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Formation of isoxazole derivatives via nitrile oxide using ammonium cerium nitrate (CAN): a novel one-pot synthesis of 3-acetyl- and 3-benzoylisoxazole derivatives

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Abstract—The reactions of alkenes and alkynes with ammonium cerium(IV) nitrate ($(NH_4)_2Ce(NO_3)_6$, CAN(IV)) in acetone under reflux gave the corresponding 3-acetyl-4,5-dihydroisoxazole and 3-acetylisoxazole derivatives. In the case of acetophenone, 3-benzoyl-4,5-dihydroisoxazole and 3-benzoylisoxazole derivatives were obtained. Reaction of acetone with CAN(IV) afforded the corresponding furoxan (3,4-diacetyl-1,2,5-oxadiazole 2-oxide) as the dimer of nitrile oxide. Moreover, it was found that yields of isoxazole derivatives were improved using ammonium cerium(III) nitrate tetrahydrate ($(NH_4)_2Ce(NO_3)_5{\cdot}4H_2O$, CAN(III))-formic acid. The reaction mechanisms based on nitration and formation of nitrile oxide mediated by CAN(IV) or CAN(III) from acetone or acetophenone are also proposed.

1. Introduction

Isoxazole derivatives are an important class of heterocyclic compounds and their chemical properties have been studied over the years. Isoxazole derivatives have served as a versatile building block in organic synthesis. They can be converted into several important synthetic units such as β-hydroxy ketones,[1–5] γ-amino alcohols,[6] α,β-unsaturated oxime,[7] and β-hydroxy nitriles.[8] For example, the transformation of β-hydroxy ketones is commonly accomplished by reduction of 4,5-dihydroisoxazoles with H_2-Raney Ni,[1] $TiCl_3$,[2] $Mo(CO)_6$,[3] and SmI_2,[4] and oxidation with ozone.[5] In addition, isoxazole derivatives have long been targeted in synthetic investigation for their known biological activities and pharmacological properties such as hypoglycemic,[9] analgesic,[10] anti-inflammatory,[11] and anti-bacterial activity.[12] Recently, Srivastava et al.[13] reported that on evaluation of HIV-inhibitory activity of 5-(2,2-dibromoacetyl)-3-phenylisoxazole, reduction of infected cells was indicated. Two methods have been employed generally to prepare isoxazole derivatives: 1,3-dipolar cycloaddition of alkenes or alkynes with nitrile oxides from the dehydrohalogenation of hydroximoyl chlorides in the presence of triethylamine,[14] and the dehydration of primary nitroalkanes with ethyl chloroformate in the presence of triethylamine.[15] In particular, it is known that the reaction of β-keto esters or α,β-unsaturated ketones with hydroxylamine yields the isoxazole derivatives via intramolcular nitrile oxide cycloaddition (INOC) by a one-pot method.[16,17]

CAN(IV) has been utilized extensively for a variety of oxidative transformations. In addition, it is known that CAN transform several alkenes and aromatic compounds into nitro compounds.[18,19] We have investigated the development of some novel reaction systems using CAN. During the course of our studies, we reported a novel α-iodination of ketones in acetic acid or alcohols,[20] a new alkoxyiodination and nitratoiodination of olefins and α,β-unsaturated esters,[21] and a new α,α′-diiodination of ketones using iodine-CAN(IV).[22] One of our group reported a one-pot synthesis of 4,5-dihydroisoxazole derivatives from alkenes by the use of CAN(IV) or CAN(III) in acetonitrile-formic acid at 57 °C for 48 h.[23] However, the yields of products were unsatisfactory because of the formation of nitroalkene and nitro alcohol from alkene as by-products. Still earlier, we described a novel one-pot synthesis of 3-acetyl- and 3-benzoylisoxazole derivatives using ammonium cerium nitrate (CAN).[24] Now, in this paper we report details concerning a new and improved synthesis of 3-acetyl- and 3-benzoylisoxazole derivatives(**1a**–**19a**, **1b**–**19b**) using CAN.

2. Results and discussion

The reaction of alkenes **1**–**13** with CAN(IV) in acetone

Keywords: Ammonium cerium(IV) nitrate; Ammonium cerium(III) nitrate; Formic acid; Isoxazole derivatives; Nitrile oxide.
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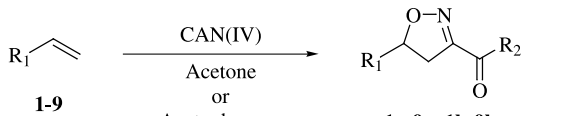


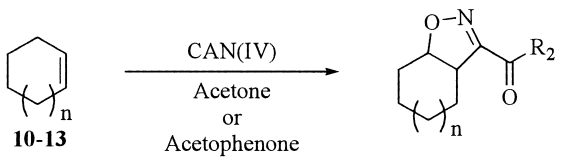
1-9

1a-9a, **1b-9b**
a : R_2=Me
b : R_2=Ph

1 : R_1=n-C_4H_9
2 : R_1=n-C_5H_{11}
3 : R_1=n-C_6H_{13}
4 : R_1=$CH_2C_6H_{11}$
5 : R_1=CH_2Ph
6 : R_1=CH_2SMe
7 : R_1=CH_2CN
8 : R_1=CH_2OPh
9 : R_1=CH_2OCOMe

CAN(IV) : $(NH_4)_2Ce(NO_3)_6$

Scheme 1.



10-13

10 : n=0
11 : n=1
12 : n=2
13 : n=3

10a-13a, **10b-13b**
a : R_2=Me
b : R_2=Ph

Scheme 2.

under reflux gave 3-acetyl-4,5-dihydroisoxazole derivatives (**1a**–**13a**). In the case of acetophenone at 80 °C, 3-benzoyl-4,5-dihydroisoxazole derivatives (**1b**–**13b**) were obtained (Schemes 1 and 2). These results are summarized in Tables 1 and 2. Compound **1a** showed absorption at 1688 (C═O) and 1577 cm^{-1} (C═N) in its IR spectrum. The CI-MS spectrum of **1a** showed an $[M+H]^+$ peak at *m/z* 170. The ^1H NMR spectrum showed a singlet at δ 2.49 (3H, $COCH_3$), and two double doublets at δ 2.76 (1H, *J*=8.4, 17.6 Hz, CH_2) and 3.16 (1H, *J*=11.0, 17.6 Hz, CH_2). The ^{13}C NMR spectra exhibited signals at 193.4, 158.3 and 84.9 ppm, which were assigned as commonly known carbonyl carbon and carbons of the 4,5-dihydroisoxazole ring, respectively. Therefore, compound **1a** was identified to be 3-acetyl-5-butyl-4,5-dihydroisoxazole. Moreover, a similar reaction using alkynes **14**–**19** afforded the corresponding 3-acetyl- and 3-benzoylisoxazole derivatives (**14a**–**19a**, **14b**–**19b**) (Scheme 3). The IR spectrum of **14a** showed absorption at 1705 (C═O) and 1593 cm^{-1} (C═N). The CI-MS spectrum of **14a** showed an $[M+H]^+$ peak at *m/z* 154. The ^1H NMR spectra exhibited a singlet at δ 6.37 (1H). The ^{13}C NMR spectra exhibited signals at 192.5, 175.5, 162.1 and 99.2 ppm, which were assigned as commonly known carbonyl carbon and carbons of the isoxazole ring, respectively. Therefore, compound **14a** was identified to be 3-acetyl-5-propylisoxazole. On the basis of these results,

Table 1. Reaction of alkenes **1**–**13** with CAN(IV) in acetone or acetophenone

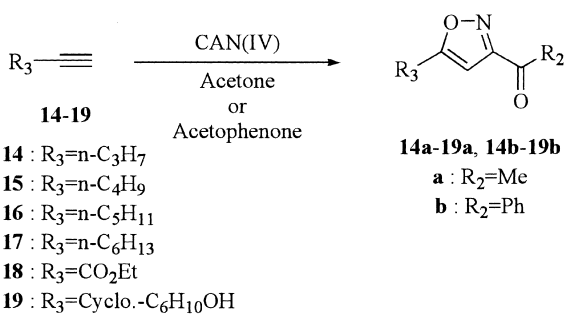
Entry[a]	Substrate	CAN(IV) (mol equiv.)	Solvent	Time (h)	Product (%)[b]
1	1-Hexene (**1**)	1.0	Acetone	15	**1a** (67)
2	1-Heptene (**2**)	1.0	Acetone	14	**2a** (72)
3	1-Octene (**3**)	0.5	Acetone	30	**3a** (47)
4	1-Octene (**3**)	1.0	Acetone	14	**3a** (72)
5	1-Octene (**3**)	1.25	Acetone	8	**3a** (68)
6	1-Octene (**3**)	1.5	Acetone	8	**3a** (62)
7	1-Octene (**3**)	2.0	Acetone	5	**3a** (54)
8	1-Octene (**3**)	4.0	Acetone	5	**3a** (35)
9	Allylcyclohexane (**4**)	1.0	Acetone	10	**4a** (69)
10	Allylbenzene (**5**)	1.0	Acetone	10	**5a** (72)
11	Allylmethylsulfide (**6**)	1.0	Acetone	5	**6a** (33)
12	Allylcyanide (**7**)	1.0	Acetone	15	**7a** (55)
13	Allylphenylether (**8**)	1.0	Acetone	10	**8a** (29)
14	Allylacetate (**9**)	1.0	Acetone	8	**9a** (44)
15	Cyclopentene (**10**)	1.0	Acetone	20	**10a** (47)
16	Cyclohexene (**11**)	1.0	Acetone	30	**11a** (22)
17	Cycloheptene (**12**)	1.0	Acetone	12	**12a** (56)
18	Cyclooctene (**13**)	1.0	Acetone	12	**13a** (59)
19	**1**	1.0	Acetophenone	18	**1b** (68)
20	**2**	1.0	Acetophenone	16	**2b** (78)
21	**3**	0.5	Acetophenone	30	**3b** (50)
22	**3**	1.0	Acetophenone	16	**3b** (77)
23	**3**	1.25	Acetophenone	10	**3b** (73)
24	**3**	1.5	Acetophenone	8	**3b** (68)
25	**3**	2.0	Acetophenone	5	**3b** (62)
26	**3**	4.0	Acetophenone	5	**3b** (27)
27	**4**	1.0	Acetophenone	16	**4b** (67)
28	**5**	1.0	Acetophenone	16	**5b** (54)
29	**6**	1.0	Acetophenone	5	**6b** (18)
30	**7**	1.0	Acetophenone	10	**7b** (60)
31	**8**	1.0	Acetophenone	12	**8b** (39)
32	**9**	1.0	Acetophenone	10	**9b** (66)
33	**10**	1.0	Acetophenone	10	**10b** (73)
34	**11**	1.0	Acetophenone	20	**11b** (49)
35	**12**	1.0	Acetophenone	10	**12b** (57)
36	**13**	1.0	Acetophenone	10	**13b** (71)

[a] Substrate (0.5 mmol), CAN(IV) (0.5–1.0 mmol), and solvent (3.0 ml) were employed under reflux.
[b] Determined by GLC analysis using *n*-dodecane as an internal hydrocarbon standard. All products were identified by satisfactory spectral data (IR, ^1H NMR, ^{13}C NMR and MS).

Table 2. Reaction of alkynes **14**–**19** with CAN(IV) in acetone or acetophenone

Entry[a]	Substrate	Solvent	Time (h)	Product (%)[b]
1	1-Pentyne (**14**)	Acetone	10	**14a** (31)
2	1-Hexyne (**15**)	Acetone	10	**15a** (45)
3	1-Heptyne (**16**)	Acetone	10	**16a** (45)
4	1-Octyne (**17**)	Acetone	14	**17a** (59)
5	Ethyl acetylenecarboxylate (**18**)	Acetone	12	**18a** (49)
6	1-Ethynyl-1-cyclohexanol (**19**)	Acetone	12	**19a** (68)
7	**14**	Acetophenone	12	**14b** (64)
8	**15**	Acetophenone	12	**15b** (66)
9	**16**	Acetophenone	12	**16b** (71)
10	**17**	Acetophenone	12	**17b** (80)
11	**18**	Acetophenone	8	**18b** (71)
12	**19**	Acetophenone	10	**19b** (49)

[a] Substrate (0.5 mmol), CAN(IV) (0.5 mmol), and solvent (3.0 ml) were employed under reflux.
[b] Determined by GLC analysis using *n*-dodecane as an internal hydrocarbon standard. All products were identified by satisfactory spectral data (IR, ^{1}H NMR, ^{13}C NMR and MS).

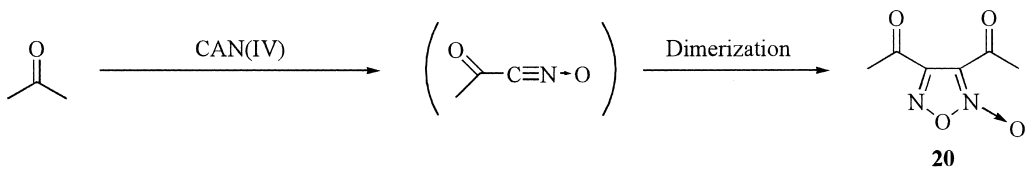


Scheme 3.

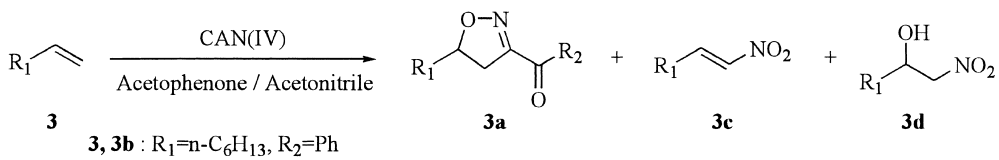
it was found that this reaction gives a novel one-pot synthesis of 3-acetyl- and 3-benzoylisoxazole derivatives (**1a**–**19a**, **1b**–**19b**) from dipolarophiles (alkenes **1**–**13** or alkynes **14**–**19**) and acetone or acetophenone using CAN(IV). When substrate (0.5 mmol), CAN(IV) (0.5 mmol: 1.0 mol equiv.), and ketone (3.0 ml) were employed (Table 1, run 4 and 21), 3-acetyl- and 3-benzoylisoxazole derivatives were obtained in good yields of 72 and 77%, respectively. But the yields of isoxazole derivatives were lowered under reaction conditions using excess CAN(IV) (Table 1, run 5–8 and 23–26). It seems that the reaction products or intermediates were further oxidized due to the oxidative power of excess CAN(IV).

It is known that nitrile oxides dimerize to furoxans. If a furoxan is confirmed in this reaction, it is possible to prove the existence of nitrile oxide as an intermediate. The formation of the dimer (3,4-diacetyl-1,2,5-oxadiazole 2-oxide (furoxan) (**20**)) of nitrile oxide generated from acetone was confirmed. As shown in Scheme 4, the reaction of acetone with CAN(IV) gave compound **20**. Its IR spectrum showed absorption at 1718 (C=O) and 1605 cm^{-1} (C=N–O). The CI-MS spectrum of **20** showed an $[M+H]^+$ peak at *m/z* 172. The ^{1}H NMR spectrum showed two singlets at δ 2.74 (3H, $COCH_3$) and 2.63 (3H, $COCH_3$). The ^{13}C NMR spectra exhibited signals at 188.9, 185.5, 153.4 and 111.5 ppm, which were assigned to 1,2,5-oxadiazole 2-oxide, respectively. Therefore, compound **20** was identified to be 3,4-diacetyl-1,2,5-oxadiazole 2-oxide (furoxan). In addition, the formation of nitrile oxide from acetophenone was confirmed in the GC-MS spectra. This result suggests that acetone is converted into the corresponding nitrile oxide via a process, which involves nitration of acetone by cerium(IV) or cerium(III), and then undergoes competitive dimerization, and 1,3-dipolarcycloaddition with the alkenes or alkynes.

In order to investigate the relationship between yields of isoxazole derivatives and ketone as a precursor of nitrile oxide in the presence of CAN(IV), the reaction of 1-octene (**3**) and acetophenone with CAN(IV) in acetonitrile as solvent was carried out (Scheme 5). These results are summarized in Figure 1. From these results, it was found that the yields of isoxazole derivatives depended on the quantity of acetophenone. The reaction of **3** (0.5 mmol) and



Scheme 4. *Reaction conditions*: acetone (3.0 ml) and CAN(IV) (1.0 mmol) were employed under reflux for 10 h.



Scheme 5.

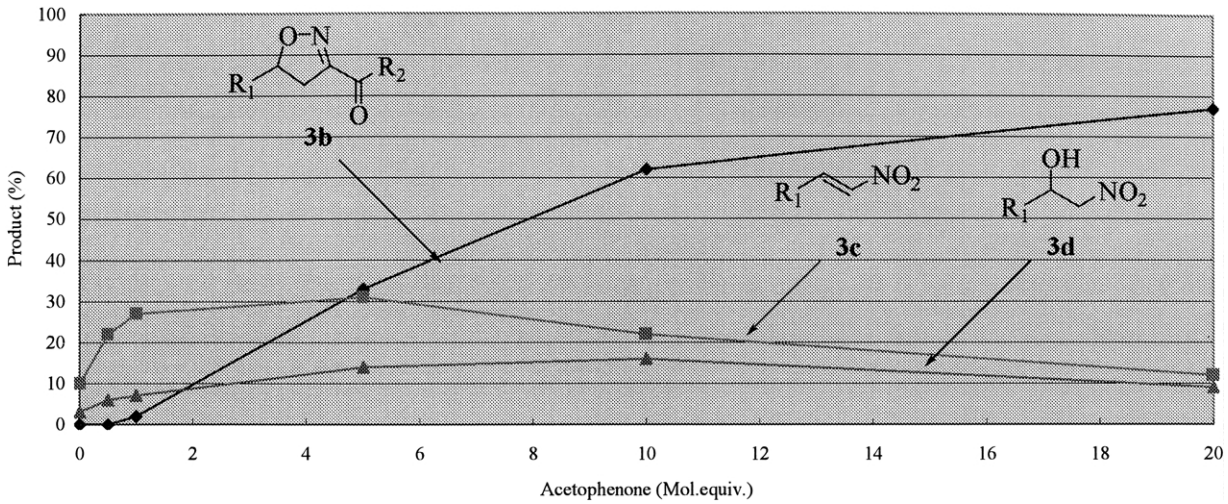
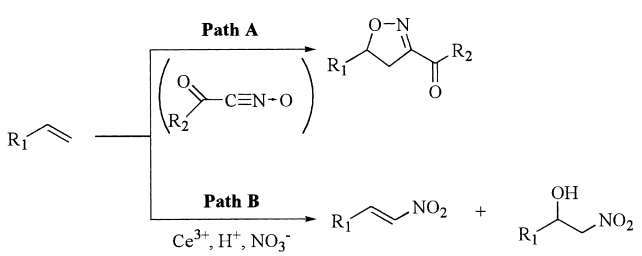


Figure 1. The relationship between acetophenone and products using CAN(IV) Reaction conditions: 1-octene (0.5 mmol), CAN(IV) (0.5 mmol), acetophenone (0–20 mol equiv.), and acetonitrile (3.0 ml) were employed for 20 h under reflux.

acetophenone (2.5 mmol, 5.0 mol equiv.) for 28 h with CAN(IV) in acetonitrile gave **3b**, 1-nitro-1-octene (**3c**),[25] and 1-nitro-2-octanol (**3d**)[25] in 33, 31 and 14% yields, respectively. In the reaction of **3** (0.5 mmol) and acetophenone (10.0 mmol, 20.0 mol equiv.) for 10 h, **3c** (12%), **3d** (9%) and **3b** (77%) as major products were obtained.

Previously, Sugiyama reported that the reaction of several alkenes and a small amount of additive such as cyclohexanone with CAN(IV) in acetonitrile-formic acid gave the corresponding 1-nitroalkenes and 1-nitro alcohols.[25] In this reaction mechanism, Ce^{4+} was at first converted into Ce^{3+} by ketones, and then the nitration of alkenes occurs by Ce^{3+}, proton, and nitrate ion. In the present reaction, it seems that the nitration by CAN(IV) proceeded by a similar reaction mechanism. Ce^{4+} was at first converted into Ce^{3+} by acetone or acetophenone, and the nitration of alkenes or ketones occurs by Ce^{3+}, proton and nitrate ion. From Figure 1, it is seen the nitration of acetone or acetophenone preferentially occurs to the nitration of alkenes under these reaction conditions using excess ketones. Therefore, the formation of nitrile oxide from acetone or acetophenone proceeds, and dipolarophiles (alkenes or alkynes) were consumed in 1,3-dipolar cycloaddition to nitrile oxide. A few by-products such as 1-nitroalkenes and 1-nitro alcohols were obtained. From these results mentioned above, it seems that this reaction proceeds via two reaction pathways: the formation of isoxazole derivatives by 1,3-dipolar cycloaddition of alkenes with nitrile oxide from acetone or acetophenone (Path A), and the formation of 1-nitroalkenes and 1-nitro alcohols from alkenes (Path B) (Scheme 6). Therefore, it seems that the reaction of Path A and B competitively proceeded, and the yields of isoxazole derivatives depended on the quantity of ketone.



Scheme 6.

We further examined the reaction conditions, to improve the yields of the isoxazole derivatives. Recently, Sugiyama

Table 3. Reaction of alkenes **1**–**13** with CAN(III)-formic acid in acetone or acetophenone

Entry[a]	Substrate	CAN(III) (mol equiv.)	Solvent	Time (h)	Product (%)[b]
1	**1**	1.0	Acetone	5	**1a** (74)
2	**2**	1.0	Acetone	5	**2a** (75)
3	**3**	0.5	Acetone	30	**3a** (47)
4	**3**	1.0	Acetone	10	**3a** (84)
5	**3**	1.25	Acetone	8	**3a** (83)
6	**3**	1.5	Acetone	5	**3a** (84)
7	**3**	2.0	Acetone	5	**3a** (83)
8	**4**	1.0	Acetone	10	**4a** (74)
9	**5**	1.0	Acetone	10	**5a** (81)
10	**6**	1.0	Acetone	5	**6a** (50)
11	**7**	1.0	Acetone	8	**7a** (72)
12	**8**	1.0	Acetone	8	**8a** (36)
13	**9**	1.0	Acetone	8	**9a** (46)
14	**10**	1.0	Acetone	5	**10a** (60)
15	**11**	1.0	Acetone	8	**11a** (36)
16	**12**	1.0	Acetone	10	**12a** (68)
17	**13**	1.0	Acetone	10	**13a** (73)
18	**1**	1.0	Acetophenone	12	**1b** (72)
19	**2**	1.0	Acetophenone	15	**2b** (84)
20	**3**	1.0	Acetophenone	15	**3b** (84)
21	**4**	1.0	Acetophenone	15	**4b** (70)
22	**5**	1.0	Acetophenone	16	**5b** (66)
23	**6**	1.0	Acetophenone	5	**6b** (35)
24	**7**	1.0	Acetophenone	10	**7b** (64)
25	**8**	1.0	Acetophenone	12	**8b** (42)
26	**9**	1.0	Acetophenone	10	**9b** (85)
27	**10**	1.0	Acetophenone	10	**10b** (82)
28	**11**	1.0	Acetophenone	20	**11b** (67)
29	**12**	1.0	Acetophenone	10	**12b** (76)
30	**13**	1.0	Acetophenone	10	**13b** (80)

[a] Substrate (0.5 mmol), CAN(III) (0.5 mol), formic acid (10.0 mol) and solvent (3.0 ml) were employed under reflux.

[b] Determined by GLC analysis using *n*-dodecane as internal hydrocarbon standard. All products were identified by satisfactory spectral data (IR, ^{1}H NMR, ^{13}C NMR and MS).

Table 4. Reaction of alkynes **14**–**19** with CAN(III)-formic acid in acetone or acetophenone

Entry[a]	Substrate	Solvent	Time (h)	Product (%)[b]
1	**14**	Acetone	8	**14a** (65)
2	**15**	Acetone	8	**15a** (70)
3	**16**	Acetone	8	**16a** (73)
4	**17**	Acetone	10	**17a** (85)
5	**18**	Acetone	8	**18a** (87)
6	**19**	Acetone	8	**19a** (85)
7	**14**	Acetophenone	8	**14b** (76)
8	**15**	Acetophenone	8	**15b** (77)
9	**16**	Acetophenone	8	**16b** (80)
10	**17**	Acetophenone	8	**17b** (85)
11	**18**	Acetophenone	5	**18b** (76)
12	**19**	Acetophenone	8	**19b** (57)

[a] Substrate (0.5 mmol), CAN(III) (0.5 mol), formic acid (10.0 mol) and solvent (3.0 ml) were employed under reflux.
[b] Determined by GLC analysis using *n*-dodecane as internal hydrocarbon standard. All products were identified by satisfactory spectral data (IR, ^{1}H NMR, ^{13}C NMR and MS).

reported that the reaction of 1-alkenes (1.5 ml) with CAN(IV) (0.6 mmol) and cyclohexanone (0.5 mmol) as additive in acetonitrile–formic acid (1.0 ml/0.5 ml) at 57 °C for 48 h gave the corresponding 4,5-dihydroisoxazole derivatives.[23] Moreover, this reaction smoothly proceeded by the use of CAN(III) instead of CAN(IV). From Figure 1 and Scheme 6, it was found that the nitration of ketones proceeds by Ce^{3+}, proton and nitrate ion. In the present reaction, we attempted to synthesize the isoxazole derivatives from alkenes with CAN(III)-formic acid instead of CAN(IV) in acetone or acetophenone. The reaction of several alkenes with CAN(III)-formic acid in acetone or acetophenone gave the corresponding 3-acetyl- and 3-benzoyl-4,5-dihydroisoxaole derivatives in preferable yields. These results are summarized in Table 3. The yields of isoxazole derivatives were increased by over 5–20%. For example, the reaction of 1-octene (**3**) with CAN(III)-formic acid in acetone under reflux for 10 h afforded 3-hexyl-5-acetyl-4,5-dihydroisoxazole (**3a**) in 84% yield (Table 3, run 3). Furthermore, in the case of several alkynes, similarly the yields of 3-acetyl- and 3-benzoylisoxaole derivatives were improved. These results are summarized in Table 4. From these results, it is apparent that these reactions using CAN(III)-formic acid efficiently afford the corresponding 3-acetyl- and 3-benzoylisoxazole derivatives in preferable yields. Also, the yields of products were not lowered under the reaction conditions using excess CAN(III) (Table 3, run 4–7). It seems that CAN(III) did not further oxidize the products.

The reaction of 1-octene (**3**) and acetophenone with CAN(III)-formic acid in acetonitrile was carried out, and the relationship between yields of products and ketone in the presence of CAN(III) is shown in Figure 2. The reaction of **3** (0.5 mmol) and acetophenone (2.5 mmol, 5.0 mol equiv.) for 28 h with CAN(III)-formic acid in acetonitrile gave **3b**, 1-nitro-1-octene (**3c**), and 1-nitro-2-octanol (**3d**) in 32, 24 and 13% yields, respectively. In the reaction of **3** (0.5 mmol) and acetophenone (10.0 mmol, 20.0 mol equiv.) for 10 h, **3b**, **3c** and **3d** were given in 82, 10 and 4% yield, respectively. As compared with the results using CAN(IV), the formation of 1-nitrooctene (**3c**) and 1-nitro-2-octanol (**3d**) was inhibited between 5 and 10%. Furthermore, the yields of product were increased by over 5%. From these results, the nitration of ketones or alkenes by Ce^{3+}, proton and nitrate ion was confirmed. Also, it seems that the nitration of ketones (Path A) efficiently proceeds under reaction conditions using CAN(III) without reduction of Ce^{4+} into Ce^{3+}. Since the formation of 1-nitroalkenes and 1-nitro alcohols was inhibited under reaction conditions using CAN(III)-formic acid, the formation of nitrile oxides from acetone or acetophenone smoothly proceeds. Therefore, the yields of isoxazole derivatives were increased.

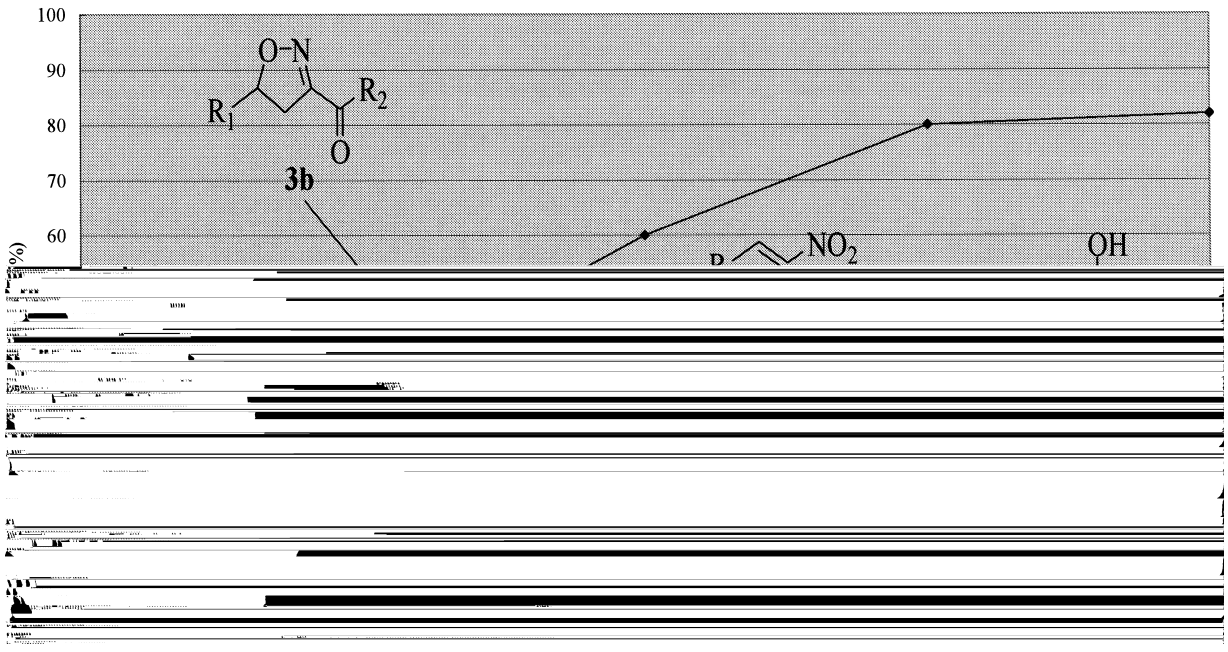
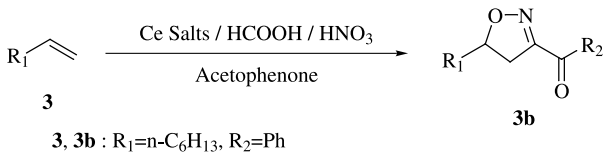


Figure 2. The relationship between acetophenone and products using CAN(III)-formic acid Reaction conditons: 1-octene (0.5 mmol), CAN(III) (0.5 mmol), formic acid (10.0 mol), acetophenone (0–20 mol equiv.), and acetonitrile (3.0 ml) were employed for 20 h under reflux.



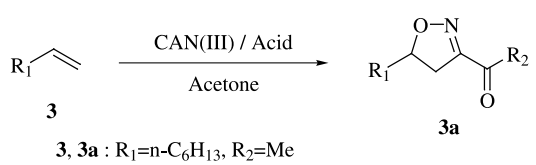
Scheme 7.

In order to investigate the reaction mechanism detailed in the formation of isoxazole derivatives, the reactions of 1-octene (**3**) with several cerium salts–formic acid in acetophenone were carried out (Scheme 7). These results are summarized in Table 5. In this reaction, isoxazole derivatives were not obtained in the absence of cerium salts and formic acid (Table 5, run 1 and 2). Also, the reaction using $Ce(OH)_4$, $Ce(NH_4)_4(SO_4)_2$, $CeCl_3$, and $Ce(CH_3COO)_3$ containing nitric acid gave isoxazole derivatives in 69, 74, 81 and 83% yields, respectively. Also, in the case of using Ce^{3+} salts, the yields of isoxazole derivatives were increased (Table 5, run 2–5). These results show this reaction in the formation of isoxazole derivatives requires Ce^{3+}, nitrate ion, and formic acid. Moreover, in order to clarify the relationship between formation of isoxazole derivatives and formic acid in this reaction mechanism, the reactions of 1-octene (**3**) with CAN(III)-several acids in acetone were carried (Scheme 8). These results are summarized in Table 6. The reaction using acetic acid, propionic acid, and benzoic acid did not proceed. However, the reaction using nitric acid, monochloroacetic acid, oxalic acid, and sulfuric acid gave isoxazole derivatives in 82, 81, 82 and 84% yield, respectively. When CAN(IV) was dissolved in acetone or acetophenone, its solution revealed high acidity. However, the solution dissolving CAN(III) did not reveal the high acidity. Furthermore, this reaction proceeds under reaction conditions using an acid containing the acidity of formic acid or above. From these results, it seems that the proton accomplishes a more essential role for this reaction mechanism than nitration of acetone and acetophenone.

Table 5. Reaction of 1-octene with Ce(IV) and Ce(III) salts in acetophenone

Run[a]	Substrate	Ce salts	Time (h)	Product (%)[b]
1	**3**	—	25	No reaction
2[c]	**3**	$Ce(OH)_4$	25	No reaction
3	**3**	$Ce(OH)_4$	12	**3b** (69)
4	**3**	$Ce(NH_4)_4(SO_4)_2$	12	**3b** (74)
5	**3**	$CeCl_3$	8	**3b** (81)
6	**3**	$Ce(CH_3COO)_3$	8	**3b** (83)

[a] Substrate (0.5 mmol), Ce salts (0.5 mol), formic acid (5.0 mmol), nitric acid (5.0 mmol), and acetophenone (3.0 ml) were employed under reflux.
[b] Determined by GLC analysis using *n*-dodecane as internal hydrocarbon standard.
[c] Substrate (0.5 mmol), Ce salts (0.5 mol), nitric acid (5.0 mmol), and acetophenone (3.0 ml) were employed under reflux. All products were identified by satisfactory spectral data (IR, ^{1}H NMR, ^{13}C NMR and MS).



Scheme 8.

Table 6. The effect of acid in the formation of isoxazole derivatives

Run	Substrate	Acid	Time (h)	Product (%)[a]
1[b]	**3**	—	70	No reaction
2[c]	**3**	CH_3COOH	25	No reaction
3[c]	**3**	CH_3CH_2COOH	25	No reaction
4[c]	**3**	C_6H_5COOH	25	No reaction
5[c]	**3**	HNO_3	15	**3a** (82)
6[c]	**3**	$ClCH_2COOH$	20	**3a** (81)
7[c]	**3**	$(COOH)_2$	15	**3a** (82)
8[d]	**3**	H_2SO_4	15	**3a** (84)

[a] Determined by GLC analysis using *n*-dodecane as internal hydrocarbon standard. All products were identified by satisfactory spectral data (IR, ^{1}H NMR, ^{13}C NMR and MS).
[b] Substrate (0.5 mmol), CAN(III) (0.5 mmol), and acetone (3.0 ml) were employed under reflux.
[c] Substrate (0.5 mmol), CAN(III) (0.5 mmol), acid (5.0 mmol) were employed under reflux.
[d] Substrate (0.5 mmol), CAN(III) (0.5 mmol), acid (0.5 mmol) were employed under reflux.

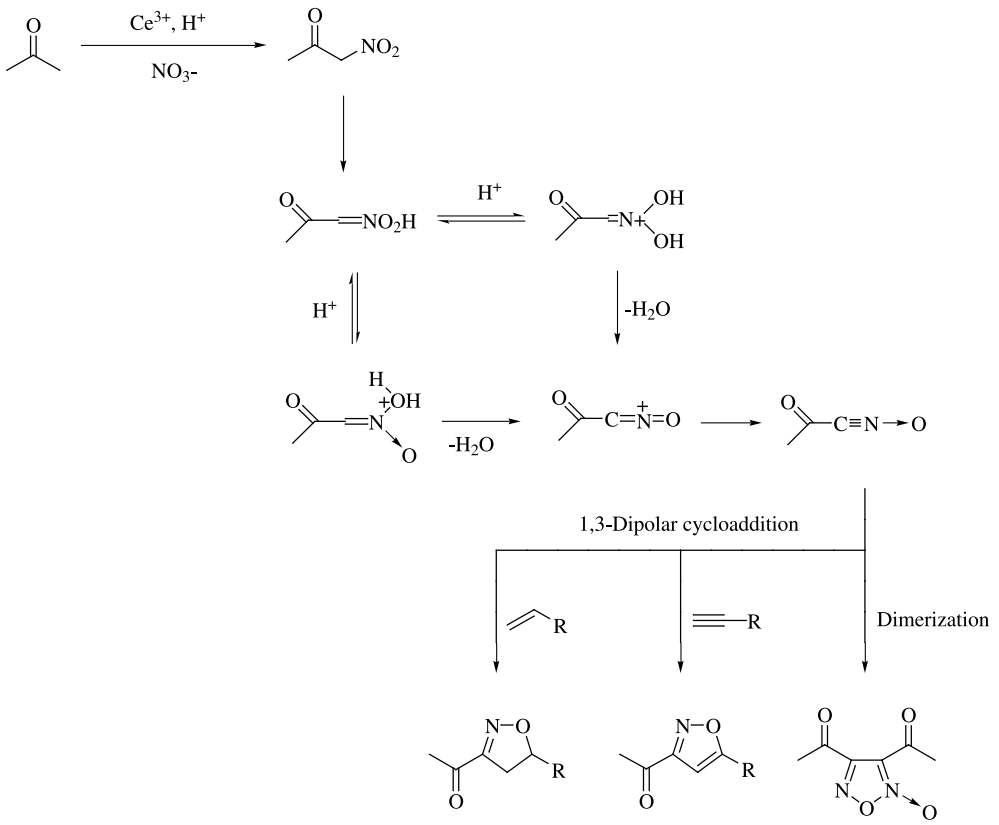
Wade and co-workers[26] reported that acid-catalyzed nitronate cycloaddition reactions gave 4,5-dihydroisoxazole and isoxazole derivatives from nitro compounds and dipolarophiles. In this reaction, nitronic esters were transformed from primary nitro ketones in the presence of nonaqueous protonic and Lewis acids or a strong acid. The protonation of nitronic esters by Lewis acids or a strong acid produced the nitroso cation with dehydration, followed by the formation of nitrile oxide from the nitroso cation. The reaction of nitrile oxide and dipolarphiles afforded the corresponding isoxazole derivatives. On the basis of this reaction mechanism, we proposed the present reaction mechanism in Scheme 9. At first, the nitration of acetone or acetophenone by Ce^{3+}, proton and nitrate ion gave the corresponding nitroketones. In the presence of proton, nitroketones were transformed into nitroso cations, followed by the formation of nitrile oxides from the nitroso cations. Finally, 3-acetyl- and 3-benzoylisoxazole derivatives were obtained by 1,3-dipolar cycloaddition of dipolarophiles (alkenes or alkynes) and nitrile oxide. In the absence of dipolarophiles, nitrile oxide dimerized into furoxan. It is known that nitrile oxides containing an acyl group were obtained from primary nitro compounds[27] and α-hydroxyimino carboxylic acids;[28] however, in this reaction nitrile oxide containing an acyl group was obtained in one-step.

In conclusion, this method is simple and efficient to obtain 3-acetyl- and 3-benzoylisoxazole derivatives. It is particularly noteworthy that this reaction affords a new synthetic method for isoxazole and 4,5-dihydroisoxazole derivatives that is more convenient than the methods used heretofore.

3. Experimental

3.1. General procedure

IR spectra were recorded on a Jasco FT-IR 230 spectrometer. ^{1}H and ^{13}C NMR spectra were measured using a JEOL GSX 400 Model spectrometer in deuteriochloroform solutions with tetramethylsilane used as an internal standard.



Scheme 9. Reaction mechanism.

GC-MS (EI) analyses were performed on a Shimazu GCMS-QP5050 with an ionizing energy of 70 eV. CIMS (*i*-butane reagent gas) were recorded on a Shimazu GCMS-QP5050 with an ionizing energy of 300 eV.

3.2. Synthesis of isoxazole derivatives using CAN(IV)

3.2.1. Typical procedures: reaction of 1-octene (3) with CAN(IV) in acetone. A mixture of 1-octene (**3**) (0.0561 g, 0.5 mmol) and ammonium cerium(IV) nitrate (0.2791 g, 0.5 mmol) in acetone (3.0 ml) was stirred under reflux for 14 h. The reaction mixture was extracted with diethyl ether (30 ml) and washed with aq. sodium hydrogencarbonate solution (2×2.0 ml), saturated aq. NaCl (2×2.0 ml), and water (2×2.0 ml). The ethereal solution was dried over Na_2SO_4 and concentrated in a vacuum. The resulting oil was chromatographed on silica gel. Elution with hexane–diethyl ether (5:1) gave 3-acetyl-5-hexyl-4,5-dihydroisoxazole (**3a**) as a pale-yellow oil (0.0581 g, 59%).

3.2.1.1. 3-Acetyl-5-butyl-4,5-dihydroisoxazole (1a). Pale-yellow oil; IR (NaCl) 1688 and 1577 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.74–4.83 (m, 1H), 3.16 (dd, *J*=11.0, 17.6 Hz, 1H), 2.76 (dd, *J*=8.4, 17.6 Hz, 1H), 2.49 (s, 3H), 1.60–1.74 (m, 2H), 1.34–1.43 (m, 4H), and 0.92 (t, *J*=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=193.4, 158.3, 84.9, 36.7, 34.9, 27.3, 26.6, 22.4, and 13.9; CIMS *m/z* 170 $[M+H]^+$; EIMS *m/z* 126 $[M-CH_3CO]^+$ (1), 112 $[M-C_4H_9]^+$ (2), 99 $[M-C_5H_{10}]^+$ (2), 85 $[M-C_6H_{12}]^+$ (4), 55 $[M-C_6H_{12}NO]^+$ (3), 43 $[M-C_7H_{12}NO]^+$ (100); HRMS Found: *m/z* 169.1103 $[M]^+$. Calcd for $C_9H_{15}NO_2$: M, 169.1103.

3.2.1.2. 3-Acetyl-5-pentyl-4,5-dihydroisoxazole (2a). Pale-yellow oil; IR (NaCl) 1688 and 1577 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.74–4.82 (m, 1H), 3.16 (dd, *J*=10.8, 17.4 Hz, 1H), 2.75 (dd, *J*=8.4, 17.4 Hz, 1H), 2.49 (s, 3H), 1.70–1.75 (m, 1H), 1.54–1.60 (m, 1H), 1.31–1.43 (m, 6H), and 0.90 (t, *J*=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=193.4, 158.3, 84.9, 36.7, 35.1, 31.5, 26.6, 24.9, 22.5, and 14.0; CIMS *m/z* 184 $[M+H]^+$; EIMS *m/z* 140 $[M-CH_3CO]^+$ (1), 112 $[M-C_5H_{11}]^+$ (2), 99 $[M-C_6H_{12}]^+$ (2), 55 $[M-C_7H_{14}NO]^+$ (3), 43 $[M-C_8H_{14}NO]^+$ (100); HRMS Found: *m/z* 183.1261 $[M]^+$. Calcd for $C_{10}H_{17}NO_2$: M, 183.1259.

3.2.1.3. 3-Acetyl-5-hexyl-4,5-dihydroisoxazole (3a). Pale-yellow oil; IR (NaCl) 1686 and 1578 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.74–4.82 (m, 1H), 3.16 (dd, *J*=11.0, 17.6 Hz, 1H), 2.75 (dd, *J*=8.6, 17.6 Hz, 1H), 2.49 (s, 3H), 1.60–1.74 (m, 4H), 1.34–1.44 (m, 6H), and 0.89 (t, *J*=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=193.4, 158.3, 84.9, 36.7, 35.2, 31.7, 29.0, 26.6, 25.1, 22.5, and 14.0; CIMS *m/z* 198 $[M+H]^+$; EIMS *m/z* 154 $[M-CH_3CO]^+$ (1), 136 $[M-CH_3CO-CH_3]^+$ (1), 112 $[M-C_6H_{13}]^+$ (2), 95 $[M-C_6H_{14}O]^+$ (2), 69 $[M-C_8H_{16}O]^+$ (2), 55 $[M-C_8H_{16}NO]^+$ (3), 43 $[M-C_9H_{16}NO]^+$ (100); HRMS Found: *m/z* 197.1428 $[M]^+$. Calcd for $C_{11}H_{19}NO_2$: M, 197.1416.

3.2.1.4. 3-Acetyl-5-cyclohexylmethyl-4,5-dihydroisoxazole (4a). Pale-yellow oil; IR (NaCl) 1686 and 1576 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.83–4.91 (m, 1H), 3.18 (dd, *J*=10.8, 17.4 Hz, 1H), 2.72 (dd, *J*=8.6, 17.4 Hz, 1H), 2.49 (s, 3H), 1.68–1.77 (m, 6H), 1.38–1.45 (m, 2H), 1.21–1.27 (m, 3H), and 0.94–1.17 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=193.4, 158.3, 83.1, 43.1, 37.8, 34.6, 33.5, 33.0, 26.6, 26.4, 26.2, and 26.1; CIMS *m/z* 210 $[M+H]^+$; EIMS *m/z* 166 $[M-CH_3CO]^+$ (1), 126 $[M-C_6H_{11}]^+$ (1), 112 $[M-C_7H_{13}]^+$ (1), 55 $[M-C_9H_{16}NO]^+$ (3), 43

$[M-C_{10}H_{16}NO]^+$ (100); HRMS Found: *m/z* 209.1407 $[M]^+$. Calcd for $C_{12}H_{19}NO_2$: M, 209, 1416.

3.2.1.5. 3-Acetyl-5-benzyl-4,5-dihydroisoxazole (5a). Pale-yellow oil; IR (NaCl) 1686 and 1577 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.21–7.33 (m, 5H), 5.01–5.06 (m, 1H), 3.05–3.13 (m, 2H), 2.83–2.91 (m, 2H), and 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$) δ=193.2, 158.2, 136.6, 129.4, 128.7, 127.0, 84.9, 40.9, 36.3, and 26.6; CIMS *m/z* 204 $[M+H]^+$; EIMS *m/z* 203 $[M]^+$ (1), 126 $[M-C_6H_5]^+$ (1), 112 $[M-C_7H_7]^+$ (2), 43 $[M-C_{10}H_{10}NO]^+$ (100); HRMS Found: *m/z* 203.0951 $[M]^+$. Calcd for $C_{12}H_{13}NO_2$: M, 203.0946.

3.2.1.6. 3-Acetyl-5-methylthiamethyl-4,5-dihydroisoxazole (6a). Pale-yellow oil; IR (NaCl) 1687 and 1578 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.97–5.04 (m, 1H), 3.24 (dd, *J*=10.8, 17.7 Hz, 1H), 3.06 (dd, *J*=7.7, 17.7 Hz, 1H), 2.81 (dd, *J*=5.0, 14.1 Hz, 1H), 2.71 (dd, *J*=6.8, 14.1 Hz, 1H), 2.50 (s, 3H), and 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$) δ=193.0, 158.2, 83.6, 38.0, 36.6, 26.7, and 16.4; CIMS *m/z* 174 $[M+H]^+$; EIMS *m/z* 173 $[M]^+$ (1), 130 $[M-CH_3CO]^+$ (1), 112 $[M-C_2H_5S]^+$ (12), 61 $[M-C_5H_6NO_2]^+$ (23), 43 $[M-C_5H_8NOS]^+$ (100); HRMS Found: *m/z* 173.0513 $[M]^+$. Calcd for $C_7H_{11}NO_2S$: M, 173.0510.

3.2.1.7. 3-Acetyl-5-cyanomethyl-4,5-dihydroisoxazole (7a). Yellow oil; IR (NaCl) 1687 and 1583 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.99–5.06 (m, 1H), 3.22 (dd, *J*=11.5, 17.8 Hz, 1H), 2.97 (dd, *J*=7.9, 17.8 Hz, 1H), 2.74–2.85 (m, 2H), and 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$) δ=192.8, 158.0, 115.2, 77.0, 39.4, 26.7, and 23.7; CIMS *m/z* 153 $[M+H]^+$; EIMS *m/z* 152 $[M]^+$ (2), 138 $[M-CH_3]^+$ (2), 112 $[M-CH_2CN]^+$ (1), 109 $[M-CH_3CO]^+$ (1), 43 $[M-C_5H_5N_2O]^+$ (100); HRMS Found: *m/z* 152.0591 $[M]^+$. Calcd for $C_7H_8N_2O_2$: M, 152.0586.

3.2.1.8. 3-Acetyl-5-phenoxymethyl-4,5-dihydroisoxazole (8a). Pale-yellow oil; IR (NaCl) 1686 and 1581 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.26–7.30 (m, 2H), 6.96–7.00 (m, 1H), 6.88–6.90 (m, 2H), 5.10–5.17 (m, 1H), 4.10 (q, *J*=4.8 Hz, 2H), 3.50 (dd, *J*=11.0, 17.6 Hz, 1H), 3.40 (dd, *J*=7.7, 17.6 Hz, 1H), and 2.52 (s, 3H); ^{13}C NMR ($CDCl_3$) δ=193.0, 158.2, 158.1, 129.6, 121.5, 114.7, 81.9, 68.3, 34.2, and 26.8; CIMS *m/z* 220 $[M+H]^+$; EIMS *m/z* 176 $[M-CH_3CO]^+$ (1), 142 $[M-C_6H_5]^+$ (1), 126 $[M-OC_6H_5]^+$ (3), 112 $[M-CH_2OC_6H_5]^+$ (4), 43 $[M-C_{10}H_{10}NO_2]^+$ (100); HRMS Found: *m/z* 219.0904 $[M]^+$. Calcd for $C_{12}H_{13}NO_3$: M, 219.0895.

3.2.1.9. 3-Acetyl-5-acetoxymethyl-4,5-dihydroisoxazole (9a). Pale-yellow oil; IR (NaCl) 1691 and 1581 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.99–5.06 (m, 1H), 4.26 (dd, *J*=3.9, 12.3 Hz, 1H), 4.16 (dd, *J*=5.5, 12.3 Hz, 1H), 3.22 (dd, *J*=11.5, 17.8 Hz, 1H), 2.97 (dd, *J*=7.9, 17.8 Hz, 1H), 2.51 (s, 3H), and 2.09 (s, 3H); ^{13}C NMR ($CDCl_3$) δ=192.8, 170.6, 158.0, 81.2, 64.4, 34.1, 26.7, and 20.7; CIMS *m/z* 186 $[M+H]^+$; EIMS *m/z* 142 $[M-CH_3CO]^+$ (1), 126 $[M-C_2H_3O_2]^+$ (5), 112 $[M-C_3H_5O_2]^+$ (5), 43 $[M-C_6H_8NO_3]^+$ (100); HRMS Found: *m/z* 185.0694 $[M]^+$. Calcd for $C_8H_{11}NO_4$: M, 185.0688.

3.2.1.10. 3-Acetyl-4,5-cyclopenta-4,5-dihydroisoxazole (10a). Pale-yellow oil; IR (NaCl) 1688 and 1571 cm^{-1}; ^1H NMR ($CDCl_3$) δ=5.05–5.27 (m, 1H), 3.80–3.85 (m, 1H), 2.46 (s, 3H), 2.14–2.19 (m, 1H), 1.90–1.96 (m, 1H), 1.68–1.83 (m, 3H), and 1.28–1.50 (m, 1H); ^{13}C NMR ($CDCl_3$) δ=193.3, 160.0, 90.8, 49.4, 35.6, 31.4, 27.0, and 23.2; CIMS *m/z* 154 $[M+H]^+$; EIMS *m/z* 153 $[M]^+$ (1), 110 $[M-CH_3CO]^+$ (4), 43 $[M-C_6H_8NO]^+$ (100); HRMS Found: *m/z* 153.0791 $[M]^+$. Calcd for $C_8H_{11}NO_2$: M, 153.0790.

3.2.1.11. 3-Acetyl-4,5-cyclohexa-4,5-dihydroisoxazole (11a). Pale-yellow oil; IR (NaCl) 1686 and 1559 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.52–4.56 (m, 1H), 3.15–3.21 (m, 1H), 2.49 (s, 3H), and 1.14–2.24 (m, 8H); ^{13}C NMR ($CDCl_3$) δ=193.6, 164.3, 83.3, 42.1, 26.8, 25.4, 24.7, 21.4, and 19.7; CIMS *m/z* 168 $[M+H]^+$; EIMS *m/z* 167 $[M]^+$ (1), 150 $[M-OH]^+$ (1), 124 $[M-CH_3CO]^+$ (4), 96 $[M-CH_3CO-C_2H_4]^+$ (3), 55 $[M-CH_3CO-C_4H_8]^+$ (3), 43 $[M-C_7H_{10}NO]^+$ (100); HRMS Found: *m/z* 167.0940 $[M]^+$. Calcd for $C_9H_{13}NO_2$: M, 167.0946.

3.2.1.12. 3-Acetyl-4,5-cyclohepta-4,5-dihydroisoxazole (12a). Pale-yellow oil; IR (NaCl) 1686 and 1560 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.87–4.93 (m, 1H), 3.52–3.58 (m, 1H), 2.47 (s, 3H), and 1.39–2.01 (m, 10H); ^{13}C NMR ($CDCl_3$) δ=193.5, 160.4, 88.2, 48.9, 31.0, 30.3, 28.2, 27.1, 26.7, and 23.8; CIMS *m/z* 182 $[M+H]^+$; EIMS *m/z* 181 $[M]^+$ (1), 138 $[M-CH_3CO]^+$ (3), 43 $[M-C_8H_{12}NO]^+$ (100); HRMS Found: *m/z* 181.1101 $[M]^+$. Calcd for $C_{10}H_{15}NO_2$: M, 181.1103.

3.2.1.13. 3-Acetyl-4,5-cycloocta-4,5-dihydroisoxazole (13a). Pale-yellow oil; IR (NaCl) 1686 and 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ=4.50–4.56 (m, 1H), 3.26–3.31 (m, 1H), 2.47 (s, 3H), 196–2.10 (m, 2H), 1.44–1.75 (m, 7H), and 1.22–1.38 (m, 3H); ^{13}C NMR ($CDCl_3$) δ=193.4, 162.7, 88.7, 47.5, 29.8, 27.1, 27.0, 25.6, 25.5, 25.1, and 24.5; CIMS *m/z* 196 $[M+H]^+$; EIMS *m/z* 152 $[M-CH_3CO]^+$ (3), 138 $[M-CH_3CO-CH_2]^+$ (1), 124 $[M-CH_3CO-C_2H_4]^+$ (1), 110 $[M-CH_3CO-C_3H_6]^+$ (1), 96 $[M-CH_3CO-C_4H_8]^+$ (1) 82 $[M-CH_3CO-C_5H_{10}]^+$ (3), 43 $[M-C_9H_{14}NO]^+$ (100); HRMS Found: *m/z* 195.1243 $[M]^+$. Calcd for $C_{11}H_{17}NO_2$: M, 195.1259.

3.2.1.14. 3-Acetyl-5-propylisoxazole (14a). Pale-yellow oil; IR (NaCl) 1705 and 1593 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.37 (s, 1H), 2.78 (t, *J*=7.6 Hz, 2H), 2.64 (s, 3H), 1.71–1.80 (m, 2H) and 1.00 (t, *J*=7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=192.5, 175.5, 162.1, 99.2, 28.6, 27.3, 20.9 and 13.6; CIMS *m/z* 154 $[M+H]^+$; EIMS *m/z* 153 $[M]^+$ (2), 138 $[M-CH_3]^+$ (1), 110 $[M-CH_3CO]^+$ (1), 43 $[M-C_6H_8NO]^+$ (100); HRMS Found: *m/z* 153.0788 $[M]^+$. Calcd for $C_8H_{11}NO_2$: M, 153.0790.

3.2.1.15. 3-Acetyl-5-butylisoxazole (15a). Pale-yellow oil; IR (NaCl) 1707 and 1593 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.36 (s, 1H), 2.76 (t, *J*=7.7 Hz, 2H), 2.63 (s, 3H), 1.67–1.74 (m, 2H), 1.34–1.45 (m, 2H), and 0.95 (t, *J*=7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=192.5, 175.6, 162.1, 99.2, 29.5, 27.2, 26.4, 22.1, and 13.6; CIMS *m/z* 168 $[M+H]^+$; EIMS *m/z* 167 $[M]^+$ (1), 152 $[M-CH_3]^+$ (1), 124 $[M-CH_3CO]^+$ (2), 43 $[M-C_7H_{10}NO]^+$ (100); HRMS Found: *m/z* 167.0929 $[M]^+$. Calcd for $C_9H_{13}NO_2$: M, 167.0946.

3.2.1.16. 3-Acetyl-5-pentylisoxazole (16a). Pale-yellow oil; IR (NaCl) 1707 and 1593 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.36 (s, 1H), 2.79 (t, *J*=7.3 Hz, 2H), 2.63 (s, 3H), 1.69–1.76 (m, 2H), 1.33–1.38 (m, 4H), and 0.91 (t, *J*=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=192.5, 175.7, 162.2, 99.2, 31.2, 27.2, 27.0, 26.7, 22.3, and 13.9; CIMS *m/z* 182 $[M+H]^+$; EIMS *m/z* 181 $[M]^+$ (1), 166 $[M-CH_3]^+$ (1), 138 $[M-CH_3CO]^+$ (1), 55 $[M-C_7H_{12}NO]^+$ (1), 43 $[M-C_8H_{12}NO]^+$ (100); HRMS Found: *m/z* 181.1097 $[M]^+$. Calcd for $C_{10}H_{15}NO_2$: M, 181.1103.

3.2.1.17. 3-Acetyl-5-hexylisoxazole (17a). Pale-yellow oil; IR (NaCl) 1707 and 1593 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.36 (s, 1H), 2.79 (t, J=7.3 Hz, 2H), 2.63 (s, 3H), 1.67–1.75 (m, 2H), 1.29–1.38 (m, 6H), and 0.89 (t, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=192.5, 175.7, 162.1, 99.1, 31.3, 28.7, 27.3, 27.0, 26.7, 22.4, and 14.0; CIMS m/z 196 $[M+H]^+$; EIMS m/z 195 $[M]^+$ (1), 180 $[M-CH_3]^+$ (1), 153 $[M-CH_3CO]^+$ (2), 55 $[M-C_8H_{14}NO]^+$ (1), 43 $[M-C_9H_{14}NO]^+$ (100); HRMS Found: m/z 195.1262 $[M]^+$. Calcd for $C_{11}H_{17}NO_2$: M, 195.1259.

3.2.1.18. Ethyl 3-acetylisoxazolecarboxylate (18a). Colorless needless from EtOH; mp 42.3–435 °C; IR (NaCl) 1710 and 1579 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.25 (s, 1H), 4.48 (q, J=7.1 Hz, 2H), 2.71 (s, 3H), and 1.47 (t, J=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=190.3, 161.8, 161.4, 155.6, 106.9, 62.2, 26.7, and 13.6; CIMS m/z 184 $[M+H]^+$; EIMS m/z 168 $[M-CH_3]^+$ (1), 140 $[M-CH_3CO]^+$ (1), 138 $[M-C_2H_5O]^+$ (2), 43 $[M-C_6H_6NO_3]^+$ (100); HRMS Found: m/z 183.0530 $[M]^+$. Calcd for $C_8H_9NO_4$: M, 183.0532.

3.2.1.19. 3-Acetyl-6-hydroxy-5-cyclohexylisoxazole (19a). Pale-yellow oil; IR (NaCl) 3400, 1706 and 1558 cm^{-1}; ^1H NMR ($CDCl_3$) δ=6.53 (s, 1H), 3.49 (brs, 1H), 2.62 (s, 3H), and 1.17–2.00 (m, 10H); ^{13}C NMR ($CDCl_3$) δ=192.3, 180.0, 161.5, 98.1, 36.1, 27.0, 24.8, 21.3, and 20.4; CIMS m/z 210 $[M+H]^+$; EIMS m/z 194 $[M-CH_3]^+$ (1), 166 $[M-CH_3CO]^+$ (2), 139 $[M-C_5H_{10}]^+$ (1), 110 $[M-C_6H_{11}O]^+$ (2), 98 $[M-C_7H_{11}O]^+$ (2), 55 $[M-C_8H_{12}NO_2]^+$ (100), 43 $[M-C_9H_{12}NO_2]^+$ (100); HRMS Found: m/z 209.1027 $[M]^+$. Calcd for $C_{11}H_{15}NO_3$: M, 209.1052.

3.2.2. Typical procedures: reaction of 1-octene (3) with CAN(IV) in acetophenone. A mixture of 1-octene (**3**) (0.0561 g, 0.5 mmol) and ammonium cerium(IV) nitrate (0.2791 g, 0.5 mmol) in acetophenone (3.0 ml) was stirred at 80 °C for 16 h. The reaction mixture was extracted with diethyl ether (30 ml) and washed with aq. sodium hydrogencarbonate solution (2×2.0 ml), saturated aq. NaCl (2×2.0 ml), and water (2×2.0 ml). The ethereal solution was dried over Na_2SO_4 and concentrated in a vacuum, followed by acetophenone removal by reduced pressure distillation. The resulting oil was chromatographed on silica gel. Elution with hexane–diethyl ether (5:1) gave 3-benzoyl-5-hexyl-4,5-dihydroisoxazole (**3b**) as a pale-yellow oil (0.0829 g, 64%).

3.2.2.1. 3-Benzoyl-5-butyl-4,5-dihydroisoxazole (1b). Pale-yellow oil; IR (NaCl) 1652 and 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.17–8.19 (m, 2H), 7.38–7.53 (m, 3H), 4.65–4.74 (m, 1H), 3.32 (dd, J=10.8, 17.4 Hz, 1H), 2.93 (dd, J=8.4, 17.4 Hz, 1H), 1.67–1.75 (m, 2H), 1.28–1.43 (m, 4H), and 0.88 (t, J=6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=186.2, 157.8, 136.0, 133.4, 130.3, 128.3, 83.4, 38.8, 35.1, 31.6, 22.6, and 14.0; CIMS m/z 232 $[M+H]^+$; EIMS m/z 231 $[M]^+$ (1), 214 $[M-OH]^+$ (1), 202 $[M-C_2H_5]^+$ (1), 185 $[M-OH-C_2H_5]^+$ (1), 174 $[M-C_4H_9]^+$ (6), 105 $[M-C_7H_{12}NO]^+$ (100), 77 $[M-C_7H_{12}NO-CO]^+$ (45); HRMS Found: m/z 231.1269 $[M]^+$. Calcd for $C_{14}H_{17}NO_2$: M, 231.1259.

3.2.2.2. 3-Benzoyl-5-pentyl-4,5-dihydroisoxazole (2b). Pale-yellow oil; IR (NaCl) 1652 and 1571 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.17–8.20 (m, 2H), 7.42–7.59 (m, 3H), 4.73–4.81 (m, 1H), 3.38 (dd, J=10.8, 17.4 Hz, 1H), 2.98 (dd, J=8.6, 17.4 Hz, 1H), 1.73–1.81 (m, 1H), 1.57–1.66 (m, 1H), 1.26–1.47 (m, 6H), and 0.90 (t, J=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=186.5, 157.8, 135.9, 133.4, 130.3, 128.3, 83.5, 38.8, 35.1, 31.5, 24.9, 22.5, and 14.0; CIMS m/z 246 $[M+H]^+$; EIMS m/z 174 $[M-C_5H_{11}]^+$ (2), 140 $[M-C_6H_5CO]^+$ (2), 105 $[M-C_8H_{14}NO]^+$ (100), 77 $[M-C_8H_{14}NO-CO]^+$ (38); HRMS Found: m/z 245.1399 $[M]^+$. Calcd for $C_{15}H_{19}NO_2$: M, 245.1416.

3.2.2.3. 3-Benzoyl-5-hexyl-4,5-dihydroisoxazole (3b). Pale-yellow oil; IR (NaCl) 1652 and 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.17–8.19 (m, 2H), 7.37–7.55 (m, 3H), 4.64–4.72 (m, 1H), 3.31 (dd, J=10.8, 17.4 Hz, 1H), 2.92 (dd, J=8.6, 17.4 Hz, 1H), 1.66–1.71 (m, 1H), 1.50–1.56 (m, 1H), 1.26–1.41 (m, 8H), and 0.87 (t, J=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=186.1, 157.9, 136.0, 133.5, 130.3, 128.3, 83.4, 38.8, 35.2, 31.8, 29.1, 25.3, 22.6, and 14.1; CIMS m/z 260 $[M+H]^+$; EIMS m/z 174 $[M-C_6H_{13}]^+$ (2), 154 $[M-C_6H_5CO]^+$ (2), 105 $[M-C_9H_{16}NO]^+$ (100), 77 $[M-C_9H_{16}NO-CO]^+$ (32); HRMS Found: m/z 259.1587 $[M]^+$. Calcd for $C_{16}H_{21}NO_2$: M, 259.1572.

3.2.2.4. 3-Benzoyl-5-cyclohexylmethyl-4,5-dihydroisoxazole (4b). Pale-yellow oil; IR (NaCl) 1653 and 1570 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.18–8.20 (m, 2H), 7.43–7.62 (m, 3H), 4.83–4.91 (m, 1H), 3.40 (dd, J=10.8, 17.4 Hz, 1H), 2.96 (dd, J=8.8, 17.4 Hz, 1H), 1.70–1.83 (m, 6H), 1.44–1.54 (m, 2H), 1.11–1.28 (m, 3H), and 0.95–0.99 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=186.6, 157.9, 135.9, 133.5, 130.3, 128.3, 81.7, 43.0, 39.5, 34.7, 33.5, 33.0, 26.4, 26.2, and 26.1; CIMS m/z 272 $[M+H]^+$; EIMS m/z 271 $[M]^+$ (2), 254 $[M-OH]^+$ (1), 228 $[M-C_3H_7]^+$ (1), 174 $[M-C_7H_{13}]^+$ (1), 166 $[M-C_6H_5CO]^+$ (1), 105 $[M-C_{10}H_{16}NO]^+$ (100), 77 $[M-C_{10}H_{16}NO-CO]^+$ (32); HRMS Found: m/z 271.1558 $[M]^+$. Calcd for $C_{17}H_{21}NO_2$: M, 271.1572.

3.2.2.5. 3-Benzoyl-5-benzyl-4,5-dihydroisoxazole (5b). Pale-yellow oil; IR (NaCl) 1652 and 1572 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.07–8.11 (m, 2H), 7.38–7.54 (m, 3H), 7.17–7.30 (m, 5H), 4.96–5.03 (m, 1H), 3.29 (dd, J=11.0, 17.6 Hz, 2H), 3.01–3.09 (m, 2H), and 2.90 (dd, J=6.2, 17.6 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ=186.3, 157.7, 136.1, 135.7, 133.5, 130.2, 129.4, 128.6, 128.3, 126.9, 83.5, 40.8, and 38.2; CIMS m/z 266 $[M+H]^+$; EIMS m/z 265 $[M]^+$ (1), 174 $[M-C_7H_7]^+$ (2), 160 $[M-C_6H_5CO]^+$ (1), 105 $[M-C_{10}H_{10}NO]^+$ (100), 77 $[M-C_{10}H_{10}NOCO]^+$ (49); HRMS Found: m/z 265.1101 $[M]^+$. Calcd for $C_{17}H_{15}NO_2$: M, 265.1103.

3.2.2.6. 3-Benzoyl-5-methylthiamethyl-4,5-dihydroisoxazole (6b). Pale-yellow oil; IR (NaCl) 1654 and 1579 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.17–8.20 (m, 2H), 7.42–7.67 (m, 3H), 4.97–5.05 (m, 1H), 3.47 (dd, J=10.8, 17.6 Hz, 1H), 3.28 (dd, J=7.7, 17.6 Hz, 1H), 2.85 (dd, J=5.1, 14.0 Hz, 1H), 2.76 (dd, J=6.8, 14.0 Hz, 1H), and 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$) δ=186.2, 157.7, 135.7, 133.6, 130.2, 128.3, 82.3, 38.6, 38.0, and 16.4; CIMS m/z 236 $[M+H]^+$; EIMS m/z 235 $[M]^+$ (1), 174 $[M-C_2H_5S]^+$ (11), 130 $[M-C_6H_5CO]^+$ (1), 105 $[M-C_5H_8NOS]^+$ (100), 77 $[M-C_5H_5NOS-CO]^+$ (77); HRMS Found: m/z 235.0662 $[M]^+$. Calcd for $C_{12}H_{13}NO_2S$: M, 235.0667.

3.2.2.7. 3-Benzoyl-5-cyanomethyl-4,5-dihydroisoxazole (7b). Yellow oil; IR (NaCl) 1654 and 1578 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.17–8.20 (m, 2H), 7.46–7.64 (m, 3H), 5.01–5.09 (m, 1H), 3.63 (dd, J=11.0, 18.0 Hz, 1H), 3.29 (dd, J=7.0, 18.0 Hz, 1H), and 2.74–2.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=185.5, 158.0, 135.3, 133.9, 130.3, 128.5, 115.5,

76.8, 39.1, and 23.7; CIMS *m/z* 215 $[M+H]^+$; EIMS *m/z* 214 $[M]^+$ (4), 174 $[M-C_2H_2N]^+$ (2), 147 $[M-C_4H_5N]^+$ (6), 105 $[M-C_5H_5N_2O]^+$ (100), 77 $[M-C_5H_5N_2O-CO]^+$ (80); HRMS Found: *m/z* 214.0749 $[M]^+$. Calcd for $C_{12}H_{10}N_2O_2$: M, 214.0742.

3.2.2.8. 3-Benzoyl-5-phenoxymethyl-4,5-dihydroisoxazole (8b). Pale-yellow oil; IR (NaCl) 1653 and 1583 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.19–8.21 (m, 2H), 7.44–7.61 (m, 3H), 7.23–7.30 (m, 2H), 6.86–6.99 (m, 3H), 5.09–5.16 (m, 1H), 4.12 (q, *J*=4.6 Hz, 2H), 3.50 (dd, *J*=11.0, 17.6 Hz, 1H), and 3.40 (dd, *J*=7.7, 17.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ=186.2, 158.2, 157.6, 135.7, 133.6, 130.3, 129.5, 128.4, 121.4, 114.6, 80.5, 68.4, and 36.3; CIMS *m/z* 282 $[M+H]^+$; EIMS *m/z* 281 $[M]^+$ (3), 188 $[M-C_6H_5O]^+$ (3), 174 $[M-C_7H_7O]^+$ (4), 105 $[M-C_{10}H_{10}NO_2]^+$ (100), 77 $[M-C_{10}H_{10}NO_2-CO]^+$ (74); HRMS Found: *m/z* 281.1050 $[M]^+$. Calcd for $C_{17}H_{15}NO_3$: M, 281.1052.

3.2.2.9. 3-Benzoyl-5-acetoxymethyl-4,5-dihydroisoxazole (9b). Pale-yellow oil; IR (NaCl) 1654 and 1578 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.05–8.16 (m, 2H), 7.35–7.58 (m, 3H), 4.94–5.01 (m, 1H), 4.25 (dd, *J*=3.7, 12.1 Hz, 1H), 4.16 (dd, *J*=5.5, 12.1 Hz, 1H), 3.41 (dd, *J*=11.4, 17.6 Hz, 1H), 3.16 (dd, *J*=7.5, 17.6 Hz, 1H), and 2.04 (s, 3H); ^{13}C NMR ($CDCl_3$) δ=185.5, 170.1, 157.2, 135.2, 133.3, 129.9, 128.0, 79.5, 64.2, 35.7, and 20.2; CIMS *m/z* 248 $[M+H]^+$; EIMS *m/z* 188 $[M-C_2H_3O_2]^+$ (7), 174 $[M-C_3H_5O_2]^+$ (8), 105 $[M-C_6H_8NO_3]^+$ (86), 77 $[M-C_6H_8NO_3-CO]^+$ (51), 43 $[M-C_{11}H_{10}NO_3]^+$ (100); HRMS Found: *m/z* 247.0859 $[M]^+$. Calcd for $C_{13}H_{13}NO_4$: M, 247.0845.

3.2.2.10. 3-Benzoyl-4,5-cyclopenta-4,5-dihydroisoxazole (10b). Pale-yellow oil; IR (NaCl) 1651 and 1566 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.14–8.16 (m, 2H), 7.43–7.60 (m, 3H), 5.23–5.26 (m, 1H), 4.07–4.12 (m, 1H), 2.19–2.24 (m, 1H), 2.01–2.05 (m, 1H), 1.69–1.91 (m, 3H), and 1.39–1.50 (m, 1H); ^{13}C NMR ($CDCl_3$) δ=186.7, 159.6, 136.5, 133.4, 130.3, 128.3, 89.6, 51.5, 35.7, 31.7, and 23.3; CIMS *m/z* 216 $[M+H]^+$; EIMS *m/z* 215 $[M]^+$ (4), 198 $[M-OH]^+$ (1), 186 $[M-CHO]^+$ (2), 172 $[M-C_2H_3O]^+$ (3), 158 $[M-C_3H_5O]^+$ (3), 144 $[M-C_4H_7O]^+$ (2), 131 $[M-C_5H_8O]^+$ (2), 110 $[M-C_6H_5CO]^+$ (4), 105 $[M-C_6H_8NO]^+$ (100), 77 $[M-C_6H_8NO-CO]^+$ (69); HRMS Found: *m/z* 215.0929 $[M]^+$. Calcd for $C_{13}H_{13}NO_2$: M, 215.0946.

3.2.2.11. 3-Benzoyl-4,5-cyclohexa-4,5-dihydroisoxazole (11b). Pale-yellow oil; IR (NaCl) 1651 and 1579 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.14–8.19 (m, 2H), 7.45–7.64 (m, 3H), 4.57–4.61 (m, 1H), 3.39–3.49 (m, 1H), 2.17–2.23 (m, 1H), 2.04–2.08 (m, 1H), 1.77–1.86 (m, 1H), 1.51–1.64 (m, 3H), and 1.25–2.36 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=186.9, 163.7, 136.2, 133.5, 130.6, 128.4, 82.1, 44.1, 25.5, 24.9, 21.6, and 19.8; CIMS *m/z* 230 $[M+H]^+$; EIMS *m/z* 229 $[M]^+$ (4), 212 $[M-OH]^+$ (1), 200 $[M-CHO]^+$ (1), 186 $[M-C_2H_3O]^+$ (2), 172 $[M-C_3H_5O]^+$ (2), 158 $[M-C_4H_7O]^+$ (4), 124 $[M-C_6H_5CO]^+$ (5), 105 $[M-C_7H_{10}NO]^+$ (100), 77 $[M-C_7H_{10}NO-CO]^+$ (71); HRMS Found: *m/z* 229.1100 $[M]^+$. Calcd for $C_{14}H_{15}NO_2$: M, 229.1103.

3.2.2.12. 3-Benzoyl-4,5-cyclohepta-4,5-dihydroisoxazole (12b). Pale-yellow oil; IR (NaCl) 1653 and 1579 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.13–8.15 (m, 2H), 7.43–7.62 (m, 3H), 4.90–4.95 (m, 1H), 3.81–3.90 (m, 1H), 1.98–2.02 (m, 2H), 1.83–1.85 (m, 2H), 1.71–1.75 (m, 2H), and 1.45–1.55 (m, 4H); ^{13}C NMR ($CDCl_3$) δ=186.9, 160.0, 136.4, 133.4, 130.3, 128.3, 86.7, 50.3, 31.0, 30.5, 28.1, 23.9, and 22.3; CIMS *m/z* 244 $[M+H]^+$; EIMS *m/z* 243 $[M]^+$ (5), 158 $[M-C_5H_9O]^+$ (4), 138 $[M-C_6H_5O]^+$ (4), 105 $[M-C_8H_{12}NO]^+$ (100), 77 $[M-C_8H_{12}NO-CO]^+$ (79); HRMS Found: *m/z* 243.1251 $[M]^+$. Calcd for $C_{15}H_{17}NO_2$: M, 243.1259.

3.2.2.13. 3-Benzoyl-4,5-cycloocta-4,5-dihydroisoxazole (13b). Pale-yellow oil; IR (NaCl) 1652 and 1579 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.14–8.18 (m, 2H), 7.43–7.63 (m, 3H), 4.54–4.60 (m, 1H), 3.54–3.59 (m, 1H), 2.02–2.13 (m, 2H), and 1.27–1.79 (m, 10H); ^{13}C NMR ($CDCl_3$) δ=186.8, 162.3, 136.5, 133.4, 130.3, 128.3, 87.5, 49.1, 29.8, 25.7, 25.5, 25.3, 25.1, and 24.6; CIMS *m/z* 258 $[M+H]^+$; EIMS *m/z* 257 $[M]^+$ (5), 228 $[M-CHO]^+$ (1), 186 $[M-C_4H_7O]^+$ (1), 172 $[M-C_5H_9O]^+$ (2), 152 $[M-C_6H_5CO]^+$ (7), 105 $[M-C_9H_{14}NO]^+$ (100), 77 $[M-C_9H_{14}NO-CO]^+$ (62); HRMS Found: *m/z* 257.1423 $[M]^+$. Calcd for $C_{16}H_{19}NO_2$: M, 257.1416.

3.2.2.14. 3-Benzoyl-5-propylisoxazole (14b). Pale-yellow oil; IR (NaCl) 1663 and 1597 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.28–8.31 (m, 2H), 7.48–7.64 (m, 3H), 6.52 (s, 1H), 2.80 (t, *J*=7.5 Hz, 2H), 1.73–1.84 (m, 2H) and 1.01 (t, *J*=7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=185.9, 174.4, 161.7, 135.7, 133.7, 130.5, 128.4, 101.6, 28.4, 20.7, and 13.5; CIMS *m/z* 216 $[M+H]^+$; EIMS *m/z* 215 $[M]^+$ (1), 105 $[M-C_6H_8NO]^+$ (100), 77 $[M-C_6H_8NO-CO]^+$ (65); HRMS Found: *m/z* 215.0924 $[M]^+$. Calcd for $C_{13}H_{13}NO_2$: M, 215.0946.

3.2.2.15. 3-Benzoyl-5-butylisoxazole (15b). Pale-yellow oil; IR (NaCl) 1663 and 1597 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.28–8.31 (m, 2H), 7.47–7.63 (m, 3H), 6.51 (s, 1H), 2.82 (t, *J*=7.7 Hz, 2H), 1.69–1.76 (m, 2H), 1.37–1.46 (m, 2H), and 0.95 (t, *J*=7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=185.9, 174.6, 161.7, 135.7, 133.7, 130.5, 128.4, 101.5, 29.3, 26.1, 22.0 and 13.5; CIMS *m/z* 230 $[M+H]^+$; EIMS *m/z* 229 $[M]^+$ (1), 105 $[M-C_7H_{10}NO]^+$ (100), 77 $[M-C_7H_{10}NO-CO]^+$ (55); HRMS Found: *m/z* 229.1083 $[M]^+$. Calcd for $C_{14}H_{15}NO_2$: M, 229.1062.

3.2.2.16. 3-Benzoyl-5-pentylisoxazole (16b). Pale-yellow oil; IR (NaCl) 1663 and 1598 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.28–8.31 (m, 2H), 7.46–7.62 (m, 3H), 6.51 (s, 1H), 2.80 (t, *J*=7.5 Hz, 2H), 1.69–1.76 (m, 2H), 1.33–1.40 (m, 4H), and 0.89 (t, *J*=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=185.7, 174.5, 161.6, 135.7, 133.6, 130.4, 128.2, 101.4, 30.9, 26.9, 26.4, 22.0, and 13.7; CIMS *m/z* 244 $[M+H]^+$; EIMS *m/z* 243 $[M]^+$ (1), 105 $[M-C_8H_{12}NO]^+$ (100), 77 $[M-C_8H_{12}NO-CO]^+$ (49); HRMS Found: *m/z* 243.1246 $[M]^+$. Calcd for $C_{15}H_{17}NO_2$: M, 243.1259.

3.2.2.17. 3-Benzoyl-5-hexylisoxazole (17b). Pale-yellow oil; IR (NaCl) 1663 and 1597 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.28–8.30 (m, 2H), 7.49–7.65 (m, 3H), 6.52 (s, 1H), 2.84 (t, *J*=7.7 Hz, 2H), 1.65–1.79 (m, 2H), 1.19–1.44 (m, 6H), and 0.90 (t, *J*=7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ=186.1, 174.7, 161.8, 135.8, 133.9, 130.6, 128.5, 101.6, 31.3, 28.7, 27.4, 26.6, 22.4, and 14.0; CIMS *m/z* 258 $[M+H]^+$; EIMS *m/z* 257 $[M]^+$ (1), 105 $[M-C_9H_{14}NO]^+$ (100), 77 $[M-C_9H_{14}NO-CO]^+$ (43); HRMS Found: *m/z* 257.1406 $[M]^+$. Calcd for $C_{16}H_{19}NO_2$: M, 257.1416.

3.2.2.18. Ethyl 3-benzoylisoxazolecarboxylate (18b). Colorless needles from EtOH; mp 51.8–53.5 °C; IR (NaCl) 1665 and 1598 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.26–8.29 (m, 2H), 7.48–7.68 (m, 3H), 7.40 (s, 1H), 4.45 (q, *J*=7.1 Hz, 2H), and 1.42 (t, *J*=7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$)

δ=184.1, 161.9, 160.9, 156.0, 135.2, 134.2, 130.4, 128.5, 109.8, 62.4, and 13.8; CIMS *m/z* 246 $[M+H]^+$; EIMS *m/z* 246 $[M]^+$ (3), 105 $[M-C_6H_6NO_3]^+$ (100), 77 $[M-C_6H_6NO_3-CO]^+$ (69); HRMS Found: *m/z* 245.0687 $[M]^+$. Calcd for $C_{13}H_{11}NO_4$: M, 245.0688.

3.2.2.19. 3-Benzoyl-6-hydroxy-5-cyclohexylisoxazole (19b). Pale-yellow oil; IR (NaCl) 3437, 1662, and 1599 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.27–8.29 (m, 2H), 7.49–7.66 (m, 3H), 6.70 (s, 1H), 3.50 (brs, 1H), and 1.19–2.02 (m, 10H); ^{13}C NMR ($CDCl_3$) δ=185.9, 178.8, 161.6, 135.6, 134.0, 130.6, 128.5, 100.7, 65.8, 36.5, 30.9, 25.0, 21.5, and 15.2; CIMS *m/z* 272 $[M+H]^+$; EIMS *m/z* 203 $[M-68]^+$ (1), 105 $[M-C_9H_{12}NO_2]^+$ (100), 77 $[M-C_9H_{12}NO_2-CO]^+$ (38); HRMS Found: *m/z* 271.1220 $[M]^+$. Calcd for $C_{16}H_{17}NO_3$: M, 271.1208.

3.2.3. Reaction of acetone with CAN(IV). A reaction mixture of acetone (3.0 ml) and CAN(IV) (0.2971 g, 0.5 mmol) was stirred under reflux for 10 h. The mixture was extracted with diethyl ether (30 ml) and washed with aq. sodium hydrogencarbonate solution (2×2.0 ml), saturated aq. NaCl (2×2.0 ml) and water (2×2.0 ml). The ethereal solution was dried over Na_2SO_4, and concentrated in a vacuum. The resulting oil was 3,4-diacetyl-1,2,5-oxadiazole 2-oxide (**20**).

3.2.3.1. 3,4-Diacetyl-1,2,5-oxadiazole oxide (20). (NaCl) 1718 and 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.74 (s, 3H) and 2.63 (s, 3H); ^{13}C NMR ($CDCl_3$) δ=188.9, 185.5, 153.4, 111.5, 29.2, 28.2; CIMS *m/z* 172 $[M+H]^+$.

3.2.4. Reaction of 1-octene (3) with CAN(III)-formic acid in acetone. A mixture of 1-octyne (**3**) (0.0561 g, 0.5 mmol), ammonium cerium (III) nitrate (0.2741 g, 0.5 mmol), and formic acid (0.2302 g, 5.0 mmol) in acetone (3.0 ml) was stirred under reflux for 10 h. After the usual work up, the resulting oil was chromatographed on silica gel. Elution with hexane–diethyl ether (5:1) gave 3-acetyl-5-hexylisoxazole (**3a**) (0.0670 g, 68%).

3.2.5. Reaction of 1-octene (3) with CAN(III)-formic acid in acetophenone. A mixture of 1-octyne (**3**) (0.0561 g, 0.5 mmol), ammonium cerium(III) nitrate (0.2741 g, 0.5 mmol), and formic acid (0.2302 g, 5.0 mmol) in acetophenone (3.0 ml) was stirred under reflux for 15 h. After the usual work up, the resulting oil was chromatographed on silica gel. Elution with hexane–diethyl ether (5:1) gave 3-benzoyl-5-hexylisoxazole (**3b**) (0.0920 g, 71%).

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