

Transformation of Organic Functional Groups with Rare-Earth Metal Compounds: The Reaction of Alkenes with Cerium (IV) Ammonium Nitrate

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Several alkenes are converted into α -nitro alkenes, β -nitro alcohols, and mono-nitrates of a diol in the presence of cerium (IV) ammonium nitrate. The products depend on the structure of alkene, and reaction conditions. It has been found that (1): a small amount of certain additive such as carbonyl compounds, hydroquinone, or so on catalyzes the reaction, though its role in the reaction is unknown, and (2): acetonitrile-formic acid 2:1 V/V is the best solvent system.

KEY WORDS: Cerium (IV) ammonium nitrate/ α -Nitro alkene/ β -Nitro alcohol/ Nitration/

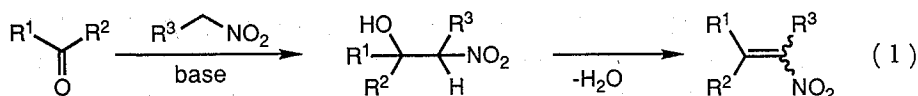
It is hard to justify at present the nomenclature of the group known as "rare earth metal", because the members of the group are no more really rare. In recent years, the advanced separation procedures have made these elements more and more easily available. Moreover, they have some interesting properties for organic chemists: (1) high coordination number, (2) oxophilicity, (3) ionic radius, (4) hardness as a Lewis acid, (5) unique oxidation-reduction system. For these reasons, recently much attention has been paid to application of rare earth metal compounds to the syntheses of organic molecules.¹⁾

The author has also been interested in finding novel transformations in organic functional groups mediated by rare earth metal compounds, especially cerium compounds and reported the development of some novel reaction systems. They are halogenation of aromatic compounds with cerium (IV) ammonium nitrate (CAN)-X₂ (X: halogen) or CAN-X⁻ system²⁾ and direct alkoxylation of anthracene derivatives with cerium (IV) trifluoroacetate-ROH system.³⁾

On the other hand, aliphatic nitro compounds have a potential and unique ability to achieve the carbon-carbon bond formation reaction, because of the strong electron-withdrawing ability and electron acceptability of the nitro group, as well as its susceptibility to the transformation into other useful functional groups (*e.g.* amino-, carbonyl- groups, and so on), and then have been used as a versatile synthetic intermediate.⁴⁾

β -Nitro alcohol and α -nitro alkene are the most familiar aliphatic nitro compounds. Various methods are reported on their syntheses.^{4,5)} Among them, the most popular one is the Henry method where a nitroalkane is treated with an aldehyde in the presence of a base (eq. 1).⁵⁾

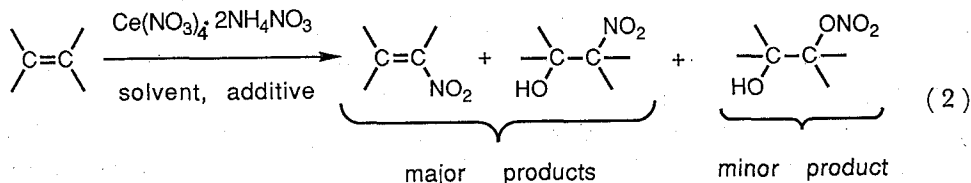
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The author wish to report a novel transformation of carbon-carbon double bond into the corresponding β -nitro alcohol and/or α -nitro alkene mediated by cerium (IV) ammonium nitrate.

RESULTS AND DISCUSSION

An appropriate amount of CAN and excess alkene were allowed to react in acetonitrile-formic acid (2:1) in the presence of small amount of additive at 50–60°C. The products shown in the eq. 2 were isolated after usual work-up and identified by elemental analyses and ^1H -NMR, ^{13}C -NMR, IR, MS-spectroscopies. Their spectra were compared with those of the corresponding authentic samples, if necessary.



Previously, it was found that, in the co-existence of catalytic amount of nitrogen dioxide and oxygen, metal halide acts as a highly selective and regiospecific halogenation agent.⁶⁾ Analogous ligand exchange reaction is expected in the present case,

Table 1. The Reaction of Alkenes with Cerium (IV) Ammonium Nitrate^{a)}

Alkene	Yield of α -nitro alkene (%) ^{b)}	Yield of β -nitro alcohol (%) ^{b)}
1-hexene	$\text{C}_4\text{H}_9\text{CH}=\text{CHNO}_2$ (32) ^{c)}	$\text{C}_4\text{H}_9\text{CH}(\text{OH})\text{CH}_2\text{NO}_2$ (157)
4-methyl-1-pentene	$(\text{CH}_3)_2\text{CHCH}_2\text{CH}=\text{CHNO}_2$ (67) ^{c)}	$(\text{CH}_3)_2\text{CHCH}_2\text{CH}(\text{OH})\text{CH}_2\text{NO}_2$ (94)
1-octene	$\text{C}_6\text{H}_{13}\text{CH}=\text{CHNO}_2$ (27) ^{c)}	$\text{C}_6\text{H}_{13}\text{CH}(\text{OH})\text{CH}_2\text{NO}_2$ (102)
1-decene	$\text{C}_8\text{H}_{17}\text{CH}=\text{CHNO}_2$ (62) ^{c)}	
2-heptene ^{h)}	$\text{C}_4\text{H}_9\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (79) ^{d)}	$\text{C}_4\text{H}_9\text{CH}(\text{OH})\text{CH}(\text{NO}_2)\text{CH}_3$ (46) ^{e)}
	$\text{C}_4\text{H}_9\text{C}(\text{NO}_2)=\text{CHCH}_3$ (36) ^{d)}	$\text{C}_4\text{H}_9\text{CH}(\text{NO}_2)\text{CH}(\text{OH})\text{CH}_3$ (43) ^{f)}
2-hexene	$\text{C}_3\text{H}_7\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (68) ^{d)}	$\text{C}_3\text{H}_7\text{CH}(\text{OH})\text{CH}(\text{NO}_2)\text{CH}_3$ (53) ^{g)}
	$\text{C}_3\text{H}_7\text{C}(\text{NO}_2)=\text{CHCH}_3$ (45) ^{d)}	$\text{C}_3\text{H}_7\text{CH}(\text{NO}_2)\text{CH}(\text{OH})\text{CH}_3$ (57) ^{g)}
2-octene	$\text{C}_5\text{H}_{11}\text{CH}=\text{C}(\text{NO}_2)\text{CH}_3$ (70) ^{d)}	$\text{C}_5\text{H}_{11}\text{CH}(\text{OH})\text{CH}(\text{NO}_2)\text{CH}_3$ (40) ^{g)}
	$\text{C}_5\text{H}_{11}\text{C}(\text{NO}_2)=\text{CHCH}_3$ (34) ^{d)}	$\text{C}_5\text{H}_{11}\text{CH}(\text{NO}_2)\text{CH}(\text{OH})\text{CH}_3$ (45) ^{g)}
2-methyl-1-pentene ⁱ⁾	$\text{C}_3\text{H}_7\text{C}(\text{CH}_3)=\text{CH}(\text{NO}_2)$ (87) ^{d)}	
cis-cyclooctene	1-nitrocyclooctene (99)	
1, 7-octadiene	$\text{C}_6\text{H}_{11}\text{CH}=\text{CH}(\text{NO}_2)$ (30) ^{c)}	$\text{C}_6\text{H}_{11}\text{CH}(\text{OH})\text{CH}_2\text{NO}_2$ (100)

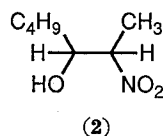
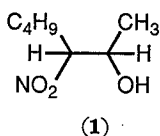
a) The reaction was carried out under the following conditions; CAN 1.6 mmol, alkene; 1.5 ml, CH_3CN ; 1.0 ml, HCOOH ; 0.5 ml, cyclohexanone; 0.4 mmol, 55–57°C, 17 h. b) The yields are based on CAN used. c) The *trans*-isomer. d) E/Z ratios are not determined. e) *syn* (*anti*): *anti* (*syn*)=49:51 f) *syn*(*anti*): *anti*(*syn*)=37:63 g) Diastereoselectivities are not determined. h) The *cis*-and *trans*-isomers gave the same result. i) N-(1,1-dimethyl butyl)-acetamide (7) was obtained as a side product.

and the results are in fact in accord with the expectations. β -Nitro alcohol and α -nitro alkene were obtained along with minor formation of mono-nitrate of a glycol. The results are summarized in Table 1. Cyclohexanone was used as an additive. The yields are calculated based on CAN used.

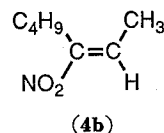
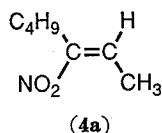
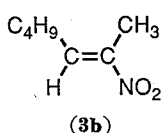
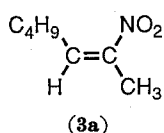
In the reaction with monosubstituted terminal alkene (1-hexene, 1-octene, 1-decene, and 4-methyl-1-pentene), β -nitro alcohol and α -nitro alkene were obtained in moderate to high yields. Closer investigation with 1-hexene showed that the compounds with the terminal nitro group are the sole products. This observation was confirmed by the comparison of $^1\text{H-NMR}$ spectra of the products with those of authentic samples that were prepared from nitromethane and valeraldehyde by the Henry method.^{7,13)} Since the nitro alcohol can be easily transformed into the corresponding nitro alkene,^{7,8)} additional attempt was not made to control the nitro alcohol/nitro alkene ratio. It turns out from $^1\text{H-NMR}$ spectrum that the nitro alkene is the *trans*-isomer.

To elucidate the limitation of the structure of alkene in the present reaction, several substituted alkene were subjected to the reaction.

Substitution of another alkyl group on the other side of alkenic carbon does not affect the reaction course: in the reaction with 2-heptene, an internal alkene, the yields of β -nitro alcohol and α -nitro alkene based on CAN used were 83% and 115%, respectively. Regioselectivities as well as diastereoselectivities were, however scarcely recognized in both products. $^1\text{H-NMR}$ spectrum of the nitro alcohol mixture exhibits four sets of doublet peaks centered at 1.246, 1.272, 1.537, and 1.543 ppm. The peaks at 1.246 and 1.272 ppm can be assigned to the protons on the carbon-2 of *syn* (*anti*) and *anti* (*syn*) isomers of the 3-nitro alcohol (**1**), respectively. On the other hand, the peaks at 1.537 and 1.543 ppm can be assigned to the protons on the carbon-2 of *syn* (*anti*) and *anti* (*syn*) isomers of 2-nitro alcohol (**2**), respectively.

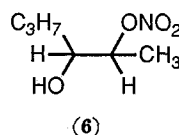
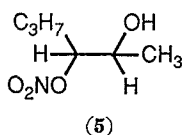


The **2/1** ratio determined from integrated intensities of the signals was 48:52 and this value agreed with the value determined from gas chromatographic data. Although each peak can not be assigned to the particular diastereoisomers (*syn* and *anti*) of **1** and **2**, the isomer ratios are 37:63 in **1** and 49:51 in **2**. In the nitro alkene, regioisomer ratio, (**3a**+**3b**)/(**4a**+**4b**) is 69/31, but it has not yet become apparent whether the nitro alkene is **3a** (**4a**) or **3b** (**4b**) or a mixture of both.

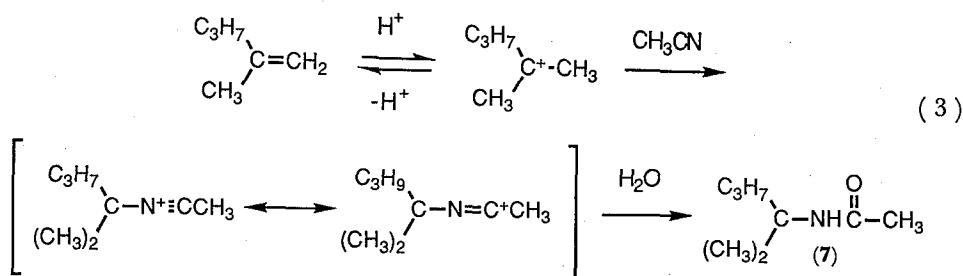


Almost the same results were obtained in *cis*-2-heptene and *trans*-2-heptene with

respect to the regioisomer and diastereomer ratios. 2-Hexene and 2-octene also yielded analogous results. However, in the products from 2-hexene, small amount of mono-nitrate of a glycol was detected. The ester may be a mixture of **5** and **6**.



However, when an additional alkyl group is substituted on the same alkenic carbon, the reaction undergoes to the different direction. In nitration of 2-methyl-1-pentene, a 1,1-disubstituted alkene, 2-methyl-1-nitro-1-pentene and N-substituted amide (**7**) were obtained in 87% and 29% yields, respectively. Under acidic conditions as that employed for the present reaction, an alkene is easily protonated to give the carbenium ion. Therefore, the amide seems to be formed according to the reactions shown in eq. 3.



It seems likely that the tertiary carbenium ion intermediate from 2-methyl-1-pentene is stable enough to afford the N-substituted amide. On the other hand, an alkene which affords the corresponding secondary carbenium ion on protonation does not yield the amide. Only a trace amount of β -nitro alcohol was isolated from the reaction under the reaction conditions employed.

The reaction proceeded smoothly and clearly in *cis*-cyclooctene, a cyclic alkene. The sole product isolated with the yield of 99% was 1-nitro-cyclooctene.

1,7-Octadiene, an isolated diene was also nitrated to afford *trans*-1-nitro-1, 7-octadiene in 30% yield.

It is worthwhile to mention about two prominent features in the reaction. First, this reaction is extremely sensitive to the solvent. Table 2 shows the effect of solvent in the reaction with 1-hexene. Acetonitrile, methanol, dimethylsulfoxide, or formic acid did not give a satisfactory result. Instead, a binary solvent, acetonitrile-formic acid, gave the best result; 1-nitro-1-hexene and 1-nitro-2-hexanol were obtained in 32% and 157% yields, respectively. The observation suggests that formic acid plays an important and special role in the reaction, since the yields of products in acetonitrile-acetic acid were moderate. Trifluoroacetic acid gave a good result for the formation of α -nitroalkene, and showed considerably different feature compared with other solvents. The ratio of acetonitrile to formic acid again plays a crucial

Table 2. Effect of Solvent in the Reaction with 1-Hexene^{a)}

Solvent (ml)	Yield of 1-nitro-1-hexene (%) ^{b)}	Yield of 1-nitro-2-hexanol (%) ^{b)}
CH ₃ CN (1.0)-HCOOH (0.5)	32	157
CH ₃ CN (1.0)-H ₂ O (0.5)	17	26
CH ₃ CN (1.5)	18	22
CH ₃ CN (1.0)-CH ₃ COOH (0.5)	28	43
CF ₃ COOH (1.5)	58	39
CH ₃ CN (1.0)-CH ₃ COOH (0.5)-H ₂ O (0.5)	9	25
CH ₃ CN (1.0)-(CH ₃ CO) ₂ O (0.5)	19	32
1-hexene (1.5)	3	3
(CH ₃) ₂ SO (1.5)	1	1
CH ₃ OH (1.5)	trace	trace
HCOOH (1.5)	7	16
CH ₃ COOH (1.5)	7	15

a) The reaction was carried out under the following conditions; CAN: 1.6 mmol, 1-hexene: 1.5 ml, 55~57°C, 17 h.

b) The yields are based on CAN used.

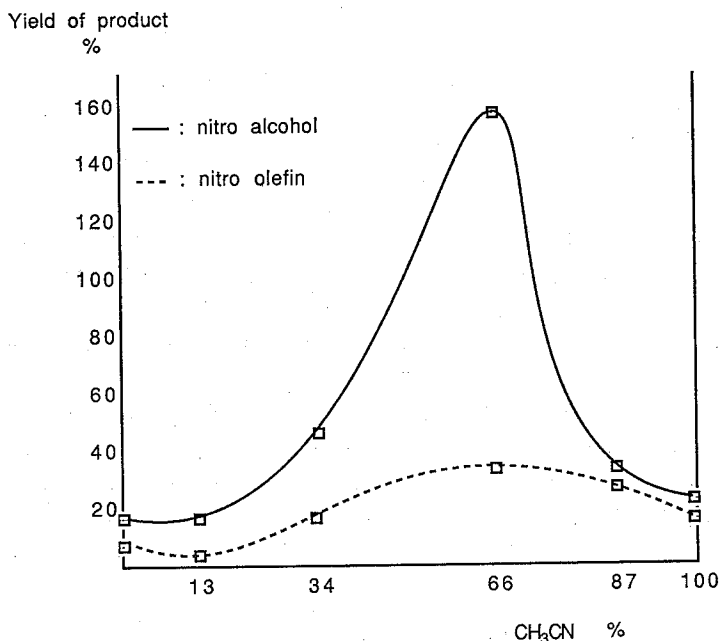


Fig. 1. Effect of CH₃CN/HCOOH (V/V) ratio in the reaction with 1-hexene on the yields of 1-nitro-2-hexanol (—) and 1-nitro-1-hexene (---).

role to the reaction. The results from the reactions in various compositions of the solvents are shown in Fig. 1, which indicates that the ratio (V/V) of 2 is the best and exclusive. This tendency is more remarkable for the formation of 1-nitro-2-hexanol than that of 1-nitro-1-hexene.

The second feature is that an additive is required to undergo the reaction smoothly. The influence of the additive on the yields of the products is shown in Table 3 for the reaction with 1-hexene. Interestingly, the reaction affords 1-nitro-1-hexene and 1-nitro-2-hexanol in only 6% and 1% yields, respectively, in the absence of an

Table 3. Effect of Additive in the Reaction with 1-Hexene^{a)}

Additive	Yield of 1-nitro-1-hexene (%) ^{b)}	Yield of 1-nitro-2-hexanol (%) ^{b)}
	6	1
cyclohexanone	32	157
cyclopentanone	30	145
acetophenone	20	19
1-heptanone	66	87
acetylacetone	52	103
hexachloroacetone	10	4
di-butyl ether	1	0
tetrahydrofuran	5	0
propanol	3	0
hydroquinone	39	107
cumene	12	6
benzene	4	0
dibutyl sulfide	7	4
dimethylsulfoxide	10	5
chloroform	9	3
benzhydrol	18	9

a) The reaction was carried out under the following conditions;
CAN: 1.6 mmol, 1-hexene: 1.5 ml, CH₃CN: 1.0 ml, HCOOH:
0.5 ml, additive: 0.4 mmol, 55~57°C, 17 h.

b) The yields are based on CAN used.

Table 4. Effect of the Amount of Additive in the Reaction with 1-Hexene^{a)}

Mole ratio cyclohexanone/CAN	Yield of 1-nitro-1-hexene (%) ^{b)}	Yield of 1-nitro-2-hexanol (%) ^{b)}
2.00	23	64
1.00	33	88
0.50	48	128
0.25	32	157
0.10	15	14
0.05	16	10
0.02	9	trace
0	6	1

a) The reaction was carried out under the following conditions;
CAN: 1.6 mmol, 1-hexene: 1.5 ml, CH₃CN: 1.0 ml, HCOOH:
0.5 ml, 55~57°C, 17 h.

b) The yields are based on CAN used.

additive. Among the additive examined, carbonyl compounds seems to give good results. However, the presence of a carbonyl group is not a necessary condition: hexachloroacetone promotes the reaction in very small extent. It seems that certain amount of electron density is required on the carbonyl oxygen in order to exert the desired effect.

Table 4 shows the effect of the mole ratio of cyclohexanone to CAN on the yield in the reaction with 1-hexene. The optimum ratio fall within the range between 0.50 and 0.25. Although it is probable that the role of the additive is based on its reducing power, the more detailed informations are required in order to understand this subject.

Generally, acetyl nitrate, nitril chloride, dinitrogen tetraoxide, dinitrogen trioxide, and nitric acid are used as the reagent to introduce a nitro group directly into a carbon-carbon double bond.⁹⁾ However, there are two significant difficulties in the reaction with these reagents. Namely, in the most case, a complex mixture of products is obtained. Separation of the mixture poses a serious limitation to the methods.⁹⁾ Of course, the difficulty in isolation decreases the yield of desired product. Secondly, there are difficulties in controlling the reaction conditions and in handling the reagents. For example, acetyl nitrate is prepared in situ by the reaction of acetic anhydride with nitric acid at 15°C. Careful control of the exothermic reaction is essential, but acetyl nitrate is not formed at lower temperatures.⁹⁾

An alkenic proton in a cycloalkene can be substituted by the nitro group by several procedures. Among them, nitro selenation,¹⁰⁾ nitro mercuration,^{4d)} or nitrocyl halogenation¹¹⁾ as well as electrode oxidation¹²⁾ were reported. Some other methods (*e.g.*, the addition of dinitrogen tetraoxide to alkene) are accompanied by many side reactions. Present method for the synthesis of 1-nitrocycloalkene is comparable to the above procedures in simplicity on the procedure, easiness of acquisition and relatively low price of the reagents and high yields. The present method will be applied to the syntheses of monosubstituted and cyclic nitro alkenes.

EXPERIMENTAL

Instruments. The ¹H-NMR, IR, and GC-MS spectra were recorded on Varian VXR-200 and JEOL JNM-GX400, Hitachi 260-50, and Hewlet-Packard 5992B GC/MS system spectrometers, respectively. Analytical GLC was carried out with a Yanaco-G-2800 gas chromatograph using 0.6 m–0.3 cm o.d. stainless column packed with 5% Silicon OV-17 on Chromosorb W. or 5% PEG 20M on Chromosorb W. and a improved Yanaco-G-2800 gas chromatograph using 25 m–0.25 mm i.d. PEG-20M bonded capillary column. The column chromatography was carried out on Silica Gel 60 (70–230 mesh, Nacalai tesque) with eluent of hexane and dichloromethane.

Materials. Cerium (IV) ammonium nitrate was offered by SEIMI Chemical Co., LTD. and used after drying at 80°C, 2 h. β -Nitro alcohols as authentic samples were prepared from the corresponding nitro alkanes and aldehydes according to the Henry method.⁷⁾ α -Nitro alkenes were obtained from the β -nitro alcohols.¹³⁾ In

each case, elemental analysis and $^1\text{H-NMR}$, IR, mass spectra gave a satisfactory results. The other chemicals were obtained from commercial source (Nacalai tesque Inc. and Wako Pure Chemical Industries, LTD.) and used after purification, if necessary.

Product Analyses. Into a mixture of CAN (9.6 mmol), cyclohexanone (2.4 mmol), acetonitrile (6.0 ml), and alkene (9.0 ml), was added 3 ml of formic acid. The mixture was stirred for 17 h. at 55–57°C and poured into 20 ml of water and extracted with dichloromethane (3 x 20 ml). The combined dichloromethane layer was washed with water, neutralized with sodium hydrogencarbonate, dried over anhydrous sodium sulfate, and the dichloromethane was removed at 50°C under reduced pressure. The residue was separated, and purified with column chromatography, and/or with distillation. The isolated products were identified by comparing their $^1\text{H-NMR}$, IR, and mass spectra with those of the corresponding authentic samples. Elemental analyses gave satisfactory results.

Quantitative Analyses. The same experiment as mentioned above was carried out in 1/6 scale. The combined dichloromethane layer was quantitatively analyzed by GLC, after an usual work-up. For the investigation of the effect of solvent composition, the reaction was run keeping the total amount of the solvent to 1.5 ml, the ratio was changed as shown in Fig. 1.

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