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Conjugate Michael Additions with Mixed Diorganozincs

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Abstract: Functionalised mixed alkyl(trimethylsilylmethyl)zinc reagents add efficiently to a wide variety of Michael acceptors in high yield and with exclusive 1,4-regioselectivity, without the need for transition metal catalysis. The trimethylsilylmethyl group behaves as a non-transferable group, and in no cases was transfer of this group observed.

In the pursuit of ever more efficient and economic means of synthesising elaborate polyfunctional compounds, strategies are required for the coupling of functionalised carbon electrophiles with equally complex carbon nucleophiles. Whilst most carbon nucleophiles are organometallic reagents, the extreme reactivity of the carbon-metal bond prevents the inclusion of sensitive functional groups on either of the coupling partners; this problem necessitates the use of a costly and time consuming protection-deprotection sequence. Even selective organometallic reagents, such as organocuprates, are themselves obtained from the corresponding lithium or magnesium compounds, and most methods for preparing these later organometallics are incompatible with sensitive groups. Organozinc chemistry with high functional group tolerance yet sufficient reactivity for a whole range of coupling reactions offers one solution to this problem.[1] However, both dialkylzincs (R_2Zn) and alkylzinc halides (RZnX) are not without their own limitations. The dialkylzincs are highly reactive, but in most reactions only one of the two functionalised groups on zinc is transferred. Alkylzinc halides are atom efficient, however, the use of this class of organometallic reagent is restricted by a lower reactivity compared to dialkylzincs.[1]

Recently, we have developed a new class of mixed zinc reagents, FG-R-$ZnCH_2SiMe_3$ **1**, which offer high reactivity together with efficiency.[2] These reagents bear one transferable functionalised group (FG-R-) and one non-transferable group, the trimethylsilylmethyl- group.[3]

$$\begin{array}{ccccc}
\text{FG-R-ZnI} & + & Me_3SiCH_2Li & \longrightarrow & \text{FG-R-}ZnCH_2SiMe_3 \\
\mathbf{2} & & \mathbf{3} & & \mathbf{1} \\
\text{FG-R-Li or FG-R-MgX} & + & Me_3SiCH_2ZnI & \longrightarrow & \text{FG-R-}ZnCH_2SiMe_3 \\
\mathbf{4} & & \mathbf{5} & & \mathbf{1} \\
(\text{FG-R})_2Zn & + & (Me_3SiCH_2)_2Zn & \rightleftharpoons & \text{FG-R-}ZnCH_2SiMe_3 \\
\mathbf{6} & & \mathbf{7} & & \mathbf{1} \\
 & & & & \text{FG-R = Alkyl, Aryl}
\end{array}$$

Scheme 1

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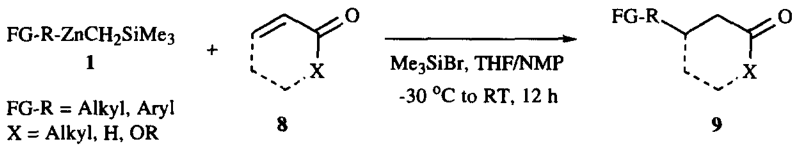
This class of reagents is easily prepared (Scheme 1) by one of three routes, either i) addition of commercially available trimethylsilylmethyllithium **3** to an organozinc halide **2**; ii) addition of an Grignard- or organolithium reagent **4** to trimethylsilylmethylzinc iodide **5**; or iii) by mixing a dialkylzinc reagent **6** with *bis*-(trimethylsilylmethyl)zinc **7**. The later method has been proven to give rise to the mixed zinc reagent as supported by extensive NMR studies.[4]

These mixed organo(trimethylsilylmethyl)zinc reagents have found use in the asymmetric addition to aldehydes,[2,5] and herein, we wish to describe the addition of there mixed organometallic reagents to a variety of Michael acceptors.

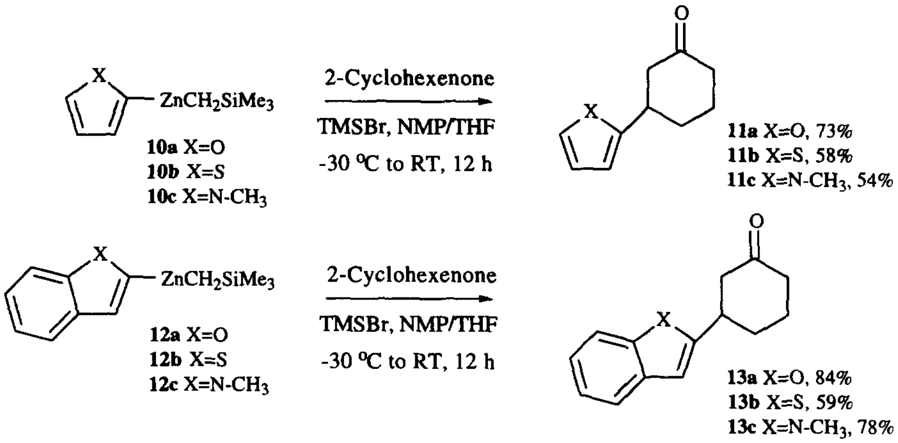
Results and Discussion

The conjugate addition of organometallic reagents to activated olefins is an important synthetic transformation[6] and numerous procedures have been documented involving stoichiometric copper reagents,[6,7] or the copper catalysed addition of magnesium,[7,8a] zinc[8b] or aluminium[8c] compounds. Recently, we have described a protocol whereby dialkylzinc reagents can be added to Michael acceptors without the need for transition metal catalysis.[9] Using a modification of this procedure, we have been able to add mixed alkyl(trimethylsilylmethyl)zinc reagents **1** to Michael acceptors **8** to give 1,4-adducts **9** in good yield (Scheme 2). The reaction is carried out in THF with addition of NMP as cosolvent, in the presence of trimethylsilyl bromide.[10]



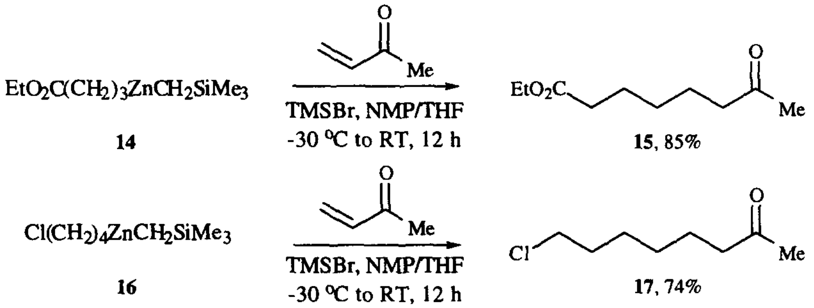
Scheme 2

Thus, the reaction of 2-lithiofuran with trimethylsilylmethylzinc iodide at -40 °C gave rise to the mixed (trimethylsilylmethyl)(2-furyl)zinc **10a**, treatment of this reagent with 2-cyclohexenone (0.7 equiv.) in the presence of trimethylsilyl bromide in a THF/NMP mixture (*ca.* 6:1) afforded the Michael adduct **11a** in 73% (Scheme 3). The reaction of 2-lithiothiophene and 2-lithio N-methylpyrrole in this manner, also gave the mixed zinc reagents **10b** and **10c** respectively. These compounds reacted with 2-cyclohexenone to give the 3-substituted cyclohexanones **11b** and **11c** in 58% and 54% yields. The efficiency of the trimethylsilylmethyl group as a non-transferable group is clearly illustrated by the way that we were able to transfer the thiophenyl group exclusively, especially as this species has itself found a crucial role as a non-transferable group in organocopper chemistry.[6] Similarly, lithiation of benzo[b]furan and transmetallation to trimethylsilylmethylzinc iodide **5**, gave the mixed zinc reagent **12a**. Again, we were able to perform a Michael addition reaction with this reagent to give the substituted cyclohexanone **13a**, in an excellent 84% yield. The sulfur and nitrogen analogues **12b** and **12c**, also reacted to give only the products of 1,4-addition **13b** and **13c** in 59% and 78% yields.



Scheme 3

The reaction is applicable to a wide range of zinc reagents. Secondary zinc species, such as cyclohexyl(trimethylsilylmethyl)zinc, can be added to both 2-cyclopentenone **18** and 2-cyclohexenone **20** (Table 1, entries 1 and 8) in good yields, 84% and 83% respectively. Likewise, mixed aryl(trimethylsilyl methyl)zinc reagents add efficiently. In these cases the mixed zinc reagent is best prepared from the corresponding aryllithium species and trimethylsilylmethylzinc iodide. For instance, the phenyl group can be added in good yield (entries 2 and 5), as can the 4-methoxyphenyl- group (entries 3 and 6). These conjugate addition reactions are not adversely effected by steric bulk, as the 2-methoxyphenyl- group can be transferred equally well when compared to its *para-* isomer (entries 6 and 7). Functionalised zinc reagents can also be used, and the Michael reaction is able to withstand the inclusion of esters (entries 10 and 11), unprotected terminal alkynes (entry 12) and halides (entry 18), without any loss of yield.



Scheme 4

The mild conditions developed in this reaction allow additions to sensitive methylvinylketone in good yield, and the functionalised mixed zinc reagents **14** and **16** add to methylvinylketone to give the functionalised ketones **15** and **17** (Scheme 4). Likewise the secondary zinc reagent (cyclohexyl) (trimethylsilylmethyl)zinc and (2-furyl group)(trimethylsilylmethyl)zinc can be added (Table 1, entries 14 and 15). β-Substituted ketones can also be used (entries 16, 17 and 18), the introduction of a methyl group in (*E*)-hex-4-en-3-one **26** results in no loss of yield, however reactions with benzylideneacetone **22** gave a Michael adduct only in poor yield (entry 13).

Table 1: Michael addition reactions of mixed organo(trimethylsilylmethyl)zinc reagents to unsaturated ketones leading to products **19a-d**, **21a-h**, **23**, **25a-b** and **27a-c**.

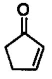
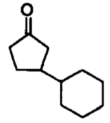
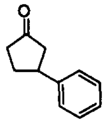
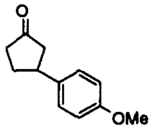
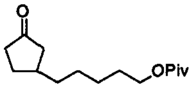
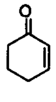
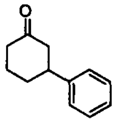
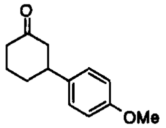
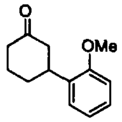
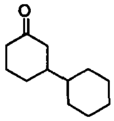
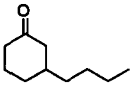
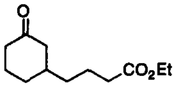
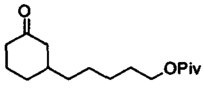
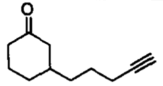
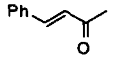
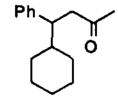
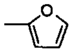
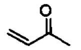
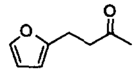
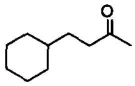
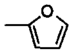
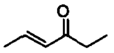
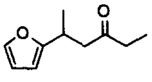
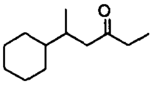
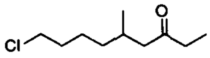
Entry	FG-R-	Michael Acceptor	Method[1]	Products	Yield[2] (%)
1	*c*-Hex	 **18**	B	 **19a**	84
2	Ph	**18**	A	 **19b**	78
3	*p*-MeOPh	**18**	A	 **19c**	87
4	PivO(CH$_2$)$_5$	**18**	C	 **19d**	60
5	Ph	 **20**	A	 **21a**	82
6	*p*-MeOPh	**20**	A	 **21b**	87
7	*o*-MeOPh	**20**	A	 **21c**	86
8	*c*-Hex	**20**	B	 **21d**	83
9	Bu	**20**	B	 **21e**	69
10	EtO$_2$C(CH$_2$)$_3$	**20**	B	 **21f**	49
11	PivO(CH$_2$)$_5$	**20**	C	 **21g**	70

Table 1: Michael addition reactions of mixed organo(trimethylsilylmethyl)zinc reagents to unsaturated ketones leading to products **19a-d**, **21a-h**, **23**, **25a-b** and **27a-c**.

Entry	FG-R-	Michael Acceptor	Method[1]	Products	Yield[2] (%)
12	$HCC(CH_2)_3$	**20**	B	 **21h**	58
13	c-Hex	 **22**	B	 **23**	38
14		 **24**	A	 **25a**	55
15	c-Hex	**24**	B	 **25b**	81
16		 **26**	A	 **27a**	95
17	c-Hex	**26**	B	 **27b**	87
18	$Cl(CH_2)_4$	**26**	B	 **27c**	71

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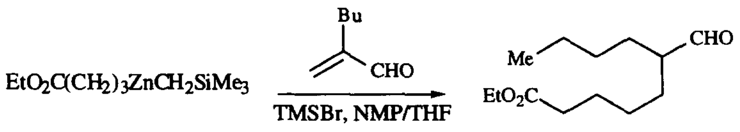
[1] Method A: Mixed zinc reagent prepared from trimethylsilylmethylzinc iodide and an organolithium reagent. Method B: from trimethylsilylmethyl lithium and organozinc halide. Method C: from *bis*-(trimethylsilylmethyl)zinc and a diorganozinc. [2] Yields refer to isolated yields of analytically pure products.

The reaction is not just applicable to ketones, unsaturated aldehydes can be used equally effectively. Whereas the addition of cuprates to unsaturated aldehydes often requires the use of a highly polar co-solvent like HMPA,[10] the addition of (trimethylsilylmethyl)(4-carbethoxybutyl)zinc **14** to 2-butylacrolein proceeds smoothly to give the aldehyde **28** as the exclusive product in 68% yield (Scheme 5). 2-Methylbutenal **37** can also undergo 1,4-addition equally well (Table 2, entries 8 and 9), to give functionalised aldehydes **38a** and **38b** in good yield.



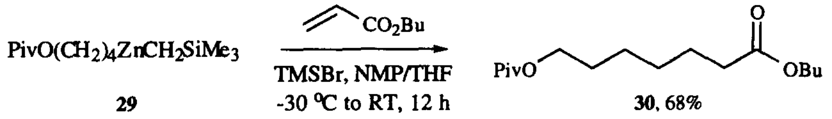
14

28, 68%

Scheme 5

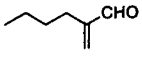
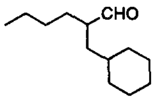
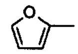
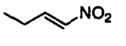
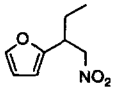
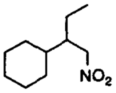
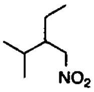
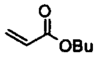
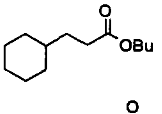
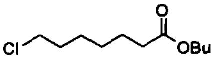
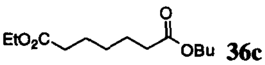
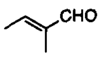
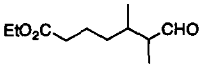
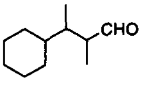
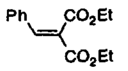
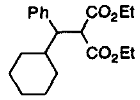
Conjugated esters, like butyl acrylate **35**, produce the expected Michael adducts in excellent yields, (4-pivaloxybutyl)(trimethylsilyl)zinc **29** undergoes 1,4-addition to give the diester **30** in 68% (Scheme 6), whilst 4-chlorobutyl-, 4-carbethoxybutyl-, and cyclohexyl- groups can also be transferred (Table 2, entries 5, 6 and

7). Finally, addition to nitroolefins, like 1-nitrobutene **33**, leads to nitroalkanes **34a**, **34b** and **34c** in 64-76% (Table 2, entries 2, 3 and 4). In no cases was transfer of the trimethylsilyl group observed.



Scheme 6

Table 2: Michael addition reactions of mixed organo(trimethylsilylmethyl)zinc reagents to unsaturated aldehydes, esters and nitro-compounds leading to products **32**, **34a-c**, **36a-c**, **38a-b** and **40**.

Entry	FG-R-	Michael Acceptor	Method	Products	Yield (%)
1	*c*-Hex	 **31**	B	 **32**	68
2		 **33**	A	 **34a**	64
3	*c*-Hex	**33**	B	 **34b**	76
4	*i*-Pr	**33**	B	 **34c**	64
5	*c*-Hex	 **35**	B	 **36a**	99
6	$Cl(CH_2)_4$	**35**	B	 **36b**	76
7	$EtO_2C(CH_2)_3$	**35**	B	 **36c**	86
8	$EtO_2C(CH_2)_3$	 **37**	B	 **38a**	51
9	*c*-Hex	**37**	B	 **38b**	91
10	*c*-Hex	 **39**	B	 **40**	82

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[1] Method A: Mixed zinc reagent prepared from trimethylsilylmethylzinc iodide and an organolithium reagent. Method B: from trimethylsilylmethyl lithium and organozinc halide. [2] Yields refer to isolated yields of analytically pure products.

In summary, we have developed a new class of organozinc reagents that will complement the existing dialkylzinc and organozinc halide reagents. We have shown that these new mixed organo(trimethylsilylmethyl)zinc reagents can undergo conjugate addition reactions to a wide range of conjugate olefins in good to excellent yields. Work is currently underway to develop an enantioselective version of this reaction using other chiral non-transferable groups.

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Experimental

General Methods. Unless otherwise indicated, all reactions were carried out under an argon atmosphere. THF was dried and freshly distilled over sodium/benzophenone and N-Methyl-2-Pyrrolidone (NMP) was distilled from calcium hydride. Zinc dust (~325 mesh) was purchased from Aldrich or Riedel-de-Haën (Germany). Reactions were monitored by gas-chromatography (GC) analysis of reaction aliquots. Fourier Transform infrared spectra (FT-IR) were recorded on a Nicolet 5 DXB spectrometer. Proton and carbon nuclear magnetic resonance spectra (^{1}H and ^{13}C-NMR) were recorded on a Bruker AC-300 (300 MHz, proton and 75.5 MHz, carbon) or a Bruker AX-200 (200 MHz, proton and 50 MHz, carbon). Mass spectra (MS) and exact mass calculations were recorded on a VG-70-250 S mass spectrometer. The ionization methods used were desorption chemical ionisation (CI) and electron impact ionisation (EI).

Starting Materials. The following starting materials were prepared according to literature procedures: *bis*-(trimethylsilylmethyl)zinc,[11] *bis*-(5-pivaloxypentyl)zinc,[12] (*E*)-1-nitrobut-1-ene[13] and trimethylsilylmethyl iodide.[14]

Standard Procedure A:- Trimethylsilylmethylzinc iodide and an organometallic reagent

3-(2-Methoxyphenyl)-1-cyclohexanone (21c): 1,2-Dibromoethane (0.2 mL) was added dropwise to a stirred mixture of zinc dust (1.57 g, 24.0 mmol) in THF (6 mL) at RT under argon, whilst heating with a heat gun to gently boil the solvent. Upon complete addition the mixture was cooled to RT and then trimethylsilyl chloride (0.2 mL) was added dropwise over 5min, again with gentle heating of the solvent. After complete addition the mixture was stirred at RT for a further 5 min. Trimethylsilylmethyl iodide (1.28 g, 6.0 mmol) was then added dropwise over 5 min and the reaction mixture was then heated at 50 °C for 3 h, and the zinc insertion reaction monitored by GC analysis.

When the reaction was complete the reaction mixture was cooled to RT and the excess zinc dust allowed to settle for 15 min. The pale grey solution was then transferred to a clean, flame dried flask and cooled to -30 °C.

Meanwhile, a solution of butyllithium (6.0 mmol) in pentane (1.27 mol L^{-1}, 4.72 mL) was added dropwise over 2 min to a stirred solution of 2-iodoanisol (1.40 g, 6.0 mmol) in THF (10 mL) at -90 °C under argon. The resulting pale yellow solution was stirred at -90 °C for 1 h and then added to a trimethylsilylmethylzinc iodide (6 mmol) solution at -30 °C. The reaction mixture was then stirred at -30 °C for 1 h.

NMP (1 mL), trimethylsilyl bromide (1.05 mL, 8.0 mmol) and then 2-cyclohexenone (0.39 mL, 4.0 mmol) were added to the reaction mixture at -30 °C and stirred at -30 °C for 2 h, before being warmed to RT and stirred overnight.

The reaction mixture was poured into saturated ammonium chloride solution (40 mL) and conc. HCl (10 drops) added and the mixture was then stirred at RT for 10 min. The resulting solution was extracted with diethyl ether (3x70 mL), and the combined organic extracts were washed with brine (50 mL), dried and finally concentrated under reduced pressure. The crude residue was then purified by column chromatography on silica using 20% diethyl ether-light petroleum as eluent to give the ketone (700 mg, 86%) as a colourless oil. ν_{max} (film) / cm^{-1} 1710, 1600, 1494, 1463, 755; δ_H (200 MHz, $CDCl_3$) 7.46-7.33 (2H, m, Ar), 7.18-7.02 (2H, m, Ar), 4.01 (3H, s, C<u>H</u>$_3$), 3.70-3.51 (1H, m, C<u>H</u>), 2.85-1.30 (8H, m, C<u>H</u>); δ_C (50 MHz, $CDCl_3$) 212.0 (s), 157.1 (s), 132.9 (s), 127.9 (d), 126.9 (d), 121.1 (d), 110.9 (d), 55.6 (q), 48.0 (t), 41.8 (t), 38.4 (d), 31.4 (t), 26.0 (t); m/z (EI) 204 (M^+, 42%, $C_{13}H_{16}O_2$ requires 204), 161 (26), 147 (100%); Found: C, 76.44; H, 7.63%. Calculated for $C_{13}H_{16}O_2$; C, 76.44; H, 7.89%.

<u>Standard Procedure B</u>:- Alkylzinc iodide and trimethylsilylmethyllithium

Ethyl 2-(carbethoxy)-3-(cyclohexyl)-3-(phenyl)propanoate (40): 1,2-Dibromoethane (0.2 mL) was added dropwise to a stirred mixture of zinc dust (1.57 g, 24.0 mmol) in THF (6 mL) at RT under argon, whilst heating with a heat gun to gently boil the solvent. Upon complete addition the mixture was cooled to RT and then trimethylsilyl chloride (0.2 mL) was added dropwise over 5 min, again with gentle heating of the solvent. After complete addition, the mixture was stirred at RT for a further 5 min. Cyclohexyl iodide (1.26 g, 6.0 mmol) was then added dropwise over 5 min, and then the reaction mixture was heated at 50 °C for 3 h, the zinc insertion reaction monitored by GC analysis.

When the insertion reaction was complete the reaction mixture was cooled to RT and the excess zinc dust allowed to settle for 15 min. The pale grey solution was then transferred to a flame dried flask and cooled to -40 °C.

A solution of trimethylsilylmethyllithium (6.0 mmol) in pentane (1.0 mol L^{-1}, 6.0 mL) was added dropwise over 3 min to the stirred solution of cyclohexyl zinc iodide at -40 °C and then stirred at -40 °C for 1 h. NMP (1 mL), trimethylsilyl chloride (1.01 mL, 8.0 mmol) and then a solution of diethyl benzylidenemalonate (0.99 g, 4.0 mmol) in THF (5 mL) were added to this reaction mixture at -60 °C. The reaction was stirred at -60 °C for 3 h, then warmed to RT and stirred overnight.

The reaction mixture was worked up as usual and the crude residue was further purified by column chromatography on silica using 30% diethyl ether-light petroleum as eluent to give the malonate (1.09 g, 82%) as a colourless oil. ν_{max} (film) / cm^{-1} 1758, 1733, 1631, 1603; δ_H (200 MHz, $CDCl_3$) 7.32-6.95 (5H, m, Ar), 4.24-3.92 (3H, m, ArC<u>H</u> and CO_2CH_2), 3.83 (1H, d, J = 11.3 Hz, $CO_2C\underline{H}CO_2$), 3.70 (2H, q, J = 7.3 Hz, $CO_2C\underline{H}_2$), 3.36-3.17 (1H, m, C<u>H</u>), 1.62-0.90 (10H, m, C<u>H</u>), 1.14 (3H, t, J = 7.3 Hz, $CH_2C\underline{H}_3$), 0.76 (3H, t, J = 7.3 Hz, $CH_2C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 168.7 (s), 167.9 (s), 138.9 (s), 129.4 (d), 127.6 (d), 126.5 (d), 61.3 (t), 60.9 (t), 55.2 (d), 50.9 (d), 40.7 (d), 31.9 (t), 28.2 (t), 26.5 (t), 26.3 (t), 26.1 (t), 14.0 (q), 13.5 (q); m/z (EI) 332 (M^+, 1%, $C_{20}H_{28}O_4$ requires 332), 250 (23), 203 (28), 172 (100%); Found: C, 71.90; H, 8.52%. Calculated for $C_{20}H_{28}O_4$; C, 72.26; H, 8.44%.

Standard Procedure C:- Dialkylzinc and *bis*-(trimethylsilylmethyl)zinc

5-(3-Oxocyclopentyl)pentyl pivolate (19d): *Bis*-(trimethylsilylmethyl)zinc (1.3 g, 6 mmol) was added slowly over 5 min to a stirred solution of *bis*-(5-pivaloxypentyl)zinc (5 mmol) in THF (6 mL) at -30 °C under argon. Upon complete addition the reaction mixture was allowed to warm to RT, and then stirred for a further 30 min.

The grey solution was then cooled to -30 °C and NMP (2 mL) was added, followed by trimethylsilyl bromide (2.4 g, 16 mmol) and finally 2-cyclopentenone (0.66 g, 8 mmol). The reaction mixture was allowed to warm slowly to RT and was then stirred for 12 h. The reaction mixture was worked up as described above and the crude residue was subjected to further purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (1.3 g, 60%) as a colourless oil. υ_{max} (film) / cm^{-1} 2960, 2933, 1729, 1159; δ_H (300 MHz, $CDCl_3$) 3.98 (2H, t, J = 6.5 Hz, $C\underline{H}_2O$), 2.32-2.06 (5H, m, $C\underline{H}$), 1.77-1.29 (10H, m, $C\underline{H}$), 1.12 (9H, s, $C\underline{H}_3$); δ_C (75 MHz, $CDCl_3$) 219.5, 178.6, 64.3, 45.3, 38.8, 38.5, 37.2, 35.6, 29.5, 28.6, 27.5, 27.2, 26.1; m/z (FD) 254 (M^+, 100%, $C_{15}H_{26}O_3$ requires 254), 85 (52), 57 (81%); Found: C, 70.72; H, 10.27%. Calculated for $C_{15}H_{26}O_3$; C, 70.82; H, 10.30%.

3-(2-Furyl)-1-cyclohexanone (11a)[15]: The reaction was carried out according to a modified **Standard Procedure A**. Furan (0.44 mL, 6.0 mmol) was added in one portion to a stirred solution of butyllithium (6.0 mmol) in pentane (1.5 mol L^{-1}, 4.0 mL) and THF (5 mL) at RT under argon. The resulting solution was stirred at RT for 30 min, and then cooled to -40 °C. A trimethylsilylmethylzinc iodide solution (6 mmol) was then added over 2 min and the mixture stirred at -40 °C for 1 h. The reaction was then carried out as described above using NMP (1 mL), trimethylsilyl bromide (1.05 mL, 8.0 mmol) and 2-cyclohexenone (0.39 mL, 4.0 mmol), to yield a crude residue was purified by column chromatography on silica using 15% diethyl ether-light petroleum as eluent to give the ketone (480 mg, 73%) as a colourless oil. ν_{max} (film) / cm^{-1} 1713, 1591, 1506, 1449; δ_H (200 MHz, $CDCl_3$) 7.29 (1H, dd, J = 1.8, 0.8 Hz, $OC\underline{H}CH$), 6.26 (1H, dd, J = 3.3, 1.8 Hz, $OCHC\underline{H}$), 6.01 (1H, dt, J = 3.3, 0.8 Hz, $OCRC\underline{H}$), 3.25-3.09 (1H, m, $C\underline{H}Ar$), 2.66 (1H, m, ddt, J = 14.3, 4.8, 1.3 Hz, $COC\underline{H}_2$), 2.49 (1H, ddd, J = 14.3, 10.3, 0.8 Hz, $COC\underline{H}_2$), 2.41-2.29 (2H, m, $COC\underline{H}_2$), 2.19-1.70 (4H, m, $C\underline{H}$); δ_C (50 MHz, $CDCl_3$) 210.0 (s), 157.0 (s), 141.2 (d), 109.9 (d), 104.4 (d), 45.5 (t), 41.1 (t), 37.5 (d), 29.8 (t), 24.3 (t); m/z (EI) 164 (M^+, 61%, $C_{10}H_{12}O$ requires 164), 107 (100%); Found: C, 72.94; H, 7.48%. Calculated for $C_{10}H_{12}O$; C, 73.15; H, 7.37%.

3-(2-Thienyl)-1-cyclohexanone (11b)[16]: The reaction was carried out according to a modified **Standard Procedure A**. A solution of butyllithium (6.0 mmol) in pentane (1.27 mol L^{-1}, 4.72 mL) was added dropwise over 2 min to a stirred solution of thiophene (0.48 mL, 6.0 mmol) in THF (5 mL) at -30 °C under argon, and then the resulting solution was stirred at -30 °C for 1 h. It was then added to a trimethylsilylmethylzinc iodide solution (6 mmol) at -30 °C, and the mixture stirred at -30 °C for 1 h. The reaction was then carried out as described above using NMP (1 mL), trimethylsilyl bromide (1.05 mL, 8.0 mmol) and 2-cyclohexenone (0.39 mL, 4.0 mmol), to yield a residue which was subjected to further purification by column chromatography on silica using 20% diethyl ether-light petroleum as eluent to give the ketone (420 mg, 58%) as a colourless oil. ν_{max} (film) / cm^{-1} 1714, 1447, 1420, 1317, 1263, 1223; δ_H (200 MHz, $CDCl_3$) 7.16 (1H, dd, J = 5.0, 1.0 Hz, $SC\underline{H}CH$), 6.93 (1H, dd, J = 5.3, 3.5 Hz, $SCHC\underline{H}$), 6.83 (1H, dt, J = 3.5, 1.0 Hz, $SCRC\underline{H}$), 3.40-3.22 (1H, m, $C\underline{H}$), 2.60 (1H, ddt, J = 14.0, 5.5, 1.7 Hz, $COC\underline{H}_2$), 2.39 (1H, ddd, J = 14.0, 11.5, 1.0 Hz, $COC\underline{H}_2$), 2.30-1.72

(6H, m, C$\underline{H}_2$); δ_C (50 MHz, $CDCl_3$) 209.7 (s), 148.2 (s), 126.6 (d), 123.1 (d), 122.7 (d), 49.2 (t), 40.9 (t), 39.5 (d), 33.6 (t), 24.7 (t); m/z (EI) 180 (M$^+$, 55%, $C_{10}H_{12}OS$ requires 180), 123 (100), 110 (45%); Found: C, 66.61; H, 7.01%. Calculated for $C_{10}H_{12}OS$; C, 66.63; H, 6.71%.

3-(1-Methyl-1*H*-2-pyrrolyl)-1-cyclohexanone (11c): The reaction was carried out according to a modified **Standard Procedure A**. N-Methylpyrrole (1.77 mL, 20.0 mmol) was added in one portion to a stirred solution of butyllithium (10.0 mmol) in pentane (1.5mol L^{-1}, 6.7 mL) and THF (10 mL) at RT under argon. The resulting pale yellow solution was then heated at 40 °C for 2 h and then cooled to RT. The solution of 2-lithiopyrrole was then added dropwise over 5 min to a stirred solution of trimethylsilylzinc iodide (6 mmol) at -40 °C and the mixture stirred at -40 °C for 45 min. NMP (1 mL), trimethylsilyl bromide (1.76 mL, 13.3 mmol) and then 2-cyclohexenone (0.64 mL, 6.7 mmol) were added and the reaction was stirred overnight, gradually warming to RT. The mixture was poured into saturated ammonium chloride solution (50 mL) and extracted with diethyl ether (3x70 mL). The combined organic extracts were washed with brine (50 mL), dried and then concentrated under reduced pressure. The crude residue was taken up in THF (50 mL) and then cooled to 0 °C. A solution of TBAF (20 mmol) in THF (1.0 mol L^{-1}, 20 mL) was added dropwise over 5 min to the crude reaction mixture and then stirred at 0 °C for 30 min. The mixture worked up as usual and the brown residue was further purified by column chromatography on silica using 15% diethyl ether-light petroleum as eluent to yield the substituted pyrrole (670 mg, 57%) as a pale yellow oil. ν_{max} (film) / cm^{-1} 1711, 1491, 1449, 1420, 1298; δ_H (200 MHz, $CDCl_3$) 6.47 (1H, dd, *J* = 2.5, 1.8 Hz, NCRC$\underline{H}$), 6.00 (1H, app. t, *J* = 3 Hz, NCHC$\underline{H}$), 5.85 (1H, dd, *J* = 3.8, 1.8 Hz, NC$\underline{H}$), 3.49 (3H, s, C$\underline{H}_3$), 3.05-2.95 (1H, m, C$\underline{H}$), 2.71-2.58 (1H, m, COC$\underline{H}_2$), 2.56-2.38 (3H, m, COC$\underline{H}_2$), 2.19-2.06 (2H, m, C$\underline{H}$), 1.90-1.68 (2H, m, C$\underline{H}$); δ_C (50 MHz, $CDCl_3$) 210.5 (s), 135.4 (s), 121.6 (d), 106.7 (d), 104.3 (d), 47.8 (t), 41.1 (t), 35.9 (q), 33.4 (d), 31.5 (t), 24.8 (t); m/z (EI) 177 (M$^+$, 74%, $C_{11}H_{15}ON$ requires 177), 134 (49), 120 (100%); Found: C, 74.43; H, 8.52; N, 8.05%. Calculated for $C_{11}H_{15}ON$; C, 74.53; H, 8.52; N, 7.90%.

3-(Benzo[b]furan-2-yl)-1-cyclohexanone (13a): The reaction was carried out according to a modified **Standard Procedure A** using trimethylsilylmethyl iodide (2.57 g, 12 mmol), 2-lithiobenzofuran (12 mmol) (prepared by deprotonation of benzo[b]furan (1.8 g, 15 mmol) at -30 °C by *n*-BuLi (12 mmol) in pentane (1.0 mol L^{-1}, 12 mL) and subsequent warming to RT for 30 min). The solution of trimethylsilylmethylzinc iodide was then added to the solution of 2-lithiobenzofuran at -50 °C and then warmed slowly to -30 °C over 1 h. The reaction was then carried out as described above using 2-cyclohexenone (0.76 g, 8 mmol), NMP (2 mL) and trimethylsilyl bromide (2.4 g, 16 mmol) to yield a crude residue. The crude residue was subjected to further purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (1.45 g, 84%) as a colourless oil. ν_{max} (film) / cm^{-1} 3059, 2941, 2865, 1711, 1584, 1454, 751; δ_H (300 MHz, $CDCl_3$) 7.48-7.38 (2H, m, Ar), 7.23-7.16 (2H, m, Ar), 6.39 (1H, s, OCRC$\underline{H}$), 3.33-3.28 (1H, m, ArC$\underline{H}$), 2.73-1.80 (8H, m, C$\underline{H}$); δ_C (75 MHz, $CDCl_3$) 210.2, 160.4, 154.9, 128.8, 124.1, 123.1, 121.1, 111.3, 102.2, 45.7, 41.7, 38.3, 30.0, 24.8; m/z (EI) 214 (M$^+$, 68%, $C_{14}H_{14}O_2$ requires 214), 171 (27), 157 (100%); Found: C, 78.46; H, 6.75%. Calculated for $C_{14}H_{14}O_2$; C, 78.43; H, 6.58%.

3-(Benzo[b]thiophen-2-yl)-1-cyclohexanone (13b): The reaction was carried out according to a modified **Standard Procedure A**. A solution of butyllithium (6.0 mmol) in pentane (1.5 mol L^{-1}, 4.0 mL) was added dropwise over 2 min to a stirred solution of benzo[b]thiophene (0.7 mL, 6.0 mmol) in THF (10 mL) at -78 °C under argon. Upon complete addition the pale yellow solution was warmed to 0 °C and then recooled to -40 °C, before addition of a trimethylsilylmethylzinc iodide solution (6 mmol) over 2 min. The resulting solution was then stirred at -40 °C for 1 h. The reaction was then carried out as described above using NMP (1 mL), trimethylsilyl bromide (1.05 mL, 8.0 mmol) and 2-cyclohexenone (0.39 mL, 4.0 mmol). The crude residue was subjected to purification by column chromatography on silica using 15% diethyl ether-light petroleum as eluent to give the substituted benzothiophene (540 mg, 59%) as a colourless oil. ν_{max} (film) / cm^{-1} 1711, 1458, 1448; δ_H (200 MHz, $CDCl_3$) 7.76-7.67 (1H, m, Ar), 7.64-7.53 (1H, m, Ar), 7.29-7.13 (2H, m, Ar), 6.96 (1H, s, SCRC$\underline{H}$), 3.39-3.24 (1H, m, ArC$\underline{H}$), 2.71-2.58 (1H, m, COC$\underline{H}_2$), 2.52-2.22 (3H, m, COC$\underline{H}_2$), 2.19-1.65 (4H, m, C$\underline{H}$); δ_C (50 MHz, $CDCl_3$) 210.6 (s), 140.5 (s), 139.1 (s), 137.7 (s), 124.3 (d), 123.9 (d), 123.0 (d), 121.4 (d), 120.5 (d), 47.5 (t), 41.3 (t), 38.0 (d), 31.1 (t), 24.9 (t); m/z (EI) 230 (M^+, 100%, $C_{14}H_{14}OS$ requires 230), 173 (93), 147 (28), 115 (28%); Found: C, 72.84; H, 6.20%. Calculated for $C_{14}H_{14}OS$; C, 73.01; H, 6.13%.

3-(1-Methyl-1*H*-2-indolyl)-1-cyclohexanone (13c): The reaction was carried out according to a modified **Standard Procedure A**. N-methylindole (1.57 mL, 12.0 mmol) was added over 1 min to a stirred solution of butyllithium (6.0 mmol) in pentane (1.5 mol L^{-1}, 4.0 mL) and THF (10 mL) at RT under argon. The resulting solution was stirred at RT for 1 h, and then cooled to -40 °C. Trimethylsilylmethylzinc iodide solution (6 mmol) was added over 2 min to this solution and then stirred at -40 °C for 1 h. The reaction was then carried out as described above using NMP (1 mL), trimethylsilyl bromide (1.05 mL, 8.0 mmol) and 2-cyclohexenone (0.39 mL, 4.0 mmol). The reaction mixture was worked up as usual to leave a crude residue which was further purified by column chromatography on silica using 25% diethyl ether-light petroleum as eluent to give the substituted indole (670 mg, 78%) as a colourless oil. ν_{max} (film) / cm^{-1} 1709, 1615, 1551, 1484, 1474; δ_H (200 MHz, $CDCl_3$) 7.48 (1H, m, dt, J = 8.0, 1.0 Hz, Ar), 7.19-6.93 (3H, m, Ar), 6.68 (1H, d, J = 0.5 Hz, NCRC$\underline{H}$), 3.56 (3H, s, C$\underline{H}_3$), 3.37-3.20 (1H, m, C$\underline{H}$), 2.64 (1H, ddt, J = 14.0, 4.7, 1.5 Hz, COC$\underline{H}_2$), 2.45 (1H, ddd, J = 13.8, 10.2, 1.0 Hz, COC$\underline{H}_2$), 2.35-1.60 (6H, m, C$\underline{H}$); δ_C (50 MHz, $CDCl_3$) 211.5 (s), 136.9 (s), 126.3 (s), 125.0 (d), 121.5 (d), 118.8 (d), 118.6 (d), 117.9 (s), 109.2 (d), 48.0 (t), 41.3 (t), 35.6 (q), 32.4 (d), 31.7 (t), 24.6 (t); m/z (EI) 227.3054 (M^+, 100%, $C_{15}H_{17}NO$ requires 227.3053), 184 (87), 170 (70), 157 (86%).

Ethyl 7-oxooctanoate (15)[17]: The reaction was carried out according to **Standard Procedure B** using ethyl 4-iodobutanoate (1.45 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and methylvinylketone (0.33 mL, 4.0 mmol) to give a crude residue which was then purified further by column chromatography on silica using 20% diethyl ether-light petroleum as eluent to give the ketoester (630 mg, 85%) as a colourless oil. ν_{max} (film) / cm^{-1} 1735, 1718, 1421, 1371, 1179, 1034; δ_H (200 MHz, $CDCl_3$) 4.07 (2H, q, J = 7.0 Hz, OC$\underline{H}_2$CH$_3$), 2.42 (2H, t, J = 7.0 Hz, COC$\underline{H}_2$), 2.27 (2H, t, J = 7.2 Hz, COC$\underline{H}_2$), 2.08 (3H s, COC$\underline{H}_3$), 1.68-1.48 (4H, m, C$\underline{H}_2$), 1.38-1.12 (5H, m, C$\underline{H}_2$ and C$\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 208.7 (s), 173.5 (s), 60.1 (t), 43.3 (t), 34.0 (t), 29.7 (q), 28.4 (t), 24.6 (t), 23.2 (t), 14.1 (q); m/z (EI) 186 (M^+, 1%, $C_{10}H_{18}O_3$ requires 186), 141 (14), 129 (61), 101 (43), 43 (100%); Found: C, 64.33; H, 9.56%. Calculated for $C_{10}H_{18}O_3$; C, 64.49; H, 9.74%.

8-Chloro-2-octanone (17)[18]: The reaction was carried out according to **Standard Procedure B** using 4-chlorobutyl iodide (1.31 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and methylvinylketone (0.33 mL, 4.0 mmol) to give a crude residue, which was then purified further by column chromatography on silica using 7% diethyl ether-light petroleum as eluent to give the chloroketone (450 mg, 74%) as a colourless oil. ν_{max} (film) / cm^{-1} 1717, 1447, 1432, 1360, 1170; δ_H (200 MHz, $CDCl_3$) 3.50 (2H, t, J = 7.0 Hz, $C\underline{H}_2Cl$), 2.41 (2H, t, J = 7.3 Hz, $C\underline{H}_2CO$), 2.11 (3H, s, $C\underline{H}_3CO$), 1.75 (2H, app. quin., J = 7 Hz, $C\underline{H}_2CH_2Cl$), 1.65-1.20 (6H, m, $C\underline{H}_2$); δ_C (50 MHz, $CDCl_3$) 208.9 (s), 44.9 (t), 43.4 (t), 32.3 (t), 29.8 (q), 28.3 (t), 26.5 (t), 23.5 (t); m/z (EI) 162 (M^+, 1%, $C_8H_{15}OCl$ requires 162), 147 (2), 126 (2), 83 (26), 58 (94), 43 (100%); Found: C, 58.82; H, 9.26%. Calculated for $C_8H_{15}OCl$; C, 59.08; H, 9.30%.

3-Cyclohexyl-1-cyclopentanone (19a)[19]: The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (1.3 g, 6 mmol), trimethylsilylmethyllithium (6 mmol), 2-cyclopentenone (0.33 g, 4 mmol), NMP (2 mL) and trimethylsilyl bromide (1.2 g, 8 mmol). The crude residue was subjected to further purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (560 mg, 84%) as a colourless oil. ν_{max} (film) / cm^{-1} 2925, 2852, 1745, 1449, 1159; δ_H (300 MHz, $CDCl_3$) 2.28-2.19 (2H, m, $C\underline{H}$), 2.09-2.04 (2H, m, $C\underline{H}$), 1.80-1.59 (7H, m, $C\underline{H}$), 1.18-1.09 (5H, m, $C\underline{H}$), 0.90-0.86 (2H, m, $C\underline{H}$); δ_C (75 MHz, $CDCl_3$) 219.4, 43.5, 43.4, 43.3, 38.9, 31.8, 30.8, 26.5, 26.4, 26.2, 26.1; m/z (EI) 166 (M^+, 24%, $C_{11}H_{18}O$ requires 166), 137 (14), 122 (12), 83 (100%); Found: C, 79.40; H, 11.09%. Calculated for $C_{11}H_{18}O$; C, 79.46; H, 10.91%.

3-Phenyl-1-cyclopentanone (19b)[20]: The reaction was carried out according to **Standard Procedure A** using trimethylsilylmethyl iodide (2.57 g, 12 mmol), phenyllithium (12 mmol), 2-cyclopentenone (0.66 g, 8 mmol), NMP (2 mL) and trimethylsilyl bromide (2.4 g, 16 mmol). The crude residue obtained subjected to purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (1.0 g, 78%) as a colourless oil. ν_{max} (film) / cm^{-1} 3085, 3062, 2897, 1742, 1603, 1495, 1151, 764, 701; δ_H (300 MHz, $CDCl_3$) 7.35-7.29 (2H, m, Ar), 7.24-7.19 (3H, m, Ar), 3.43-3.33 (1H, $C\underline{H}Ar$), 2.61 (1H, dd, J = 18.3, 7.5 Hz, $COC\underline{H}_2$), 2.43-2.24 (4H, m, $C\underline{H}$), 1.97-1.93 (1H, m, $C\underline{H}$); δ_C (75 MHz, $CDCl_3$) 218.1, 143.2, 128.7, 126.8, 126.7, 45.8, 42.2, 38.9, 31.2; m/z (EI) 160 (M^+, 93%, $C_{11}H_{12}O$ requires 160), 131 (13), 117 (50), 104 (100%); Found: C, 82.41; H, 7.71%. Calculated for $C_{11}H_{12}O$; C, 82.46; H, 7.54%.

3-(4-Methoxyphenyl)-1-cyclopentanone (19c)[20]: The reaction was carried out according to a modified **Standard Procedure A** using trimethylsilylmethyl iodide (2.57 g, 12 mmol), 4-methoxyphenyllithium (12 mmol) (prepared by the iodine-lithium exchange from 4-methoxyiodobenzene (2.8 g, 12 mmol) and *n*-BuLi (12 mmol) in pentane (1.0 mol L^{-1}, 12 mL) at -90 °C and stirred for 30 min). The solution of trimethylsilylmethylzinc iodide was added to the solution of 4-methoxyphenyllithium at -90 °C and then warmed to -30 °C slowly over 1 h. The reaction was then carried out as described above with 2-cyclopentenone (0.66 g, 8 mmol), NMP (2 mL) and trimethylsilyl bromide (2.4 g, 16 mmol) to yield a crude residue, which was subjected to further purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (1.32 g, 87%) as a colourless oil. ν_{max} (film) / cm^{-1} 3033, 2960, 2937, 1743, 1612, 1582, 1515, 1249, 1034, 832; δ_H (300 MHz, $CDCl_3$) 7.15 (2H, d, J = 8.6 Hz, Ar), 6.81 (2H, d, J = 8.6 Hz, Ar), 3.71 (3H, s, $OC\underline{H}_3$), 3.33-3.21 (1H, m, $ArC\underline{H}$), 2.53 (1H, dd, J = 18.1, 7.5 Hz, COC$\underline{H}_2$), 2.40-2.12 (4H, m, C$\underline{H}$), 1.92-1.78 (1H, m, C$\underline{H}$); δ_C (75 MHz, CDCl$_3$) 218.0, 158.3, 135.1, 127.6, 113.6, 55.1, 45.8, 41.3, 38.7, 31.3; m/z (EI) 190 (M$^+$, 93%, $C_{12}H_{14}O_2$ requires 190), 161 (29), 147 (20), 134 (100%); Found: C, 75.54; H, 7.47%. Calculated for $C_{12}H_{14}O_2$; C, 75.76; H, 7.41%.

3-Phenyl-1-cyclohexanone (21a)[16, 20]: The reaction was carried out according to **Standard Procedure A** using trimethylsilylmethyl iodide (2.57 g, 12 mmol), phenyllithium (12 mmol), 2-cyclohexenone (0.76 g, 8 mmol), NMP (2 mL) and trimethylsilyl bromide (2.4 g, 16 mmol). The crude residue was subjected to purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (1.15 g, 82%) as a colourless oil. ν_{max} (film) / cm^{-1} 3028, 2938, 2866, 1711, 1603, 756, 701; δ_H (300 MHz, CDCl$_3$) 7.30-7.25 (2H, m, Ar), 7.20-7.15 (3H, m, Ar), 2.97-2.93 (1H, m, ArC$\underline{H}$), 2.53-2.30 (4H, m, C$\underline{H}$), 2.09-1.99 (2H, m, C$\underline{H}$), 1.82-1.64 (2H, m, C$\underline{H}$); δ_C (75 MHz, CDCl$_3$) 210.8, 144.4, 128.7, 126.7, 126.6, 48.9, 44.7, 41.2, 32.8, 25.5; m/z (EI) 174 (M$^+$, 88%, $C_{12}H_{14}O$ requires 174), 131 (73), 117 (100%); Found: C, 82.50; H, 8.50%. Calculated for $C_{12}H_{14}O$; C, 82.71; H, 8.09%.

3-(4-Methoxyphenyl)-1-cyclohexanone (21b)[20]: The reaction was carried out according to a modified **Standard Procedure A** using trimethylsilylmethyl iodide (2.57 g, 12 mmol), 4-methoxyphenyllithium (12 mmol) (prepared by the iodine-lithium exchange from 4-methoxyiodobenzene (2.8 g, 12 mmol) and *n*-BuLi (12 mmol) in pentane (1.0 mol L^{-1}, 12 mL) at -90 °C stirred for 30 min). The solution of trimethylsilylmethylzinc iodide was added to the solution of 4-methoxyphenyllithium at -90 °C and then warmed to -30 °C slowly over 1 h. The reaction was then carried out as described above using 2-cyclohexenone (0.76 g, 8 mmol), NMP (2 mL) and trimethylsilyl bromide (2.4 g, 16 mmol) to yield a crude residue. This yellow oil was subjected to further purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (1.42 g, 87%) as a colourless oil. ν_{max} (film) / cm^{-1} 3031, 2937, 2865, 1711, 1612, 1515, 1256, 1034, 829; δ_H (300 MHz, CDCl$_3$) 7.12 (2H, d, J = 8.6 Hz, Ar), 6.83 (2H, m, J = 6.8 Hz, Ar), 3.76 (3H, s, OC$\underline{H}_3$), 2.95-2.90 (1H, m, ArC$\underline{H}$), 2.53-2.35 (4H, m, C$\underline{H}$), 2.12-2.08 (2H, m, C$\underline{H}$), 1.81-1.73 (2H, m, C$\underline{H}$); δ_C (75 MHz, CDCl$_3$) 210.9, 158.3, 136.6, 127.5, 114.0, 55.2, 49.2, 43.9, 41.1, 33.0, 25.5; m/z (EI) 204 (M$^+$, 44%, $C_{13}H_{16}O_2$ requires 204), 161 (19), 147 (100%); Found: C, 76.28; H, 7.91%. Calculated for $C_{13}H_{16}O_2$; C, 76.44; H, 7.89%.

3-Cyclohexyl-1-cyclohexanone (21d)[21]: The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (2.5 g, 12 mmol), trimethylsilylmethyllithium (12 mmol), NMP (2 mL), 2-cyclohexenone (0.76 g, 8 mmol) and trimethylsilyl bromide (2.4 g, 16 mmol). The crude residue was subjected to purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (1.2 g, 83%) as a colourless oil. ν_{max} (film) / cm^{-1} 2925, 2853, 1714, 1449, 1094; δ_H (300 MHz, CDCl$_3$) 2.28-2.16 (2H, m, C$\underline{H}$), 2.06-1.97 (2H, m, C$\underline{H}$), 1.69-1.50 (8H, m, C$\underline{H}$), 1.33-0.78 (8H, m, C$\underline{H}$); δ_C (75 MHz, CDCl$_3$) 212.4, 45.6, 44.7, 42.7, 41.6, 30.0, 29.9, 28.5, 26.6, 26.5, 26.4, 25.6; m/z (EI) 180 (M$^+$, 2%, $C_{12}H_{20}O$ requires 180), 162 (2), 137 (8), 97 (100%); Found: C, 79.78; H, 11.12%. Calculated for $C_{12}H_{20}O$; C, 79.94; H, 11.18%.

3-Butyl-1-cyclohexanone (21e)[16]: The reaction was carried out according to **Standard Procedure A** using trimethylsilylmethyl iodide (2.57 g, 12 mmol), *n*-BuLi (12 mmol) in pentane (1.5 mol L^{-1}, 8 mL), NMP (2 mL), 2-cyclohexenone (0.76 g, 8 mmol) and trimethylsilyl bromide (2.4 g, 16 mmol). The crude residue was subjected to further purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (0.85 g, 69%) as a colourless oil. ν_{max} (film) / cm^{-1} 2959, 2929, 1715, 1448; δ_H (300 MHz, $CDCl_3$) 2.32-2.17 (3H, m, C$\underline{H}$), 1.97-1.58 (5H, m, C$\underline{H}$), 1.28-1.21 (7H, m, C$\underline{H}$), 0.83-0.79 (3H, m, C$\underline{H}$); δ_C (75 MHz, $CDCl_3$) 211.5, 47.9, 41.3, 38.8, 36.0, 31.1, 28.6, 25.0, 22.4, 13.7; m/z (EI) 154 (M^+, 7%. $C_{10}H_{18}O$ requires 154), 111 (23), 97 (100%); Found: C, 77.65; H, 11.83%. Calculated for $C_{10}H_{18}O$; C, 77.86; H, 11.76%.

Ethyl 4-(3-oxocyclohexyl)butanoate (21f)[7c]: The reaction was carried out according to **Standard Procedure B** using ethyl 4-iodobutanoate (2.9 g, 12 mmol), trimethylsilylmethyllithium (12 mmol), NMP (2 mL), 2-cyclohexenone (0.76 g, 8 mmol) and trimethylsilyl bromide (2.4 g, 16 mmol). The crude residue was subjected to further purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (0.84 g, 49%) as a colourless oil. ν_{max} (film) / cm^{-1} 2935, 2867, 1733, 1714, 1247; δ_H (300 MHz, $CDCl_3$) 4.05 (2H, q, J = 7.1 Hz, OC$\underline{H}_2$), 2.36-2.17 (4H, m, C$\underline{H}$), 2.21 (2H, t, J = 6.5 Hz, COC$\underline{H}_2$), 1.98-1.58 (6H, m, C$\underline{H}$), 1.33-1.20 (3H, m, C$\underline{H}$), 1.17 (3H, t, J = 7.1 Hz, OCH$_2$C$\underline{H}_3$); δ_C (75 MHz, $CDCl_3$) 211.3, 173.2, 60.1, 47.9, 41.3, 38.7, 35.8, 34.1, 30.9, 25.1, 21.9, 14.1; m/z (EI) 212 (M^+, 1%, $C_{12}H_{20}O_3$ requires 212), 167 (3), 121 (9), 97 (100%); Found: C, 67.80; H, 9.61%. Calculated for $C_{12}H_{20}O_3$ C, 67.89; H, 9.49%.

5-(3-oxocyclohexyl)pentyl pivalate (21g): The reaction was carried out according to a modified **Standard Procedure C** using *bis*-(5-pivaloxypentyl)zinc (5 mmol), *bis*-(trimethylsilylmethyl)zinc (1.3 g, 6 mmol), NMP (2 mL), 2-cyclohexenone (0.76 g, 8 mmol) and trimethylsilyl bromide (2.4 g, 16 mmol). The crude residue was subjected to further purification by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (1.5 g, 70%) as a colourless oil. ν_{max} (film) / cm^{-1} 2933, 2862, 1726, 1286, 1157; δ_H (300 MHz, $CDCl_3$) 3.80 (2H, t, J = 6.6 Hz, C$\underline{H}_2$O), 2.15-1.00 (17H, m, C$\underline{H}$), 0.95 (9H, s, C$\underline{H}_3$); δ_C (75 MHz, $CDCl_3$) 210.9, 177.9, 63.8, 47.7, 41.1, 38.6, 38.3, 36.1, 30.9, 28.2, 26.8, 25.9, 25.6 24.9; m/z (EI) 268 (M^+, 1%, $C_{16}H_{28}O_3$ requires 268), 166 (6), 123 (17), 110 (10), 97 (100%); Found: C 71.61; H, 10.65%. Calculated for $C_{16}H_{28}O_3$; C, 71.60; H, 10.51%.

3-(4-Pentynyl)-1-cyclohexanone (21h): The reaction was carried out according to **Standard Procedure B** using 5-iodo-1-pentyne (1.94 g, 10 mmol), trimethylsilylmethyllithium (10 mmol), trimethylsilyl bromide (1.32 mL, 10 mmol), NMP (1 mL) and 2-cyclohexenone (0.48 mL, 5.0 mmol) to give a crude residue. This residue was purified further by column chromatography on silica using 20% diethyl ether-light petroleum as eluent to give the ketone (480 mg, 58%) as a colourless oil. ν_{max} (film) / cm^{-1} 3290, 2116, 1711, 1457, 1448, 1346, 1227; δ_H (300 MHz, $CDCl_3$) 2.46-2.15 (6H, m, C$\underline{H}$), 2.10-1.88 (4H, m, C$\underline{H}$), 1.84-1.70 (1H, m, C$\underline{H}$), 1.68-1.30 (5H, m, C$\underline{H}$); δ_C (75 MHz, $CDCl_3$) 211.4 (s), 84.0 (s), 68.5 (d), 47.9 (t), 41.3 (t), 38.5 (d), 35.5 (t), 31.1 (t), 25.5 (t), 25.1 (t), 18.4 (t); m/z (EI) 164.1204 (M^+, 9%, $C_{11}H_{16}O$ requires 164.1204), 149 (11), 136 (16), 123 (30), 121 (84), 97 (100%).

4-Cyclohexyl-4-phenyl-2-butanone (23)[22]: The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (1.26 g, 6 mmol), trimethylsilyl bromide (1.05 mL, 8.0 mmol), NMP (1 mL) and benzylidene acetone (580 mg, 4.0 mmol) to give a crude residue, which was then purified further by column chromatography on silica using 20% diethyl ether-light petroleum as eluent to give the ketone (350 mg, 38%) as a white crystalline solid, this solid was finally recrystallised from ethanol. m.p. 61-63 °C. ν_{max} (KBr) / cm^{-1} 1709, 1447, 1420, 1372, 748, 699; δ_H (200 MHz, $CDCl_3$) 7.52-7.29 (5H, m, Ar), 3.22-3.08 (1H, m, ArC$\underline{H}$RR'), 3.04-2.91 (2H, m, C$\underline{H}_2$CO), 2.18 (3H, s, C$\underline{H}_3$), 2.08-0.94 (11H, m, C$\underline{H}$); δ_C (50 MHz, $CDCl_3$) 208.2 (s), 143.3 (s), 128.1 (d), 128.0 (d), 126.0 (d), 47.3 (t), 47.1 (d), 42.9 (q), 32.9 (t), 31.0 (t), 30.4 (d), 26.4 (t); m/z (EI) 230 (M$^+$, 6%, $C_{16}H_{22}O$ requires 230), 172 (100), 148 (56), 105 (39%); Found: C, 83.10; H, 9.77%. Calculated for $C_{16}H_{22}O$; C, 83.43; H, 9.63%.

4-(2-Furyl)-3-butanone (25a)[23]: The reaction was carried out according to **Standard Procedure A** as described for 3-(2-furyl)-1-cyclohexanone (11a) using furan (0.44 mL, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and methylvinylketone (0.33 mL, 4.0 mmol) to give a crude residue, which was purified by column chromatography on silica using 15% diethyl ether-light petroleum as eluent to give the ketone (510 mg, 92%) as a colourless oil. ν_{max} (film) / cm^{-1} 1718, 1508, 1413, 1364, 1165, 1008; δ_H (200 MHz, $CDCl_3$) 7.14 (1H, dd, *J* = 2.0, 0.8 Hz, OCRC$\underline{H}$), 6.12 (1H, dd, *J* = 3.3, 2.0 Hz, OCHC$\underline{H}$), 5.84 (1H, dd, *J* = 3.3, 0.8 Hz, OC$\underline{H}$CH), 2.82-2.58 (4H, m, C$\underline{H}_2$), 2.02 (3H, s, COC$\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 207.2 (s), 154.4 (s), 141.0 (d), 110.1 (d), 105.1 (d), 41.6 (t), 29.8 (q), 22.1 (t); m/z (EI) 138 (M$^+$, 66%, $C_8H_{10}O_2$ requires 138), 95 (56), 81 (100%); Found: C, 69.31; H, 7.33%. Calculated for $C_8H_{10}O_2$; C, 69.54; H, 7.29%.

4-Cyclohexyl-2-butanone (25b)[24]: The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (1.26 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and methylvinylketone (0.33 mL, 4.0 mmol) to give a crude residue, which was then purified further by column chromatography on silica using 5% diethyl ether-light petroleum as eluent to give the ketone (500 mg, 81%) as a colourless oil. ν_{max} (film) / cm^{-1} 1719, 1449, 1357, 1162; δ_H (200 MHz, $CDCl_3$) 2.38 (2H, t, *J* = 7.5 Hz, C$\underline{H}_2$CO), 2.09 (3H, s, C$\underline{H}_3$CO), 1.70-1.55 (5H, m, C$\underline{H}$), 1.45-1.38 (2H, m, C$\underline{H}_2$), 1.20-1.05 (4H, m, C$\underline{H}$), 0.95-0.80 (2H, m, C$\underline{H}$); δ_C (50 MHz, $CDCl_3$) 209.5 (s), 41.3 (t), 37.2 (d), 33.0 (t), 31.2 (t), 29.8 (q), 26.5 (t), 26.2 (t); m/z (EI) 154 (M$^+$, 5%, $C_{10}H_{18}O$ requires 154), 136 (8), 121 (16), 96 (64), 43 (100%); Found: C, 77.47; H, 11.88%. Calculated for $C_{10}H_{18}O$; C, 77.87; H, 11.76%.

5-(2-Furyl)-3-hexanone (27a): The reaction was carried out according to **Standard Procedure A** as described for 3-(2-furyl)-1-cyclohexanone (11a) using furan (0.44 mL, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and (*E*)-hex-4-en-3-one (0.46 mL, 4.0 mmol) to give a crude residue. This residue was further purified by column chromatography on silica using 10% diethyl ether-light petroleum as eluent to give the ketone (630 mg, 95%) as a colourless oil. ν_{max} (film) / cm^{-1} 1714, 1508, 1459, 1413, 1148, 1011; δ_H (200 MHz, $CDCl_3$) 7.23 (1H, dd, *J* = 1.8, 0.8 Hz, OCRC$\underline{H}$), 6.20 (1H, dd, *J* = 3.3, 1.8 Hz, OCHC$\underline{H}$), 5.92 (1H, dd, *J* = 3.3, 0.8 Hz, OC$\underline{H}$CH), 3.47-3.26 (1H, m, ArC$\underline{H}$), 2.76 (1H, dd, *J* = 16.3, 6.0 Hz, CHC$\underline{H}_2$), 2.48 (1H, dd, *J* = 16.3, 7.8 Hz, CHC$\underline{H}_2$), 2.32 (2H, t, *J* = 7.5 Hz, C$\underline{H}_2$CH$_3$), 1.18 (3H, d, *J* = 7.0 Hz, CHC$\underline{H}_3$), 0.97 (3H, t, *J* = 7.5 Hz, CH$_2$C$\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 209.9 (s), 159.0 (s), 140.9 (d), 110.0 (d), 103.7 (d), 48.0 (t), 36.4 (t), 28.9 (d), 18.9 (q), 7.6 (q); m/z (EI) 166.0993 (M$^+$, 30%, $C_{10}H_{14}O_2$ requires 166.0993), 137 (20), 109 (47), 95 (100%).

5-Cyclohexyl-3-hexanone (27b)[21]: The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (1.26 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and (*E*)-hex-4-en-3-one (0.46 mL, 4.0 mmol) to give a crude residue. The crude oil was then purified further by column chromatography on silica using 2% diethyl ether-light petroleum as eluent to give the ketone (630 mg, 87%) as colourless oil. ν_{max} (film) / cm^{-1} 1714, 1449, 1413, 1377, 1114; δ_H (200 MHz, $CDCl_3$) 2.51-2.32 (3H, m, C$\underline{H}$), 2.16 (1H, dd, *J* = 15.8, 9.1 Hz, C$\underline{H}$CH$_3$), 2.00-1.82 (1H, m, C$\underline{H}$), 1.80-1.53 (5H, m, C$\underline{H}$), 1.32-0.90 (6H, m, C$\underline{H}$), 1.03 (3H, t, *J* = 7.3 Hz, CH$_2$C$\underline{H}_3$), 0.80 (3H, d, *J* = 15.8 Hz, CHC$\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 212.0 (s), 47.1 (t), 42.7 (d), 36.3 (t), 34.2 (d), 30.3 (t), 29.0 (t), 26.7 (t), 26.6 (t), 26.6 (t), 16.6 (q), 7.8 (q); m/z (EI) 182 (M^+, 1%, $C_{12}H_{22}O$ requires 182), 153 (16), 135 (40), 110 (100%); Found: C, 78.96; H, 12.38%. Calculated for $C_{12}H_{22}O$; C, 79.06; H, 12.16%.

9-Chloro-5-methylnonan-3-one (27c): The reaction was carried out according to **Standard Procedure B** using 4-chlorobutyl iodide (1.31 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and (*E*)-hex-4-en-3-one (0.46 mL, 4.0 mmol) to give a crude residue. This residue was treated with TBAF as described for 3-(1-Methyl-1*H*-2-pyrrolyl)-1-cyclohexanone (11c) and then purified further by column chromatography on silica using 2% diethyl ether-light petroleum as eluent to give the chloroketone (540 mg, 71%) as a colourless oil. ν_{max} (film) / cm^{-1} 1714, 1459, 1377, 1114; δ_H (200 MHz, $CDCl_3$) 3.53 (2H, t, *J* = 6.5 Hz, C$\underline{H}_2$Cl), 2.46-2.17 (4H, m, C$\underline{H}_2$CO), 2.02 (1H, m, C$\underline{H}$), 1.76 (2H, app. quin., *J* =7 Hz, C$\underline{H}_2$CH$_2$Cl), 1.53-1.10 (4H, m, C$\underline{H}_2$), 1.04 (3H, t, *J* = 7.3 Hz, C$\underline{H}_3$CH$_2$), 0.89 (3H, d, *J* = 6.5 Hz, CHC$\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 211.4 (s), 49.7 (t), 45.0 (t), 36.5 (t), 36.0 (t), 32.5 (t), 29.0 (d), 24.2 (t), 19.7 (q), 7.7 (q); m/z (EI) 190 (M^+, 4%, $C_{10}H_{19}OCl$ requires 190), 163 (8), 161 (23), 97 (27), 72 (100%); Found: C, 62.89; H, 10.18%. Calculated for $C_{10}H_{19}OCl$; C, 62.98; H, 10.04%.

Ethyl 6-(formyl)decanoate (28): The reaction was carried out according to **Standard Procedure B** using ethyl 4-iodobutanoate (1.45 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and 2-butyl acrolein (0.53 mL, 4.0 mmol). The reaction mixture was poured into a saturated aqueous ammonium chloride solution (50 mL) and extracted with diethyl ether (3x50 mL). The combined ethereal extracts were washed with brine (50 mL) and dried. Silica (10g) was added and the resulting mixture stirred for 1 h to hydrolyze the silyl enol ether. After filtration and evaporation of the solvent under reduced pressure, the residue was further purified by column chromatography on silica using 15% diethyl ether-light petroleum as eluent to give the aldehyde (650 mg, 71%) as a colourless oil. ν_{max} (film) / cm^{-1} 1736, 1706, 1465, 1375, 1184; δ_H (200 MHz, $CDCl_3$) 9.54 (1H, d, *J* = 3.0 Hz, C$\underline{H}$O), 4.05 (2H, t, *J* = 7.2 Hz, OC$\underline{H}_2$CH$_3$), 2.20 (1H, t, *J* = 7.4 Hz, C$\underline{H}$CHO), 2.25-2.10 (1H, m, C$\underline{H}$), 1.70-1.18 (13H, m, C$\underline{H}$), 1.23 (3H, t, *J* = 7.2 Hz, OCH$_2$C$\underline{H}_3$), 0.82 (3H, t, *J* = 6.8 Hz, CH$_2$C$\underline{H}_3$); δ_C (75 MHz, $CDCl_3$) 205.3 (s), 173.5 (d), 60.2 (t), 51.7 (d), 34.0 (t), 29.1 (t), 28.5 (t), 28.4 (t), 26.5 (t), 25.0 (t), 22.7 (t), 14.2 (q), 13.8 (q); m/z (EI) 200.1769 (M-CO$^+$, 9%, $C_{12}H_{24}O_2$ requires 200.1768), 171 (14), 152 (24), 128 (66), 101 (100%).

Butyl 7-(*tert*-butylcarbonyloxy)heptanoate (30): The reaction was carried out according to **Standard Procedure B** using 4-iodobutyl pivalate (1.70 g, 6 mmol), trimethylsilyl bromide (1.06 mL, 8.0 mmol), NMP (1 mL) and butyl acrylate (0.57 mL, 4.0 mmol) to give a crude residue after 48 h, which was then purified further by column chromatography on silica using 8% diethyl ether-light petroleum as eluent to give the diester (780 mg, 68%) as a colourless oil. ν_{max}(film) / cm^{-1} 1732, 1480, 1462, 1285, 1159; δ_H (200 MHz, $CDCl_3$) 4.02-3.88 (4H, m, $C\underline{H}_2O$), 2.20 (2H, t, J = 7.4 Hz, $C\underline{H}_2CO$), 1.60-0.70 (15H, m, $C\underline{H}$), 1.09 (9H, s, $C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 178.5 (s), 173.7 (s), 64.2 (t), 64.1 (t), 38.7 (s), 34.2 (t), 30.6 (t), 29.1 (t), 28.7 (t), 26.9 (q), 25.6 (t), 24.8 (t), 19.1 (t), 13.6 (q); m/z (EI) 213.1490 (M^+-C_4H_9O, 2%, $C_{12}H_{21}O_3$ requires 213.1489), 184 (5), 173 (13), 159 (15), 85 (31), 57 (100%).

2-Cyclohexylmethylhexanal (32)[25]: The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (1.26 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and 2-butylacrolein (0.53 mL, 4.0 mmol) and worked up with TBAF as described for 3-(1-Methyl-1*H*-2-pyrrolyl)-1-cyclohexanone (11c), to give a crude residue which was purified further by column chromatography on silica using 2% diethyl ether-light petroleum as eluent to give the aldehyde (530 mg, 68%) as a colourless oil. ν_{max} (film) / cm^{-1} 1706, 1449, 1292, 1274, 1187; δ_H (200 MHz, $CDCl_3$) 9.52 (1H, d, J = 3.5 Hz, $C\underline{H}O$), 2.42-2.24 (1H, m, $C\underline{H}CHO$), 1.78-1.46 (7H, m, $C\underline{H}$), 1.42-1.12 (10H, m, $C\underline{H}$), 0.96-0.82 (5H, m, $C\underline{H}$); δ_C (50 MHz, $CDCl_3$) 205.7 (s), 49.4 (d), 36.8 (d), 35.6 (t), 33.7 (t), 33.2 (t), 29.2 (t), 26.5 (t), 26.2 (t), 22.7 (t), 13.8 (q); m/z (EI) 166.1721 (M-CH_2O^+, 14%, $C_{12}H_{23}$ requires 166.1721), 109 (41), 96 (46), 82 (100%).

2-(1-Nitromethylpropyl)furan (34a)[26]: The reaction was carried out according to **Standard Procedure A** as described for 3-(2-furyl)-1-cyclohexanone (11a) using trimethylsilylmethyl iodide (1.67 g, 7.8 mmol), furan (0.53 g, 7.8 mmol), trimethylsilyl chloride (1.32 mL, 10.4 mmol), NMP (2 mL) and 1-nitrobutene (520 mg, 5.2 mmol) for 48h, to give a crude residue which was purified by column chromatography on silica using 2% diethyl ether-light petroleum as eluent to give the nitroalkane (430 mg, 64%) as a colourless oil. ν_{max} (film) / cm^{-1} 1556, 1380, 1150, 1011; δ_H (200 MHz, $CDCl_3$) 7.29 (1H, dd, J = 1.8, 0.7 Hz, $OC\underline{H}CH$), 6.24 (1H, dd, J = 3.1 Hz, 1.8 Hz, $OCHC\underline{H}$), 6.08 (1H, dd, J = 3.1, 0.7 Hz, $OCRC\underline{H}$), 4.62-4.42 (2H, m, $C\underline{H}_2NO_2$), 3.53-3.38 (1H, m, $ArC\underline{H}$), 1.80-1.58 (2H, m, $C\underline{H}_2CH_3$), 0.84 (3H, t, J = 7.5 Hz, $CH_2C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 152.4 (s), 142.1 (d), 110.2 (d), 107.2 (d), 78.2 (t), 39.4 (d), 24.1 (t), 11.2 (q); m/z (EI) 169.0737 (M^+, 5%, $C_8H_{11}NO_3$ requires 169.0737), 122 (100%), 94 (60).

1-(1-Nitromethylpropyl)cyclohexane (34b): The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (1.26 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and 1-nitrobutene (404 mg, 4.0 mmol) to give a crude residue, which was then purified further by column chromatography on silica using 2% diethyl ether-light petroleum as eluent to give the nitroalkane (560 mg, 76%) as a colourless oil. ν_{max} (film) / cm^{-1} 1552, 1449, 1384, 1250, 1098; δ_H (300 MHz, $CDCl_3$) 4.38 (1H, dd, J = 12.0, 6.5 Hz, $C\underline{H}_2NO_2$), 4.25 (1H, dd, J = 12.0, 7.5 Hz, $C\underline{H}_2NO_2$), 2.04-0.98 (14H, m, $C\underline{H}$), 0.92 (3H, t, J = 7.4 Hz, $C\underline{H}_3$);δ_C (75 MHz, $CDCl_3$) 77.7 (t), 44.5 (d), 38.6 (d), 29.8 (t), 29.4 (t), 26.6 (t), 26.5 (t), 21.5 (t), 11.4 (q); m/z (EI) 169.1468 (M-O^+, 7%, $C_{10}H_{19}NO$ requires 169.1469), 95 (18), 83 (69), 55 (100%).

2-Methyl-3-nitromethylpentane (34c): The reaction was carried out according to **Standard Procedure B** using *iso*-propyl iodide (1.52 g, 9 mmol), trimethylsilylmethyllithium (9 mmol), trimethylsilyl chloride (1.15 mL, 9.0 mmol), NMP (1 mL) and 1-nitrobutene (455 mg, 4.5 mmol), for 36 h, to give a crude residue, which was then purified further by column chromatography on silica using 1% diethyl ether-light petroleum as eluent to give the nitroalkane (420 mg, 64%) as a colourless oil.ν_{max} (film) / cm^{-1} 1556, 1466, 1384, 1261, 1097, 1022; δ_H (200 MHz, $CDCl_3$) 4.37 (1H, dd, J = 12.0, 6.5 Hz, $C\underline{H}_2NO_2$), 4.26 (1H, dd, J = 12.0, 7.2 Hz,

$C\underline{H}_2NO_2$), 2.12-1.95 (1H, m, $C\underline{H}CH_2NO_2$), 1.90-1.70 (1H, m, $C\underline{H}(CH_3)_2$), 1.60-1.19 (2H, m, $C\underline{H}_2CH_3$), 0.94 (3H, d, *J* = 7.4 Hz, $CHC\underline{H}_3$), 0.91 (3H, d, *J* = 7.4 Hz, $CHC\underline{H}_3$), 0.90 (3H, t, *J* = 6.8 Hz, $CH_2C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 77.5 (t), 44.9 (d), 28.0 (d), 21.2 (t), 18.9 (q), 18.6 (q), 11.2 (q); m/z (EI) 98 (M^+-HNO_2, 3%, C_7H_{14} requires 98), 84 (8), 69 (21), 57 (100%); Found: C, 57.84; H, 10.39; N, 9.72%. Calculated for $C_7H_{15}NO_2$; C, 57.90; H, 10.41; N, 9.65%.

Butyl 3-cyclohexylpropanoate (36a): The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (1.26 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and butyl acrylate (0.57 mL, 4.0 mmol) to give a crude residue, which was then purified further by column chromatography on silica using 2.5% diethyl ether-light petroleum as eluent to give the ester (0.86 g, 99%) as a colourless oil. ν_{max} (film) / cm^{-1} 1738, 1450, 1310, 1166; δ_H (200 MHz, $CDCl_3$) 4.05 (2H, t, *J* = 6.5 Hz, $OC\underline{H}_2$), 2.28 (2H, t, *J* = 7.0 Hz, $C\underline{H}_2CO$), 1.75-1.10 (17H, m, $C\underline{H}$), 0.94 (3H, t, *J* = 7.0 Hz, $C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 174.2 (s), 64.0 (t), 37.2 (d), 32.9 (t), 32.4 (t), 31.9 (t), 30.7 (t), 26.5 (t), 26.2 (t), 19.1 (t), 13.7 (q); m/z (EI) 212.1779 (M^+, 3%, $C_{13}H_{24}O_2$ requires 212.1779), 183 (6), 157 (28), 139 (34), 129 (51), 97 (62), 56 (100%).

Butyl 7-chlorohexanoate (36b): The reaction was carried out according to **Standard Procedure B** using 4-chlorobutyl iodide (1.31 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and butyl acrylate (0.57 mL, 4.0 mmol) to give a crude residue which was then purified further by column chromatography on silica using 2% diethyl ether-light petroleum as eluent to give the chloroester (670 mg, 76%) as a colourless oil. ν_{max} (film) / cm^{-1} 1737, 1463, 1306, 1250, 1180; δ_H (200 MHz, $CDCl_3$) 4.00 (2H, t, *J* = 6.6 Hz, $OC\underline{H}_2$), 3.46 (2H, t, *J* = 6.7 Hz, $C\underline{H}_2Cl$), 2.23 (2H, t, *J* = 7.4 Hz, $C\underline{H}_2CO$), 1.84-1.18 (12H, m, $C\underline{H}$), 0.86 (3H, t, *J* = 7.2 Hz, $C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 173.7 (s), 64.1 (t), 44.9 (t), 34.1 (t), 32.3 (t), 30.6 (t), 28.3 (t), 26.4 (t), 24.7 (t), 19.1 (t), 13.7 (q); m/z (EI) 165 (M-$C_4H_8^+$, 24%, $C_7H_{13}O_2Cl$ requires 165), 149 (11), 147 (41), 83 (32), 56 (100%); Found: C, 59.75; H, 9.59%. Calculated for $C_{11}H_{21}O_2Cl$; C, 59.85; H, 9.59%.

1-Butyl 7-ethyl pimelate (36c): The reaction was carried out according to **Standard Procedure B** using ethyl 4-iodobutanoate (1.45 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and butyl acrylate (0.57 mL, 4.0 mmol) to give a crude residue. The crude oil was then purified further by column chromatography on silica using 15% diethyl ether-light petroleum as eluent to give the diester (840 mg, 86%) as a colourless oil. ν_{max} (film) / cm^{-1} 1737, 1465, 1373, 1249, 1180; δ_H (200 MHz, $CDCl_3$) 4.14-3.94 (4H, m, $OC\underline{H}_2$), 2.27 (4H, app. t, *J* = 7.5 Hz, $C\underline{H}_2CO$), 1.68-1.47 (6H, m, $C\underline{H}_2$), 1.40-1.16 (7H, m, $C\underline{H}_2$ and $C\underline{H}_3$), 0.88 (3H, t, *J* = 7.5 Hz, $C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 173.5 (s), 173.4 (s), 64.4 (t), 60.5 (t), 33.9 (2xt), 30.5 (t), 28.4 (t), 24.5 (t), 24.4 (t), 19.0 (t), 14.1 (q), 13.5 (q); m/z (EI) 244 (M^+, 1%, $C_{13}H_{24}O_4$ requires 244), 199 (31), 171 (100%); Found: C, 63.61; H, 10.04%. Calculated for $C_{13}H_{24}O_4$; C, 63.90; H, 9.90%.

Ethyl 6-formyl-5-methylheptanoate (38a): The reaction was carried out according to **Standard Procedure B** using ethyl 4-iodobutanoate (1.45 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and (*E*)-2-methylbutenal (0.39 mL, 4.0 mmol) to give a crude residue. This residue was then purified further by column chromatography on silica using 20% diethyl ether-light petroleum as eluent to give the ester (410 mg, 51%) as a colourless oil, as a mixture of diastereomers (3:2). ν_{max} (film) / cm^{-1} 1732, 1461, 1375, 1246,

1179. Major diastereomer: δ_H (200 MHz, $CDCl_3$) 9.61 (1H, d, *J* = 2.0 Hz, $C\underline{H}O$), 4.09 (2H, q, *J* = 7.2 Hz, $C\underline{H}_2CH_3$), 2.34-2.20 (3H, m, $C\underline{H}CO$ and $C\underline{H}_2CO_2Et$), 2.15-1.28 (5H, m, $C\underline{H}$), 1.22 (3H, t, *J* = 7.2 Hz. $OCH_2C\underline{H}_3$), 1.02 (3H, d, *J* = 7.0 Hz, $CHC\underline{H}_3$), 0.96 (3H, d, *J* = 7.0 Hz, $CHC\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 205.4 (d), 173.4 (s), 60.2 (t), 51.3 (d), 34.2 (t), 33.5 (d), 32..5 (t), 22.5 (t), 17.2 (q), 14.2 (q), 9.8 (q). Minor diastereomer: δ_H (200 MHz, $CDCl_3$) 9.58 (1H, d, *J* = 1.3 Hz, $C\underline{H}O$), 4.10 (2H, q, *J* = 7.2 Hz, $OC\underline{H}_2CH_3$), 2.34-2.20 (3H, m, $C\underline{H}CO$ and $C\underline{H}_2CO_2Et$), 2.15-1.28 (5H, m, $C\underline{H}$), 1.23 (3H, t, *J* = 7.2 Hz, $OCH_2C\underline{H}_3$), 0.97 (3H, d, *J* = 7.0 Hz, $CHC\underline{H}_3$), 0.81 (3H, d, *J* = 6.7 Hz, $CHC\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 205.3 (d), 173.4 (s), 60.2 (t), 50.3 (d), 34.2 (t), 34.0 (t), 33.3 (d), 22.7 (t), 17.2 (q), 15.3 (q), 8.0 (q). m/z (EI) 172.1456 ($M-CO^+$, 11%, $C_{10}H_{20}O$ requires 172.1456), 155 (19), 143 (62), 109 (54), 55 (100%).

3-Cyclohexyl-2-methylbutanal (38b): The reaction was carried out according to **Standard Procedure B** using cyclohexyl iodide (1.26 g, 6 mmol), trimethylsilyl chloride (1.02 mL, 8.0 mmol), NMP (1 mL) and (*E*)-2-methylbutenal (0.39 mL, 4.0 mmol) to give a crude residue, which was then purified further by column chromatography on silica using 3% diethyl ether-light petroleum as eluent to give the aldehyde (610 mg, 91%) as a colourless oil, as a mixture of diastereomers (3:2). ν_{max} (film) / cm^{-1} 1726, 1449, 1285, 1267, 1188. Major diastereomer: δ_H (200 MHz, $CDCl_3$) 9.64 (1H, d, *J* = 2.8 Hz, $C\underline{H}O$), 2.42-2.26 (1H, m, $C\underline{H}CHO$), 1.85-1.10 (12H, m, $C\underline{H}$), 1.05 (3H, d, *J* = 6.8 Hz, $C\underline{H}_3$), 0.89 (3H, d, *J* = 7.0 Hz, $C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 206.1 (d), 49.6 (d), 39.7 (d), 39.3 (d), 31.8 (t), 28.4 (t), 26.7 (t), 26.5 (t), 26.5 (t), 14.0 (q), 11.6 (q). Minor diastereomer: δ_H (200 MHz, $CDCl_3$) 9.59 (1H, d, *J* = 1.5 Hz, $C\underline{H}O$), 2.57-2.42 (1H, m, $C\underline{H}CHO$), 1.85-1.10 (12H, m, $C\underline{H}$), 0.96 (3H, d, *J* = 7.0 Hz, $C\underline{H}_3$), 0.76 (3H, d, *J* = 7.0 Hz, $C\underline{H}_3$); δ_C (50 MHz, $CDCl_3$) 206.1 (d). 48.2 (d), 40.3 (d), 37.6 (d), 31.3 (t), 29.6 (t), 26.5 (t), 26.4 (t), 26.4 (t), 12.5 (q), 8.2 (q). m/z (EI) 138.1402 ($M-CH_2O^+$, 12%, $C_{10}H_{18}$ requires 138.1403), 127 (13), 111 (100%).

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