

SILICA SUPPORTED PERCHLORIC ACID: AN EFFICIENT CATALYST FOR THE SYNTHESIS OF *CIS*-ISOQUINOLONIC ACIDS

JAISHREE L.SOMWANSHI,* N.D.SHINDE, B.A.ARBAD, MAZHAR FARUQUI

Department of Chemistry , Shri Madhavrao Patil College, Murum, 413 605, India
email : jayshri.somwanshi@rediffmail.com

Abstract

An efficient preparation of *cis*-isoquinolonic acids employing a one-pot condensation reaction of homophthalic anhydride, aromatic aldehydes and anilines using silica supported perchloric acid is described. Short reaction times, high yields with high purity, mild reaction conditions and recyclability of supported catalyst are the features of this protocol.

Keywords: *cis*-Iso quinolonic acids, One-pot, Silica supported per chloric acid.

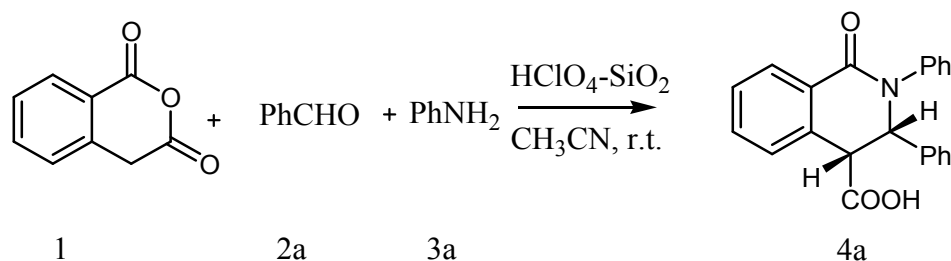
Introduction

Tetrahydroisoquinolonic acid derivatives exhibit a wide range of biological activities including psychotropic, anti- inflammatory, anti-allergetic and estrogenic behaviour.¹ Iso quinolonic acids are precursors for the total synthesis of naturally occurring phenanthridine alkaloids² and Indeno isoquinolines³. The three component condensation of homophthalic anhydride, amines, and aldehydes is a popular method for the synthesis of iso quinolonic acids. Several methods have been reported for the synthesis of isoquinolonic acids and their derivatives⁴⁻⁹. However, many of these methods often involve the use of expensive reagents, extended reaction times.

The use of heterogeneous catalysts has received great interest in organic synthesis due to economic and environmental considerations. Silica supported perchloric acid has been used as an efficient heterogeneous catalyst for many organic transformations¹⁰⁻¹⁷ because of its advantages such as less expensive, ease of preparation, moisture-insensitive and ease of handling.

Results and Discussion

We investigated the reaction of homophthalic anhydride (**1**) with benzaldehyde (**2a**) and aniline (**3a**) in the presence of silica supported perchloric acid (Scheme 1). The reaction proceeded smoothly at ambient temperature to afford the corresponding *cis*-1-oxo-2,3-diphenyl-1,2,3,4-tetrahydro-4-isoquinolinecarboxylic acid (**4a**) in high yield.



Scheme 1. Synthesis of *cis*-Isoquinolonic acid derivative (4a).

The product was obtained as a *cis*-diastereomer, which was established on the basis of the coupling constants of the hydrogens in the ^1H NMR spectra of the product. As solvent, acetonitrile appeared to give the best results. Encouraged by this result, we carried out this reaction of homophthalic anhydride (1) with a variety of aldehydes and anilines under similar conditions, furnishing the respective *cis*-isoquinolonic acids in very good yields (Table 1). The reactions were clean and the products were obtained in excellent yields and with high diastereoselectivity. In all reactions, the product was obtained as a *cis*-diastereomer. All the products were characterized by ^1H NMR and IR spectroscopy, and mass spectrometry. Enhanced reaction rates, excellent yields, and high *cis*-selectivity are the features observed in this protocol.

Experimental

Melting points were recorded on Buchi R-535 apparatus. IR spectra were recorded on a Perkin-Elmer FT-IR 240-c spectrophotometer using KBr disk. ^1H -NMR Spectra were recorded on Gemini-200 spectrometer in CDCl_3 using TMS as internal standard. Mass spectra were recorded on a Finnigan MAT 1020 mass spectrometer operating at 70 eV.

Preparation of perchloric acid adsorbed on silica gel ($\text{HClO}_4\text{-SiO}_2$):

The preparation of silica supported perchloric acid was carried out following a reported procedure¹⁸.

General procedure for the synthesis of *cis*-1-oxo-2,3-diphenyl-1,2,3,4-tetrahydro-4-isoquinolinecarboxylic acid(4a): A mixture of homophthalic anhydride (1 mmol), benzaldehyde (1 mmol), aniline (1 mmol) and $\text{HClO}_4\text{-SiO}_2$ (100 mg, 0.05 mmol) in acetonitrile (5ml) was stirred for an appropriate time and monitored by TLC. After completion of the reaction, the solvent was evaporated under reduced pressure. Then, Ethyl acetate was added to the reaction mixture, and the resulting mixture was filtered to recover the catalyst. The Ethyl acetate filtrate layer was concentrated. The crude product was passed through a short pad of silica gel using diethyl ether and pentane (1:1) as eluent to obtain pure *cis*-isoquinolonic acids in 79–90% yields. All the pure products were identified by their spectroscopy data.

Spectral data for selected compounds

1-Oxo-2,3-diphenyl-1,2,3,4-tetrahydro-4-isoquinolinecarboxylic acid (4a) : White solid, m.p. 196-198 °C (lit⁷-198°C); IR (KBr) ν : 3035, 1723, 1635, 1496, 1223, 1025, 771, 698 cm^{-1} . ^1H NMR (CDCl_3) δ : 4.86 (d, 1H, J = 6.0 Hz), 5.41 (d, 1H, J = 6.0 Hz), 7.10 (m, 8H), 7.39 (m, 3H), 7.71 (d, 1H, J = 8.0 Hz), 8.19 (dd, 1H, J = 2.1, 8.0 Hz). MASS (ESI-MS): m/z 344 $[\text{M}+\text{H}]^+$ 366 $[\text{M}+\text{Na}]^+$.

(3*S*,4*R*)-2-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)-1-oxo-1,2,3,4-tetrahydroisoquinoline-4-carboxylic acid (4f) : White solid, mp 120 °C ¹H NMR (CDCl₃) δ : 3.60(s,3H) 3.78(s,3H),4.76 (d, 1H, *J*=6.0 Hz), 5.34(d, 1H, *J*=6.0 Hz), 6.50-6.68 (m, 3H),7.12-7.34(m,3H),7.40-7.58(m,2H),7.65-7.80(m,2H) 8.15 (dd, 1H, *J*= 8.0 Hz) MASS (ESI-MS) : *m/z* 438 [M+H]⁺.

3-(4-methoxyphenyl)-1-oxo-2-phenethyl-1,2,3,4-tetrahydro-4-isoquinoline-carboxylic acid (4i) : White solid, mp 162-165°C (lit⁷-166°C). IR (KBr) ν : 2936,1739,1614,1570,1256,1175,1028,749. ¹H NMR (CDCl₃) δ : 2.80-3.10 (m, , 3H), 3.72 (s, 3H), 4.10-4.25 (m,1H), 4.38 (d, 1H, *J*=6.0 Hz) 4.74 (d, 1H, *J*=6.0 Hz), 6.64 (d, 2H, *J*=8.0 Hz), 6.90 (d,2H, *J*= 8.0 Hz), 7.15-7.65 (m,8 H), 8.16 (dd, 1H, *J*= 2.0, 8.0 Hz). MASS (ESI-MS) : *m/z* 402 [M+H]⁺ 424 [M+Na]⁺.

Conclusion

In summary, It was shown that silica supported perchloric acid can be used as an efficient heterogeneous catalyst for the one-pot condensation reaction between aldehydes, amines, and homophthalic anhydride to afford *cis*-Isoquinolonic acids. The present method offers significant advantages such as mild reaction conditions, high conversions, high selectivity, simple work-up, environmentally benign, recyclability of supported catalyst and excellent yields.

Acknowledgements

Authors Jaishree L.Somwanshi and N.D.Shinde are thankful to UGC for providing funding.

References

1. a) Johnson, J. V.; Rauckman, B. S.; Baccanari, P. D.; Roth, B. J. *Med.Chem.* 32, 1942 (1989). b) Gray, N. M.; Dappen, M. S.; Cheng, B. K.; Cordi, A. A.; Biesterfeldt, J. P.; Hood, W. F.; Monahan, J. B. *J.Med.Chem.* 34, 1283 (1991).
2. a) Cushman, M.; Chen, J.K.; *J.Org.Chem.* 52, 1517 (1987). b) Fodor, L.; Szabo, J.; Bernath, G.; Sohar, P. *J.Heterocyclic.Chem.* 26, 33 (1989). c) Cushman, M.; Abbaspour, A.; Gupta, Y. P. *J.Am.Chem.Soc.* 105, 2873 (1983).
3. Cushman, M.; Chen, L. G. *J.Org.Chem.* 43, 286 (1978).
4. Cushman, M.; Madaj, E. J. *J.Org.Chem.* 52, 907 (1987).
5. Yu, N.; Bourel, L.; Deprez, B.; Gesquiere, J. C. *Tetrahedron Lett.* 39, 829 (1998).
6. Yu, N.; Poulain, R.; Gesquiere, J. C. *Synlett* 355 (2000).
7. Yadav, J. S.; Reddy, B. V. S.; Saritha Raj, K.; Prasad, A. R. *Tetrahedron* 59,1805 (2003).
8. Azizian, J.; Mohammadi, A. A.; Karimi, A. R.; Mohammadizadeh, M. R. *J.Org. Chem.* 70, 350 (2005).
9. Vara, Y.; Bello, T.; Aldaba, E.; Arrieta, A.; Pizarro, J. L.; Arriortua, M. I.; Lopez, X.; Cossio, F. P. *Org.Lett.* 10, 4759 (2008).
10. a) Chakraborti, A. K.; Gulhane, R. *Chem.Commun.* 1896 (2003). b) Shaterian, H. R.; Yarahmadi, H.; Ghashang, M. *Tetrahedron* 64, 1263 (2008).
11. a) Agarwal, A.; Vankar, Y.D. *Carbohydrate Res.* 340 1661 (2005). b) Agarwal, A.; Rani, S.; Vankar, Y.D. *J.Org.Chem.* 69, 6137 (2004).
12. Khan, A.T.; Ghosh, S.; Choudhury, L.H. *Eur.J.Org.Chem.* 2226 (2006).
13. Chakraborti, A.K.; Chankeshwara, S.V. *Org.Biomol.Chem.* 4, 2769 (2006).
14. Mandal, P. K.; Misra, A. K. *Lett.Org.Chem.* 3, 848 (2006).

15. Khan, A. T.; Ghosh, S.; Choudhury, L. H. *Eur.J.Org.Chem.* 9, 2226 (2006).
16. Khatik, G. L.; Sharma, G.; Kumar, R.; Chakraborti, A. K. *Tetrahedron.* 63, 1200 (2007).
17. Kamble, V. T.; Jamode, V. S.; Joshi, N. S.; Biradara, A. V.; Deshmukh, R. Y. *Tetrahedron Lett.* 47, 5573 (2006).
18. Shaterian, H. R.; Yarahmadi, H.; Ghashang, M. *Tetrahedron.* 64, 1263 (2008).

Received on February 25,2013.

Table 1. Silica supported perchloric acid promoted synthesis of *cis*-Isoquinolonic acids.

S.No.	R ₁ (-CHO)	R ₂ (-NH ₂)	product	time (h)	yield(%)
A	Ph	Ph	4a	7.0	79
B	Ph	C ₆ H ₅ CH ₂	4b	6.1	84
C	2-Me C ₆ H ₄	4-MeO C ₆ H ₄	4c	6.0	90
D	Ph	4-Me C ₆ H ₄	4d	6.4	81
E	4-MeO C ₆ H ₄	4-Me C ₆ H ₄	4e	6.2	87
F	3,4-(MeO) ₂ C ₆ H ₄	4-Cl C ₆ H ₄	4f	6.0	85
G	Ph	4-Cl C ₆ H ₄	4g	6.2	80
H	Ph	4-MeO C ₆ H ₄	4h	6.3	83
I	4-MeO C ₆ H ₄	C ₆ H ₅ CH ₂ CH ₂	4i	6.0	90
J	4-Cl C ₆ H ₄	4-Me C ₆ H ₄	4l	6.0	80
K	4-OMe C ₆ H ₄	C ₆ H ₅ CH ₂	4m	6.2	88
L	3,4-(MeO) ₂ C ₆ H ₄	Ph	4n	6.4	87
M	C ₄ H ₃ S	Ph	4o	5.5	85
N	4-NO ₂ C ₆ H ₄	4-Me C ₆ H ₄	4p	7.5	74