Asian Journal of Chemistry; Vol. 23, No. 4 (2011), 1417-1420

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

MINI REVIEW

Progress in Synthesis of α-Aminophosphonic Acid(ate) Analogues

BING JING LIU[1], CHANG CHUN CEN[1], MING SHU WU[1,*] and DU LIN KONG[2]

[1]College of Chemistry and Chemical Engineering, Hainan Normal University, Haikou 571158, Hainan Province, P.R. China
[2]Key Laboratory of Tropical Medicinal Plant Chemistry Ministry of Education, Hainan Normal University, Haikou 571158, Hainan Province, P.R. China

*Corresponding author: Fax: +86 898 65889422; Tel: +86 898 65889422; E-mail: wumingshu@126.com

(*Received*: 20 March 2010; *Accepted*: 22 November 2010) AJC-9326

As the isosteric or bio-isosteric analogues of the corresponding α-amino acids, α-aminophosphonic acids have diversed and interested in biological and biochemical properties. This article reviews the recent studies on the progress in synthesis of α-aminophosphonates, which were reviewed with 81 references.

Key Words: α-Aminophosphonic acid, Synthesis, Progress.

INTRODUCTION

Aminophosphonic acid, as phosphorus analogues of natural amino acids[1-3], the third category of amino acid, which were found in biological after following amino sulfonic acid and amino carboxylic acid[4]. Especially the phosphorus atom with tetrahedral structure has played an important part in the development of organic chemistry in recent several decades. In addition, it has already been found a number of important physiological functions too. It has excellent resistance to plant viruses[5-11], bactericidal[12-17], weeding[18-20], plant growth regulators[21-24], antioxidant[25,26], damage to biological membranes[27-29], enzyme inhibition[30,31], antitumor[32] and other wide range of biological activity. Besides, with the role of prevention of metal corrosion[33]. Many organic chemist committed to the synthesis of aminophosphonic acid research and development in some extraordinary important ways.

In this paper, the synthesis of α-amino-phosphonic acid(ate) since year 2000 has been reviewed.

Synthesis from aldehyde(ketone), amine and phosphite esters: The first step is aldehyde(ketone) and the amine to imine or by $SnCl_2$ deoxidized nitrile compounds and then obtained α-aminophosphonic acid(ate)[34-44] with the addition of sub-phosphonate, yield of 25-98 % and this is a very wide method of synthesis.

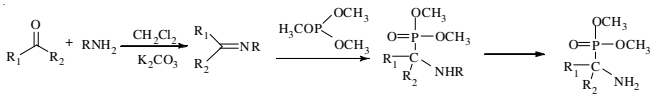

Fig. 1. Route of synthesis from aldehyde (or ketone), amine and phosphite esters

The solvents used H_2O[45-48],$ClCH_2CH_2Cl$[48-52], THF[48,53,54], DMF[55], phMe[56], F_3CCH_2OH[57], MeCN[58-60], Me_2CO[61]. The catalyst in step to restore used Al_2O_3[62], MeS^+Br^-[63], $Mg(ClO_4)_2$[64], CdI_2[65], Ga[66], Mg[67], $MgSO_4$[67], $(NH_4)_2Ce(NO_3)_6$[53], $TaCl_5$-SiO_2[50], $ZrOCl_2$[68], $InCl_3$[69] for better yield.

Lv *et al.*[70] reported that a series of α-aminophosphonates bearing the ferrocenyl moiety were obtained by the addition of diethyl phosphite to an azomethine bond of Schiff bases. X-ray crystallography of 3h reveals that it belongs to triclinic system P-1 space group, with a = 0.9728 nm, b = 1.1056 nm, c = 1.3713 nm, α = 108.445(2)°, β = 98.649(2)°, γ = 104.890(2)°, final R = 0.049, wR = 0.1152.

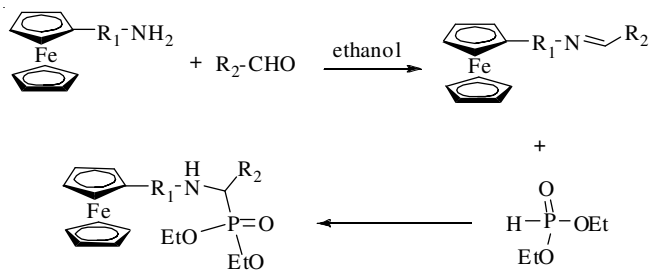

Fig. 2. Synthesis of novel ferrocenyl α-aminophosphonic acid(ate)

Song *et al.*[71] have recently reported that some novel O,O'-diakyl-α-(6-methoxybenzothiazol-2-ylamino)-4-fluoro-phenylphosphonates (**3**) have been synthesized through the reaction of Schiff base with dialkyl phosphite. The crystal of compound A (R = *i*-Pr) belongs to tetragonal with space group $I_4(1)/a$, a = 2.1055(3) nm, b = 2.1055(3) nm, c = 2.0521(5)

nm, α = 90.00°, β = 90.00°, γ = 90.00°, V = 0.9098(3) nm^3, Z = 16, Dc = 1.321 mg/m^3, μ = 0.250 mm^{-1}, F(000) = 3808. There exists an intramolecular hydrogen bond [N(2)-H(2)···O(1)] in the molecule.

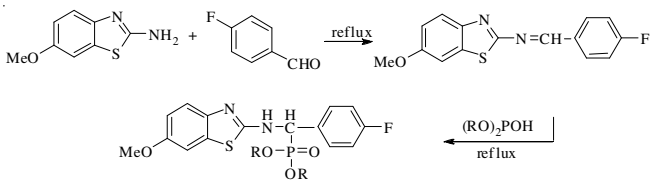

Fig. 3. Synthesis of α-aminophosphonic acid derivitaves

In addition, the reaction mechanism was proposed by Bhagat and Chakraborti[64].

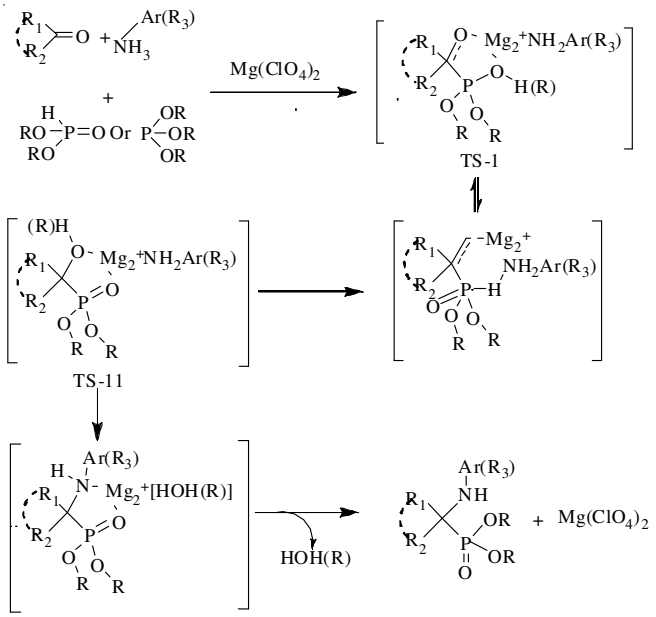

Fig. 4. Reaction mechanism of synthesis from aldehyde(ketone), amine and phosphite esters

From the preparation of Grignard reagent: This method has used Grignard reagent and imine phosphonate in THF or Et_2O as solvent to generate the corresponding α-aminophosphonic acid(ate)[72-74], the product and Grignard reagent are continued to generate *tert*-amine ring. Yield of 68-97 % in the method.

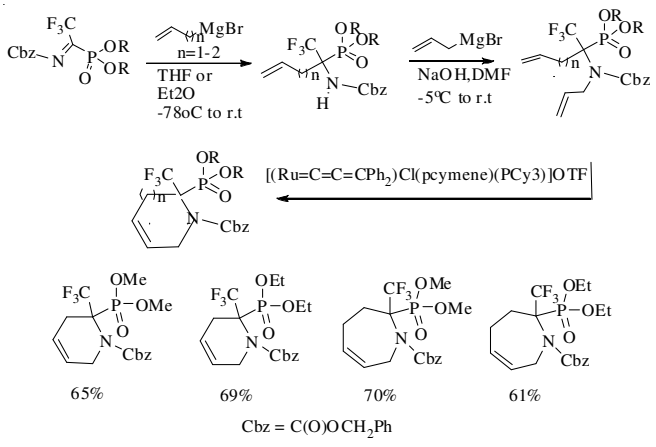

Fig. 5. Route of preparation of Grignard reagent

Synthesis through sulfoxide and chloride: The reaction of aldehydes-(ketones), sulfoxides, chloride and phosphite were studied by Chen and Yuan[75], following A, B, C 3 routes to synthesis intermediate product M, then M has been hydrolyzed for α-amino phosphonic acid(ate). The synthesis has a short routes and sulfoxide is a very good ligand and the alkylating agent, so the way has a better yield (83-85 %).

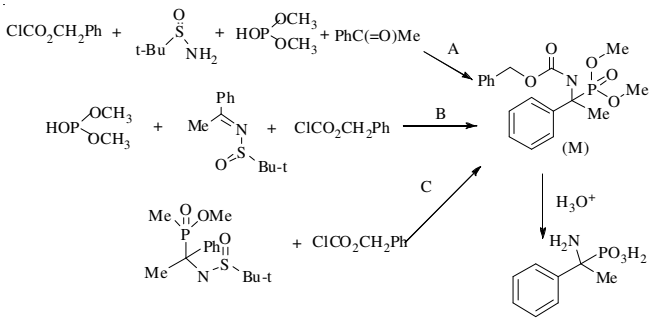

Fig. 6. Route of synthesis through sulfoxide and chloride

Preparation through the iodomethane and the diazo reaction: The aldehydes(ketones), chloride, phosphorous acid and iodomethane in the corresponding catalytic with the diazo methane have generated α-aminophosphonic acid(ate)[76]. But due to being used in explosives, such as diazo, this method is restricted to use.

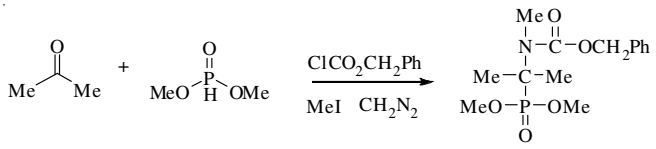

Fig. 7. Route of synthesis through sulfoxide and chloride

Through the reaction of alkynes and amine: This method is the reaction of amines with alkynes in the catalytic Me_2AlCl, generated corresponding onco-amine that is deoxidized by H_2/Pd to generate the corresponding α-amino phosphonic acid(ate)[53], production of this method is a higher rate of between 68-97 %.

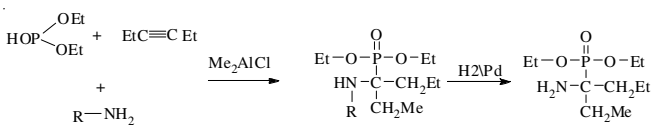

Fig. 8. Route through the reaction of alkynes and amine

Through quaternary ammonium synthesis: The sulfonate of quaternary ammonium and phosphite at a catalyst of LiCl and THF as solvent have responsed to α-aminophosphonic acid(ate)[74], with a higher yield of the reaction, between 69-75 %.

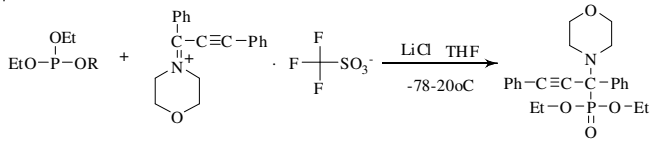

Fig. 9. Route through quaternary ammonium synthesis

Synthesis through cyclopropane lactone: Jászay *et al.*[77] reported the phosphonate replaced cyclopropane lactone then ammoniated and protected by hydroxyl silicon ether. The reaction undergoes Hoffmann degradation, which took off the protection base and acid hydrolyzed to α-aminophosphonic acid(ate), the yield of isomers rate is 82 %.

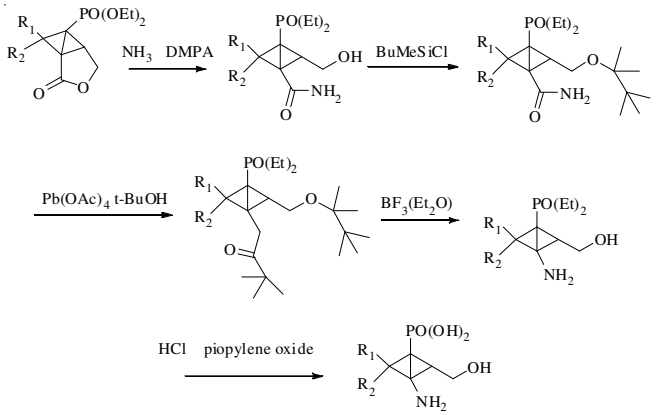

Fig. 10. Cyclopropane lactone leading to the formation of α-aminophosphonic acid(ate)

Synthesis from CS_2 and hydrazine: Cheng *et al.*[78] have used hydrazine and CS_2 in the solvent of acetic acid to synthesis a series of s-triazolo[2,1,-b]-1',3',4'-thiadiazole compounds that responsed with DIPPH to series of N-containing triazolo thiadiazole of the α-amino phosphonate derivatives, the reaction time is 7-8 h.

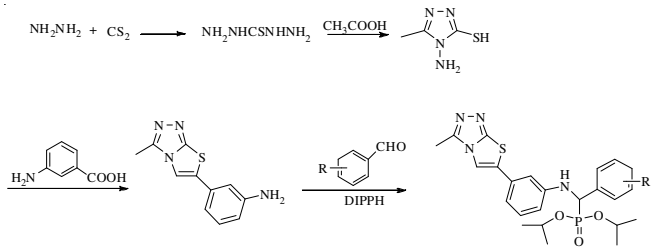

Fig. 11. Route of Synthesis from CS_2 and hydrazine

Preparation through the N-tosyl aldimines: Treatment of N-tosyl aldimines with dialkyl trimethylsilyl phosphites at 0 ºC in the presence of iodine as a catalyst afforded the corresponding sulfonamide phosphonates in excellent yields within 1.5 to 2.5 h was carried out by Biswanath *et al.*[79].

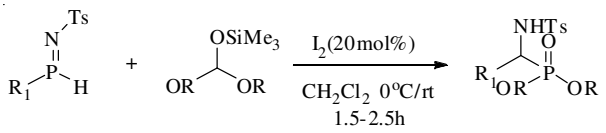

Fig. 12. Route of Preparation through the N-Tosyl Aldimines

Through the reaction of ammonium: Aminomethylphosphonic acid is synthesized by using the following material H_3PO_4, NH_4Cl and HCHO. The influences of the ratio of material, reaction temperature and time on the yield are also studied by Hu *et al.*[80]. The yield is 60-86 %. Due to easier operation, lower cost and accessible material, it is an valuable production with promising future.

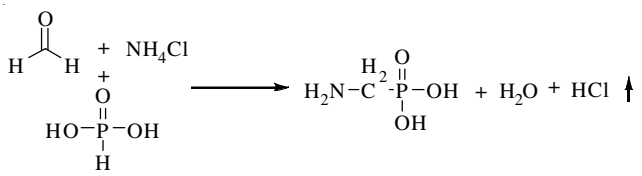

Fig. 13. Synthesis of α-aminophosphonic acid(ate) by NH_4Cl

The α-aminophosphonates were synthesized by Wu and Zhang[81] under solvent-free conditions on an acidic silica gel support using aromatic aldehydes, diethyl phosphite and anhydrous ammonium acetate as starting materials in moderate yields 40-83 %.

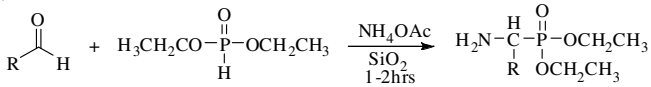

Fig. 14. NH_4OAc leading to the formation of α-aminophosphonic acid(ate)

To sum up, one can see that studies on the synthesis of phosphonate are extremely invigorates in recent years and increasing new compounds, new synthetic methods, emerging continued synthetic route. Both high-yield and high selectivity of the new ways, besides the reaction mechanism, the reaction steps are studied in-depth. Applications has been extended to α-amino acid re-modification of the entire skeleton, by changing P, α carbon and the amine part of the group structure or through the introduction of the special nature of the atom has synthesized new compound, It's a great promising to receive active compounds by directly chemical synthesis and develop new drugs with high-efficiency, low-toxicity, low-residue.

REFERENCES

1. M. Horiguchi and M.Kandasu, *Nature*, **184**, 901 (1959).
2. J.A. Alhadeff and G.D. Davies, *Biochemistry*, **9**, 4866 (1970).
3. B.A. Song and M.G. Jiang, *Chin. J. Org. Chem.*, **24**, 843 (2004).
4. Z.Y. Cao, Z.C. Fan, W.Z. Shen, L.L. Chen and J.C. Xu, *Chin. J .Org. Chem.*, **9**, 543 (1989).
5. H.K. Yung, J.H. Shim, J.Z. Wu, W.D. Zhong, Z. Hong and J.L. Girardet, *J. Med. Chem.*, **48**, 2867 (2005).
6. B.A. Song, M.G. Jiang, Y.L. Wu, X.Q. He, Y. Song, L.H. Jin, G. Liu and D.Y. Hu, *Chin. J .Org. Chem.*, **23**, 967 (2003).
7. H.Y. Li, R.Y. Chen and K.T. Ren, *Sci. China, Ser. B.*, **27**, 112 (1997).
8. Z.G. Li, R.Q. Huang, Z. Yang and H.Y. Li, *Chem. J. Chin. Univ.*, **19**, 1970 (1998).
9. Z.G. Li, R.Q. Huang and R.L. Shao, *Chin. J. Org. Chem.*, **19**, 519 (1999).
10. Q. Dai and Chen Ru yu. *Chem. J . Chin. Univ.*, **18**, 1992 (1997).
11. L. Cao, Y.G. Wang, X.J. Song and G.H. Liu, *Chin. J . Org. Chem.*, **25**, 1007 (2005).
12. A.B. Czerwonka, B.B. Lejczak and P. Kafarski, *Amino Acids*, **12**, 101 (1997).
13. C.M. Qi, Y.F. Wang, G.X. Zhang, X.F. Guo, X.X. Chen, Y. Ling and W.Y. Chen, *Chin. J. Med. Chem.*, **11**, 329 (2001).
14. H.Z. Yang, J.W. Wang and M.R. Cheng, *Chem. J. Chin. Univ.*, **10**, 254 (1989).
15. K.S. Zhang, L.J. Mu and Y.X. Long, *Chem. J. Chin. Univ.*, **2**, 741 (1999).
16. S.M. Lu and R.Y. Chen, *Chin. J. Synth. Chem.*, **3**, 270 (1999).
17. F.M. Sun, D.Q. Shi, M.M. Tian and X.S. Tan, *Chem. J. Chin. Univ.*, **27**, 2092 (2006).
18. R.Y. Chen and Q. Dai, *Sci. China, Ser. B.*, **25**, 591 (1995).
19. D.Q. Shi and R.Y. Chen, *Chin. J. Appl. Chem.*, **19**, 780 (2002).
20. J. Tanaka and E.J. Kuwnao, *Fac. Agric. Kyushu Univ.*, **30**, 20 (1986).
21. X.F. Liu, Y. Wang and Z.X. Chen, *Chin. J. Appl. Chem.*, **1**, 40 (2005).
22. P. Kafarski, B. Lejczak, R. Tyka, L. Koba, E. Pliszczak and P. Wieczorek, *J. Plant. Growth Regul.*, **14**, 199 (1995).

23. K. Bielecki and Dzimaska, *J. Biosci.*, **56**, 995 (2001).
24. J. Yang, B.X. Lu and Y.G. Wang, *Chin. J. Appl. Chem.*, **19**, 117 (2002).
25. X.Y. Mei, H. He and J.L. Yuan, *Hubei Agric. Sci.*, **11**, 34 (1998).
26. H. Kleszczynska, J. Sarapuk and D. Dziamska, *Cell Mol. Biol. Lett.*, **69**, 271 (2001).
27. H. Kleszczynska, J. Sarapuk and A. Dziamaks, *Cell Mol. Biol. Lett.*, **5**, 415 (2000).
28. J. Sarpauk, K. Bielecki and Z. Trela, *Acta Soc. Bot. Pol.*, **71**, 223 (2002).
29. Z. Trela, H. Kleszczynska and J. Sarpaku, *J. Biosci.*, **56**, 838 (2001).
30. B. Stowasser, K.H. Budta, J.Q. Li, A. Peymana and D. Ruppert, *Tetrahedron Lett.*, **33**, 6625 (1992).
31. F.R. Atherton, M.J. Hali, C.H. Hassall, R.W. Lambert and P.S. Ringrose, *Agents Chemother.*, **15**, 677 (1979).
32. X.J. Liu, R.Y. Chen and Y.Y. Yang, *Chem. J. Chin. Univ.*, **23**, 1299 (2002).
33. X.L. Gao and C.F. Zhu, *Mater. Prot.*, **37**, 19 (2004).
34. B. Kaboudin and K. Moradi, *Tetrahedron Lett.*, **46**, 2989 (2005).
35. B.C. Ranu and A. Hajra, *Green Chem.*, **4**, 551 (2002).
36. P.Y. Zhuang, F.L. Rui and P. Jun, *Chem. Lett.*, **34**, 1042 (2005).
37. P. Sibille, S. Lopez, I. Brabet, O. Valenti, N. Oueslati, Fl. Gaven, C. Goudet, H.O. Bertrand, J. Neyton, J.M. Marino, M. Amalric, J.P. Pin and F.C. Acher, *J. Med. Chem.*, **50**, 3585 (2007).
38. L.S. Boulos, R. Shabana and Y.M. Shaker, *Heteroatom Chem.*, **11**, 57 (2000).
39. M.M. Kabachnik, E.V. Zobnina and P. Beletskaya, *Synlett*, 1393 (2005).
40. F. Meyer, A. Laaziri, A.M. Papini, J. Uziel and S. Juge, *Tetrahedron*, **60**, 3593 (2004).
41. S. Bhagat and K.A. Chakraborti, *J. Org. Chem.*, **72**, 1263 (2007).
42. M. Xia and Y.D. Lu, *Ultrason. Sonochem.*, **14**, 235 (2007).
43. F. Habib, I. Nasser and S. Sara, *Synthesis*, 2692 (2004).
44. S. Chandrasekhar, C. Narsihmulu, S.S. Sultana, B. Saritha and S.J. Prakash, *Synlett*, 505 (2003).
45. M.M. Kabachnik, T.N. Ternovskaya, E.V. Zobnina and I.P. Beletskaya, **38**, 484 (2002).
46. P.P. Sun, X. Yang and Z.X. Hu, *Chem. Inform.*, **4**, 240 (2006).
47. L.E. Kaïm, L. Grimaud and S. Hadrot, *Tetrahedron Lett.*, **47**, 3945 (2006).
48. J.C. Wilt, M. Pink and J.N. Johnston, *Chem. Commun.*, **35**, 4177 (2008).
49. S. Simon and R. Joachim, *Synthesis*, 2011 (2001).
50. S. Chandrasekhar, S.J. Prakash, V. Jagadeshwar and C. Narsihmulu, *Tetrahedron Lett.*, **42**, 5561 (2001).
51. M. Kabachnic, E. Zobnina, V. Pavlov, I. Konstantinov, G. Ponomarev and I. Beletskaya, *Russ. Chem. B*, **54**, 262 (2005).
52. E.D. Matveeva, T.A. Podrugina, M.V. Prisyazhnoi, I.N. Rusetskaya and N.S. Zefirov, *Russ. Chem. B*, **56**, 798 (2007).
53. E. Haak, I. Bytschkov and S. Doye, *Eur. J. Org. Chem.*, 457 (2002).
54. A. Atmani, J.C. Combret and C. Malhiac, *Tetrahedron Lett.*, **41**, 6045 (2000).
55. P.M. Cullis and M.J. Harger, *J. Chem. Soc. Perkin Trans. II,* 1538 (2002).
56. I.I. Stoikov and S.A. Repejkov, *Heteroatom Chem.*, **11**, 518 (2000).
57. E.D. Matveeva, T.A. Podrugina, M.V. Prisyazhnoi and N.R. Zefirov, *Vestn. Russ. Chem. Bull.*, **56**,798 (2007).
58. F. Xu, Y.Q. Luo, J.T. Wu and Q. Shen, *Heteroatom Chem.*, **17**, 389 (2006).
59. Z.P. Zhan and J.P. Li, *Synth. Commun.*, **35**, 2501 (2005).
60. E.D. Matveeva, T.A. Podrugina, E.V. Tishkovskaya and D. Elena, *Synlett*, 2321 (2003).
61. D.C. Danila, X.Y. Wang, H. Hubble, I.S. Antipin and E. Pinkhassik, *Bioorg. Med. Chem. Lett.*, **18**, 2320 (2008).
62. K. Babak and R. Nazari, *Tetrahedron Lett.*, **42**, 8211 (2001).
63. S. Kudrimoti and V.R. Bommena, *Tetrahedron Lett.*, **46**, 1209 (2005).
64. S. Bhagat and A.K. Chakraborti, *J. Org. Chem.*, **72**, 3158 (2007).
65. M. Kabachnik, E. Zobnina and I. Beletskaya, *Russ. J. Org. Chem.*, **41**, 505 (2005).
66. P.P. Sun, Z.X. Hu and Z.H. Huang, *Synth. Commun.*, **34**, 4293 (2004).
67. E.D. Matveeva, T.A. Podrugina, E.V. Tishkovskaya, L.G. Tomilova and S. Nikolay, *Synlett*, 2321 (2003).
68. S. Bhagat and A.K. Chakraborti, *J. Org. Chem.*, **73**, 6029 (2008).
69. D. Biswanath, K. Damodar and N.A. Bhunia, *J. Org. Chem.*, **109**, 257 (2009).
70. E.N. Lv, Y. Xu, C.L. Ran, H.H. Liu, C.J. Qiao, Y.T. Fan and Y. Zhu, *Chin. J. Org. Chem.*, **28**, 1375 (2008).
71. B.A. Song, Y.P. Hong, L.H. Jin, S.Z. Yang and H.H. Zhi, *Chin. J. Org. Chem.*, **25**, 1001 (2005).
72. S.N. Osipov, O.I. Artyushin, A.F. Kolomiets, C. Bruneau, M. Picquet and P.H. Dixneuf, *Eur. J. Org. Chem.*, 3891 (2001).
73. S.N. Osipov, O.I. Artyushin and A.F. Kolomiets, *Mendeleev. Commun.*, **10**, 192 (2000).
74. M. Reisser, A. Maier and G. Maas, *Eur. J. Org. Chem.*, 2071 (2003).
75. Q.Y. Chen and C.Y. Yuan, *Synthesis*, 3779 (2007).
76. P.M. Cullis and H.J. Martin, *J. Chem. Soc., Perkin Trans. II*, 1538 (2002).
77. Z.M. Jászay, G.M. Keserü, G. Clementis, I. Petneházy, K. Kováts and L. Toke, *Heteroatom Chem.*, **12**, 90 (2001).
78. L.X. Cheng, L.L. Guo, Y.C. Cao, S.X. Rong, C.L. Zhao and Y. Fen, *Chin. J. Org. Chem.*, **26**, 233 (2006).
79. D. Biswanath, B. Penagaluri, K. Maddeboina, V. Boyapati and C.R. Gandolla, *J. Org. Chem.*, **74**, 4393 (2009).
80. M.J. Hu, Z.W. Chang and Y.Y. Ding, *Guizhou. Chem. Ind.*, **29**, 15 (2004).
81. M.S. Wu and X.Z. Zhang, *J. Chem. Res.*, **8**, 562 (2008).