Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron Letters 49 (2008) 1538–1541
Tetrahedron Letters

Synthesis of aryl-hydrazones via ultrasound irradiation in aqueous medium

Ana Cristina Lima Leite *, Diogo Rodrigo de M. Moreira, Lucas Cunha Duarte Coelho, Frederico Duarte de Menezes, Dalci José Brondani *

LabSINFA—Laboratory for the Planning, Synthesis and Evaluation of Pharmaceutical Products, Department of Pharmaceutical Science, Centre for Health Science, Federal University of Pernambuco, 50740-520 Recife, PE, Brazil

Received 11 November 2007; revised 15 December 2007; accepted 18 December 2007

Abstract

The synthesis of aryl-hydrazones from aromatic aldehydes/ketones and hydrazides (semicarbazide, thiosemicarbazide and aminoguanidine) is described using aqueous medium (acid conditions) under ultrasound irradiation with short reaction times (20–30 min), the reactions occurring at room temperature and giving rise to good to excellent yields of the products, along with the diastereoselectivities. The procedure is also simple and clean.

Keywords: Hydrazones; Aqueous medium; Ultrasound irradiation; Condensation

Aryl-hydrazones, such as semicarbazones, thiosemicarbazones and guanyl hydrazones, are important compounds for drug design,[1] as possible ligands for metal complexes,[2] organocatalysis[3] and also for the preparation of heterocyclic rings.[4]

At present a broad range of methods for synthesizing imines[5] in the presence of catalysts are available: $ZnCl_2$,[6] $TiCl_2$,[7] K-10,[8] $MgSO_4$-PPTL,[9] $Mg(ClO_4)_2$[10] and also SiO_2–$NaHSO_4$ (under MW irradiation condition).[11] More recently, ultrasound irradiation has been used to give rise to the formation of a series of Schiff bases (aryl–aryl and aryl–alkyl), under solvent-free conditions[12] or using SiO_2 as a catalyst in ethanol,[13] with short reaction times (10–20 min) and high yields.

For aryl-hydrazones, most reaction methods described to date involve the use of methanol as a solvent without catalysts at reflux, although ethanol and acid catalysis (or *p*-toluenesulfonic acid in dried toluene) are required if the carbonyl compounds bear a strong electron-withdrawing group.[14] Improvements in yields of the aryl-hydrazones synthesis have been achieved when MW-irradiation at solvent-free conditions were used.[15] In some cases, a mixture of isomers (*Z* and *E*) is reported, mainly for reaction procedures that are only possible at high temperatures or for prolonged reaction periods.[16]

At the same time, many addition/condensation reactions have been demonstrated to occur in aqueous media (such as: Barbier and Mannich-type reactions, Diels–Alder cycloaddition, and Knoevenagel condensation).[17] Water is the cheapest and safest solvent available, and in the presence of reactive functional groups, protection and deprotection processes are often unnecessary. In fact, total solubility is required for efficient reaction in water, and thus, either organic co-solvents or heating are almost always employed.[18] Although Schiff and colleagues have reported that the presence of water is a disadvantage in imine synthesis, three works have shown that such reactions can be effective in completely aqueous media under mild conditions.[19] More recently, a protocol for the synthesis of aryl- and heterocyclic-hydrazones from aryl-hydrazine

* Corresponding authors. Tel./fax: +55 81 2126 8511 (A.C.L.L.).
E-mail addresses: ana.leite@pq.cnpq.br (A. C. L. Leite), dalci@ufpe.br (D. J. Brondani).

0040-4039/$ - see front matter © 2007 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2007.12.103

and aldehydes/ketones has been described with excellent yields using polystyrene sulfonic acid as a catalyst under MW irradiation (100 °C) in water.[20] However, the literature does not report the general synthesis of aryl-hydrazones (such as thiosemicarbazones, semicarbazones, or guanyl hydrazones) in aqueous media using ultrasound irradiation, nor the diastereoselectivities for these compounds.

Taking into account its application to studies of medicinal chemistry and its use for obtaining metal complexes, we describe here an efficient and rapid aryl-hydrazone synthesis process using ultrasound irradiation in an aqueous medium (Scheme 1).

The reactions were carried out in parallel on a microscale: 2 mL of water, 1 mmol of amine, 1 mmol of aryl-aldehyde/ketone and irradiated with ultrasound (low intensity) for 20–30 min at rt (30 °C), and the precipitate was then filtered and washed (in H_2O or EtOH).

First, the reaction of *p*-methoxybenzaldehyde (**1a**) and thiosemicarbazide (**2a**) was used as the model reaction in the simplest manner, by mixing the amines and the aldehydes directly in water, without adding any co-solvent or catalyst, at rt and irradiating for 20–30 min with ultrasound (Table 1). However, the yield was only 45% under these conditions (entry 1). When the reaction was run between 40 and 60 °C, the yields only improved to 55% and 65%, respectively (entries 2 and 3), and no improvement was observed in the case of solid aldehydes/ketones.

The effect of acidity is very important in this reaction, as it protonates the carbonyl carbon in the first step to produce the formation of imines.[5] Subsequently, acetic acid and inorganic salts were tested. $KHSO_4$ and NH_4Cl showed good yields comparable to acetic acid, and thus the use of acid conditions proved to be crucial, because of the effect of acidity and also in helping to produce total solubility of the carbonyl compounds. By contrast, under basic conditions, only a moderate yield was detected (entry 11). The addition of water-miscible co-solvents (0.5 mL, MeOH or EtOH) brought about a considerable improvement, mainly in the case of more lipophilic aldehydes/ketones.

When activated SiO_2 was used as catalyst[13] in water or ethanol (Table 1, entry 12), the yield was comparable with that produced using acetic acid, but generated more problems due to the precipitation accompanying the product, and, in this case, it was necessary to use toluene or ethyl acetate to separate aryl-hydrazone (**3a**) of the SiO_2. We observed that the application of ultrasound irradiation significantly increased the reaction rates and yields

Table 1
Aqueous medium-promoted condensation of 4-methoxybenzaldehyde (**1a**) with thiosemicarbazide (**2a**) via ultrasound irradiation

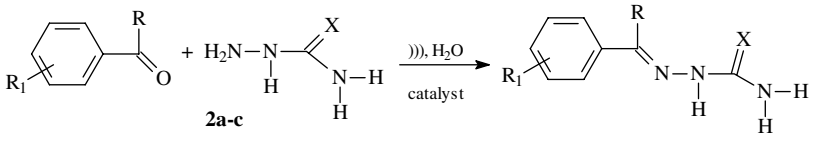
Entry	Catalyst	Co-solvent	Temp (°C)	Yield[a] (%)
1	None	None	30	45[b]
2	None	None	40	55[b]
3	None	None	60	65[b] (68)[g]
4	HOAc[c]	None	30	98
5	HOAc	None	60	98
6	None	EtOH[d]	60	75 (78)[g]
7	HOAc	EtOH[d]	30	98
8	NH_4Cl[e]	None	60	90
9	NH_4Cl	EtOH[d]	30	95
10	$KHSO_4$[f]	None	60	85
11	NaOAc	None	30	65
12	SiO_2 (5 equiv)	None	30	80 (85)[h]

[a] Determined as isolated products after 20 min.
[b] The starting materials were mostly recovered.
[c] Five drops (0.1 mL).
[d] A mixture (5:1) of water and co-solvent.
[e] Saturated solution (pH 5.0).
[f] Solution at 10% wt (pH 4.5).
[g] After 30 min.
[h] Using ethanol.

(20–30 min) compared to the traditional stirring for 4–6 h for the reaction between aldehyde **1a** and hydrazide **2a** (at rt).

The reaction can be carried out effectively with a wide variety of aldehydes/ketones and hydrazides using the optimal condition described in entry 4. Excellent results were obtained in most cases, with the formation of crystalline products and the same diastereoselectivity (only one isomer isolated).[21] Aromatic ketones proved to be less reactive and did not furnish the best yields, these being only moderate to good. Low yield (>20%) was obtained in the condensation reaction with benzophenone (showing reduced electrophilicity of the carbonyl carbon under powerful resonance) under the conditions of entry 5 (Table 1), even after 1 h. In the case of cinnaldehyde and arylthioacetaldehyde the use of a co-solvent (0.5 mL EtOH) or a large amount of acetic acid (0.5 mL) provided better results than the use of a complete aqueous medium. Furthermore, cinnaldehyde derivatives did not precipitate at the end of reaction, and had to be isolated by freezing them overnight and then filtering.

Similarly, the use of semicarbazide (chloridrate) or aminoguanidine [22] (carbonate) also furnished the desired products under the reaction conditions at good to excellent yields



2a: X=S thiosemicarbazide
2b: X = O semicarbazide
2c: X = NH aminoguanidine

Scheme 1. Synthetic route for aryl-hydrazones.

Table 2
Synthesis of aryl-hydrazones

Entry	Aldehyde/ketone	Hydrazides	Time (min)	Yield (%)
1	*p*-Methoxybenzaldehyde	3b	20	95
2	*p*-Methoxybenzaldehyde	3c	20	98
3	2-Furaldehyde	3a	20	95 (92)[a]
4	2-Furaldehyde	3b	20	90
5	2-Furaldehyde	3c	20	98
6	3,4-Di-chlorobenzaldehyde	3a	30	85
7	3,4-Di-chlorobenzaldehyde	3b	30	90
8	3,4-Di-chlorobenzaldehyde	3c	30	88
9	*p*-Bromobenzaldehyde	3a	20	85
10	*p*-Bromobenzaldehyde	3b	20	92
11	*p*-Bromobenzaldehyde	3c	20	84 (80)[a]
12	Cinnaldehyde	3a	20	90
13	Cinnaldehyde	3b	20	94 (90)[a]
14	Cinnaldehyde	3c	20	90
15	*p*-Hydroxybenzaldehyde	3a	20	80[b]
16	*p*-Hydroxybenzaldehyde	3b	20	95[b]
18	*p*-Hydroxybenzaldehyde	3c	20	85[b]
19	Arylthioacetaldehyde	3a	20	90
20	Arylthioacetaldehyde	3b	20	90
21	Arylthioacetaldehyde	3c	20	85
22	Acetophenone	3a	30	80
23	Acetophenone	3b	30	85
24	Acetophenone	3c	30	80
25	*p*-Chloroacetophenone	3a	20	85
26	*p*-Chloroacetophenone	3b	20	88
27	*p*-Chloroacetophenone	3c	30	75

[a] Scale-up of 10 mmol, using 15 mL of water and 0.4 mL of acetic acid.
[b] After the filtration, the water from the reaction was extracted with dichloromethane three times and the combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo.

(Table 2). Moreover, the reactions proceeded normally even when 2 equiv of enolizable aldehyde was used, and no aldol adducts were observed as possible by-products.[23] We tried the condensation of N^1-(*tert*-butyloxycarbonyl)thiosemicarbazide with aldehyde **1a**, but aryl-hydrazone **3a** was not obtained under these conditions. No reaction was detected for arylthioacetaldehyde diethyl acetal with hydrazide **2a**, and acetal was collected unaltered after prolonged reaction time (1 h). Subsequently, the reactions described in entries 3, 11, and 13 (Table 2) were shown to be efficient on a 10 mmol scale.

One crucial feature of this reaction procedure was the total solubilization of the hydrazide starting material in water when sonicated for 2 min and hence, the aldehyde/ketone was added dropwise to the mixture and resulted in an initially homogenous reaction mixture that was smoothly precipitated during the reaction.

Finally, we decided to compare the MW irradiation conditions for obtaining aryl-thiosemicarbazone **3a**. As summarized in Table 3, the use of MW-irradiation led to good yield of product **3a** in 4 min of reaction when $NaHSO_4$–SiO_2 was used as catalyst, and moderate yields were achieved at solvent-free conditions or with five drops of DMF, but the presence of a by-product was unfortunately also observed in all these reactions. This probably occurred as a result of some kind of degradation or desulfuration involving the thiocarbonyl carbon of the thiosemicarbazide when it was microwave heated, as described by Siemion and co-workers.[24] However, it was difficult to make the correct assignments of this by-product, which we hope will be reported elsewhere in the future. Thus, the use of MW-assisted reactions show extraordinary ability to achieve the aryl-hydrazones synthesis from hydrazine hydrate or phenyl hydrazine as previously described[15,20] and in the case of the aryl-thiosemicarbazones synthesis is still much more problematic due to the different reactivity and feasible degradation for the thiosemicarbazide.

Table 3
Comparative study of the reaction between aldehyde **1a** and hydrazide **2a** by microwave irradiation

Conditions[a]	Yield[b] (%)
2 min, $T_{max} = 100$ °C, solvent free	40
4 min, $T_{max} = 100$ °C, solvent free	60
4 min, $T_{max} = 100$ °C, DMF (five drops)	60
4 min, $T_{max} = 150$ °C, solvent free	70
4 min, $T_{max} = 150$ °C, $NaHSO_4$–SiO_2[c]	78
4 min, $T_{max} = 150$ °C, DMF (five drops)[d]	75

[a] Using a domestic microwave oven.
[b] After recrystallization.
[c] As described in Ref. 11
[d] As described in Ref. 30.

The experimental procedures for the synthesis[25] and the full assignment of NMR and IR spectra for the new compounds are provided in Refs. 28,29.

In conclusion, we have discovered a practical, mild, and rapid procedure for ultrasound-accelerated synthesis of aryl-hydrazones from aromatic aldehydes/ketones and hydrazides in the presence of an aqueous medium (under acid conditions) at room temperature. This method furnishes the products very quickly with good to excellent yields, compatible with the commonly-used amine/carbonyl protecting groups, simplifies the work-up and does not harm the environment.

Acknowledgments

We would like to thank the Brazilian National Research Council (CNPq) for financial support. F.D.M. and L.C.D.C. also received a CNPq grant and D.R.M.M. is a fellow of CAPES. Our thanks are also due to the Department of Fundamental Chemistry, UFPE, for recording the ^1H, ^{13}C NMR and IR spectra of all compounds and to Professor R. M. Srivastava (DQF-UFPE) for helpful discussions.

References and notes

1. (a) Beraldo, H.; Gambino, D. *Mini-Rev. Med. Chem.* **2004**, *4*, 31–39; (b) Greenbaum, D. C.; Mackey, Z.; Hansell, E.; Doyle, P.; Gut, J.; Caffrey, C. R.; Lehrman, J.; Rosenthal, P. J.; McKerrow, J. H.; Chibale, K. *J. Med. Chem.* **2004**, *47*, 3212–3219.
2. (a) Costa, R. F. F.; Rebolledo, A. P.; Matencio, T.; Calado, H. D. R.; Ardisson, J. D.; Cortes, M. E.; Rodrigues, B. L.; Beraldo, H. *J. Coord. Chem.* **2005**, *58*, 1307–1319; (b) Rebolledo, A. P.; Vieites, M.; Gambino,

D.; Piro, O. E.; Castellano, E. E.; Zani, C. L.; Souza-Fagundes, E. M.; Teixeira, L. R.; Batista, A. A.; Beraldo, H. *J. Inorg. Biochem.* **2005**, *99*, 698–706.
3. (a) Lemay, M.; Ogilvie, W. W. *J. Org. Chem.* **2006**, *71*, 4663–4666; (b) Lemay, M.; Aumand, L.; Ogilvie, W. W. *Adv. Synth. Catal.* **2007**, *349*, 441–444; (c) Lemay, M.; Ogilvie, W. W. *Org. Lett.* **2005**, *7*, 4141–4144.
4. (a) Salgm-Goksen, U.; Gokhan-Kelekci, N.; Goktas, O.; Koysal, Y.; Kilic, E.; Isik, S.; Aktay, G.; Ozalp, M. *Bioorg. Med. Chem.* **2007**, *15*, 5738–5751; (b) Leite, A. C. L.; de Lima, R. S.; Moreira, D. R. D.; Cardoso, V. D. O.; de Brito, A. C. G.; dos Santos, L. M. F.; Hernandes, M. Z.; Kiperstok, A. C.; de Lima, R. S.; Soares, M. B. P. *Bioorg. Med. Chem.* **2006**, *14*, 3749–3757; (c) Bondock, S.; Khalifa, W.; Fadda, A. A. *Eur. J. Med. Chem.* **2007**, *42*, 948–954.
5. For an review on imine, see: Layer, R. W. *Chem. Rev.* **1963**, *63*, 489–510.
6. Billman, J. H.; Tai, K. M. *J. Org. Chem.* **1958**, *23*, 535–539.
7. Weingart, H.; Chupp, J. P.; White, W. A. *J. Org. Chem.* **1967**, *32*, 213–214.
8. (a) Vaas, R. S.; Dudas, J.; Varma, R. S. *Tetrahedron Lett.* **1999**, *40*, 4951–4954; (b) Landge, S. M.; Atanassova, V.; Thimmaih, M.; Torok, B. *Tetrahedron Lett.* **2007**, *48*, 5161–5164.
9. Branchaud, B. P. *J. Org. Chem.* **1983**, *48*, 3531–3538.
10. Chakraborti, A. K.; Bhagat, S.; Rudrawar, S. *Tetrahedron Lett.* **2004**, *45*, 7641–7644.
11. Bazgir, A. *J. Chem. Res.* **2006**, *1*, 1–2.
12. Yu, Y. *Asian J. Chem.* **2007**, *19*, 2476–2478.
13. Guzen, K. P.; Guarezemini, A. S.; Orfão, A. T. G.; Cella, R.; Pereira, C. M. P.; Stefani, H. A. *Tetrahedron Lett.* **2007**, *48*, 1845–1848.
14. (a) Aguirre, G.; Boiani, L.; Cerecetto, H.; Fernandez, M.; Gonzalez, M.; Denicola, A.; Otero, L.; Gambino, D.; Rigol, C.; Olea-Azar, C.; Faundez, M. *Bioorg. Med. Chem.* **2004**, *12*, 4885–4893; (b) Cerecetto, H.; Maio, R. D.; González, M.; Risso, M.; Sagrera, G.; Seoane, G.; Denicola, A.; Pellufo, G.; Quijano, C.; Stoppanie, A. O. M.; Paulino, M.; Olea-Azarg, C.; Basombríoh, M. G. *Eur. J. Med. Chem.* **2000**, *35*, 343–350.
15. (a) Jeselnik, M.; Varma, R. S.; Polanc, S.; Kocevar, M. *Chem. Commun.* **2001**, 1716–1717; (b) Joselnik, M.; Varma, R. S.; Polanc, S.; Kocevar, M. *Green Chem.* **2002**, *4*, 35–38.
16. (a) Bastos, A. M. B.; Alcântara, A. F. C.; Beraldo, H. *Tetrahedron* **2005**, *61*, 7045–7053; (b) Siles, R.; Chen, S. E.; Zhou, M.; Pinney, K. G.; Trawick, M. L. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 4405–4409.
17. (a) Narayan, S.; Muldoon, J.; Finn, M. G.; Fokin, V. V.; Kolb, H. C.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2005**, *44*, 3275–3279; (b) Deb, M. L.; Bhuyan, P. J. *Tetrahedron Lett.* **2005**, *46*, 6453–6456; (c) Dallinger, D.; Kappe, C. O. *Chem. Rev.* **2007**, *107*, 2563–2591; (d) Li, C. J. *Tetrahedron Lett.* **1996**, *52*, 5643–5668; (e) Silva, R. A.; Estevan, I. H. S.; Bieber, L. W. *Tetrahedron Lett.* **2007**, *48*, 7680–7682.
18. (a) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159–164; (b) Lindstrom, U. M. *Chem. Rev.* **2002**, *102*, 2751–2771; (c) Maya, V.; Raj, M.; Singh, V. K. *Org. Lett.* **2007**, *9*, 2593–2595.
19. (a) Simion, A.; Simion, C.; Kanda, T.; Nagashima, S.; Mitoma, Y.; Yamada, T.; Mimura, K.; Tashiro, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2071–2078; (b) Rivera, A.; Rios-Motta, J.; Leon, F. *Molecules* **2007**, *11*, 858–866; (c) Jarrahpour, A. A.; Khalili, D. *Molecules* **2006**, *11*, 59–63.
20. Polshelttiwar, V.; Varma, R. S. *Tetrahedron Lett.* **2007**, *48*, 5649–5652.
21. Spectroscopic analysis (^{1}H NMR) of the aryl-hydrazones obtained led us to establish that only one isomer was always formed, despite the fact that chemical shift data for the N*H* (imine) and ArC*H*N showed signs of being one singlet, in accordance with the results observed on the GC analysis and related in Ref. 2b,15a.
22. Aromatic guanyl hydrazones were visualized on the TLC plates using iodine vapor or by spraying a solution of H_2SO_4 10% wt and the R_f values were determined for MeOH/CH_2Cl_2 2:8.
23. Wagner, E. C. *J. Org. Chem.* **1954**, *19*, 1862–1881.
24. Siemion, P.; Kapusniak, J.; Koziol, J. J. *Carbohydr. Polym.* **2006**, *66*, 104–109.
25. *General procedure*: Synthesis of 1-(*p*-methoxybenzylidene)thiosemicarbazone (**3a**): Thiosemicarbazide (**2a**, 91 mg, 1 mmol) was added to a vessel flask containing 2 mL of water, immersed in a water bath (30 °C) and sonicated for 2 min in Unique Model 1400 A ultrasonic laboratory (220 V, 100 W, 40 kHz). Afterwards the aldehyde **1a** (136 mg, 1 mmol) and acetic acid (0.1 mL) were added dropwise to the mixture reaction. Upon completion of the reaction (20–30 min), the product was filtered, washed with water (20 mL) and ethyl ether (5 mL), dried in vacuo, and, if necessary, recrystallized from ethanol/water (1:5) for the aryl-thiosemicarbazones and aryl-semicarbazones; and with dichloromethane for the aryl-guanyl hydrazones. The diastereoselectivities of the products were determined using GC and NMR analysis. All aryl-hydrazones previously described presented m.p., NMR and IR data in accordance with the literature.[26,27]
26. Messeder, J. C.; Tinoco, L. W.; Figueroa-Vilar, J. D.; Souza, E. M.; de Castro, S. L. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 3079–3084.
27. Du, X.; Guo, C.; Hansell, E.; Doyle, P. S.; Caffrey, C. R.; Holler, T. P.; McKerrow, J. H.; Cohen, F. E. *J. Med. Chem.* **2002**, *45*, 2695–2707.
28. We have observed that some aryl-thiosemicarbazones exhibit two non-equivalent singlets for the imine proton (CHNN*H*), due to the intramolecular hydrogen-bond between the thiocarbonyl carbon and the imine proton, when it was recorded using DMSO-d_6, although these were not observed in the case of aryl-semicarbazones and aromatic guanyl hydrazones.
29. Compound *N*-(3-phenylethylidene)thiosemicarbazone: mp: 111–112 °C (from ethanol); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 6.82–6.90 (m, 1H, CH); 6.98 (d, $J = 10$ Hz, 1H, CH); 7.28–7.53 (m, 3H, Ar); 7.56–7.73 (d, 2H, Ar); 7.62 (s, 1H, NH_2); 7.90 (d, $J = 7.0$ Hz, 1H, CH=N); 8.17 (s, 1H, NH_2); 11.40 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ 125.11; 126.98; 128.94; 135.91; 138.92; 144.76 (CH=N); 177.69 (C=S). IR (KBr, cm^{-1}) ν 3409 (NH_2). 3257 (NH); 1587 (C=N); 1283 (C=S).
Compound *N*-(3-phenylethylidene)semicarbazone: mp: 127–8 °C (from ethanol); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 6.31 (s, 2H, NH_2); 6.86–6.89 (m, 2H, CH); 7.26–7.39 (m, 3H, Ar); 7.51–7.54 (d, $J = 10$ Hz, 2H, Ar); 7.69 (d, $J = 5$ Hz, 1H, CH=N); 10.22 (s, 1H, NH); ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ 125.58; 125.67; 126.67; 128.44; 128.87; 136.16; 141.84 (CH=N); 156.48 (C=O). IR (KBr, cm^{-1}) ν 3435 (NH_2). 3188 (NH); 1640 (C=O); 1601 (C=N).
Compound *N*-(3-phenylethylidene)aminoguanidine: mp: 139 °C (from ethanol); ^{1}H NMR (DMSO-d_6, 300 MHz): δ 6.51 (s, 1H, NH_2); 6.79 (d, $J = 12$ Hz, 1H, CH); 7.50 (m, 1H, CH); 7.90–8.11 (m, 5H, Ar and 1H of NH_2); 8.12 (d, $J = 8$ Hz, CH=N); 11.93 (s, 1H, NH). ^{13}C NMR (DMSO-d_6, 75.5 MHz): δ 125.07; 126.58; 127.01; 129.04; 128.87; 136.19; 141.84 (CH=N); 159.87 (C=NH). IR (KBr, cm^{-1}) ν 3409 (NH_2). 3257 (NH); 1619 (C=N).
30. Zamani, K.; Faghihi, K.; Bagheri, S.; Kalhor, M. *Indian J. Chem., Sect. B* **2004**, *43*, 2716–2718.