Regioselective and Green Synthesis of Nitro Aromatic Compounds Using Polymer-Supported Sodium Nitrite/$KHSO_4$

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ABSTRACT: Polymer supported reagents have become the subject of considerable and increasing interest as insoluble materials in the organic synthesis. Use of polymeric reagents simplifies routine nitration of aromatic compounds because it eliminates traditional purification. In this article, the use of readily available cross-linked poly(4-vinylpyridine) supported sodium nitrite, [P_4-Me] NO_2, as an efficient polymeric nitrating agent in the presence of $KHSO_4$ is described. A good range of available aromatic compounds were also subjected to nitration in the presence of [P_4-Me] $NO_2/KHSO_4$. This reagent is regioselective and chemoselective nitrating polymeric reagent for activated aromatic rings. In this procedure, the work-up is easy, and the spent polymeric reagent is easily regenerated and reused. © 2011 Wiley Periodicals, Inc. J Appl Polym Sci 120: 2830–2834, 2011

Key words: nitration; aromatic compounds; polymeric reagent; nitro group

INTRODUCTION

Electrophilic aromatic nitration is one of the most important reactions in organic Chemistry. Nitro aromatic compounds are useful intermediates for the preparation of other compounds, particularly amines by reduction of nitro groups.[1–5]

Nitroaromatic compounds are widely studied because of their application as solvents, dyes, pharmaceuticals, perfumes, agrochemicals, explosives, and plastics in the industry.[2]

There are many useful reagents for nitration such as concentrated nitric acid,[6] mixtures of nitric acid with sulfuric acid,[7] nitric acid in acetic anhydride,[8] nitrate salts in trifluoroacetic anhydride,[9] ozone and nitrogen dioxide,[10] N_2O_5 and $Fe(acac)_3$,[11] N-nitropyridinium and quinolinium salts,[12] nitric acid and trifluoromethanesulfonic acid[13] or trifluoromethanesulfonic anhydride,[14] metal nitrates in sulfuric acid,[15–17] lanthanide(III) nosylates,[18] guanidinium nitrate,[19] potassium nitrate or nitric acid and boron trifluoride monohydrate mixtures,[20] and sodium nitrate/chlorotrimethyl silane and aluminium chloride mixtures.[21] Many of these reactions have been carried out in the presence of protic or Lewis acids. However, the majority of the reported methods for nitration of aromatic compounds suffer from disadvantages such as low regioselectivity,[11,22–24] over nitration,[23,24] competitive oxidation of substrates,[24–27] strongly acidic media,[19,25,28,29] oxidation of the reagents,[19,25,23] safety problems (storage, handling, and using toxic transition metal cations such as Hg^{2+}, Cu^{2+}, etc.),[15–17] and the work-up is needed several steps.[25–27]

These disadvantages have encouraged the researchers for extensive efforts to use alternative reagents including solid acids,[1,16,23,27,30–32] other sources of NO_2^+ (Nitronium salts,[14,22] N-nitropyridinum salt,[33] nitrogen oxide,[11,23] and peroxynitrite[34]), organic nitrating agents (acetyl nitrate, benzoyl nitrate, and trimethylsilyl nitrate),[35,36] etc.[18,37,38]

Although there are numerous applications of solid supported reagents and scavengers in literature,[39–52] but to the best of our knowledge, there is no report on the nitration of aromatic compounds based on polymer-supported nitrating reagents.

Recently, sodium nitrite is supported on cross-linked poly(4-vinyl pyridine) and is used for synthesis of nitroalkanes[47] and N-nitrosation of secondary amines.[48,51]

In continuing of our studies on application of cross-linked poly(4-vinyl pyridine) supported sodium nitrite in organic synthesis,[47,48,51] herein we report a green, clean, and simple method for nitration of activated aromatic compounds by using cross-linked poly(4-vinylpyridinie) supported sodium nitrite, [P_4-Me] NO_2, in the presence of $KHSO_4$.

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TABLE I
Nitration of Activated Aromatic Compounds with $[P_4\text{-}Me]\ NO_2/KHSO_4$

$$Ar{-}H + KHSO_4 \xrightarrow[\text{Acetonitrile, reflux}]{[P_4{-}Me]NO_2} Ar{-}NO_2$$

Entry	Substrate	Products[a]	Time	Yield (%)[b]
1	Phenol	*o*-nitrophenol (trace) + *p*-nitrophenol (61%)	2 (h)	68
2	Phenol	*o*-nitrophenol (15%) + *p*-nitrophenol (73%) + 2,4-dinitrophenol (11%)	6 (h)	88
3	Hydroquinone	2-Nitrohydroquinone (65%) + Quinone (34%)	30 (min)	99
4	Catechol	4-nitrocatechol	20 (min)	87
5	*p*-nitrophenol	2,4-dinitrophenol	9 (h)	Trace
6	*p*-cresol	4-Methyl-2-nitrophenol	3 (h)	83
7	*o*-cresol	2-Methyl-4-nitrophenol (54%) +2-Methyl-5-nitrophenol (37%)	4 (h)	91
8	Biphenyl	No reaction	9 (h)	0.0
9	2-Naphtol	1-Nitro-2-naphtol	4 (h)	95
10	Toluene	No reaction	9 (h)	0.0
11	*m*-xylene	No reaction	9 (h)	0.0
12	*N*,*N*-dimethyl aniline	*N*,*N*-dimethyl-4-nitro aniline	4 (h)	74

[a] The structure were confirmed by comparison of the FTIR and ^{1}H- and ^{13}C-NMR spectra with those of authentic specimen.

[b] Yields refer to isolated total products.

EXPERIMENTAL

Chemicals

All Chemical substrates were either prepared in our laboratory or were purchased from Fluka (Buchs, Switzerland), Merck and Aldrich chemical companies (Milwaukee, WI). Poly(4-vinylpyridine) cross-linked with 2% divinylbenzene (DVB) was commercial product (Fluka). Poly(N-methyl-4-vinylpyridinium) iodide

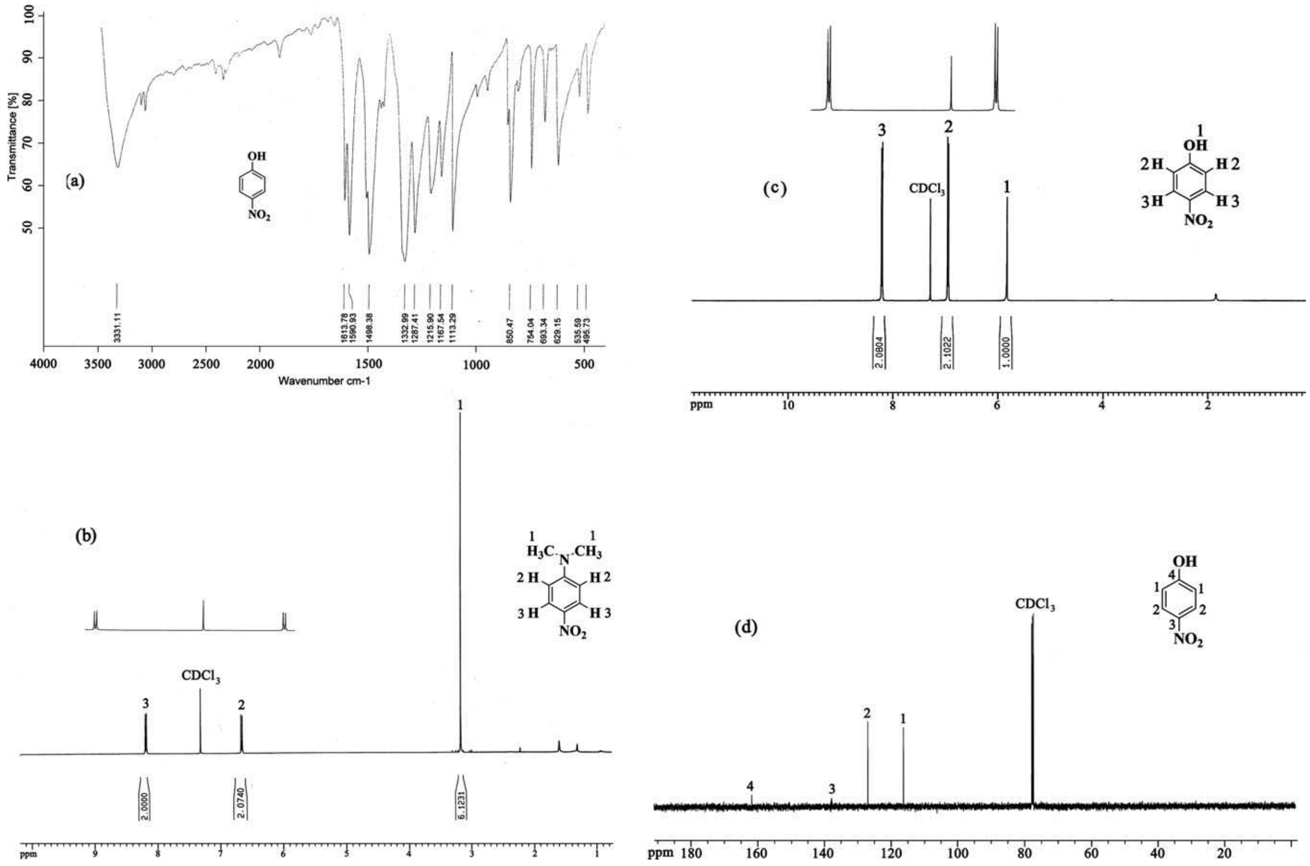


Figure 1 (a) FTIR, (c) ^{1}H-NMR, and (d) ^{13}C-NMR spectra of *p*-nitrophenol; and (b) ^{1}H-NMR spectrum of *N*,*N*-dimethyl-4-nitroaniline.

and [P$_4$-Me] NO$_2$ were prepared according to previously our reported procedures.[47,48]

Progress of the reaction was followed by thin layer chromatography (TLC) using silica gel Poly Gram SIL G/UV 254 plates. All products were characterized by comparison of their FTIR, ^{1}H-NMR and ^{13}C-NMR spectra, TLC, and physical data with authentic samples. All yields refer to the isolated products. FTIR, ^{1}H-NMR, and ^{13}C-NMR spectra were run on a Bruker, Equinox (model 55) and Bruker AC 500, Aveance DPX spectrophotometer (using tetramethylsilane as internal reference), respectively.

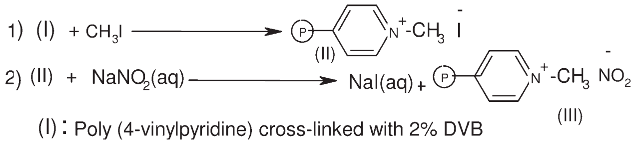
The capacity of [P$_4$-Me] NO$_2$ was determined by potentiometric titration with a 0.1 N solution of silver nitrate. The activity of [P$_4$-Me] NO$_2$ was found to be 3.8 mmol/g of the polymer.

General procedure for nitration of activated aromatic compounds with [P$_4$-Me] NO$_2$/KHSO$_4$ in acetonitrile at reflux conditions

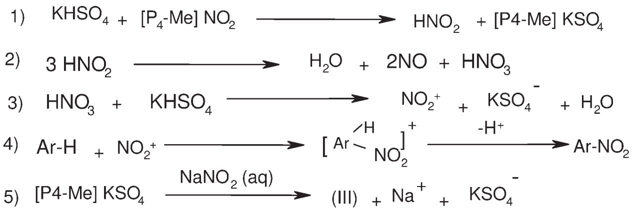
To a suspension of [P$_4$-Me] NO$_2$ (1.23 g, 3 mmol) and KHSO$_4$ (0.2 g, 1.47 mmol) in acetonitrile (5 mL) was added an activated aromatic compound (1 mmol) and the mixture was stirred at reflux conditions. The progress of the reaction was monitored by TLC. After completion of the reaction, the suspension was filtered and washed with acetonitrile (2 × 5 mL), and the filtrate was dried with MgSO$_4$. The nitro aromatic compounds in good to high total yields were obtained by the evaporation of the solvent (Table I). If further purification or isomeric separation was needed, flash chromatography on silica gel [eluent: *n*-hexane-ethyl acetate (80 : 20)] provides highly pure products. The spent polymeric reagent was regenerated by treatment with sodium nitrite solution.

Nitration of phenol with [P$_4$-Me] NO$_2$/KHSO$_4$ in acetonitrile at reflux conditions

To a suspension of [P$_4$-Me] NO$_2$ (1.23 g, 3 mmol) and KHSO$_4$ (0.2 g, 1.47 mmol) in acetonitrile (5 mL), 94 mg (1 mmol) of phenol was added, and the mixture was stirred at reflux conditions for 2 h. The suspension was filtered, washed with acetonitrile (2 × 5 mL), and the filtrate was dried with MgSO$_4$. Evaporation of the solvent was obtained the *p*-nitro phenol product in 68% yield (but if the stirring was continued for 6 h, the mixture of *p*-nitro phenol and *o*-nitro phenol were obtained in 88% total yield). The progress of the reaction was monitored by TLC. After completion of the reaction, the suspension was filtered and washed with acetonitrile (2 × 5 mL), and the filtrate was dried with MgSO$_4$. Highly pure *p*-nitro phenol (73%) and *o*-nitro phenol (15%) products were obtained by flash chromatography on silica gel [eluent: *n*-hexane-ethyl acetate (80 : 20)] (Table I). The absence of dinitrophenols was ascertained by GC/MS analyses of the crude reaction mixture. Selected spectra data for some nitro aromatic prepared are given below and some selected FTIR, ^{1}H-NMR, and ^{13}C-NMR spectra are shown in Figure 1.

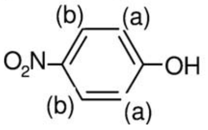


Scheme 1 Preparation of [P$_4$-Me] NO$_2$.



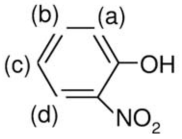
Scheme 2 The plausible mechanism for nitration of aromatic compounds.

***p*-nitrophenol**

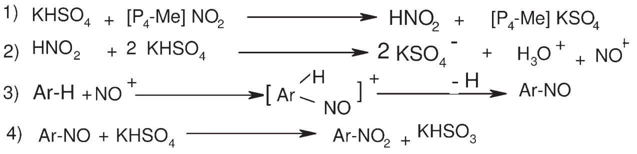


FTIR (KBr), ν (cm^{-1}): 3331 (O—H), 3000 (C—H, aromatic), 1614 and 1590 (C=C, aromatic), 1498 (N=O, asymmetric), 1333, (N=O, symmetric), 1215 (C—O) and 1113 (C—N); ^{1}H-NMR (500 MHz, CDCl$_3$), δ (ppm): 5.833 (1H, OH), 6.949–6.967 (2H, H$_a$, d, J = 9.1 Hz), 8.207–8.225(2H, H$_b$, d, J = 9.1 Hz); ^{13}C-NMR (125 MHz, CDCl$_3$), δ (ppm): 116.1 (C$_a$), 126.7(C$_b$), 138 (C-NO$_2$) and 161.6 (C—OH).

***O*-nitrophenol**



FTIR (KBr), ν (cm^{-1}): 3378 (O—H), 3050–3090 (C—H, aromatic), 1614 and 1606, 1625 and 1593 (C=C, aromatic), 1498 (N=O, asymmetric), 1337, (N=O, symmetric), 1268, 1261 (C—O) and 1111 (C—N); ^{1}H-



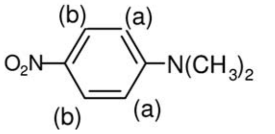
Scheme 3 The alternative plausible mechanism for nitration of aromatic compounds.

TABLE II
Nitration of Phenol with Different Methods

		Isolated yield (%)		
Entry	Reagent	*o*-nitrophenol	*p*-nitrophenol	References
1	$NaNO_2/KHSO_4$	63	12	55
2	$NaNO_2$/Silica sulfuric acid	30	20	30
3	HNO_3/Sulfated titania	68.6	2.3	56
4	HNO_3/Microemulsion	50	50	9
5	$Mn(NO_3)_3.2H_2O$	60	40	57
6	$Cu(NO_3)_2.2H_2O$	40	60	57
7	$Fe(NO_3)_3.9H_2O$	50	50	57
8	$ZrO(NO_3)_2.XH_2O$	40	60	58
9	$NaNO_3/Mg(HSO_4)_2$	36	26	59
10	HNO_3/P_2O_5/Silica gel	10	90	28
11	$NaNO_3$/Silica sulfuric acid/Wet SiO_2	0.0	85	60
12	$KHSO_4/[P_4\text{-Me}]\ NO_2$	15	73	–

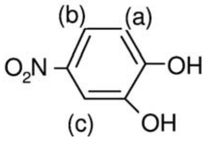
NMR (500 MHz, $CDCl_3$), δ (ppm): 10.57 (1H, OH), 6.995 (1H, H_c, m), 7.161 (1H, H_a, t), 7.575 (1H, H_b, m) and 8.103(1H, H_d, t).

N,*N*-dimethyl-4-nitroaniline



FTIR (KBr), ν (cm^{-1}): 3088 (C—H, aromatic) 2955 (C—H, CH_3), 1600, 1592 and 1530 (C=C, aromatic), 1484 (N=O, asymmetric), 1383, (N=O, symmetric), 1201 (C—O) and 1117 (C—N); ^{1}H-NMR (500 MHz, $CDCl_3$), δ (ppm): 3.160 (6H, s, CH_3), 6.644–6.663(2H, H_b, d, J = 9.42 Hz), 7.578–7.584(2H, H_a, d, J = 9.42 Hz).

4-Nitro-1,2-benzenediol



FTIR (KBr), ν (cm^{-1}): 3351 (O—H), 3050–3080 (C—H, aromatic), 1631 and 1606 and 1590 (C=C, aromatic), 1499 and 1448 (N=O, asymmetric), 1393 and 1336 (N=O, symmetric), 1281, 1185 (C—O) and 1122 and 1082 (C—N); ^{1}H-NMR (500 MHz, $CDCl_3$), δ (ppm): 10.3 (2H, OH), 6.93 (1H, H_a, d, J = 9Hz), 7. 64 (1H, H_c, s) and 7.67 (1H, H_b, d, J = 9Hz).

RESULTS AND DISCUSSION

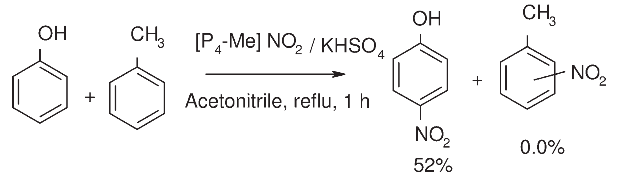
Cross-linked poly(4-vinylpyridine) supported sodium nitrite prepared according to our previous reported procedure[47,48] and used as an efficient procedure for chemoselective and regioselective nitration of aromatic compounds (Scheme 1).

The advantages of this method over conventional classical method is mild reaction conditions, stability, safe handling, regioselectivity, chemoselectivity, mildness of polymeric nitrating reagent, and very simple work-up (only filtration, drying and evaporation of the solvent, if the conversion is completed and only one isomer is obtained). In addition, there is current research and general interest in heterogeneous systems because of the importance such systems have in industry and in developing technologies.[53] We have investigated a number of different reaction conditions based upon the generation of HNO_3, and it was observed that $[P_4\text{-Me}]\ NO_2/KHSO_4$ is a regioselective and chemoselective nitrating reagent for nitration of activated aromatic compounds. Also it was observed that acetonitrile is the best solvent among other organic solvents for nitration reaction.

A good range of available aromatic compounds were also subjected to nitration in the presence of $[P_4\text{-Me}]\ NO_2/KHSO_4$. It was found that the reaction is most useful for activated aromatic compounds such as phenol, catechol, hydroquinone, beta-naphthol, and *N*,*N*-dimethyl aniline, and the reaction fails completely for less activated aromatic compounds such as biphenyl, *m*-xylene or toluene (Table I).

For this new system, the *in situ* generation of nitronium ion (NO_2^+) mechanism may be proposed. The plausible mechanism is given in Scheme 2.

The reaction of $KHSO_4$ and $[P_4\text{-Me}]\ NO_2$ gives HNO_2 [eq. (1) in Scheme 2]. It is well known that nitrous acid decomposes to nitric acid particularly when warmed,[54] [eq. (2) in Scheme 2]. Nitric acid



Scheme 4 The chemoselectivity of [P4-Me] $NO_2/KHSO_4$.

provides nitronium ion (NO_2^+) as an electrophile that substituted on activated aromatic rings [eq. (3) and (4) in Scheme 2]. The spent polymeric reagent was regenerated by treatment with sodium nitrite solution [eq. (5) in Scheme 2]. The regenerated polymeric reagent has the same capacity as the original form. The alternative mechanism, involving the generation of nitrosonium ion (NO^+) and nitrosation followed by oxidation to obtain the nitro compound (Scheme 3). Similar mechanisms are proposed by Heravi et al. for synthesis of ortho-nitrophenol using $NaNO_2/KHSO_4$.[55]

The superior regioselectivity of our method is clear and can be justified by comparison of percentages of para isomers with previously reported protocols (Table II). To demonstrate the chemoselectivity of this method, a competitive reaction was performed between phenol and toluene. It was observed that nitration of phenol occurred exclusively, whereas toluene remained intact in the reaction mixture after 1 h (Scheme 4).

CONCLUSIONS

Poly(4-vinylpyridine) supported sodium nitrite was easily synthesized and used for the efficient and selective nitration of activated aromatic compounds to their corresponding nitroaromatic compounds in the presence of $KHSO_4$. Ease of product isolation, stability, safe handling, regioselectivity, chemoselectivity, and mildness of this polymeric nitrating reagent make it a useful addition to other methods used in the organic synthesis.

References

1. Samajdar, S.; Becker, F. F.; Banik, B. K. Tetrahedron Lett 2000, 41, 8017.
2. Esakkidurai, T.; Pitchumani, K. J Mol Catal A Chem 2002, 185, 305.
3. Botvay, A.; Mathe, A.; Poppl, L. Polymer 1999, 40, 4965.
4. Tasneem, A. M. M.; Rajanna, K. C.; Saiparakash, P. K. Synth Commun 2001, 31, 1123.
5. Min, S.; Shi-Cong, C. J Fluorine Chem 2002, 113, 207.
6. Fetscher, C. A. Org Synth 1963, 4, 735.
7. Robertson, G. R. Org Synth 1932, 1, 389.
8. Sparks, A. K. J Org Chem 1966, 31, 2299.
9. Crivello, J. V. J Org Chem 1981, 46, 3056.
10. Suzuki, H.; Mori, T. J Chem Soc Perkin Trans 2 1996, 677.
11. Bak, R. R.; Smallridge, A. J. Tetrahedron Lett 2001, 42, 6767.
12. Olah, G. A.; Narang, S. C.; Olah, J. A.; Pearsian, R. L.; Cupas, C. A. J Am Chem Soc 1980, 102, 3507.
13. Coon, C. L.; Blucher, W. G.; Hill, M. E. J Org Chem 1973, 38, 4243.
14. Olah, G. A.; Reddy, V. P.; Prakash, G. K. S. Synthesis 1992, 1087.
15. Olah, G. A.; Krishnamurthy, V. V.; Narang, S. C. J Org Chem 1982, 47, 596.
16. Cornelis, A.; Laszlo, P. Synthesis 1985, 909.
17. Mellor, J. M.; Mittoo, S.; Parkes, R.; Millar, R. W. Tetrahedron 2000, 56, 8019.
18. Parac-Vogt, T. N.; Binnemans, K. Tetrahedron Lett 2004, 45, 3137.
19. Ramana, M. M. V.; Malik, S. S.; Parihar, J. A. Tetrahedron Lett 2004, 45, 8681.
20. Olah, G. A.; Wang, Q.; Li, X.; Bucsi, I. Synthesis 1992, 1085.
21. Olah, G. A.; Ramaiah, P.; Sandford, G.; Orlinkov, A.; Prakash, G. K. S. Synthesis 1994, 468.
22. Olah, G. A.; Kuhn, S. J. J Am Chem Soc 1962, 84, 3684.
23. Peng, X.; Suzuki, H.; Lu, C. Tetrahedron Lett 2001, 42, 4357.
24. Iranpoor, N.; Firouzabadi, H.; Heydari, R. Synth Commun 1999, 29, 3295.
25. Strazzolini, P.; Giumanini, A. G.; Runcio, A. Tetrahedron Lett 2001, 42, 1387.
26. Bozell, J. J.; Hoberg, J. O. Tetrahedron Lett 1988, 39, 2261.
27. Bahulayan, D.; Narayan, G.; Sreekumar, V.; Lalithambika, M. Synth Commun 2002, 32, 3565.
28. Hajipour, A. R.; Rouho, A. E. Tetrahedron Lett 2005, 46, 8307.
29. Yi, W. B.; Cai, C. J Fluorine Chem 2008, 129, 524.
30. Riego, J. M.; Sedin, Z.; Zaldivar, J. M.; Marziano, N. C.; Tortato, C. Tetrahedron Lett 1996, 37, 513.
31. Zolfigol, M. A.; Chasemi, E.; Madrakian, E. Synlett 2003, 191.
32. Zolfigol, M. A.; Madrakian, E.; Chasemi, E. Molecules 2002, 7, 734.
33. Bosnich, B.; Nyholm, R. S.; Pauling, P. J.; Tobe, M. L. J Am Chem Soc 1968, 90, 4742.
34. Nonoyama, N.; Chiba, K.; Hisatome, K.; Suzuki, H.; Shintani, F. Tetrahedron Lett 1999, 40, 6933.
35. Rodrigues, J. A. R.; Fitho, A. P. D. O.; Moran, P. J. S.; Custodio, R. Tetrahedron 1999, 55, 6733.
36. Kimura, M.; Kajita, K.; Naoyuki, O.; Morosawa, S. J Org Chem 1990, 55, 4887.
37. Frost, C. G.; Hartley, J. P.; Griffin, D. Tetrahedron Lett 2002, 43, 4789.
38. Rajagopal, R.; Srinivasan, K. V. Ultrason Sonochem 2003, 10, 41.
39. Sherrington, D. C.; Hodge, P. Synthesis and Separations Using Functional Polymers; John Wiley and Sons, New York, 1988.
40. Sherrington, D. C.; Hodge, P. Polymer Supported Reactions in Organic Synthesis; John Wiley and Sons, New York, 1980.
41. Takemoto, K.; Inaki, Y.; Ottenbrite, R. M. Functional Monomers and Polymers; Marcel Dekker Inc.; New York, 1987.
42. Akelah, A.; Sherrington, D. C. Chem Rev 1981, 81, 577.
43. Akelah, A.; Sherrington, D. C. Polymer 1984, 24, 1369.
44. Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, R. I.; Taylor's, J. J Chem Soc Perkin Trans 1 2000, 2, 3815.
45. Tamami, B.; Iranpoor, N.; Karimi Zarchi, M. A. Polymer 1993, 34, 2011.
46. Tamami, B.; Karimi Zarchi, M. A. Eur Polym J 1995, 13, 715.
47. Karimi Zarchi, M. A.; Zarei, A. J Chin Chem Soc 2005, 52, 309.
48. Karimi Zarchi, M. A.; Noei, J. J Appl Polym Sci 2007, 104, 1064.
49. Karimi Zarchi, M. A. J Chin Chem Soc 2007, 54, 1299.
50. Karimi Zarchi, M. A.; Mirjalili, B. F.; Ebrahimi, N. Bull Korean Chem Soc 2008, 29, 1079.
51. Karimi Zarchi, M. A.; Noei, J. J Appl Polym Sci 2009, 114, 2134.
52. Karimi Zarchi, M. A.; Mirjalili, B. F.; Kheradmand, A. A. J Appl Polym Sci 2009, 115, 237.
53. Turro, N. J. Tetrahedron 1987, 43, 1589.
54. Cotton, F. A.; Wilkinson, G.; Gaus, P. L. Advanced Inorganic Chemistry, 3rd ed.; Wiley Interscience, New York, 1972; p 358.
55. Heravi, M. M.; Oskooie, H. A.; Baghernejad, B. J Chin Chem Soc 2007, 54, 1299.
56. Sunajadevi, K. R.; Sugunan, S. Catal Commun 2005, 6, 611.
57. Anuradha, V.; Srinivas, P. V.; Aparna, P.; Madhusudana Rao, J. Tetrahedron Lett 2006, 47, 4933.
58. Selvan, J. J. P.; Suresh, V.; Rajesh, K.; Reddy, S. R.; Venkateswarlu, Y. Tetrahedron Lett 2006, 47, 2507.
59. Zolfigol, M. A.; Ghaemi, E.; Madrakian, E. Molecules 2001, 6, 614.
60. Zolfigol, M. A.; Mirjalili, B. B. F.; Bamoniri, A.; Karimi Zarchi, M. A.; Zarei, A.; Khazdooz, L.; Noei, J. Bull Korean Chem Soc 2004, 25, 1414.