SHORT PAPER

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Regioselective synthesis of *syn*-oximes using 3Å molecular sieves in a solventless system

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Regioselective synthesis of *syn*-oximes using 3Å molecular sieves under solvent-free condition is described.

Keywords: regioselective synthesis, *syn*-oximes

Oximes are one of the most useful protecting groups and are extensively used for isolation, purification and characterisations of carbonyl compounds.[1] They are also widely used as the precursor in the synthesis of wide variety of organic compounds.[2] An efficient, mild and eco-friendly procedure for their preparation would therefore be of much interest. Although the literature contains quite a number of methods concerning the synthesis of oximes, careful scrutiny of the products reveals the presence of *syn* and *anti* regioisomers.[3] Existing methods for the synthesis of oximes consist of nitrosation at a carbon bearing an active hydrogen,[4] addition of hydroxylamine to aldehydes and ketones,[5] addition of NOCl to olefins,[6] addition of Grignard reagents to conjugate bases of nitro compounds,[7] photolysis of nitrites (Barton reaction),[8] oxidation of primary amines[9] and reduction of nitro compounds.[10]

These methods have their own merits and drawbacks. One disadvantage which all of these methods possess is that they are conducted in organic solvents. Solvents are not only expensive but they are hazardous to the environment. A literature survey showed only one report[11] of the synthesis of oximes in a solventless system.[11] However this procedure can be generalised for aromatic aldehydes and ketones and requiring NaOH as basic media.

In view of the current emphasis on solid state synthesis[12] and on green chemistry,[13] there is merit in developing a solventless preparation of oximes using an inexpensive and non-polluting catalyst.

Condensation of hydroxylamine with aldehydes and ketones which is most common method of synthesis of oximes, usually takes place in a mixture of water and ethanol requiring warming or even reflux in most cases.[3b] Use of molecular sieves has been reported as promoting agent in organic synthesis.[14] In continuation of our interest in conducting of organic synthesis in solventless system,[15] in this communication we report the use of 3Å molecular sieves to catalyse the condensation of carbonyl compound and hydroxylamine to obtain the corresponding oximes in a solvent-free condition.

In a typical procedure a mixture of benzaldehyde and hydroxylamine hydrochloride were ground thoroughly with an equivalent weight of 3Å molecular sieves relative to carbonyl compounds at room temperature. Usual work up afforded *syn*-benzaldoxime in 98% yield. To assess the generality of method, a wide variety of carbonyl compounds were treated similarly to give the corresponding oximes in high to excellent yields. The yield of reaction of benzophenone (entry 17) is moderate (Table 1).

Table 1 Synthesis of oximes catalysed by 3Å molecular sieves in solventless system

Entry	R_1	R_2	Found m.p./°C (b.p.)	Reported m.p./°C (b.p.)	Ref.	Yields/%[a]
1	CH_3	C_6H_5	59–61	60	3a,d	95
2	CH_3	4-$CH_3C_6H_4$	85–87	88	3a,d	96
3	CH_3	4-$OCH_3C_6H_4$	80–83	81–82	3a,d	95
4	CH_3	4-OHC_6H_4	141–143	144–145	3a,d	94
5	CH_3	4-BrC_6H_4	126–129	128–129	3a,d	96
6	CH_3	4-ClC_6H_4	93–95	95	3a,d	98
7	CH_3	4-$NO_2C_6H_4$	170–173	174	3a,d	96
8	C_3H_7	H	50–53	53–54	3a,d	98
9	C_3H_7	CH_3	(161–164)	(167)	3a,d	84
10	C_2H_5	C_2H_5	(165–169)	(164–166)	3a	80
11	H	C_6H_5	35–38	31–33	3b,d	98
12	H	4-$OCH_3C_6H_4$	60–63	65	3a,d	97
13	H	4-$CH_3C_6H_4$	75–77	79–80	3a,d	98
14	H	2-OHC_6H_4	55–58	57	3a,d	96
15	Cyclohexyl		83–86	87–88	3c	80
16	H	4-N,N-$(CH_3)_2C_6H_4$	140–143	144	3c	93
17	C_6H_5	C_6H_5	143–146	144	3c	30

[a]Yields refer to isolated products.

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It is interesting to mention that a careful examination of the TLC which was eluted in $CHCl_3$,^{1}HNMR spectra and melting or boiling points of these oximes showed the predominant formation of *syn*-oximes. The *syn*-oximes are easily distinguishable from those of *anti* by chemical shifts of hydrogens *cis* to the hydroxyl group.[3a,16] These ^{1}HNMR spectra and melting or boiling points were compared with those of authentic samples reported previously.[2a,3a-d,16]

In conclusion, 3Å molecular sieves are a convenient, efficient and environmentally benign catalyst for conversion of carbonyl compounds to the corresponding oximes in high to excellent yields. The method enjoys eco-friendly conditions since the consumption of solvent is minimum.

Experimental

All carbonyl compounds were commercially available. 3Å Molecular sieves were purchased from Merck. All products are known compounds and were characterised by comparison of their physical and spectroscopic data with those of the authentic samples.

Preparation of syn-oximes. General procedure: A mixture of an appropriate carbonyl compound (2.2 mmol), hydroxylamine hydrochloride (2.2 mmol) and powdered 3Å molecular sieves (1:1 w/w respect to carbonyl compound), were grinded thoroughly for 10 min. The reaction mixture was set aside for further 5 min at ambient temperature. To the crude $CHCl_3$ (2×10 ml) was added and filtered off.The solvent was evaporated to dryness and the residue was appropriately distilled or crystalised from suitable solvent to afford the syn-oxime (Table 1).

Typical 1HNMR data of products($CDCl_3$ as solvent, δ *relative to TMS):* Compounds **1:** δ 2.30(s,3H,CH_3); 7.30–7.70(m,5H,ArH); 9.50–9.80(broad,=NOH), **2:** δ 2.40(s,3H, CH_3); 2.50(s,3H, *p*–CH_3); 7.32(d,2H,*J*=8.4 Hz, ArH); 7.57(d,2H, *J*=8.4 Hz, ArH); OH is unobserved, **3:** δ 2.40(s,3H,CH_3); 3.90(s,3H,OCH3); 6.95(d,2H, *J*=8.4 Hz, ArH); 7.63(d,2H, *J*=8.4 Hz, ArH); OH is unobserved, **4:** δ 2.00(s,3H,CH_3); 6.52(d,2H, *J*=8.4 Hz, ArH); 7.35(d,2H, *J*=8.4 Hz, ArH); 9.40(broad, =NOH);10.50 (broad, 1H, *p*-OH), **5:** δ 2.30(s,3H,CH_3); 7.45–7.55(m,4H,ArH); 9.10–9.60(broad,=NOH), **7:** d2.65(s,3H,CH_3); 8.07(d,2H, *J*=9.0 Hz, ArH); 8.30(d,2H, *J*=9.0 Hz, ArH); OH is unobserved, **9:** δ 0.90(t,3H,CH_3-CH_2); 1.60–1.80(m,2H, CH_3-CH_2CH_2); 1.90(s,3H,CH_3-C=NOH); 2.30–2.40(m,2H,CH_3-CH_2-CH_2); 9.00(broad,C=NOH), **11:** δ 7.20–7.40(m,5H,ArH); 8.20(s,1H,H-C=N); 8.90–9.20(broad, =NOH), **12:** δ 3.85(s,3H, *p*-OCH_3); 6.91(d,2H, *J*=8.4 Hz, ArH); 7.54(d,2H, *J*=8.4 Hz, ArH); 8.10 (s,1H,H-C=N); OH is unobserved, **13:** δ 2.40(s,3H,*p*-CH_3); 7.25(d,2H, *J*=8.4 Hz, ArH); 7.56(d,2H, *J*=8.4 Hz, ArH); 8.20(s,1H, H-C=N); 8.90–9.20(broad,=NOH).

$$R_1R_2C{=}O + NH_2OH{,}HCl \xrightarrow[\text{solventless}]{\text{3Å molecular sieves}} R_1R_2C{=}NOH$$

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