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# Functionalization of Carboxylate Multi Walled Carbon Nanotube with pyrano[2,3-d]pyrimidinone Derivatives by DABCO as a Catalyst in Green Media

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**Abstract**

1, 4-Diazabicyclo [2.2.2] octane (DABCO) was employed as a catalyst for one-pot synthesis of pyrano[2,3-d] pyrimidinone derivatives and MWNT- pyrimidinones from condensation reactions of aromatic aldehydes, malononitrile and thiobarbituric acid and MWNT-COCl . This method delivers the advantages of a simple method, environment friendly procedure, mild reaction conditions and high returns. The materials were characterized by Fourier transform infrared spectroscopy, nuclear magnetic resonance, mass spectroscopy, elemental analysis, scanning electron microscopy and Thermogravimetric analysis.

***Keywords**: MWNT, Pyrano[2,3-d]pyrimidinone , Thiobarbuturbic acid, Malononitrile, Aldehyde.*

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## Introduction

Owing to their pharmacological activity, Barbituric (BA) and thiobarbituric acids (TBA), as well as their various substituted derivatives, are significant compounds in biological chemistry and medicine. Their biological activity is primarily relevant to tautomerism and acid-base equilibria and, in turn, to the nature of the substituents [1-3]. It is well-known that barbituric acid itself has no consequences on the fundamental nervous system [4], however, it is a precursor to medical barbiturates which can be lethal in excessive amounts [5]. In a study, is has shown that in mice, barbituric acid would cause liver and kidney weight increase[6]. Barbituric acid is also a precursor to derivatives that have been proven to possess antibacterial activity[7, 8] and for tumor inhibitory agents [9]. Thus, determination of trace amounts of barbituric acid is very significant both in the study of biological and industrial operations.

Synthesis of fused heterocycles has been interesting for scientists for many decades. One of the premier of these compounds is pyrano[2,3-d]pyrimidinonethat has a widespread usage in pharmaceutical and biological active compounds like diuretic, anticoagulant, antitumor, antiallergic, cardiotonic, antihypertensive and anticancer activity[10-12].These nitrogen-containing heterocycles are used in the industrial preparation of pigments and dyes [13] and luminescence compounds [14]. There are many simple and straightforward protocols for synthesis of pyrano [2,3-d]pyrimidinone scaffolds, consisting of ultrasonic methods [15], DABCO[16], Zn[(L) proline]$_2$[17], alumina[18], ionic liquids [19, 20], DAHP[21], CAN[22], electrocatalyst [23]. Some of them have own merit and limitations, that harsh reaction condition, organic solvent, effluent pollution and hard work-up are some of these disadvantages. So the environment-friendly methods have been our inspirations in this paper, as we investigated the synthesis of MWNT- pyrano[2,3-d]pyrimidinone, from amidation of MWNT- COCl and pyrimidinone derivatives.

## Experimental

*Material and methods*

All reagents and solvents were obtained from Merck Chemical Inc. (Darmstadt, Germany), and MWCNT–COOH (95% purity, 20–30 nm; Netvino Co. Ltd) was purchased and used as received. The FT-IR spectrum was recorded using KBr tablets on a Nexus 870 FT-IR spectrometer (Thermo Nicolet, Madison, WI). SEM was used to examine the morphology of the MWCNTs. SEM measurement was implemented the XL30 electron microscope (Philips, Amsterdam, Netherlands). Elemental analyses of samples were performed using a Series II 2400 (Perkin Elmer, Waltham, MA). TGA analysis was taken on a Mettler TA 4000 Systems under nitrogen atmosphere at rate of

10 C°/min. whole synthesized compound were characterized by comparison of their M.P with reported in the literature.

*General procedure for synthesis of 7-Amino-6-cyano-5-(Aryl) 4-oxo-2-thioxo-5H- pyrano[2,3-d] pyrimidinone(**4a-g**)*

A mixture of aromatic aldehyde (1 mmol), malononitrile (1.2 mmol), thiobarbituric acid (1 mmol), and 1, 4-diazabicyclo [2.2.2] octane (DABCO) (10 mol %) in $H_2O$ (10 ml) and EtOH (10 ml) was stirred at room temperature for 2 h. After completion of the reaction, the solid product was collected by filtration and purified by washing with aqueous ethanol.

***7-Amino-6-cyano-5-(4-bromophenyl)-4-oxo-2-thioxo-5H-pyrano[2,3-d]pyrimidinone*** **(4a)**

White color powder, IR (KBr) ($\nu_{max}$/cm$^{-1}$): 3370 ($NH_2$), 3189 (NH), 2220 (C≡N), 1684 (C=O), 1567.

***7-amino-6-cyano-5-(3-chlorophenyl)-4-oxo-2-thioxo-5H-pyrano [2,3-d]pyrimidinone*** **(4b)**

White color powder, IR (KBr) ($\nu_{max}$ /cm$^{-1}$): 3375, 3320 ($NH_2$), 3194 (NH), 2892 (CH), 2195 (C≡N), 1680 (C=O), 1569 (C=S).

***7-Amino-6-cyano-5-(2, 3 -dichloro phenyl)-4-oxo-2-thioxo-5H-pyrano [2,3-d]pyrimidinone*** **(4c)**

White color powder, IR (KBr) ($\nu_{max}$ /cm$^{-1}$): 3460, 3316 ($NH_2$), 3172,3064 (NH), 2190 (C≡N), 1671 (C=O), 1574.

***7-amino-6-cyano-5-(3-nitrophenyl)-4-oxo-2-thioxo-5H-pyrano[2,3-d] pyrimidinone*** **(4d)**

White color powder, m.p. IR (KBr) ($\nu_{max}$ /cm$^{-1}$): 3385, 3311 ($NH_2$), 3194(NH), 2202(C≡N), 1683 (C=O), 1573 (C=S).

***7-Amino-6-cyano-5-(4-nitrophenyl)-4-oxo-2-thioxo-5H-pyrano[2,3-d]pyrimidinone*** **(4e)**

White color powder, IR (KBr) ($\nu_{max}$ /cm$^{-1}$): 3369, 3265 ($NH_2$), 3190 (NH), 2201(C≡N), 1684 (C=O), 1517(C=S).

***7-Amino-6-cyano-5-(4-trifluoromethyl)-4-oxo-2-thioxo-5H-pyrano[2,3-d]pyrimidinone*** **(4f)**

Pale yellow powder, IR (KBr) ($\nu_{max}$ /cm$^{-1}$): 3383 ($NH_2$), 3186 (NH), 2198 (C≡N), 1697 (C=O), 1671, 1637.

***7-Amino-6-cyano-5-(2,4-dichlorophenyl)-4-oxo-2-thioxo-5H-pyrano[2,3-d]pyrimidinone*(4g)**

White color powder, IR (KBr) ($\nu_{max}$ /$cm^{-1}$): 3388 ($NH_2$), 3306, 3198(NH), 2196 (C≡N), 1687 (C=O), 1647.

*Synthesis of MWNT-COCl* ***(10)***

MWNT–COOH (60 mg) (20–30 nm; Netvino Co. Ltd) was sonicated in 90 mL of N, N-dimethyl formamide (DMF) for 45 minutes to give a homogeneous suspension. Then, Oxalyl chloride (2.5 mL) was added dropwise to the MWNT suspension at 0°C under nitrogen atmosphere. The mixture was stirred at 0°C for 2 hours and followed at room temperature for the same duration. Finally, the solvent evaporated under vacuum.

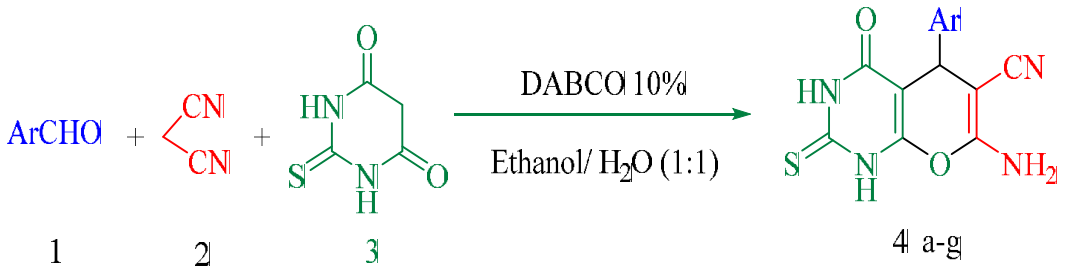
*Synthesis of MWNT-pyrimidinones* ***(11a-h)***

A mixture of aromatic aldehyde (1 mmol), malononitrile (1.2 mmol), thiobarbituric acid (1 mmol), and 1, 4- diazabicyclo[2.2.2]octane (DABCO) (10 mol %) dissolved in DMF, then MWNT-COCl (0.1 gr) was added. The reaction mixture was stirred at 95°C for 24 hours. Afterward, after cooling to room temperature, the mixture was filtered and washed thoroughly with DMF, ethyl alcohol, and THF. Subsequently, the black solid was vacuum-dried at room temperature for five hours.

**Results and discussion**

*Synthesis of pyrano [2, 3-d] pyrimidine*

pyrano[2,3-d] pyrimidinone derivative (4a-g) were achieved by the three-component condensation reaction of aldehyde, malononitrile, thiobarbituric acid in the presence of DABCO at room temperature(Scheme 1).




**Scheme 1**. synthesis of pyrano[2,3-d] pyrimidinone (**4a–g**).

In order to determine the optimum conditions, the reaction of the thiobarbituric acid, malononitrile with 4-bromo-benzaldehyde and various amount of DABCO was carried out with ethanol under reflux condition. As can be seen the optimum yield was achieved in %10 mol of catalyst. In

continue, investigation of solvent and temperature was executed, and the best yield was seen in the $H_2O$-ethanol in 1:1 ratio at room temperature (Table 1). To survey of catalyst efficiency, the reactions of series of representative aldehydes carried out with malononitrile and thiobarbituric acid (Table 2). Reactions were very clean so that pyranopyrimidinones (**4a-g**) were obtained as a sole product during suitable times in good to high yields.

**Table 1**. Optimization of the reaction conditions for synthesis of **4a**.

| Entry | Condition | Cat. (% mol) | Yield |
|---|---|---|---|
| 1 | Ethanol-reflux | 3 | 62 |
| 2 | Ethanol-reflux | 5 | 78 |
| 3 | Ethanol-reflux | 10 | 86 |
| 4 | Ethanol-reflux | 15 | 88 |
| 5 | $CH_3CN$-reflux | 10 | 53 |
| 6 | $H_2O$-reflux | 10 | 65 |
| 7 | $CH_2Cl_2$-reflux | 10 | 56 |
| 8 | $H_2O$-Ethanol-reflux | 10 | 92 |
| 9 | $H_2O$-Ethanol- r.t | 10 | 89 |
| 10 | $H_2O$-Ethanol- 50 | 10 | 92 |

**Table 2**. Synthsis of pyrano[2,3-d] pyrimidinone 4a–g in aqueous ethanol using DABCO.

| Ar | Product | Yield[a] | M.P(found) | M.P(reported) |
|---|---|---|---|---|
| 4-Br-$C_6H_4$ | 4a | 89 | 236 | 238[20] |
| 3-Cl-$C_6H_4$ | 4b | 83 | 237-238 | 234-237[24] |
| 2,3-$Cl_2$-$C_6H_3$ | 4c | 91 | 257-258 | 257-258[25] |
| 3-$O_2N$-$C_6H_4$ | 4d | 96 | 233.5-234 | 230-233[24] |
| 4-$O_2N$-$C_6H_4$ | 4e | 92 | 235-236 | 232-235[24] |
| 4-$CF_3$-$C_6H_4$ | 4f | 95 | 239-240 | 239-240[25] |
| 2,4-$Cl_2$-$C_6H_3$ | 4g | 85 | 238.5-239.5 | 238.5-239.5[25] |

[a]*:Isolated yield*

The structures of compounds **4(a-g)** were proved from their IR spectral data and melting point. $^1$HNMR and $^{13}$C NMR spectroscopy were especially useful to clarify the structures of products. Thus, all of the products displayed a single peak at about $\delta$ =4.22–4.85ppm for H-5 in the $^1$H NMR spectra, and also a distinctive signal at $\delta$ =35–36ppm for C-5 in the $^{13}$C NMR spectra[25].

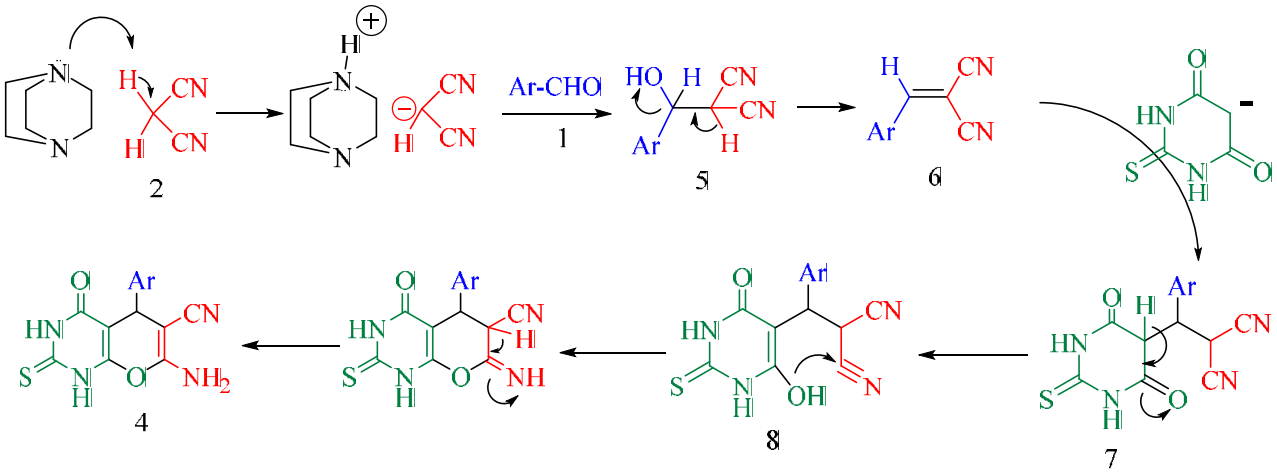
**Table 3.** Performance comparison of various catalyst with DABCO in pyrano[2,3-d]pyrimidinone synthesis.

| Entry | Catalyst | Solvent | Condition | Time | Yield | Ref. |
|---|---|---|---|---|---|---|
| 1 | [BMIm]BF4 | - | 90 °C | 3-5 h | 82-95 | [26] |
| 2 | DAHP | Ethanol | r.t | 2 h | 71-81 | [27] |
| 3 | - | $H_2O$ | )))) | 1-3 h | 62-78 | [28] |
| 4 | Nano-sawdust-OSO3H | Ethanol | reflux | 8-25 min | 69-94 | [24] |
| 5 | SBA-pr-SO3H | - | 140 °C | 5-45 min | 30-90 | [29] |
| 6 | DABCO | $H_2O$-EtOH | r.t | 2 h | 83-96 | This work |

The time and yield of the synthesized product via DABCO comprised with some catalyst in Table 3. It is obvious that the difference in condition and yields is due to the DABCO activity.

Although we have not yet set up the mechanism of the one-pot reaction between benzaldehyde derivatives, malononitrile and thiobarbituric acid in the presence of DABCO, a possible explanation is presented in scheme 2. We suggest that DABCO is an effective catalyst for the formation of pyrano[2,3-d]pyrimidinone.

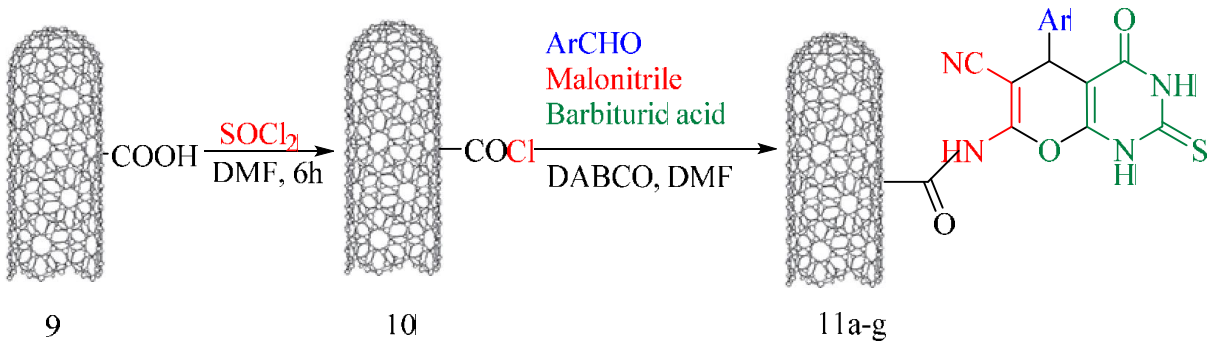
The high reactivity of the ammonium group was utilized to facilitate Knoevenagel condensation between aryl aldehyde **1** and malononitrile **2**, which proceeds via intermediate **5** and, after dehydration, Olefin **6** is produced. DABCO also catalyzes the generation of a proposed carboanion thiobarbituric acid and this intermediateadds to olefin **6** to generate **7**.the final product 4, was obtained after proton transfer in molecule 7, cyclization and tautomerization of the intermediate **8** (Scheme 2).




**Scheme 2.** The proposed mechanism for the synthesis of pyrano [2,3-d] pyrimidinone by DABCO.

*Synthesis of MWNT- pyrimidinones* (**11a-g**)

Functionalization of MWNT with pyrimidinone derivatives executed with this procedure. firstly, MWNT–COOH was reacted with Oxalyl chloride in DMF to achieve the MWNT–COCl. Then a four-component reaction was carried out with a kind of aromatic aldehyde (Table 1), malononitrile, thiobarbituric acid, and MWNT–COCl in the presence of DABCO to producing the MWNT-pyrimidinones (Scheme 3). The products were characterized by SEM, TGA, and elemental analysis.




**Scheme 3.** Synthesis route of modified MWNT- pyrimidinones.

Elemental analysis of the modified MWNT-COOH **9** and **11(a-g)** are shown in Table 4. the atomic percentages ofhydrogen and nitrogen of (**11a-g**) as compared with MWNT-COOH indicated that **9** is successfully functionalized with 7-Amino-6-cyano-5-(Aryl)4-oxo-2-thioxo-5H-pyrano[2,3-d] pyrimidinone.

**Table 4.** Elemental analysis of the modified MWNT.

| **Sample** | **%C** | **%H** | **%N** |
|---|---|---|---|
| MWNT-COOH | 96.40 | 0.04 | 0 |
| 11a | 83.50 | 2.45 | 3.03 |
| 11b | 82.56 | 2.34 | 3.10 |
| 11c | 81.67 | 2.36 | 3.11 |
| 11d | 83.75 | 2.58 | 2.85 |
| 11e | 81.65 | 2.31 | 2.87 |
| 11f | 82.98 | 2.39 | 3.15 |
| 11g | 75.45 | 1.95 | 3.87 |

Morphology of functionalized nanotubes (**11a, 11d, 11f**) were studied by scanning electron microscopy and the results are shown in figure 1. It is seen that the functionalized nanotubes show the presence of smaller agglomeration and aggregation. Also, after functionalization CNTs have been slightly shortened in contrast of pristine MWNT.

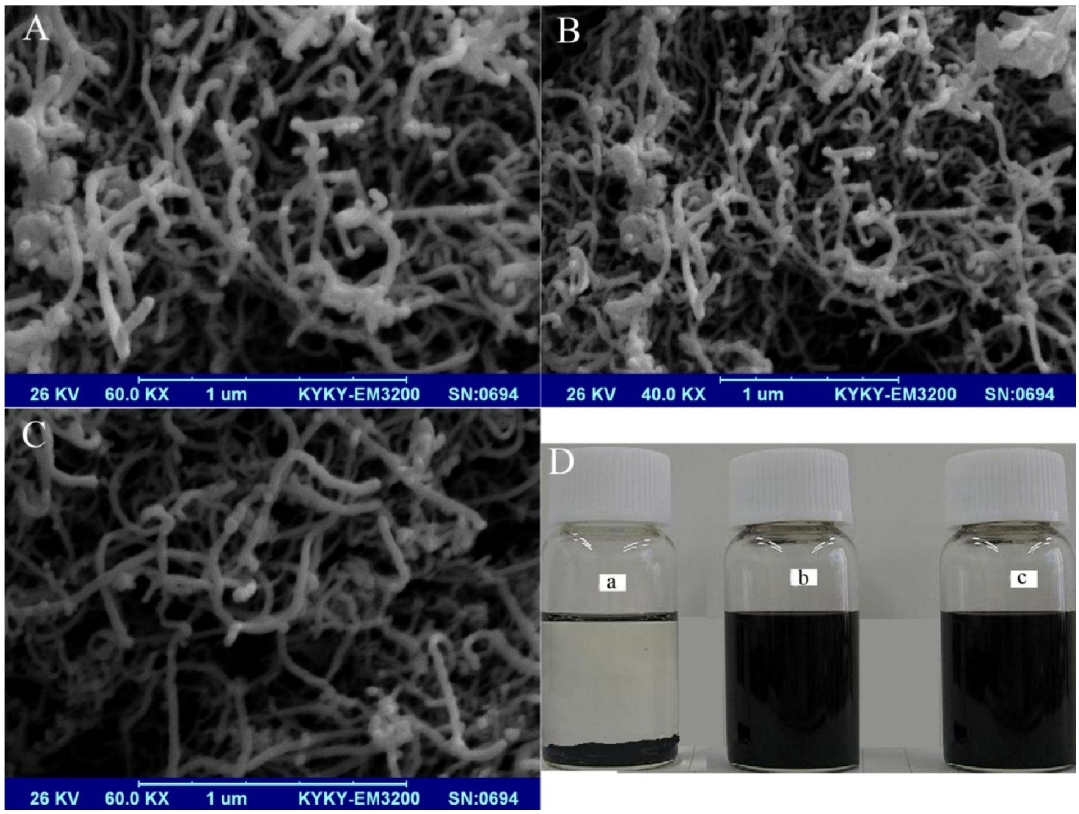



**Figure1.** SEM images of A :(**11a**), B:(**11d**), C:(**11f**) and D: dispersion of MWNT in DMSO (a) and 11a in DMSO (b) and DMF (c).

Because of the hydrophobic property of nanotubes and presence of van der Waals attraction between tubes, they show a little dispersibility in water[30]. The functionalized MWNTs have better dispersibility rather than the MWNT pristine, due to their organic functionalization.

The content of the pyrano[2,3-d] pyrimidinone attached to the MWNTs was investigated according to the comparison of mass losses of MWNT-COOH and **11a** and **11b** upon heating in nitrogen atmosphere(figure 2). The MWNT-COOH is more stable and was decomposed about 2.5% till 700 °C. After fictionalization, the TGA patterns show two stages of weight loss for the 11a and 11b. The first stage region at around 200 °C can be assigned to the loss of moisture and solvents molecules (about 3%). The second loss weight (about 21%) at region 200-700 °C are assigned to the decomposition of the pyrano[2,3-d] pyrimidinone groups mobilized on the MWNTs. The results show that the pyrano[2,3-d] pyrimidinone group grafted successfully on the surface of MWNTs.

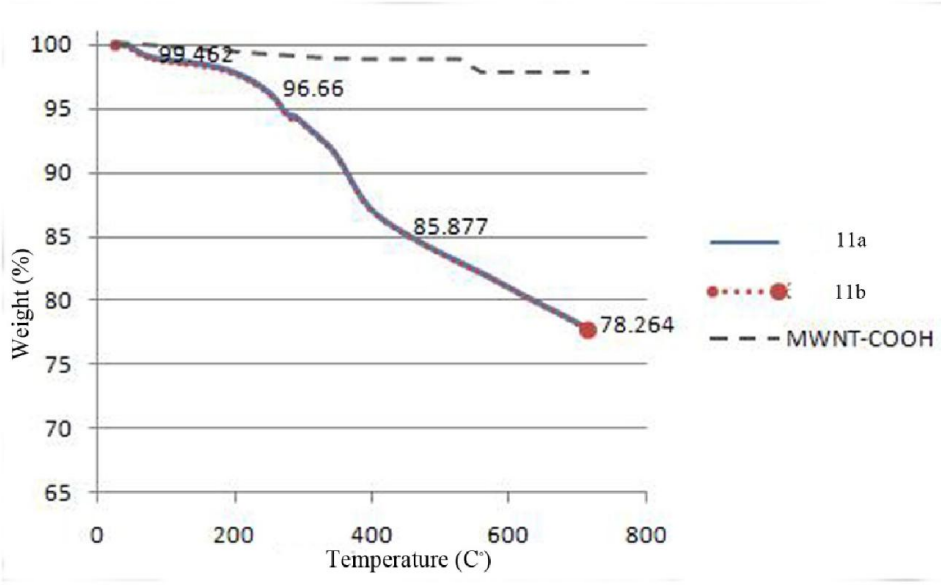



**Figure 2.** TGA curves of MWNT-COOH and modified-MWNT in the $N_2$.

## Conclusion

We have developed an easier, practically convenient, novel, ecologically safe method for the synthesis of pyrano[2,3-*d*] pyrimidinone derivatives using a green chemistry protocol. The use of DABCO as a green catalyst not only gave high yields of products, but also offered a procedure that does not use harmful organic solvents. In summary, we have introduced pyrano[2,3-*d*] pyrimidinone derivatives onto the surface of nanotubes via reaction with MWNT–COOH. Functionalization was demonstrated by their SEM images, as well as TGA and elemental analysis.

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## References

[1] G. Hawley, Condeses Chemical Dictionary, 10th ed., Nostrand Reihold (1981).

[2] R.M. Acheson, Introduction to the chemistry of heterocyclic compounds (1967).

[3] D. Brown, R. Evans, T. Batterham, The Pyrimidines Supplements, Wiley Interscience, New York (1970).

[4] D.R. Wesson, D.E. Smith, Barbiturates: Their use, misuse, and abuse, Human Sciences (1977).

[5] H. Matther, Acute Barbiturate Poisoning, Excerpta Medica, amsterdam (1971).

[6] A. Reid, M. Turnbull, *Arch. Int. Pharmacodyn. Ther.,* 211, 49 (1974).

[7] P. Prisyazhnyuk, G. Palii, Y. Volyanskii, A. Lopushanskii, E. Opanasenko, *Khim.-Farm. Zh.,* 10, 46 (1976).

[8] M. Omar, *Egypt. J. Pharm. Sci.,* 38, 281 (1997).

[9] A. Kreutzberger, *Arzneimittelforschung.,* 28, 1684 (1978).

[10] S.I. Alqasoumi, A.M. Al-Taweel, A.M. Alafeefy, E. Noaman, M.M. Ghorab, *Eur. J. Med. Chem.,* 45, 738 (2010).

[11] A. El-Gazzar, H. Hafez, G. Nawwar, *Eur. J. Med. Chem.,* 44, 1427 (2009).

[12] M.M. Hanna, *Eur. J. Med. Chem.,* 55, 12 (2012).

[13] N. Patel, A. Mehta, *Asian J. Chem.,* 13, 1385 (2001).

[14] S. Całus, E. Gondek, A. Danel, B. Jarosz, M. Pokładko, A. Kityk, *Mater. Lett.,* 61, 3292 (2007).

[15] M.H. Mosslemin, M.R. Nateghi, *Ultrason. Soochem.,* 17, 162 (2010).

[16] J. Azizian, A. Shameli, S. Balalaie, M. Mehdi Ghanbari, S. Zomorodbakhsh, M. Entezari, S. Bagheri, G. Fakhrpour, *Orient. J. Chem.,* 28, 327 (2012).

[17] J. Yu, H. Wang, *Synth. Commun.,* 35, 3133 (2005).

[18] A. Mobinikhaledi, N. Foroughifar, M.A. Bodaghi Fard, *Synth. React. Inorg. Met. Org. Nano Met. Chem.,* 40, 179 (2010).

[19] O.G. Jolodar, F. Shirini, M. Seddighi, *Chinese J. Catal.,* 38, 1245 (2017).

[20] N. Seyyedi, F. Shirini, M.S. Nikoo Langarudi, *RSC Adv.,* 6, 44630 (2016).

[21] S. Balalaie, S. Abdolmohammadi, H.R. Bijanzadeh, A.M. Amani, *Mol. Divers.,* 12, 85 (2008).

[22] A. Dandia, S.L. Gupta, S. Bhaskaran, *European Chemical Bulletin,* 2, 836 (2013).

[23] H. Kefayati, M. Valizadeh, A. Islamnezhad, *Anal. Bioanal. Electrochem.,* 6, 80 (2014).

[24] B. Sadeghi, M. Bouslik, M. Shishehbore, *J. Iran. Chem. Soc.,* 12, 1801 (2015).

[25] M. Bararjanian, S. Balalaie, B. Movassag, A. Amani, *J. Iran. Chem. Soc.,* 6, 436 (2009).

[26] J. Yu, H. Wang, *Synthetic Commun.,* 35, 3133 (2005).

[27] S. Balalaie, S. Abdolmohammadi, H.R. Bijanzadeh, A.M. Amani, *Mol Divers.,* 12, 85 (2008).

[28] T.-S. Jin, L.-B. Liu, Y. Zhao, T.-S. Li, *J. Chem. Res.,* 2005, 162 (2005).

[29] G.M. Ziarani, S. Faramarzi, S. Asadi, A. Badiei, R. Bazl, M. Amanlou, *DARU J. Pharm. Sci.,* 21, 3 (2013).

[30] C. Zhao, L. Ji, H. Liu, G. Hu, S. Zhang, M. Yang, Z. Yang, *J. Solid. State. Chem.,* 177, 4394 (2004).