Original Article: Application of Ninhydrin as an Efficient and Novel Catalyst for The Preparation of 2-Amino-4H-Pyran Derivatives

Bita Baghernejad* | **Mahsa Fiuzat**

Department of Chemistry, Payame Noor University, PO BOX 19395-4697 Tehran, Iran

Use yor device to scan and read the article online

Citation B. Baghernejad. Application of Ninhydrin as an Efficient and Novel Catalyst for The Preparation of 2-Amino-4H-Pyran Derivatives. *J. Appl. Organomet. Chem.*, **2021**; *1*(1):17-21.

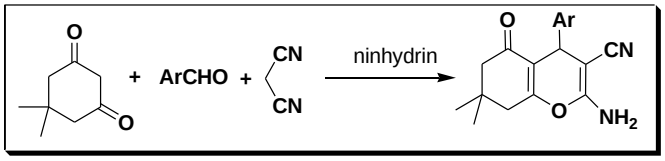
https://doi.org/10.22034/jaoc.2021.277050.1007

Article info:
Received: March 10, 2021
Accepted: March 28, 2021
Available Online: April 1, 2021
ID: **JAOC-2103-1007**
Checked for Plagiarism: **Yes**
Peer Reviewers Approved by:
Dr. SUNIL V. GAIKWAD
Editor who Approved Publication:
Professor Dr. Abdelkader Zarrouk

Keywords:
2-Amino-4H-Pyran, Multi–Component Reaction, One-Pot, Ninhydrin.

ABSTRACT

Benzopyranes and their derivatives are of interest due to their wide range of biological and medicinal properties. In this study, 2-amino-4H-pyran derivatives were obtained through a one-step multi-component reaction of aromatic aldehyde, malononitrile and dimedone in the presence of ninhydrin as a catalyst in water with high efficiency and short time.



Introduction

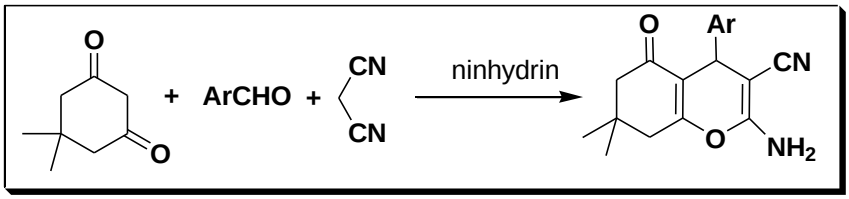
Pyran derivatives are a large group of organic compounds that have important chemical properties and are of great biological and pharmacological importance. Benzopyran is a derivative of this group that is found in nature [1]. Benzopyranes are present in the structure of various plant species and their welded rings are flat and have anti-allergic, antimicrobial, anti-influenza, anti-tumor, anti-fungal, anti-cancer properties and are used in industry in pigments [3-7]. Because these compounds are found in small quantities in natural resources and are very difficult and expensive to extract, chemists are forced to synthesize these very valuable compounds [8]. Benzene pyran cations are present in the red, purple, and blue pigments of flower petals, known as anthocyanins and glycosides.

There are many studies on the synthesis of pyranes, but most of them have shortcomings such as high reaction time, problem purification methods, low efficiency and the use of toxic

***Corresponding Author:** *Bita Baghernejad(bitabaghernejad@yahoo.com)*

solvents. Therefore, the need to invent new methods under suitable conditions for the environment for the synthesis of pyran derivatives is of great importance [9-19].

Given our strong desire to develop highly suitable methods for the preparation of heterocyclic derivatives, in this report, we introduced ninhydrin catalyst as a suitable catalyst for the preparation of 2-amino-4H-pyran under reflux conditions (Scheme 1).



1 2 3 4(a-g)

Scheme 1. synthesis of 2-amino-4H-pyran

Result and Discussion

Because of our recent interest in developing useful method for synthesis of heterocyclic compounds having biological properties, in this study, we selected ninhydrin as a useful catalyst for the synthesis of 2-amino-4H-pyrans. The reaction of malononitrile, aldehydes and dimedone in the presence of ninhydrin as a catalyst in water as a solvent produced 2-amino-4H-pyranes with high efficiency.

It should be noted that the effect of substitution type on the aromatic ring has no noticeable effect on the reaction efficiency. These compounds were obtained with high efficiency in a short time. The results are shown in Table 1.

Table1. Preparation of 2-amino-4H-Pyran derivatives using ninhydrin as a catalyst

Entry	X	Product	Yield (%)[a]	m.p.(°C)	
				Found	Reported [20]
1	H	4a	93	224-225	226-228
2	4-Cl	4b	96	206-208	207-209
3	4-NO_2	4c	97	178-179	177-178
4	3-NO_2	4d	98	210-212	208-211
5	4-CH_3	4e	93	213-215	214-216
6	4-OCH_3	4f	91	200-202	198-200
7	4-OH	4g	90	205-207	206-208
8	2-Cl	4h	95	209-211	208-210

In other words, we accomplished effects of varied solvents for the preparation of 4a. This reaction was investigated in the presence of different solvents. For instance, chloroform, dichloromethane, water, Ethanol, and solvent-free were used. It is evident from data that, the best yields were achieved in water (Table 3).

To optimize the amount of catalyst, various amounts (0.01, 0.02, 0.03, 0.05, and 0.08 g) of ninhydrin were used. The results presented in the Table 3 revealed that 0.05 g of ninhydrin had the best efficiency.

After comparing the results for the synthesis of 4a with other methods, we found that the ninhydrin catalyst performed the reaction faster and with higher efficiency (Table 4).

The proposed mechanism for the preparation of 2-amino-4H-Pyrans using ninhydrin is shown in Scheme 2.

Table 2. Preparation of 4a using various solvents by ninhydrin as a catalyst

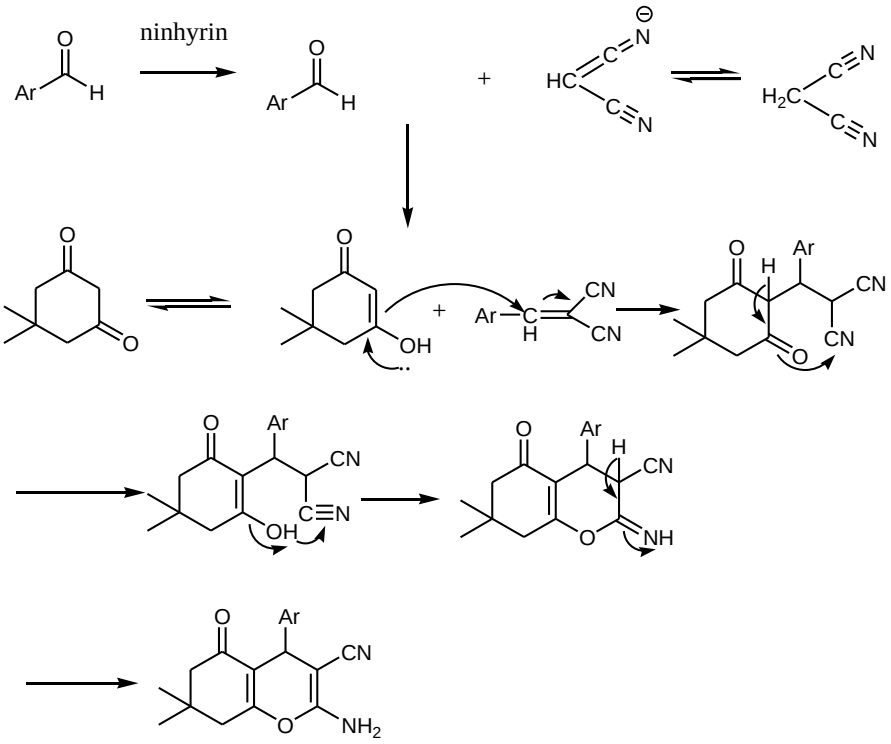
Entry	Solvent	Yield(%)[a]
1	C_2H_5OH	87
2	THF	69
3	CH_3CN	85
4	Solvent-free	90
5	$CHCl_3$	73
6	water	93

Table 3. Analogy of amount of catalysts for the preparation of 4a

Entry	Solvent	Yield (%)[a]
1	0.02g	80
2	0.03g	89
3	0.05g	93
4	0.08g	93

Table 4. Analogy of different catalysts for the preparation of 4H-Pyrans

Entry	Catalyst	Yield (%)	Time(min)	Ref
1	NaBr	60-95	15-20	[21]
2	(S)-Proline	78-98	30	[22]
3	HDMBAB	84-93	7-8(h)	[23]
4	Na_2SeO_4	80-98	3(h)	[24]
5	TMAH	79-93	2(h)	[23]
6	TBAF	73-98	30-300	[25]
7	MgO	90-96	22-33	[26]
8	ninhydrin	90-98	15-20	Present study



Scheme 2.

Conclusion

Due to the great interest in inventing new methods for the synthesis of heterocyclic compounds and the use of water as a solvent in chemical reactions, we reported here a facile and improved protocol for preparation of 4H-pyrans, from malononitrile, benzaldehydes, dimedon and ninhydrin as a catalyst in water at ambient conditions.

Among the advantages of this method in general can be mentioned the following:

- Reaction in aqueous medium is a clean, non-toxic and environmentally friendly reaction. On the other hand, water is a cheap substance with the highest abundance compared to other solvents.
- Separation of products is done by simple filtering with filter paper and the percentage of products lost during the purification process is very small.
- The yield of the reactions was high and the compounds were easily obtained by crystallization in ethanol solvent.
- The reaction is a single-phase three-component compression, so there is no need to separate the interface, thus saving time, energy and costs.

Acknowledgments

The authors are grateful to Payame Noor University for financial support

Orcid:

Bita Baghernejad: https://orcid.org/0000-0002-1733-0829
Mahsa Fiuzat: https://orcid.org/0000-0003-3492-7341

References

[1] G.R. Green, J.M. Evans, A.K. Vong, *In Comprehensive Heterocyclic Chemistry II*, *Vol 5*; Katrizky, A. R.; Rees, C. W.; Scriven, E. F. V.; Eds.; Pergamon Press: Oxford. **1995**, 469. [Google Scolar]
[2] W.O. Foye, *Principal di Chemico Farmaceutica*; Piccin: Padova, Italy, **1991**, 416. [Link], [Google Scholar]
[3] C.S. Konkoy, D.B. Fick, S.X. Cai, N.C. Lan, J.F.W. Keana, PCT Int. Appl. WO 0075123, **2000**, *Chem. Abstr.*, **2001**, *134*, 29313a. [Google Scholar]
[4] D.J. Macquarrie, *Tetrahedron Lett.*, **1998**, *39*, 4125-4128. [crossref], [Google Scholar], [Publisher]
[5] R.A. Holton, A.D. Williams, R.M. Kennedy, *J. Org. Chem.*, **1986**, *51*, 5480-5482. [crossref], [Google Scholar], [Publisher]
[6] A. Lubineau, J. Auge, *Tetrahedron Lett.*, **1992**, *33*, 8073-8074. [crossref], [Google Scholar], [Publisher]
[7] R. Maggi, R. Ballini, G. Sartori, R. Sartorio, *Tetrahedron Lett.*, **2004**, *45*, 2297-2299. [crossref], [Google Scholar], [Publisher]
[8] D. Armesto, W.M. Horspool, N. Martin, A. Ramos, C. Seaone, *J. Org. Chem.*, **1989**, *54*, 3069-3073. [crossref], [Google Scholar], [Publisher]
[9] L. Bonsignore, G. Loy, D. Secci, Calignano, Eur. *J. Med. Chem.*, **1993**, *28*, 517-520. [crossref], [Google Scholar], [Publisher]
[10] R. Bernetti, F. Mancini, C.C. Price, *J. Org. Chem.*, **1962**, *27*, 2863-2865. [crossref], [Google Scholar], [Publisher]
[11] C. Wiener, C.H. Schroeder, B. D. West, K. P. Link, *J. Org. Chem.,* **1962**, *27*, 3086-3088. [crossref], [Google Scholar], [Publisher]
[12] A.S. Prasad, J.S. Sandhu, J.N. Baruah, *J. Heterocycl. Chem.*, **1984**, *21*, 1657-1659. [crossref], [Google Scholar], [Publisher]
[13] H. Junek, H. Aigner, *Cehm. Ber.*, **1973**, *106,* 914-921. [crossref], [Google Scholar], [Publisher]
[14] I. Devi, B.S.D. Kumar, P.J. Bhuyan *Tetrahedron Lett.*, **2003**, *44*, 8307-8310. [crossref], [Google Scholar], [Publisher]
[15] P. B. Hiremath, K. Kantharaju, *Chem. Select.*, **2020**, *5*, 1896-1906. [crossref], [Google Scholar], [Publisher]
[16] S. Amirnejati, A. Nosrati, R. Peymanfar, Sh. Javanshir, *Research. Chem. Int.*, **2020**, *46*, 3683-3701. [crossref], [Google Scholar], [Publisher]
[17] F. Auria-Luna, M.C. Gimeno, R.P. Herrera, *Scientific. Report.*, **2020**, *10*, 11594. [crossref], [Google Scholar], [Publisher]
[18] M.A. Wanzheng, A. Ebadi; Jimenez, *G. Rsc Adv.*, **2019**, *9*, 12801-12812. [crossref], [Google Scholar], [Publisher]

[19] Z.J. Karimi, B. Pooladian, *Scientific. World*. Journal, **2012**, *10*, 208796. [crossref], [Google Scholar], [Publisher]
[20] S.J. Gao, Y. Guo, C. Shi, D. Lu, *Synth. Commun*., **2002**, *32*, 2137-2141. [crossref], [Google Scholar], [Publisher]
[21] I. Devi, P.J. Bhuyan, *Tetrahedron. Lett*., **2004**, *45*, 8626-8631. [crossref], [Google Scholar], [Publisher]
[22] T. Sh. Jin, A.Q. Wang, F. Shi, L. Sh. Han, L. B. Liu, T. Sh. Li, *Arkivoc*, **2006**, (*Xiv*), 78-91. [crossref], [Google Scholar], [Publisher]
[23] S. Balalaie, M. Bararjanian, A. M. Amini, B. Movassagh, *Tetrahedron Lett*., **2005**, *35*, 264-274. [crossref], [Google Scholar], [Publisher]
[24] R. Hekmatshoar, S. Majedi, Kh. Bakhtiari, *Catal. Commun*., **2007**, *9*, 308-312. [crossref], [Google Scholar], [Publisher]
[25] Sh. Gao, H. Ch. Tsai, Ch. Tseng, Ch-Fa. Yao, *Tetrahedron*., **2008**, *64*, 9143-9148. [crossref], [Google Scholar], [Publisher]
[26] M. Seifi, H. Sheibani, *Catal Lett*., **2008**, *126*, 275-282. [crossref], [Google Scholar], [Publisher]