

Synthesis of Poly-Substituted Quinolines via Friedländer Hetero-Annulation Reaction Using Silica-Supported P₂O₅ under Solvent-Free Conditions

Hasaninejad, Alireza*[†]

Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr, I.R. IRAN

Zare, Abdolkarim*[†]

Department of Chemistry, Payame Noor University (PNU), Tehran, I.R. IRAN

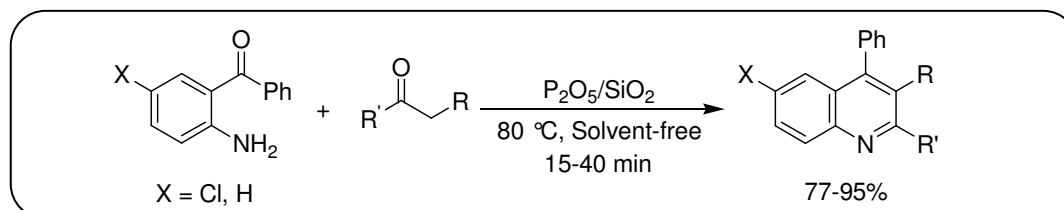
Zolfigol, Mohammad Ali

Faculty of Chemistry, Bu-Ali Sina University, Hamedan, I.R. IRAN

Abdeshah, Marzieh; Ghaderi, Arash; Nami-Ana, Fatemeh

Department of Chemistry, Faculty of Sciences, Persian Gulf University, Bushehr, I.R. IRAN

ABSTRACT: A highly efficient, simple and green solvent-free protocol for the preparation of poly-substituted quinolines via Friedländer hetero-annulation reaction between 2-aminoaryl ketones and carbonyl compounds in the presence of silica-supported P₂O₅ (P₂O₅ / SiO₂) is described. In this method, the title compounds are obtained in high to excellent yields and in short reaction times.



KEY WORDS: Quinoline, Friedländer hetero-annulation, P₂O₅/SiO₂, Solvent-free, Green chemistry.

INTRODUCTION

Quinoline derivatives are of importance as they have various biological and pharmaceutical activities such as antimalarial, antibacterial, anti-inflammatory, anti-asthmatic,

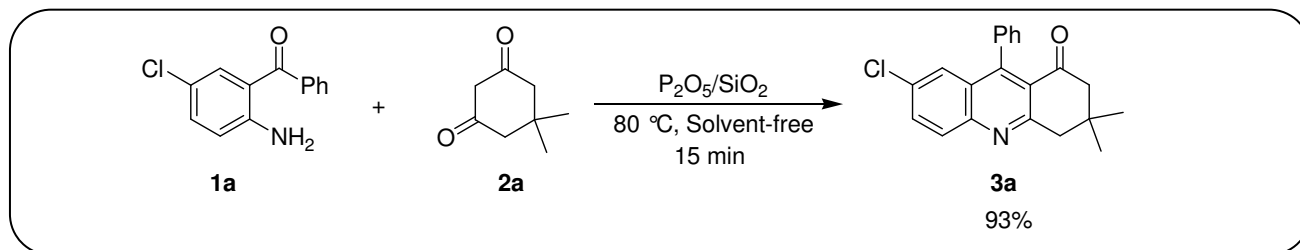
anti-hypertensive, and tyrosine kinase inhibiting properties [1-4]. In addition, poly-substituted quinolines can achieve hierarchical self-assembly into a variety of

* To whom correspondence should be addressed.

+ E-mail: ahasaninejad@yahoo.com ; abdolkarimzare@yahoo.com

1021-9986/11/1/73

9/\$/2.90



Scheme 1: Friedländer synthesis of poly-substituted quinolines.

meso and nano structures with enhanced photonic and electronic properties [5-7]. Therefore, development of new efficient protocols for the synthesis of quinoline derivatives is of interest in both medicinal chemistry and synthetic organic chemistry. Some methods such as Skraup, Doebner-Von Miller, Pfitzinger, Conrad-Limpach and Combes procedures have been reported for the preparation of quinolines [1,3,8-12]; nevertheless, Friedländer hetero-annulation is still one of the most simple and straightforward approaches for the preparation of poly-substituted quinolines [13]. Friedländer reaction is acid or base-catalyzed condensation of 2-aminoaryl ketones with carbonyl compounds containing a reactive α -methylene group followed by cyclodehydration [14 - 32]. This reaction is generally carried out by refluxing an aqueous or alcoholic solution of the reactants in the presence of a base at high temperature [14,15]. Other catalysts which have been reported for the synthesis of quinolines via Friedländer reaction include protic and Lewis acids such as $\text{HClO}_4/\text{SiO}_2$ [16], $\text{NaHSO}_4/\text{SiO}_2$ [17], amberlyst-15 [18], trifluoroacetic acid [19], concentrated HCl [20], cellulose sulfuric acid [21], sulfamic acid [22], $\text{Zr}(\text{HSO}_4)_4$ [23], $\text{Y}(\text{OTf})_3$ [24], zirconium tetrakis(dodecyl sulfate) [25], NaAuCl_4 [26,27], $\text{Ag}_3\text{POW}_{12}\text{O}_{40}$ [28], $\text{Bi}(\text{OTf})_3$ [29], $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ [30], I_2 [31], and neodymium nitrate [32]. However, most of the reported protocols for synthesis of quinolines have some disadvantages including long reaction times, low product yields and use of hazardous and expensive catalysts. Moreover, this reaction is usually carried out in harmful organic solvents such as acetonitrile, THF, DMF and DMSO; therefore, workup of the reaction mixture is not only cumbersome but also the green aspect of the reaction is annihilated by using these solvents specially DMF. Consequently, search for finding a simple, green, rapid, inexpensive and efficient procedure for the preparation of these important heterocycles is in demand.

Reactions on solid-supports under solvent-free conditions are currently the subject of considerable attention for synthetic chemists to develop eco-friendly techniques because these heterogeneous organic reactions have many advantages, such as ease of handling, low corrosion, minimum execution time, environmentally safe disposal and waste minimization by developing cleaner synthetic routes [33-51]. Consequently, it is important to note that the combination of heterogeneous catalysis with the use of solvent-free conditions represent a suitable way toward the so-called ideal synthesis.

Phosphorus pentoxide supported on silica gel ($\text{P}_2\text{O}_5/\text{SiO}_2$) is an inexpensive, green, and heterogeneous catalytic system which has been used in several organic transformations, such as the synthesis of bis(indolyl)methanes [50], synthesis of *N*-sulfonyl imines [51], oxime preparation [52], conversion of aldehydes to acylals [53], selective deprotection of acylals [54], oxidation of sulfides to sulfoxides [55], acetalization of carbonylic compounds [56], nitration of aromatic compounds [57], esterification [58], Fries rearrangement [59], Schmidt reaction [60], direct sulfonylation of aromatic rings [61], and conversion of aldehydes to nitriles [62]. In this paper, we report an efficient one-pot synthesis of various substituted quinolines via Friedländer hetero-annulation between 2-aminoaryl ketones and different carbonyl compounds in the presence of catalytic amounts of $\text{P}_2\text{O}_5/\text{SiO}_2$ under solvent free conditions at 80°C (Scheme 1).

EXPERIMENTAL SECTION

All chemicals were purchased from Merck or Fluka chemical companies. Silica gel 60, 0.063-0.200 mm (70-230 mesh ASTM) was used as the support. ^1H and ^{13}C NMR spectra were recorded at 90 and 22.5 MHz, respectively (δ in ppm). Microanalyses were performed on a Perkin-Elmer 240-B microanalyzer. Melting points were recorded on a Stuart Scientific apparatus SMP3 (UK) in open capillary tubes.

Table 1: Effect of amount of P_2O_5/SiO_2 and temperature on the reaction of 2-amino-5-chlorobenzophenone (2 mmol) with dimedone (3 mmol).

| Entry | Amount of catalyst (g) | Temperature (°C) | Time (min) | Yield (%) ^a |
|-------|------------------------|------------------|------------|------------------------|
| 1 | 0.2 | 80 | 50 | 71 |
| 2 | 0.4 | 80 | 15 | 93 |
| 3 | 0.6 | 80 | 15 | 93 |
| 4 | 0.4 | 40 | 150 | 47 |
| 5 | 0.4 | 60 | 50 | 85 |
| 6 | 0.4 | 70 | 35 | 90 |
| 7 | 0.4 | 90 | 15 | 93 |

a) Isolated yield

Table 2: Comparative the hetero-annulation reaction between 2-amino-5-chlorobenzophenone and dimedone using P_2O_5/SiO_2 in solution conditions versus the solvent-free method.

| Entry | Solvent | Temperature (°C) | Time (min) | Yield (%) ^a |
|-------|--------------|------------------|------------|------------------------|
| 1 | Solvent-free | 80 | 15 | 93 |
| 2 | EtOH | Reflux | 300 | 81 |
| 3 | CH_2Cl_2 | Reflux | 480 | 40 |
| 4 | $CHCl_3$ | Reflux | 300 | 52 |
| 5 | CH_3CN | Reflux | 300 | 76 |
| 6 | THF | Reflux | 300 | 64 |

a) Isolated yield.

Preparation of P_2O_5/SiO_2 Catalytic System

A mixture of SiO_2 (1.4 g) and P_2O_5 (0.6 g) was ground vigorously to give P_2O_5/SiO_2 catalytic system (30% w/w) as a white powder (2 g) [50,51].

General Procedure for the Preparation of Quinoline Derivatives

To a mixture of 2-aminoaryl ketone (2 mmol) and carbonyl compound (3 mmol) in a 10 mL round-bottomed flask connected to a reflux condenser was added P_2O_5/SiO_2 (0.4 g). The resulting mixture was stirred in an oil-bath (80 °C) for the appropriate time (Table 3). After completion of the reaction, as monitored by TLC, the reaction mixture was cooled to room temperature and EtOAc (40 mL) was added to it, stirred for 3 min and filtered. The solvent was evaporated and the crude product was purified by column chromatography on silica gel eluted with EtOAc-*n*-hexane (1:9).

Some Selected Physical and Spectral Data of the Products

7-Chloro -3,3- dimethyl -9- phenyl -3,4- dihydroacridin-1(2H)-one (3a)

Yellow solid, m.p. 211-212 °C (Lit. [19] m.p. 208-210 °C). ¹H NMR ($CDCl_3$): δ 1.15 (s, 6H), 2.56 (s, 2H), 3.25 (s, 2H), 7.21-7.95 (m, 8H). ¹³C NMR ($CDCl_3$): δ 28.3, 32.2, 48.3, 54.2, 123.3, 126.7, 127.9, 128.1, 128.3, 130.3, 132.4, 136.8, 147.4, 150.0, 161.4, 197.5. Anal. calcd. for $C_{21}H_{18}ClNO$: C, 75.11; H, 5.40; N, 4.17. Found: C, 75.36; H, 5.26; N, 4.35.

(6- Chloro -2- methyl -4- phenylquinolin -3-yl) (phenyl) methanone (3d)

White solid, m.p. 217-218 °C (Lit. [31] m.p. 217 °C). ¹H NMR ($CDCl_3$): δ 2.62 (s, 3H), 7.25-8.03 (m, 13H). ¹³C NMR ($CDCl_3$): δ 23.9, 124.9, 126.1, 128.2, 128.5, 129.2, 129.9, 130.6, 130.9, 132.4, 133.6, 134.2, 136.9, 144.7,

Table 3: The solvent-free synthesis of poly-substituted quinolines via Friedländer hetero-annulation between 2-aminoaryl ketones and carbonyl compounds using P_2O_5/SiO_2 at 80 °C.

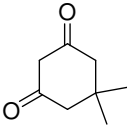
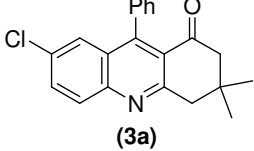
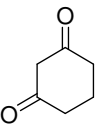
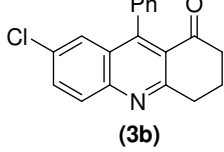
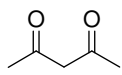
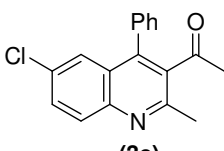
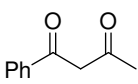
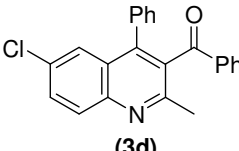
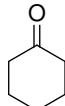
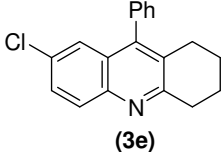

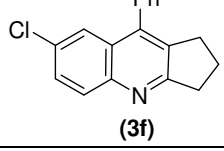
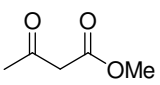
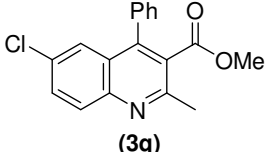
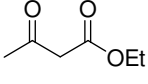
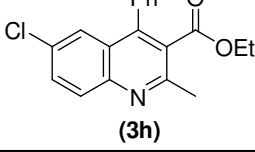
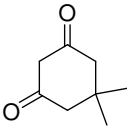
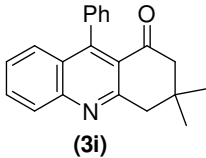
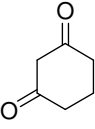
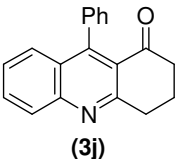
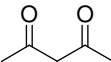
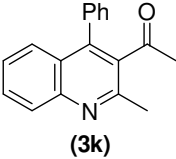
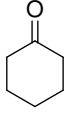
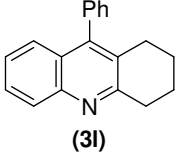
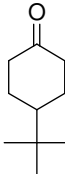
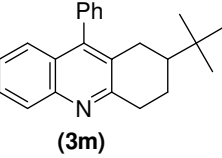
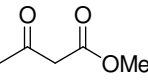
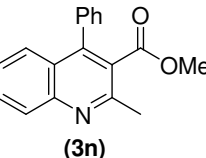
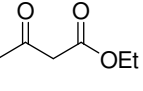
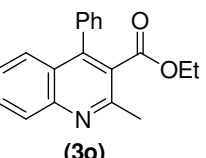
| Entry | Carbonyl Compound | Product ^a | Time (min) | Yield (%) ^b | M.p. °C (Lit.) |
|-------|---|--|------------|------------------------|---------------------------|
| 1 |  |  (3a) | 15 | 93 | 211-212 (208-210) [19] |
| 2 |  |  (3b) | 15 | 95 | 187-189 (185-189) [19] |
| 3 |  |  (3c) | 15 | 93 | 156-157 (152-153) [21] |
| 4 |  |  (3d) | 40 | 77 | 217-218 (217) [31] |
| 5 |  |  (3e) | 20 | 87 | 165-166 (165) [31] |
| 6 |  |  (3f) | 20 | 86 | 99-101 (104-105) [21] |
| 7 |  |  (3g) | 20 | 93 | 136-137 (135) [31] |
| 8 |  |  (3h) | 20 | 91 | 101-102 (101) [31] |

Table 3: Continued

| Entry | Carbonyl Compound | Product ^a | Time (min) | Yield (%) ^b | M.p. °C (Lit.) |
|-------|---|--|------------|------------------------|---------------------------|
| 9 |  |  (3i) | 35 | 94 | 192-193 (191-192) [19] |
| 10 |  |  (3j) | 30 | 91 | 158-159 (156-158) [19] |
| 11 |  |  (3k) | 15 | 88 | 109-110 (112-113) [21] |
| 12 |  |  (3l) | 20 | 85 | 143-145 (139) [17] |
| 13 |  |  (3m) | 25 | 87 | 134-136 (132-133) [30] |
| 14 |  |  (3n) | 30 | 91 | 106-107 (107) [25] |
| 15 |  |  (3o) | 30 | 88 | 100-102 (96) [17] |

148.3, 155.1, 197.2. Anal. calcd. for $C_{23}H_{16}ClNO$: C, 77.20; H, 4.51; N, 3.97. Found: C, 77.41; H, 4.39; N, 4.11.

Ethyl 2-methyl-4-phenylquinoline-3-carboxylate (3o)

Yellow solid, m.p. 100-102 °C (Lit. [17] m.p. 96 °C). 1H NMR ($CDCl_3$): δ 0.86 (t, 3H, $J = 7.7$ Hz), 2.71 (s, 3H), 3.93 (q, 2H, $J = 7.7$ Hz), 7.35-7.95 (m, 9H). ^{13}C NMR ($CDCl_3$): δ 13.5, 23.4, 61.2, 125.1, 126.4, 127.4, 128.4, 129.2, 130.3, 135.5, 146.6, 147.1, 154.4, 168.0. Anal. calcd. for $C_{19}H_{17}NO_2$: C, 78.33; H, 5.88; N, 4.81. Found: C, 78.16; H, 5.97; N, 4.69.

RESULTS AND DISCUSSION

We have previously used solid-supported catalysts in several organic transformations [35-40,50,51,63,64]. One of these green catalytic systems is P_2O_5/SiO_2 that it is easily prepared by mixing of P_2O_5 and SiO_2 , and grounding them. We have successfully applied this catalyst for the preparation of bis(indolyl)methanes [50], and N-sulfonyl imines [51]. Considering these subjects and also the unique properties of P_2O_5/SiO_2 , we decided to extend application of this catalyst in organic synthesis. Herein, we found that P_2O_5/SiO_2 can efficiently catalyze Friedländer hetero-annulation between 2-aminoaryl ketones and carbonyl compounds to give quinoline derivatives. At first, the condensation of 2-amino-5-chlorobenzophenone (1a) (2 mmol) with dimedone (2a) (3 mmol) was examined in the presence of different amounts of P_2O_5/SiO_2 (30% w/w) at range of 40-90 °C under solvent-free conditions in order to optimize the reaction conditions with respect to the amount of the catalyst and temperature (Scheme 1). As Table 1 indicates, reasonable results were obtained when the reaction was performed using 0.4 g of the catalyst at 80 °C.

In another set of experiments, efficiency and capacity of the solvent-free procedure in comparison with solution conditions were studied. For this purpose, a mixture of 2-amino-5-chlorobenzophenone (2 mmol), dimedone (3 mmol) and P_2O_5/SiO_2 (0.4 g) was stirred in some solvents (10 mL) at 80 °C or under reflux conditions (Table 2). As it can be seen in Table 2, the solvent-free method is more efficient.

To assess the generality and scope of the method, the reaction was examined with different carbonyl compounds and 2-aminoaryl ketones. As it is shown in table 3, reactions of 2-amino-5-chlorobenzophenone or

2-aminobenzophenone with various kinds of carbonyl compounds including cyclic and acyclic β -diketones, aliphatic and aromatic β -diketones, ketones and β -ketoesters proceeded efficiently and the desired products were obtained in high to excellent yields and in short reaction times. Thus, the method is highly efficient and general. Moreover, in most of the entries, 2-amino-5-chlorobenzophenone in comparison with 2-aminobenzophenone afforded the corresponding quinolines in shorter reaction times.

CONCLUSIONS

In summary, we have developed a new method for the synthesis of poly-substituted quinolines via Friedländer hetero-annulation reaction between 2-aminoaryl ketones and carbonyl compounds. The advantages of this method are the efficiency, generality, high yields, short reaction times, low cost, cleaner reaction profile, simplicity, ease of preparation of the catalyst, ease of product isolation, and compliance with the green chemistry protocols.

Acknowledgements

The authors thank Persian Gulf University and Payame Noor University (PNU) Research Councils for the financial support of this work.

Received : Aug. 4, 2009 ; Accepted : Nov. 24, 2010

REFERENCES

- [1] Jones G., "Comprehensive Heterocyclic Chemistry II", Katritzky, A.R., Rees, C.W. and Scriven, E.F.V. (Eds.), Pergamon: New York, Pyridines and Their Benzoderivatives Synthesis, **5** (1996).
- [2] Yates F.S., "Comprehensive Heterocyclic Chemistry", Boulton, A.J. and McKillop, A. (Eds.), Pergamon Press, New York, The Structure Reaction Synthesis and uses of Heterocyclic Compounds, **2** (1984).
- [3] Jones G., "The Chemistry of Heterocyclic Compounds", Weissberger, A. and Taylor, E.C. (Eds.), John Wiley and Sons, Chichester, **32** (1977).
- [4] Bilker O., Lindo V., Panico M., Etien, A.E., Paxton T., Dell A., Rogers M., Sinden R.E., Morris H.R., Identification of Xanthurenic Acid as the Putative Inducer of Malaria Development in the Mosquito, *Nature*, **392**, p. 289 (1998).
- [5] Aggarwal A.K., Jenekhe S.A., New Conjugated Polyanthrazolines Containing Thiophene Moieties in the Main Chain *Macromolecules*, **24**, p. 6806 (1991).

- [6] Jenekhe S.A., Lu L., Alam M.M., New Conjugated Polymers with Donor-Acceptor Architectures: Synthesis and Photophysics of Carbazole-Quinoline and Phenothiazine-Quinoline Copolymers and Oligomers Exhibiting Large Intramolecular Charge Transfer, *Macromolecules*, **34**, p. 7315 (2001).
- [7] Zhang X., Shetty A.S., Jenekhe S.A., Electroluminescence of Multicomponent Conjugated Polymers. 1. Roles of Polymer/Polymer Interfaces in Emission Enhancement and Voltage-Tunable Multicolor Emission in Semiconducting Polymer/Polymer Heterojunctions, *Macromolecules*, **33**, p. 2069 (2000).
- [8] Cho C.S., Oh B.H., Kim T.J., Shim S.C., Synthesis of Quinolines via Ruthenium-Catalysed Amine Exchange Reaction Between Anilines and Trialkylamines, *J. Chem. Soc., Chem. Commun.*, **1885**, and references cited therein (2000).
- [9] Jiang B., Si Y.C., Zn(II)-Mediated Alkynylation-Cyclization of *O*-Trifluoroacetyl Anilines: One-Pot Synthesis of 4-Trifluoromethyl-Substituted Quinoline Derivatives, *J. Org. Chem.*, **67**, p. 9449 (2002).
- [10] Mansake R.H., Kulka M., The Skraup Synthesis of Quinolines, *Org. React.*, **7**, p. 59 (1953).
- [11] Linderman R.J., Kirolos, S.K., Regioselective Synthesis of Trifluoromethyl Substituted Quinolines from Trifluoroacetyl Acetylenes *Tetrahedron Lett.*, **31**, p. 2689 (1990).
- [12] Theclitou M.E., Robinson L.A., Novel Facile Synthesis of 2,2,4 Substituted 1,2-Dihydroquinolines via a Modified Skraup Reaction, *Tetrahedron Lett.*, **43**, p. 3907 (2002).
- [13] Friedländer P., Ueber *O*-Amidobemaldehyd, *Chem. Ber.*, **15**, p. 2572 (1882).
- [14] Cheng C.C., Yan S., The Friedlander Synthesis of Quinolines, *Org. React.*, **28**, p. 37 (1982).
- [15] Gladiali S., Chelucci G., Mudadu M.S., Gastaut M.A., Thummel R.P., Friedländer Synthesis of Chiral Alkyl-Substituted 1,10-Phenanthrolines, *J. Org. Chem.*, **66**, p. 400 (2001).
- [16] Narasimhulu M., Reddy T.S., Mahesh K.C., Prabhakar P., Rao C.B., Venkateswarlu Y., Silica Supported Perchloric Acid: A Mild and Highly Efficient Heterogeneous Catalyst for the Synthesis of Poly-Substituted Quinolines via Friedlander Hetero-Annulation, *J. Mol. Catal. A: Chem.*, **266**, p. 114 (2007).
- [17] Desai U.V., Mitragotri S.D., Thopate T.S., Pore D.M., Wadgaonkar P.P., A Highly Efficient Synthesis of Trisubstituted Quinolines Using Sodium Hydrogensulfate on Silica Gel as a Reusable Catalyst, *ARKIVOC*, **xv**, 198 (2006).
- [18] Das B., Damodar K., Chowdhury N., Kumar R.A., Application of Heterogeneous Solid Acid Catalysts for Friedlander Synthesis of Quinolines, *J. Mol. Catal. A: Chem.*, **274**, p. 148 (2007).
- [19] Shaabani A., Soleimani E., Badri, Z., Trifluoroacetic Acid as an Efficient Catalyst for the Synthesis of Quinoline, *Synth. Commun.*, **37**, p. 631 (2007).
- [20] Muscia G.C., Bollini M., Carnevale J.P., Bruno A.M., Asis S.E., Microwave-Assisted Friedländer Synthesis of Quinolines Derivatives as Potential Antiparasitic Agents, *Tetrahedron Lett.*, **47**, p. 8811 (2006).
- [21] Shaabani A., Rahmati A., Badri Z., Sulfonated Cellulose and Starch: New Biodegradable and Renewable Solid Acid Catalysts for Efficient Synthesis of Quinolines, *Catal. Commun.*, **13** (2008).
- [22] Yadav J.S., Rao P.P., Sreenu D., Rao R.S., Kumar V.N., Nagaiah K., Prasad A.R., Sulfamic Acid: an Efficient, Cost-Effective and Recyclable Solid Acid Catalyst for the Friedlander Quinoline Synthesis, *Tetrahedron Lett.*, **46**, p. 7249 (2005).
- [23] Zolfigol M.A., Salehi P., Ghaderi A., Shiri M., A Catalytic and Green Procedure for Friedlander Quinoline Synthesis in Aqueous Media, *Catal. Commun.*, 1214 (2007).
- [24] De S.K., Gibbs R.A., A Mild and Efficient One-Step Synthesis of Quinolines, *Tetrahedron Lett.*, **46**, p. 1647 (2005).
- [25] Zolfigol M.A., Salehi P., Ghaderi A., Shir, M., Tanbakouchian Z., An Eco-Friendly Procedure for the Synthesis of Polysubstituted Quinolines Under Aqueous Media, *J. Mol. Catal. A: Chem.*, **259**, p. 253 (2006).
- [26] Atechian S., Nock N., Norcross R.D., Ratni H., Thomas A.W., Verron J., Masciadri R., New Vistas in Quinoline Synthesis, *Tetrahedron*, **63**, p. 2811 (2007).
- [27] Arcadi A., Chiarini M., Giuseppe S.D., Marinelli F., A New Green Approach to the Friedlander Synthesis of Quinolines, *Synlett*, 203 (2003).
- [28] Yadav J.S., Reddy B.V.S., Sreedhar P., Srinivasa R.R., Nagaiah K., Silver Phosphotungstate: A Novel

- and Recyclable Heteropoly Acid for Friedländer Quinoline Synthesis, *Synthesis*, 2381 (2004).
- [29] Yadav J.S., Reddy B.V.S., Premalatha K., Bi(OTf)₃-Catalyzed Friedlander Hetero-Annulation: A Rapid Synthesis of 2,3,4-Trisubstituted Quinolines, *Synlett*, 963 (2004).
- [30] Bose D.S., Kumar R.K., An Efficient, High Yielding Protocol for the Synthesis of Functionalized Quinolines via the Tandem Addition/Annulation Reaction of *O*-Aminoaryl Ketones with *A*-Methylene Ketones, *Tetrahedron Lett.*, **47**, p. 813 (2006).
- [31] Zolfigol M.A., Salehi P., Ghaderi A., Shiri M., Iodine Catalyzed Friedlander Quinoline Synthesis Under Solvent-Free Conditions, *J. Chin. Chem. Soc.*, **54**, p. 267 (2007).
- [32] Varala R., Enugala R., Adapa S.R., Efficient and Rapid Friedlander Synthesis of Functionalized Quinolines Catalyzed by Neodymium(III) Nitrate Hexahydrate, *Synthesis*, 3825 (2006).
- [33] Clark J.H., Rhodes C.N., "Clean Synthesis Using Porous Inorganic Solid Catalysts and Supported Reagents", 1st ed., Royal Society of Chemistry, UK (2000).
- [34] Kybett A.P., Sherrington D.C., "Supported Catalysts and Their Applications", 1st ed., Royal Society of Chemistry, UK (2001).
- [35] Zare A., Hasaninejad A., Beyzavi M.H., Moosavi Zare A.R., Khalafi-Nezhad A., Asadi F., Baramaki L., Jomhori-Angali S., Ghaleh-Golabi R., KF/Al₂O₃ as a Highly Efficient, Green, Heterogeneous, and Reusable Catalytic System for the Solvent-Free Synthesis of Carboacyclic Nucleosides via Michael Addition reaction, *Synth. Commun.*, **39**, p. 139 (2009).
- [36] Zare A., Hasaninejad A., Moosavi-Zare A.R., Beyzavi M.H., Khalafi-Nezhad A., Pishahang N., Parsaee Z., Mahdavinassab P., Hayati N., KF/Al₂O₃ as a Highly Efficient Reagent for the Synthesis of *N*-Aryl Derivatives of Pyrimidine and Purine Nucleobases, *ARKIVOC*, **xvi**, 178 (2008).
- [37] Zare A., Hasaninejad A., Shekouhy M., Moosavi Zare A.R., A Green Solventless Protocol for the Synthesis of *N*-Sulfonylimines in the Presence of Silica Sulfuric Acid as an Efficient, Heterogeneous and Reusable Catalyst, *Org. Prep. Proced. Int.*, **40**, p. 457 (2008).
- [38] Khalafi-Nezhad A., Zare A., Parhami A., Soltani Rad M.N., Nejabat G.R., Highly Regioselective *N*-Alkylation of Benzotriazole Under Solvent-Free Conditions, *J. Iran. Chem. Soc.*, **4**, 271 (2007).
- [39] Hasaninejad A., Zare A., Sharghi H., Shekouhy M., Khalifeh R., Salimi Beni A., Moosavi Zare A.R., A Solvent-Free Protocol for Facile Condensation of Indoles with Carbonyl Compounds using Silica Chloride as a New, Highly Efficient, and Mild Catalyst, *Can. J. Chem.*, **85**, p. 416 (2007).
- [40] Khalafi-Nezhad A., Parhami A., Soltani Rad M.N., Zolfigol M.A., Zare A., A Catalytic Method for Chemoselective Detritylation of 5'-Tritylated Nucleosides Under Mild and Heterogeneous Conditions Using Silica Sulfuric Acid as a Recyclable Catalyst, *Tetrahedron Lett.*, **48**, p. 5219 (2007).
- [41] Alinezhad H., Tajbakhsh M., Soleimani R., Selective Oxidation of Benzylic and Allylic Alcohols with NaOCl/Silica Gel System, *J. Iran. Chem. Soc.*, **6**, p. 288 (2009).
- [42] Niknam K., Saberi D., Sadegheyan M., Deris A., Silica-Bonded S-Sulfonic Acid: an Efficient and Recyclable Solid Acid Catalyst for the Synthesis of 4,40-(arylmethylene) bis(1H-pyrazol-5-Ols), *Tetrahedron Lett.*, **51**, p. 692 (2010).
- [43] Khalilzadeh M.A., Hosseini A., Tajbakhsh M., Mohannazadeh F., LiAlH₄/Silica Chloride as a New Chemoselective System for Reduction of Carbonyl Compounds and Phosphine Oxides, *J. Iran. Chem. Soc.*, **5**, p. 699 (2008).
- [44] Zolfigol M.A., Salehi P., Shiria M., Rastegar T.F., Ghaderi A., Silica Sulfuric Acid as an Efficient Catalyst for the Friedländer Quinoline Synthesis from Simple Ketones and *Ortho*-Aminoaryl Ketones Under Microwave Irradiation, *J. Iran. Chem. Soc.*, **5**, p. 490 (2008).
- [45] Niknam K., Saberi D., Nouri Sefat M., Silica-Bonded S-Sulfonic Acid as a Recyclable Catalyst for Chemoselective Synthesis of 1,1-Diacetates, *Tetrahedron Lett.*, **50**, p. 4058 (2009).
- [46] Mohammadpoor-Baltork I., Moghadam M., Tangestaninejad S., Mirkhani V., Zolfigol M.A., Hojati S.F., Silica Sulfuric Acid Catalyzed Synthesis of Benzoxazoles, Benzimidazoles and Oxazolo[4,5-*b*] Pyridines under Heterogeneous and Solvent-Free Conditions, *J. Iran. Chem. Soc.*, **5**, p. S65 (2008).

- [47] Terauchi T., Machida S., Komba S., A New Method for Cleavage of Silicon-Carbon Linkers on Glass Plate Supports with Applications to Solid-Phase Syntheses on Silica Resins, *Tetrahedron Lett.*, **51**, p. 1497 (2010).
- [48] Niknam K., Saberi D., Silica-Bonded N-Propyl Sulfamic Acid as an Efficient Catalyst for the Formylation and Acetylation of Alcohols and Amines under Heterogeneous Conditions, *Tetrahedron Lett.*, **50**, p. 5210 (2009).
- [49] Mohammadpoor-Baltork I., Zolfigol M.A., Abdollahi-Alibeik M., Novel and Chemoselective Dehydrogenation of 2-Substituted Imidazolines with Potassium Permanganate Supported on Silica Gel, *Tetrahedron Lett.*, **45**, p. 8687 (2004).
- [50] Hasaninejad A., Zare A., Sharghi H., Niknam K., Shekouhy M., P_2O_5/SiO_2 as an Efficient, Mild, and Heterogeneous Catalytic System for the Condensation of Indoles with Carbonyl Compounds under Solvent-Free Conditions *ARKIVOC*, **xiv**, 39 (2007).
- [51] Hasaninejad A., Zare A., Sharghi H., Shekouhy M., P_2O_5/SiO_2 an Efficient, Green and Heterogeneous Catalytic System for the Solvent-Free Synthesis of N-Sulfonyl Imines, *ARKIVOC*, **xi**, p. 64 (2008).
- [52] Eshghi H., Gordi Z., P_2O_5/SiO_2 as an Efficient Reagent for the Preparation of Z-Aldoximes under Solvent-Free Conditions, *Phosphorus, Sulfur, and Silicon*, **180**, p. 1553 (2005).
- [53] Mirjalili M., Zolfigol M., Bamoniri A., An Efficient Conversion of Aldehydes to Their Corresponding Acylals with P_2O_5/SiO_2 under Mild Condition, *Phosphorus, Sulfur, and Silicon*, **179**, p. 19 (2004).
- [54] Eshghi H., Shafieyoon P., P_2O_5/SiO_2 as an Efficient Reagent for Selective Deprotection of 1,1-Diacetates Under Solvent-Free Conditions, *J. Chin. Chem. Soc.*, **52**, p. 155 (2005).
- [55] Hajipour A., Kooshki R.B., Ruoho A.E., Nitric Acid in the Presence of Supported P_2O_5 on Silica Gel: an Efficient and Novel Reagent for Oxidation of Sulfides to the Corresponding Sulfoxides, *Tetrahedron Lett.*, **46**, p. 5503 (2005).
- [56] Mirjalili B., Zolfigol M., Bamoniri A., Amrollahi M., Hazar, A. An Efficient Procedure for Acetalization of Carbonyl Compounds with P_2O_5/SiO_2 , *Phosphorus Sulfur, and Silicon*, **179**, p. 1397 (2004).
- [57] Hajipour A.R., Ruoho A.E., Nitric Acid in the Presence of P_2O_5 Supported on Silica Gel: a Useful Reagent for Nitration of Aromatic Compounds under Solvent-Free Conditions, *Tetrahedron Lett.*, **46**, p. 8307 (2005).
- [58] Eshghi H., Rafei M., Karimi M.H., P_2O_5/SiO_2 as an Efficient Reagent for Esterification of Phenols in Dry media, *Synth. Commun.*, **31**, p. 771 (2001).
- [59] Eshghi H., Rafie Gordi M.Z., Bohloli M., Improvement of Selectivity in the Fries Rearrangement and Direct Acylation Reactions by Means of P_2O_5/SiO_2 Under Microwave Irradiation in Solvent-Free Media, *J. Chem. Res.*, 763 (2003).
- [60] Eshghi H., Hassankhani A., P_2O_5/SiO_2 -Catalyzed One-Pot Synthesis of Amides from Ketones via Schmidt Reaction under Microwave Irradiation in Dry media, *Synth. Commun.*, **36**, p. 2211 (2006).
- [61] Hajipour A.R., Zarei A., Khazdooz L., Pourmousavi S.A., Mirjalili B.F., Ruoho A.E., Direct Sulfonylation of Aromatic Rings with Aryl or Alkyl Sulfonic Acid Using Supported P_2O_5/Al_2O_3 , *Phosphorus, Sulfur, and Silicon*, **180**, p. 2029 (2005).
- [62] Eshghi H., Gordi Z., Microwave-Assisted Efficient One-Pot Synthesis of Nitriles from Aldehydes in the Presence of P_2O_5/SiO_2 in Solvent-Free Media, *Phosphorus, Sulfur, and Silicon*, **180**, p. 619 (2005).
- [63] Hasaninejad Niknam A.K., Zare A., Farsimadan E., Shekouhy M., Silphox [$POCl_3 \cdot n(SiO_2)_n$] as a New, Efficient, and Heterogeneous Reagent for the Synthesis of Benzimidazole Derivatives Under Microwave Irradiation, *Phosphorus, Sulfur, and Silicon*, **184**, p. 147 (2009).
- [64] Khalafi-Nezhad A., Zare A., Parhami R., Soltani Rad M.N., Nejabat G.R., Microwave-Assisted N-Nitroarylation of Some Pyrimidine and Purine Nucleobases, *Can. J. Chem.*, **84**, p. 979 (2006).