Original Research Paper

JIC

Journal of Industrial Catalysis
Vol. 1, No. 2, 2024, 38-42.

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU) as a highly efficient catalyst for the production of fluorescent 3*H*-imidazo[4,5-*a*]acridine-11-carbonitriles

Mehrdad Mazrouei, Mehdi Pordel,* Abolghasem Davoodnia and S. Ali Beyramabadi

Department of Chemistry, Mashhad Branch, Islamic Azad University, Mashhad, Iran

**Corresponding author. E-mail: mehdipordel58@mshdiau.ac.ir*

Received 22 August 2024; accepted 10 October 2024

Abstract

1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), an amidine compound, is widely utilized in organic synthesis as a catalyst, complexing ligand, and non-nucleophilic base. Its applications include serving as a catalyst, a resin curing agent, and for separating fullerenes in conjunction with trimethylbenzene. On the other hand, acridine derivatives, a type of nitrogen heterocycle, are used in producing dyes and drugs. Some are efficient fluorescent chemosensors for metal ions and valuable stains for cell cycle determination. Combining acridine with the imidazole nucleus may enhance their properties. In this study, the synthesis of 3H-imidazo[4,5-a]acridine-11-carbonitriles was achieved by reacting 1-alkyl-5-nitro-1H-benzoimidazoles with 2-(4-methoxyphenyl)acetonitrile and benzyl cyanide, involving nucleophilic substitution of hydrogen. Notably, the catalytic influence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) remarkably led to the high yields of the synthesized compounds. Structural verification of the synthesized dyes was accomplished through comprehensive physical spectral and analytical data analysis.

Keywords: *DBU, Catalyst, Imidazo[4,5-a]acridine, Nucleophilic substitution of hydrogen*

1. Introduction

Fluorescent heterocyclic compounds are of significant interest due to their unique electrical and optical properties, making them valuable for various applications. These compounds serve as emitters for electroluminescence devices, and molecular probes for biochemical research, and are utilized in traditional textile and polymer fields, as well as fluorescent whitening agents and photoconducting materials [1-3].

The significance of five-membered heterocyclic imidazole derivatives is increasing due to their diverse optical applications, including their use as fluorescence compounds, dyes, and TPA materials, which involve the simultaneous absorption of two photons to excite a molecule to a higher energy state. Moreover, several commercial fluorescent brighteners for synthetic fibers contain an imidazole moiety [4-6].

Acridine derivatives, a type of tricycle nitrogen heterocycle, have been instrumental in producing dyes and valuable drugs. Certain acridine derivatives have proven to be efficient fluorescent chemosensors for recognizing transition metal ions such as Hg2+ and as emitters for luminescence studies. For instance, acridine orange (3,6-dimethylaminoacridine) serves as a valuable stain for cell cycle determination. The combination of the acridine moiety with the imidazole nucleus may further enhance their properties [7-12].

1,8-Diazabicyclo[5.4.0]undec-7-ene, commonly referred to as DBU, is an amidine compound utilized in organic synthesis as a catalyst, complexing ligand, and non-nucleophilic base., or more commonly DBU, is a chemical compound and belongs to the class of amidine compounds. It is used in organic synthesis as a catalyst, a complexing ligand, and a non-nucleophilic base. In the realm of organic chemistry, DBU is utilized as a ligand and base reagent. When serving as a base, protonation transpires at the imine nitrogen. Additionally, Lewis acids have the capacity to coordinate with the same nitrogen atom. These attributes render DBU suitable for implementation as a catalyst, for instance, as a curing agent for epoxy resins and polyurethane. It is also employed in conjunction with trimethylbenzene for the separation of fullerenes [13-15].

Imidazo[4,5-a]acridines with notable fluorescence attributes have been successfully synthesized through the reaction of 1-alkyl-5-nitro-1H-benzoimidazoles with 2-(4-methoxyphenyl)acetonitrile and benzyl cyanide. This process, which entails nucleophilic substitution of hydrogen, was catalyzed by DBU, resulting in the production of high yields of the desired products.

2- Experimental method

2.1. Materials

Methanol, N,N-Dimethylformamide (DMF), methyl iodide, benzyl chloride, ethyl bromide, n-propyl bromide, n-butyl bromide, iso-butyl bromide, 5-nitro-1H-

benzimidazole, benzyl cyanide, 2-(4-methoxyphenyl)acetonitrile and DBU were purchased from Merck. Potassium hydroxide was purchased from Sigma-Aldrich. All solvents were dried according to standard procedures. Compounds 1a–f were synthesized as in literature [16].

2.2. Equipment

Melting points were measured on an Electrothermaltype-9100 melting-point apparatus. The IR (as KBr discs) spectra were obtained on a Tensor 27 spectrometer and only noteworthy absorptions are listed. The 1H NMR (400 MHz) spectra were recorded on a Bruker Avance DRX-400 spectrometer in deuterated chloroform (CDCl3). Chemical shifts are reported in parts per million downfield from tetramethylsilane (TMS) as the internal standard; coupling constant J is given in hertz.

2.3. General procedure for the synthesis of 3a–g from 1a–f and 2a,b.

1-Alkyl-5-nitro-1H-benzimidazole 1a–f (1 mmol) and 2a,b (1 mmol) were added with stirring to a solution of DBU (1 mmol) in methanol (30 mL). The mixture was stirred at rt for 2 h. After concentration at reduced pressure, the precipitate was collected by filtration, washed with water, following with cold EtOH and acetone respectively, and then air dried to give crude 3a–g. More purification was achieved by crystallization from suitable solvent such as MeOH or EtOH.

8-Methoxy-3-methyl-3H-imidazo[4,5-a]acridine-11-carbonitrile (3a). Compound 3a was obtained as shiny yellow needles (EtOH), (85%), m.p.: 319–321 °C; IR (KBr disk): CN 2240 cm 1; 1H NMR: δ 4.03 (s, 3 H, OMe); 4.43 (s, 3 H, Me); 7.48 (dd, 1 H, H(9); J1 = 9.0 Hz, J2 = 2.2 Hz); 7.91 (d, 1 H, H(7), J = 2.2 Hz); 8.06 (d, 1 H, H(10) J = 9.5 Hz); 8.17 (s, 1 H, H(2)); 8.35 (d, 1 H, H(5) J = 9.0 Hz); 8.43 (d, 1 H, H(4), J = 9.5 Hz) ppm.

3-Ethyl-8-methoxy-3H-imidazo[4,5-a]acridine-11-carbonitrile (3b). Compound 3b was obtained as shiny yellow needles (EtOH), (79%), m.p.: 288–290 °C; IR (KBr disk): CN 2240 cm 1; 1H NMR: δ 1.62 (t, 3 H, CH2CH3, J = 7.2 Hz,); 4.03 (s, 3 H, OMe); 4.41 (q, 2 H, CH2CH3, J= 7.2 Hz); 7.50 (dd, 1 H, H(9); J1 = 9.0 Hz, J2 = 2.2 Hz); 7.90 (d, 1 H, H(7), J = 2.2 Hz); 8.08 (d, 1 H, H(10) J = 9.5 Hz); 8.19 (s, 1 H, H(2)); 8.31 (d, 1 H, H(5) J = 9.0 Hz); 8.43 (d, 1 H, H(4), J = 9.5 Hz) ppm.

8-Methoxy-3-propyl-3H-imidazo[4,5-a]acridine-11-carbonitrile (3c). Compound 3c was obtained as shiny yellow needles (MeOH), (83%), m.p.: 269–271 °C; IR (KBr disk): CN 2240 cm 1; 1H NMR: δ 1.01 (t, 3 H, CH2CH2CH3, J = 7.0 Hz); 1.89–2.01 (m, 2 H, CH2CH2CH3); 4.03 (s, 3 H, OMe); 4.32 (t, 2 H, CH2CH2CH3, J = 7.2 Hz); 7.50 (dd, 1 H, H(9); J1 = 9.0 Hz, J2 = 2.2 Hz); 7.89 (d, 1 H, H(7), J = 2.2 Hz); 8.08 (d, 1 H, H(10) J = 9.5 Hz); 8.17 (s, 1 H, H(2)); 8.33 (d, 1 H, H(5) J = 9.0 Hz); 8.42 (d, 1 H, H(4), J = 9.5 Hz) ppm.

3-Butyl-8-methoxy-3H-imidazo[4,5-a]acridine-11-carbonitrile (3d). Compound 3d was obtained as shiny yellow needles (MeOH), (82%), m.p.: 259–263 °C; IR (KBr disk): CN 2240 cm 1; 1H NMR: δ 0.98 (t, 3 H, CH2CH2CH2CH3, J = 7.0 Hz); 1.29–1.39 (m, 2 H, CH2CH2CH2CH3); 1.89–2.01 (m, 2 H, CH2CH2CH2CH3); 4.02 (s, 3 H, OMe); 4.27 (t, 2 H, CH2CH2CH2CH3, J = 7.1 Hz); 7.49 (dd, 1 H, H(9); J1 = 9.0 Hz, J2 = 2.2 Hz); 7.89 (d, 1 H, H(7), J = 2.2 Hz); 8.09 (d, 1 H, H(10) J = 9.5 Hz); 8.16 (s, 1 H, H(2)); 8.32 (d, 1 H, H(5) J = 9.0 Hz); 8.43 (d, 1 H, H(4), J = 9.5 Hz) ppm.

3-Isobutyl-8-methoxy-3H-imidazo[4,5-a]acridine-11-carbonitrile (3e). Compound 3e was obtained as shiny yellow needles (MeOH), (86%), m.p.: 262–264 °C; IR (KBr disk): CN 2240 cm 1; 1H NMR: δ 0.90 (d, 6 H, CH2CH(CH3)2, J = 6.4 Hz); 2.15– 2.19 (m, 1H, CH2CH(CH3)2); 4.32 (d, 2H, CH2CH(CH3)2, J = 7.2 Hz,); 7.48 (dd, 1 H, H(9); J1 = 9.0 Hz, J2 = 2.2 Hz); 7.90 (d, 1 H, H(7), J = 2.2 Hz); 8.08 (d, 1 H, H(10) J = 9.5 Hz); 8.14 (s, 1 H, H(2)); 8.33 (d, 1 H, H(5) J = 9.0 Hz); 8.44 (d, 1 H, H(4), J = 9.5 Hz) ppm.

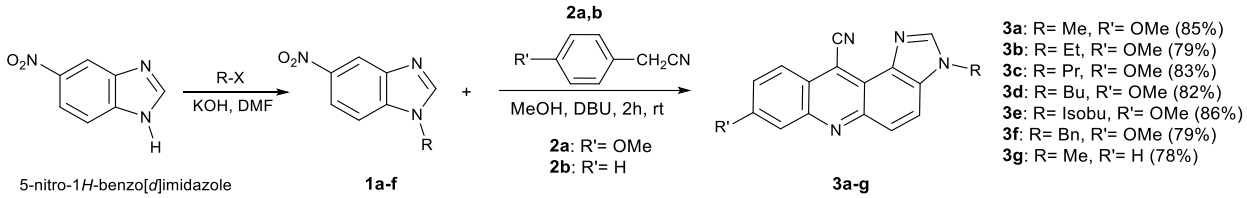
3-Benzyl-8-methoxy-3H-imidazo[4,5-a]acridin-11-carbonitrile (3f). Compound 3f was obtained as shiny yellow needles (MeOH), (79%), m.p.: 270–272 °C; IR (KBr disk): CN 2240 cm 1; 1H NMR: δ 4.03 (s, 3 H, OMe); 5.41 (s, 2 H, CH2Ph); 7.13-7.25 (m, 5 H, Ar); 7.48 (dd, 1 H, H(9); J1 = 9.0 Hz, J2 = 2.2 Hz); 7.91 (d, 1 H, H(7), J = 2.2 Hz); 8.06 (d, 1 H, H(10) J = 9.5 Hz); 8.18 (s, 1 H, H(2)); 8.34 (d, 1 H, H(5) J = 9.0 Hz); 8.44 (d, 1 H, H(4), J = 9.5 Hz) ppm.

3-Methyl-3H-imidazo[4,5-a]acridin-11-carbonitrile (3g). Compound 3g was obtained as shiny yellow needles (MeOH), (78%), m.p.: 242–245 °C; IR (KBr disk): CN 2240 cm 1; 1H NMR: δ 4.35 (s, 3 H, Me); 7.69–7.80 (m ,3 H, Ar), 8.11 (d, 1 H, J= 9.0 Hz, Ar-H), 8.20 (s, 1 H, Ar-H), 8.49 (d, 1 H, J= 9.0 Hz, Ar-H), 8.57 (dd, 1 H, J= 8.4, 1.2 Hz, Ar-H), ppm.

3- Results

3-1- 3.1. Synthesis and structures of the compounds 3a–g in the presence of DBU

Firstly, the precursor 1-alkyl-5-nitro-1H-benzoimidazoles (1a–f) were synthesized by reacting 5-nitro-1H-benzimidazole with various alkyl halides in N, N-dimethylformamide (DMF) at room temperature [16]. Subsequently, we conducted an investigation to determine the optimal reaction conditions for producing of 3H-imidazo[4,5-a]acridines by examining the reaction between 1 mmol of compounds 1a and 2a in the presence of 1 mmol of DBU under various conditions. The results



Scheme 1. Synthesis of fluorescent dyes 3a–g in the presence of DBU as basic catalyst

Table 1. Determining the best reaction conditions in treatment of **1a** with **2a** under different condition in the synthesis of 3*H*-imidazo[4,5-*a*]acridines in the presence of DBU

Entry	Solvent	Temperature	Time (h)	Yield (%)
1	THF	rt	10	15
2	THF	Reflux	10	23
3	CH_2Cl_2	rt	10	17
4	CH_2Cl_2	reflux	5	19
5	CH_3CN	rt	15	25
6	CH_3CN	reflux	10	29
7	MeOH	rt	2	85
8	MeOH	reflux	2	86
9	Solvent free	120 °C	>10	-

Table 2. Synthesis of **3a-g** by the reaction of **1a-f** with **2a,b** in the presence of DBU as an basic catalyst in MeOH

Entry	R	R´	Product	Time (h)	Yield (%)[a]	m.p °C	
						Found	Reported
1	Me	OMe	**3a**	2	85	319-321	320–322 [18]
2	Et	OMe	**3b**	2	79	288–290	288–289 [18]
3	Pr	OMe	**3c**	2	83	269-271	268–270 [18]
4	Bu	OMe	**3d**	2	82	259–263	260–262 [18]
5	Iso-but	OMe	**3e**	2	86	262–264	260–262 [18]
6	Bn	OMe	**3f**	2	79	270–272	271–273 [18]
7	Me	H	**3g**	2	78	242–245	245–247 [18]

[a]The products were characterized by comparison of their spectroscopic and physical data with authentic samples synthesized by the procedure given in the references

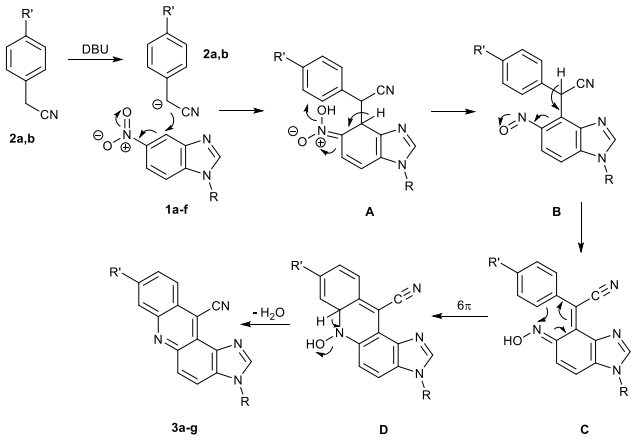
depicted in Table 1 indicate that the most favorable outcome was observed when MeOH was used as the solvent under room temperature conditions (entry 7).

With the optimized reaction conditions established, our investigation delved into the potential of the DBU for the preparation of 3H-imidazo [4,5-a]acridines using DBU (Scheme 1).

The generation of compounds 3a-g is tentatively explicated through Scheme 2. The ring closure ensues via an electrocyclic pathway, wherein intermediate C undergoes conversion to D, succeeded by dehydration, resulting in synthesizing compounds 3a-g [17–27].

The structural assignments of compounds 3a–g were based on the analytical and spectral data. For example, in the 1H NMR spectrum of 3a revealed the doublet of doublet signal at δH 7.48 ppm (J1 = 9.0 Hz and J2 = 2.2 Hz), the doublet signals at δ 7.91 ppm with meta J (2.2 Hz), δH 8.06 ppm, δH 8.35 ppm and δH 8.43 ppm and singlet signal at δH 8.17 ppm assignable to six protons of aromatic rings. Moreover, the FT-IR spectrum of 3a in KBr showed an absorption band at 2240 cm-1 corresponding to cyanide group.

Table 3 presents a comparative analysis aimed at evaluating the efficacy of the current method for the synthesis of 3H-imidazo[4,5-a]acridines concerning alternative methodology. The findings outlined in Table 3 demonstrate that employing DBU as a base instead of potassium hydroxide yields up to16% increase in the efficiency of preparing compounds 3a-g. Furthermore, this choice of base/catalyst (DBU) reduces the reaction time necessary for the preparation of these compounds. The heightened efficiency and reduced reaction time can be attributed to the superior performance of DBU as a hindered base in comparison to potassium hydroxide, primarily due to greater spatial crowding, which effectively curtails side reactions and facilitates accelerated reactions.



Scheme 2. The reaction mechanism for the formation of **3a–g.**

4-Conclusion

The 3H-imidazo [4,5-a]acridine-11-carbonitriles were successfully synthesized by reacting 1-alkyl-5-nitro-1H-benzoimidazoles with 2-(4-methoxyphenyl)acetonitrile and benzyl cyanide. This reaction, catalyzed by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), yielded high product yields. The structural confirmation of the synthesized dyes was conclusively achieved through physical spectral and analytical data.

Acknowledgments

We would like to express our sincere gratitude to the Research Office, Mashhad Branch, Islamic Azad University, Mashhad-Iran, for financial support of this work.

Conflict of Interest

The authors declare that they have no conflicts of interest.

References

1. Z. Yaneva, D. Ivanova, N. Nikolova, M.Toneva Biotechnology & Biotechnological Equipment. 36 (2022) 1.
2. S.C. Lee, S. Park, H. So, G. Lee, K.T. Kim, C. Kim. Sensors.23 (2020) 4764.
3. L.C. Lee, KK. Lo. Chemical Reviews.25 (2024) 25.
4. C. Wang, J. Fu, K. Yao, K. Xue, K. Xu, X. Pang Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 15(2018) 403.
5. Y. Dai, K. Xu, Q. Li, C. Wang, X. Liu, P. Wang. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy.15 (2016) 1.
6. A. Visscher, S. Bachmann, C. Schnegelsberg, T. Teuteberg, R.A. Mata, D. Stalke. Dalton Transactions. 45(2016) 5689.
7. H. Sajid, K. Ayub, M. Arshad, T. Mahmood. Computational and Theoretical Chemistry.1 (2019) 112509.
8. K .Anju, A. Sumita, S Gayathri, R Vasanthi, K. Rajendran.. ACS omega.18 (2019) 12357.
9. M.C. Nunes, F. dos Santos Carlos, O. Fuganti, L.A. da Silva, H.T. Ribas, S.M. Winnischofer, F.S. Nunes. Journal of Fluorescence. 30 (2020) 235.
10. F. dos Santos Carlos, L.A. da Silva, C. Zanlorenzi, F.S. Nunes. Inorganica Chimica Acta.1 (2020)119634.
11. S. Chemate, Y. Erande, D. Mohbiya, N. Sekar. RSC advances. 6(2016)84319.
12. M.Z.Baig, H. Oh, Y.A. Son. Dyes and Pigments. 1(2022)110159.
13. S.K. Boddu, N. Ur Rehman, T.K. Mohanta, A. Majhi, Green Chemistry Letters and Reviews.15 (2022)765.
14. J. Muzart. ChemistrySelect. 5(2020)11608.
15. C. Larrivée-Aboussafy, B.P. Jones, KE. Price, MA. Hardink, R.W. Mc Laughlin, B.M. Lillie, J.M. Hawkins, Vaidyanathan R. Organic Letters. 15(2010)324.

16. P. N. Preston, The Chemistry of Heterocyclic Compounds, Benzimidazoles and Cogeneric Tricyclic Compounds, John Wiley & Sons, 40(1980) 87.
17. M. J. Frisch, G. W. Trucks, H. B. Schlegel, Scuseria G E, et al. (1998) Gaussian 98, Revision A.7; Gaussian, Inc.: Pittsburgh PA
18. V. Maroofi, M. Pordel, H. Chegini, S. Ramezani. Journal of fluorescence.25 (2015)1235.
19. L.R. Daghigh, M .Pordel, A. Davoodnia, M. Jajarmi.. Medicinal Chemistry Research. 24(2015)3912.
20. H. Alipoor, M. Pordel, A. Morsali. Journal of Chemical Research.41 (2017)371.
21. H. Alipoor, M. Pordel, A. Morsali. Russian Journal of Organic Chemistry. 53(2017)53.
22. M. Faramarzi, M. Pordel, A. Morsali. Russian Journal of Organic Chemistry.56 (2020)1438.
23. M.R. Toosi, Pordel M, M.R. Bozorgmehr. Journal of Chemical Health Risks.14 (2024)159.
24. J. Mohammadi, M. Pordel, M.R. Bozorgmehr Pharmaceutical Chemistry Journal. 15(2024)1.
25. F Zonozi, S.A. Beyramabadi, M. Pordel, A. Morsali, Research on Chemical Intermediates. 43(2017)1829.
26. F. Zonozi, M. Pordel, Beyramabadi SA, Morsali A. Progress in Reaction Kinetics and Mechanism.41 (2016)365.
27. F. Zonozi, M. Pordel, Beyramabadi SA, Morsali A. Heterocyclic Letters. 8(2018)587.