Tetrahedron Letters 51 (2010) 5933–5936

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Application of cyclic-1,3-diketones in domino and multicomponent reactions: facile route to highly functionalized chromeno[2,3-*d*]pyrimidinones and diazabenzo[*b*]fluorenones under solvent-free conditions

Ram Kumar, Keshav Raghuvanshi, Rajiv K. Verma, Maya S. Singh *

Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi 221005, India

ARTICLE INFO

Article history:
Received 16 July 2010
Revised 3 September 2010
Accepted 6 September 2010
Available online 21 September 2010

Keywords:
Multicomponent reaction
Chromeno[2,3-*d*]pyrimidinones
Diazabenzo[*b*]fluorenones
$InCl_3$
P_2O_5
Solvent-free conditions

ABSTRACT

A facile and efficient protocol for the synthesis of chromeno[2,3-*d*]pyrimidinones and diazabenzo[*b*]fluorenones has been developed by one-pot three-component cyclocondensation of aldehydes, cyclic-1,3-diketones and 1,3-dimethylbarbituric acid in the presence of $InCl_3$ or P_2O_5 under solvent-free conditions.

© 2010 Elsevier Ltd. All rights reserved.

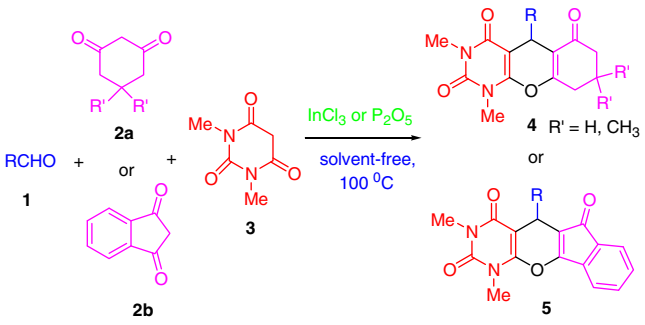
The interesting and diverse biological activities[1,2] of dihydropyrimidinones (DHPMs) have been explored through the generation of libraries of compounds via microwave, solid-phase, and fluorous-phase technologies.[2] Chromene derivatives are widely present in plants including edible vegetables and fruits,[3] and are promising compounds in the field of medicinal chemistry.[4] Stealthins isolated from *Streptomyces ciridochromogenes* as potent radical scavengers are the first known members of natural benzo[*b*]fluorenones, a recently discovered class of metabolites.[5,6] Recently, anthracene derivatives have been synthesized and screened for their antibacterial and antifungal activities.[7] Diazaanthracene derivatives[8] have been utilized as dye-forming components for copying methods, whereas polyazaanthracenes are useful precursors for preparing bioluminescent substrates and light-emitting components for organic light-emitting devices,[9] and are utilized as potential DNA intercalators.[10]

Multicomponent reactions (MCRs) being highly flexible, selective, and convergent in nature have a significant part of today's arsenal of methods in organic synthesis.[11] MCRs leading to interesting heterocyclic scaffolds are useful for the construction of diverse chemical libraries of 'drug like' molecules.[12,13] The possibility of performing chemical reactions in the absence of solvent has been receiving more attention now-a-days.[14] The examples reported[14–16] demonstrate that solvent-free reactions are generally faster giving higher selectivities and excellent yields. It is evident from the recent literature that indium trichloride[17] has invoked enormous interest as a green and potential Lewis acid catalyst for the construction of carbon–carbon and carbon–heteroatom bonds,[18] due to its air and water compatibility, good reactivity[19] and remarkable ability to suppress side reactions in acid sensitive substrates. Phosphorous pentoxide is a mild, selective, and readily biodegradable reagent, which has also been utilized widely in various organic transformations.[20–22] Recently, chromeno[2,3-*d*]pyrimidinones have been synthesized by one-pot three-component condensation of barbituric acids, aldehydes, and cyclohexane-1,3-diones in refluxing ethanol in the presence of *p*-toluenesulfonic acid.[23] However, the above method suffers from drawbacks such as longer reaction time (4–8 h) and the need for an acidic catalyst in high mole percentage. As part of our ongoing research program on the development of new protocols in heterocyclic synthesis,[24] we report herein a one-pot three-component synthesis[25] of chromeno[2,3-*d*]pyrimidinones (**4**) and 6,10-dihydro-5-oxa-6,8-diazabenzo[*b*]fluorene-7,9,11-triones (**5**) promoted by $InCl_3$ or P_2O_5 under solvent-free conditions (Scheme 1).

Initially, the three-component cyclocondensation of 4-bromobenzaldehyde (1.0 mmol), dimedone (1.0 mmol), and 1,3-dimethylbarbituric acid (1.2 mmol) as a model reaction was performed in refluxing dichloromethane in the presence of different catalysts such as CAN (30 mol %, 22 h), P_2O_5 (20 mol %, 14 h), and $InCl_3$ (10 mol %, 8 h) separately, resulting the desired product **4** in 42%, 58%, and 72% yields, respectively. Further, to optimize the reaction

* Corresponding author. Fax: +91 542 2368127.
E-mail address: mssinghbhu@yahoo.co.in (M.S. Singh).

0040-4039/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2010.09.017



Scheme 1. Coupling of aldehydes (**1**), cyclic-1,3-diketones (**2**), and 1,3-dimethylbarbituric acid (**3**) to yield **4** and **5**.

conditions, the above model reaction was carried out in the absence of solvent at 100 °C with the above respective catalysts to give 50%, 80%, and 85% yields within 25–45 min. Subsequently, we carried out another set of reactions under similar conditions taking 4-nitrobenzaldehyde (1.0 mmol), cyclohexan-1,3-dione (1.0 mmol) and 1,3-dimethylbarbituric acid (1.2 mmol) giving the desired product **4** in 52%, 83%, and 88% yields, respectively. The results show that under solvent-free condition the catalytic activities of $InCl_3$ and P_2O_5 increased significantly. Thus, $InCl_3$ was found to be a better choice than P_2O_5 and provides the desired products exclusively in good yields and high purity.

A test reaction using 4-nitrobenzaldehyde (1.0 mmol), dimedone (1.0 mmol), and 1,3-dimethylbarbituric acid (1.2 mmol) at 100 °C in the absence of solvent and catalyst was performed to establish the real effectiveness of the catalyst. It was found that only trace amount of the desired product was obtained even after 8 h of heating (Table 1, entry 1). After optimization, 10 mol % of $InCl_3$ and 20 mol % of P_2O_5 were found to be effective for the progress of the reaction. The effect of temperature was also studied and the optimum temperature of the reaction was found to be 100 °C (Table 1). The best results were obtained when the reactions were carried out with 10 mol % of $InCl_3$ or 20 mol % of P_2O_5 at 100 °C (Table 1, entry 6). In this process P_2O_5 not only acts as promoter but also as water scavenger, which plays an important role in accelerating the reactions.

To explore the generality of the reaction, we extended our study with different aromatic aldehydes and cyclic-1,3-diketones. The

Table 1
Optimization of conditions for the synthesis of **4**[a]

Entry	Temp (°C)	Loading (mol %)		Time (min)		Yield[b] (%)	
		Method A ($InCl_3$)	Method B (P_2O_5)	Method A ($InCl_3$)	Method B (P_2O_5)	Method A ($InCl_3$)	Method B (P_2O_5)
1	100	No catalyst		8 h		Trace	
2	80	5	10	70	85	62	58
3	100	5	10	45	65	75	70
4	120	5	10	40	50	76	72
5	80	10	20	50	60	74	66
6	100	10	20	25	30	92	84
7	120	10	20	25	30	90	82
8	80	15	25	40	50	78	72
9	100	15	25	25	30	92	84
10	120	15	25	25	30	90	82

[a] Reaction conditions: 4-nitrobenzaldehyde (1.0 mmol), dimedone (1.0 mmol), and 1,3-dimethylbarbituric acid (1.2 mmol).
[b] Isolated yields.

Table 2
$InCl_3$ and P_2O_5 promoted cyclocondensation of aldehydes, cyclic-1,3-diketones, and 1,3-dimethylbarbituric acid[a]

Entry	R	1,3-Diketone (**2**)	Time (min)		Yield[b] (%)	
			Method A ($InCl_3$)	Method B (P_2O_5)	Method A ($InCl_3$)	Method B (P_2O_5)
4a	*p*-F·C_6H_4	Dimedone	30	40	85	81
4b	*p*-NO_2·C_6H_4	Dimedone	25	30	92	84
4c	*m*-NO_2·C_6H_4	Dimedone	35	38	89	85
4d	*o*-NO_2·C_6H_4	Dimedone	30	40	82	78
4e	*p*-MeO·C_6H_4	Dimedone	35	45	78	74
4f	*o*-MeO·C_6H_4	Dimedone	40	50	74	72
4g	*p*-Cl·C_6H_4	Dimedone	28	36	86	82
4h	*m*-Cl·C_6H_4	Dimedone	25	37	84	75
4i	*p*-Me·C_6H_4	Dimedone	30	35	80	78
4j	*m*-OH·C_6H_4	Dimedone	35	45	78	75
4k	*p*-Br·C_6H_4	Dimedone	25	32	85	80
4l	C_6H_5	Dimedone	25	30	88	84
4m	2-OH-3-MeO·C_6H_3	Dimedone	40	60	78	73
4n	*p*-NO_2·C_6H_4	Cyclohexane-1,3-dione	25	35	88	83
4o	*p*-Me·C_6H_4	Cyclohexane-1,3-dione	35	40	75	72
4p	*p*-Br·C_6H_4	Cyclohexane-1,3-dione	28	38	82	78
4q	2,4-Cl_2·C_6H_3	Cyclohexane-1,3-dione	30	42	78	75
4r	*o*-Cl·C_6H_4	Cyclohexane-1,3-dione	35	40	78	76
4s	C_6H_5	Cyclohexane-1,3-dione	25	35	85	78
5a	*p*-Me·C_6H_4	Indane-1,3-dione	35	40	55	50
5b	*p*-NO_2·C_6H_4	Indane-1,3-dione	32	40	57	52
5c	*p*-Br·C_6H_4	Indane-1,3-dione	35	42	53	48

[a] For the experimental procedure, see Ref. 25.
[b] Yield of isolated and purified products.

results of synthesis of a series of 9-oxa-1,3-diazaanthracene-2,4,5-triones (**4**) and 5-oxa-6,8-diazabenzo[*b*]fluorene-7,9,11-triones (**5**) are summarized in Table 2. This protocol tolerates a variety of aromatic aldehydes containing both electron-withdrawing and electron-donating substituents at *ortho*-, *meta*- or *para*-positions. However, when some aliphatic aldehydes such as propionaldehyde, isobutyraldehyde, cinnamaldehyde, and cyclohexanecarboxaldehyde were used in this protocol under the above optimized conditions, it led to a mixture of products in low yields. This may be attributed to the aldol condensation as a side reaction.

In conclusion, we have developed a convenient one-pot three-component cyclocondensation reaction between aromatic aldehydes, cyclic-1,3-diketones, and 1,3-dimethylbarbituric acid for the preparation of 9-oxa-1,3-diazaanthracene-2,4,5-triones and 6,10-dihydro-5-oxa-6,8-diaza-benzo[*b*]fluorene-7,9,11-triones of potential synthetic and pharmacological interest. Solvent-free conditions, good yields of the products, and the use of simple and readily available starting materials are the main advantages of this method.

Acknowledgments

This work was carried out under the financial support from Council of Scientific and Industrial Research (Grant No. 01(2260)/08/EMR-II) and Department of Science and Technology (Grant No. SR/S1/OC-66/2009), New Delhi. R.K. is grateful to MDLLC, Michigan, USA for the financial assistance. R.K.V. thanks CSIR, New Delhi for his senior research fellowship.

References and notes

1. (a) Stadler, A.; Kappe, C. O. *J. Comb. Chem.* **2001**, *3*, 624–630; (b) Wipf, P.; Cunningham, A. *Tetrahedron Lett.* **1995**, *36*, 7819–7822; (c) Valverde, M. G.; Dallinger, D.; Kappe, C. O. *Synlett* **2001**, 741–744; (d) Rovnyak, G. C.; Atwal, K. S.; Hedberg, A.; Kimball, S. D.; Moreland, S.; Gougoutas, J. Z.; O'Reilly, B. C.; Schwartz, J.; Malley, M. F. *J. Med. Chem.* **1992**, *35*, 3254–3263; (e) Patil, A. D.; Kumar, N. V.; Kokke, W. C.; Bean, M. F.; Freyer, A. J.; De Brosse, C.; Mai, S.; Truneh, A.; Faulkner, D. J.; Carte, B.; Breen, A. L.; Hertzberg, R. P.; Johnson, R. K.; Westley, J. W.; Potts, B. C. M. *J. Org. Chem.* **1995**, *60*, 1182–1188; (f) Zorkun, I. S.; Sarac, S.; Celebi, S.; Erol, K. *Bioorg. Med. Chem.* **2006**, *14*, 8582–8589.
2. (a) Kappe, C. O. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 49–51; (b) Studer, A.; Jeger, P.; Wipf, P.; Curran, D. P. *J. Org. Chem.* **1997**, *62*, 2917–2924; (c) Barrow, J. C.; Nantermet, P. G.; Selnick, H. G.; Glass, K. L.; Rittle, K. E.; Gilbert, K. F.; Steele, T. G.; Homnick, C. F.; Freidinger, R. M.; Ransom, R. W.; Kling, P.; Reiss, D.; Broten, T. P.; Schorn, T. W.; Chang, R. S. L.; O'Malley, S. S.; Olah, T. V.; Ellis, J. D.; Barrish, A.; Kassahun, K.; Leppert, P.; Nagarathnam, D.; Forray, C. *J. Med. Chem.* **2000**, *43*, 2703–2718; (d) Kappe, C. O. *Eur. J. Med. Chem.* **2000**, *35*, 1043–1052; (e) Folkers, K.; Johnson, T. B. *J. Am. Chem. Soc.* **1933**, *55*, 3784–3791; (f) Sweet, F.; Fissekis, J. D. *J. Am. Chem. Soc.* **1973**, *95*, 8741–8749; (g) Kappe, C. O. *J. Org. Chem.* **1997**, *62*, 7201–7204; (h) Hu, E. H.; Sidler, D. R.; Dolling, U.-H. *J. Org. Chem.* **1998**, *63*, 3454–3457; (i) Vdovina, S. V.; Mamedov, V. A. *Russ. Chem. Rev.* **2008**, *77*, 1017–1053.
3. Curini, M.; Cravotto, G.; Epifano, F.; Giannone, G. *Curr. Med. Chem.* **2006**, *13*, 199–222.
4. (a) Elinson, M. N.; Dorofeev, A. S.; Feducovich, S. K.; Gorbunov, S. V.; Nasybullin, R. F.; Stepanov, N. O.; Nikishin, G. I. *Tetrahedron Lett.* **2006**, *47*, 7629–7633; (b) Sun, W.; Cama, L. J.; Birzin, E. T.; Warrier, S.; Locco, L.; Mosley, R.; Hammond, M. L.; Rohrer, S. P. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1468–1472; (c)*Coumarins: Biology, Applications and Mode of Action*; O'Kennedy, P., Thornes, R. D., Eds.; John Wiley & Sons: Chichester, U.K., 1997.
5. For recent examples of biologically active chromene derivatives, see: Borges, F.; Roleira, F.; Milhazes, N.; Santana, L.; Uriarte, E. *Curr. Med. Chem.* **2005**, *12*, 887–916.
6. (a) Tangmouo, J. G.; Meli, A. L.; Komguem, J.; Kuete, V.; Ngounou, F. N.; Lontsi, D.; Beng, V. P.; Choudhary, M. I.; Sondengam, B. L. *Tetrahedron Lett.* **2006**, *47*, 3067–3070; (b) Gore, M. P.; Gould, S. J.; Weller, D. D. *J. Org. Chem.* **1991**, *56*, 2289–2291; (c) Mohri, S.; Stefinovic, M.; Snieckus, V. *J. Org. Chem.* **1997**, *62*, 7072–7073.
7. Khafagy, M. M.; Ashraf, H. F.; Abd El-Wahab Eid, F. A.; El-Agrody, A. M. *ILFarmaco* **2002**, *57*, 715–722.
8. Kast, H.; Dunkelmann, G. U.S. Patent 3931182, 1976.
9. Textbooks: (a) *Industrial Dyes: Chemistry, Properties, Applications*; Hunger, K., Ed.; Wiley-VCH: Verlag GmbH & Co. KGaA, Weinheim, 2003; (b) Hachiya, S.; Hashizume, D.; Maki, S.; Niwa, H.; Hirano, T. *Tetrahedron Lett.* **2010**, *51*, 1401–1403.
10. Ebrahimlo, A. R. M.; Khalafy, J.; Marjani, A. P.; Prager, R. H. *ARKIVOC* **2009**, 17–30.
11. For recent reviews, see: (a) Guillena, G.; Ramon, D. J.; Yus, M. *Tetrahedron: Asymmetry* **2007**, *18*, 693–700; (b) D'Souza, D. M.; Muller, T. J. J. *Chem. Soc. Rev.* **2007**, *36*, 1095–1108; (c) Tietze, L. F.; Kinzel, T.; Brazel, C. C. *Acc. Chem. Res.* **2009**, *42*, 367–378; (d) Aliaga María, J.; Ramon Diego, J.; Yus, M. *Org. Biomol. Chem.* **2010**, *8*, 43–46; (e) Sunderhaus, J. D.; Martin, S. F. *Chem. Eur. J.* **2009**, *15*, 1300–1308; (f) Scheffelaar, R.; Paravidino, M.; Znabet, A.; Schmitz, R. F.; de Kanter, F. J. J.; Lutz, M.; Spek, A. L.; Guerra, C. F.; Bickelhaupt, F. M.; Groen, M. B.; Ruijter, E.; Orru, R. V. A. *J. Org. Chem.* **2010**, *75*, 1723–1732; (g) Marek, I. *Tetrahedron* **2005**, *61*, 11309–11519; (h)*Multicomponent Reactions*; Zhu, J., Bienaym'e, H., Eds.; Wiley-VCH: Weinheim, 2005; (i) Basso, A.; Banfi, L.; Riva, R.; Guanti, G. *J. Org. Chem.* **2005**, *70*, 575–579.
12. (a) Hulme, C.; Gore, V. *Curr. Med. Chem.* **2003**, *10*, 51–80; (b) Sunderhaus, J. D.; Dockendorff, C.; Martin, S. F. *Org. Lett.* **2007**, *9*, 4223–4226; (c) Armstrong, R. W.; Combs, A. P.; Tempest, P. A.; Brown, S. D.; Keating, T. A. *Chem. Res.* **1996**, *29*, 123–131; (d) Lieby-Muller, F.; Constantieux, T.; Jean Rodriguez, J. *J. Am. Chem. Soc.* **2005**, *127*, 17176–17177; (e) Chebanov, V. A.; Saraev, V. E.; Desenko, S. M.; Chernenko, V. N.; Knyazeva, I. V.; Groth, U.; Glasnov, T. N.; Kappe, C. O. *J. Org. Chem.* **2008**, *73*, 5110–5118.
13. (a) Dax, S. L.; McNally, J. J.; Youngman, M. A. *Curr. Med. Chem.* **1999**, *6*, 255–270; (b) Willy, B.; Muller, T. J. *Eur. J. Org. Chem.* **2008**, 4157–4168; (c) Heravi, M. M.; Baghernejad, B.; Oskooie, H. A.; Hekmatshoar, R. *Tetrahedron Lett.* **2008**, *49*, 6101–6103; (d) Dömling, A. *Comb. Chem. High Throughput Screening* **1998**, *1*, 1–22; (e) Evdokimov, N. M.; Kireev, A. S.; Yakovenko, A. A.; Antipin, M. Y.; Magedov, I. V.; Kornienko, A. *J. Org. Chem.* **2007**, *72*, 3443–3453.
14. (a) Metzger, J. O. *Angew. Chem., Int. Ed.* **1998**, *37*, 2975–2978; (b) Varma, R. S. *Green Chem.* **1999**, 43–55; (c) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025–1074; (d) Varma, R. S. *Pure Appl. Chem.* **2001**, *73*, 193–198; (e) Tanaka, K.; Toda, F. In *Solvent-free Organic Synthesis*; Wiley-VCH, GmbH, 2003; (f) DeSimone, J. M. *Science* **2002**, *297*, 799–803.
15. (a) Loh, T.-P.; Huang, J.-M.; Goh, S.-H.; Vittal, J. J. *Org. Lett.* **2000**, *2*, 1291–1294; (b) Hajipour, A. R.; Arbabian, M.; Ruoho, A. E. *J. Org. Chem.* **2002**, *67*, 8622–8624; (c) Yadav, L. D. S.; Singh, S. *Synthesis* **2003**, 63–66; (d) Lee, J. C.; Bae, Y. H. *Synlett* **2003**, 507–508; (e) Xu, Z.-B.; Lu, Y.; Guo, Z.-R. *Synlett* **2003**, 564–566.
16. (a) Azizi, N.; Saidi, M. R. *Organometallics* **2004**, *23*, 1457–1458; (b) Azizi, N.; Saidi, M. R. *Eur. J. Org. Chem.* **2003**, 4630–4633; (c) Azizi, N.; Saidi, M. R. *Org. Lett.* **2005**, *7*, 3649–3651; (d) Khan, N. H.; Agrawal, S.; Kureshy, R. I.; Abdi, S. H. R.; Singh, S.; Jasra, R. V. *J. Organomet. Chem.* **2007**, *692*, 4361–4366; (e) Khan, N. H.; Agrawal, S.; Kureshy, R. I.; Abdi, S. H. R.; Singh, S.; Suresh, E.; Jasra, R. V. *Tetrahedron Lett.* **2008**, *49*, 640–644; (f) Kureshy, R. I.; Singh, S.; Khan, N. H.; Abdi, S. H. R.; Suresh, E.; Jasra, R. V. *J. Mol. Catal. A: Chem.* **2007**, *264*, 162–169.
17. For reviews see: (a) Li, C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149–11176; (b) Sharma, S. D.; Hazarika, P.; Konwar, D. *Tetrahedron Lett.* **2008**, *49*, 2216–2220.
18. (a) Loh, T. P.; Pei, J.; Cao, G. Q. *Chem. Commun.* **1996**, 1819–1820; (b) Li, Z.; Zhang, J.; Li, C. J. *Tetrahedron Lett.* **2002**, *44*, 153–156; (c) Zhang, J.; Li, C. J. *J. Org. Chem.* **2002**, *67*, 3969–3971; (d) Babu, G.; Perumal, P. T. *Tetrahedron Lett.* **1997**, *38*, 5025–5026; (e) Loh, T. P.; Wei, L. L. *Synlett* **1998**, 975–976; (f) Ranu, B. C. *Eur. J. Org. Chem.* **2000**, 2347–2356; (g) Ranu, B. C.; Hajra, A.; Jana, U. *J. Org. Chem.* **2000**, *65*, 6270–6272.
19. Ranu, B. C.; Hajra, A.; Jana, U. *Org. Lett.* **1999**, *1*, 1141–1143.
20. (a) Eshghi, H.; Gordi, Z. *Synth. Commun.* **2003**, *33*, 2971–2978; (b) Mirjalili, B. F.; Zolfigol, M. A.; Bamoniri, A.; Amrollahi, M. A.; Hazar, A. *Phosphorus, Sulfur Silicon* **2004**, *179*, 1397–1401; (c) Eshghi, H.; Gordi, Z. *Phosphorus, Sulfur Silicon* **2005**, *180*, 619–623; (d) Massah, A. R.; Dabagh, M.; Shahidi, S.; Naghash, H. J.; Momeni, A. R.; Aliyan, H. *J. Iran. Chem. Soc.* **2009**, *6*, 405–411; (e) Nandi, G. C.; Samai, S.; Kumar, R.; Singh, M. S. *Tetrahedron Lett.* **2009**, *50*, 7220–7222; (f) Kumar, R.; Nandi, G. C.; Verma, R. K.; Singh, M. S. *Tetrahedron Lett.* **2010**, *51*, 442–445.
21. (a) Ren, R. X.; Zueva, L. D.; Ou, W. *Tetrahedron Lett.* **2001**, *42*, 8441–8443; (b) Eshghi, H.; Shafieyoon, P. *Phosphorus, Sulfur Silicon* **2004**, *179*, 2149–2152; (c) Eshghi, H.; Gordi, Z. *Phosphorus, Sulfur Silicon* **2004**, *179*, 1341–1346; (d) Hajipour, A. R.; Zarei, A.; Ruoho, A. E. *Tetrahedron Lett.* **2007**, *48*, 2881–2884.
22. (a) Hajipour, A. R.; Kooshki, B.; Ruoho, A. E. *Tetrahedron Lett.* **2005**, *46*, 5503–5506; (b) Hajipour, A. R.; Ruoho, A. E. *Tetrahedron Lett.* **2005**, *46*, 8307–8310; (c) Eshghi, H.; Rahimizadeh, M.; Saberi, S. *Chin. Chem. Lett.* **2008**, *19*, 1063–1067; (d) Zarei, A.; Hajipour, A. R.; Khazdooz, L.; Mirjalili, B. F.; Zahmatkesh, S. *J. Mol. Catal. A: Chem.* **2009**, *301*, 39–46.
23. Ghahremanzadeh, R.; Fereshtehnejad, F.; Bazgir, A. *Chem. Pharm. Bull.* **2010**, *58*, 516–520.
24. (a) Nandi, G. C.; Samai, S.; Kumar, R.; Singh, M. S. *Tetrahedron* **2009**, *65*, 7129–7134; (b) Samai, S.; Nandi, G. C.; Kumar, R.; Singh, M. S. *Tetrahedron Lett.* **2009**, *50*, 7096–7098; (c) Samai, S.; Nandi, G. C.; Singh, P.; Singh, M. S. *Tetrahedron* **2009**, *65*, 10155–10161; (d) Nandi, G. C.; Samai, S.; Singh, M. S. *Synlett* **2010**, 1133–1137; (e) Verma, R. K.; Ila, H.; Singh, M. S. *Tetrahedron* **2010**, *66*, 7389–7398; (f) Samai, S.; Nandi, G. C.; Singh, M. S. *Tetrahedron Lett.* **2010**, *51*, 5555–5558.
25. *General procedure for the synthesis of compounds* **4** *and* **5***:* To a ground mixture of aldehyde (1.0 mmol), cyclic-1,3-diketone (1.0 mmol), and 1,3-dimethylbarbituric acid (1.2 mmol), $InCl_3$ (10 mol %) or P_2O_5 (20 mol %) was added and the whole reaction mixture was heated at 100 °C for a set period of time (Table 2) till the completion of the reaction (monitored by TLC). After the completion of the reaction, water (20 mL) was added and the appeared precipitate was extracted with ethyl acetate (3 × 20 mL). The combined organic extract was washed with water followed by brine, and dried over anhydrous $MgSO_4$. The solvent was evaporated under vacuum to give the product, which was purified by column chromatography over silica gel using EtOAc–hexane (1:2) as eluent.

Data for some selected compounds: 10-(4-Fluorophenyl)-1,3,7,7-tetramethyl-6,7,8,10-tetrahydro-1H-9-oxa-1,3-diazaanthracene-2,4,5-trione (**4a**)*:* white solid, mp 177–178 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.05, 1.14 (2s, 6H, 2 × CH_3), 2.25 (q, J = 4.5 Hz, 2H, CH_2), 2.58 (s, 2H, CH_2), 3.26, 3.48 (2s, 6H, 2 × NCH_3), 4.95 (s, 1H, CH), 6.90–6.95 (m, 2H, ArH), 7.28–7.30 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.4, 28.1, 29.0, 29.1, 32.3, 40.5, 50.5, 92.0, 114.9, 115.2, 115.9, 129.7, 129.8, 138.9, 150.4, 151.1, 161.1, 161.2, 195.6. IR (KBr): ν = 2954, 1721, 1675, 1660, 1518 cm^{-1}. MS (m/z): 385 [M+1]$^+$. Anal. Calcd for $C_{21}H_{21}FN_2O_4$ (384.4): C, 65.62; H, 5.51; N, 7.29. Found: C, 65.50; H, 5.35; N, 7.46.

10-(4-Methoxyphenyl)-1,3,7,7-tetramethyl-6,7,8,10-tetrahydro-1H-9-oxa-1,3-diazaanthracene-2,4,5-trione (**4e**)*:* white solid, mp 205–207 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.99, 1.09 (2s, 6H, 2 × CH_3), 2.19 (q, J = 6.9 Hz, 2H, CH_2), 2.45 (s, 2H, CH_2), 3.39, 3.41 (2s, 6H, 2 × NCH_3), 3.73 (s, 3H, OCH_3), 4.69 (s, 1H, CH), 6.74 (d, J = 8.4 Hz, 2H, ArH), 8.32 (d, J = 8.7 Hz, 1H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.4, 28.2, 28.9, 29.3, 32.4, 33.3, 40.5, 50.5, 56.1, 90.1, 115.3, 121.9, 122.1, 128.3, 135.7, 145.1, 147.3, 150.3, 152.4, 161.2, 161.5, 194.5. IR (KBr): ν = 2923, 1699, 1634, 1623, 1567, 1501, 1475 cm^{-1}. MS (m/z): 397 [M+1]$^+$. Anal. Calcd for $C_{22}H_{24}N_2O_5$ (396.4): C, 66.65; H, 6.10; N, 7.07. Found: C, 66.39; H, 6.35; N, 7.29.

10-(4-Methylphenyl)-1,3,7,7-tetramethyl-6,7,8,10-tetrahydro-1H-9-oxa-1,3-diazaanthracene-2,4,5-trione (**4i**)*:* white solid, mp 184–186 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.06, 1.13 (2s, 6H, 2 × CH_3), 2.24 (s, 3H, $ArCH_3$), 2.25 (q, J = 4.8 Hz, 2H, CH_2), 2.57 (q, J = 2.7 Hz, 2H, CH_2), 3.24, 3.47 (2s, 6H, 2 × NCH_3), 4.83 (s, 1H, CH), 7.05 (d, J = 7.8 Hz, 2H, ArH), 7.20 (d, J = 7.8 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 27.5, 28.1, 29.0, 29.1, 32.3, 32.7, 40.5, 50.6, 92.4, 116.2, 128.0, 128.9, 136.4, 140.1, 150.4, 151.1, 160.9, 161.3, 195.6. IR (KBr): ν = 2941, 1709, 1689, 1668, 1533 cm^{-1}. MS (m/z): 381 [M+1]$^+$. Anal. Calcd for $C_{22}H_{24}N_2O_4$ (380.4): C, 69.46; H, 6.36; N, 7.36. Found: C, 69.36; H, 6.19; N, 7.49.

10-(3-Hydroxyphenyl)-1,3,7,7-tetramethyl-6,7,8,10-tetrahydro-1H-9-oxa-1,3-diazaanthracene-2,4,5-trione (**4j**)*:* white solid, mp 232–233 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.07, 1.13 (2s, 6H, 2 × CH_3), 2.26 (s, 2H, CH_2), 2.57 (q, J = 6.3 Hz, 2H, CH_2), 3.26, 3.48 (2s, 6H, 2 × NCH_3), 4.84 (s, 1H, CH), 4.97 (s, 1H, OH), 6.62 (d, J = 7.8 Hz, 2H, ArH), 6.85 (s, 1H, ArH), 7.08–7.13 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.6, 28.2, 28.9, 29.2, 32.3, 32.9, 40.5, 50.6, 92.1, 114.0, 115.8, 116.1, 119.8, 129.3, 144.5, 150.4, 151.3, 155.8, 161.1, 161.2, 196.0. IR (KBr): ν = 3493, 2943, 1711, 1692, 1671, 1529 cm^{-1}. MS (m/z): 383 [M+1]$^+$. Anal. Calcd for $C_{21}H_{22}N_2O_5$ (382.4): C, 65.96; H, 5.80; N, 7.33. Found: C, 65.72; H, 5.59; N, 7.49.

6,8-Dimethyl-10-p-tolyl-6,10-dihydro-5-oxa-6,8-diazabenzo[b]fluorene-7,9,11-trione (**5a**)*:* red solid, mp 265–267 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3H, $ArCH_3$), 2.94, 3.37 (2s, 6H, 2 × NCH_3), 4.74 (s, 1H, CH), 6.94 (d, J = 7.8 Hz, 2H, ArH), 7.10 (d, J = 7.5 Hz, 2H, ArH), 7.27–7.34 (m, 2H, ArH), 7.45–7.61 (m, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3, 31.4, 31.9, 51.3, 120.9, 122.5, 123.8, 125.7, 128.6, 129.2, 129.9, 131.0, 133.8, 134.0, 168.3, 193.4. IR (KBr): ν = 3129, 3081, 2951, 2867, 1689, 1652, 1649, 1642, 1487 cm^{-1}. MS (m/z): 387 [M+1]$^+$. Anal. Calcd for $C_{23}H_{18}N_2O_4$ (386.4): C, 71.49; H, 4.70; N, 7.25. Found: C, 71.37; H, 4.41; N, 7.13.

6,8-Dimethyl-10-(4-nitrophenyl)-6,10-dihydro-5-oxa-6,8-diaza-benzo[b]fluorene-7,9,11-trione (**5b**)*:* red solid, mp 210–212 °C (dec). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.99, 3.35 (2s, 6H, 2 × NCH_3), 4.87 (s, 1H, CH), 7.37 (d, J = 6.6 Hz, 2H, ArH), 7.64–7.81 (m, 4H, ArH), 8.17 (d, J = 8.7 Hz, 2H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 31.9, 32.7, 53.2, 121.9, 122.1, 123.2, 125.9, 129.9, 130.1, 130.6, 131.9, 134.5, 134.9, 167.9, 195.4. IR (KBr): ν = 3154, 3069, 2945, 2896, 1712, 1689, 1649, 1635, 1477 cm^{-1}. MS (m/z): 418 [M+1]$^+$. Anal. Calcd for $C_{22}H_{15}N_3O_6$ (417.3): C, 63.31; H, 3.62; N, 10.07. Found: C, 63.45; H, 3.79; N, 10.31.