Efficient, Mild and One Pot Synthesis of *N,N'*-Bis(salicylidene)arylmethanediamines *via* Three Component Reaction under Solvent Free Conditions

Hossein Naeimi,* Khadijeh Rabiei, and Fariba Salimi

*Department of Chemistry, Faculty of Science, University of Kashan, Kashan 87317, I.R. Iran. *E-mail: naeimi@kashanu.ac.ir*
Received May 8, 2008

An economical and environmental friendly method has been developed for the synthesis of *N,N'*-bis(salicylidene)-arylmethanediamine derivatives. This procedure were carried out through one pot three component reaction of two different aromatic aldehydes and ammonium acetate salt in the presence of a base under free solvent conditions at room temperature. The Schiff base products were purely obtained in excellent yields and short reaction times.

Key Words : Schiff base, Three component, Solvent free, Aromatic aldehydes

Introduction

Schiff base ligands represent one of the most widely utilized classes of ligands in coordination chemistry.[1] Their complexes find many important catalytic applications ranging from asymmetric epoxidation,[2] Lewis acid assisted organic transformations,[3] ring opening of epoxides,[4] to various types of polymerization,[5-8] as well as their widespread use as model compounds for the study of the active sites of metallo-enzymes[9] and other applications such as; solid phase extraction of metal iones,[10] preparation of the ion selective electrodes[11-15] and etc. With attention to the importance of these ligands, each year many literatures have been published from synthesis of these compounds through two component reactions to their application in different fields for various purposes.

Recently multi-component reactions constitute an especially attractive synthetic strategy for rapid and efficient library generation due to the fast that the products are formed in a single step and the diversity can be achieved simply by varying the reacting components.[16] The importance of these one-pot three component reactions in such synthesis has been demonstrated in the Mannich, Ugi, Biginell and aza-Baylish-Hillman reactions.[17-20]

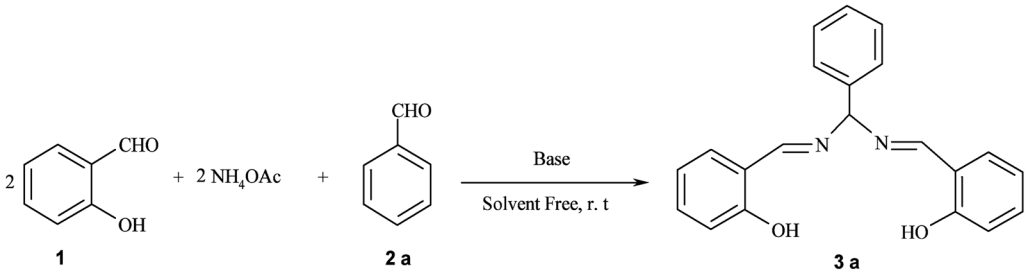
Some of multicomponent reactions have been reported in solvent free or solid phase reactions.[21] The development of cleaner technologies is a major in green chemistry. Among the several aspects of green chemistry, the reduction or replacement of volatile organic solvents from the reaction medium is of out most importance.[22] The solid-state reaction or solvent free reaction has many advantages: reduced pollution, low costs and simplicity in process and handling. These factors are especially important in industry.[23] For the increasing environmental and economical concerns in recent years, it is now essential for chemists to search environmentally reactions as many as possible. Because of these economical and environmental reasons and in conjunction with ongoing work in our laboratory on the preparation of double Schiff bases and their complexes,[24,25] here we decide to report the synthesis of various Schiff bases from salicylaldehyde and other aromatic aldehydes by one pot three component reactions at room temperature under mild and solvent free conditions.

Results and Discussion

In this reaction, the aromatic aldehydes were reacted with ammonium acetate salt in the presence of a base to afford *N,N'*-bis(salicylidene)-arylmethanediamine derivatives.

Firstly, 2 moles salicylaldehyde and 1 mol benzaldehyde were treated with 2 moles NH_4OAc at room temperature in the presence of a base under solvent free conditions, a yellow product was obtained in high yield and short reaction time (Scheme 1).

In order to study the effect of the base, the reaction was carried out in the presence of various bases. The results are indicated in Table 1. As can be seen in this Table, it was remarkably enhanced given a good to excellent yields of the desired products. The reaction in absence of a base was afforded the product with low yield even with an extension



1 2 a 3 a

Scheme 1

Table 1. The reaction of salicylaldehyde, benzaldehyde and ammonium acetate in the presence of various bases at room temperature

Entry	Base	Time/min	Yeild/%
1	$NaHCO_3$	20	55
2	NaO_2CCH_3	15	60
3	KOH	10	90
4	NaOH	10	90
5	Pyridine	10	35
6	NEt_3	120	90
7	None	Over Night	30

of the reaction time to over night (entry 7, Table 1).

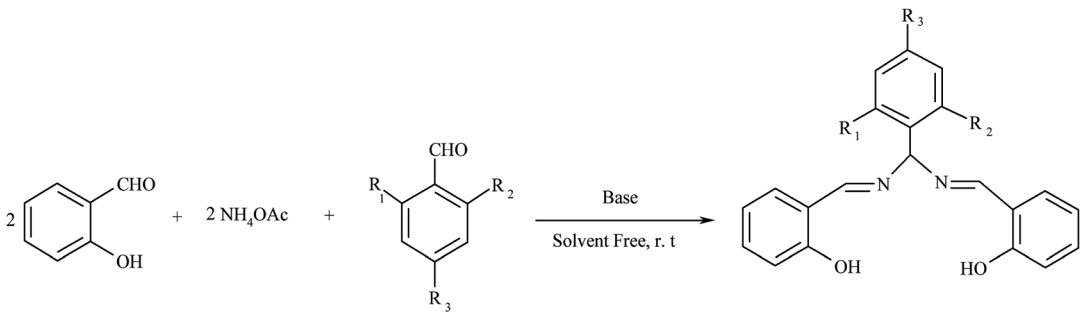
In respect to the results in Table 1, we infer that the base may play a main role in the reaction. As shown in this Table, potassium hydroxide, sodium hydroxide and triethylamine are the most effective bases in the reaction process. After the completion of the reaction, the yellow oil substance was obtained. Then, by dissolving the oil product in methanol and cooling, the yellow crystalline product was obtained in high yield.

In continuation of this study due to the generation of represented procedure, the various aromatic aldehydes with salicylaldehyde and ammonium acetate in the presence of triethylamine have been investigated (Scheme 2 and 3). The corresponding results are summarized in Table 2. In these reactions, the optimum amount of the used base as catalyst for all of the various aldehydes was 0.05 mol for 1 mol of salicylaldehyde. As shown in Table 2, at the same amount of catalyst, the condensation reaction of two different aldehydes with ammonium acetate were yielded novel Schiff bases **3a-3j** in the rang of 80-98% yields and reaction times between 4 and 15 minutes.

The structure of products has been identified by physical and spectroscopic data. In the IR spectra, the characteristic Schiff base C=N stretching frequency is formed in the region between υ = 1600-1700 cm^{-1} as a signal strong band. The OH stretching frequency is found at υ = 3250-3600 cm^{-1} with particular width. In the ^1H NMR spectra, the broad signal around the δ = 12.5-13.1 ppm are assigned to the protons of the hydroxyl groups. Two protons of CH=N have the same chemical shifts in δ = 8.50-8.90 ppm. The signal around the δ = 6.00-6.65 ppm is assigned to the protons of the NCHN and the signals around the δ = 6.60-7.90 ppm is assigned to the protons of aromatic rings (HC=CH).

Conclusion

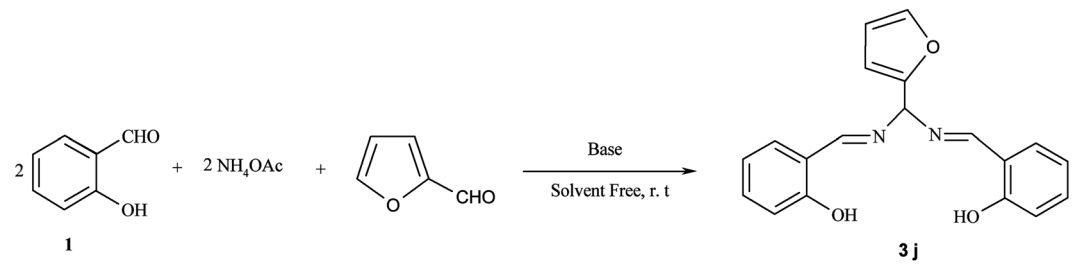
This efficient, mild and new method for preparation of double Schiff bases, *N,N'*-bis(salicylidene)-arylmethanediamines, have some advantages such as; availability of catalyst base, simplicity of the reaction, excellent yields of reaction products, short reaction times, simple work-up and environmentally friendly reaction conditions. These reactions have been occurred at room temperature under solvent free conditions.



1 **2a-i** **3a-i**

2a) $R_1 = R_2 = R_3 = H$
2b) R_1= OH, $R_2 = R_3 = H$
2c) R_1= OMe, $R_2 = R_3 = H$
2d) $R_1 = R_3$= OMe, $R_2 = H$
2e) $R_1 = R_2 = H$, R_3 = Me
2f) $R_1 = R_2 = H$, R_3 = Cl
2g) $R_1 = R_3$= Cl, $R_2 = H$
2h) $R_1 = R_2$ = Cl, $R_3 = H$
2i) $R_1 = R_2 = H$, $R_3 = NO_2$

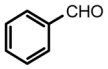
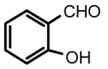
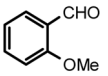
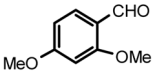
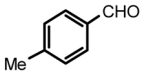
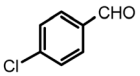
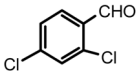
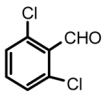
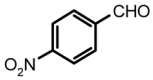
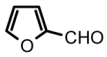
Scheme 2



1 **3j**

Scheme 3

Table 2. The reaction of salicylaldehyde, ammonium acetate and different aromatic aldehydes in the presence of NEt_3 at room temperature

Entry	Aromatic Aldehydes	Time/min	M. P/°C	Product	Yield/%
1		10	118-120	**3a**	90
2		7	164-166	**3b**	96
3		4	145-147	**3c**	98
4		12	90-92	**3d**	92
5		15	98-100	**3e**	80
6		8	113-115	**3f**	92
7		10	130-132	**3g**	95
8		10	154-156	**3h**	95
9		12	116-118	**3i**	88
10		12	87-89	**3j**	80

Experimental Section

Materials. All the materials were of commercial reagent grade. The salicylaldehyde and other aldehyde compounds were purified by standard procedures. The purity of them was determined by thin layer chromatography (TLC) and gas chromatography (GC).

Apparatus. IR spectra were recorded as KBr pellet on a Perkin-Elmer 781 Spectrophotometer and an Impact 400 Nickolet FTIR Spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in d_6-DMSO on a Bruker DRX-400 spectrometer for sample as indicated with tetramethylsilane as internal reference. Mass spectra were recorded on a Finnigan MAT 44S, by Electron Ionization (EI) mode with an ionization voltage of 70 eV. The elemental analyses (C, H, N) were obtained from a Carlo ERBA Model EA 1108 analyzer.

Melting points were obtained with a Yanagimoto micro melting point apparatus are uncorrected. The purity determination of the substrates and reactions monitoring by the solvent system were accomplished by TLC on silica-gel polygram SILG/UV 254 plates (from Merck Company).

General procedure for synthesis of *N,N′*-bis(salicylidene)-arylmethanediamines. To a mixture of salicylaldehyde (0.38 g, 3 mmol) and benzaldehyde (0.16 g, 1.5 mmol) was added NH_4OAc (0.25 g, 3.27 mmol) in the presence of the NEt_3 (0.12 mL) as a base by stirring in one portion. The mixture stirring is continued to 10 minutes. The progress of the reaction was monitored by TLC. After the completion of the reaction, oil pail yellow substance was obtained. Then, by dissolving the oil yellow mixture in 1.5 mL MeOH and cooling for one night, a yellow solid was precipitated. The solid product was filtered off and washed with cold MeOH. The crude product was purified by recrystallization from ethanol and the pure Schiff base, *N,N′*-bis(salicylidene)-phenylmethanediamine was obtained in 90% yield, m.p = 118-120 °C. The Schiff base products were identified by physical and spectroscopic data.

***N,N′*-Bis(salicylidene)-phenylmethanediamine (3a):** pail yellow solid; mp 118-120 °C; IR (KBr)/ υ (cm^{-1}) 3300-3500 (br, OH), 1625 (s, C=N), 1450, 1550 (Ar); ^{1}H NMR/DMSO/δ ppm: 6.1 (s, 1H, NCHN), 6.63-7.35 (m, 13H), 8.6 (s, 2H, HC=N), 12.80 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 90, 118, 119, 119.5, 127.5, 130.1, 130.3, 138, 161, 167; UV ($CHCl_3$)/λ_{max} (nm) 320 (w), 260 (s); MS: m/z = 331 (M^+ + 1, 3), 330 (M^+, 9), 210 (60), 209 (80), 91 (70), 89 (100), 77 (50); Anal. Calcd. For C. H. N: 76.36 (C), 5.45 (H), 8.48 (N); Found: 76.36 (C), 5.46 (H), 8.49 (N).

***N,N′*-Bis(salicylidene)-2-hydroxy-phenylmethanediamine (3b):** yellow solid; mp 164-166 °C; IR (KBr)/υ (cm^{-1}): 3250-3450 (br, OH), 1622 (s, C=N), 1450, 1550 (Ar); ^{1}H NMR/DMSO/δ ppm: 6.1 (s, 1H, NCHN), 6.6-7.5 (m, 12H), 8.5 (s, 2H, HC=N); 9.7 (s, 1H, OH); 12.96 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 90, 117, 119.6, 120, 127.5, 130.2, 130.3, 138, 165, 167; UV ($CHCl_3$)/λ_{max} (nm) 322 (w), 261 (s); MS: m/z = 348 (M^+ + 1, 2), 347 (M^+, 8), 225 (55), 224 (65), 107 (70), 108 (100), 77 (20); Anal. Calcd. For C. H. N: 72.62 (C), 5.46 (H), 8.07 (N); Found: 72.63 (C), 5.48 (H), 8.07 (N).

***N,N′*-Bis(salicylidene)-2-methoxy-phenylmethanediamine (3c):** yellow solid; mp 145-147 °C; IR (KBr)/υ (cm^{-1}) 3375-3625 (br, OH), 1625 (s, C=N), 1450, 1510 (Ar); ^{1}H NMR/DMSO/δ ppm: 2.3 (3H, OCH_3), 6.2 (s, 1H, NCHN), 6.7-7.4 (m, 12H), 8.6 (s, 2H, HC=N),12.90 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 60, 90, 117, 119, 119.2, 129.5, 130.2, 130.3, 138, 165, 170; UV ($CHCl_3$)/λ_{max} (nm) 324 (w), 262 (s); MS: m/z = 361 (M^+ + 1, 2), 360 (M^+, 6), 241 (50), 240 (80), 120 (70), 119 (100), 77 (15); Anal. Calcd. For C. H. N: 73.3 (C), 5.5 (H), 7.8 (N); Found: 72.69 (C), 5.48 (H), 8.07 (N).

***N,N′*-Bis(salicylidene)-2,4-dimethoxy-phenylmethanediamine (3d):** yellow solid; mp 90-92 °C; IR (KBr)/υ (cm^{-1}) 3300-3600 (br, OH), 1620 (s, C=N), 1450-1510 (Ar); ^{1}H NMR/DMSO/δ ppm: 2.4 (s, 6H, 2 OCH_3), 6.3 (s, 1H, NCHN), 6.8-7.7 (m, 11H), 8.7 (s, 2H, HC=N), 12.95 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 60, 92, 117, 119, 119.2, 129.5, 130.2, 146.2, 147, 166, 170; UV ($CHCl_3$)/λ_{max} (nm) 324 (w), 262 (s); MS: m/z = 390 (M^+ + 1, 3), 389 (M^+, 9), 270 (47), 269 (78), 149 (70), 148 (100), 77 (20); Anal. Calcd. For C. H. N: 70.95 (C), 5.398 (H), 7.19 (N); Found: 70.97 (C), 5.40 (H), 7.19 (N).

***N,N′*-Bis(salicylidene)-4-methyl-phenylmethanediamine (3e):** pail yellow solid; mp 98-100 °C; IR (KBr)/υ (cm^{-1})

3200-3500 (br, OH), 1623 (s, C=N),1495, 1573 (Ar); ^{1}H NMR/DMSO/δ ppm: 2.1 (s, 3H, CH_3), 6.3 (s, 1H, NCHN), 6.9-7.4 (m, 12H), 8.9 (s, 2H, HC=N), 13.1 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 21.59, 90.24, 117, 119.53, 119.88, 127.5, 130.3, 133.94, 138, 139, 161, 167; UV ($CHCl_3$)/λ_{max} (nm) 320 (w), 261 (s); MS: m/z = 345 (M^+ + 1, 4), 344 (M^+, 9), 224 (70), 223 (82), 104 (85), 103 (100), 77 (10); Anal. Calcd. For C. H. N: 73.3 (C), 5.5 (H), 7.8 (N); Found: 72.69 (C), 5.48 (H), 8.07 (N).

***N,N′*-Bis(salicylidene)-4-chloro-phenylmethanediamine (3f):** pail yellow solid; mp 115-117 °C; IR (KBr)/υ (cm^{-1}) 3300-3550 (br, OH), 1625 (s, C=N),1486, 1572 (Ar), 790 (C-Cl); ^{1}H NMR/DMSO/δ ppm: 6.2 (s, 1H, NCHN), 6.9-7.9 (m, 12H), 8.9(s, 2H, HC=N), 12.9 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 90.2, 117, 119.33, 120.88, 127.5, 130.3, 132.94, 136, 144, 165, 169; UV ($CHCl_3$)/λ_{max}(nm) 320 (w), 261 (s); MS: m/z = 366.5 (M^+ + 2, 2), 364.5 (M^+, 7), 245.5 (50), 243.5 (74), 125.5 (64), 123.5(100), 77 (18); Anal. Calcd. For C. H. N: 69.13 (C), 4.67 (H), 7.68 (N); Found: 69.14 (C), 4.69 (H), 7.68 (N).

***N,N′*-Bis(salicylidene)-2,4-dichloro-phenylmethanediamine (3g):** pail yellow solid; mp 130-132 °C; IR (KBr)/υ (cm^{-1}) 3400-3600 (br, OH), 1619 (s, C=N), 1490, 1570 (Ar), 785 (C-Cl); ^{1}H NMR/$DMSO_3$/δ ppm: 6.3 (s, 1H, NCHN), 6.7-7.5 (m, 11H), 8.7 (s, 2H, HC=N), 12.5 (s, H, 2 OH); ^{13}C NMR/DMSO/δ ppm: 90.6, 117, 119.33, 120.88, 127.5, 130.3, 133.94, 138, 149, 165, 170; UV ($CHCl_3$)/λ_{max} (nm) 323 (w), 262 (s); MS: m/z = 401 (M^+ + 2, 3), 399 (M^+, 5), 280 (58), 278 (84), 161 (64), 159 (100), 77 (23); Anal. Calcd. For C. H. N: 63.16 (C), 4.00 (H), 7.00 (N); Found: 63.16 (C), 4.02 (H), 7.03 (N).

***N,N′*-Bis(salicylidene)-2,6-dichloro-phenylmethanediamine (3h):** pail yellow solid; mp 154-156 °C; IR (KBr)/υ (cm^{-1}) 3400-3600 (br, OH), 1619 (s, C=N), 1490, 1576 (Ar), 760 (C-Cl); ^{1}H NMR/DMSO/δ ppm: 6.65 (s, 1H, NCHN), 6.7-7.6 (m, 11H), 8.9 (s, 2H, HC=N), 13.7 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 95, 119.30, 120.89, 127.5, 130.3, 135.94, 138, 151, 165, 170; UV ($CHCl_3$)/λ_{max} (nm) 323 (w), 262 (s); MS: m/z = 401 (M^+ + 2, 3), 399 (M^+, 5), 280 (60), 278 (85), 161 (67), 159 (100), 77 (23); Anal. Calcd. For C. H. N: 63.16 (C), 4.00 (H), 7.00 (N); Found: 63.16 (C), 4.02 (H), 7.03 (N).

***N,N′*-Bis(salicylidene)-4-nitro-phenylmethanediamine (3i):** yellow solid; mp 116-118 °C; IR (KBr)/υ (cm^{-1}) 3400-3600 (br, OH), 1622 (s, C=N), 1480, 1570 (Ar), 1350, 1530 (N=O); ^{1}H NMR/DMSO/δ ppm: 6.4 (s, 1H, NCHN), 6.5-7.6 (m, 12H), 8.9 (s, 2H, HC=N), 12.64 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 89.9, 117.30, 119.6, 120, 124.9, 132.94, 134.2 148, 148.9, 160.9, 167; UV ($CHCl_3$)/λ_{max} (nm) 323 (w), 262 (s); MS: m/z = 376 (M^+ + 1, 6), 375 (M^+, 10), 255 (65), 254 (80), 134 (85), 134 (100), 91 (20); Anal. Calcd. For C. H. N: 67.2 (C), 4.5 (H), 11.2 (N); Found: 67.3 (C), 4.52 (H), 11.2 (N).

***N,N′*-Bis(salicylidene)-2-furylmethanediamine (3j):** pail yellow solid; mp 87-89 °C; IR (KBr)/υ (cm^{-1}) 3400-3550 (br, OH), 1622 (s, C=N), 1480, 1510 (Ar); ^{1}H NMR/DMSO/δ ppm: 6.4 (s, 1H, NCHN), 6.5-7.6 (m, 11H), 8.5 (s, 2H, HC=N), 12.8 (s, 2 OH); ^{13}C NMR/DMSO/δ ppm: 94.9, 117, 119.6, 122, 133.9, 135.94, 136.2, 148.9, 160.9, 170; UV ($CHCl_3$)/λ_{max} (nm) 319 (w), 260 (s); MS: m/z = 321 (M^+ + 1, 4), 320 (M^+, 12), 200 (75), 79 (55), 78 (100), 91 (30); Anal. Calcd. For C. H. N: 71.25 (C), 5.00 (H), 8.75 (N); Found: 71.26 (C), 5.02 (H), 8.75 (N).

Acknowledgments. We are grateful to The University of Kashan Research Council for the partial support of this work.

References

1. Nimitsiriwat, N.; Marshall, E. L.; Gibson, V. G.; Elsegood, M. R. J.; Dale, S. H. *J. Am. Chem. Soc.* **2004**, *26*, 13598.
2. (a) Samsel, E. G.; Srinivasan, K.; Kochi, J. K. *J. Am. Chem. Soc.* **1985**, *107*, 7606. (b) Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801. (c) Irie, R.; Noda, K.; Ito, Y.; Matsumoto, N.; Katsuki, T. *Tetrahedron Lett.* **1990**, *31*, 7345. (d) Sigman, M. S.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1998**, *120*, 4901.
3. Atwood, D. A.; Jegier, J. A.; Rutherford, D. *J. Am. Chem. Soc.* **1995**, *117*, 6779.
4. Sharghi, H.; Naeimi, H. *Bull. Chem. Soc. Jpn.* **1999**, *72*, 1525.
5. Younkin, T. R.; Connor, E. F.; Henderson, J. I.; Friedrich, S. K.; Grubbs, R. H.; Bansleben, D. A. *Science* **2000**, *287*, 460.
6. Satio, J.; Mitani, M.; Matsui, S.; Mohri, J.; Kojoh, S.; Kashiwa, N.; Fujita, T. *Angew. Chem. Int. Ed.* **2001**, *40*, 2918.
7. Jones, D. J.; Gibson, V. C.; Green, S. M.; Maddox, P. J. *J. Chem. Soc. Chem. Commun*. **2002**, *10*, 1038.
8. O'Reilly, R. K.; Gibson, V. C.; White, A. J. P.; Williams, D. J. *J. Am. Chem. Soc.* **2003**, *125*, 8450.
9. (a) Berkassel, A. *Bioorg. Chem.* **1991**, *19*, 101. (b) Feichtinger, D.; Plattner, D. A. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1718.
10. Shamsipur, M.; Ghiasvand, A. R.; Sharghi, H.; Naeimi, H. *Anal. Chim. Acta* **2000**, 271.
11. Shamsipur, M.; Sadeghi, S.; Naeimi, H.; Sharghi, H. *Polish J. Chem*. **2000**, *74*, 231.
12. Alizadeh, N.; Ershad, S.; Naeimi, H.; Sharghi, H.; Shamsipur, M. *Fresenius J. Anal. Chem*. **1999**, *365*, 511.
13. Mazlum Ardakany, M.; Ensafi, A. A.; Naeimi, H.; Dastanpour, A.; Shamelli, A. *Sensors and Actuators B* **2003**, 441.
14. (a) Khorrami, A. R.; Naeimi, H.; Fakhari, A. R. *Talanta* **2004**, *64*, 13. (b) Shamsipur, M.; Saeidi, M.; Yari, A.; Yaganeh-Faal, A.; Mashhadizadeh, M. H.; Azimi, Gh.; Naeimi, H.; Sharghi, H. *Bull. Korean Chem. Soc.* **2004**, *25*, 629.
15. Shamsipur, M.; Yousefi, M.; Hosseini, M.; Ganjali, M. R.; Sharghi, H.; Naeimi, H. *Anal. Chem*. **2001**, *73*, 2869.
16. Azizian, J.; Mohammadi, A. A.; Karimi, A. R.; Mohammadizadeh, M. R. *J. Org. Chem*. **2005**, *70*, 350.
17. Ugi, I.; Domling, A.; Werner, B. *J. Heterocyclic Chem.* **2000**, *37*, 697.
18. Ugi, I. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 810.
19. Kappe, C. O. *Eur. J. Med. Chem*. **2000**, *35*, 1043.
20. Balan, D.; Adolfsson, H. *Tetrahedron Lett.* **2003**, *44*, 2521.
21. Hartmut, R.; Gunther, J. *Tetrahedron Lett.* **1998**, *39*, 2729.
22. Rajinder, S. V.; Vasudevan, V. N. *Pure Appl. Chem.* **2001**, *73*, 1309.
23. Tanka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 102.
24. Ghoreishi, S. M.; Naeimi, H.; Navid, M. D. *Bull. Korean Chem. Soc.* **2005**, *26*, 548.
25. (a) Mazloum Ardakani, M.; Jamshidpoor, M.; Naeimi, H.; Heidarnezhad, A. *Bull. Korean Chem. Soc.* **2006**, *27*, 1127. (b) Naeimi, H.; Sharghi, H.; Salimi, F.; Rabiei, Kh. *Heteroatom Chem*. **2008**, *19*, 43.