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Preparation of α-Substituted Acroleins via the Reaction of Aldehyde or the Corresponding Ozonide with Dihalomethane and Diethylamine

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Abstract: Treatment of aldehydes or the corresponding ozonides with a mixture of dibromomethane and diethylamine afforded α-substituted acroleins in modest to good yields. The β-carbon of the acrolein (**nc**, n = 1-16) derived from dibromomethane. Functional groups, such as ketone, hydroxy, acetoxy, bromide, iodide, ester are compatible with this reaction condition. The relative rates and yields of this transformation in dichloromethane were found to be in the following order: CH_2I_2 > CH_2Br_2 > CH_2Cl_2.

INTRODUCTION

Recently, we found that the ozonides derived from mono- and 1,1-di-substituted olefins reacted with secondary amines in the presence of 4 Å molecular sieves in refluxing CH_2Cl_2 to give the corresponding tertiary amines in good yields. This transformation included four sequential reactions (*i.e.* ozonide formation, ozonide ring fragmentation, enamine formation, and reductive amination) in the same flask.[1] For example, the ozonide **1a'** prepared from 4-phenyl-1-butene (**1**) reacted with 2.5 mol equiv. of *N*-methylbenzylamine under the described condition to give tertiary amine **1d** in 72% yield (Eq. 1).[1] When *N*-methylbenzylamine was replaced with diethylamine to react with ozonide **1a'**, the α-benzylacrolein (**1c**) was formed in 62% yield. There is no reductive amination product **1d** (Eq. 2).[2] Furthermore, when CH_2Br_2, instead of CH_2Cl_2, was used as the solvent in Eq. 1, the α-benzylacrolein (**1c**) was formed as the major product in 71% yield along with the reductive amination product **1d** (2% yield) and 1-aminoindan **1e** (3% yield) resulting from the intramolecular iminium ion cyclization (Eq. 3). In other words, the reaction pathway can be altered completely by changing the

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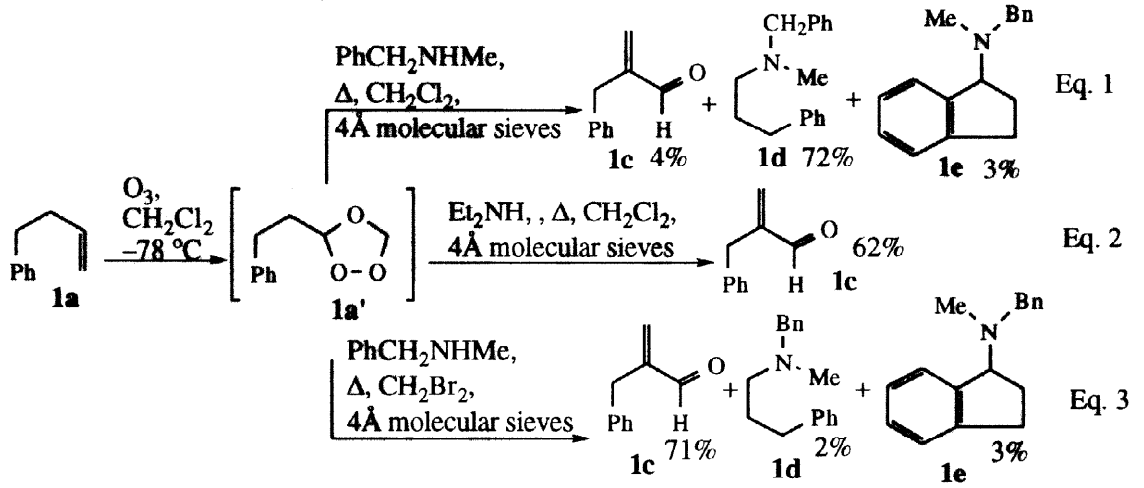


structures of the secondary amines or dihalomethanes. These results can be rationalized as follows. The enamine formation from *N*-methylbenzylamine and an aldehyde is a facile process. Therefore, the reductive amination occurred in Eq. 1. On the other hand, diethylamine is a poor reagent for the enamine formation probably due to its high volatility (b.p. 55 °C).[3] Therefore, diethylamine would prefer to react with dichloromethane to give a reactive intermediate which subsequently reacted with the aldehyde to give the acrolein derivatives **1c**. Interestingly, when dibromomethane was used as the solvent, *N*-methylbenzylamine preferred to nucleophilically attack dibromomethane rather than the aldehyde so that the α-substituted acrolein was formed as the major product. The results illustrated by Eq. 2 and 3 indicated that dihalomethane provided one carbon unit in the major product. Indeed, in the presence of a secondary amine, methylene chloride is known to serve both as solvent and reactant under high[4] or atomospheric pressure[5] at room temperature. Methylenebisamines were proposed as the intermediates. Mannich products have been obtained in modest to good yields by reacting the proposed intermediate with ketones[4b], enamines[5d], or indoles[4d]. Enolizable aldehydes have been used in the Mannich base formation; however, side products arising from subsequent aldol condensation of the resulting β-amino aldehyde often occur. Best results are achieved with α-branched aldehydes, which produce Mannich bases without enolizable protons.[6] Mannich base formation from an aldehyde followed by deamination, a two-step sequence reaction, was reported to prepare α–substituted acroleins.[7] α–Substituted acroleins are very important and useful compounds in organic synthesis. To the best of our knowledge, there is no literature precedent for the enal formation from monosubstituted ozonide and dihalomethane in the presence of diethylamine as shown in Eq. 2. In this report, we will describe the scope of our method in the preparation of α–substituted acroleins.

RESULTS AND DISCUSSION

In order to find the optimal conditions for this interesting transformation, a solution of 4-phenyl-1-butene (**1a**) in CH_2Cl_2 was subjected to the general ozonolysis procedure. The resulted ozonide solution was then reacted with a secondary amine under several different conditions and the results were listed in Table 1. Several findings are also noteworthy. The molecular sieves is not required for this reaction (Entries 1 and 2)

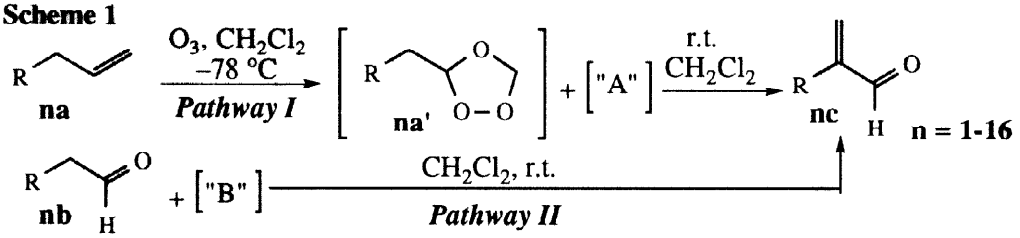
and 2.5 molar equivalents of diethylamine are enough to obtain enal **1c** in 61% yield. The characteristic absorptions of its ^1H NMR spectrum are two singlets (δ 6.06 and 6.09 ppm) due to the olefinic protons. The assignment of the signal at δ 6.06 to the proton *cis* to the carbaldehyde group was confirmed by 2D-NOESY NMR technique. Extra diethylamine did not improve the chemical yield at all (Entries 2, 3 and 4). Better

Table 1. Reaction of ozonide (**1a'**), derived from 4-phenyl-1-butene (**1a**), with dihalomethane and diethylamine to give 2-benzylacrolein (**1c**).

Entry	Molar Eq. of Et_2NH	Solvent	Temp.(°C)	Time (h)	Yield (%)
1	2.5 [a]	CH_2Cl_2 (0.2 M)[b]	refluxing	24	61
2	2.5	CH_2Cl_2 (0.2 M)	refluxing	24	61
3	4	CH_2Cl_2 (0.2 M)	refluxing	24	62
4	10	CH_2Cl_2 (0.2 M)	refluxing	24	62
5	2.5	CH_2Br_2 (0.2 M)	55	0.8	81
6	2.5	CH_2Br_2 (10 mol equiv.) in CH_2Cl_2 (0.2 M)	55	16	71
7	2.5	CH_2I_2 (6 mol equiv.) in CH_2Cl_2 (0.2 M)	55	3	74
8	3[c]	CH_2Br_2 (10 mol equiv.) in CH_2Cl_2 (0.2 M)	r.t.	0.5	72

[a] In the presence of 4Å molecular sieves. [b] 0.2 M means the concentration of the ozonide in CH_2X_2 (X=Cl, Br). [c] A solution of of Et_2NH and CH_2Br_2 was heated at 55 °C for 1.5 h prior to its addition to the ozonide in CH_2Cl_2.

Scheme 1



Reagents: A mixture of CH_2Br_2 (15 mol equiv.) and Et_2NH (5 mol equiv.) was heated to 55 °C for 1.5 h to give reactive species expressed as "A"; A mixture of CH_2Br_2 (15 mol equiv.) and Et_2NH (3 mol equiv.) was heated to 55 °C for 1.5 h to give reactive species expressed as "B"

chemical yields with a shorter reaction time were obtained when the solvent was changed from CH_2Cl_2 to CH_2Br_2 (Entries 2 and 5). The mixed solvent such as CH_2Br_2 in CH_2Cl_2 or CH_2I_2 in CH_2Cl_2 could also improve the yields (Entries 2, 6 and 7). A mixture of diethylamine and CH_2Br_2 was preheated to 55 °C for 1.5 h in an attempt to generate the reactive species in advance. This preheated mixture was then added to a solution of ozonide **1a'** in CH_2Cl_2 at -78 °C. The cooling bath was removed and the reaction mixture was warmed to room temperature. The reaction was found to be complete within 1 h and acrolein **1c** was formed in 72% yield (Entries 8). In light of its efficiency this procedure was used in further investigations. It is worthy to mention

that this preheated mixture was concentrated *in vacuo* to give the orange solid which was not effective to react with ozonide **1a'** any more.

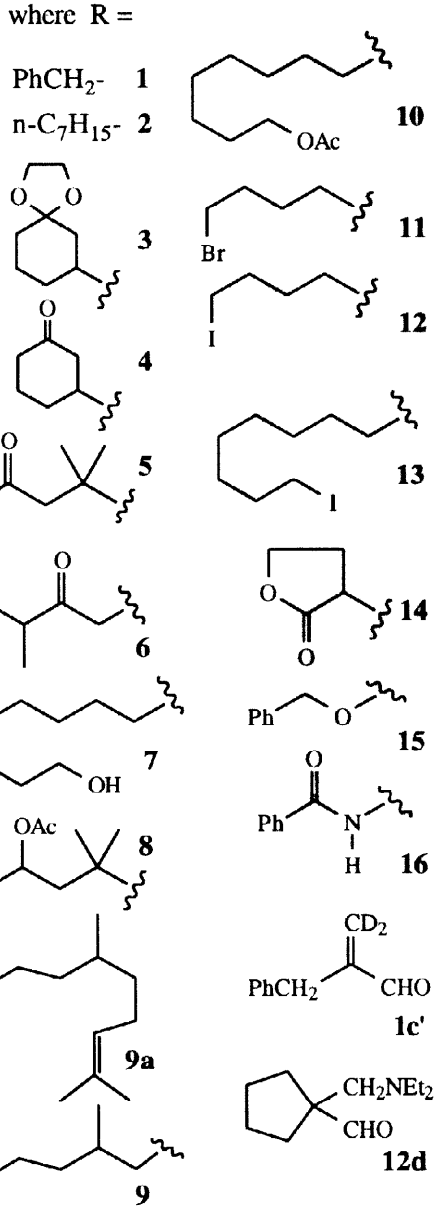
Table 2. α-Substituted acrolein formation from olefin *via* ozonide (pathway I) or from aldehyde (pathway II)

Entry	Starting Material	Pathway I Yield (%)	Starting Material	Pathway II Yield (%)
1	**1a**	**1c** 72	**1b**	**1c** 87
2	**1a**	**1c'** 63[a]	**1b**	**1c'** 75
3	**2a**	**2c** 51	**2b**	**2c** 62
4	**3a**	**3c** 67	**3b**	**3c** 72
5	**4a**	**4c** 63	**4b**	**4c** 73
6	**5a**	**5c** 65	**5b**	**5c** 68
7	**6a**	**6c** 50	**6b**	**6c** 66
8	**7a**	——[b]	**7b**	**7c** 64
9	**8a**	**8c** 68	**8b**	**8c** 76
10	**9a**	**9c** 61	**9b**	**9c** 69
11	**10a**	——[b]	**10b**	**10c** 63
12	**11a**	——[b]	**11b**	**11c** 73
13	**12a**	——[b]	**12b**	**12c** 54[c]
14	**13a**	——[b]	**13b**	**13c** 68
15	**14a**	**15c** 50	**14b**	**14c** 64
16	**15a**	**16c** 61	**15b**	**15c** 73
17	**16a**	**17c** 42	**16b**	**16c** 0

$RCH_2CH{=}CH_2$ **na**
RCH_2CHO **nb**

where R =

$PhCH_2$- **1**
$n\text{-}C_7H_{15}$- **2**



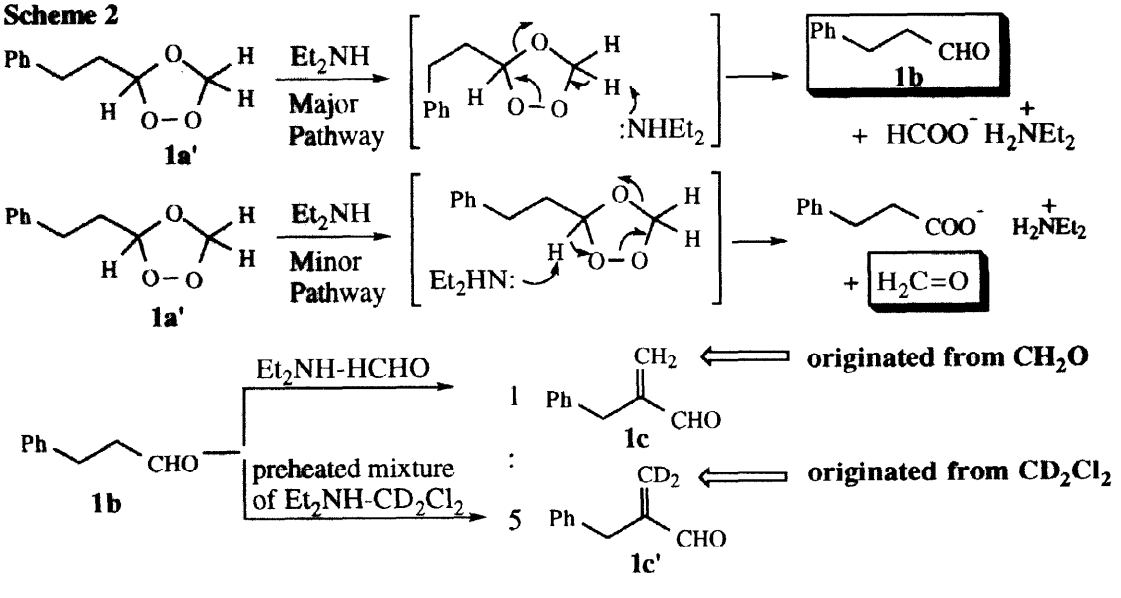
[a] **1c'** : **1c** = 5 : 1; [b] They were not tried; [c] The by-product **12d** was formed in 8% yield.

We have previously reported that aldehydes are formed in good yield from the reaction of monosubstituted ozonides with tertiary or secondary amines.[8] Therefore, 3-phenylpropionaldehyde should serve as an intermediate leading to 2-benzylacrolein (**1c**) in Eq. 3. It is interesting to compare the results of α-

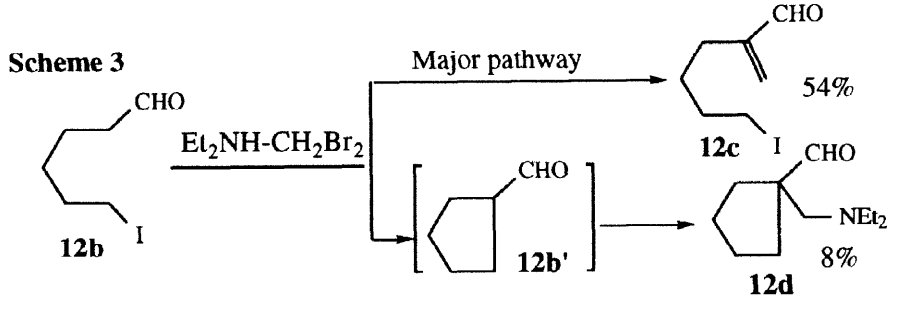
substituted-acrolein formation from olefin **na** *via* ozonide **na'** (pathway I) and from the corresponding aldehyde **nb** directly (pathway II) under similar conditions (Scheme I). The results were listed in Table 2. Most of the aldehydes utilized in pathway II have to be prepared either from the oxidation of the corresponding alcohols or from the ozonolysis of the corresponding terminal olefins.[8]

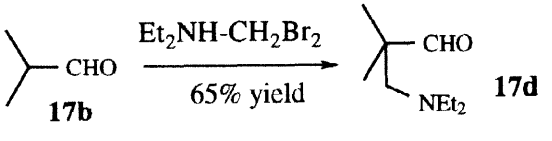
We tried to prepare the deuterium-labeled acrolein. The solution of Et_2NH-CD_2Cl_2 in acetonitrile was heated at 80 °C in the sealed tube for 24 h. The resulted solution reacted with aldehyde **1b** at room temperature to give β,β-dideuterated acrolein **1c'** in 71% yield (Entry 2, Table 2). Two deuteriums were labeled at β-carbon with 100% enrichment. However, under the same condition, both compounds **1c** and **1c'** were formed in 61% yields in a ratio of 1 : 5 *via* pathway I (Entry 2). The formation of compound **1c** was explained as follows. The deprotonation of the ozonide ring proton by Et_2NH from the less hindered side (minor pathway) gave formaldehyde, which might react with Et_2NH to obtain a reactive intermediate. This intermediate will react subsequently with aldehyde **1b** (generated from the major pathway) to give compound **1c** as a minor product (Scheme 2).

Scheme 2



Scheme 3





Eq. 4

Our reaction condition is so mild that many functional groups survived during the α-methylene group formation. The chemoselective formation of α-methylene aldehyde in the presence of a keto group is possible, and the protection of the keto groups is actually not necessary (Entries 4-7) Apparently, the keto functionality is quite unreactive to the preheated mixture of Et_2NH and CH_2Br_2. The α-methylenation is insensitive to the steric hindrance and it can be achieved at a position α to the quaterary carbon center in good yield (Entry 6). The reactions are also compatible to several functionalities such as hydroxy (Entry 8), acetoxy (Entries 9-11), bromo (Entry 12), iodo (Entries 13-14), and ester (Entry 15) groups . In the case of 6-iodohexanal (**12b**), not only the α-methylenation product **12c** was formed in 54% yield, but also Mannich base **12d** was isolated in 8% yield (Entry 13). The explanation of compound **12d** formation was shown in Scheme 3. Intramolecular alkylation occurred as a minor pathway to give cyclic aldehyde **12b'**, which further reacted with a preheated mixture of Et_2NH-CH_2Br_2 to give the Mannich base **12d**. Indeed, we also found that isobutyraldehyde (**17b**) reacted with a mixture of Et_2NH-CH_2Br_2 to give the Mannich base **17d** in modest yield (Eq. 4). The intramolecular cyclization didn't happen when 6-bromohexanal (**11b**) (Entry 12) or 9-iododecyl aldehyde (**13b**) (Entry 14) was used under the same condition. This method is also applicable to the preparation of the oxygen- and nitrogen-containing acroleins in modest yields (Entries 16 and 17). It is important to point out that we have diificulty to prepare aldehyde **16b** from compound **16a** *via* ozonolysis followed by reduction with Me_2S. Fortunately, compound **16c** can be prepared from pathway I in 42% yield (Entry 17).

The detailed mechanism of this transformation is still not clear. Mannich base should be formed first in our reaction, and the deamination of β-diethylaminoaldehydes to give α-substituted acroleins must be a facile process under our reaction conditions. The mechanism of this reaction remains to be studied.

CONCLUSION

In summary, the reactive intermediate generated from the reaction of diethylamine and dibromomethane is an effective ingredient to convert the monosubstituted ozonides or aldehydes to the α-substituted acroleins. It is a general, facile and economic method to carry out the α-methylenation of the aldehyde. A wide range of the functionalities were compatible to our reaction conditions. This newly developed reaction conditions represent an excellent example of using dihalomethane as an one carbon source in organic synthesis.

EXPERIMENTAL

All reactions were carried out under nitrogen. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Ozone was prepared with a Fisher ozone generator (Model 501). Melting points were determined by using a Yanaco micro melting point apparatus and were uncorrected. The ^1H and ^{13}C-NMR spectra were recorded on a Bruker AC 200 and ACP 300 spectrometer, and chemical shifts were given in ppm downfield from tetramethylsilane (TMS). IR spectra were taken with a Perkin Elmer 882 spectrophotometer and only noteworthy absorptions were listed. Mass spectra were measured on a VG 70-250S mass spectrometer by electronic impact at 70 eV (unless otherwise indicated).

General Procedure for the Ozonolysis of Terminal Alkenes: A two-necked flask fitted with a glass tube to admit ozone, a $CaCl_2$ drying tube and a magnetic stirring bar is charged with 0.1-0.2 M of terminal

alkene **na** (n = 1-16) in CH_2Cl_2. The flask is cooled to -78 °C and ozone is bubbled through the solution. When the solution turns blue, ozone addition is stopped. Nitrogen is passed through the solution until the blue color is discharged. The resulted solution was employed directly to the further reaction.

Reaction of Ozonide 1a' with $PhCH_2NHMe$, 4Å Molecular Sieves in Refluxing CH_2Cl_2: The solution of 4-phenyl-1-butene (**1a**) (227 mg, 1.7 mmol) in CH_2Cl_2 (9 mL) was subjected to the general ozonolysis procedure. To the resulted solution was added $PhCH_2NHMe$ (618 mg, 5.1 mmol), 4Å molecular sieves (2 g) and the reaction mixture was heated to reflux for 20 h. The reaction mixture was concentrated, and chromatographed on silica gel by elution with EtOAc/hexane to give compound **1c** (10 mg, 4% yield), **1d** (293 mg, 72% yield) and **1e** (12 mg, 3% yield).

Reaction of Ozonide 1a' with $PhCH_2NHMe$ in CH_2Br_2 at 65 °C: The solution of 4-phenyl-1-butene (**1a**) (372 mg, 2.8 mmol) in CH_2Cl_2 (14 mL) was subjected to the general ozonolysis procedure. The reaction was concentrated *in vacuo* to give the crude product **1a'** which was redissolved in a mixture of CH_2Br_2 (14 mL) and $PhCH_2NHMe$ (1018 mg, 8.4 mmol). After 24 h at 65 °C, the reaction mixture was concentrated, and chromatographed on silica gel by elution with EtOAc/hexane to give compound **1c** (290 mg, 71% yield), **1d** (13 mg, 2% yield), and **1e** (20 mg, 3% yield).

Reaction of Ozonide 1a' with Et_2NH in Refluxing CH_2Cl_2: The solution of 4-phenyl-1-butene (**1a**) (185 mg, 1.4 mmol) in CH_2Cl_2 (7 mL) was subjected to the general ozonolysis procedure. To the resulted solution was added Et_2NH (256 mg, 3.5 mmol, 2.5 mol equivalents) and the reaction mixture was heated to reflux for 24 h. The reaction mixture was concentrated, and chromatographed on silica gel by elution with EtOAc/hexane to give compound **1c** (127 mg, 62% yield). Note: When 2.5-10 mol equivalents of Et_2NH were used in this reaction, the yields of compound **1c** were 60-62%.

Reaction of Ozonide 1a' with Et_2NH in a Mixture of CH_2Br_2-CH_2Cl_2 at 55 °C: The solution of 4-phenyl-1-butene (**1a**) (180 mg, 1.4 mmol) in CH_2Cl_2 (7 mL) was subjected to the general ozonolysis procedure. To the resulted solution was added Et_2NH (249 mg, 3.5 mmol, 2.5 mol equiv.) and CH_2Br_2 (1 mL, 14 mmol) and the reaction mixture was heated to 55 °C for 16 h. The reaction mixture was concentrated, and chromatographed on silica gel by elution with EtOAc/hexane to give compound **1c** (122.2 mg, 62% yield).

General Procedure of Pathway I to Give α-Substituted Acroleins Starting from Alkenes : The standard procedure for the sequential ozonolysis of alkene and Et_2NH-CH_2Br_2 treatment is illustrated below with 4-phenyl-1-butene (**1a**). The solution of 4-phenyl-1-butene (**1a**) (529 mg, 4 mmol) in CH_2Cl_2 (8 mL) was subjected to the general ozonolysis procedure.

A mixture of Et_2NH (1.46 g, 2.1 mL, 20 mmol) and CH_2Br_2 (4.2 mL, 60 mmol) was heated to 55 °C for 1.5 h to give a yellow solution and then cooled to room temperature. To a solution of ozonide **1a'** in CH_2Cl_2 generated above was added a preheated mixture of Et_2NH-CH_2Br_2 at -78 °C. After the addition, the cooling bath was removed and the reaction mixture was stirred at room temperature. The reaction was completed in 1.5 h. The reaction mixture was concentrated, and chromatographed on silica gel by elution with EtOAc/hexane to give the desired product **1c** in 72% yield (421 mg).

General Procedure of Pathway II to Give α-Substituted Acroleins Starting from Aldehydes: The standard procedure for the reaction of aldehyde and Et_2NH-CH_2Br_2 is illustrated below with 3-phenylpropionaldehyde (**1b**). A mixture of Et_2NH (0.93 mL, 9 mmol) and CH_2Br_2 (3.2 mL, 45 mmol) was

heated to 55 °C for 1.5 h and then cooled to room temperature. To a solution of phenylpropionaldehyde (**1b**) (0.40 mL, 3 mmol) in 6 mL of CH_2Cl_2 was added the preheated mixture of Et_2NH-CH_2Br_2 at room temperature. The reaction was completed in 1.5 h. The reaction mixture was concentrated, and chromatographed on silica gel by elution with EtOAc/hexane to give the desired product **1c** (359 mg) in 82% yield.

2-Benzylprop-2-enal (1c): colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.55 (s, 2H, CH_2), 6.03 (s, 1H, $=CH_2$), 6.08 (s, 1H, $=CH_2$), 7.15-7.30 (m, 5H), 9.58 (s, 1H, CHO); ^{13}C NMR (50 MHz, $CDCl_3$) δ 34.06 ($-\underline{C}H_2$), 126.37 ($=\underline{C}H_2$), 128.47, 129.07, 135.20 ($\underline{C}$=CH2), 138.05, 149.64, 193.94 (CHO); IR (neat) (ν, cm^{-1}): 1684 (C=O, s), 1600 (m), 1429 (m), 1311 (m), 1073 (m), 949 (s); MS (32 eV, m/z): 146 (M^+, 75), 145 (M^+-1, 60), 117 (M^+-CHO, 98), 116 (100), 115 (93), 91 (75); HRMS (m/z): 146.0737 (M^+, $C_{10}H_{10}O$, Calcd 146.0731).

***N*-Benzyl-*N*-methyl-3-phenylpropylamine (1d):** Brown viscous liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.78-1.91 (m, 2H), 2.18 (s, 3H), 2.33 (t, J = 7.3 Hz, 2H), 2.56 (t, J = 7.7 Hz, 2H), 3.39 (s, 2H), 7.07-7.23 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 29.14, 33.54, 42.11, 56.83, 62.23, 125.64, 126.85, 128.15, 128.22, 128.39, 129.01, 139.15, 142.38; IR (neat) (ν, cm^{-1}): 2945 (w), 1605 (w), 1253 (m), 1114 (s), 1074 (s), 1024 (m); MS (32 eV, m/z): 239 (M^+, 10), 134 (100), 91 (92); HRMS (m/z): 239.1671 (M^+, $C_{17}H_{21}N$, Calcd 239.1674).

1-(*N*-Benzyl-*N*-methylamino)indan (1e): Brown viscous liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.16 (s, 3H, N-Me), 2.17-2.40 (m, 4H), 2.74 (d, J = 5.5 Hz, 1H), 3.49 (s, 2H, N-CH_2), 7.14-7.32 (m, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 36.41, 37.09, 42.64, 60.21, 62.59, 125.79, 127.13, 128.23, 128.35, 129.28, 129.66, 139.42, 140.89; IR (neat) (ν, cm^{-1}): 3029 (w), 2946 (m), 1599 (m), 1446 (m), 1247 (m), 1105 (s), 1073 (s); MS (32 eV, m/z): 239 (M^+, 12), 134 (M^+-CH_2Ph-CH_2, 100), 91 (89); HRMS (m/z): 239.1668 (M^+, $C_{17}H_{21}N$, Calcd 239.1674).

2-Benzyl-3,3-dideuteroprop-2-enal (1c'): A mixture of 3-phenylpropionaldehyde (**1b**) (242 mg, 1.8 mmol), Et_2NH (1.9 mL, 18 mmol), CD_2Cl_2 (mininium isotopic purity 99.9 atom % D, 2.3 mL, 36 mmol) and CH_3CN (5 mL) was heated to 80 °C for 24 h in a sealed tube. The reaction mixture was concentrated, and chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired product **1c'** (173 mg) in 63% yield as a colorless liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.55 (s, 2H, CH_2Ar), 7.15-7.34 (m, 5H), 9.59 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.01 (CH_2Ar), 126.38, 128.48, 129.08, 134.35 (quin, J = 24 Hz, $=CD_2$), 138.13, 149.59 (α-C), 193.83 (C=O); IR (neat) (ν, cm^{-1}): 1687 (s), 1253 (m), 1103 (s); MS (60 eV, m/z): 149 (M^++1, 10), 148 (M^+, 100), 147 (M^+-1, 70), 119 (71), 118 (70), 117 (90), 91 (32), 78 (28); HRMS (m/z): 148.0857 (M^+, $C_{10}H_8OD_2$, Calcd 148.0857).

2-*n*-Heptylprop-2-enal (2c): Colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, J = 6.7 Hz, 3H), 1.26-1.30 (m, 8H), 1.35-1.47 (m, 2H), 2.24 (t, J = 7.5 Hz, 2H), 5.98 (s, 1H, $=CH_2$), 6.24 (s, 1H, $=CH_2$), 9.54 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.84, 22.45, 27.64, 28.88, 29.11, 31.63, 133.37 ($=CH_2$), 150.43 ($-\underline{C}=CH_2$), 194.30 (C=O); IR (neat) (ν, cm^{-1}): 1686 (s), 1456 (m), 1103 (m), 945 (s); MS (29 eV, m/z): 154 (M^+, 8), 123 (30), 111 (32), 98 (53), 97 (100), 81 (28), 71 (68); HRMS (m/z): 154.1359 (M^+, $C_{10}H_{18}O$, Calcd 154.1358).

3-(1'-Hydroformyl-1'-ethenyl)cyclohexanone ethylene ketal (3c): 3-Allylcyclohexanone, prepared from the reaction of 2-cyclohexen-1-one, allyltrimethylsilane and titanium tetrachloride (*i.e.* Sakurai-Hosomi reaction),[9] was protected as a ethylene ketal (**3a**).[10] Compound (**3a**) was converted to compound (**3c**) according to standard protocol described above in 67% yield. Pale yellow liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.08-1.80 (m, 8H), 2.70-2.80 (m, 1H), 3.96 (br s, 4H), 5.99 (s, 1H), 6.23 (s, 1H), 9.52 (s, 1H, CHO); ^{13}C NMR (50 MHz, $CDCl_3$) δ 23.15, 30.49, 33.68, 34.60, 39.32, 64.05 (CH_2O), 64.17 (CH_2O), 108.64 (O-C-O), 132.79 (=CH_2), 153.81 (-C=CH_2), 194.05 (C=O); IR (neat) (ν, cm^{-1}): 1689 (s), 1225 (s), 1154 (m), 1085 (s), 1034 (m); MS (60 eV, m/z): 196 (M^+, 2), 167 (15), 153 (36), 99 (80), 86 (100); HRMS (m/z): 196.1096 (M^+, $C_{11}H_{16}O_3$, Calcd 196.1099).

3-(1'-Hydroformyl-1'-ethenyl)cyclohexanone (4c): Aldehyde **4b**, prepared from alkene **4a** according to our reported procedure,[8a, 8b] was converted to enal **4c** by standard protocol described above in 72% yield. Pale yellow liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.55-1.81 (m, 2H), 1.93-2.25 (2H), 2.25-2.91 (m, 4H), 2.91-3.05 (m, 1H), 6.12 (s, 1H, =CH_2), 6.61 (s, 1H, =CH_2), 9.54 (s, 1H, CHO); ^{13}C NMR (50 MHz, $CDCl_3$) δ 24.66, 29.60, 36.42, 40.92, 45.43, 133.84 (=CH_2), 151.93 (-C=CH_2), 193.61 (C=O), 210.08 (CHO); IR (neat) (ν, cm^{-1}): 1689 (s), 1419 (w), 1219 (w), 1099 (w); MS (29 eV, m/z): 152 (M^+, 3), 151 (M^+-1, 3), 112 (100), 97 (98), 84 (71), 69 (68); HRMS (m/z): 152.0835 (M^+, $C_9H_{12}O_2$, Calcd 152.0837).

5-Oxo-3,3-dimethylhexanal (5b): Compound **5a** was prepared by Sakurai-Hosomi reaction.[9] The solution of compound **5a** (364 mg, 2.6 mmol) in CH_2Cl_2 (13 mL) was subjected to the general ozonolysis procedure, followed by addition of Et_3N (0.71 mL, 5.2 mmol).[8a, 8b] The reaction was warmed slowly to room temperature. The reaction was completed in 1 h. The reaction mixture was concentrated under reduced pressure. The residue was chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired product **5b** (274 mg) in 74% yield as a pale yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (s, 6H), 2.10 (s, 3H), 2.54 (s, 4H), 9.86 (t, J = 1.3 Hz, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.95, 31.77, 32.53, 52.91, 53.52, 202.35 (C=O), 207.72 (C=O); IR (neat) (ν, cm^{-1}): 2949 (s), 1710 (s), 1365 (m), 1159 (m); MS (60 eV, m/z): 143 (M^++1, 6), 142 (M^+, 8), 127 (23), 114 (15), 99 (32), 85 (100); HRMS (m/z): 142.0959 (M^+, $C_8H_{14}O_2$, Calcd 142.0994).

5-Oxo-3,3-dimethyl-2-methylenehexanal (5c): Pale yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.23 (s, 6H), 2.02 (s, 3H), 2.94 (s, 2H), 6.01 (s, 1H, =CH_2), 6.39 (s, 1H, =CH_2), 9.51 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.58, 31.24, 35.56, 51.77, 135.17 (=CH_2), 155.70 (-C=CH_2), 195.02 (C=O), 207.40 (C=O); IR (neat) (ν, cm^{-1}): 2952 (s), 1698 (s), 1436 (m), 1354 (m), 1172 (m), 953 (m); MS (60 eV, m/z): 155 (M^++1, 6), 154 (M^+, 8), 139 (32), 126 (62), 111 (100), 97 (88), 69 (58); HRMS (m/z): 154.0988 (M^+, $C_9H_{14}O_2$, Calcd 154.0994).

6-Methyl-5-oxo-1-heptene (6a): Compound **6a** was prepared as a colorless liquid according to the literature.[11] ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.06 (d, J = 7.2 Hz, 6H), 1.81-2.09 (hept, J = 7.2 Hz, 1H), 2.29 (q, J = 7.4 Hz, 2H), 2.52 (t, J = 7.4 Hz, 2H), 4.92-5.05 (m, 2H, =CH_2), 5.72-5.83 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.15, 27.75, 39.39, 40.82, 115.04 (=CH_2), 137.35, 213.75 (C=O); IR (neat) (ν, cm^{-1}): 1710 (s), 1637 (w), 1461 (m), 1372 (m), 1250 (m), 1096 (m), 914 (m); MS (60 eV, m/z): 127 (M^++1, 37),

126 (M^+, 3), 98 (70), 91 (40), 83 (100), 69 (63), 62 (50); HRMS (m/z): 126.1081 (M^+, $C_8H_{14}O$, Calcd 126.1045).

5-Methyl-4-oxohexanal (6b): Compound **6a** was converted to aldehyde **6b** as a colorless oil in 78% yield according to our reported procedure.[8a, 8b] ^1H NMR (300 MHz, $CDCl_3$) δ 1.12 (d, J = 7.1 Hz, 6H, CH_3), 2.66 (hept, J = 7.1 Hz, 1H), 2.77-2.80 (m, 4H), 9.80 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.18, 32.30, 37.42, 40.72, 200.47 (C=O), 212.35 (C=O); IR (neat) (ν, cm^{-1}): 2952 (m), 1709 (s), 1378 (m), 1089 (m), 1018 (m); MS (60 eV, m/z): 129 (M^++1, 5), 128 (M^+, 3), 100 (38), 85 (100), 71 (23), 62 (15); HRMS (m/z): 128.0837 (M^+, $C_7H_{12}O_2$, Calcd 128.0837).

5-Methyl-2-methylene-4-oxohexanal (6c): Pale yellow liquid; ^1H NMR (200 MHz, $CDCl_3$) δ 1.14 (d, J =6.9 Hz, 6H, CH_3), 2.72 (hept, J = 6.9 Hz, 1H), 3.41 (s, 2H), 6.23 (s, 1H, =CH_2), 6.37 (s, 1H, =CH_2), 9.53 (s, 1H, CHO); ^{13}C NMR (50 MHz, $CDCl_3$) δ 18.16, 39.19, 41.14, 136.86 (=CH_2), 143.52 (-C=CH_2), 193.30 (C=O), 210.18 (C=O); IR (neat) (ν, cm^{-1}): 2928 (s), 1697 (s), 1450 (w), 1243 (m), 1043 (m).

2-(8'-Hydroxyoctyl)prop-2-enal (7c): Pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26-1.58 (m, 12H), 1.75-1.85 (br, 1H, -OH), 2.23 (t, J = 7.4 Hz, 2H), 3.62 (t, J = 6.6 Hz, 2H, -CH_2OH), 5.99 (s, 1H, =CH_2), 6.24 (s, 1H, =CH_2), 9.53 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.61, 27.65, 29.09, 29.20, 32.64, 62.80, 133.86 (=CH_2), 150.35 (-C=CH_2), 194.74 (C=O); IR (neat) (ν, cm^{-1}): 3050-3650 (br), 2934 (s), 2855 (s), 1685 (s), 1460 (m), 1349 (m), 1052 (m), 950 (m); MS (60 eV, m/z): 184 (M^+, 6), 183 (M^+-1, 2), 154 (10), 137 (12), 123 (18), 111 (23), 97 (41), 81 (45), 67 (54), 55 (100), 41 (80); HRMS (m/z): 184.1456 (M^+, $C_{11}H_{20}O_2$, Calcd 184.1463).

6-Acetoxy-4,4-dimethyl-1-heptene (8a): Sodium borohydride (93.2 mg, 2.5 mmol) was added to a stirred solution of ketone **5a** (230 mg, 1.6 mmol) in 8 mL of ethanol. Stirring is continued for 2 h at RT. The reaction mixture was concentrated, followed by the addition of 10 mL of saturated solution of ammonium chloride. The mixture was extracted three times with 15 mL of ether. The combined organic phase were washed with brine and dried over Na_2SO_4. The solvent was evaporated and the residue was chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired alcohol (198 mg, 1.4 mmol) in 72% yield. The alcohol (198 mg, 1.4 mmol), acetic anhydride (185 mg, 1.8 mmol), pyridine (143 mg, 1.8 mmol) and a catalytic amount of *N,N*-dimethylaminopyridine (10 mg) were dissolved in 10 mL of CH_2Cl_2 and stirred at RT for 12 h. The reaction mixture was evaporated *in vacuo* and the residue was chromatographed on a silica gel column by elution with EtOAc/hexane to give the acetate **8a** as a colorless liquid in 86% yield (120 mg, 1.2 mmol). ^1H NMR (200 MHz, $CDCl_3$) δ 0.92 (s, 3H), 0.93 (s, 3H), 1.24 (d, J = 6.2 Hz, 3H), 1.28 (dd, J = 14.9 and 2.8 Hz, 1H), 1.68 (dd, J = 14.9 and 8.7 Hz, 1H), 2.00 (d, J = 7.3 Hz, 2H), 2.05 (s, 3H, OAc), 4.98-5.16 (m, 3H), 5.75-5.96 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.46, 22.15, 27.14, 32.83, 47.03, 47.13, 69.44, 117.10, 135.20, 170.51 (C=O); IR (neat) (ν, cm^{-1}): 1734 (s), 1367 (m), 1242 (s); MS (60 eV, m/z): 184 (M^+, 2), 183 (4), 163 (20), 149 (21), 149 (23), 136 (22), 123 (33), 109 (32), 95 (33), 83 (100), 73 (42); HRMS (m/z): 183.1414 (M^+-1, $C_{11}H_{19}O_2$, Calcd 183.1385).

5-Acetoxy-3,3-dimethylhexanal (8b): Compound **8a** was converted to aldehyde **8b** as a colorless oil in 72% yield according to our reported procedure.[8a, 8b] Colorless liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 1.07 (s, 3H), 1.08 (s, 3H), 1.23 (d, J = 16.1 Hz, 3H), 1.46 (dd, J = 15.0 and 2.4 Hz, 1H), 1.84 (dd, J = 14.9 and 9.0 Hz, 1H), 2.01 (s, 3H, OAc), 2.28 (qd, J = 15.3 and 2.7 Hz, 2H), 5.03-5.13 (m, 1H), 9.83 (t, J = 2.7 Hz,

1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.42, 22.01, 27.78, 28.15, 32.84, 47.52, 54.73, 68.11, 170.49 (C=O), 202.74 (HC=O); IR (neat) (ν, cm^{-1}): 2967 (s), 1725 (s), 1457 (m), 1372 (s), 1245 (s), 1128 (m), 1050 (m), 1023 (m); MS (60 eV, m/z): 187 (M^++1, 1), 186 (M^+, 1), 126 (32), 111 (41), 83 (100), 69 (35); HRMS (m/z): 187.1287 (M^++1, $C_{10}H_{19}O_3$, Calcd 187.1334).

5-Acetoxy-3,3-dimethyl-2-methylenehexanal (8c): Pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 1.17 (d, *J* = 6.5 Hz, 3H, CH_3), 1.22 (s, 3H), 1.24 (s, 3H), 1.74 (dd, *J* = 14.7 and 2.4 Hz, 1H), 1.93 (s, 3H, OAc), 2.31 (dd, *J* = 14.7 and 9.6 Hz, 1H), 4.85-4.91 (m, 1H, CHOAc), 5.98 (s, 1H, $=CH_2$), 6.27 (s, 1H, $=CH_2$), 9.58 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.17, 21.59, 27.15, 28.02, 36.23, 44.96, 68.50, 133.92 ($=CH_2$), 156.23 ($-C=CH_2$), 170.31 (C=O), 194.50 (C=O); IR (neat) (ν, cm^{-1}): 1730 (s), 1693 (s), 1611 (w), 1449 (m), 1369 (s), 1243 (s), 1128 (m), 1043 (m); MS (60 eV, m/z): 199 (M^++1, 3), 198 (M^+, 3), 154 (30), 138 (18), 123 (100), 109 (30), 95 (53), 83 (39), 67 (59); HRMS (m/z): 199.1330 (M^++1, $C_{11}H_{19}O_3$, Calcd 199.1334).

6-Acetoxy-4-methylhexanal (9b): Citronellyl acetate **9a** was converted to aldehyde **9b** as a colorless oil in 90% yield according to our reported procedure.[8a, 8b] ^1H NMR (300 MHz, $CDCl_3$) δ 0.93 (d, *J* = 6.3 Hz, 3H), 1.46-1.72 (m, 5H), 2.03 (s, 3H, CH_3C=O), 2.43-2.49 (m, 2H), 4.05-4.15 (m, 2H), 9.77 (t, *J* = 1.9 Hz, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.85, 20.61, 28.46, 29.23, 34.98, 41.14, 62.25 (CH_2O), 170.67 (C=O) , 201.89 (C=O); IR (neat) (ν, cm^{-1}): 1729 (s), 1453 (m), 1366 (m), 1236 (s), 1038 (m); MS (60 eV, m/z): 172 (M^+, 1), 171 (M^+-1, 2), 129 (12), 112 (18), 78 (53), 69 (100), 61 (75); HRMS (m/z): 171.1070 (M^+-1, $C_9H_{15}O_3$, Calcd 171.1021).

6-Acetoxy-4-methyl-2-methylenehexanal (9c): Pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (d, *J* = 6.6 Hz, 3H), 1.40-1.47 (m, 1H), 1.64-1.81 (m, 2H), 2.04 (s, 3H, OAc), 2.10 (dd, *J* = 13.6 and 7.8 Hz, 1H), 2.30 (dd, *J* = 13.6 and 6.1 Hz, 1H), 4.04-4.15 (m, 2H), 6.08 (s, 1H, $=CH_2$), 6.27 (s, 1H, $=CH_2$), 9.54 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.04, 20.76, 28.58, 35.03, 35.11, 62.44 (CH_2O), 135.26 ($=CH_2$), 148.45 ($-C=CH_2$), 170.87 (C=O), 194.35 (C=O); IR (neat) (ν, cm^{-1}): 1732 (s), 1682 (s), 1453 (m), 1366 (m), 1236 (s), 1045 (m); MS (60 eV, m/z): 185 (M^++1, 2), 184 (M^+, 1), 142 (43), 124 (M^+-HOAc, 39), 115 (37), 109 (100), 81 (97); HRMS (m/z): 185.1163 (M^++1, $C_{10}H_{17}O_3$, Calcd 185.1178).

10-Acetoxy-2-methylenedecanal (10c): Pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 1.31-1.65 (m, 12H), 2.04 (s, 3H, -OAc), 2.23 (t, *J* = 7.2 Hz, 2H), 4.05 (t, *J* = 6.8 Hz, 2H, $-CH_2OAc$), 5.98 (s, 1H, $=CH_2$), 6.24 (s, 1H, $=CH_2$), 9.54 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.92, 25.80, 27.69, 28.53, 29.07, 29.13, 64.53, 133.78 ($=CH_2$), 150.40 ($-C=CH_2$), 171.12 (OAc), 194.66 (C=O); IR (neat) (ν, cm^{-1}): 2934 (s), 2857 (s), 1737 (s), 1689 (s), 1460 (m), 1363 (m), 1238 (s), 1034 (m), 947 (m); MS (60 eV, m/z): 226 (M^+, 6), 209 (3), 184 (20), 166 (10), 137 (11), 123 (16), 112 (23), 91 (33), 81 (39), 67 (44), 55 (63), 43 (100); HRMS (m/z): 226.1562 (M^+, $C_{13}H_{22}O_3$, Calcd 226.1569).

6-Bromohexanal (11b): 6-Bromohexanol (2.0 g, 11.0 mmol) and pyridinium chlorochromate (PCC) (3.57 g, 16.6 mmol) are stirred for 3 h at 0 °C in 25 mL of dichloromethane. The reaction mixture was concentrated *in vacuo* and diluted with ethyl ether (20 mL). The solution was filtered through Celite and the oxidation reagent was washed three times with 20 mL of ether. The combined filtrates were evaporated and the residue was chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired aldehyde **11b** as a

pale yellow liquid in 79% yield (1.56 g). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.44-1.54 (m, 2H), 1.61-1.72 (m, 2H), 1.80-1.93 (m, 2H), 2.48 (td, J = 7.3 and 1.3 Hz, 2H, α-CH_2), 3.42 (t, J = 6.6 Hz, 2H, CH_2Br), 9.77 (t, J = 1.3 Hz, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.91, 27.38, 32.19, 33.31, 43.37, 202.05 (C=O); IR (neat) (ν, cm^{-1}): 1714 (s), 1457 (m), 1388 (m), 1264 (m); MS (60 eV, m/z): 181 (M^++1, 5), 180 (M^+, 3, when Br = 81), 179 (M^++1, 5), 178 (M^+, 3, when Br = 79), 164 (3), 162 (3), 152 (18), 150 (18), 115 (18), 99 (48), 81 (100); HRMS (m/z): 179.0051 (M^++1, $C_6H_{12}BrO$, Calcd 179.0072 when the exact mass of bromine is 78.9183).

6-Bromo-2-methylenehexanal (11c): Pale yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.65 (quin, J = 6.3 Hz, 2H), 1.88 (quin, J = 7.0 Hz, 2H), 2.28 (t, J = 7.3 Hz, 2H), 3.41 (t, J = 6.7 Hz, 2H), 6.03 (s, 1H, =CH_2), 6.28 (s, 1H, =CH_2), 9.54 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.25, 26.83, 32.18, 33.21, 134.14 (=CH_2), 149.58 (-C=CH_2), 194.35 (C=O); IR (neat) (ν, cm^{-1}): 1730 (s), 1434 (m), 1253 (m); MS (60 eV, m/z): 192 (M^+, 3, when Br = 81), 191 (M^+-1, 3), 190 (M^+, 3, when Br = 79), 189 (M^+-1, 3), 111 (100), 93 (4), 67 (61); HRMS (m/z): 189.999 (M^+, $C_7H_{11}BrO$, Calcd 189.9993 when the exact mass of Br is 78.9183).

6-Iodohexanol (12a'): A mixture of 6-bromohexanol (1.5 g, 8.3 mmol) and KI (20.6 g, 124.3 mmol) in 90 mL of acetone was heated up to reflux for 40 h. The precipitate was collected by filtration and washed with 20 mL of acetone. The combined filtrates were evaporated and the residue was chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired 6-iodohexanol (**12a'**) as a pale yellow liquid (1.61 g) in 85% yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40-1.68 (m, 7H), 1.79-1.88 (m, 2H), 3.19 (t, J = 6.9 Hz, 2H, CH_2I), 3.64 (t, J = 6.2 Hz, 2H, CH_2O); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.89, 24.68, 30.21, 32.44, 33.39, 62.69; IR (neat) (ν, cm^{-1}): 3000-3600 (s), 1452 (m), 1423 (m), 1197 (m), 1050 (m); MS (60 eV, m/z): 229 (M^++1, 1), 155 (10), 101 (41), 83 (100); HRMS (m/z): 229.0089 (M^++1, $C_6H_{14}IO$, Calcd 229.0089).

6-Iodohexanal (12b): 6-Iodohexanol was oxidized by PCC to give compound **12b** in 73 % yield according to the procedure described in the preparation of compound **11b**. This compound will turn pink at room temperature slowly. ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.42-1.49 (m, 2H), 1.59-1.71 (m, 2H), 1.80-1.90 (m, 2H), 2.45 (td, J = 6.9 and 1.3 Hz, 2H, α-CH_2), 3.19 (t, J = 6.7 Hz, 2H, CH_2I), 9.78 (t, J = 1.3 Hz, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.24, 20.95, 29.95, 33.13, 43.59 (CH_2I), 202.04 (C=O); IR (neat) (ν, cm^{-1}): 1721 (s), 1453 (m), 1425 (m), 1354 (m), 1206 (s), 1167 (s), 1121 (s); MS (60 eV, m/z): 225 (M^+-1, 2), 127 (8, I^+), 99 (40, M^+-I), 81 (100); HRMS (m/z): 224.9770 (M^+-1, $C_6H_{10}IO$, Calcd 224.9776).

6-Iodo-2-methylenehexanal (12c): Colorless liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55-1.63 (m, 2H), 1.80-1.89 (m, 2H), 2.27 (t, J = 7.4 Hz, 2H), 3.20 (t, J = 6.7 Hz, 2H, CH_2I), 6.04 (s, 1H, =CH_2), 6.29 (s, 1H, =CH_2), 9.55 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.33, 26.67, 28.59, 32.94, 134.36 (=CH_2), 149.57 (-C=CH_2), 194.54 (C=O); IR (neat) (ν, cm^{-1}): 2933 (s), 1688 (s), 1435 (m), 1212 (m); MS (60 eV, m/z): 239 (M^++1, 3), 155 (10), 127 (8), 111 (100), 93 (43), 77 (19), 67 (68); HRMS (m/z): 238.9923 (M^++1, $C_7H_{12}IO$, Calcd 238.9933).

1-*N*,*N*-Diethylaminomethylcyclopentanecarboxaldehyde (12d): Compound **12d** was formed as the minor product during the preparaion of compound **12c**. Pale yellow liquid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, J = 7.3 Hz, 6H), 1.41-2.03 (m, 8H), 2.47 (q, J = 7.3 Hz, 4H), 2.69 (s, 2H), 9.55 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.44, 24.90, 31.73, 47.52, 59.35, 59.46, 205.19 (C=O); IR (neat) (ν, cm^{-1}):

2962 (s), 1719 (s), 1450 (m), 1374 (m), 1291 (w), 1200 (m); MS (60 eV, m/z): 183 (M^+, 1), 182 (3), 168 (12), 86 (100); HRMS (m/z): 182.1539 (M^+-1, $C_{10}H_{20}NO$, Calcd 182.1545).

2-(8'-Iodooctyl)prop-2-enal (13c): 11-Iodoundec-1-ene (**13a**)[12] was was converted to enal **13c** as a pale yellow liquid by standard protocol described above in 68% yield. ^1H NMR (300 MHz, $CDCl_3$) δ 1.28-1.50 (m, 10H), 1.81 (quin, J = 7.1 Hz, 2H), 2.24 (t, J = 7.4 Hz, 2H), 3.18 (t, J = 6.9 Hz, 2H, $-CH_2I$), 5.99 (s, 1H, $=CH_2$), 6.25 (s, 1H, $=CH_2$), 9.54 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 7.23, 27.67, 28.37, 29.10, 30.40, 33.46, 133.94 ($=CH_2$), 150.34 ($-\underline{C}=CH_2$), 194.74 (C=O); IR (neat) (ν, cm^{-1}): 2930 (s), 2855 (s), 1688 (s), 1624 (w), 1456 (m), 1348 (m), 1223 (m), 1177 (m), 942 (m); MS (60 eV, m/z): 294 (M^+, 6), 263 (3), 217 (3), 167 (18), 149 (44), 123 (51), 107 (28), 93 (40), 81 (50), 67 (48), 55 (100), 41 (95); HRMS (m/z): 294.0479 (M^+, $C_{11}H_{19}OI$, Calcd 294.0481).

2-Allyl-γ-butyrolactone (14a): Compound **14a** was prepared according to the literature procedure.[13] Colorless liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 1.96-2.04 (m, 1H), 2.26-2.41 (m, 2H), 2.57-2.68 (m, 2H), 4.16-4.36 (m, 2H, CH_2O), 5.09-5.17 (m, 2H, $=CH_2$), 5.75-5.84 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.56, 34.08, 38.58, 66.32 (CH_2O), 117.37, 134.24, 178.57 (C=O); IR (neat) (ν, cm^{-1}): 1765 (s), 1736 (w), 1441 (m), 1373 (m), 1165 (s), 1018 (s), 919 (s); MS (60 eV, m/z): 127 (M^++1, 8), 126 (M^+, 6), 97 (20), 82 (39), 67 (100); HRMS (m/z): 127.0752 (M^++1, $C_7H_{11}O_2$, Calcd 127.0759).

2-(2'-Oxoethyl)-γ-butyrolactone (14b): 2-Allyl-γ-butyrolactone (**14a**) was converted to aldehyde **14b** as a colorless oil in 71% yield according to our reported procedure.[8] Colorless liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 1.89-2.03 (m, 1H), 2.45-2.60 (m, 1H), 2.71 (dd, J = 18.3 and 8.1 Hz, 1H, CH_2-CHO), 2.96-3.12 (m, 2H), 4.20-4.29 (m, 1H), 4.29-4.44 (m, 1H), 9.81 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.56, 33.66, 43.99, 66.64, 178.28 (O-C=O), 198.83 (CHO); IR (neat) (ν, cm^{-1}): 1758 (s), 1718 (s), 1377 (s), 1209 (s), 1161 (s), 1021 (s); MS (60 eV, m/z): (M^++1, 10), 112 (30), 95 (74), 81 (28), 67 (100); HRMS (m/z): 141.0522 (M^++1, $C_7H_9O_3$, Calcd 141.0552).

2-(1'-Formyl-1'-ethenyl)-γ-butyrolactone (14c): Pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 2.16-2.27 (m, 1H), 2.52-2.61 (m, 1H), 3.61 (t, J = 9.9 Hz, 1H, HC-CO_2-), 4.26-4.35 (m, 1H, CH_2O), 4.42-4.49 (m, 1H, CH_2O), 6.30 (s, 1H, $=CH_2$), 6.53 (s, 1H, $=CH_2$), 9.56 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.02, 39.75, 66.63, 136.72 ($=CH_2$), 145.71 ($-\underline{C}=CH_2$), 176.10 (O-C=O), 192.51 (C=O); IR (neat) (ν, cm^{-1}): 1765 (s, O-C=O), 1678 (s, CHO), 1628 (m), 1477 (w), 1450 (w), 1371 (s), 1322 (s), 1265 (s), 1214 (s), 1019 (s), 969 (s); MS (60 eV, m/z): 141 (M^++1, 8), 140 (M^+, 3), 112 (31), 95 (75), 81 (28), 67 (100); HRMS (m/z): 141.0522 (M^++1, $C_7H_9O_3$, Calcd 141.0552).

2-Bezyloxyprop-2-enal (15c): Pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 4.90 (s, 2H, OCH_2), 5.12 (d, J = 3.0 Hz, 1H), 5.22 (d, J = 3.0 Hz, 1H), 7.24-7.36 (m, 5H), 9.29 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 70.09 (OCH_2), 103.49 ($=CH_2$), 127.31, 128.10 ($-\underline{C}=CH_2$), 128.52, 135.54, 158.12, 187.88 (C=O); IR (neat) (ν, cm^{-1}): 3061 (m), 3034 (m), 1702 (s), 1609 (s), 1306 (s), 1043 (s), 858 (s); MS (28 eV, m/z): 162 (M^+, 2), 144 (1), 133 (6), 120 (8), 91 (100), 65 (10); HRMS (m/z): 162.0685 (M^+, $C_{10}H_{10}O_2$, Calcd 162.0681).

2-(*N*-Benzoylamino)prop-2-enal (16c): Colorless liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 5.68 (s, 1H, $=CH_2$), 7.32 (s, 1H, $=CH_2$), 7.46-7.59 (m, 3H), 7.87 (d, J = 7.8 Hz, 2H), 8.46 (br s, 1H, NH), 9.25 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 118.10 ($=CH_2$), 127.02, 128.80, 132.27, 133.74, 139.78, 165.65 (N-

C=O), 189.05 (HC=O); MS (56 eV, m/z): 175 (M^+, 28), 105 (100), 77 (68); HRMS (m/z): 175.0628 (M^+, $C_{10}H_9NO_2$, Calcd 175.0633).

3-*N,N*-Diethylamino-2,2-dimethylpropanal (17d): A mixture of Et_2NH (1.56g, 8.9 mmol) and CH_2Br_2 (2.2 g, 30 mmol) was heated to 55 °C for 1.5 h to give a yellow solution and then cooled to room temperature. To a solution of isobutyraldehyde (216 mg, 3 mmol) in 5 mL of CH_2Cl_2 was added a preheated mixture of Et_2NH-CH_2Br_2 generated above at RT. The reaction was completed in 5 min. The reaction mixture was concentrated, and chromatographed on a silica gel column by elution with EtOAc/hexane to give the desired product **17d** (307 mg) in 65% yield as a pale yellow liquid; ^1H NMR (300 MHz, $CDCl_3$) δ 0.85 (br t, J = 6.4 Hz, 6H), 0.95 (br s, 6H), 2.30-2.45 (m, 6H), 9.45 (s, 1H, CHO); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.72, 20.27, 47.48 (β-C), 48.27, 61.47, 206.64 (C=O); IR (neat) (ν, cm^{-1}): 1730 (s), 1434 (m), 1253 (m); MS (60 eV, m/z): 158 (M^++1, 2), 157 (M^+, 2), 129 (18), 93 (35), 86 (73), 62 (100); HRMS (m/z): 158.1568 (M^++1, $C_9H_{20}NO$, Calcd 158.1545).

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