optimization of solvent for the preparation of [TCT-DMF] Complex

Sr. no.	Solvent	Time (h)/Yield[a] (%)	Time (h)/Yield[a] (%)	Time (h)/Yield[a] (%)
1	DMF	2/00	3/68	4/68
2	DCM	2/00	**3/89**	4/85
3	$CHCl_3$	2/00	3/65	4/66
4	Toluene	2/00	3/62	4/64
5	CH_3CN	2/00	3/68	4/70
6	Nitrobenzene	2/00	3/65	4/66
7	THF	2/00	3/60	4/62

[a]Isolated yield:

Table 2 Synthesis of coumarin carbaldehyde derivatives under Microwave method:

Sr. no.	Compound	Molecular structure	Molecular formula	Yield(%)/Time(min)	Melting Point (^{0}C)
1	2a		$C_{10}H_6O_4$	79/4	160-162
2	2b		$C_{11}H_8O_4$	**93/3**	120-122
3	2c		$C_{12}H_{10}O_4$	86/3	148-150
4	2d		$C_{13}H_{12}O_4$	82/4	159-161
5	2e		$C_{11}H_8O_4$	85/4	140-142
6	2f		$C_{11}H_8O_5$	84/4	180-182

Reaction condition: Cyanuric chloride (0.11 mol) and DMF (0.13 mol) and DCM (45ml) in a round bottom flask and stirred for 3h at room temperature, white colored precipitate formed [TCT-DMF] to this reagent, coumarin (**1**) (0.098 mol) under MWI condition.
[a]Isolated yield

General procedure for the synthesis of formyl coumarin derivatives (2a-2f):
Microwave method:
Cyanuric chloride (0.11 mol) and DMF (0.13 mol), were added to 40ml of DCM as solvent in a round bottom flask and stirred for 3h at room temperature, white colored precipitate formed [TCT-DMF] to this reagent, coumarin (**1**) (0.040 mol) and minimum amount of solvent DCM was added the mixture of compound was subjected to microwave synthesizer programmed at 150 watt, 100°C for 3-4 min. Progress of reaction was monitored by TLC. The reaction mixture was then cooled to room temperature water was added, stirred for few minutes then organic layer was extracted with water. The precipitates were filtered, dried and crystallized from ethanol yield 79-93%. If necessary products were purified by column chromatography)

Spectral Characterization data *(2a-2f):*

4-hydroxy-2-oxo-2H-chromene-3-carbaldehyde (2a):

IR (cm^{-1}): 3326, 1730.

^{1}H NMR: δ ppm = 13.5 (s, 1H), 10.36 (s, 1H), 7.40-7.90 (m, 4H)

^{13} NMR: δ ppm = 190.4, 178.2, 160.9, 150.9, 128.1, 125.3, 115.4, 114.2, 95.3

Mass: [M^{+}+1]; 190.026

4-methoxy-2-oxo-2H-chromene-3-carbaldehyde (2b):

IR (cm^{-1}): 1720, 1316

^{1}H NMR: δ ppm = 3.56–3.60 (s, 3H), 10.30–10.42 (s, 1H), 7.40-7.91 (m, 4H)

^{13} NMR: δ ppm = 190.3, 181.2, 162.4, 153.2, 128.1, 125.2, 123.2, 117.2, 116.3, 92.2, 60.1

Mass: [M^{+}+1]; 204.0422

4-ethoxy-2-oxo-2H-chromene-3-carbaldehyde (2c):

IR (cm^{-1}): 2862, 1720, 1624

^{1}H NMR: δ ppm = 1.22–1.42 (t, 3H), 4.02–4.12 (q, 2H), 10.41 (s, 1H), 7.40-7.90 (m, 4H)

^{13} NMR: δ ppm = 191.3, 180.2, 162.2, 152.1, 128.3, 125.1, 123. 117.4, 116, 94.2, 60.3, 15.3

Mass: [M^{+}+1]; 218.057

2-oxo-4-propoxy-2H-chromene-3-carbaldehyde (2d):

IR (cm^{-1}): 2860, 1728

^{1}H NMR: δ ppm = 0.98-1.12 (t, 3H), 1.78-1.82 (m, 2H), 4.02 (t, 2H), 10.40-1.52 (s, 1H), 7.32-7.85 (m, 4H)

^{13} NMR: δ ppm = 191.2, 180.3, 162, 152, 128.2, 126.1, 123.3, 117.2, 90, 68, 23.1, 10.5

Mass: [M^{+}+1]; 232.0735

7-hydroxy-4-methyl-2-oxo-2H-chromene-8-carbaldehyde (2e):

IR (cm^{-1}):3350, 1730, 1618

^{13} NMR: δ ppm = 12.20-12.32 (s, 1H), 10.60–10.69 (s, 1H), 7.70-7.80 (d, 1H), 6.90 (d, 1H), 6.14–6.26 (s, 1H), 2.32-2.45 (s, 3H)

^{13} NMR: δ ppm = 191.3, 165, 160, 152, 150, 135, 120, 115, 112, 20.2

Mass: [M^{+}+1]; 204.0421

7,8-dihydroxy-4-methyl-2-oxo-2H-chromene-6-carbaldehyde (2f):

IR (cm^{-1}): 3356, 1725

^{1}H NMR: δ ppm = 2.41–2.53 (s, 3H), 10.30–10.40 (s, 1H), 5.32-5.42 (s, 2H), 6.20-6.33 (s, 1H)

^{13} NMR: δ ppm = 192.3, 161.1, 152.2, 152, 151.2, 140.3, 125.2, 120.3, 115.2, 112.1, 20.3

Mass: [M^{+}+1]; 220.0371

Conclusions

Herein we first time report formylation of hydroxy coumarin and substituted coumarins using an environmentally benign reagent [TCT-DMF] in good to excellent yield, cleaner reaction in very short reaction time under the condition of MWI method.

Acknowledgement

Authors are thankful to the Principal, Vivekanand College, Aurangabad for provide necessary facilities for this work.

References

i. Kayser, O.; Kolodziej, H. *Planta Med*. **(1997)**, 63, 508-510.

ii. Wang, C. J.; Hsieh, Y. J.; Chu, C. Y.; Lin, Y. L.; Tseng, T. H.; *Cancer Lett.* **(2002)**, 183, 163 168.

iii. Luchini, A. C.; Rodrigues, O. P.; Cestary, S. H.; Seito, L. N.; Witaicenis, A.; Pelizzon, C. H.; Stasi, L. C. D. *Bio. Pharma. Bull.***(2008)**, 31, 1343-1350.

iv. Erans, D. A.; Sacks, C. E.; Kleschick, W. A.; Taber, T. R. *J. Am. Chem. Soc.***(1979)**, 101, 6789.

v. (a) Vukovic, N.; Sukodolak, S.; Solugic, S.; Niciforovic, N. *Arch Pharma. Res*. **(2010)**, 33,5 15.; (b)Yamato, M.; *J. Pharma. Soc. Japan*, **(1992)**, 112, 81.

vi. Kokotos, G.; Tzougraki, C. *J.Chem. Soc. Perkin Trans*. **(1991)**, 2, 495.
vii. Maheshwara, M.; Siddaiah, V.; Damu, G. L.; Rao, Y. K. *J. Mol. Catalysis A Chem*., **(2006)**, 255, 49 52.
viii. Seetharamaiyer.; Padmanabhan.; Rajkumar, Peri.; Devid, J.; Triggle. *Syn. Comm*. **(1996),** 26, 4, 827 821.
ix. Naik, R. M.; Thakor, V. M. *Journal of Org. chem.*, **(1957)**, 22, 12, 1626-29.
x. Andrea, Sabatie.; Daniel, Vegh.; Andre, Laupy.; Lubomir, Hoch. *ARKIVOC*, (2001), (vi),122 128.
xi. Kirpichenok, M. A.; Baukiulv, V. M.; Karandashova, L. A.; Grandberg, I. F. *Chem. Heterocyclic Comp.*, **(1991)**, 27, 11, 1193-99.
xii. Mehdi, Shariat.; Mohd, Wahid S.; Zuriati, Zakaria. *Chemistry Central Journal*, **(2013)**, 7:58, 1-6.
xiii. Venkanna, P.; Rajanna, K. C.; Satish Kumar M.; Ansari, M. B.; Mohazzan Ali, M. *Tetrahedron Lett.*,**(2015)**, 56, 5164-5167.
xiv. L, De, Luca.;Giacomelli, G.; Porcheddu A. *Org Lett*. **(2002)**, 4, 553–555.
xv. Thilagavathy, R.; Kavitha, H. P.; Arulmozhi, R.; Vennila, J. P.; Manivannan, V.*Acta Crystallogr Sect E- Struct Rep***(2009)**, 65, 127.
xvi. Khajavi, M. S.; Shariat, S. M. *Heterocycles,* (2005), 65, 1159–1165.
xvii. Vilsmeier, A.; Haack, A. *Ber. dtsch. Chem. Ges*. **(1927)**, 60, 119–122.
xviii. (a) Jutz, C. *Adv. Org. Chem.***(1976)**, 9, 225–342.; (b) Seshadri, S. *J. Sci. Ind. Res*. **(1973)**, 32, 128–149.
xiv. Naik, R. M.; Thakur, V. M. *J. Org. Chem.*, **(1957)**, 22, 12, 1626–1629
xv. George, A.; Olah, Lena.;Ohannesian, Massoud.; Arvanaghi. *Chem. Rev*., **(1987)**, 87, 4, 671 686
xvi. (a) Houben, J. *Ber, Dtsch. chem. Ges*. **(1926)**, 59, 2878-2891; (b) Hoesch, K. *Ber, Dtsch. chem. Ges.**(1957),** 48, 1122-1133*
xvii. James, C.; Duff, *J. Chem. Soc*., **(1941**), 547-550
xviii. Duff, J. C. Bills, E. J.; *J. Chem. Soc*., **(1932),** 1987-1988
xix. Ian, M.; Downie, Martyn, J.; Khamis, F.; Shuhaibar. *Tetrahedron,* **(1993)**, 4, 9, 19, 4015 4034.
xx. William, E.; Smith, *J. Org. Chem.*, **(1972)**, 37, 24, 3972–3973
xxi. (a) Duff, J.; Bills, E.; *Journal of Chem. Soc.*, **(1932)**, 1987.; (b) Ferguson, L. N. *Chem. Review.***(1946)**, 38, 230.
xxii. Duff, J.; Bills, E. *Journal of Chem. Soc.*, **(1934)**, 1305.
xxiii. Caddic, K.S. *Tetrahedron*.(**1995),** 51, 38, 10403-10432.
xxiv. SethuramanIndumathi.; SubbuPerumal.; Natarajan Anbananthanb. *Green Chem*. (**2012)**, 14, 3361 3367.
xxv Pramod, K. *Current Microwave Chemistry*. (**2015)**, 2, 144-149.
xxvi. Jadhav, S. A.; Shioorkar, M. G.; Chavan, O. S.; Sarkate, A. P.; Shinde, D. B.; Pardeshi, R. K *Heterocyclic Letters,* **(2015)**, 5, 3, 375 382.
xxvii. Jadhav, S. A.; Shioorkar, M. G.; Chavan, O. S.; Sarkate, A. P.; Shinde, D. B.; Pardeshi, R. K *Chemistry and Materials Research*, **(2015)**, 7, 8, 105-111.
xxviii. Jadhav S. A. , Mahesh G. Shioorkar, Omprakash S. Chavan, Rajendra K. Pardeshi, *Europian Journal of Pharmaceutical Medicinal Res*.; (**2016**), 3(1), 233-238.; xxix. Santosh, A. Jadhav.; Pardeshi, R. K.; Shioorkar, M. G.; Chavan, O. S.; Vaidya, S. R., *Der Pharma Chemica,* **(2015)**, 7, 2, 127-131.
xxix. Jadhav, S. A.; Shioorkar, M. G.; Chavan, O. S.; Sarkate, A. P.; Shinde, D. B.; Pardeshi, R. K., *European Journal of Chemistry*, (**2015)**, 6 (4) 410-416.
xxx. Jadhav S. A. , Mahesh G. Shioorkar, Omprakash S. Chavan, Mohammad A. Baseer and Rajendra K. Pardeshi, *Org. Chem. International Journal.* (**2016)**, 90, 37490-37495.

Received on November 5, 2015.