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Nitrite Ionic Liquids (IL-ONO and [bmim]NO_2) as Effective Nitrosonium Sources for the Synthesis of α-Oximinoketones under Mild Heterogeneous Conditions

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Ketones and β-diketones were nitrosated and converted to their corresponding α-oximinoketones using task-specific ionic liquids, 1-(4-nitritobutyl)-3-methylimidazolium chloride, IL-ONO, and 1-butyl-3-methylimidazolium nitrite at room temperature. The results from two ionic liquids are comparable and showed that these IL's are effective nitrosonium sources for the preparation of oximinoketones. The protocol is rapid, the yields are excellent, and the method is simple.

Keywords β-diketones, ketones, malonodiamide, oximinoketones, ionic liquids

Introduction

Large number of organic compounds especially heterocyclic one containing an oximino group have pharmacological properties.[1,2] Some oxime derivatives present a fungi toxic and herbicide effect,[3,4] or act as growth regulators for plants.[5] Various important organic compounds such as amino acids,[6] nitrosopyrazoles[7] and 2-vinylimidazoles[8] have been synthesized from α-oximinoketones. Nitrosation chemistry is very attractive for organic and biological chemists[9-11] and many works have been reported about the synthetic and mechanistic aspects of nitrosation or transnitrosation.[12,13] Nitrous acid is the most general reagent which is used for nitrosation and is generated from sodium nitrite and a mineral acid.[14,15] Alkyl nitrites,[16,17] nitrosyl salts,[18,19] Fremy's salt,[20] bis(triphenylphosphine)nitrogen (1+) nitrite,[21] alkyl thionitrite and thionitrate,[22] polymer-supported nitrosation reagent,[23] nitrosonium ethyl sulfate,[24] and [NO^+•Crown•$H(NO_3)_2^-$][25] have been used as nitrosating agents.

Weekly coordination of organic cations such as 1-butyl-3-methylimidazolium, *N*-alkylpyridinium or tetraalkylammonium with inorganic anions such as Cl^-, BF_4^- or HSO_4^- produced ionic liquids, which have attracted chemist's interest due to their interesting physical and chemical properties.[26,27] Many of these compounds known as task-specific ionic liquids (TSILs) are able to play dual roles as catalyst and/or reagent and solvent, which have been reported in the literature. TSILs contain functional groups which are covalently bonded to cation or anion in these compounds. TSILs have been increasingly used in synthetic organic chemistry.[28-32] In this work we wish to report the two nitrite functionalized ionic liquids as new reagents for the nitrosation of ketons and β-diketones (Figure 1).

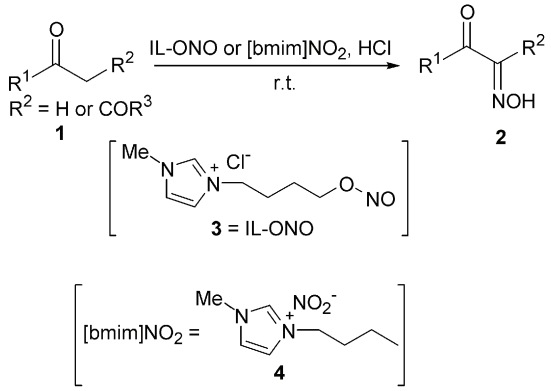

Figure 1 Synthesis of oximinoketones using IL-ONO or [bmim]NO_2.

Results and Discussion

The task-specific nitrite ionic liquids, 1-(4-nitritobutyl)-3-methylimidazolium chloride (**3**) and 1-butyl-3-methylimidazolium nitrite (**4**) were prepared according to our recently published paper[33] and from the anion exchange of [bmim]Cl respectively. First of all, we found that activated methylene compounds, such as benzoylacetone (**1a**) and dibenzoylmethane (**1b**) could be transformed into the corresponding oximes **2a** and **2b** respectively by simply grinding (45—50 min) at room temperature (in a mortar with a pestle) with 1 equiv. of

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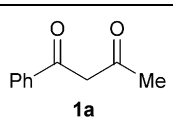
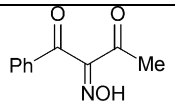
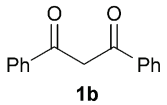
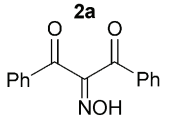
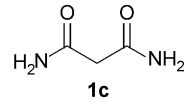
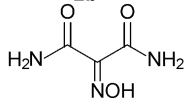
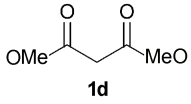
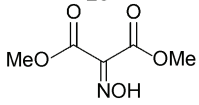
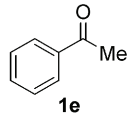
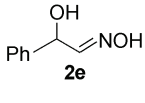
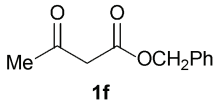
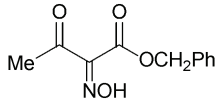
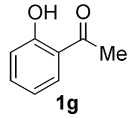
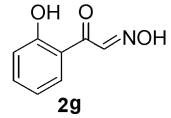
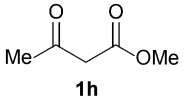
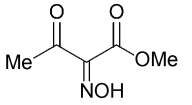
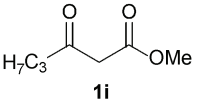
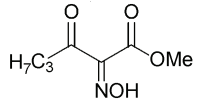
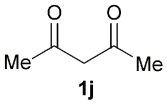
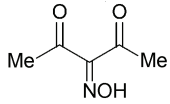
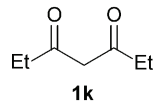
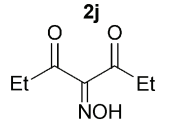
IL-ONO over acidic alumina. For optimization, different factors such as reaction temperature, reactants ratios and solid supports (silica gel, neutral alumina and molecular sieves 3 Å) in the presence of various Lewis acids ($AlCl_3$, $ZnCl_2$ and $TiCl_4$) were studied. No significant improvement in the yields of products **2a** and **2b** were observed under different grinding conditions. So, we decided to examine this reaction under heterogeneous aqueous condition in the presence of HCl. Under these conditions, dibenzoylmethane was converted to related oximinoketone **2b**, using one equivalent of IL-ONO in 80% yield over 4 h. Also, there was no need to heat the reaction mixture. For optimization, the reaction was studied with different molar ratios of the dibenzoylmethane, IL-ONO and HCl. The best ratio was found to be 1∶1.1∶1.25 and the related product **2b** was prepared in 89% yield over 2.5 h. Increasing the amount of ionic liquid led to the mixture of products such as nitrosoarene derivatives via electrophilic aromatic nitrosation of benzene ring. With optimized conditions in hand, we examined the nitrosation of some other ketones and diketones (Table 1). Acetophenone **1e** afforded the product **2e** in 82% yield over 2.5 h. *O*-Hydroxyacetophenone **1g** led to the related oximinoketnoe product in lower yield (65%) in comparison with acetophenone and nitrosoarene derivative product was also isolated in this reaction. Diketones (**1f**, **1h** and **1i**) containing two sites for nitrosation, were nitrosated selectively at activated site but the nitrosated product at other site was also isolated in very lower yield for these reactants. Excellent results were obtained with malonodiamide **1c** and dimethylmalonate **1d**. ^{1}H NMR and ^{13}C NMR spectroscopic data showed that two *syn* and *anti* isomers of products **2a** and **2e**—**2i** were formed in this procedure. The spectroscopic data of the major isomer were given in the experimental section.

1-Butyl-3-methylimidazolium nitrite was also examined to transform the activated methylene compounds, benzoylacetone (**1a**) and dibenzoylmethane (**1b**) into their related oximes **2a** and **2b** under above described optimized conditions. It was found that there are no significant differences in the results from the using of two ILs in this procedure. For comparison, the results of the nitrosation of some ketones and diketones using two ILs are gathered in Table 2. In order to evaluate the preparative value of the present methodology we carried out these reactions with 0.5 mol of benzoylacetone and oximinoketone **2a** was obtained in high yield.

In conclusion, the task-specific nitrite containing ionic liquids, IL-ONO and [bmim]NO_2, act as excellent alternative reagents for the synthesis of oximinoketones. Easy and clean work-up, and high yields make this procedure an attractive method for organic synthesis. This simple procedure is highly selective and contamination by-products is avoided. We believed that the present methodology is an important addition to existing methodologies.

Table 1 Synthesis of oximinoketones using task-specific nitrite ionic liquids IL-ONO or [bmim]NO_2[a]

Entry	Ketone/Diketone	Product	m.p./℃
1	 **1a**	 **2a**	129—131
2	 **1b**	 **2b**	145—149
3	 **1c**	 **2c**	168—170
4	 **1d**	 **2d**	129—132
5	 **1e**	 **2e**	123—125
6	 **1f**	 **2f**	—
7	 **1g**	 **2g**	—
8	 **1h**	 **2h**	—
9	 **1i**	 **2i**	—
10	 **1j**	 **2j**	—
11	 **1k**	 **2k**	—

[a] Excess HCl was used for the reaction of **1c**.

Experimental

General information

All reagents were purchased from Merck Company and used without further purification. Infrared spectra were recorded in KBr and were determined on a Perkin Elmer FT-IR spectrometer. ^{1}H NMR spectra were obtained in DMSO-d_6 solution from Bruker Avance AC-400 MHz and ^{13}C NMR spectra at 100 MHz on the

Table 2 Comparison of the results of nitrosation using IL-ONO with $[bmim]NO_2$

Product	Time/h		Yield[a]/%	
	$[bmim]NO_2$	IL-ONO	$[bmim]NO_2$	IL-ONO
2a	3	3	88[b]	90[b]
2b	2.5	2.5	90	89
2c	3.5	3.5	95	95
2d	3	3	92	94
2e	2.5	2.5	83[b]	82[b]
2f	3	3	85[b]	84[b]
2g	3.5	3.5	63[b]	65[b]
2h	3.5	3.5	88	89
2i	3	3	85[b]	85[b]
2j	3	3	65	68
2k	3	3	72	75

[a] Isolated yield. [b] Total yield of two isomeric products.

aforementioned instruments.

Elemental analyses were carried out on a Perkin-Elmer 240C elemental analyzer and are reported in percent atomic abundance. All melting points were measured in an open glass-capillaries using Stuart melting point apparatus.

Preparation of 1-butyl-3-methylimidazolium nitrite, $[bmim]NO_2$

1-Butyl-3-methylimidazolium chloride was prepared from the reaction of *N*-methylimidazole with *n*-butylchloride at 80 ℃ under neat conditions.[34] Sodium nitrite (23 mmol) was added to a solution of this freshly prepared ionic liquid (20 mmol) in dichloromethane (10 mL) and stirred for 24 h at room temperature. The suspension was filtered to remove the precipitated sodium chloride salt and the organic layer washed with water (8 mL×3) until no precipitation of AgCl occurred in aqueous phase on addition of a concentrated $AgNO_3$ solution. The solvent and other volatile materials were removed from organic layer in vacuum and the resulting ionic liquid was stirred with activated charcoal for 12 h, after which the ionic liquid was passed through a short alumina column(s) (acidic and/or neutral) to give a colorless ionic liquid, which was dried at 100 ℃ in vacuum for 24 h or until no visible signs of water present in the IR spectrum. Yields were generally 75%—82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.05 (t, J=8.24 Hz, 3H, CH_3), 1.41—1.43 (m, 2H, CH_2), 1.76—1.78 (m, 2H, CH_2), 3.83 (s, 3H, NCH_3), 3.97 (t, J=8.14 Hz, 2H, CH_2), 7.21 (d, J=7.24 Hz, 1H, ArH), 7.40 (d, J=7.24 Hz, 1H, ArH), 9.12 (broad, 1H, ArH); ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 11.7, 18.3, 25.6, 36.4, 37.8, 124.7, 126.8, 140.0; IR (KBr) ν: 1652, 1617, 1532, 1350, 1190 cm^{-1}. Anal. calcd for $C_8H_{15}N_3O_2$: C 51.88, H 8.16, N 22.69; found C 52.12, H 8.21, N 22.58.

Synthesis of oximinoketones using IL-ONO or $[bmim]NO_2$

Diketone or ketone (12 mmol) and concentrated hydrochloric acid (15 mmol) were added in water or in mixed alcohol-water (10 mL) and mixed vigorously at room temperature. While stirring the mixture, a solution of ionic liquid (13.2 mmol) in water (8 mL) is added slowly. The reaction mixture was left to stirring at room temperature for a time as shown in Table 1. The participated products were filtered and washed three times with cold water to afford the crude oximinoketone (**2a**—**2i**). The crude solid products were purified by recrystallization from water/ethanol.

Selected spectroscopic data

1-Phenyl-1,2,3-butanetrione-2-oxime (2a) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.61—7.68 (m, 4H, PhH), 7.75—7.79 (m, 2H, PhH), 7.81—7.85 (m, 4H, PhH), 12.87 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 114.05, 128.74, 130.00, 141.10, 154.87, 162.36; IR (KBr) ν_{max}: 3383 (br, OH), 1701, 1685, 1590, 1458, 1370 cm^{-1}. Anal. calcd for $C_{10}H_9NO_3$: C 62.82, H 4.74, N 7.33; found C 63.02, H 4.75, N 7.31.

1,3-Diphenyl-1,2,3-propanetrione-2-oxime (2b) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.51 (s, 3H, Me), 7.56—7.60 (m, 2H, PhH), 7.71—7.75 (m, 1H, PhH), 7.77—7.80 (m, 2H, PhH), 13.04 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 19.78, 112.25, 127.12, 128.45, 144.80, 148.32, 158.14, 160.21; IR (KBr) ν_{max}: 3379 (br, OH), 1689, 1579, 1451, 1372 cm^{-1}. Anal. calcd for $C_{15}H_{11}NO_3$: C 71.14, H 4.38, N 5.53; found C 71.23, H 4.39, N 5.52.

Malonamide-2-one-2-oxime (2c) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.73—7.79 (br, 2H, NH_2), 7.32—7.36 (br, 2H, NH_2), 12.04 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, MHz) δ: 138.63, 159.32, 162.52; IR (KBr) ν_{max}: 3431 (br, OH), 3310 (NH_2), 3211 (NH_2), 1680, 1675, 1437, 1261 cm^{-1}. Anal. calcd for $C_3H_5N_3O_3$: C 27.49, H 3.84, N 32.05; found C 28.14, H 3.85, N 31.58.

Methyl 4-methoxy-2,3-dione-2-oxime butanoate (2d) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.25 (s, 3H, OCH_3), 3.68 (s, 3H, OCH_3), 3.75 (s, 2H, OCH_2), 12.68 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 59.65, 60.25, 68.89, 135.25, 161.87, 163.45; IR (KBr) ν_{max}: 3330 (br, OH), 1743, 1691, 1627, 1437, 1388 cm^{-1}. Anal. calcd for $C_6H_9NO_5$: C 41.15, H 5.18, N 8.00; found C 42.10, H 5.16, N 7.98.

1-Phenyl-1,2-ethanedione-2-oxime (2e) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 7.73—7.77 (m, 2H, PhH), 7.81—7.85 (m, 3H, PhH), 12.75 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 112.32, 117.65, 125.63, 128.45, 148.63, 161.54; IR (KBr) ν_{max}: 3421 (br, OH), 1688, 1685, 1614, 1450, 1318 cm^{-1}. Anal. calcd for $C_8H_7NO_2$: C 64.42, H 4.73, N 9.39; found C 64.87, H 4.71, N 9.35.

Benzyl 2,3-dione-2-oxime butanoate (2f) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.50 (s, 3H, Me), 3.95 (s, 2H, OCH_2), 7.52—7.58 (m, 2H, PhH), 7.67—7.72 (m,

1H, PhH), 7.75—7.78 (m, 2H, PhH), 13.08 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 36.78, 71.41, 113.63, 117.87, 119.56, 122.36, 149.79, 160.52, 163.53; IR (KBr) ν_{max}: 3331 (br, OH), 1746, 1698, 1627, 1498, 1379 cm^{-1}. Anal. calcd for $C_{11}H_{11}NO_4$: C 59.73, H 5.01, N 6.33; found C 60.23, H 4.99, N 6.32.

1-(2-Hydroxyphenyl)-1,2-ethanedione-2-oxime (2g) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 6.35 (br, 1H, OH), 7.41—7.45 (m, 2H, PhH), 7.60—7.65 (m, 1H, PhH), 7.75—7.78 (m, 2H, PhH), 12.82 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 114.32, 117.56, 119.75, 121.32, 122.52, 122.98, 149.96, 165.85; IR (KBr) ν_{max}: 3449 (br, OH), 1684, 1531, 1384 cm^{-1}. Anal. Calcd for $C_8H_7NO_3$: C 58.18, H 4.27, N 8.48; found C 59.08, H 4.26, N 8.46.

Methyl 2,3-dione-2-oxime hexanoate (2h) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 1.05 (t, J=8.24 Hz, 3H, CH_3), 1.15—1.17 (m, 2H, CH_2), 2.64 (t, J=8.24 Hz, 2H, CH_2), 3.65 (s, 3H, OCH_3), 12.89 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 15.52, 18.45, 23.36, 62.52, 145.56, 158.89, 164.75; IR (KBr) ν_{max}: 3354 (br, OH), 1726, 1694, 1627, 1458, 1374 cm^{-1}. Anal. calcd for $C_7H_{11}NO_4$ C 48.55, H 6.40, N 8.09; found C 48.74, H 6.43, N 8.08.

Methyl 2,3-dione-2-oxime butanoate (2i) ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.35 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 13.34 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 31.25, 62.53, 147.69, 161.53, 165.82; IR (KBr) ν_{max}: 3448 (br, OH), 1751, 1654, 1452, 1373 cm^{-1}. Anal. calcd for $C_5H_7NO_4$: C 41.38, H 4.86, N 9.65; found C 41.42, H 4.88, N 9.63.

2,4-Dione-3-oxime pentane ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.15 (s, 3H, CH_3), 13.04 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 31.25, 137.79, 159.51, 161.72; IR (KBr) ν_{max}: 3437 (br, OH), 1747, 1634, 1425, 1351 cm^{-1}. Anal. calcd for $C_5H_7NO_3$: C 46.51, H 5.46, N 10.85; found C 46.53, H 5.47, N 10.83.

3,5-Dione-4-oxime heptane ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 2.24 (s, 3H, CH_3), 13.02 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 150 MHz) δ: 30.16, 32.42, 136.70, 159.43, 160.63; IR (KBr) ν_{max}: 3435 (br, OH), 1748, 1641, 1430, 1356 cm^{-1}. Anal. calcd for $C_5H_{11}NO_3$: C 53.49, H 7.05, N 8.91; found C 53.50, H 7.06, N 8.89.

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References

[1] Mohan, R. R. *Indian Drugs* **1991**, *29*, 120.
[2] Plate, R. *EP 559279*, **1993**.
[3] Benoit, R.; Sauter, H.; Kirstgen, R. *EP 498188*, **1992**.
[4] Misslitz, U.; Meyer, N.; Kast, J. *DE 418623*, **1991**.
[5] Lazonova, K.; Vasilev, G.; Kalcheva, V. *Dokl Bulg Akad Nauk* **1992**, *44*, 115.
[6] McOmie, J. F. W. *Protective Groups in Organic Chemistry*, Plenum Press, London and New York, **1973**, p. 46.
[7] Cameron, M.; Gowenlock, B. G.; Boyed, A. S. F. *J. Chem Soc., Perkin Trans. 2* **1996**, 2271.
[8] Veronese, A. C.; Vecchiati, G.; Sferra, S.; Orlandini, P. *Synthesis* **1985**, *3*, 300.
[9] Williams, D. L. H. *Nitrosation*, Cambridge University Press, **1988**, p. 77.
[10] Williams, D. L. H. *Supplement F2*, *In the Chemistry of Amino*, *Nitroso*, *Nitro and Related Groups*, John Wiley and Sons Ltd, New York, **1996**, p. 665.
[11] Keefer, L. K.; Williams, D. L. H. *Methods in Nitric Oxide Research*, John Wiley and Sons Ltd, New York, **1996**, p. 509 and references cited therein.
[12] Garcia Rio, L.; Leis, J. R.; Moreira, J. A.; Norberto, F. *J. Org. Chem.* **2001**, *66*, 381.
[13] Garcia Rio, L.; Leis, J. R.; Iglesias, E. *J. Org. Chem.* **1997**, *62*, 4712.
[14] *Vogels Text Book of Practical Organic Chemistry*, Longman, 4th ed., London and New York, **1986**,
[15] Sheriner, R. L.; Reynold, T. L.; Fuson, C.; Curtin, D. Y.; Morrill, T. C. *The Systematic Identification of Organic Compounds*, 6th ed., John Wiley and Sons, New York, **1980**, p. 220.
[16] Fuson, R. G. *Reaction of Organic Compounds*, *a Textbook for the Advanced Student*, John Wiley & Sons Inc, New York, **1962**, p. 535.
[17] Wagner, R. B.; Zook, H. D. *Synthetic Organic Chemistry*, John Wiley & Sons Inc, New York, **1953**, pp. 739—745.
[18] Graham, A.; Williams, D. L. H. *J. Chem. Soc., Perkin Trans. 2* **1992**, 747.
[19] Leis, R. J.; Pena, M. E.; Williams, D. L. H.; Mawson, S. D. *J. Chem. Soc., Perkin Trans. 2* **1998**, 157.
[20] Castedo, L.; Riguera, R.; Vezquez, M. P. *J. Chem. Soc. Chem. Commun*. **1983**, 301.
[21] Fanning, J. C.; Keefer, L. K.; Larry, K. *J. Chem. Soc. Chem. Commun*. **1987**, 955.
[22] Kim, Y. H.; Park, Y. J.; Kim, K. *Tetrahedron Lett*. **1989**, *30*, 2833.
[23] Lardy, C.; Tournier, L.; Prunier, M.; Valeur, E. *Tetrahedron Lett*. **2010**, *51*, 2277.
[24] Zyk, N. V.; Nesterov, E. E.; Khiobystov, A. N.; Zefirov, N. S. *Russ. Chem. Bull.* **1999**, *48*, 506.
[25] Zolfigol, M. A.; Zebarjadian, M. H.; Chehardoli, G.; Keypour, H.; Salehzadeh, S.; Shamsipur, M. *J. Org. Chem*. **2001**, *66*, 3619.
[26] Marsh, K. N.; Boxall, J. A.; Lichtenthaler, R. *Fluid Phase Equilibria* **2004**, *219*, 93.
[27] Keskin, S.; Kayrak-Talay, D.; Akman, U.; Hortacsu, Ö. *Supercritical Fluids* **2007**, *43*, 150.
[28] Zhao, H.; Yu, N.; Ding, Y.; Tan, R.; Liu, C.; Yin, D.; Qiu, H.; Yin, D. *Microporous Mesoporous Mater*. **2010**, *136*, 10.
[29] Wang, L.; Li, H. P. *Tetrahedron* **2009**, *65*, 364.Bi, W.; Tian, M.; Zhou, J.; Row, K. H. *J. Chromatogr. B* **2010**, *878*, 2243.
[30] Bi, W.; Tian, M.; Zhou, J.; Row, K. H. *J. Chromatogr. B* **2010**, *878*, 2243.
[31] Yadav, L. D. S.; Patel, R.; Rai, V. K.; Srivastava, V. P. *Tetrahedron Lett*. **2007**, *48*, 7793.
[32] Sun, J.; Cheng, W.; Fan, W.; Wang, Y.; Meng, Z.; Zhang, S. *Catal. Today* **2009**, *148*, 361.
[33] Valizadeh, H.; Shomali, A. *Dyes Pigments*. **2010**, doi: 10.1016/j.dyepig. 11.010.
[34] Burrell, A. K.; Del Sesto, R. E.; Baker, S. N.; McCleskey, T. M.; Baker, G. A. *Green Chem*. **2007**, *9*, 449.

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