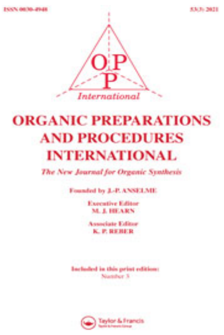


OPP
International

ORGANIC PREPARATIONS AND PROCEDURES INTERNATIONAL

The New Journal for Organic Synthesis

Founded by J.-P. ANSELME

Executive Editor
M. J. HEARN

Associate Editor
K. P. REBER

Included in this print edition:
Number 3

Taylor & Francis
Taylor & Francis Group

Organic Preparations and Procedures International

The New Journal for Organic Synthesis

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/uopp20

Dendrimer-Functionalized Magnetic Graphene Oxide for Knoevenagel Condensation

Behrooz Maleki, Fatemeh Taheri, Reza Tayebee & Fatemeh Adibian

To cite this article: Behrooz Maleki, Fatemeh Taheri, Reza Tayebee & Fatemeh Adibian (2021) Dendrimer-Functionalized Magnetic Graphene Oxide for Knoevenagel Condensation, Organic Preparations and Procedures International, 53:3, 284-290, DOI: 10.1080/00304948.2021.1875799

To link to this article: https://doi.org/10.1080/00304948.2021.1875799

ORGANIC PREPARATIONS AND PROCEDURES INTERNATIONAL
2021, VOL. 53, NO. 3, 284–290
https://doi.org/10.1080/00304948.2021.1875799

EXPERIMENTAL PAPER

Dendrimer-Functionalized Magnetic Graphene Oxide for Knoevenagel Condensation

Behrooz Maleki[a], Fatemeh Taheri[a], Reza Tayebee[a], and Fatemeh Adibian[b]

[a]Department of Chemistry, Hakim Sabzevari University, Sabzevar, Iran; [b]School of Chemistry, Damghan University, Damghan, Iran

ARTICLE HISTORY Received 14 June 2020; Accepted 30 September 2020

A great deal of attention has been paid to developing methods for heterogenizing homogeneous catalysts in order to combine the advantages of both homogeneous and heterogeneous catalysis.[1] Among these methods, the binding of catalysts to organic polymer solids[2] or inorganic solids[3] is widely used. Although the heterogenized catalysts can be recycled and easily separated from the reaction mixtures, they are significantly less reactive and selective than their homogeneous counterparts. For this reason, there is a need to find new methods and strategies in order to overcome these limitations.

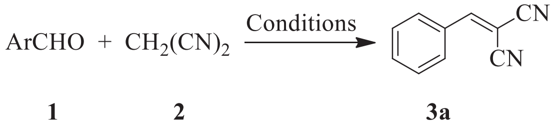
Graphene oxide (GO) and functionalized GOs are suitable for achieving this purpose. GO has a large amount of functional groups on its basal plane, and these allow for the modification of GO for further applications.[4–6] The large surface area and functional groups act as active sites. GO is a suspension in pure water but generally aggregates in salt solutions or in biological solutions.[7] To overcome this problem and also to permit easy separation by an external magnet, magnetic nanoparticles have been used. Magnetic nanoparticles (MNPs) such as magnetite (Fe_3O_4) are of much current interest because of their magnetic and electrical properties, high specific surface area, unique catalytic powers and wide applications.[8–10]

Dendrimers are a comparatively new class of polymeric materials. They are highly branched, monodisperse macromolecules. The structure of these materials has a great impact on their physical and chemical properties. As a result of their unique characteristics, including enormous surface areas in relation to volume, the presence of internal cavities and the possibility of encapsulating guest molecules, dendrimers are suitable for a wide range of biomedical and industrial uses. For example, polyamidoamine (PAMAM), has been beneficially applied.[11–14]

We now describe a useful synthetic organic method based on combining the features of magnetic nanoparticles, GO and dendrimers. The objective of this strategy is to homogenize a heterogeneous catalyst. Thus we sought to: *(i)* use magnetic nanoparticles to minimize the support for the immobilization of the catalyst, while at the same time keeping it easily separable; and *(ii)* use the dendrimerization process to produce organic arms on the support. The latter action will enhance the compatibility of the material with the medium, allow it to mimic real homogeneous catalysts and promote our

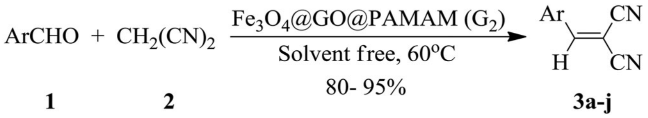
CONTACT Behrooz Maleki b.maleki@hsu.ac.ir Department of Chemistry, Hakim Sabzevari University, Sabzevar, Iran

Table 1. Optimization of reaction conditions for **3a**.[a]



Entry	Catalyst (g)	Conditions	Time (min)	Yield (%)
1	Fe_3O_4@GO@PAMAM (G_2) (0.008)	Solvent-free/60 °C	20	95
2	Fe_3O_4@GO@PAMAM (G_2) (0.007)	Solvent-free/60 °C	20	85
3	Fe_3O_4@GO@PAMAM (G_2) (0.008)	Solvent-free/50 °C	20	82
4	Fe_3O_4@GO@PAMAM (G_2) (0.008)	Solvent-free/70 °C	20	92
5	Fe_3O_4@GO@PAMAM (G_2) (0.008)	Solvent-free/25 °C	60	42
6	Fe_3O_4@GO (0.008)	Solvent-free/60 °C	20	20
7	Fe_3O_4@GO@PAMAM (G_1) (0.008)	Solvent-free/60 °C	20	75
8	Fe_3O_4@GO@PAMAM (G_2) (0.008)	Water/60 °C	20	40
9	Fe_3O_4@GO@PAMAM (G_2) (0.008)	Ethanol/60 °C	20	32
11	–[b]	Solvent-free/60 °C	30	–[c]

[a] Reaction conditions: benzaldehyde (1 mmol) and malononitrile (1.2 mmol).
[b] This reaction was carried out in the absence of Fe_3O_4@GO@PAMAM (G_2).
[c] No product **3a** observed.



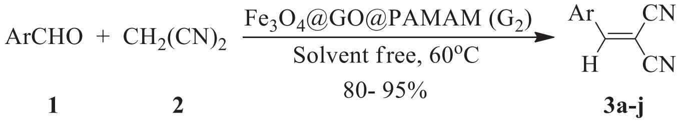
Scheme 1. Synthesis of benzylidenemalononitrile derivatives catalyzed by Fe_3O_4@GO@PAMAM (G_2).

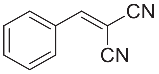
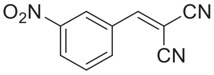
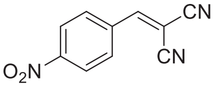
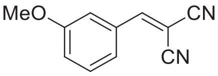
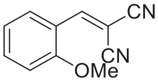
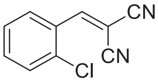
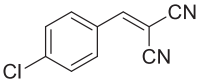
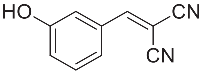
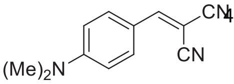
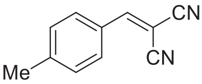
synthetic purpose. We thus grew a PAMAM dendron on nanomagnetite Fe_3O_4@GO. The preparation of the Fe_3O_4@GO@PAMAM (G_2) was accomplished according to a procedure described in the literature.[15]

The Knoevenagel condensation of aldehydes with compounds containing activated methylene groups is an important reaction for C = C bond formation in organic compounds. Because of its simplicity, economy and efficiency, this process is frequently used,[16–21] and we may note the use of numerous catalysts, including rare-earth (RE) exchanged NaY zeolite [RE(72%)NaY],[22] cetyltrimethyl ammonium bromide (CTMAB),[23] MgO/ZrO_2,[24] Zn^{2+} exchanged Hß (Znß),[25] polyvinyl chloride supported tetraethylenepentamine (PVC-TEPA),[26] Na_2S/Al_2O_3,[27] magnesium fluoride,[28] Ni–SiO_2,[29] ceria-zirconia (C/Z-30/70),[30] La_2O_3–MgO/KOH,[31] guanidine supported on magnetic nanoparticles Fe_3O_4 (Fe_3O_4@guanidine),[32] BEA or TS-1 or CuBTC or FeBTC,[33] gallium chloride ($GaCl_3$),[34] polyvinyl amine coated Fe_3O_4@SiO_2 (Fe_3O_4@SiO_2-PVAm),[35] Fe_3O_4@UiO-66-NH_2,[36] *N*-(3-trimethoxysilylpropyl)diethylenetriamine) coated (Fe_3O_4@SiO_2-3N),[37] Fe_3O_4@P4VP@ZIF-8,[38] magnetic Fe_3O_4@SiO_2@Ni-Zn-Fe layered double hydroxide (LDH) (Fe_3O_4@SiO_2@Ni-Zn-Fe LDH),[39] and fiber (PAN_PF-3).[40]

In furtherance of our studies of organic reactions in the presence of benign heterogeneous and homogeneous catalysts,[41–50] we now demonstrate the preparation of benzylidenemalononitrile (BMN) derivatives by Knoevenagel condensation of benzaldehydes (1 mmol) and malononitrile (1.2 mmol) using [Fe_3O_4@GO@PAMAM (G_2)] as catalyst (Scheme 1).

Table 2. Preparation of benzylidenemalononitrile derivatives (**3a-j**).



Entry	Product (3a-j)	Time (min)	Yield (%)	m.p (°C)	
				Found	Reported
3a		20	95	80-82	81-82[23]
3b		30	95	102-104	101-103[27]
3c		30	90	159-161	161-162[27]
3d		15	86	103-105	102-104[40]
3e		15	80	79-80	80-81[27]
3f		35	82	85-87	84-86[32]
3g		30	90	164-166	162-163[23]
3h		40	90	151-152	148-150[40]
3i		40	90	178-180	179-180[23]
3j		60	85	136-137	137-138[27]

To define the best conditions for this reaction, we optimized the type and amount of catalyst, temperature and solvent. Our study started by using benzaldehyde (1 mmol) and malononitrile (1.2 mmol) in a model reaction. Our results on optimization are shown in Table 1. The best results are represented by Entry 1, when the model reaction was carried out in the presence of Fe_3O_4@GO@PAMAM (G_2) (0.008 g) under solvent-free conditions at 60 °C.

To probe the generality of this reaction we reacted malononitrile with ten aryl aldehydes substituted with both electron-withdrawing and electron-donating groups, including aldehydes with *ortho* substituents. The experiments were repeated three times for

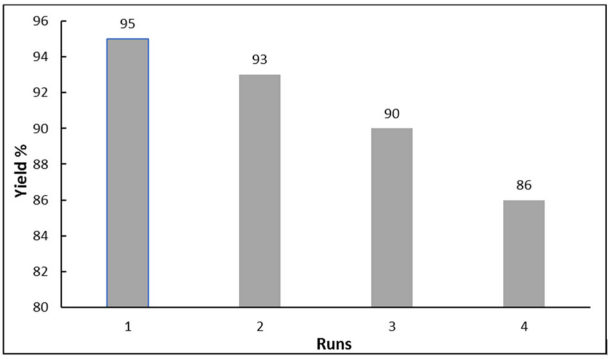


Figure 1. Reusability of Fe_3O_4@GO@PAMAM (G_2).

each aldehyde and the average yields are reported in Table 2. The products were formed in high to excellent yields (see Experimental section; mean yield 88%).

The recyclability of the Fe_3O_4@GO@PAMAM (G_2) was checked in the model reaction under optimized conditions. After completing the reaction, 1 mL ethanol was added to the reaction mixture and then the catalyst was easily separated using an external magnet. Fe_3O_4@GO@PAMAM (G_2) was reused in the model reaction after washing with acetone and deionized water and drying. As shown in Figure 1, the nanocatalyst could be reused in four reaction runs before considerable loss in activity was observed.

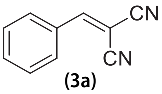
Table 3 shows the efficiency of the present procedure for the synthesis of 2-benzylidene malononitrile (**3a**), compared with previously reported procedures in the literature. The data suggest that Fe_3O_4@GO@PAMAM (G_2) stands among the best catalysts and has the desirable attributes of high yield, short reaction time and the avoidance of solvents.

In conclusion, our work illustrates the advantages of heterogenizing homogeneous catalysts in order to improve synthetic organic preparations. The efficiency of Fe_3O_4@GO@PAMAM (G_2) as a reusable and highly effective catalyst was illustrated for the synthesis of benzylidenemalononitrile derivatives through the Knoevenagel reaction. Over-all, this synthetic approach provides excellent yields and short reaction times. Among the green characteristics of this method are low waste generation, the avoidance of solvent, simple work-up, easy separation and reusability of catalyst. We hope that our catalyst can be applied for the promotion of a wide range of Knoevenagel reactions and other related reactions.

Experimental section

All reagents were obtained from commercial sources. Melting points were determined on an Electrothermal 9200 apparatus and are uncorrected. IR spectra were recorded at room temperature on a Shimadzu 435-U-04 spectrophotometer using KBr disks and are reported in cm^{-1}. A Bruker DRX-400 Avance spectrometer was used for recording ^1H and ^{13}C NMR spectra at 400 MHz and 100 MHz in $CDCl_3$ or DMSO-d_6 using tetramethylsilane as an internal standard. First order aromatic couplings were within the expected range and are not enumerated. The catalyst was prepared according to the method previously described.[15]

Table 3. Comparison of methods for the synthesis of 2-benzylidene malononitrile (**3a**).

	Conditions	Time (min)	Yield (%)
 (3a)	Fe_3O_4@GO@PAMAM (G_2)/Solvent-free/60 °C	20	95
	RE(72%)NaY/CH_3CN/rt[22]	720	78
	CTMAB/H_2O/rt[23]	90	91
	MgO/ZrO_2/Solvent-free/60 °C[24]	20	93
	Znß/Solvent-free/140 °C[25]	360	16
	PVC-TEPA/EtOH/reflux[26]	60	75
	$Na_2S/Al_2O_3/CH_2Cl_2$/reflux[27]	20	90
	MgF_2/EtOH/rt[28]	150	93
	Ni–SiO_2/Toluene/reflux[29]	900	100
	C/Z-30/70/EtOH/reflux[30]	50	82
	Fe_3O_4@UiO-66-NH_2-3/DMF/80 °C[36]	60	73
	Fe_3O_4@SiO_2-3N/Water/75 °C[37]	12	93
	Fe_3O_4@P4VP@ZIF-8/Toluene/23 °C[38]	120	99
	Fe_3O_4@SiO_2@Ni-Zn-Fe/EtOH/reflux[40]	90	92

General procedure for synthesis of benzylidenemalononitrile derivatives (3a-j) catalyzed by Fe_3O_4@GO@PAMAM (G_2)

Fe_3O_4@GO@PAMAM (G_2) (0.008 g) was added to a mixture of the benzaldehyde (1 mmol) and malononitrile (1.2 mmol). The mixture was heated at 60 °C on an oil bath under solvent-free conditions for the appropriate time (Table 2). The progress of reaction was monitored by TLC (silica gel; n-hexane:ethyl acetate, 4:1). After completion of the reaction, 1 mL ethanol was added to the mixture and then the nanocatalyst was easily separated using an external magnet. The resulting mixture was poured into crushed ice to precipitate the product. The product was filtered off and was recrystallized from ethanol (96%) to get the respective pure 2-benzylidenemalononitrile derivatives (**3a-j**). All of the compounds in this study were known and were identified by matching their melting points with the literature values cited in Table 2. For the sake of completeness, representative IR, ^{1}H-NMR and ^{13}C-NMR are provided below for compounds **3d** and **3h**.

2-(3-Methoxybenzylidene)malononitrile (3d)

IR (KBr) 3039, 2217, 1575, 1470, 1249, 756, 613 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 8.47 (s, 1H, CH), 7.95-7.97 (d, 1H, CH, aromatic), 7.66-7.70 (d, 1H, CH aromatic), 7.13-7.24 (m, 2H, 2CH aromatic), 3.906 (s, 3H, OCH_3); ^{13}C-NMR (DMSO-d_6,100 MHz) δ: 159.10, 156.50, 136.99, 129.33, 120.39, 120.35, 114.88, 113.73, 112.89, 81.99, 56.52.

2-(3-Hydroxybenzylidene)malononitrile (3h)

IR (KBr) 3359, 3014, 2235, 1573, 1467, 781, 673 cm^{-1}; ^{1}H-NMR (DMSO-d_6, 400 MHz) δ: 8.44 (s, 1H, CH), 7.07-7.09 (d, 1H, CH aromatic), 7.35-7.43 (m, 3H, 3CH aromatic), 10.13 (s, 1H, OH); ^{13}C-NMR (DMSO-d_6, 100 MHz) δ: 162.10, 158.34, 132.86, 131.06, 122.50, 122.27, 116.57, 114.76, 113.66, 81.58.

Acknowledgment

The authors are grateful to the Research Council of Hakim Sabzevari University for partial support of this work.

ORCID

Behrooz Maleki http://orcid.org/0000-0002-3740-7096
Reza Tayebee http://orcid.org/0000-0003-1211-1472
Fatemeh Adibian http://orcid.org/0000-0002-6365-9780

References

1. R. Abu-Reziq, H. Alper, D. Wang and M. L. Post, *J. Am. Chem. Soc.*, **128**, 5279 (2006). doi:10.1021/ja060140u
2. N. E. Leadbeater and M. Marco, *Chem. Rev.*, **102**, 3217 (2002). doi:10.1021/cr010361c
3. C. E. Song and S. G. Lee, *Chem. Rev.*, **102**, 3495 (2002). doi:10.1021/cr0103625
4. M. Tarahomi, H. Alinezhad and B. Maleki, *Appl. Organometal. Chem.*, **33**, e5203 (2019).
5. E. Rezaei-Seresht, M. Bakhshi-Noroozi, B. Maleki, *Polycycl. Arom. Compds.*, (2020). doi:10.1080/10406638.2019.1708417.
6. M. Baghayeri, H. Alinezhad, M. Tarahomi, M. Fayazi, M. Ghanei-Motlagh and B. Maleki, *Appli. Surface Sci.*, **478**, 87 (2019). doi:10.1016/j.apsusc.2019.01.201
7. D. Li, M. B. Müller, S. Gilge, R. B. Kaner and G. G. Wallace, *Nat. Nanotechol.*, **3**, 101 (2008). doi:10.1038/nnano.2007.451
8. S. Hemmati, P. Mohammadi, A. Sedrpoushan and B. Maleki, *Org. Prep. Proced. Int.*, **50**, 465 (2018). doi:10.1080/00304948.2018.1525668
9. A. Khojastehnezhad, B. Maleki, B. Karrabi and E. Rezaei Seresht, *Org. Prep. Proced. Int.*, **49**, 338 (2017). doi:10.1080/00304948.2017.1342505
10. B. Maleki, H. Alinezhad, H. Atharifar, R. Tayebee and A. Vedad Mofrad, *Org. Prep. Proced. Int.*, **51**, 301 (2019). doi:10.1080/00304948.2019.1600132
11. H. Alinezhad, M. Tarahomi, B. Maleki and A. Amiri, *Appl. Organometal. Chem.*, **33**, e4661 (2019). doi:10.1002/aoc.4661
12. F. Adibian, A. R. Pourali, B. Maleki, M. Baghayeri and A. Amiri, *Polyhedron*, **175**, 114179 (2020). doi:10.1016/j.poly.2019.114179
13. B. Maleki, O. Reiser, E. Esmaeilnezhad and H. J. Choi, *Polyhedron*, **162**, 129 (2019). doi:10.1016/j.poly.2019.01.055
14. B. Maleki, M. Baghayeri, M. Ghanei-Motlagh, F. Mohammadi Zonoz, A. Amiri, F. Hajizadeh, A. R. Hosseinifar and E. Esmaeilnezhad, *Measurement*, **140**, 81 (2019). doi:10.1016/j.measurement.2019.03.052
15. W. Xiao, B. Yan, H. Zeng, Q. Liu, *Carbon*, **105**, 655 (2016). doi:10.1016/j.carbon.2016.04.057
16. H. N. Borah, M. L. Deb, R. C. Boruah, P. J. Bhuyan, *Tetrahedron Lett.*, **46**, 3391 (2005). doi:10.1016/j.tetlet.2005.03.091
17. F. Freeman, *Chem. Rev.*, **80**, 329 (1980). doi:10.1021/cr60326a004
18. A. Ying, L. Wang, F. Qiu, H. Hu and J. Yang, *C. R. Chim.*, **18**, 223 (2015). doi:10.1016/j.crci.2014.05.012
19. G. Srikanth, U. K. Ray, D. Srinivas Rao, P. B. Gupta, P. Lavanya and A. Islam, *Synth. Commun.*, **42**, 1359 (2012). doi:10.1080/00397911.2010.539894
20. S. M. Lai, C. P. Ng, R. Martin-Aranda and K. L. Yeung, *Microporous Mesoporous Mater.*, **66**, 239 (2003). doi:10.1016/j.micromeso.2003.09.014
21. S. Guihéneuf, L. Paquin, F. Carreaux, E. Durieu, T. Roisnel, L. Meijer and J.-P. Bazureau, *Mol. Diver.*, **18**, 375 (2014). doi:10.1007/s11030-014-9509-7
22. T. I. Reddy and R. S. Varma, *Tetrahedron Lett.*, **38**, 1721 (1997). doi:10.1016/S0040-4039(97)00180-9

23. S. Wang, Z. J. Ren, W. G. Cao and W. Tong, *Synth. Commun.*, **31**, 673 (2001). doi:10.1081/SCC-100103255
24. M. B. Gawande and R. V. Jayaram, *Catal. Commun.*, **7**, 931 (2006). doi:10.1016/j.catcom.2006.03.008
25. S. Saravanamurugan, M. Palanichamy, M. Hartmann and V. Murugesan, *Appl. Catal. A Gen.*, **298**, 8 (2006). doi:10.1016/j.apcata.2005.09.014
26. F. Dong, Y. Q. Li and R. F. Dai, *Chin. Chem. Lett.*, **18**, 266 (2007). doi:10.1016/j.cclet.2007.01.023
27. M. M. Heravi, K. Bakhtiari, S. Taheri and H. A. Oskooie, *J. Chin. Chem. Soc.*, **54**, 1557 (2007). doi:10.1002/jccs.200700219
28. R. M. Kumbhare and M. Sridhar, *Catal. Commun.*, **9**, 403 (2008). doi:10.1016/j.catcom.2007.07.027
29. V. R. Pullabhotla, A. Rahman and S. B. Jonnalagadda, *Catal. Commun.*, **10**, 365 (2009). doi:10.1016/j.catcom.2008.09.021
30. G. Postole, B. Chowdhury, B. Karmakar, K. Pinki, J. Banerji and A. Auroux, *J. Catal.*, **269**, 110 (2010). doi:10.1016/j.jcat.2009.10.022
31. Y. Wei, S. Zhang, S. Yin, C. Zhao, S. Luo and C. Au, *Catal. Commun.*, **12**, 1333 (2011). doi:10.1016/j.catcom.2011.05.010
32. A. Rostami, B. Atashkar and H. Gholami, *Catal Commun.*, **37**, 69 (2013). doi:10.1016/j.catcom.2013.03.022
33. M. Opanasenko, A. Dhakshinamoorthy, M. Shamzhy, P. Nachtigall, M. Horacek, H. Garcia and J. Cejka, *Catal. Sci. Technol.*, **3**, 500 (2013). doi:10.1039/C2CY20586F
34. L. Muralidhar and C. R. Girija, J. Saud. *Chem. Soc.*, **18**, 541 (2014). doi:10.1016/j.jscs.2011.10.024
35. F. Zamani and E. Izadi, *Chin. J. Catal.*, **35**, 21 (2014). doi:10.1016/S1872-2067(12)60685-8
36. Y. Zhang, T. Dai, F. Zhang, J. Zhang, G. Chu and C. Quan, *Chin. J. Catal.*, **37**, 2106 (2016). doi:10.1016/S1872-2067(16)62562-7
37. J. B. M. de Resende Filho, G. P. Pires, J. M. G. de Oliveira Ferreira, E. E. S. Teotonio and J. A. Vale, *Catal. Lett.*, **147**, 167 (2017). doi:10.1007/s10562-016-1916-1
38. Z. Miao, F. Yang, Y. Luan, X. Shu and D. Ramella, *J. Solid. State Chem.*, **256**, 27 (2017). doi:10.1016/j.jssc.2017.07.032
39. M. Gilanizadeh and B. Zeynizadeh, *New J. Chem.*, **42**, 8553 (2018). doi:10.1039/C8NJ00788H
40. G. Li, J. Xiao and W. Zhang, *Green Chem.*, **13**, 1828 (2011). doi:10.1039/c0gc00877j
41. B. Maleki and H. Veisi, *Org. Prep. Proced. Int.*, **52**, 232 (2020). doi:10.1080/00304948.2020.1752606
42. B. Maleki, R. Rooky, E. Rezaei Seresht, R. Tayebee, *Org. Prep. Proced. Int.*, **49**, 557 (2017). doi:10.1080/00304948.2017.1384282
43. B. Maleki, *Org. Prep. Proced. Int.*, **48**, 303 (2016). doi:10.1080/00304948.2016.1165061
44. B. Maleki, M. Raei, E. Akbarzadeh, H. Ghasemnejad Borsa, A. Sedrpoushan, S. Sedigh Ashrafi and M. N. Dehdashti, *Org. Prep. Proced. Int.*, **48**, 62 (2016). doi:10.1080/00304948.2016.1127102
45. B. Maleki, M. Chahkandi, R. Tayebee, S. Kahrobaei, H. Alinezhad and S. Hemmati, *Appl. Organomet. Chem.*, **33**, e5118 (2019).
46. B. Maleki, M. Raei, H. Alinezhad, R. Tayebee and A. Sedrpoushan, *Org. Prep. Proced. Int.*, **50**, 288 (2018). doi:10.1080/00304948.2018.1462055
47. B. Maleki, R. Nejat, H. Alinezhad, S. M. Mousavi, B. Mahdavi and M. Delavari, *Org. Prep. Proced. Int.*, **52**, 328 (2020). doi:10.1080/00304948.2020.1765655
48. H. Atharifar, A. Keivanloo and B. Maleki, *Org. Prep. Proced. Int.*, doi:10.1080/00304948.2020.1799672
49. B. Maleki, *Org. Prep. Proced. Int.*, **48**, 81 (2016). doi:10.1080/00304948.2016.1127104
50. A. Jamshidi, B. Maleki, F. M. Zonoz and R. Tayebee, *Mater. Chem. Phys.*, **209**, 46 (2018). doi:10.1016/j.matchemphys.2018.01.070