Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron Letters
Tetrahedron Letters 45 (2004) 4759–4762

Silica supported MoO_3: a mild heterogeneous catalyst for the Beckmann rearrangement and its application to some sugar derived ketoximes ☆

Mohan K. Dongare,* Vivekanand V. Bhagwat, C. V. Ramana and Mukund K. Gurjar

National Chemical Laboratory, Dr. Homi Bhabha Road, Pune-411008, India

Received 5 January 2004; revised 7 April 2004; accepted 13 April 2004

Abstract—Silica supported molybdenum(VI) oxide (20%) has been explored as a new solid catalyst for the Beckmann rearrangement and the results are compared in parallel with the known β-zeolite as a catalyst for the same transformation. Both catalysts were found to facilitate the rearrangement under mild conditions and the conditions employed were tolerable for protecting groups such as isopropylidene, cyclohexylidene and PMB are commonly employed in carbohydrate chemistry.

The Beckmann rearrangement is a well-known transformation of keto-oximes to *N*-substituted amides in the presence of an acid.[1] Generally, strong Brønstead/Lewis acids ranging from stoichiometric to catalytic amounts are employed in order to accomplish the Beckmann rearrangement. To circumvent the harsh reaction conditions generally used for the Beckmann rearrangement coupled with a desire to use clean and environmentally benign reusable catalysts, various heterogeneous catalysts such as zeolites, mesoporous materials and metal oxides,[2,3] various solid acid catalysts[4] including B_2O_3 supported on Al_2O_3,[5] TiO_2 doped on $AlPO_4$,[6] SiO_2/Al_2O_3,[7,8] tungsten oxide,[8,9] FSM-16 and MCM-41[10] have been used either in solution or in the vapor phase.

Molybdenum oxide without support or supported on SiO_2 or Al_2O_3 is a well-known solid acid catalyst useful for acid catalyzed reactions such as the oxidation of ammonia to elemental N_2[11] and the synthesis of diphenyl carbonate from dimethyl carbonate and phenol.[12] Among the supported oxides, V_2O_5/SiO_2, ZrO_2/SiO_2, PbO/SiO_2 and MoO_3/SiO_2 **1**, MoO_3/SiO_2 has revealed the highest activity and selectivity for esterification.[12] One added advantage of the MoO_3/SiO_2 catalyst is the availability of standard protocols for the preparation of catalysts with the molybdenum percentage varying from 5–30%. In this communication we would like to present our results on the utilization of the MoO_3/SiO_2 catalyst for the Beckmann rearrangement. In addition, we evaluated its efficiency vis-à-vis β-zeolite **2**, the latter having already been employed as a catalyst for the Beckmann rearrangement.

The silica supported MoO_3 catalyst was prepared by the sol–gel method using ammonium molybdate $[(NH_4)_6Mo_7O_{24}{\cdot}4H_2O]$ and ethyl silicate-40 as molybdenum and silica sources, respectively, followed by drying and calcination at 500 °C. The catalyst was characterized for chemical composition as well as structural characterization by atomic absorption spectroscopy and X-ray diffraction analysis. Chemical analysis of MoO_3/SiO_2 showed the composition of the catalyst as 19.5 mol% MoO_3 and 80.5 mol% SiO_2. The XRD pattern of MoO_3/SiO_2 showed the presence of a MoO_3 crystalline phase supported on amorphous silica. The BET surface area and pore size distribution measurements showed the mesoporous nature (pore diameter of 79 Å) and the surface area of the material as 145 m^2/g indicating the high dispersion of MoO_3 on the amorphous silica support. The TPD analyses of MoO_3/SiO_2 and β-zeolite are shown in Figure 1. MoO_3/SiO_2 showed a higher number of weaker acid sites than β-zeolite. The

Keywords: Beckmann rearrangement; Solid acid; β-Zeolite; Molybdenum oxide; Glucose diacetonide.
☆ Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.04.068
* Corresponding author. Tel./fax: +91-20-25893761; e-mail: dongare@cata.ncl.res.in

0040-4039/$ - see front matter © 2004 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2004.04.068

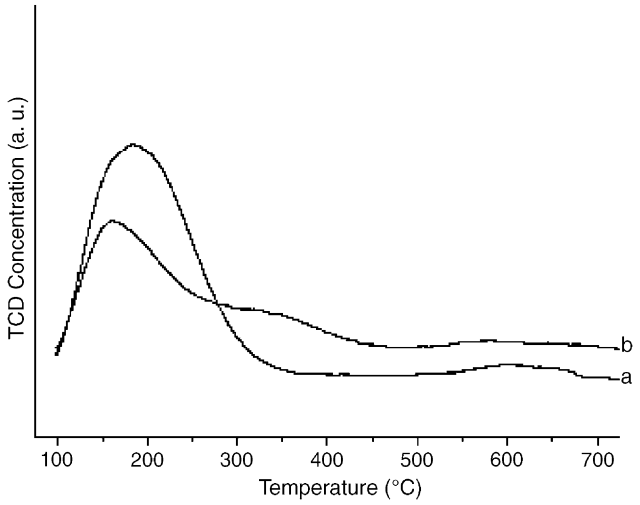
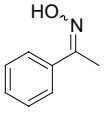
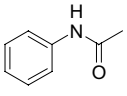
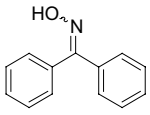
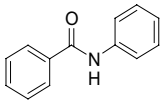
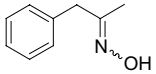
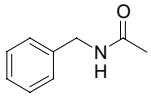
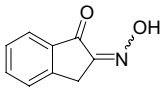
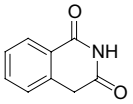
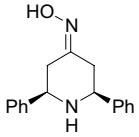
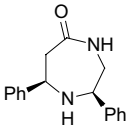
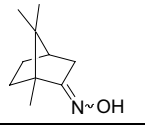
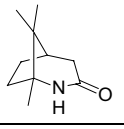


Figure 1. NH_3-TPD of (a) Mo/SiO_2 and (b) β-zeolite.

total acidity of β-zeolite was found to be 0.781 mmol/g while that of MoO_3/SiO_2 was 1.104 mmol/g.

After characterization of catalyst **1** in comparison with **2**, we proceeded further to investigate its applicability for Beckmann rearrangements. Attempted Beckmann rearrangement of various oximes derived from simple ketones (Table 1) with catalyst **1** gave excellent yields, and the regioselectivities in the cases of unsymmetrical ketoximes were high as expected.[13] Similar results were obtained when beta zeolite was used instead of MoO_3/SiO_2 as the catalyst.

Table 1. Beckmann rearrangement using solid acid catalysts **1** and **2**

Entry	Starting material	Product	Yield (%)	
			β-Zeolite	MoO_3/SiO_2
1			92	95
2			94	97
3			81	91
4			83	87
5			79	89
6			83	96

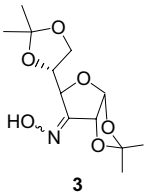
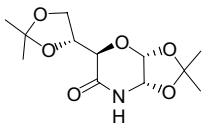
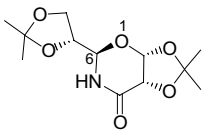
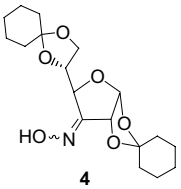
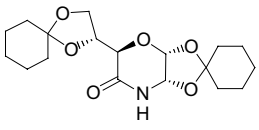
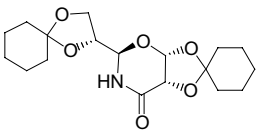
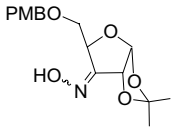
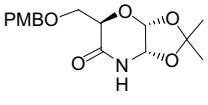
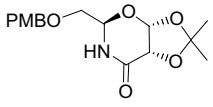
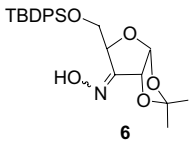
Representative procedure for the rearrangement of benzophenone oxime: A suspension of the catalyst (12.3 mg) and benzophenone oxime (5.0 mmol) in ethanol (10 mL) under argon was heated under reflux for 18 h. The reaction mixture was diluted with water and repeatedly extracted with ether. The combined organic layer was washed with brine, dried (magnesium sulfate) and concentrated. The residue was purified by flash column chromatography on silica gel to give benzanilide in 97% yield (with catalyst **1**) and 94% yield (with catalyst **2**).

Encouraged by the results obtained with aromatic as well as aliphatic oximes, we next focused our attention with the oximes derived from carbohydrates. To the best of our knowledge, there is no report concerning the Beckmann rearrangement of sugar oximes. However, oximes derived from erythronolides[14] and cyclohexitol[15] derivatives have been shown to undergo the Beckmann rearrangement yielding valuable drug candidates such as azythromycin, and polyhydroxycyclic lactams with varying ring sizes. Nonetheless, the use of catalytic methods is scarce. We chose the oximes **3**–**6**, which can be easily derived from glucose (Table 2; **3** and **4**) and xylose (Table 2; **5** and **6**).

The rearrangement of sugar-oxime **3** was carried out in the presence of catalyst **1** or **2** in refluxing ethanol. With both catalysts, the reactions are clean and resulted in inseparable regioisomeric mixtures. The amides **7** and **8** were obtained in very good yields and with moderate regioselectivity (3:2). The structures of the major **7** and the minor **8** isomers were determined with the help of ^1H NMR, COSY and NOESY spectra.[16] In the ^1H NMR spectra, H(3) of the major isomer **7** resonated downfield, ca. 0.25 ppm, with respect to the minor isomer **8**. Whereas, H(6) of the minor isomer **8** resonated 0.48 ppm downfield with respect to the major isomer **7**. This clearly established that in isomer **7**, C(5) is a carbonyl carbon while C(4) is a carbonyl carbon in the minor isomer **8**. Additionally, the long-range coupling observed $^5J_{3,6} = 1.3$ Hz (confirmed by selective irradiation experiments) in both isomers clearly indicated a *trans*-relationship between these protons thus excluding epimerization/inversion at C(6) during the rearrangement. This was further substantiated by the NOESY spectrum, where there was no coupling between H(6) and H(2)/H(3) for both isomers.

Having established the configuration of the two isomers resulting from oxime **3**, we next focused on oximes **4**–**6**. As indicated in Table 2, with oximes **4** and **5**, the rearrangement was smooth and resulted in regiomeric mixtures. In the case of the TBDPS oxime **6** (Table 2, entry 4), we encountered a complex reaction mixture presumably because of the cleavage of TBDPS under these conditions. The regioselectivity for oximes **3**–**5** was found to be independent of the catalyst used. This indicated that both catalysts can facilitate the rearrangement but the regioselectivity is governed by stereoelectronic

Table 2. Beckmann rearrangement of sugar oximes

Entry	Starting material	Products		Yield (%)[a]	
				β-Zeolite	MoO_3/SiO_2
1	 **3**	 **7**	 **8**	85 (3:2)	82 (3:2)
2	 **4**	 **9**	 **10**	84 (3:2)	87 (3:2)
3	 **5**	 **11**	 **12**	71 (3:1)	70 (3:1)
4	 **6**	Complex reaction mixture			

[a] Ratio of isomers in parentheses.

factors. Also, the protecting groups employed that is ketals (isopropylidene and cyclohexylidene) and benzyl ether are stable under the reaction conditions.

To conclude, a simple and convenient solid acid (β-zeolite and MoO_3/SiO_2) catalyzed Beckmann rearrangement has been reported. For the first time the Beckmann rearrangement on carbohydrate templates using solid catalysts has been evaluated. Commonly employed protecting groups in carbohydrate chemistry such as isopropylidene and cyclohexylidene systems and benzyl ethers were found to be stable under the conditions employed. Work in the direction of exploring the potential of the resulting [1,3]-oxazinone and morpholinone derivatives as chiral intermediates is in progress.

Supplementary material: ^1H, ^1H–^1H COSY, NOESY and ESI-MS of compounds **7/8**.

Acknowledgement

V.V.B. thanks CSIR (New Delhi) for the financial assistance in the form of a Research Fellowship.

References and notes

1. (a) Nubbemeyer, U. *Top. Curr. Chem.* **2001**, *216*, 125–196; (b) Craig, D. *Compd. Org. Synth.* **1999**, *7*, 689–702; (c) Abele, E.; Lukevics, E. *Heterocycles* **2000**, *53*, 2285–2336.
2. O'Sullivan, P.; Forni, L.; Hodnett, B. K. *Ind. Eng. Chem. Res.* **2001**, *40*, 1471–1475.
3. (a) Kusama, H.; Yamashita, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 373–377; (b) Laurent, A.; Jacquault, P.; De Martino, J. L.; Hamelin, J. *J. Chem. Soc., Chem. Commun.* **1995**, 1101; (c) Baldwin, J. E.; Vollmer, H. E.; Lee, V. *Tetrahedron Lett.* **1999**, *40*, 5401–5404; (d) Olah, G. A.; Fung, A. P. *Synthesis* **1981**, 473–474.
4. (a) Holdrich, W. F.; van Bekkum, H. *Stud. Surf. Sci. Catal.* **1991**, *58*, 631; (b) Holdrich, W. F. *Stud. Surf. Sci. Catal.* **1989**, *46*, 193; (c) Sato, H. *Catal. Rev. Sci. Eng.* **1997**, *39*, 395–424; (d) Tatsumi, T. *Curr. Opin. Solid State Mater. Sci.* **1997**, *2*, 76.
5. (a) Takamiya, N.; Tsunoda, H.; Suzuki, S.; Murai, S. *Nippon Kagaku Kaishi* **1978**, 799–804; (b) Sato, S.; Hasebe, S.; Sakurai, H.; Urabe, K.; Izumi, Y. *Appl. Catal.* **1987**, *29*, 107–115; (c) Sato, S.; Urabe, K.; Izumi, Y. *J. Catal.* **1986**, *102*, 99–108.
6. (a) Haber, J.; Szybalska, U. *Faraday Discuss. Chem. Soc.* **1981**, *72*, 263; (b) Bautista, F. M.; Campelo, J. M.; Garcia, A.; Luna, D.; Marinas, J. M.; Moreno, M. S. *Stud. Surf. Sci. Catal.* **1993**, *78*, 615.
7. Murakami, Y.; Saeki, Y.; Ito, K. *Nippon Kagaku Kaishi* **1978**, 21–26.
8. Yashima, T.; Horie, S.; Saito, S.; Hara, N. *Nippon Kagaku Kaishi* **1977**, 77–81.
9. Kob, N.; Drago, R. S. *Catal. Lett.* **1997**, *49*, 229–234.
10. (a) Nakajima, T.; Nakajima, T.; Meshima, S. *Nippon Kagaku Kaishi* **1997**, 565–569; (b) Dai, L. X.; Koyama, K.; Tatsumi, T. *Catal. Lett.* **1998**, *53*, 211–214.
11. (a) Lietti, L.; Ramis, G.; Busca, G.; Bregani, F.; Forzatti, P. *Catal. Today* **2000**, *61*, 187–195; (b) Biermann, J. J. P.; Janssen, F. J. J. G.; De Boer, M.; Van Dillen, A. J.; Geus, J. W.; Vogt, E. T. C. *J. Mol. Catal.* **1990**, *60*, 229–238.

12. Ono, Y.; Fu, Z. H. *J. Mol. Catal. A Chem.* **1997**, *118*, 293–299.
13. (a) Shriner, R. L.; Neumann, F. W. *Chem. Rev.* **1944**, *35*, 351–425; (b) Miyajima, G.; Sasaki, Y.; Suzuki, M. *Chem. Pharm. Bull.* **1971**, *19*, 2301–2307; (c) Egli, R. A. *Helv. Chim. Acta* **1970**, *53*, 47–53; (d) Ravindran, T.; Jeyaraman, R.; Murray, R. W.; Singh, M. *J. Org. Chem.* **1991**, *56*, 4833–4840; (e) Senthilkumar, U. P.; Jeyaraman, R.; Murray, R.; Singh, M. *J. Org. Chem.* **1992**, *57*, 6006–6014; (f) Rudakov, G. A. *Chemistry and technology of camphor*, 2nd ed., 1976.
14. (a) Kobrehel, G.; Djokic, S. U.S.-4,517,359, 1985 to Pliva, *Chem. Abstr.* **1982**, *98*, 17006; (b) Bright, G. M. U.S.-4,474,768, 1984 to Pfizer; *Chem. Abstr.* **1984**, *102*, 46227; (c) Djokic, S.; Kobrehel, G.; Lazarevski, G.; Lopotar, N.; Tam-burasev, Z.; Kamenar, B.; Nagl, A.; Vickovic, I. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1881–1890; (d) Yang, B. V.; Goldsmith, M.; Rizzi, J. P. *Tetrahedron Lett.* **1994**, *3*, 5, p 3025; (e) Bayod-Jasanada, M.; Carbajo, R. J.; López-Ortiz, F. *J. Org. Chem.* **1997**, *62*, 7479–7481.
15. (a) Albertini, E.; Barco, A.; Benetti, S.; De Risi, C.; Pollini, G. P.; Zanirato, V. *Tetrahedron* **1997**, *50*, 17171–17194; (b) Albertini, E.; Barco, A.; Benetti, S.; De Risi, C.; Pollini, G. P.; Zanirato, V. *Synlett* **1996**, 29–30; (c) Wu, M. H.; Jacobsen, E. N. *Tetrahedron Lett.* **1997**, *38*, 1693–1696.
16. Major isomer **7**: IR ($CHCl_3$) 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 3H), 1.41 (s, 3H), 1.43 (s, 3H), 1.51 (s, 3H), 3.96–4.10 (m, H-8, H-8′), 4.30 (dt, H-7, $J = 6.3$, 4.9 Hz, *irrdn. at* 4.77 → t, $J = 6.3$ Hz), 4.76 (dd, H-6, $J = 4.7$, 1.2 Hz, *irrdn. at* 5.28 → d, $J = 4.7$ Hz), 5.28 (dd, H-3, $J = 4.4$, 1.2 Hz, *irrdn. at* 4.76 → d, $J = 4.3$ Hz, *irrdn. at* 5.94 → d, $J = 1.2$ Hz), 5. 94 (d, H-2, $J = 4.4$ Hz, *irrdn. at* 5.28 → br s), 8.87 (br s, H–N); ^{13}C NMR (75 MHz, $CDCl_3$) 25.3, 26.3, 27.4, 65.4, 74.3, 76.9, 77.4, 104.8, 110.2, 113.8, 157.9 ppm. Minor isomer **8**: IR ($CHCl_3$) 1740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.33 (s, 3H), 1.39 (s, 3H), 1.44 (s, 6 H), 3.96–4.10 (m, H-8, H-8′, *irrdn. at* 5.24 → change), 4.49 (dt, H-7, $J = 6.9$, 2.3 Hz, *irrdn. at* 5.24 → t, $J = 6.7$ Hz), 5.03 (dd, H-3, $J = 4.4$, 1.3 Hz, *irrdn. at* 5.24 → d, $J = 4.1$ Hz, *irrdn. at* 6.01 → d, $J = 1.3$ Hz), 5.24 (dd, H-6, $J = 2.4$, 1.3 Hz, *irrdn. at* 5.03 → d, $J = 2.0$ Hz, *irrdn. at* 4.49 → d, $J = 1.3$ Hz, *irrdn. at* 6.01 → no change), 6.01 (d, H-2, $J = 4.4$ Hz, *irrdn. at* 5.03 → s), 8.80 (br s, H–N); ^{13}C NMR (75 MHz, $CDCl_3$) 26.1, 27.4, 27.6, 64.9, 77.4, 77.7, 79.1, 104.6, 109.8, 114.1, 158.5 ppm. MS-ESI: 274.2 (49%, $[M+1]^+$).
Anal. Calcd for $C_{12}H_{19}NO_6$:C, 52.74; H, 7.01; N, 5.13. Found: C, 52.67; H, 7.18; N, 4.95.