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A general route to α-alkyl (*E*)-α,β-unsaturated aldehydes

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Abstract

Bis(trimethylsilyl)-*tert*-butylaldimines **3** react with aldehydes in the presence of zinc bromide at room temperature to give, after hydrolysis, the desired α-alkyl α,β-ethylenic aldehydes in good yield and with very high *E* stereoselectivity. The reaction was believed to proceed via the α-silyl β-siloxyimines **4**.

Keywords: α,α-Bis(trimethylsilyl)-*tert*-butylaldimines; α,β-Unsaturated aldehydes; Zinc bromide

1. Introduction

The direct conversion of an aldehyde into a conjugated enal by two-carbon unit introduction is a very attractive reaction since unsaturated aldehydes are useful intermediates in organic synthesis. Among the numerous methods that have been developed for this purpose, α,α-bis(trimethylsilyl)-*tert*-butylacetaldimine **1** is now the reagent of choice for this homologation because of its ease of preparation, clean product obtained and the very high *E* selectivity of the ethylenic aldehyde prepared (Scheme 1).

The preparation, reactivity and synthetic applications of **1** have been reported [1] and this organosilicon reagent is now commercially available. We had just examined at the end of our previous article, the behavior of the α,α-bis(trimethylsilyl)-*tert*-butylpropionaldimine **3a** (Scheme 2).

In this paper, we report an account of our investigations concerning the extension of our methodology to various disilylated aldimines and show that α-alkyl unsaturated aldehydes can be easily prepared using this route.

2. Results and discussion

2.1. Preparation of α,α-disilylated aldimines *3*

Various α,α-bis(trimethylsilyl)-*tert*-butylaldimine **3** (R = methyl, ethyl, *n*-propyl, *n*-butyl, *n*-pentyl) were prepared in one-pot from the corresponding aldimines, lithium diisopropylamide (LDA) and chlorotrimethylsilane (Scheme 3). However, a two-step preparation of **3**, with isolation the monosilylated aldimine **2**, turned out to be less advantageous.

2.2. Reaction of the disilylated propionaldimine *3a* with benzaldehyde

Our goal is to study the reaction of **3** with a large panel of aldehydes to prepare the corresponding α,β-unsaturated α-alkyl aldehydes. A methodological study has been carried out to obtain the best yield and the high *E* stereoselectivity. Thus, we first examined the condensation of α,α-bis(trimethylsilyl)-*tert*-butylpropionaldimine **3a** (R = Me) with benzaldehyde in the presence of several catalysts to determine the best reaction conditions (Table 1).

2.2.1. Lewis acid catalyst

As shown in Table 1, several Lewis acids were investigated (entries 1–8). First (entry 1) benzaldehyde was treated

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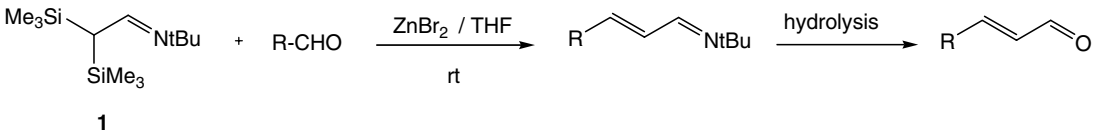
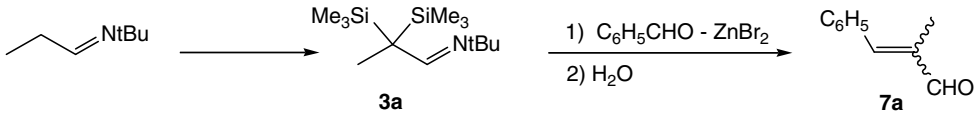
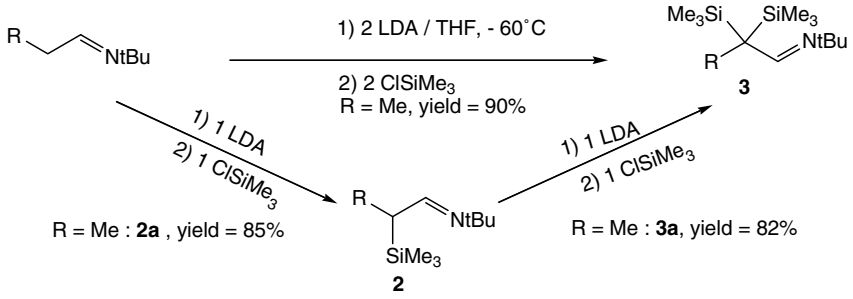


Scheme 1.



Scheme 2.

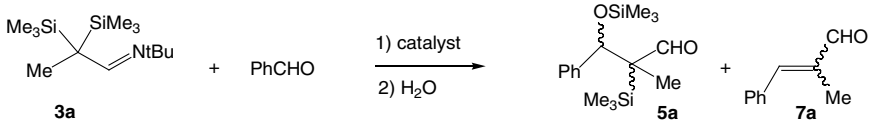


Scheme 3.

with **3a** in the presence of one equivalent of zinc bromide in THF at room temperature for 5 h; after hydrolysis, the reaction affords only the corresponding enal **7a** in almost quantitative yield with very high *E* stereoselectivity.

The intermediate **5a** seems to eliminate hexamethyldisiloxane less easily when the same reaction is achieved with catalytic amount of zinc bromide (entry 3) or at lower temperature (entry 2). However, this elimination could be

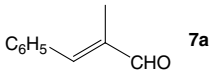
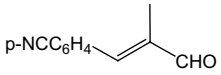
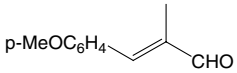
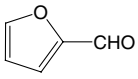
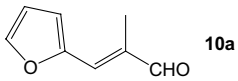
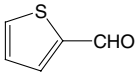
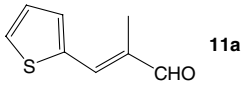
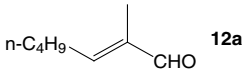
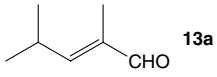
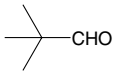
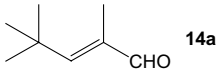
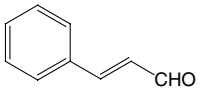
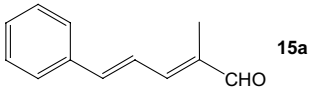
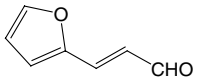
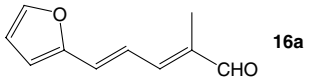
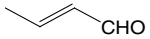
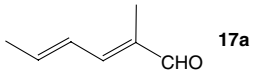
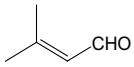
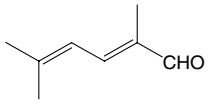
Table 1
Reaction of α,α-(bistrimethylsilyl)-*N*-*tert*-butylpropionaldimine **3a** with benzaldehyde in the presence of various catalysts



Entry	Catalyst	Solvent	Reactions conditions	Yield (%)[a] **5a**	Yield (%)[a] **7a**	**7a** *E*/*Z*[b]
1	1 eq. $ZnBr_2$	THF	5 h at r.t.	0	95	100/0
2	1 eq. $ZnBr_2$	THF	7 h at 0 °C	34	48	74/26
3	10% $ZnBr_2$	THF	24 h at r.t.	73	9	92/8
4	10% $ZnBr_2$	Toluene	24 h at r.t.	80	15	96/4
5	1 eq. $ZnBr_2$	Toluene	24 h at r.t.	75	19	98/2
6	10% HgI_2	Toluene	8 h at r.t.	95	0	–
7	1 eq. $TiCl_4$	CH_2Cl_2	5 h at −60 °C	0	42	21/79
8	1 eq. $TiCl_4$	CH_2Cl_2	1 h at −60 °C, 4 h at r.t.	0	85	51/49
9	10% TBAF	THF	8 h at r.t.	64	26	67/33
10	1 eq. TBAF	THF	8 h at r.t.	0	93	55/45
11	10% CsF	THF	24 h at r.t.	0	16	32/68
12	1 eq. CsF	THF	24 h at r.t.	0	17	33/67
13	10% CsF	DMSO	5 h at r.t.	0	73	83/17
14	1 eq. CsF	DMSO	5 h at r.t.	0	88	42/58
15	10% NaF	THF	24 h at r.t.	24	6	63/37
16	1 eq. NaF	THF	24 h at r.t.	24	6	64/36

[a] Estimated by ^{1}H NMR on the crude reaction mixture with respect to nonreacted benzaldehyde (molar percentage).
[b] The stereoselectivity of the compound **7a** is determined by the ^{1}H NMR spectrum of the crude product.

Table 2
Synthesis of α-methyl α,β-unsaturated aldehydes using reagent **3a**

Entry	Starting aldehydes	Time (h)	Obtained aldehydes	Yield (%)[a]	*E*/*Z*[b]	Reference
1	C_6H_5CHO	5	 **7a**	95	100/0	[3]
2	*p*-CNC_6H_4CHO	7	 **8a**	89	100/0	[4]
3	*p*-$MeOC_6H_4CHO$	5.5	 **9a**	80	100/0	[4]
4		8	 **10a**	92	96/4	[5]
5		7	 **11a**	93	96/4	[6]
6	$CH_3(CH_2)_3CHO$	6	 **12a**	96	100/0	[7]
7		24	 **13a**	93	100/0	[8]
8		24	 **14a**	93	100/0	[9]
9		5	 **15a**	81	89/11	[10]
10		5.5	 **16a**	89	86/14	[11]
12		7	 **17a**	85	83/17	[12]
13		6	 **18a**	96	90/10	[13]

[a] Isolated yield.
[b] The stereoselectivity of each compound is determined by the ^1H NMR spectrum of the crude product.

suppressed completely using mercuric iodide in toluene (entry 6).

One particular aspect of the reaction carried out with titanium tetrachloride (entries 7 and 8) is the poor influence of the temperature on the nature of the obtained adduct. Indeed, at −60 °C or at room temperature, α-methylcinnamaldehyde **7a**, the single reaction product, was obtained.

2.2.2. Fluoride ion catalyst

We have found that fluoride ion was also efficient as catalyst for reaction of **3a** with benzaldehyde. Some of the results are reported in Table 1. It is obvious from the results obtained that the reaction works faster and gives better yields when tetrabutylammonium fluoride is used (entry 10). However, with cesium fluoride, DMSO is necessary to obtain good yield of the expected enal **7a** (entries 13 and 14).

From the reported examples of various catalysts that promoted reaction of **3a** with benzaldehyde, zinc bromide (one equivalent) in THF can be considered as the most active catalyst for the preparation of (*E*)-unsaturated aldehydes.

2.3. Stereoselective synthesis of α-methyl (*E*)-α,β-unsaturated aldehydes

The reaction of **3a** has been performed on structurally different aldehydes. α-Methyl unsaturated aldehydes obtained are listed in Table 2. As can be seen from the data, the reaction was effective for a large class of aldehydes. Aromatic and heteroaromatic aldehydes were tested and gave the corresponding α-methyl enals in high yield and with excellent *E* stereoselectivity (entries 1–5). The reaction was also very efficient with saturated aldehydes

(entries 6–8). Homologation of α,β-ethylenic aldehydes was achieved efficiently; indeed, conjugated unsaturated aldehydes resulting from 1,2-addition were exclusively formed in good yields (entries 9–12).

2.4. Extension to other α,α-disilylated aldimines

We next investigated the scope and limitations of this new method leading to α-alkyl α,β-unsaturated aldehydes. For this, the reaction has been performed with four α,α-disilylated aldimines **3** (R = ethyl, *n*-propyl, *n*-butyl, *n*-pentyl) on various aldehydes. The results are summarized in Table 3. In all cases, the expected α-alkylenals were obtained in good yield and with excellent *E* stereoselectivity.

2.5. Reaction mechanism and stereochemistry

A tentative reaction mechanism and explanation of the *E* stereoselectivity were postulated. For this, our investigations were focused on the reaction of **3a** with benzaldehyde.

When the reaction was carried out in the presence of catalytic amounts of mercuric iodide at room temperature, only the sensitive intermediates **4a** (*anti* + *syn*) were isolated in 95% overall yield (Scheme 4). The diastereoselectivity of the reaction, as shown by ^{1}H NMR (δ_{H_a} = 4.77 and 4.61 ppm), is in the range 82/18.

The major problem concerned with the stereochemistry of the intermediates **4a**: which is *syn* and which is *anti*? Since suitable crystals were not obtained for rigorous assignments by X-ray spectroscopy, we sought another approach to determine the configuration of these diastereoisomers.

The mixture of diastereoisomers (*syn* + *anti*) **4a** previously obtained was treated with 1 equivalent of $ZnBr_2$ in THF at room temperature (Scheme 4). The unsaturated imines **6a** (*E* + *Z*) were formed. Their *E*/*Z* ratio (80/20) corresponds to the ratio (82/18) of the starting silylimines **4a**. Since elimination of hexamethyldisiloxane is highly regulated to the *anti* manner in acidic medium [2], the major diastereoisomer is assigned to the *anti* **4a** and the minor isomer to the *syn* **4a**. Quenching the ethylenic imines **6a** (*E*/*Z* = 80/20) with water affords the enals **7a** (*E*/*Z* = 80/20).

Interestingly, addition of zinc bromide (1 eq.) in THF at room temperature to another preformed intermediates **4a** (*anti*/*syn* = 40/60), followed by quenching the reaction with water, leads to the formation (*E*) and (*Z*) **7a** in the ratio *E*/*Z* = 40/60. From these results, we can assume that geometrical ratio of unsaturated aldehydes **7a** reflects the diastereochemical ratio of the intermediates **4a**.

Moreover, we can reasonably speculate that *anti* **4a** was the only intermediate when the reaction was carried out with benzaldehyde in the presence of one equivalent of $ZnBr_2$ in THF at room temperature (Scheme 5).

In the presence of the other catalysts, the stereochemical outcome of this aldolisation–olefination reaction seems to be intriguing.

3. Conclusion

Our results demonstrate clearly the practical utility of these disilylated aldimines as excellent reagents for direct synthesis of α-alkyl (*E*)-unsaturated aldehydes.

4. Experimental

4.1. General information

All reactions involving water-sensitive compounds are carried out in oven-dried glassware and under nitrogen atmosphere. Unless otherwise noted, starting materials were purchased from commercial sources and used as received. All the solvents are dried and distilled prior to use.

LDA was prepared in situ from diisopropylamine and *n*-butyl lithium (1.6 M solution in hexane). Zinc bromide was prepared by heating ground zinc and 1,2-dibromoethane in THF for 16 h at reflux [1]. The starting imines were prepared from the corresponding aldehydes and *tert*-butylamine in pentane [24]. ^{1}H and ^{13}C NMR spectra were recorded at 250 or 300 MHz using $CDCl_3$ as solvent. Chemical shifts are given in ppm (*J* in Hz) relative to chloroform. Flash chromatography was done on Merck grade 60 silica gel (230–400 mesh) using mixtures of hexane and ethyl acetate as eluent. Melting points were uncorrected.

4.2. Preparation of α,α-bis(trimethylsilyl)-tert-butylaldimines 3

4.2.1. General procedure

To a cooled (−60 °C) solution of LDA (100 mmol) in anhydrous THF (50 mL) was added a solution of N-*tert*-butylaldimine (50 mmol) in THF (5 mL). The resulting mixture was stirred at −60 °C for 18 h. Trimethylchlorosilane was added in two portions: the first portion (50 mmol) was added at −60 °C and the solution was stirred for 5 h at this temperature, then the second portion (50 mmol) was added. After being stirred at the same temperature for 1 h, the solution was gradually warmed to room temperature and filtered through a pad of celite. The solvent was removed under reduced pressure and distillation of the remaining oil gave the disilylated aldimines **3**.

4.2.2. α,α-Bis(trimethylsilyl)-tert-butylpropionaldimine (3a)

b.p.: 110 °C/15 mm Hg; yield = 82%.

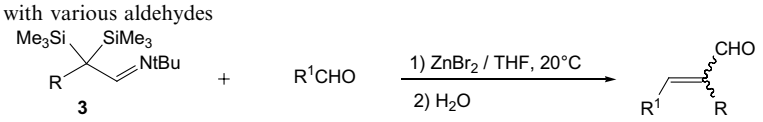
^{1}H NMR (250 MHz, $CDCl_3$) δ 0.05 (s, 18H), 1.13 (s, 9H), 1.21 (s, 3H), 7.74 (s, 1H). Anal. Calc. for $C_{13}H_{31}NSi_2$: C, 60.75; H, 12.16. Found: C, 60.71; H, 12.10%.

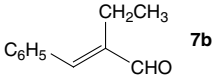
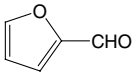
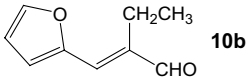
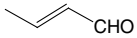
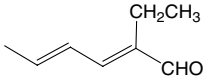
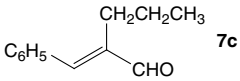
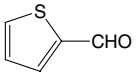
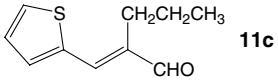
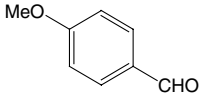
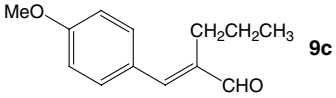
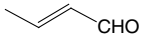
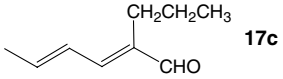
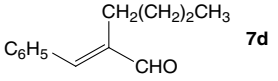
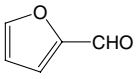
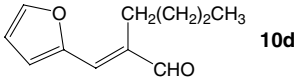
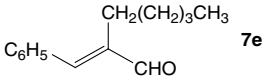
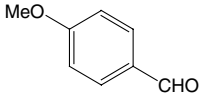
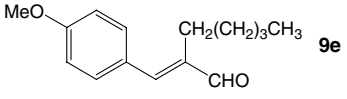
4.2.3. α,α-Bis(trimethylsilyl)-tert-butylbutyraldimine (3b)

b.p.: 118 °C/15 mm Hg; yield = 74%.

^{1}H NMR (250 MHz, $CDCl_3$) δ 0.01 (s, 18H), 0.92 (t, 3H, *J* = 7.4 Hz), 1.07 (s, 9H), 1.78 (q, 2H, *J* = 7.4 Hz), 7.53 (s, 1H). Anal. Calc. for $C_{14}H_{33}NSi_2$: C, 61.91; H, 12.25. Found: C,61.72 ; H, 12.15%.

Table 3
Reaction of numerous reagents **3** with various aldehydes



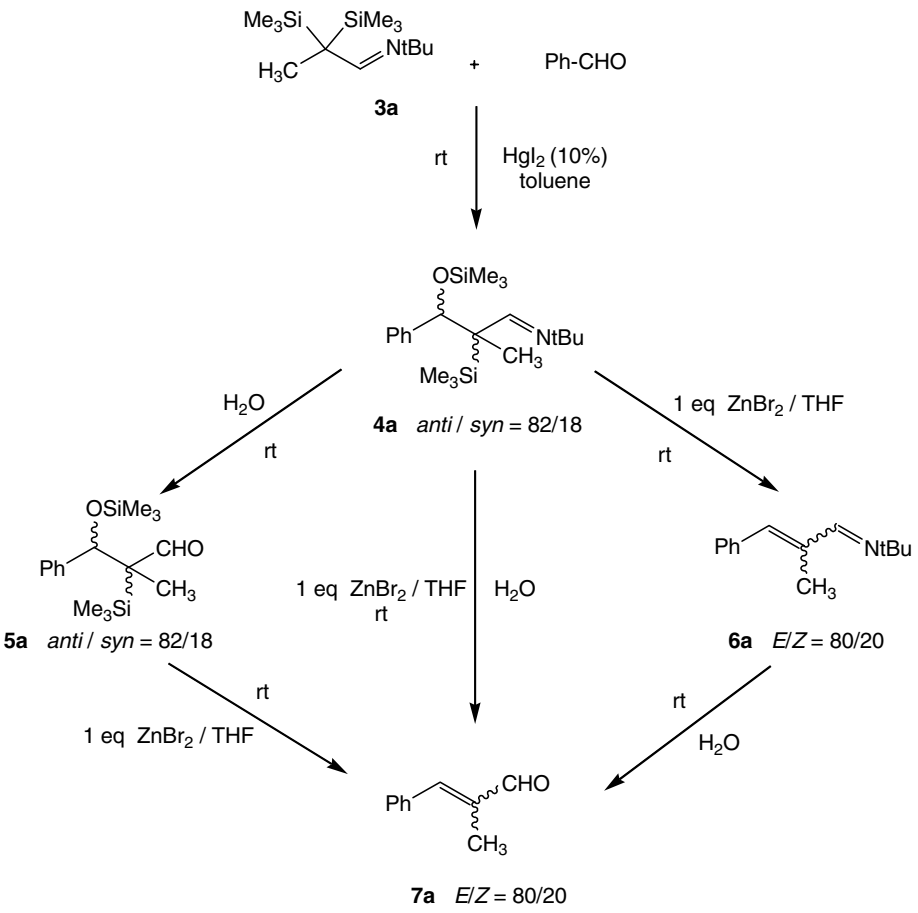
Entry	R^1CHO	R	Time (h)	Obtained aldehydes	Yield (%)[a]	E/Z[b]	Reference
1	C_6H_5CHO	Ethyl	24	 **7b**	86	95/5	[14]
2		Ethyl	14	 **10b**	75	91/9	[15]
3		Ethyl	12	 **17b**	89	72/28	[16]
4	C_6H_5CHO	*n*-Propyl	14	 **7c**	70	93/7	[17]
5		*n*-Propyl	24	 **11c**	51	100/0	[18]
6		*n*-Propyl	24	 **9c**	76	100/0	[17]
7		*n*-Propyl	24	 **17c**	89	77/23	[19]
8	C_6H_5CHO	*n*-Butyl	14	 **7d**	97	91/9	[20]
9		*n*-Butyl	14	 **10d**	90	95/5	[21]
10	C_6H_5CHO	*n*-Pentyl	14	 **7e**	48	88/12	[22]
11		*n*-Pentyl	24	 **9e**	68	100/0	[23]

[a] Isolated yield.
[b] The stereoselectivity of each compound is determined by the ^1H NMR spectrum of the crude product.

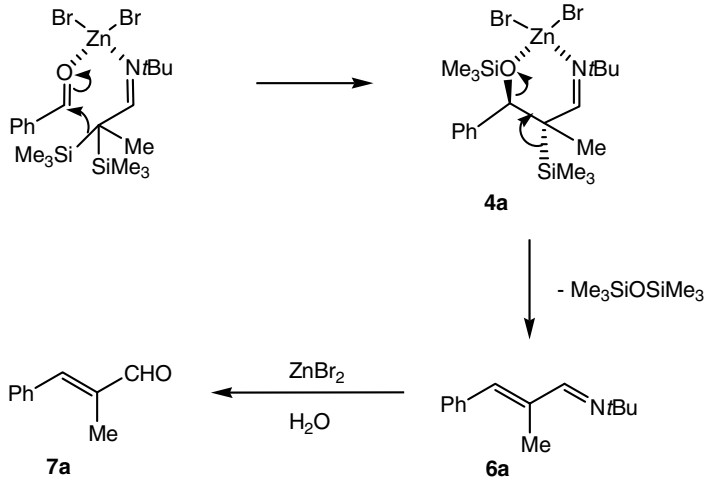
*4.2.4. α,α-Bis(trimethylsilyl)-tert-butylpentaldimine (**3c**)*
b.p.: 124 °C/15 mm Hg; yield = 74%.
^1H NMR (250 MHz, $CDCl_3$) δ 0.08 (s, 18H), 0.93 (t, 3H, $J = 7.1$ Hz), 1.15 (s, 9H), 1.55 (m, 2H), 1.73 (t, 2H, $J = 7.4$ Hz), 7.60 (s, 1H). Anal. Calc. for $C_{15}H_{35}NSi_2$: C, 63.08; H, 12.35. Found: C, 63.18; H, 12.25%.

*4.2.5. α,α-Bis(trimethylsilyl)-tert-butylhexanaldimine (**3d**)*
b.p.: 136 °C/15 mm Hg; yield = 80%.
^1H NMR (250 MHz, $CDCl_3$) δ 0.08 (s, 18H), 0.93 (t, 3H, $J = 6.9$ Hz), 1.16 (s, 9H), 1.33 (m, 4H), 1.76 (t, 2H, $J = 7.9$ Hz), 7.68 (s, 1H). Anal. Calc. for $C_{16}H_{37}NSi_2$: C, 64.13; H, 12.45. Found: C, 64.23; H, 12.15%.

*4.2.6. α,α-Bis(trimethylsilyl)-tert-butylheptanaldimine (**3e**)*
b.p.: 146 °C/15 mm Hg; yield = 79%.
^1H NMR (250 MHz, $CDCl_3$) δ 0.10 (s, 18H), 0.92 (t, 3H, $J = 7.0$ Hz), 1.16 (s, 9H), 1.31 (m, 6H), 1.78 (t, 2H,



Scheme 4.



Scheme 5.

$J = 7.2$ Hz), 7.69 (s, 1H). Anal. Calc. for $C_{17}H_{39}NSi_2$: C, 65.09; H, 12.53. Found: C, 65.29; H, 12.13%.

4.3. Preparation of α-alkyl α,β-unsaturated aldehydes

4.3.1. General procedure

A detailed procedure for reaction of **3** with aldehydes in the presence of one equivalent of zinc bromide is given below. All the reactions are conducted in a similar manner. Reaction times and yields are reported in Tables 2 and 3. Physical, spectral and analytical data for the obtained unsaturated aldehydes follow.

To a solution of the corresponding aldehyde (10 mmol) and zinc bromide (10 mmol) in THF (10 mL), was added a solution of **3** (10 mmol) in THF (5 mL) dropwise at room temperature. The reaction is checked using TLC until

disappearance of the starting aldehyde. The resulting red solution is then quenched with water (20 mL) and stirred for 1 h at room temperature. The precipitate is filtered through a pad of celite. The aqueous layer is extracted with ether (3×20 mL) and the organic layers are dried over $MgSO_4$. The solvent is removed under reduced pressure and the crude product is purified by flash chromatography to give the unsaturated aldehydes.

*4.3.2. (E)-α-Methylcinnamaldehyde (**7a**)*

Column flash chromatography was done using hexane/ethyl acetate (95/5) as eluent. Oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06 (s, 3H, CH_3), 7.24 (s, 1H, H-3), 7.37–7.61 (m, 5H, ArH), 9.57 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 10.7, 128.5, 129.5, 129.8, 134.9, 138.1, 149.6, 195.3.

IR ($CDCl_3$) 1676 cm^{-1} (C=O), 1624 cm^{-1} (C=C). Anal. Calc. for $C_{10}H_{10}O$: C, 82.16; H, 6.89. Found: C, 82.36; H, 6.69%.

*4.3.3. (E)-4-(2-Methyl-3-oxopropenyl)benzonitrile (**8a**)*

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent. m.p.: 100 °C (Lit 4: 113–114 °C).

^{1}H NMR (250 MHz, $CDCl_3$) δ 2.00 (s, 3H, CH_3), 7.24 (s, 1H, H-3), 7.56; 7.68 (A_2B_2, 4H, $J = 8.4$ Hz, $J = 8.4$ Hz, ArH), 9.57 (s, 1H, H-1); ^{13}C NMR (62.9 MHz, $CDCl_3$) 10.8, 110.7, 116.4, 128.6, 130.2, 137.5, 138.8, 144.8, 192.9.

IR ($CDCl_3$) 1681 cm^{-1} (C=O), 1615 cm^{-1} (C=C). Anal. Calc. for $C_{11}H_9NO$: C, 77.17; H, 5.30. Found: C, 77.37; H, 5.52%.

*4.3.4. (E)-4-Methoxy-α-methylcinnamaldehyde (**9a**)*

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent. Oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 2.07 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 6.97; 7.52 (A_2B_2, 4H, $J = 8.8$ Hz, $J = 8.8$ Hz, ArH), 7.19 (s, 1H, H-3), 9.53 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 10.9, 55.5, 114.2, 127.9, 132.1, 136.1, 149.8, 160.2, 195.5.

IR ($CDCl_3$) 1674 cm^{-1} (C=O), 1605 cm^{-1} (C=C). Anal. Calc. for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.64; H, 6.35%.

*4.3.5. (E)-3-Furan-2-yl-2-methylpropenal (**10a**)*

Column flash chromatography was done using hexane/ethyl acetate (95/5) as eluent. Oil.

^{1}H NMR (250 MHz, $CDCl_3$) δ 2.03 (s, 3H, CH_3), 6.57 (dd, 1H, $J = 3.3$ Hz, $J = 3.4$ Hz, ArH-2), 6.78 (d, 1H, $J = 3.3$ Hz, ArH-1), 6.03 (s, 1H, H-3), 7.62 (d, 1H, $J = 3.4$ Hz, ArH-3), 9.49 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 10.4, 112.5, 116.4, 134.8, 135.3, 145.2, 151.5, 194.0.

IR ($CDCl_3$) 1679 cm^{-1} (C=O), 1623 cm^{-1} (C=C). Anal. Calc. for $C_8H_8O_2$: C, 70.57; H, 5.92. Found: C, 70.17; H, 5.82%.

*4.3.6. (E)-2-Methyl-3-thiophen-2-propenal (**11a**)*

Column flash chromatography was done using hexane/ethyl acetate (95/5) as eluent. m.p.: 31–33 °C (Lit 6: 27–30 °C).

^{1}H NMR (250 MHz, $CDCl_3$) δ 2.09 (s, 3H, CH_3), 7.18 (dd, 1H, $J = 3.7$ Hz, $J = 5.1$ Hz, ArH-2), 7.22 (d, 1H, $J = 3.7$ Hz, ArH-1), 7.28 (s, 1H, H-3), 7.39 (d, 1H, $J = 5.1$ Hz, ArH-3), 9.52 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 10.6, 127.7, 131.0, 132.6, 135.0, 138.7, 141.8, 194.1.

IR ($CDCl_3$) 1680 cm^{-1} (C=O), 1616 cm^{-1} (C=C). Anal. Calc. for C_8H_8OS: C, 63.13; H, 5.30. Found: C, 61.91; H, 5.19%.

*4.3.7. (E)-2-Methyl-hept-2-enal (**12a**)*

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent. Oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (t, 1H, $J = 7.2$ Hz, CH_3), 1.42 (m, 4H, $2CH_2$), 1.74 (s, 3H, CH_3), 2.37 (td, 2H, $J = 7.1$ Hz, $J = 7.4$ Hz, CH_2=), 6.50 (t, 1H, $J = 7.4$ Hz, H-3), 9.44 (s, 1H, H-1); ^{13}C NMR (62.9 MHz, $CDCl_3$) 13.1, 17.6, 21.6, 28.3, 32.8, 135.2, 148.1, 193.7.

IR ($CDCl_3$) 1681 cm^{-1} (C=O), 1625 cm^{-1} (C=C). Anal. Calc. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.34; H, 11.21%.

*4.3.8. (E)-2,4-Dimethylpent-2-enal (**13a**)*

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent.Oil.

^{1}H NMR (250 MHz, $CDCl_3$) δ 1.46 (d, 6H, $J = 7.2$ Hz, $2CH_3$), 1.77 (s, 3H, CH_3), 2.86 (m, 1H, H-4), 6.30 (d, 1H, $J = 8.4$ Hz, H-3), 9.39 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 9.6, 22.1, 29.0, 138.3, 161.7, 195.8.

IR ($CDCl_3$) 1700 cm^{-1} (C=O), 1640 cm^{-1} (C=C). Anal. Calc. for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 74.55; H, 10.58%.

*4.3.9. (E)-2,4,4-Trimethylpent-2,4-dienal (**14a**)*

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent. Oil.

^{1}H NMR (250 MHz, $CDCl_3$) δ 1.19 (s, 9H, $3CH_3$), 1.81 (s, 3H, CH_3), 6.23 (s, 1H, H-3), 9.33 (s, 1H, H-1); ^{13}C NMR (62.9 MHz, $CDCl_3$) 7.8, 26.1, 27.8, 135.4, 162.9, 194.8.

IR ($CDCl_3$) 1705 cm^{-1} (C=O), 1650 cm^{-1} (C=C). Anal. Calc. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.54; H, 11.38%.

*4.3.10. (E,E)-2-Methyl-5-phenylpenta-2,4-dienal (**15a**)*

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent. m.p.: 59–60 °C (Lit 10: 60–61 °C).

^{1}H NMR (250 MHz, $CDCl_3$) δ 1.95 (s, 3H, CH_3), 6.99 (d, 1H, $J = 15.7$ Hz, H-5), 7.25 (dd, 1H, $J = 10.6$ Hz, $J = 15.7$ Hz, H-4), 7.33–7.40 (m, 5H, ArH), 7.52 (d, 1H, $J = 10.6$ Hz, H-3), 9.50 (s, 1H, H-1); ^{13}C NMR (75 MHz,

$CDCl_3$) 10.5, 125.6, 128.0, 130.4, 132.2, 136.1, 138.7, 142.1, 149.5, 195.0.

IR ($CDCl_3$) 1670 cm^{-1} (C=O), 1618 cm^{-1} (C=C). Anal. Calc. for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 83.56; H, 7.11%.

4.3.11. (E,E)-5-Furan-2-yl-2-methylpenta-2,4-dienal (**16a**)

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent. m.p.: 52 °C (Lit 11: 50 °C).

^1H NMR (250 MHz, $CDCl_3$) δ 1.92 (s, 3H, CH_3), 6.46 (d, 1H, $J = 4.7$ Hz, ArH-1), 6.51 (dd, 1H, $J = 11.7$ Hz, $J = 15.0$ Hz, H-4), 6.74 (d, 1H, $J = 15.0$ Hz, H-5), 6.93 (d, 1H, $J = 11.7$ Hz, H-3), 7.00 (dd, 1H, $J = 3.6$ Hz, $J = 4.7$ Hz, ArH-2), 7.09 (d, 1H, $J = 3.6$ Hz, ArH-3), 9.47 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 9.6, 112.3, 112.8, 121.8, 127.2, 137.8, 145.3, 150.6, 152.3, 194.4.

IR ($CDCl_3$) 1740 cm^{-1} (C=O), 1650 cm^{-1} (C=C). Anal. Calc. for $C_{10}H_{10}O_2$: C, 74.06; H, 6.21. Found: C, 74.1; H, 6.02%.

4.3.12. (E,E)-2-Methylhexa-2,4-dienal (**17a**)

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent. Oil.

^1H NMR (250 MHz, $CDCl_3$) δ 1.85 (s, 3H, CH_3), 1.96 (d, 3H, $J = 7.8$ Hz, CH_3), 6.28 (m, 1H, H-5), 6.56 (dd, 1H, $J = 11.0$ Hz, $J = 16.4$ Hz, H-4), 6.84 (d, 1H, $J = 11.0$ Hz, H-3), 9.44 (s, 1H, H-1); ^{13}C NMR (62.9 MHz, $CDCl_3$) 14.2, 25.9, 126.8, 134.8, 139.3, 148.1, 194.1.

IR ($CDCl_3$) 1677 cm^{-1} (C=O), 1637 cm^{-1} (C=C). Anal. Calc. for $C_7H_{10}O$: C, 76.33; H, 9.15. Found: C, 76.03; H, 9.01%.

4.3.13. (E)-2,5-Dimethylhexa-2,4-dienal (**18a**)

Column flash chromatography was done using hexane/ethyl acetate (90/10) as eluent. Oil.

^1H NMR (250 MHz, $CDCl_3$) δ 1.81 (s, 3H, CH_3), 1.95 (s, 6H, $2CH_3$), 6.26 (d, 1H, $J = 11.8$ Hz, H-4), 7.07 (d, 1H, $J = 11.8$ Hz, H-3), 9.47 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 7.3, 17.1, 25.2, 119.3, 133.4, 143.2, 145.8, 193.3.

IR ($CDCl_3$) 1680 cm^{-1} (C=O), 1638 cm^{-1} (C=C). Anal. Calc. for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.18; H, 9.24%.

4.3.14. (E)-α-Ethylcinnamaldehyde (**7b**)

Column flash chromatography was done using hexane/ether (23/1) as eluent. Oil.

^1H NMR (300 MHz, $CDCl_3$) δ 1.14 (t, 3H, $J = 7.7$ Hz, CH_3), 2.56 (q, 2H, $J = 7.7$ Hz, CH_2), 7.20 (s, 1H, H-3), 7.39–7.52 (m, 5H, ArH), 9.54 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 12.8, 18.0, 128.3, 128.8, 129.6, 134.9, 144.4, 149.5, 195.5.

IR ($CDCl_3$) 1679 cm^{-1} (C=O), 1626 cm^{-1} (C=C). Anal. Calc. for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.16; H, 7.35%.

4.3.15. (E)-3-Furan-2-yl-2-ethylpropenal (**10b**)

Column flash chromatography was done using hexane/ether (25/1) as eluent. Oil.

^1H NMR (300 MHz, $CDCl_3$) δ 1.07 (t, 3H, $J = 7.3$ Hz, CH_3), 2.64 (q, 2H, $J = 7.3$ Hz, CH_2), 6.56 (dd, 1H, $J = 3.3$ Hz, $J = 3.7$ Hz, ArH-2), 6.77 (d, 1H, $J = 3.7$ Hz, ArH-1), 6.93 (s, 1H, H-3), 7.62 (d, 1H, $J = 3.3$ Hz, ArH-3), 9.45 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 12.7, 18.1, 112.6, 116.5, 134.8, 141.1, 145.4, 151.2, 194.1.

IR ($CDCl_3$) 1676 cm^{-1} (C=O), 1632 cm^{-1} (C=C). Anal. Calc. for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.68; H, 6.31%.

4.3.16. (E,E)-2-Ethylhexa-2,4-dienal (**17b**)

Column flash chromatography was done using hexane/ether (23/1) as eluent. Oil.

^1H NMR (300 MHz, $CDCl_3$) δ 0.99 (t, 3H, $J = 7.7$ Hz, CH_3), 1.94 (d, 3H, $J = 6.9$ Hz, CH_3), 2.34 (q, 2H, $J = 7.7$ Hz, CH_2), 6.27 (m, 1H, H-5), 6.55 (dd, 1H, $J = 11.4$ Hz, $J = 16.2$ Hz, H-4), 6.77 (d, 1H, $J = 11.4$ Hz, H-3), 9.38 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 13.7, 17.3, 19.1, 127.0, 140.7, 141.8, 149.0, 194.9.

IR ($CDCl_3$) 1677 cm^{-1} (C=O), 1637 cm^{-1} (C=C). Anal. Calc. for $C_8H_{12}O$: C, 77.38; H, 9.74. Found: C, 77.08; H, 9.14%.

4.3.17. (E)-α-Propylcinnamaldehyde (**7c**)

Column flash chromatography was done using hexane/ether (23/1) as eluent. Oil.

^1H NMR (300 MHz, $CDCl_3$) δ 0.98 (t, 3H, $J = 7.3$ Hz, CH_3), 1.51 (m, 2H, $CH_2\beta$), 2.51 (t, 2H, $J = 8.1$ Hz, $CH_2\alpha$), 7.21 (s, 1H, H-3), 7.38–7.51 (m, 5H, ArH), 9.54 (s, 1 H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 14.2, 21.5, 26.6, 128.7, 129.4, 129.5, 134.9, 143.1, 149.8, 195.6.

IR ($CDCl_3$) 1677 cm^{-1} (C=O), 1623 cm^{-1} (C=C). Anal. Calc. for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.12; H, 8.01%.

4.3.18. (E)-4-Methoxy-α-propylcinnamaldehyde (**9c**)

Column flash chromatography was done using hexane/ether (23/10) as eluent. Oil.

^1H NMR (300 MHz, $CDCl_3$) δ 0.99 (t, 3H, $J = 7.3$ Hz, CH_3), 1.52 (m, 2H, $CH_2\beta$), 2.52 (t, 2H, $J = 8.0$ Hz, $CH_2\alpha$), 3.84 (s, 3H, OCH_3), 7.11 (s, 1H, H-3), 6.96 ; 7.48 (A_2B_2, 4H, $J = 8.8$ Hz, $J = 8.8$ Hz, ArH), 9.48 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 14.3, 21.4, 26.6, 55.3, 114.0, 127.6, 131.8, 140.9, 150.0, 160.8, 195.7.

IR ($CDCl_3$) 1673 cm^{-1} (C=O), 1602 cm^{-1} (C=C). Anal. Calc. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.02; H, 7.70%.

4.3.19. (E)-2-Propyl-3-thiophen-2-propenal (**11c**)

Column flash chromatography was done using hexane/ether (21/1) as eluent. Oil.

^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, 3H, $J = 7.3$ Hz, CH_3), 1.49 (m, 2H, $CH_2\beta$), 2.58 (t, 2H, $J = 8.1$ Hz, $CH_2\alpha$), 7.15 (dd, 1H, $J = 5.1$ Hz, $J = 5.1$ Hz, ArH-2),

7.36 (m, 2H, ArH-3, H-3), 7.58 (d, 1H, $J = 5.1$ Hz, ArH-1), 9.48 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 14.3, 21.1, 26.9, 127.6, 131.0, 133.2, 139.7, 141.9, 143.5, 194.5.

IR ($CDCl_3$) 1673 cm^{-1} (C=O), 1614 cm^{-1} (C=C). Anal. Calc. for $C_{10}H_{12}OS$: C, 66.63; H, 6.71; S, 17.79. Found: C, 66.16; H, 6.51%.

*4.3.20. (E,E)-α-Propylhexa-2,4-dienal (**17c**)*

Column flash chromatography was done using hexane/ether (25/10) as eluent. Oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.91 (t, 3H, $J = 7.5$ Hz, CH_3), 1.41 (m, 2H, $CH_2\beta$), 1.93 (d, 3H, $J = 6.6$ Hz, CH_3), 2.30 (t, 2H, $J = 7.7$ Hz, $CH_2\alpha$), 6.27 (m, 1H, H-5), 6.52 (dd, 1H, $J = 11.0$ Hz, $J = 11.4$ Hz, H-4), 6.80 (d, 1H, $J = 11.0$ Hz, H-3), 9.37 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 14.0, 19.1, 22.3, 25.8, 127.3, 140.3, 140.7, 149.7, 195.1.

IR ($CDCl_3$) 1673 cm^{-1} (C=O), 1636 cm^{-1} (C=C). Anal. Calc. for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.62; H, 10.41%.

*4.3.21. (E)-α-Butylcinnamaldehyde (**7d**)*

Column flash chromatography was done using hexane/ether (27/1) as eluent. Oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (t, 3H, $J = 7.0$ Hz, CH_3), 1.33–1.50 (m, 4H, $CH_2\beta$, $CH_2\gamma$), 2.53 (t, 2H, $J = 7.0$ Hz, $CH_2\alpha$), 7.18 (s, 1H, H-3), 7.35–7.50 (m, 5H, ArH), 9.53 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 13.8, 23.0, 24.5, 30.0, 128.2, 128.7, 128.9, 129.5, 129.6, 134.9, 143.3, 149.7, 195.6.

IR ($CDCl_3$) 1678 cm^{-1} (C=O), 1623 cm^{-1} (C=C). Anal. Calc. for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.62; H, 8.41%.

*4.3.22. (E)-3-Furan-2-yl-2-butyl-propenal (**10d**)*

Column flash chromatography was done using hexane/ether (28/1) as eluent. Oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93 (t, 3H, $J = 7.3$ Hz, CH_3), 1.41 (m, 4H, $CH_2\beta$, $H_2\gamma$), 2.63 (t, 2H, $J = 7.3$ Hz, $CH_2\alpha$), 6.56 (dd, 1H, $J = 3.3$ Hz, $J = 3.3$ Hz, ArH-2), 6.77 (d, 1H, $J = 3.3$ Hz, ArH-1), 6.94 (s, 1H, H-3), 7.61 (d, 1H, $J = 3.3$ Hz, ArH-3), 9.46 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 14.1, 22.9, 24.5, 30.4, 112.6, 116.5, 135.2, 139.8, 145.3, 151.3, 194.4.

IR ($CDCl_3$) 1675 cm^{-1} (C=O), 1625 cm^{-1} (C=C). Anal. Calc. for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.01; H, 7.52%.

*4.3.23. (E)-α-Amylcinnamaldehyde (**7e**)*

Column flash chromatography was done using hexane/ether (25/10) as eluent. Oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3H, $J = 7.3$ Hz, CH_3), 1.32–1.38 (m, 4H, $CH_2\gamma$, $CH_2\delta$), 1.47–1.53 (m, 2H, $CH_2\beta$), 2.52 (t, 2H, $J = 7.3$ Hz, $CH_2\alpha$), 7.19 (s, 1H, H-3), 7.37–7.51 (m, 5H, ArH), 9.55 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 14.1, 22.3, 24.7, 27.9, 32.0, 128.9, 129.5, 129.9, 130.1, 134.4, 134.9, 143.3, 149.7, 195.6.

IR ($CDCl_3$) 1700 cm^{-1} (C=O), 1680 cm^{-1} (C=C). Anal. Calc. for $C_{14}H_{18}O$: C, 83.12; H, 8.97. Found: C, 82.99; H, 8.77%.

*4.3.24. (E)-4-Methoxy-α-pentylcinnamaldehyde (**9e**)*

Column flash chromatography was done using hexane/ether (23/10) as eluent. Oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, 3H, $J = 7.3$ Hz, CH_3), 1.34–1.39 (m, 4H, $CH_2\gamma$, $CH_2\delta$), 1.40–1.50 (m, 2H, $CH_2\beta$), 2.53 (t, 2H, $J = 7.3$ Hz, $CH_2\alpha$), 3.85 (s, 3H, OCH_3), 6.96 ; 7.49 (A_2B_2, 4H, $J = 8.8$ Hz, $J = 8.8$ Hz, ArH), 7.10 (s, 1H, H-3), 9.48 (s, 1H, H-1); ^{13}C NMR (75 MHz, $CDCl_3$) 14.0, 22.4, 24.6, 27.7, 32.1, 55.3, 114.3, 127.6, 131.5, 141.2, 149.7, 160.7, 195.6.

IR ($CDCl_3$) 1674 cm^{-1} (C=O), 1601 cm^{-1} (C=C). Anal. Calc. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.10; H, 8.28%.

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