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Cerium (IV) ammonium nitrate (CAN) initiated *O*-alkylation of oximes with *N*-vinyl lactams

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Abstract

O-Alkylation of oximes with *N*-vinylpyrrolidin-2-one or *N*-methyl-*N*-vinylacetamide was efficiently initiated by a catalytic amount of cerium (IV) ammonium nitrate (CAN), giving the corresponding oxime ether derivatives in good yield.

Keywords: Cerium (IV) ammonium nitrate; *O*-Alkylation; Oxime; *N*-Vinylpyrrolidin-2-one; *N*-Methyl-*N*-vinylacetamide

With a rather high reduction potential value of +1.61 V *vs.* NHE (normal hydrogen electrode), cerium (IV) ammonium nitrate (CAN) has emerged as a powerful one-electron oxidant [1]. CAN offers several advantages like easy handling, non-toxicity, and good solubility in organic solvents. It has been noted that more than 2 equiv. of CAN are required inevitably in most CAN-mediated oxidations, whereas catalytically CAN-induced reactions have scarcely been reported [2]. So making CAN catalytic performance should be a main focus of future on CAN chemistry.

Addition of organometallic reagents or radical species to oxime ethers have become an important protocol for many chemical conversions [3,4]. In general, oxime ethers have been prepared either by the condensation of *O*-alkyl hydroxylamine with a corresponding aldehyde or by the reaction of oximes with alkyl halides under basic conditions [5]. Recently, new methods have been developed upon transition metal-catalyzed allylic substitution of oximes [6], Michael addition [7], Cu-catalyzed cross-coupling reaction [8], and cation radical tris(aryl)aminium oxidation of *O*-alkylation of oximes with *N*-vinyl lactams [9]. In the present work we will report CAN initiated *O*-alkylation of oximes (1) with *N*-vinyl lactams, in which the corresponding oxime ethers (**3** or **4**) were produced in good yield.

We started with the addition reaction of (*E*)-4-chlorobenzaldehyde oxime (**1e**) to *N*-vinylpyrrolidin-2-one (**2a**, Scheme 1). It was used to optimize the reaction conditions and found that 10 mol% of CAN resulted in the formation of **3e** in a yield of 95%. Although the reaction proceeded also readily in the presence of only 2 mol% of CAN, a slightly lower yield was obtained and the reaction time was largely prolonged. It was still found that more than 10 mol% of CAN lead to a dramatic decrease in the yield of adducts and promoted decomposition of products. In some cases, the product of decomposition, 4-chlorobenzaldehyde, was detected. The solvent effects were then investigated using 10 mol% of CAN. Both of dichloromethane and acetonitrile were found to be the most favorable solvents.

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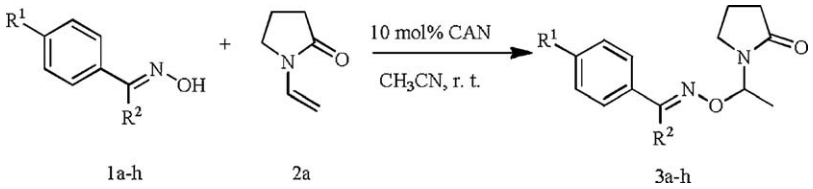


1a-h 2a 3a-h

Scheme 1.

The substrate scope for aldoximes (entries 1–7, Table 1) was extended under the optimized conditions. It shows that the reaction occurred satisfactorily in good yield and that an electron-withdrawing substituent bearing on the phenyl ring of **1** led to a higher yield (entries 4–7, Table 1), whereas an electron-donating group (entries 1 and 3, Table 1) resulted in a lower yield and a longer reaction time. This might be attributed to the lower oxidation potential of **1a** and **1c**, compared with those bearing an electron-withdrawing group [10], and partial decomposition of substrates. Replacement of **2a** by *N*-methyl-*N*-vinylacetamide **2b** proved to be encouraging (entries 9 and 10, Table 1 and Scheme 2). Nevertheless, two rotamers exhibiting double sets of ^{1}H NMR spectroscopy existed in the latter due to the restricted rotation of the amide bond, as having been reported previously [9b]. The conformation of rotamer **4** (major) and **4′** (minor) was deduced by NOE difference spectrum correlations. NOE enhancement of O–CH–N proton signals (q, 5.86) for **4** or NCH_3 proton signals for **4′** (q, 2.80) was observed on irradiation of $NCOCH_3$ protons (s, 2.25–2.02). The ratio of **4** to **4′** was estimated to be *ca*. 3:1 (Table 1).

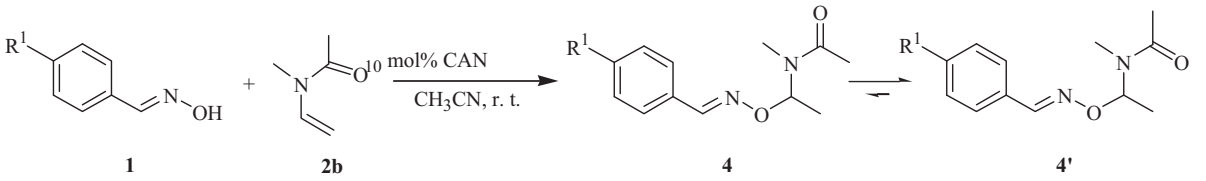
Addition of ketoximes (**1i**–**1l**) and 2-furaldehyde oxime (**1m**) to **2a** also occurred under the same conditions, giving the corresponding products **3** (entries 11–15, Table 1).

To identify the most possible reaction mechanism, some tests were carried out: (a) The reaction was performed both in the absence of CAN and in the presence of cerium trichloride or cerium trinitrate. No reaction took place in the former, and only a small amount of oximes converted to oxime ethers after 24 h in the latter; and (b) the aqueous extraction from the acetonitrile reaction solution was subjected to a test of color fading of methyl orange solution, which is characteristic of Ce^{4+}. It failed to fade the color of methyl orange solution. These observations suggest: (a) CAN most likely serves as a one-electron oxidant in the CAN initiated reaction. Because the oxidation potentials of **2a** (1.12 V *vs*. SCE [12]) and **2b** (1.51 V *vs*. SCE [11]) are significantly lower than those of **1a**–**1g** (1.45–2.14 V *vs*. Ag/AgCl electrode) [10], enamide **2** will be preferentially oxidized by CAN, giving the corresponding cation radical $\mathbf{2}^+$,

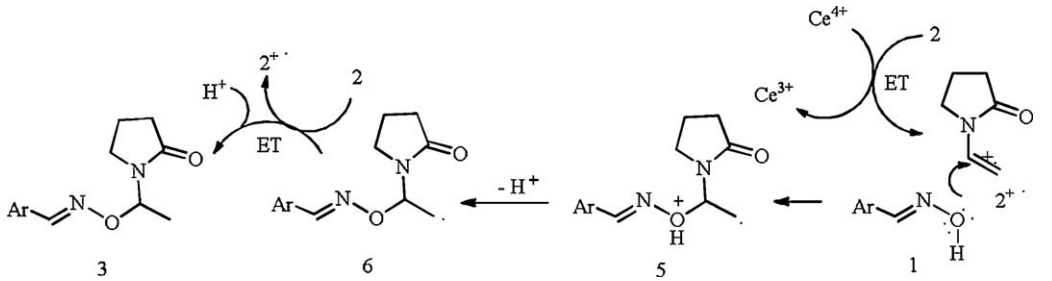
Table 1
CAN initiated addition of oximes **1** to *N*-vinyl lactams **2a** or **2b**[a].

Entry		Oximes		Lactam	Time[b] (h)	Product	Yield of **3** or **4**[c] (%)
		Ar (R)	R^2				
1	**1a**	*p*-CH_3OPh	H	**2a**	3	**3a**	73
2	**1b**	Ph	H	**2a**	1.5	**3b**	87
3	**1c**	*p*-CH_3Ph	H	**2a**	3	**3c**	85
4	**1d**	*o*-ClPh	H	**2a**	1	**3d**[d]	89
5	**1e**	*p*-ClPh	H	**2a**	1	**3e**	95
6	**1f**	*p*-NO_2Ph	H	**2a**	1.5	**3f**	91
7	**1g**	*m*-NO_2Ph	H	**2a**	2	**3g**[e]	88
8	**1h**	*o*-OHPh	H	**2a**	2	**3h**[e]	83
9	**1c**	*p*-CH_3Ph	H	**2b**	2	**4c** (3.2:1)[d]	72
10	**1e**	*p*-ClPh	H	**2b**	2	**4e** (2.7:1)[d]	88
11	**1i**	Ph	CH_3	**2a**	2	**3i**	82
12	**1j**	*p*-NO_2Ph	CH_3	**2a**	2	**3j**[e]	85
13	**1k**	Ph	Ph	**2a**	2	**3k**[e]	90
14	**1l**	CH_3	CH_3	**2a**	2.5	**3l**[e]	84
15	**1m**	2-Furyl	H	**2a**	1.5	**3m**	85

[a] Reaction conditions: oximes (1.05 mmol), *N*-vinyl lactams (1 mmol), CAN (0.10 mmol), CH_3CN (10 mL), r.t.
[b] The reaction time.
[c] Isolated yields of the products after column chromatography.
[d] The ratio of **4** to **4′** was evaluated using the characteristic ^{1}H NMR peaks for O-C*H*-N at 5.86 (**4**) and 6.57 (**4′**).
[e] Five new compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy, EI-MS, and HRMS.



Scheme 2.



Scheme 3.

and (b) Ce^{4+} was reduced to Ce^{3+} during the course of reaction, and a possible acid-induced process would be ruled out, for no reduction of CAN would be detected if CAN acted as a Lewis acid catalyst [2b]. As such, a cation radical-mediated *O*-alkylation of oximes as depicted in Scheme 3 is proposed to rationalize the reaction. [13]

In conclusion, we present herein a simple, novel, highly efficient method for *O*-alkylation of oximes with *N*-vinylpyrrolidin-2-one or *N*-methyl-*N*-vinylacetamide by using CAN as an initiator. This entry offers several advantages like short reaction time, good yields, ready availability of the initiator, and mild reaction conditions.

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[13] General procedure: An anhydrous acetonitrile solution (10 mL) of 1 (1.05 mmol) and 2 (1 mmol) was dropwise added to an acetonitrile solution (10 mL) of CAN (0.10 mmol) at ambient temperature under stirring. After the reaction was completed as monitored by TLC, it was diluted with water and extracted with 3 × 10 mL of dichloromethane. The crude organic solution was then extracted three times with water to remove inorganic salts. The organic phase was dried over anhydrous magnesium sulfate, filtered, and the solvent was removed under reduced pressure. The product was separated by silica gel column chromatography eluted with ethyl acetate/acetone (v/v 3:1) to afford the pure oxime ether as a unique product. Selective data for **3g**: Colorless oil; IR (KBr) ν 2988, 2956, 1697, 1532, 1418, 1352, 1282, 1269, 1087, 958 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.30 (m, 1H), 8.17–8.20 (m, 1H), 8.11 (s, 1H), 7.95–7.97 (m, 1H), 7.53 (m, 1H), 6.16 (q, 1H, J = 6.0 Hz), 3.42–3.48 (m, 2H), 2.42–2.46 (m, 2H), 2.00–2.03 (m, 2H), 1.48 (d, 3H, J = 6.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.7, 148.4, 147.2, 133.8, 132.3, 129.7, 124.4, 122.8, 80.9, 41.7, 31.6, 18.1, 16.9; MS-EI (70 eV): m/z (rel. int., %) = 277 (0.01), 166 (1.2), 113 (7.5), and 112 (100); HR-ESI-MS: m/z calcd for $C_{13}H_{15}N_3O_4$ + H: 278.1135. Found: 278.1136.