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Reaction of α,β-unsaturated ketones with cerium(IV) salts in alcohol

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Reaction of α,β-unsaturated ketones with cerium(IV) salts or lanthanide triflates in alcohols gave good yields of the corresponding β-alkoxy compounds. In the case of 2-cyclopentenone and 2-cyclohexenone, the 1,1,3-trialkoxy acetal derivatives were obtained preferentially accompanied by β-alkoxyketone, except 2-cycloheptenone. However, in the reaction of 2-cycloheptenone with alcohol using cerium(IV) sulfate (CS)-molecular sieve, 1,1,3-trialkoxy derivatives were obtained. Also, in the cases of 1-penten-3-one, 4-hexen-3-one and 3-hepten-2-one, 1,1,3-trialkoxy derivatives were obtained preferentially. Copyright © 2006 John Wiley & Sons, Ltd.

KEYWORDS: Michael addition; acetalization; 1,1,3-trialkoxycycloalkane; β-alkoxy ketone; α,β-unsaturated ketone

INTRODUCTION

β-Alkoxy ketones are usually used as intermediates for natural product synthesis. It is known that the Michael reaction of alcohols and α,β-unsaturated ketones under basic conditions is one of the hardest synthetic transformations to achieve efficiently, because β-alkoxy ketones revert to starting materials via the retro Michael reaction.[1] Thus, such Michael reactions need to use strongly basic conditions or non-basic conditions using Pd(II) catalysts.[2–6] Hayashi and Nishimura reported that high pressure, which was realized by freezing water in a sealed autoclave, has been successfully applied to a high-yield Michael reaction of alcohols and α,β-unsaturated ketones in the presence of a catalytic amount of DMAP and $LiClO_4$.[7]

In previous work, we have reported a novel α-iodination of ketones to afford the corresponding iodo ketones;[8,9] a new alkoxyiodination and nitratoiodination of olefins;[10,11] new oxidative aromatization of α,β-unsaturated cyclohexenones;[12] and a new α,α'-diiodination of ketones using iodine–ammonium cerium(IV) nitrate (CAN).[13]

Still earlier, we described oxidation of 2-substituted cycloalkanones with cerium(IV) sulfate tetrahydrate (CS) in alcohols and acetic acid;[14,15] cerium(IV) sulfate mediated oxidative addition of 1-phenylcycloalkenes and styrene derivatives in methanol for synthesis of 1,2-dimethoxy compound;[16] preparative conversion of oxime to parent carbonyl compounds by cerium(IV) sulfate in acetonitrile and alcohol;[17] esterification of alkene with cerium(IV) sulfate in carboxylic acid;[18] and formation of isoxazole derivatives via nitrile oxide using ammonium cerium nitrate.[19,20] Through our studies, we have found that iodine–CAN, CAN and CS are useful reagents for the synthesis of a large number of iodo compounds, C–C bond cleavage compounds, and dihydroisoxazole and isoxazole derivatives.

Here, we report on the synthesis of 1,1,3-trialkoxy or 3-alkoxy derivatives from α,β-unsaturated ketones (2-cyclopentenone, 2-cyclohexenone, 2-cycloheptenone, 1-penten-3-one, 4-hexen-3-one and 3-hepten-2-one) with cerium(IV) sulfate using molecular sieves in alcohols.

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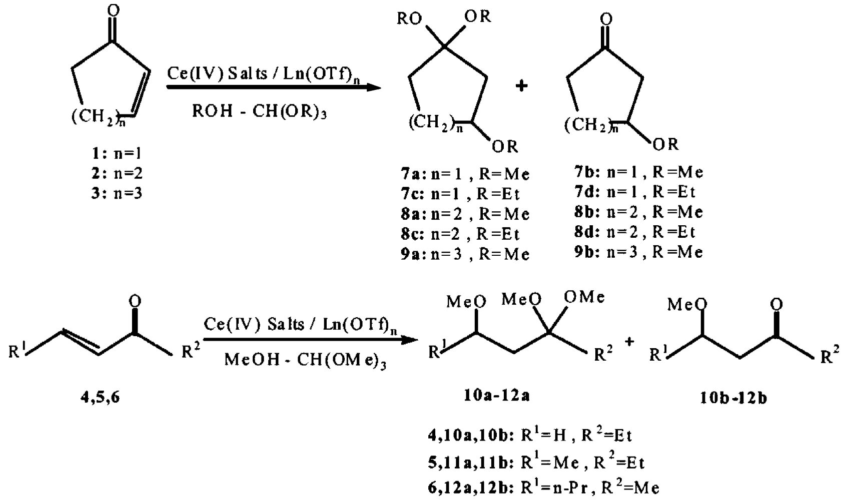

Scheme 1.

RESULTS AND DISCUSSION

The reaction of 2-cyclohexenone (**2**) with CAN or CS in methanol at 50 °C for 4.0 h gave 1,1,3-trimethoxycyclohexane (**8a**) and 3-methoxycyclohexanone (**8b**), (64, 66%, **8a** : **8b** = 70 : 30, 84 : 16), respectively (see Scheme 1). In the case containing trimethyl orthoformate using CS at 0 °C for 4.0 h, **8a** and **8b** were obtained 92% of the time (**8a** : **8b** = 94 : 6). It is known that lanthanide triflates are stable in aqueous media and can act as Lewis acid catalysts in several carbon–carbon bond forming reactions. Accordingly, we thought that, if we used lanthanide triflates, 1,1,3-trialkoxy derivatives may be obtained in high selectivity. In the reaction of **2** with $Yb(OTf)_3$ in methanol–trimethyl orthoformate at 0 °C for 3.0 h, the compound **8a** was obtained preferentially (88%, **8a** : **8b** = 100 : 0). These results are summarized in Table 1.

As can be seen from Table 1, cerium (IV) salts or lanthanide triflates act as Lewis acids, so that 2-cyclohexenone (**2**) transforms into 3-methoxycyclohexanone (**8b**). From these results, it is considered that the first step of this reaction occurs by 1,4-addition and then proceeds to 1,1,3-trialkoxy derivatives by acetalization. The reaction provides a new, simple method for preparing 3-methoxycyclohexanone dimethyl acetal. The reaction of 2-cyclohexenone (**2**) at 0 °C with CS gave 1,1,3-trimethoxycyclohexane (**8a**) and 3-methoxycyclohexanone (**8b**; 92%, **8a** : **8b** = 94 : 6). Also, the reaction with $Yb(OTf)_3$ gave only compound **8a** (88%, **8a** : **8b** = 100 : 0). On the basis of these results, reactions run using $Yb(OTf)_3$ (Table 1, runs 4, 16, 27, 32 and 36) at 0 °C are best for acetalization. Reactions using other catalysts [CAN, CS, $Ce(OTf)_4$, $Sc(OTf)_3$] are also effective for acetalization.

However, in the case of cycloheptenone, 1,1,3-trimethoxy derivative was not obtained. In the cases of **1**, **2** or **7** with EtOH and $CH(OEt)_3$ using Ce(IV) salts or $Ln(OTf)_n$, 1,1,3-triethoxy derivatives were obtained. These results are summarized in Table 2.

As can be seen from Table 2, cerium(IV) salts or lanthanide triflates are effective as Lewis acids, although the yields are inferior to those of trimethoxy derivatives. It was found that the CS–MS system gave better results than $Yb(OTf)_3$ for synthesis of triethoxy derivatives. Moreover, we tried effective methods for expensive CS. The reaction of **2** with CS, $CH(OMe)_3$, molecular sieve (3 or 4 Å) and methanol was carried out at room temperature. Trimethoxy derivatives were obtained preferentially. These results are summarized in Table 3. As seen from the results, these systems (CS–MS 3 or 4 Å) were more effective for synthesis of 1,1,3-trialkoxy derivatives from α,β-unsaturated ketone. In particular, it is interesting that the reaction of cycloheptenone with the CS–MS system provides a good yield of 1,1,3-trimethoxy derivative **9a**, but with $Yb(OTf)_3$, **9a** was not obtained. From these results, it seems that molecular sieves take water generated from the reaction system.

In conclusion, this method is simple and convenient for Michael reaction and acetalization from α,β-unsaturated ketone. It is particularly noteworthy that this reaction affords new synthetic methods for Michael addition and acetalization.

EXPERIMENTAL

IR spectra were recorded using a Jasco FT/IR-230 grating infrared spectrometer. ^{1}H- and ^{13}C-NMR spectra were measured using a Joel GSX-400 model spectrometer in deuteriochloroform with TMS as an internal standard. High-resolution MS spectra were measured on a Joel JMS-01SG-2 instrument equipped with a JMA-DA 7000 data system.

Typical procedures 1

A mixture of 2-cyclohexenone (**2**; 123 mg, 1.28 mmol), CAN (140 mg, 0.26 mmol), methanol (5 ml) and trimethyl

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Table 1. Reaction of 2-cycloalkenone with MeOH and CH(OMe)3 using Ce(IV) salts or Ln(OTf)$_n$

Run	Substrate	Catalyst[a]	Temperature (°C)	Time (h)	Product	Yield (%)	Ratio[b]
1	**1**[c]	CAN	0	2.0	**7a** : **7b**	56	83 : 17
2	**1**	CS	0	2.0	**7a** : **7b**	52	88 : 12
3	**1**	Ce(OTf)$_4$	0	2.0	**7a** : **7b**	57	67 : 33
4	**1**	Yb(OTf)$_3$	rt	3.0	**7a** : **7b**	87	100 : 0
5	**2**[d]	CAN	rt	5.0	**8a** : **8b**	76	81 : 19
6	**2**	CAN	0	4.0	**8a** : **8b**	75	95 : 5
7	**2**	CS	rt	5.0	**8a** : **8b**	79	95 : 5
8	**2**	CS	0	4.0	**8a** : **8b**	92	94 : 6
9	**2**	Ce(OTf)$_4$	rt	3.0	**8a** : **8b**	74	71 : 29
10	**2**	Ce(OTf)$_4$	0	4.0	**8a** : **8b**	72	94 : 6
11	**2**	Sc(OTf)$_3$	rt	3.0	**8a** : **8b**	87	95 : 5
12	**2**	Sc(OTf)$_3$	0	3.0	**8a** : **8b**	99	97 : 3
13	**2**	Yb(OTf)$_3$	rt	3.0	**8a** : **8b**	85	100 : 0
14	**2**	Yb(OTf)$_3$	0	3.0	**8a** : **8b**	88	100 : 0
15	**3**[d]	CAN	50	4.0	**9b**	95	
16	**3**	CAN	reflux	2.0	**9b**	78	
17	**3**	CS	50	4.0	**9b**	95	
18	**3**	Sc(OTf)$_3$	50	4.0	**9b**	87	
19	**3**	Yb(OTf)$_3$	50	3.5	**9b**	78	
20	**4**[c]	CAN	50	4.0	**10a** : **10b**	52	83 : 17
21	**4**[c]	CS	50	4.0	**10a** : **10b**	57	32 : 68
22	**4**[c]	Ce(OTf)$_4$	50	3.0	**10a** : **10b**	59	89 : 11
23	**4**[c]	Yb(OTf)$_3$	50	3.0	**10a** : **10b**	73	96 : 4
24	**4**[c]	Sc(OTf)$_3$	50	3.0	**10a** : **10b**	45	64 : 36
25	**5**[d]	CAN	50	5.0	**11a** : **11b**	70	65 : 35
26	**5**[c]	CS	50	4.0	**11a** : **11b**	57	20 : 80
27	**5**[d]	Ce(OTf)$_4$	50	3.0	**11a** : **11b**	59	15 : 85
28	**5**[d]	Yb(OTf)$_3$	50	3.0	**11a** : **11b**	73	80 : 20
29	**5**[c]	Sc(OTf)$_3$	50	3.0	**11a** : **11b**	45	26 : 74

[a] Reaction conditions: substrate (1.28 mmol), Ce(IV) salts [or Ln(Otf)$_n$] (0.26 mmol) and MeOH (5 ml) were employed.
[b] Product ratios were determined from the peak area of ^{1}H-NMR spectrum.
[c] CH(OMe)3 (6.38 mmol).
[d] CH(OMe)3 (12.75 mmol).

orthoformate (1.353 g, 12.75 mmol) was stirred at 0 °C for 4.0 h. The reaction mixture was poured into water and extracted with ether. The ethereal solution was washed with water, dried and concentrated. The reaction mixtures (75%, **8a** : **8b** = 95 : 5) were chromathographed on silica gel. Elution with hexane–ether (1 : 1) gave the 1,1,3-trimethoxycyclohexane (**8a**) and 3-methoxycyclohexanone (**8b**). The product ratio was determined from the peak area of ^{1}H-NMR spectrum.

Typical procedures 2

A mixture of 2-cycloheptenone (**3**; 141 mg, 1.28 mmol), CS (103 mg, 0.26 mmol), molecular sieve (100 mg), methanol (5 ml) and trimethyl orthoformate (1.353 g, 12.75 mmol) was stirred at 0 °C for 4.0 h. The reaction mixture was poured into water and extracted with ether. The ethereal solution was washed with water, dried and concentrated. The reaction mixtures (90%, **9a** : **9b** = 93 : 7) were chromathographed on silica gel. Elution with hexane–ether (1 : 1) gave the 1,1,3-trimethoxycycloheptane (**9a**) and 3-methoxycycloheptanone (**9b**). The product ratio was determined from the peak area of ^{1}H-NMR spectrum.

*1,1,3-Trimethoxycyclopentane (**7a**)*

IR (NaCl) 1099 and 1051 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 1.70$–1.83 (m, 3H), 1.89–1.97 (m, 3H), 2.13–2.19 (m, 1H), 3.18 (s, 3H), 3.22 (s, 3H), 3.29 (s, 3H) and 3.83(m, 1H). ^{13}CNMR (CDCl3) $\delta = 29.6$, 32.2, 40.8, 48.9, 49.6, 56.7, 79.9 and 110.1. HRMS Found: m/z 160.1124; calcd for $C_8H_{16}O_3$: M, 160.1100.

*3-Methoxycyclopentanone (**7b**)*

IR (NaCl) 1735 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 1.20$ (t, 3H), 2.13 (m, 3H), 2.34 (m, 3H) 3.49 (m, 2H) and 4.17 (m, 1H). ^{13}CNMR (CDCl$_3$) $\delta = 15.4$, 29.1, 35.9, 45.0, 64.1, 76.5 and 217.4. HRMS Found: m/z 114.0682; calcd for $C_6H_{10}O_2$: M, 114.0681.

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Table 2. Reaction of 2-Cycloalkenone with EtOH and CH(OEt)3 using Ce(IV) Salts or Ln(OTf)$_n$

Run	Substrate	Catalyst[a]	Temperature (°C)	Time (h)	Product	Yield (%)	Ratio[b]
1	**1**	CAN	0	2.0	**7c : 7d**	58	69 : 31
2	**1**	CS	0	2.0	**7c : 7d**	62	58 : 42
3	**1**	CS–MS 3 Å	0	2.0	**7c : 7d**	72	95 : 5
4	**1**	Ce(OTf)$_4$	0	2.5	**7c : 7d**	64	52 : 48
5	**1**	Yb(OTf)$_3$	0	2.5	**7c : 7d**	69	84 : 16
6	**1**	Sc(Otf)$_3$	0	2.0	**7c : 7d**	61	84 : 16
7	**2**	CAN	40	2.0	**8c : 8d**	88	89 : 11
8	**2**	CS	40	2.0	**8c : 8d**	89	88 : 12
9	**2**	Ce(OTf)$_4$	rt	2.0	**8c : 8d**	90	93 : 7
10	**2**	Yb(OTf)$_3$	40	2.0	**8c : 8d**	89	91 : 9
11	**2**	Sc(Otf)$_3$	rt	2.0	**8c : 8d**	89	80 : 20

[a] Reaction conditions: substrate (1.28 mmol), Ce(IV) salts [or Ln(Otf)$_n$] (0.26 mmol), CH(OEt)3 (2.55 mmol), and EtOH (5 ml) were employed.
[b] Product ratios were determined from the peak area of ^{1}H-NMR spectrum.

Table 3. Reaction of 2-cycloalkenone or alkenone with ROH, CH(OR)$_3$ and Ce(IV) salts using molecular sieves

Run	Substrate	Catalyst[a]	Temperature (°C)	Time (h)	Product	Yield (%)	Ratio[b]
1	**1**	CS–MS 3 Å	rt	2.0	**7a : 7b**	70	90 : 10
2	**1**	CS–MS 3 Å	0	2.0	**7a : 7b**	50	62 : 38
3	**1**	CS–MS 3 Å	0	2.0	**7a : 7b**	68	97 : 3
4	**1**	CS–MS 4 Å	rt	2.0	**7a : 7b**	70	76 : 24
5	**1**	CS–MS 4 Å	0	2.0	**7a : 7b**	57	89 : 11
6	**1**	CS–MS 4 Å	0	4.0	**7a : 7b**	62	99 : 1
7	**1**	CS–MS 3 Å	0	2.0	**7c : 7d**	86	88 : 12
8	**1**	CS–MS 3 Å	0	5.0	**7c : 7d**	82	85 : 15
9	**1**	CS–MS 4 Å	0	2.0	**7c : 7d**	80	88 : 12
10	**1**	CS–MS 4 Å	0	5.0	**7c : 7d**	87	91 : 9
11	**2**	CS–MS 3 Å	60	3.0	**8a : 8b**	83	98 : 2
12	**2**	CS–MS 3 Å	rt	5.0	**8a : 8b**	86	91 : 9
13	**2**	CS–MS 3 Å	0	5.0	**8a : 8b**	83	87 : 13
14	**2**	CS–MS 4 Å	60	3.0	**8a : 8b**	88	98 : 2
15	**2**	CS–MS 4 Å	rt	5.0	**8a : 8b**	95	97 : 3
16	**2**	CS–MS 4 Å[c]	rt	5.0	**8a : 8b**	98	100 : 0
17	**3**	CS–MS 3 Å	rt	7.0	**9a : 9b**	89	93 : 7
18	**3**	CS–MS 3 Å	0	7.0	**9a : 9b**	88	90 : 10
19	**3**	CS–MS 4 Å	rt	7.0	**9a : 9b**	90	92 : 8
20	**3**	CS–MS 4 Å	0	7.0	**9a : 9b**	90	93 : 7
21	**5**	CS–MS 3 Å	50	3.0	**11a : 11b**	57	91 : 9
22	**5**	CS–MS 4 Å	50	3.0	**11a : 11b**	59	77 : 23
23	**6**	CS–MS 3 Å	rt	3.0	**12a : 12b**	80	83 : 17
24	**6**	CS–MS 4 Å	rt	3.0	**12a : 12b**	82	66 : 34

[a] Reaction conditions: substrate (1.28 mmol), Ce(IV) sulfate (0.26 mmol), CH(OR)$_3$ (6.38 mmol), MS (100 mg) and MeOH (5 ml) were employed.
[b] Product ratios were determined from the peak area of ^{1}H- NMR spectrum.
[c] Powder was used.

*1,1,3-Triethoxycyclopentane (**7c**)*

IR (NaCl) 1054 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 1.17$ (m, 9H), 1.68 (m, 1H), 1.79 (m, 2H), 1.96 (m, 2H), 2.24 (m, 1H), 3.46 (m, 6H) and 3.94(m, 1H). ^{13}CNMR (CDCl$_3$) $\delta = 15.45, 15.49, 15.51$, 30.0, 32.9, 41.9, 56.4, 57.3, 64.2, 78.0 and 109.32. HRMS Found: m/z 202.1584; calcd for $C_{11}H_{22}O_3$: M, 202.1570.

*3-Ethoxycylopentanone (**7d**)*

(NaCl) 1745, 1157, 1120 and 1079 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 1.20$ (t, 3H), 2.13 (m, 3H), 2.34 (m, 3H), 3.49 (m, 2H) and 4.17 (m, 1H). ^{13}CNMR (CDCl$_3$) $\delta = 15.4$, 29.1, 35.9, 45.0, 64.1, 76.5 and 217.4. HRMS Found: m/z 128.0799; calcd for $C_7H_{12}O_2$: M,128.0838.

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*1,1,3-Trimethoxycyclohexane (**8a**)*

IR (NaCl) 1164, 1096 and 1060 cm^{-1}. ^{1}HNMR(CDCl$_3$) $\delta =$ 1.06–1.39 (m, 4H), 1.66 (m, 1H), 1.97 (m, 2H), 2.40 (m, 2H), 3.15 (s, 3H), 3.21 (s, 3H) and 3.35 (s, 3H). ^{13}CNMR(CDCl3) $\delta = 19.6$, 31.2, 31.8, 38.5, 47.4, 47.7, 55.9, 76.9 and 101.0. HRMS Found: m/z 174.1298; calcd for $C_9H_{18}O_3$: M, 174.1256.

*3-Methoxycyclohexanone (**8b**)*

IR (NaCl) 1720 and 1102 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 1.70$ (m, 1H), 1.85 (m, 1H), 2.01 (m, 1H), 2.32 (m, 2H), 2.48 (dd, $J = 7.0$, 14.0 Hz, 1H), 2.60 (dd, $J = 4.0$, 14.0 Hz, 1H), 3.33 (s, 3H) and 3.68 (m, 1H). ^{13}CNMR (CDCl$_3$) $\delta = 20.6$, 29.3, 41.1, 47.1, 55.9, 78.1 and 209.6. HRMS Found: m/z 128.0827; calcd for $C_7H_{12}O_2$: M, 128.0838.

*1,1,3-Triethoxycyclohexane (**8c**)*

IR (NaCl) 1103, 1081 and 1056 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta =$ 1.15–1.26 (m, 14H), 1.62 (m, 1H), 2.02 (m, 2H), 2.39 (m, 1H), 3.42 (m, 2H) and 3.52 (m, 4H). ^{13}CNMR (CDCl$_3$) $\delta = 15.5$, 15.6, 15.8, 19.9, 31.9, 32.9, 40.1, 55.0, 55.2, 63.4, 75.4 and 100.9. HRMS Found: m/z 216.1677; calcd for $C_{12}H_{24}O_3$: M, 216.1726.

*3-Ethoxycyclohexanone (**8d**)*

IR (NaCl) 1718 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 1.18$ (t, 3H), 1.73 (m, 2H), 2.00 (m, 2H), 2.31 (t, 2H), 2.44 (dd, $J = 7.0$, 14.0 Hz, 1H), 2.62 (dd, $J = 4.0$, 14.0 Hz, 1H), 3.48 (m, 2H) and 3.74 (m, 1H). ^{13}CNMR (CDCl$_3$) $\delta = 15.5$, 20.7, 30.1, 41.1, 47.7, 63.6, 76.5 and 209.8. HRMS Found: m/z 142.1014; calcd for $C_8H_{14}O_2$: M, 142.0994.

*1,1,3-Trimethoxycycloheptanone (**9a**)*

IR (NaCl) 1130, 1089 and 1050 cm^{-1}: ^{1}HNMR (CDCl$_3$) $\delta =$ 1.36–1.82 (m, 8H), 1.88 (m, 1H), 2.04 (m, 1H), 2.30 (m, 1H), 3.17 (s, 3H), 3.18 (s, 3H) and 3.32 (s, 3H); ^{13}CNMR (CDCl$_3$) $\delta = 21.8$, 25.4, 34.8, 36.2, 42.3, 47.84, 47.89, 56.1, 77.2 and 101.8. HRMS Found: m/z 174.1225; calcd for $C_9H_{18}O_3$: M, 174.1256.

*3-Methoxycycloheptanone (**9b**)*

IR (NaCl) 1704 and 1096 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta =$ 1.64–1.98 (m, 6H), 2.44 (m, 2H), 2.75 (dd, $J = 2.0$, 14.0 Hz, 1H), 2.82 (dd, $J = 8.0$, 14.0 Hz, 1H), 3.33 (s, 3H) and 3.55 (m, 1H). ^{13}CNMR (CDCl$_3$) $\delta = 23.9$, 24.4, 35.1, 44.2, 48.4, 56.2, 75.9 and 212.0. HRMS Found: m/z 142.1025; calcd for $C_8H_{14}O_2$: M, 142.0994.

*1,3,3-Trimethoxypentane (**10a**)*

IR (NaCl) 1120, 1086 and 1065 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 0.87$ (t, 3H), 1.56 (q, 2H), 1.92 (t, 2H), 3.16 (s, 6H), 3.32 (s, 3H) and 3.37 (t, 2H). ^{13}CNMR (CDCl$_3$) $\delta = 8.15$, 26.0, 31.7, 47.6, 58.7, 68.5 and 102.63. HRMS Found: m/z 162.1244; calcd for $C_8H_{18}O_3$: M, 162.1256.

*1-Methoxy-3-pentanone (**10b**)*

IR (NaCl) 1714 and 1116 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 1.06$ (t, 3H), 2.47 (q, 2H), 2.66 (t, 2H), 3.33 (s, 3H) and 3.65 (t, 2H). ^{13}CNMR (CDCl$_3$) $\delta = 7.6$, 36.6, 42.4, 58.8, 67.7 and 209.7. HRMS Found: m/z 116.0872; calcd for $C_6H_{12}O_2$: M, 116.0837.

*2,4,4-Trimethoxyhexane (**11a**)*

IR (NaCl) 1141, 1085 and 1060 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 0.86$ (t, 3H), 1.17 (t, 3H), 1.67 (m, 2H), 1.88 (m, 2H), 2.42 (m, 1H), 3.136 (s, 3H), 3.138 (s, 3H) and 3.298 (s, 3H). ^{13}CNMR (CDCl$_3$) $\delta = 8.1$, 19.9, 25.8, 38.8, 47.5, 47.7, 56.0, 73.5 and 103.1. HRMS Found: m/z 176.1437; calcd for $C_9H_{20}O_3$: M, 176.1413.

*5-Methoxy-3-hexanone (**11b**)*

IR (NaCl) 1716 and 1094 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 1.04$ (t, 3H), 1.16 (d, 3H), 2.40 (dd, $J = 5.0$, 15.0 Hz, 1H), 2.46 (m, 2H), 2.69 (dd, $J = 7.0$, 15.0 Hz, 1H), 3.30 (s, 3H) and 3.80 (m, 1H). ^{13}CNMR (CDCl$_3$) $\delta = 7.6$, 19.2, 37.0, 49.4, 56.3, 73.3 and 209.9. HRMS Found: m/z 130.0967; calcd for $C_7H_{14}O_2$: M, 130.0994.

*2,2,4-Trimethoxyheptane (**12a**)*

IR (NaCl) 1199, 1087 and 1052 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 0.93$ (t, 3H), 1.33 (s, 3H), 1.37 (m, 2H), 1.48 (m, 2H), 1.76 (m, 2H), 3.16 (s, 3H), 3.19 (s, 3H) and 3.30 (s, 3H). ^{13}CNMR (CDCl$_3$) $\delta = 14.3$, 18.2, 21.7, 36.6, 41.1, 47.9, 48.0, 56.1 and 101.2. HRMS Found: m/z 190.1537; calcd for $C_{10}H_{22}O_3$: M, 190.1564.

*4-Methoxy-2-heptanone (**12b**)*

IR (NaCl) 1718 and 1093 cm^{-1}. ^{1}HNMR (CDCl$_3$) $\delta = 0.93$ (t, 3H), 1.20–1.53 (m, 4H), 2.18 (s, 3H), 2.45 (dd, $J = 5.0$ and 16.0 Hz, 1H), 2.67 (dd, $J = 7.0$ and 16.0 Hz, 1H), 3.33 (s, 3H) and 3.67 (m, 1H). ^{13}C-NMR (CDCl$_3$) $\delta = 19.2$, 40.0, 52.9, 53.1, 56.1, 73.5 and 102.3. HRMS Found: m/z 144.1110; calcd for $C_8H_{16}O_2$: M, 144.1151.

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