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$HClO_4$-SiO_2 Nanoparticles as an Efficient Catalyst for Three-Component Synthesis of Triazolo[1,2-a]Indazole-Triones

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Abstract**—**An environmentally benign protocol for the one-pot, three-component synthesis of Triazolo[1,2-a]indazole-1,3,8-trione derivatives by condensation of dimedone, urazole and aromatic aldehydes catalyzed by $HClO_4/SiO_2$ NPS as an ecofriendly catalyst with high catalytic activity and reusability at 100ºC under solvent-free conditions is reported. The reaction proceeds to completion within 20-30 min in 77-86% yield.

Keywords**—**One-pot reaction, Dimedone, Triazoloindazole, Urazole.

I. Introduction

MULTICOMPONENT reactions (MCRs) are chemical transformations in which three or more reactants forma product derived from all of the inputs [1]. Although the term MCR is used interchangeably with 'cascade', 'domino' and 'one-pot' processes, a somewhat specific definition is useful for direct comparison. Conducting successive reactions in a reaction vessel can be an efficient way to access molecular diversity. That said, a series of 'two-component' reactions requiring a specific order of addition is functionally and practically different than many MCRs in which the components can be added in any order [2]. Another important distinction lies in the definition of a 'component' versus a 'reagent.' For maximumutility in the assembly of complex products, each component should be present in the final product and, to a certain extent, be independently variable from the other components [3].

In recent years, use of heterogeneous catalysts has received considerable interest in various disciplines including organic synthesis. They are advantageous over their homogeneous counterparts due to the prime advantage that, in most cases, the catalyst can be recovered easily and reused. Silica-supported perchloric acid ($HClO_4$–SiO_2) has been used as an efficient heterogeneous catalyst for many organic transformations because of its low cost, ease of preparation, catalyst recycling, and ease of handling [4]–[9].

Herein, as a part of our continued interest in catalysis by nanoparticles, we report a convenient and facile one pot method for the synthesis Triazolo[1,2-a]indazole-triones **4** via Three-Component reaction between Dimedon **1** , 4-phenylurazole **2** and aromatic aldehydes **3** under solvent-free conditions in the present of $HClO_4/SiO_2$ NPs (Fig. 1).

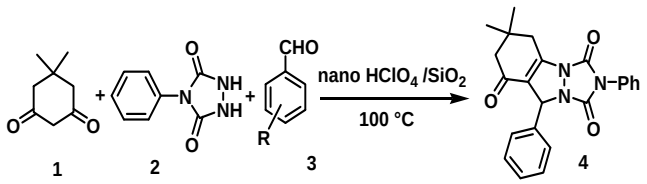

Fig. 1 Synthesis of Triazolo[1,2-a]indazole-1,3,8-trione derivatives

II. Results and Discussion

Our initial efforts focused on the search for a catalyst for the condensation reaction between dimedone, urazoles and aromatic aldehydes. For this purpose, the condensation reaction between dimedone **1** (1 mmol), 4-phenylurazole **2** (1 mmol) and 4-chlorobenzaldehyde **3a** (1 mmol) as a simple model substrate for the synthesis of 6,7-Dihydro-6,6-dimethyl-2-phenyl-9-(4- chloro-phenyl)-[1,2,4]-triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione (**4a**) in the presence of $HClO_4$–SiO_2 NPs under solvent-free conditions was selected as a model reaction in the presence of different catalytic systems and the results are summarized in (Table I).

TABLE I
Compared Performances of Various Catalysts for the Model Reaction [A]

Entry	Catalyst	Reaction conditions	Time (min)	Yield[b] (%)
1	ZnO NPs	Solvent-free,100 ºC	25	0
2	MgO NPs	Solvent-free,100 ºC	25	0
3	CuO NPs	Solvent-free,100 ºC	25	0
4	ZrO_2 NPs	Solvent-free,100 ºC	25	0
5	$HClO_4/SiO_2$	Solvent-free,100 ºC	25	62
6	$HClO_4/SiO_2$ NPs	Solvent-free,100 ºC	25	86

[a] Reaction conditions: Dimedon (1 mmol), 4-phenylurazole (1 mmol), 4-chlorobenzaldehyde (1 mmol); catalyst: $HClO_4$–SiO_2 NPs (20 mol%); temp: 100ºC; solvent free. [b] Isolated yields.

With the best catalyst in hand, we then studied the influence of different amounts of catalyst and temperature on the reaction time and yield for the model reaction. (Table II)

The efficacy of our protocol was well evaluated using a wide range of aldehydes. As indicated in Table III, it seemed that there was no remarkable electronic effect from the substituents on aldehyde moiety, since the aryl aldehydes with

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both electrondonating and electron-withdrawing groups could be applied as efficient candidates for the synthesis of corresponding triazolo[1,2- a]indazolone derivatives in good yields. Compounds **4i** and **4j** were new and their structures were deduced by elemental and spectral analysis. but compounds **4a-h** were known and their structures were deduced by comparison of melting points and spectral data with authentic samples [10]-[12] (Table III).

TABLE II
OPTIMIZATION AMOUNT OF HCLO4–SIO2 NPS AND REACTION TEMPERATURE FOR PREPARATION 6,7-DIHYDRO-6,6-DIMETHYL-2-PHENYL-9-(4- CHLORO-PHENYL)-[1,2,4]-TRIAZOLO[1,2-A]INDAZOLE-1,3,8(2H,5H,9H)-TRIONE [A]

Entry	Catalyst (g%)	Temp(°C)	Time (min)	Yield[b] (%)
1	$HClO_4$-SiO_2 NPs(0.02)	100	30	62
2	$HClO_4$-SiO_2 NPs(0.03)	100	15	80
3	$HClO_4$-SiO_2 NPs(0.03)	100	25	86
4	$HClO_4$-SiO_2 NPs(0.04)	100	25	83
5	$HClO_4$-SiO_2 NPs(0.03)	120	25	83
6	$HClO_4$-SiO_2 NPs(0.03)	80	25	77

[a] Reaction conditions: Dimedon (1 mmol), 4-phenylurazole, (1 mmol), 4-chlorobenzaldehyde (1 mmol); catalyst: $HClO_4$–SiO_2 NPs (20 mol%); temp: 100ºC; solvent free. [b] Isolated yields.

TABLE III
THREE-COMPONENT REACTION OF DIMEDON, 4-PHENYLURAZOLE AND AROMATIC ALDEHYDES CATALYZED BY HCLO4-SIO2 NPS UNDER SOLVENT-FREE CONDITIONS[A]

Entry	Ar	Time(min)	Yield[b] (%)	M.P. (°C)	mp[lit] (°C)
4a	4-Cl-C_6H_4	25	86	167	(166–168)[10]
4b	2-Cl-C_6H_4	20	79	172	(175–177)[10]
4c	C_6H_5	25	78	200	(187–189)[11]
4d	4-NO_2-C_6H_4	20	81	180	(126–128)[11]
4e	4-MeO-C_6H_4	30	78	175	(176-180)[12]
4f	4-Br-C_6H_4	25	80	185	(184–186)[12]
4g	3-Br-C_6H_4	30	81	180	(174–176)[12]
4h	4-Me-C_6H_4	30	79	165	(173–175)[12]
4i	2-Me-C_6H_4	25	77	184	(New product)
4j	2-NO_2-C_6H_4	20	80	168	(New product)

[a] Reaction conditions: Dimedon (1 mmol), 4-phenylurazole (1 mmol), aromatic aldehydes (1 mmol); catalyst: $HClO_4$–SiO_2 NPs (20 mol%); temp: 100ºC; solvent free. [b] Isolated yields.

A possible mechanism for the formation of the products is shown in Scheme 2. The reaction occurs via initial formation of heterodiene **5**, by standard Knoevenagel condensation of aldehyde **1** and dimedone **2**. Subsequent Michael-type addition of the urazole **3** to **5** followed by cyclization affords the corresponding product **4** (Fig. 2).

Another advantage of this approach could be related to the reusability of the catalyst. We found that the catalyst could be separated from the reaction mixture simply by centrifuge and washing with ethanol and dried at 100 °C. The reusability of $HClO_4$–SiO_2 NPs was checked by the reaction of Dimedon **1**, 4-phenylurazole **2** and aromatic aldehydes **3** under optimized reaction conditions. The results show that the catalyst can be used effectively three times with slight decreasing in catalytic activity, 86%, 80% and 77% (Table IV). Therefore, the recyclability of the catalyst makes the process economically and potentially viable for commercial applications.

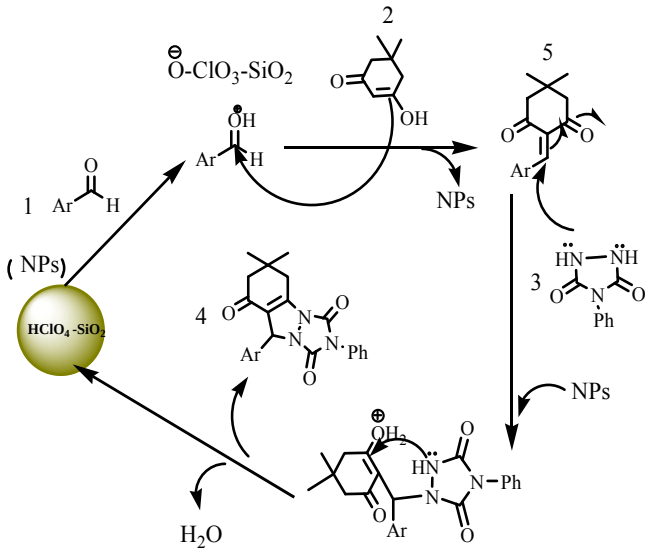

Fig. 2 Suitable mechanism for the formation of triazole[1,2-a]indazole triones

TABLE IV
RECYCLABILITY OF THE CATALYST [A]

No of cycles[a]	Run1	Run2	Run3
Yield[b] (%)	86	80	77
Time (min)	25	25	25

[a] Reaction conditions: Dimedon (1 mmol), 4-phenylurazole (1 mmol), aromatic aldehydes (1 mmol); catalyst: $HClO_4$–SiO_2 NPs (20 mol%); temp: 100ºC; solvent free. [b] Isolated yields.

III. EXPERIMENTAL

A. General

Melting points were determined with an Electrothermal 9100 apparatus. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR-470 spectrometer. ^1H and ^{13}C NMR spectra were recorded on Bruker DRX-500 Avance spectrometer at solution in $CDCl_3$ using TMS as internal standard. The chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and were used without further purification. The stable silicagel nanoparticles is easily prepared [13] and used for preparation of catalyst ($HClO_4$–SiO_2 NPs).

B. Synthesis of Perchloric acid Supported on Silicagel Nanoparticles Nanoparticles

The reagent was prepared by combining 70% aqueous $HClO_4$ (1.8 g, 12.5 mmol) with nano silicagel (23.7 g) in diethyl ether (70 mL). It was stirred for 3h at room temperature. The mixture was concentrated and the residu dried under vacuum at 100°C for 72h to afford $HClO_4$– SiO_2 NPs (0.5 mmol g−1) as a free flowing powder. The dimensions of nanoparticles were observed with SEM (Fig. 3). The sizes of particles are between 20 and 30 nm.

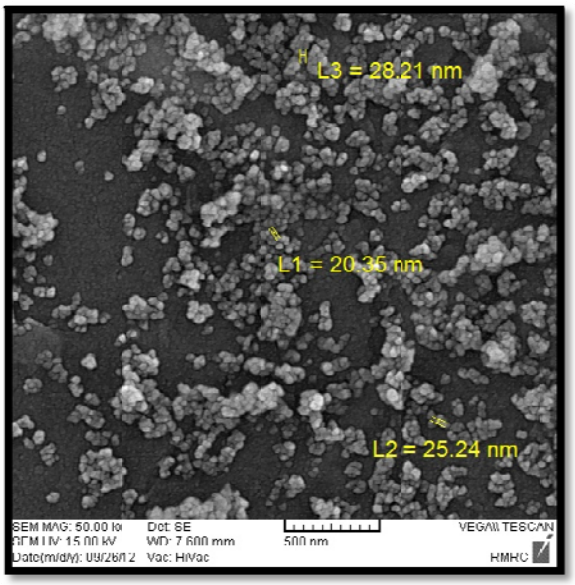

Fig. 3 SEM image of Perchloric Acid Supported on Silica ($HClO_4/SiO_2$ NPs)

C. General Procedure

A mixture of Dimedon (1.0 mmol), 4-phenylurazole (1.0 mmol), aromatic aldehyde (1.0 mmol) and $HClO_4$-SiO_2 NPs (0.03 g, 20 mol %) in solvent-free conditions was heated at 100ºC. The reaction was monitored by thin layer chromatography. The reaction went to completion around 20–30 min. After completion of the reaction, the reaction mixture was cooled at room temperature. The solid residue was dissolved in hot ethanol and centrifuged to separate the catalyst. By recrystallization from ethyl acetate–n-hexane (1:2), pure products were obtained.

D. Spectral Data

6,7-Dihydro-6,6-dimethyl-2-phenyl-9-(4-chlorophenyl)-[1,2,4]-triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)- trione (**4a**).

White powder (86%); mp 167 °C, IR (KBr) (ν_{max}, cm^{-1}): 1780, 1720, 1665. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (6H, s, $2CH_3$), 2.33 (2H, s, CH_2), 2.90 (2H, AB system, $^2J_{HH}$ = 18.7 Hz, CH_2), 6.18 (1H, s, CH), 7.38–7.49(9H, m, H–Ar) (ppm). ^{13}C NMR (75 MHz, $CDCl_3$): *δ* = 28.2, 28.7, 34.7, 35.5, 51.2, 63.5, 119.7, 125.6, 128.6, 128.8, 129.0, 129.4, 130.7, 134.6, 135.6, 149.1, 151.0, 151.3, 192.0 (ppm); Anal. Calcd for $C_{23}H_{20}ClN_3O_3$: C, 65.48; H, 4.78; N, 9.96. Found: C, 65.35; H, 4.92; N, 9.80.

6,7-Dihydro-6,6-dimethyl-2-phenyl-9-(2-chlorophenyl)-[1,2,4]-triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)- trione (**4b**).

White powder (79%); mp 172°C, IR (KBr) (ν_{max}, cm^{-1}): 2966, 1777, 1728, 1658. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (6H, s, $2CH_3$), 2.32 (2H, AB system, $^2J_{HH}$ = 16.7 Hz, CH_2), 2.93 (2H, AB system, $^2J_{HH}$ = 18.3 Hz, CH_2), 6.35 (1H, s, CH), 7.32–7.47(9H, m, H-Ar) (ppm). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.3, 28.9, 34.6, 35.4, 51.2, 63.6, 118.5, 125.8, 127.6, 128.7, 129.3, 130.5, 130.7, 130.8, 131.3, 131.9, 132.8, 148.4, 150.0, 150.7, 191.8 (ppm). Anal. Calcd for $C_{23}H_{20}ClN_3O_3$: C, 65.48; H, 4.78; N, 9.96. Found: C, 65.40; H, 4.73; N, 9.87.

6,7-dihydro-6,6-dimethyl-2,9-diphenyl-[1,2,4]-triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione (**4c**).

White powder (78%); mp 200 °C, IR (KBr) (ν_{max}, cm^{-1}): 2957, 1778, 1730, 1655. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22 (6H, s, $2CH_3$), 2.35 (2H, s, CH_2), 2.93(2H, AB system, $^2J_{HH}$ = 18.0 Hz, CH_2), 6.23 (1H, s, CH), 7.35–7.49 (10H, m, H–Ar) (ppm). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.3, 28.7, 34.8, 35.5, 51.3, 64.1, 120.1, 125.6, 127.1, 128.8, 128.9, 129.3, 130.7, 136.8, 149.0, 150.7, 151.0, 192.0(ppm). Anal. Calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85. Found: C, 71.45; H, 5.39; N, 10.93.

6,7-Dihydro-6,6-dimethyl-2-phenyl-9-(4-nitrophenyl)-[1,2,4]-triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione(**4d**).

White powder (81%); mp 180 °C, IR (KBr) (ν_{max}, cm^{-1}): 1788, 1730, 1660. 1H NMR (300 MHz, $CDCl_3$): δ = 1.19 (3H, s, CH_3), 1.21 (3H, s, CH_3), 2.34 (2H, s, CH2), 2.92 (2H, AB system, $^2J_{HH}$ = 18.7 Hz, CH_2), 6.30 (1H, s, CH), 7.46–8.27(9H, m, H-Ar) (ppm). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.2, 28.7, 34.8, 35.6, 51.2, 63.3, 119.2, 124.1, 125.6, 128.2, 129.0, 129.4, 130.5, 143.9, 148.0, 149.2, 151.6, 191.9(ppm). Anal. Calcd for $C_{23}H_{20}N_4O_5$: C, 63.88; H, 4.66; N, 12.96. Found: C, 63.82; H, 4.58; N, 12.88.

6,7-Dihydro-6,6-dimethyl-2-phenyl-9-(4-metoxyphenyl)-[1,2,4]-triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)-trione(**4e**).

White solid (78%); mp 175 °C, IR (KBr) (ν_{max}, cm^{-1}): 1782, 1723, 1668. ^{1}H NMR (300 MHz, $CDCl_3$): δ = (ppm) 1.21 (6H, s, $2CH_3$), 2.10(3H, s, CH_3) 2.40 (2H, s, CH_2), 2.92 (2H, s, CH_2), 6.19 (1H, s, CH), 7.20–7.49 (9H, m, H-Ar); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.2, 28.3, 35.5, 40.8, 50.6, 63.4, 115.2, 125.6,128.2, 128.5, 128.8, 129.1, 129.3, 129.8,135.4, 142.7, 150.9, 162.4, 196.3(ppm).Anal. Calcd for $C_{24}H_{23}N_3O_4$: C, 69.06; H, 5.51; N, 10.08. Found: C, 69.15; H, 5.59; N, 10.28.

6,7-Dihydro-6,6-dimethyl-2-phenyl-9-(4-bromophenyl)-[1,2,4]-triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)- trione (**4f**).

White powder (80%); mp 185°C, IR (KBr) (ν_{max}, cm^{-1}): 1789, 1726, 1660. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 (6H, s, $2CH_3$), 2.33 (2H, s, CH_2), 2.90 (2H, AB system, $^2J_{HH}$ = 19.6 Hz, CH_2), 6.17 (1H, s, CH), 7.32–7.54(9H, m, H–Ar) (ppm). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.3, 28.7, 34.8, 35.5, 51.2, 63.6, 119.7, 122.9, 125.6, 128.8, 129.4, 130.6, 132.1, 135.9, 149.1, 150.9, 151.2, 191.9 (ppm). Anal. Calcd for $C_{23}H_{20}BrN_3O_3$: C, 59.24; H, 4.32; N, 9.01. Found: C, 59.29; H, 4.41; N, 8.93.

6,7-Dihydro-6,6-dimethyl-2-phenyl-9-(3-bromophenyl)-[1,2,4]-triazolo[1,2-a]indazole-1,3,8(2H,5H,9H)- trione (**4g**).

White powder (79%); mp 165°C, IR (KBr) (ν_{max}, cm^{-1}): 2946, 1774, 1729, 1665. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19 (3H, s, CH_3), 1.21 (3H, s, CH_3), 2.34 (2H, AB system, $^2J_{HH}$ = 16.4 Hz, CH_2), 2.92 (2H, AB system, $^2J_{HH}$ = 19.7 Hz, CH_2), 6.17(1H, s, CH), 7.24–7.58 (9H, m, H-Ar) (ppm). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.3, 28.6, 34.8, 35.5, 51.2, 63.4, 119.6, 122.9, 125.6, 126.1, 128.9, 129.4, 130.0, 130.4, 130.6,

131.9, 139.2, 149.1, 151.1, 151.3, 191.9 (ppm). Anal. Calcd for $C_{23}H_{20}BrN_3O_3$: C, 59.24; H, 4.32; N, 9.01. Found: C, 59.31; H, 4.28; N, 8. 94

IV. Conclusion

In conclusion, we have demonstrated that $HClO_4$-SiO_2 nanoparticles can be used as green and reusable and heterogeneous catalyst for efficient synthesis of triazoloindazoles under solvent-free conditions. Simple reaction, one-pot, and work-up procedures make it a useful protocol for the synthesis of these classes of compounds.

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References

[1] J. Zhu, H. Bienayme, *Multicomponent Reactions*, wiley-vch weinheim, 2005.
[2] L. Weber, K. Illgen, M. Almstetter, Discovery of New "Multi Component Reactions with Combinatorial Methods" *Synlett*. 1999, 366-374.
[3] A. Doemling "Recent developments in isocyanide based multicomponent reactions in applied chemistry" *Chem. Rev*. 2006, 106, 17-89.
[4] A. K. Misra, P. Tiwari,G. Agnihotri, "Ferrier Rearrangement Catalyzed by $HClO_4$-SiO_2: Synthesis of 2,3-Unsaturated Glycopyranosides" *Synthesis* 2005, 260.
[5] G. Agnihotri, A. K. Misra, "Mild and efficient method for the cleavage of benzylidene acetals using $HClO_4$–SiO_2 and direct conversion of acetals to acetates" *Tetrahedron Lett*. 2007, 48, 7553.
[6] P.Tiwari, A.K. Misra, "Selective removal of anomeric O-acetate groups in carbohydrates using $HClO_4$–SiO_2" *Tetrahedron Lett.* 2007*,* 48*, 7422.*
[7] M.A. Bigdeli, M. M. Heravi, G. H. Mahdavinia, "Silica supported perchloric acid ($HClO_4$-SiO_2): A mild, reusable and highly efficient heterogeneous catalyst for the synthesis of 14-aryl or alkyl-14H dibenzo[a,j]xanthenes*" J. Mol. Cata. A-Chem*. 2007, 275, 25.
[8] A.T. Khan, S. Ghosh, L. H.Choudhury, "Perchloric Acid Impregnated on Silica Gel ($HClO_4$/SiO_2): A Versatile Catalyst for Michael Addition of Thiols to the Electron-Deficient Alkenes" *Eur. J. Org. Chem*. 2006, 9, 2226.
[9] L.Q. Wu, C.G. Yang, C. Zhang, L. M. Yang, "$HClO_4$-SiO_2 and $NaHSO_4$-SiO_2: Two Efficient Heterogeneous Catalysts for Synthesis of N-Acylsulfonamides under Solvent-free Conditions" *Lett . Org . Chem*. 2009, 6,234.
[10] A. Bazgir, M.Seyyedhamzeh, Z. Yasaei, P. Mirzaei, "A novel three-component method for the synthesis of triazolo[1,2-a]indazole-triones" *Tetrahedron Lett*. 2007, 48, 8790-8794.
[11] M.A. Chari, G. Karthikeyan, A. Pandurangan, T.S. Naidu, B. Sathyaseelan, J. Zaidi, A. Vinu, "Synthesis of triazolo indazolones using 3D mesoporous aluminosilicate catalyst with nanocage structure " *Tetrahedron Lett*. 2010. 51, 2629.
[12] M. Kidwai, R. Chauhan, " Sulfamic acid: an efficient, cost-effective and recyclable catalyst for the synthesis of triazole[1,2-a]indazole-trione derivatives" *Communication*. 2012, 2, 7660–7665.
[13] K. Lee, A. N. Sathyagal, and A. V. McCormick, "A closer look at an aggregation model of the Stober process," *Colloids and Surfaces* A 1998,144, 115–125.

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