Indian Journal of Chemistry
Vol. 61, December 2022, pp. 1303-1308
DOI: 10.56042/ijc.v61i12.69445

Ag nanoparticle promoted synthesis of 1,8-dioxo-decahydroacridines at room temperature

Akbar Shirazi, Seyed Mohammad, Vahdat Seyed Meysam* & Baghbanian
Department of Chemistry, Ayatollah Amoli Branch, Islamic Azad University, Amol, Iran
*E-mail: vahdat_mohammad@yahoo.com

Received 11 July 2021; accepted (revised) 18 November 2022

The three component condensation reaction of aldehydes with dimedone and ammonium acetate or anilines happened in the presence of Ag nanoparticles as a heterogeneous catalyst at room temperature in ethanol.Ag nanoparticles can suitably be handled and removed from the reaction mixture, generating the experimental process simple and green.The significant features of this method are suitable conversions, cleaner reaction profiles and short reaction time. The catalyst is recycled and reused for five successive times without loss of structure and significant activity.

Keywords: Ag nanoparticles, 1,8-Dioxo-decahydroacridines, Ethanol solvent, Heterogeneous catalyst, Three component reaction

The use of solid heterogeneous catalysts has extended substantial attention both in academia and industrial investigation owing to their distinctive properties for example improved reactivity as well as recyclability of the catalyst, straightforward workup, selectivity and the environmentally friendly reaction conditions[1,2].

Nanoscience and nanotechnology has developed one of the most explored fields. Because of the probability to influence substance at atomic level, nanotechnology lets to control detailed properties to achieve different materials. Materials which size is shrank to the nanoscale often display novel and individual properties, remarkable for academia research and valuable from scientific viewpoint[3-5]. Silver nanoparticles are often applied for uses in photo-catalysis[6-8]. Meanwhile further noble metals for example Rh, Pt, Pd and Au are very expensive, Ag nanoparticles may attend as a much more cost-efficient solution. Furthermore, Ag nanoparticles dispersed on metal oxide supports are of attention since they are appropriate catalysts for numerous uses.[9,10]

Multicomponent reactions have engrossed much attention and have been applied to produce highly functionalized and complex molecules in a single synthetic process. It is an advanced approach for synthetic organic chemists to generate combinatorial libraries of varied organic molecules which are pharmacologically significant and it has afforded effective main skeletons in present drug discovery. Furthermore, the benefits of MCRs are structural variety, high selectivity, high atom-economy and simpler process[11].

1,8-Dioxo-decahydroacridine derivatives are functionalized 1,4-dihydropyridines[12]. It is well acknowledged that 1,8-dioxo-decahydroacridines have a broad variety of biological uses display antitumor properties[13] but carcinogenic activity has moreover been acknowledged[14]. Because of its planar structure, 1,8-dioxo-decahydroacridines chromophore tag at times has superb DNA binding properties. The synthesis of 1,8-dioxo-decahydroacridine compounds[15] as potential bis-intercalating agents has been widely investigated. These compounds are currently applied for the treatment of platelet anti-aggregator activity, cardiovascular diseases counting hypertension[16,17], diabetes[18,19], Alzheimer's disease[20] and tumors[21]. Also, these compounds can be applied as dyes.[22,23] Several approaches are improved for the synthesis of 1,8-dioxo-decahydroacridines by using numerous catalysts such as sulfonated organic heteropoly acid salts[24], [2-MPyH]OTf[25], Cu(II) Schiff base[26], $\{[HMIM]C(CN)_3\}$[27], *p*-dodecylbenezenesulfonic acid,[28] ceric ammonium nitrate[29] and Brønsted acidic imidazolium salts containing perfluoroalkyl tails[12].

In continuation of our work on the multicomponent synthesis of organic compounds[30,31], we here report the synthesis of 1,8-dioxo-decahydroacridines by using Ag nanoparticles as a benign and facile catalyst (2 mol%) in the three component condensation reaction between aldehydes, dimedone and ammonium acetate or anilines in ethanol solvent at room temperature (Scheme 1).

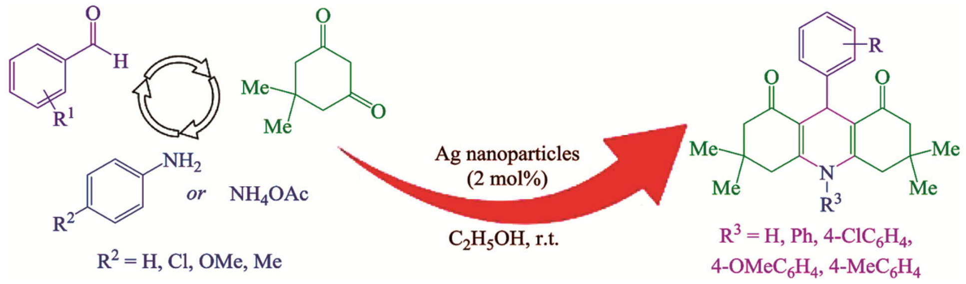
Experimental Details

General methods

Ag nanoparticles were purchased from commercial center. All chemicals were acquired from Merck or Fluka Chemical Companies. The ^{1}H NMR (400 MHz) spectra were run on a Bruker DRX-400 MHz spectrometer, δ in parts per million (ppm) corresponding to TMS as internal standard by using $CDCl_3$ and DMSO-d_6 as solvent. Melting points were recorded on a Thermo Scientific apparatus in open capillary tubes and all are uncorrected.FT-IR spectra were recoreded on FT-IR Bruker (WQF-510) spectrometer.

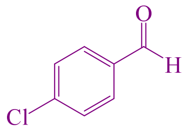
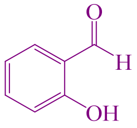
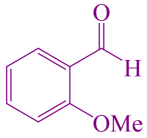
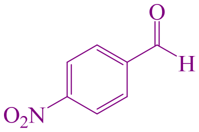
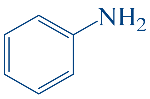
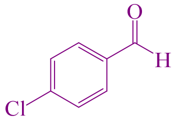
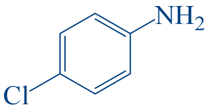
General procedure for theAg nanoparticles catalyzed synthesis of 1,8-dioxo-decahydroacridines

A mixture of aldehydes (1 mmol), dimedone (2 mmol; 0.280 g), ammonium acetate (1 mmol; 0.077 g) or anilines (1 mmol) and Ag nanoparticles (2 mol%) was magnetically stirred in ethanol (2 mL) as a solvent at room temperature for the specified time (Table 1). After the TLC shows the disappearance of starting materials, the hot ethanol (10 mL) was added and the soluble crude product was filtered to separate the Ag nanoparticles catalyst. The filtrate was concentrated under vacuum at 80°C and the crude product was purified by crystallization in ethanol to give pure 1,8-



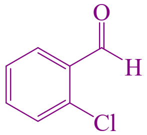
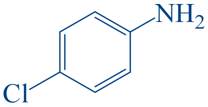
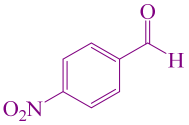
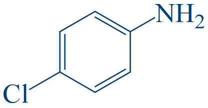
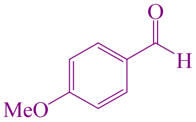
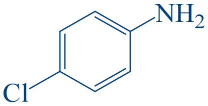
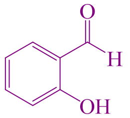
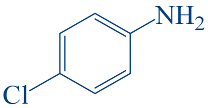
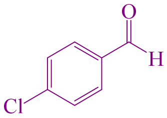
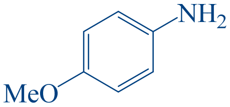
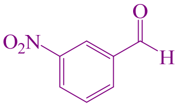
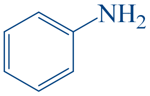
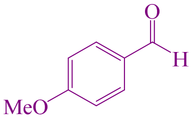
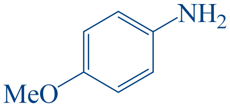
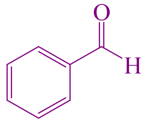
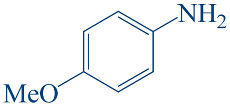
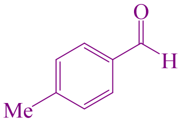
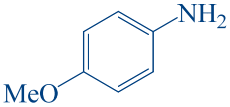
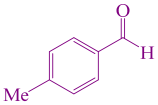
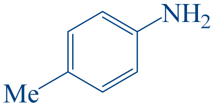
Scheme 1 — Synthesis of 1,8-dioxo-decahydroacridines by using Ag nanoparticles as a benign and facile catalyst

Table 1 — Ag nanoparticles catalyzed synthesis of 1,8-dioxo-decahydroacridines.[a]

Entry	Aldehyde	Amine	Time (min)	Yield (%)[b]	M.p. (°C)
1		NH_4OAc	60	91	289-294
2		NH_4OAc	40	92	293-297
3		NH_4OAc	30	93	293-295
4			5	96	183-190
5			20	93	290-292

(*Contd.*)

Table 1 — Ag nanoparticles catalyzed synthesis of 1,8-dioxo-decahydroacridines.[a] (*Contd.*)

Entry	Aldehyde	Amine	Time (min)	Yield (%)[b]	M.p. (°C)
6			30	95	299-303
7			10	94	187-192
8			55	90	278-284
9			5	95	203-207
10			20	97	275-281
11			25	97	278-279
12			40	92	212-214
13			35	93	215-216
14			30	94	237-239
15			30	95	296-298

[a]Reaction condition: aldehydes (1.0 mmol), dimedone (2.0 mmol; 0.280 g); ammonium acetate (1 mmol; 0.077 g) anilines (1.0 mmol), Ag nanoparticles (2 mol%), C_2H_5OH (2 mL), r.t.; [b]Isolated yield

dioxo-decahydroacridines in appropriate yields as specified in Table 1. The Ag nanoparticles catalyst filtered was washed three times with ethanol (3×10 mL), dried at 80°C for 3 h and reused. The isolated product yield after four successive runs is decreased to 91%. Selected products were achieved characterized by melting point and spectroscopic methods such as FT-IR and ^{1}H NMR and have been known by the comparison of the spectral data with those reported.

Spectral data for selected compounds

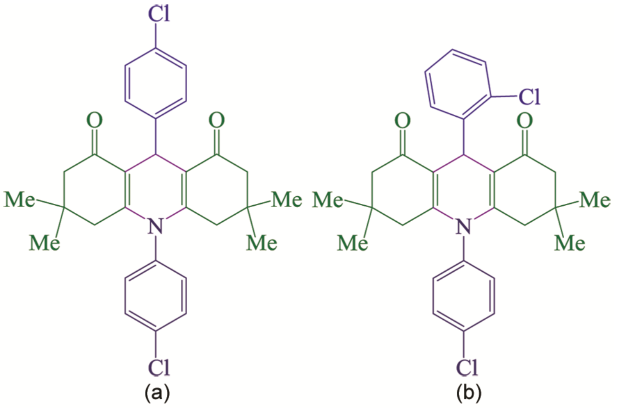
9,10-Bis(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione (Table 1, entry 5): White crystalline solid; M.p.: 290-292°C; Yield: 93 %; FT-IR (KBr) (υ_{max}, cm^{-1}): 2958, 1639, 1486, 1365,1292,1219; ^{1}H NMR (400 MHz, $CDCl_3$): δ=0.85 (s, 6H), 0.99 (s, 6H), 1.83-2.10 (m, 4H), 2.15-2.25 (m, 4H), 5.26 (s, 1 H), 7.20-7.59 (m, 8H).

9-(2-Chlorophenyl)-10-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8-(2H,5H)-dione (Table 1, entry 6): White crystalline solid;M.p.: 299-303°C; Yield: 95 %; FT-IR (KBr) (υ_{max}, cm^{-1}): 3055, 2952, 1641, 1521, 1363, 1221;^{1}H NMR (400 MHz, DMSO-d_6): δ=0.87 (s, 6H), 1.21 (s, 6H),1.94-2.25 (m, 8H),5.25 (s, 1H), 6.67-7.67 (m, 8H).

The structures of selected products are given in Fig. 1 and spectral images of FT-IR and ^{1}H NMR of selected products are given in Supplementary Information.

Results and Discussion

To synthesize 1,8-dioxo-decahydroacridines in a further effective way, and to decrease the reaction time and the amount of catalyst requisite, the reaction of 4-nitrobenzaldehyde (1.0 mmol; 0.151 g), dimedone (2.0 mmol; 0.280 g) and aniline (1.0 mmol; 0.093 g; 0.091 mL) was chosen as a typical system. Various amounts of Ag nanoparticles were initial studied for the typical reaction. The result is known in Table 2 (Table 2, entries 1-3). These studiesdisplayed that enhanced results could be attained by using 2 mol% of Ag nanoparticles in ethanol (2 mL) at room temperature.



(a) (b)

Fig. 1 — Structures of (a) 9,10-Bis(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione and (b) 9-(2-Chlorophenyl)-10-(4-chlorophenyl)-3,3,6,6-tetramethyl-3,4,6,7,9,10-hexahydroacridine-1,8(2H,5H)-dione

The current optimization investigations exposed that yield improved with the catalyst load up to 2 mol% and use of larger amounts of the Ag nanoparticles catalyst did not progress the yields whereas shrinking the amount of catalyst led to shrank yields (Table 2, entries 1-4). The insignificant amount of the target product was produced in the absence of catalyst.Among the green solvents CH_3CH_2OH, H_2O, CH_3CO_2Et, toluene and CH_3CN studied in this reaction, CH_3CH_2OH was found as the solvent of select which afforded the best rate and yield (Table 2, entries 4-8). As seen in Table 2 (entries 9 and 10), the reaction yield progressively reduces with increasing the temperature from 25°C to 50°C and 75°C. Apparently, higher temperatures may reason the increase of side product generation by using Ag nanoparticles catalyst.

Various aldehydes and anilines underwent condensation with dimedone by this process to afford related 1,8-dioxo-decahydroacridines by using Ag nanoparticles as a benign and facile catalyst (Table 1). No side product was identified in any reaction. Several aldehydes containing electron-withdrawing or electron-donating substituents (*ortho*-, *meta*- and *para*-substituted) used satisfactory in this reaction and provide the 1,8-dioxo-decahydroacridines in good to superb yield. Consequently, we attain that the electronic nature of substituents of the aldehyde has no noteworthy effect on the reaction time and isolate yield. Also, we establish that aromatic amines including electron-donating substituents gave the target product in short reaction time and high yield.

The recyclability of Ag nanoparticles was studied in typical reaction. After end of the reaction, the hot

Table 2 — Optimization of reaction conditions in the synthesis of target product.^{a}

Entry	Catalyst amount (%)	Solvent	Time (min)	Yield (%)^b
1	–	CH_3CH_2OH	60	15
2	0.5	CH_3CH_2OH	20	84
3	1	CH_3CH_2OH	10	89
4	2	CH_3CH_2OH	5	96
5	2	H_2O	15	85
6	2	CH_3CO_2Et	35	79
7	2	Toluene	40	75
8	2	CH_3CN	30	80
9	2	CH_3CH_2OH (50 ^{0}C)	5	87
10	2	CH_3CH_2OH (75 ^{0}C)	5	73

^{a}Reaction condition: 4-nitrobenzaldehyde (1.0 mmol; 0.151 g), dimedone (2.0 mmol; 0.280 g); aniline (1.0 mmol; 0.093 g; 0.091 mL), solvent (2 mL), r.t.; ^{b}Isolated yield ethanol (10 mL) was added to reaction mixture and the Ag nanoparticles catalyst was filtered (the reaction mixture was soluble in hot ethanol). At that time, the recovered catalyst was washed three times with ethanol and after dryness was reused in the subsequentsame run. This procedure was repeated for four successive runs and the selected product was attained in good yields (Fig. 2).

The plausible mechanism for the Ag nanoparticles catalyzed synthesis of 1,8-dioxo-decahydroacridines is presented in Scheme 2[26]. Firstly, the Ag nanoparticles activate the carbonyl group of aldehyde **1**. Then, the first molecule of dimedone **2** was tautomerized to enol form and reacted with an activated aldehyde **1** *via* Knoevenagel condensation | to provide intermediate **5** by elimination of one molecule of H_2O. At that timesecond molecule of dimedone **2**(in the enol form) was reacted with **5** *via* Michael addition to afford intermediate **6**. In the next step nucleophilic attack of aniline derivatives or ammonia (*in situ* formed by ammonium acetate) **3** to carbonyl group of **6** provides intermediate **7** by elimination of second molecule of H_2O which tautomerized to intermediate **8**. Lastly, intermediate **8** was cyclized by the nucleophilic attack of amine group on carbonyl group and afford 1,8-dioxodecahydroacridines **4** by removal of other molecule of water.

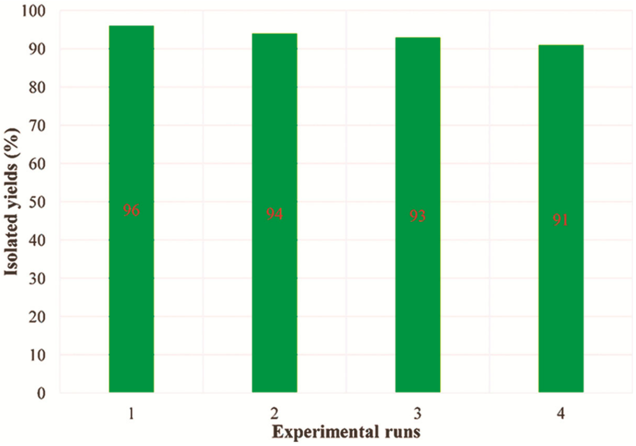
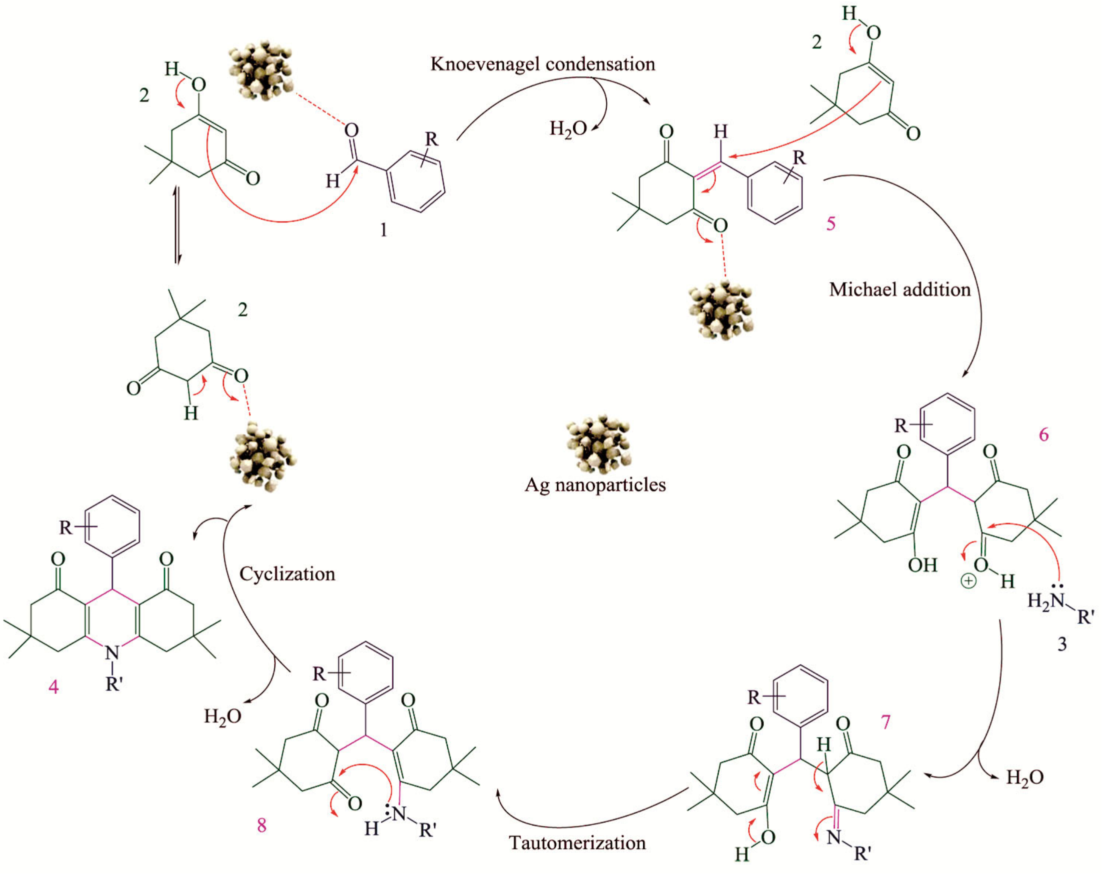


Fig. 2 — Recyclability studies of Ag nanoparticles catalyst in typical reaction after 5 min



Scheme 2 — Plausible mechanism for the Ag nanoparticles catalyzed synthesis of 1,8-dioxo-decahydroacridines

Conclusion

From the results of the above study, in can be concluded that the Ag nanoparticles is a really appropriate heterogeneous catalyst for the synthesis of 1,8-dioxo-decahydroacridines by using condensation between aldehydes, dimedone and ammonium acetate or anilines. The reaction was performed in ethanol solvent at room temperature. The favorable points of this technique are economical catalyst, benign and simple reaction process, easy product separation, short reaction time, high yields and safety, as compared to the other technique counterparts.

Supporting Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

Acknowledgement

The authors are thankful for facilities provided to carry out research in chemistry research laboratory at Ayatollah Amoli Branch, Islamic Azad University.

References

1 (a) Clark J H & Rhodes C N, *Clean Synthesis Using Porous Inorganic Solid Catalysts and Supported Reagents,* 1st ed. (Royal Society of Chemistry, UK) 2000, p. 117.
2 (a) Salehi P, Zolfigol M A, Shirini F & Baghbanzadeh M, *Curr Org C*hem, 10 (2006) 2171; (b) Khalafi-Nezhad A, Parhami A, Soltani Rad M N, Zolfigol M A & Zare A, *Tetrahedron Lett*, 48 (2007) 5219.
3 Koo O M, Rubinstein I & Onyuksel H, *Nanomedicine*, 1 (2005) 193.
4 Sahoo S K, Parveen S & Panda J J, *Nanomedicine*, 3 (2007) 20.
5 Corbett J, McKeown P A, Peggs G N & Whatmore R, *CIRP Ann Manuf Technol*, 49 (2000) 523.
6 Hirakawa T & Kamat P V, *J Am Chem Soc*, 127 (2005) 3928.
7 Elahifard M R, Rahimnejad S, Haghighi S & Gholami M R, *J Am Chem Soc*, 129 (2007) 9552.
8 Awazu K, Fujimaki M, Rockstuhl C, Tominaga J, Murakami H, Ohki Y, Yoshida N & Watanabe T, *J Am Chem Soc*, 130 (2008) 1676.
9 Oliveira A L D, Wolf A & Schuth F, *Catal Lett*, 73 (2001) 157.
10 Lei Y, Mehmood F, Lee S, Greeley J, Lee B, Seifert S, Winans R E, Elam J W, Meyer R J, Redfern P C, Teschner D, Schlogl R, Pellin M J, Curtiss L A & Vajda S, *Science*, 328 (2010) 224.
11 (a) Domling A, *Chem Rev*, 106 (2006) 17; (b) Cariou A C C, Clarkson G J & Shipman M, *J Org Chem*, 73 (2008) 9762; (c) Umkeherer M, Kalinski C, Kolb J & Burdack C, *Tetrahedron Lett*, 47 (2006) 2391; (d) Alizadeh A, Mobahedi F & Esmaili A, *Tetrahedron Lett*, 47 (2006) 4469; (e) Domling A & Ugi I, *Angew Chem Int Ed*, 39 (2000) 3168.
12 Shen W, Wang L M, Tian H, Tang J & Yu J J, *J Fluorine Chem*, 130 (2009) 522.
13 Baguley B C, Zhuang L & Marshall E M, *Cancer Chemother Pharmacol*, 36 (1995) 244.
14 Croisy-Delcey M, Croisy A, Zajdela F & Lhoste J M, *J Med Chem*, 26 (1983) 303.
15 Filloux N & Galy J P, *Synlett*, 7 (2001) 1137.
16 Bossert F, Meyer H & Wehinger E, *Angew Chem Int Ed*, 20 (1981) 762.
17 Nakayama H & Kasoaka Y, *Heterocycles*, 42 (1996) 901.
18 Godfraid T, Miller R & Wibo M, *Pharmacol Rev*, 38 (1986) 321.
19 Mannhold R, Jablonka B, Voigt W, Schonafinger K & Schraven E, *Eur J Med Chem*, 27 (1992) 229.
20 Bretzel R G, Bollen C C, Maeser E & Federlin K F, *Drugs Future*, 17 (1992) 465.
21 Boer R & Gekeler V, *Drugs Future*, 20 (1995) 499.
22 Shanmugasundaram P, Prabahar K J & Ramakrishnan V T, *J Heterocycl Chem*, 30 (1993) 1003.
23 Murugan P, Shanmugasundaram P, Ramakrishnan V T, Venkatachalapathy B, Srividya N, Ramamurthy P, Gunasekharan K & Velmurugan D, *J Chem Soc Perkin Trans*, 2 (1998) 999.
24 Vahdat S M, Khaksar S, Akbari M & Baghery S, *Arabian J Chem*, 12 (2019) 1515.
25 Alinezhad H, Tajbakhsh M, Norouzi M, Baghery S & Rakhtshah J, *J Chem Sci*, 125 (2013) 1517.
26 Vahdat S M, Mardani H R, Golchoubian H, Khavarpour M, Baghery S & Roshankouhi Z, *Comb Chem High Throughput Screening*, 16 (2013) 2.
27 Zolfigol M A, Bahrami-Nejad N & Baghery S, *J Mol Liq*, 218 (2016) 558.
28 Jin T S, Zhang J S, Guo T T, Wang A Q & Li T S, *Synthesis*, 12 (2004) 2001.
29 Kidwai M & Bhatnagar D, *Chem Pap*, 64 (2010) 825.
30 (a) Zolfigol M A, Baghery S, Moosavi-Zareb A R & Vahdat S M, *J Mol Catal A Chem*, 409 (2015) 216; (b) Maleki B, Baghayeri M, Vahdat S M, Mohammadzadeh A & Akhoondi S, *RSC Adv*, 5 (2015) 46545.
31 (a) Vahdat S M, Ghafouri R S & Baghery S, *J Chem Sci*, 126 (2014) 579; (b) Vahdat S M, Chekin F, Hatami M, Khavarpour M, Baghery S & Roshankouhi Z, *Chinese J Catal,* 34 (2013) 758; (c) Chekin F, Vahdat S M & Asadi M J, *Russian J Appl Chem*, 89 (2016) 816; (d) Yazdani S, Hatami M & Vahdat S M, *Turkish J Chem*, 38 (2014) 388; (e) Vahdat S M, Khavarpour M & Mohanazadeh F, *J Appl Chem*, 9 (2015) 41.