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Intramolecular Carbometallation of Organozinc Reagents.

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abstract: The intramolecular cyclization reaction of primary or secondary alkenylzincs leads to a cyclopentylmethylzinc derivatives in a totally regiospecific 5-exo-trig cyclization in the presence of a highly sensitive function.

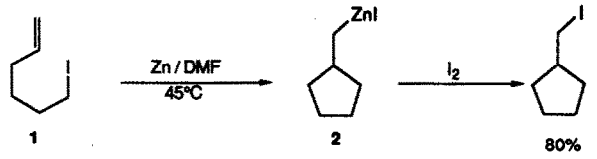
Regio and stereoselective construction of carbocycles is one of the most important operation in organic synthesis[1]. Intramolecular additions of cations[2] or radicals[3] to carbon-carbon double bonds are a topic of intense current interest. Such reactions are particularly valuable for the formation of five or six-membered rings in situations where such transformations must be effected in the presence of sensitive functionalities. A major disadvantage of this otherwise powerful methodology is the fact that the produced radical is difficult to trap in an intermolecular reaction, to give a functionalized product[4] : an alternative to these radical cyclizations should be provided by the cyclization of various organometallic derivatives. Despite the pioneering work of Richey and Hill on the cyclization of Grignard reagents[5] and the following studies of different authors showing the high propensity of various organometallics of 5-hexenyl type to cyclize (m = Li, Mg, Al, Ga, In)[6], the controversies about the mechanism of the reaction as well as the lack of method to produce in high yield such organometallics, with a minimum of side product formation, and without the intervention of free-radical process, have limited the scope of this reaction. The development of a clean, rapid halogen-metal exchange reaction[7] by treatment of an appropriate iodoalkene with terbutyllithium provides now an anionic route to metallated carbocycles[8]. Since then, some developments have been brought in the intramolecular carbocyclization from methyl seleno compounds[9], Shapiro degradation of trisylhydrazones[10], reductive lithiation of phenyl thioethers[11], tin-lithium exchange[12], titanium mediated carbocyclization[13], and carbon-carbon bond cleavage[14].

However, all these organometallic reagents, due to the highly reactive nature of the carbon-metal bond often preclude the presence of functional groups. Thus, the development of methods allowing the preparation of functionalized organometallic compounds is of great importance[15a]. Recent advances[15b,15c] in the accessibility of

organozinc compounds and in the applications of these less reactive organometallic reagents in synthetic chemistry have prompted an examination of the reaction of 6-iodo-1-hexene **1** with zinc.

Carbocyclization of primary organozinc reagents.

Thus, **1** reacts with zinc at 40°C in DMF to afford the 5-hexen-1-ylzinc iodide and cyclizes to the five-membered ring **2** in a totally regiospecific 5-exo-trig cyclization, the cyclized organozinc iodide being characterized by iodinolysis and the corresponding product isolated in 80% yield.



Scheme 1

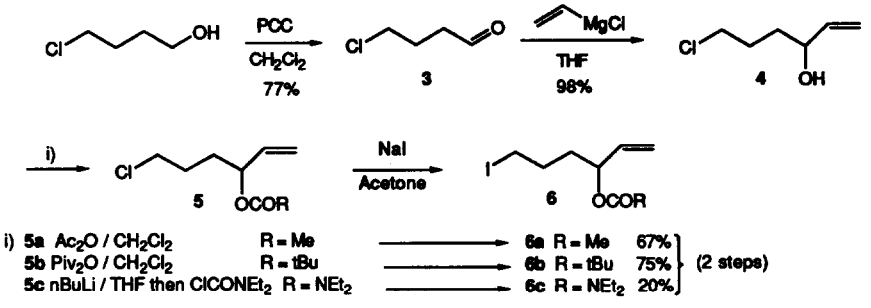
However, cyclization was slow in coordinating solvents such DMF or THF, which are required for oxidative insertion of zinc, and we have observed that decreasing the Lewis basicity of the solvent considerably speeds up the reaction and allows to carry out the carbocyclisation at lower temperatures. Thus, we decided to generate a very reactive zinc metal by the reduction of zinc bromide with lithium naphtalenide in THF[17] (eq 1)

$$ZnBr_2 + Li,\ Naphthalene \longrightarrow Zn^* + LiBr + Naphthalene \qquad (eq.\ 1)$$

The highly reactive zinc produced by this reaction is washed several times with dry ether and then allows the easy oxidative insertion in an alkyl iodide in ether (eq 2) :

$$Zn^* + RI \xrightarrow{Et_2O} RZnI \qquad (eq.2)$$

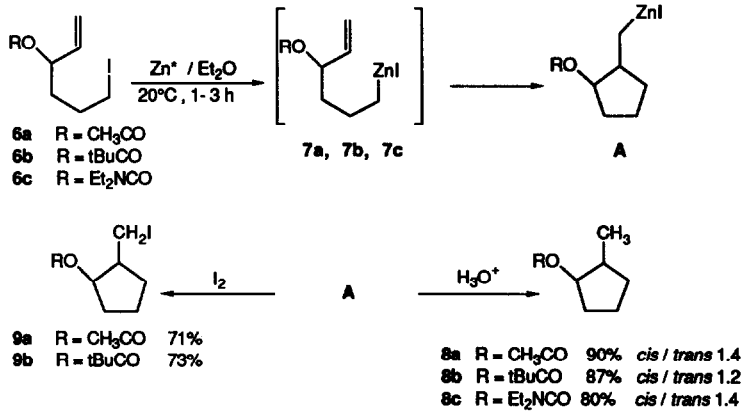
Having in hand an efficient way to produce activated zinc in ether, we then decided to study the cyclization of 5-hexenyl zinc iodides bearing a sensitive function in the allylic position. In order to test the possibility of this proposal, several iodo derivatives were prepared as shown in the following scheme :



Scheme 2

Oxidation[18] of commercially available 4-chloro-1-butanol with PCC in CH_2Cl_2 leads to 4-chloro-1-butanal **3** which upon treatment with vinylmagnesium chloride affords the secondary alcohol **4**. The latter is respectively functionnalized with acetic anhydride, pivaloic anhydride or lithiated and allowed to react with N,N-diethyl-carbamoylchloride[19]. Compounds **5a, 5b, 5c** were subjected to iodine/chlorine exchange using NaI in refluxing acetone.

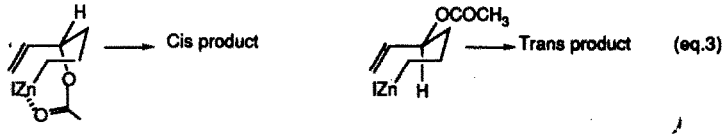
Reactions of iodides **6a, 6b, 6c** were generally performed with a 2 to 3 fold excess of activated zinc in Et_2O at room temperature. In all cases, we observed a clean and rapid insertion of activated zinc metal into the carbon-iodine bond leading to the acyclic zinc derivatives **7a, 7b, 7c** in low concentration, which cyclized rapidly at room temperature in less than 1h prior to the addition of the electrophiles which served to deliver functionnalized methylcyclopentanes[20] in good to excellent chemical yields.



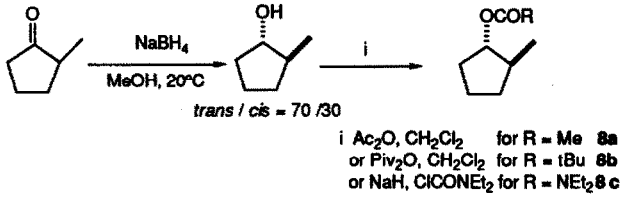
Scheme 3

Although alkenes are not generally thought of as good sites of nucleophilic attack, when an ester function is present, these results clearly show that organozinc iodides are able to

cyclize[21], for the first time, with functionnalized derivatives. The high propensity of organozinc iodide to form a metallated cyclic product is probably due to the internal metal-double bond interaction[22]. However, the diastereomeric ratio is disappointing (*cis /trans* = 1.4 for **8a** and **8c** and 1.2 for **8b**). This can be explained if one takes into account the chair-like transition state which has been proposed[28] and supported by theoretical calculations for this type of process[23,8h,8i]. In terms of such a model, the lack of stereocontrol is attributed to a mixture of steric and chelation interaction : the acetoxy group may occupy an unfavorable axial position in which it chelates the zinc atom. Unfortunately, even the more highly chelating allylic carbamate does not improve the diastereomeric ratio.

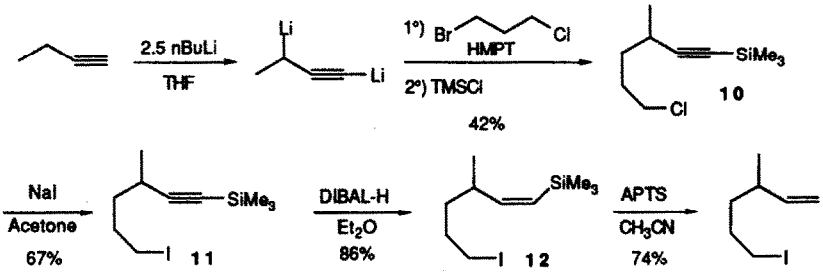


The stereochemistry of the cyclized products were deduced from the literature data[30] for **8a** and from comparison with authentic samples prepared from 2-methylcyclopentanone[31] for **8b** and **8c**.



Scheme 4

For comparison purposes, we also examined the behaviour of the methyl substituted analogues, for which we have devised a new strategy of synthesis :

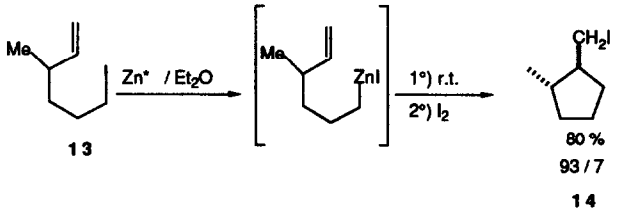


Scheme 5

The dimetallation of butyne[24] followed respectively by the introduction of 1 equivalent of 1-bromo-3-chloropropane and TMSCl leads to the alkyne **10** in 42% yield of isolated product. The transhalogenation followed by a semi-reduction of the alkyne **11** into the Z

vinyl silane **12** was carried out according to Zweifel[25], and finally the smooth desilylation[26] by treatment of the latter with APTS in CH_3CN leads to the desired 6-iodo-3-methyl-1-hexene **13** in good overall yield.

Olefinic organozinc iodides were generated at room temperature, as illustrated in scheme 6, by oxidative insertion of activated zinc in Et_2O, and underwent ring closure as shown by iodinolysis of the corresponding cyclized organometallic.

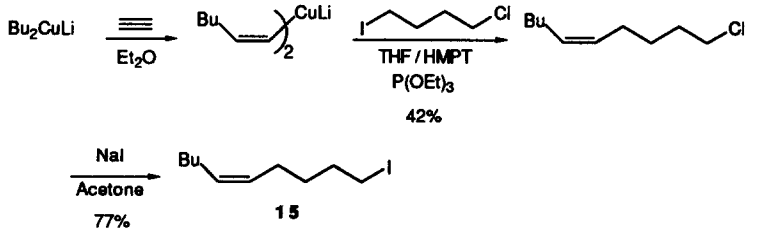


Scheme 6

The diastereomeric ratio as well as the chemical yield are the same in our zinc mediated cyclization as they are in the lithium mediated one[8c] (80%, *trans / cis* = 93/7). This result indicates clearly that the stereocontrol is attributed to steric interactions where the methyl group occupies a pseudoequatorial position in the cyclohexane chair-like transition state. The big discrepancy between a methyl group and a heteroatom in an allylic position has already been noted in a lithium carbocyclization[6b].

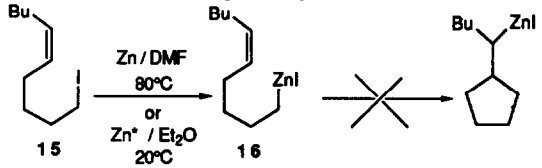
The trans isomer obtained upon cyclisation of **13** is the same as the one generated in the cyclization of substituted 5-hexen-1-yl radical[27], but in the case of the organometallic derivatives (organozinc halides and organolithiums), the cyclization is more stereoselective (*trans / cis* = 93 / 7) than the corresponding radical reactions (*trans / cis* = 82 / 18).

However, radical intermediates have been proposed [28,21c], in the reaction of alkyl halides with zinc, whereas a mechanistic study on the intramolecular conjugate addition reactions via organozinc compounds suggests that, only a small part of the cyclization product might result from a radical-mediated pathway[29], the major being anionic. In order to discriminate these two hypotheses, we investigated the carbocyclization of an organozinc iodide prepared as described before, on a 1,2-disubstituted double bond. Thus, (Z)-1-iodo-5-decene **15** was prepared according to the following scheme :



Scheme 7

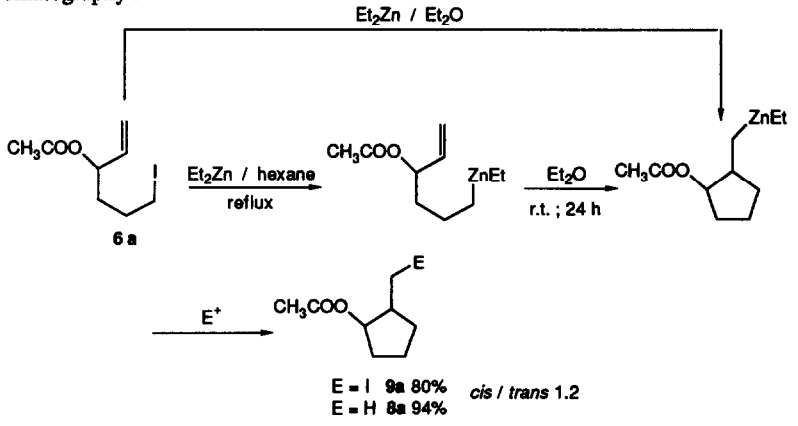
The organozinc iodide **16** was generated from the corresponding iodide **15**, but it does not cyclize to the five-membered ring upon standing for 12h at room temperature. Moreover, the pure Z stereochemistry of the double bond remained unchanged after the process. This ruled out a scenario that would have involved radical ring closure of **16** followed by reduction to the anion and ring opening since it would have led, at least, to partial equilibration of the double bond geometry.



Scheme 8

Another proof of the anionic nature of the carbocyclization was given by the following experiment : treatment of **6a** with activated zinc in ether at 0°C and quenching an aliquot with an 1N HCl solution, showed after 20 min the presence of the linear organozinc reagent to an extent of 30%. By warming to room temperature, the amount of this reduction product decreased while the amount of cyclization product increased concomitantly. The only explanation of these experimental results is that the cyclic product derives from an anionic cyclization.

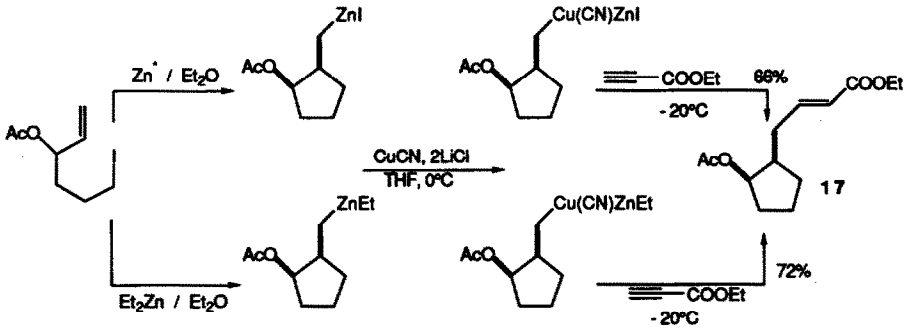
Recently, P. Knochel et al[21a,32] have reported that primary organic iodides undergo an iodine-zinc exchange reaction when treated with an excess of Et_2Zn (5 equiv., neat, 50-55°C, 10-40h) and several functional groups can be present in the organic iodides. In order to get further insights into the carbocyclization of dialkylzinc instead of organozinc iodides, we used **6a** as precursor. When **6a** was refluxed with Et_2Zn (2 equiv.) in hexane for 3h, the formation of the linear organozinc reagent occured to an extent of 70-80%, the balance consisting in the starting iodide (10-15%) and cyclized organozinc reagent (10-15%) as shown by hydrolysis of an aliquot and analysis by gas chromatography :



Scheme 9

Removal of hexane and addition of dry diethyl ether resulted in a complete cyclization reaction after 12 to 24 hours, a longer reaction time than the one observed with the organozinc *iodide*. Meanwhile, the diastereomeric ration is still low (*cis* / *trans* = 1.2). During this study, we have also observed that the same iodine-ethylzinc exchange reaction can be directly performed in Et_2O using Et_2Zn (2 equiv.) in 36 to 48 hours[33]. Notheworthy is the fact that ether is the solvent of choice for organozinc cyclization since at most 15% cyclization occured in refluxing hexane after 3 hours.

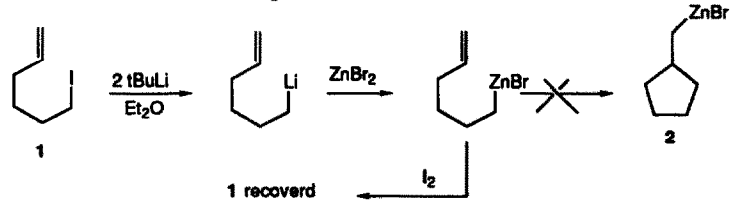
So, both methods (activated zinc of Rieke and Et_2Zn) allow the carbocyclization of hexenyl iodides with a sensitive function thanks to the less reactive nature of these organometallics. However, this lack of reactivity can be circumvented by transmetallation to a more reactive copper reagent by addition of copper salt[14,15,34].This organocopper derivative is especially convenient, since it can react with a variety of electrophiles :



Scheme 10

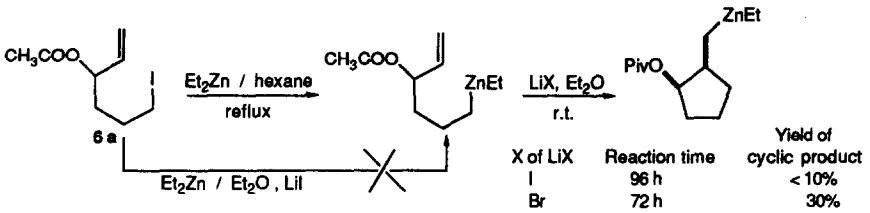
Thus, the bifunctional derivative were obtained in good chemical yield by 1,4-addition on ethylpropiolate.

Although the direct iodine to Zn exchange allows cyclisations of *functionalized* molecules, we studied the iodine to organolithium and to organozinc iodide exchanges of the simple 1-iodo-5-hexene, and noticed the tremendous importance of the nature of lithium halides present in the solution. Indeed, as shown in scheme 11, the cyclization somehow similar to that of scheme 1 does not operate any more, although performed in ether !. The only difference lies in the presence of LiI (formed in the first step[7]) and LiBr (formed in the transmetallation step).



Scheme 11

We, thus, decided to study the influence of lithium halides on the carbocyclization reaction . When **6a**, was stirred with Et_2Zn (2 equiv.) in the presence of LiI (2 equiv.) in dry ether, no exchange nor cyclization occured and the starting iodide was quantitatively recovered. In a second step, the linear organozinc reagent was generated in refluxing hexane, as previously described, and the desired lithium halides (1.5 to 2 equiv.) were added :



X of LiX	Reaction time	Yield of cyclic product
I	96 h	< 10%
Br	72 h	30%
Cl	48 h	> 90%

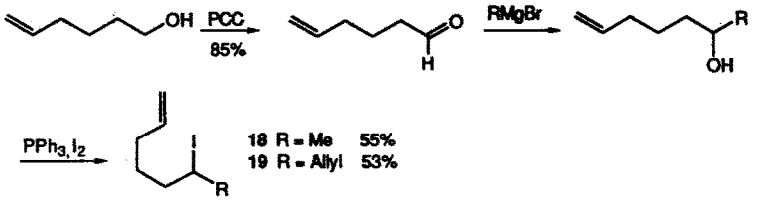
Scheme 12

No cyclization product was observed by addition of lithium iodide, only 20-30% with lithium bromide, even after 72h at room temperature, but the cyclization reached completion after usual reaction time with lithium chloride. These results clearly demonstrate the influence of lithium iodide and bromide on the reactivity of the linear reagent.

Lithium halides (Br or I) may well modify the Lewis character of the zinc atom, probably via a zincate species[35], and prevent the efficient coordination of the zinc atom to the double bond, coordination which is required for the carbocyclization. Thus, in the Rieke's method, it is essential to wash the active zinc thoroughly since the lithium naphtalenide reduction of zinc bromide also generates lithium bromide (see eq. 1) which is detrimental to the success of the reaction. Indeed, the insertion of Rieke's zinc in presence of LiBr leads to the linear organozinc iodide but not to the cyclic product.

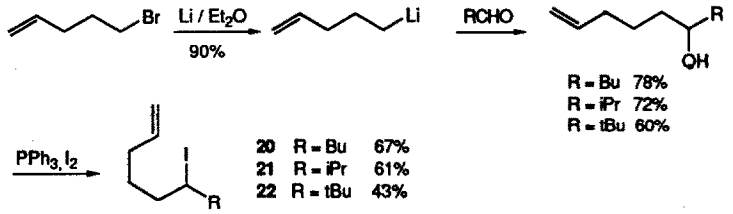
Carbocyclization of secondary organozinc reagents.

A severe limitation is observed when ω-ethylenic *secondary* organometallic reagents are used. Treatment of ω-ethylenic secondary iodides with *ter*BuLi at -78°C leads mainly to Wurtz type coupling and elimination[6c]. Furthermore, the stereoselectivity of the cyclisation is a function of the order of mixing the reagents[8h]. On the other hand, the intramolecular addition of ω-ethylenic secondary Grignard reagents requires harsh conditions[5e]. Notable exceptions are the cases of α-alkoxyalkyllithiums, α-aminoalkyllithiums[12,36], the metalla-ene reactions[37] and the ω-ethylenic propargylic zinc reagents[38]. Thus, by analogy with the carbocyclization of primary organozinc derivatives, we investigated the cyclization of secondary organozinc iodides. The secondary iodides have been prepared as follows for R = Me, allyl :

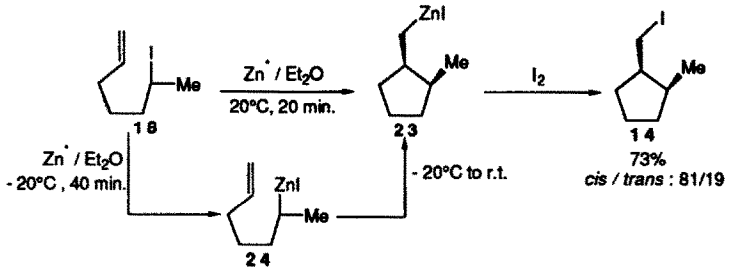


Oxidation[18] of 5-hexenol provided 5-hexenal which upon addition of Grignard reagents followed by conversion of the alcohol to the iodide[39] led respectively to **18** and **19** in 55 and 53 % yield from the aldehyde.

For the secondary alkyl iodides (R = Bu, iPr, tBu), the synthetic scheme was the following one : 5-bromopentene was converted to the lithium reagent which was added to various aldehydes and the corresponding alcohols converted to the iodides[39] :



Treatment of 6-iodo-1-heptene **18** with Rieke's zinc in ether, quantitatively leads to the cyclized organozinc iodide **23** in less than 20 min[40], as shown by iodinolysis of the reaction mixture[41] :

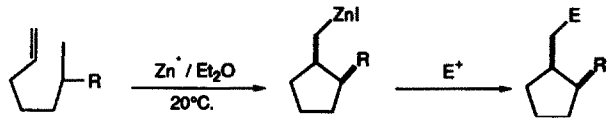


Scheme13

At lower temperatures, we have observed a clean and rapid oxidative insertion of activated zinc metal into the carbon-iodine bond leading to the acyclic zinc derivative **24** in 95% yield (as shown by comparison of hydrolysed and iodinolyzed aliquots) contaminated by 5% of cyclized product. The formation of the linear organozinc iodide **24** and its subsequent cyclization by warming to room temperature can be taken as a hint

to the absence of a one-electron transfer process in the cyclization. The scope of this cyclization is quite broad : alkyl groups can be primary, secondary and tertiary :

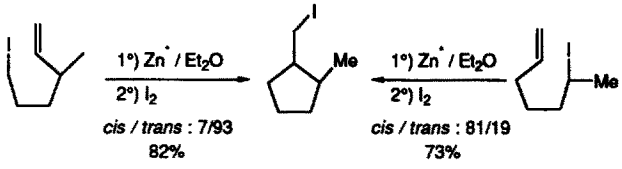
Table 1



Entry	R	Time[a]	E^+	Product[b] (Yield %)	*cis/trans*[c] ratio
1	Me	20 mn	I_2	**14** *cis*	81/19
	18			E=I (73)	
2	nBu	20 mn	H_3O^+	**25** E=H	73/27
	20			(60)	
3	nBu	20 mn	I_2	**26** E=I	73/27
	20			(68)	
4	iPr	2 h	I_2	**27** E=I	73/27[d]
	21			(78)	
5	t-Bu	3 h	I_2	**28** E=I	62/38[d]
	22			(60)	

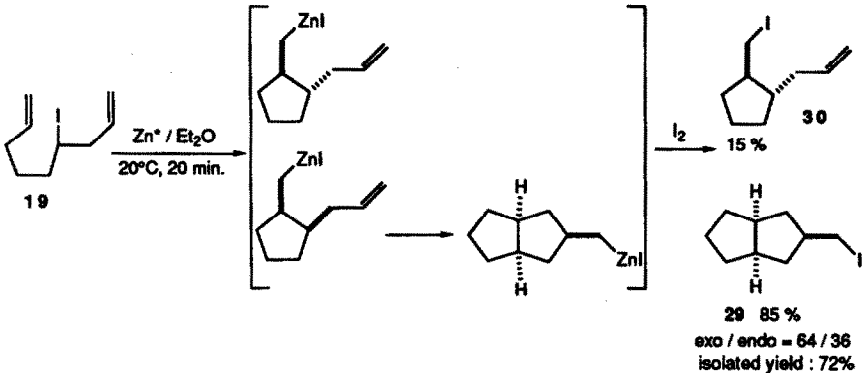
a) Necessary time for the transformation of linear organozinc iodide into the cyclic derivative.b) Yield of isolated product by chromatography on silica gel. c) The cis/trans ratio was determined by ^1H and ^{13}C NMR spectroscopy.d) The stereochemistry has been deduced from the preceding exemples.

These reactions are of synthetic value for the obtention, at will, of the two diastereomers, starting from the primary or the secondary iodides[41] :



Scheme 14

This method allows the performance of tandem-cyclization reactions. The dienic iodide **19** gives after intramolecular carbozincation and iodinolysis, the bicyclic product **29** (85%; cis-ring junction >99%, exo/endo = 64/36) and the monocyclic trans product **30** (15%) :

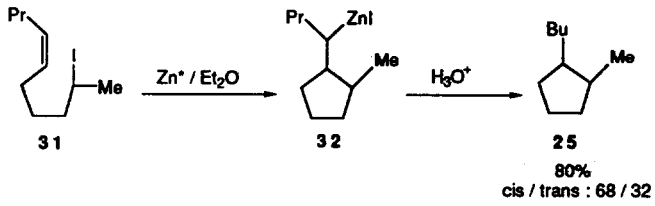


Scheme 15

In all these reactions, the cis stereoselectivity observed is attributed to steric interactions which favor a geometry in which the R substituent preferentially occupies an outside position in the chair-like transition state. The pronounced cis stereoselectivity of the reaction is opposite to the trans usually observed[6c,8h,5e,12,36]. It may be that organolithium or organomagnesium cyclizations, in contrast to the zinc one, proceed through a rather "product-like" transition state. The highly covalent nature of the carbon-zinc bond as well as the favorable intramolecular association of the zinc atom with the double bond[22] may explain the cis stereoselectivity observed here.

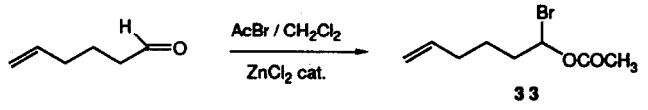
Scheme 16

However, the transition state leading to the cis isomer may be destabilized by nonbonded interactions between the alkyl group (R) and the incipient zinciomethylene unit. The steric bulk of the former may decrease the diastereoselectivity. This is effectively the case (compare entries 1, 3, 5, table I). Recently, it has been shown that various unsaturated secondary iodides undergo a radical cyclization in the presence of Et_2Zn and a catalytic amount of Pd^{II} salts providing the same organometallic, although the mechanism is totally different[42]. An other very promising result is that the secondary organozinc derivative **31** undergoes a smooth carbocyclization in ether, at room temperature, into a 1,2-*disubstituted* double bond to afford a new secondary zinc iodide[43] **32** in 80% yield, with a 68/32 *cis / trans* diastereomeric ratio, as shown by the hydrolyzed compound **25.**

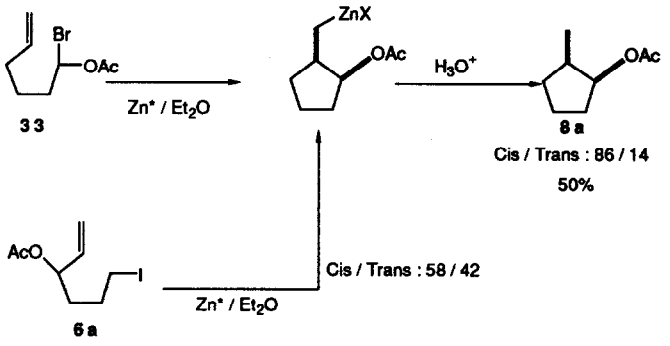


Scheme 17

Another very promising result comes from the cyclization of α-bromoalkyl acetate **33** which can be readily obtained according to Neuenschwander's method[44], and metallated according to P. Knochel at the α position to oxygen[45] :



Thus, the latter upon treatment with Zn* in ether leads to **8a** in moderate yields (the balance being the uncyclized material) but with a much better diastereomeric *cis / trans* ratio (86/44) than the one obtained (58/42) via the strategy depicted in scheme 3 :



Scheme 18

This approach constitutes a very interesting route to the synthesis of functionalized carbocycles, the moderate chemical yield in this reaction comes from the difficulty to obtain the starting material as a very pure compound.

Conclusions.

The results described above demonstrate that, with a method in hand for the facile preparation of organozinc reagents by direct insertion of zinc metal in Et_2O, or by using an iodine-zinc exchange reaction, the intramolecular cyclization reaction of *primary* or

secondary alkenylzincs leads to a cyclopentylmethylzinc derivatives in a totally regiospecific 5-exo-trig cyclization in the presence of a highly sensitive function.

EXPERIMENTAL SECTION

Experiments involving organometallics were carried out under a positive pressure of dry nitrogen. All glasswares were oven dried at 150°C overnight and assembled quickly while hot under a stream of nitrogen. Liquid nitrogen was used as a cryogenic fluid and all indicated temperatures, unless otherwise stated, refer to internal ones. Ether and THF were distilled from sodium benzophenone ketyl. Dichloromethane, triethylamine, N,N,N',N'-tetramethylethylenediamine (TMEDA), and trimethylchlorosilane (TMSCl) were distilled from calcium hydride. HMPA was dried from CaO and then distilled at 80°C (1mmHg) from calcium hydride. $ZnBr_2$ was melted under a stream of nitrogen and handled as 1M etheral solution . LiCl and LiBr were dried at 120°C at 0.1 mmHg for at least four hours before use. Dry LiI was purchased and used as received. $CuBr.Me_2S$ was prepared by dissolution of CuBr in dimethylsulfide, followed by precipitation with n-pentane. Organolithium and organomagnesium reagents were titrated with 2-butanol (1M in toluene) using respectively 1,10-phenantroline or 2,2'-biquinolyl as indicators[46]. NMR spectra have been recorded on either a JEOL GSX 400, BRUCKER AC 200, JEOL FX 90 Q, in $CDCl_3$. Chemical shifts are reported in part per million (ppm) relative to tetramethylsilane (TMS) as an internal standard (0.1 %) in ^1H NMR spectra. When a trimethylsilyl moiety was present within the molecule $CHCl_3$ itself was used as a reference. In ^{13}C NMR spectra, $CDCl_3$ (δ=77.2 ppm) has been used as a reference.

Cyclization of Functionalized Organozinc Reagents

4-Chloro-1-butanal (3)
A solution of freshly distilled 4-chloro-1-butanol (8 g, 73.7 mmol) in dry dichloromethane (20 ml) was added all at once to a suspension of pyridinium chlorochromate (23.8 g, 1.5 equiv) in dry dichloromethane (200 ml), and the resultant mixture was stirred for 3 hours at room temperature. It was then diluted with dry ether, filtered through a pad of celite and neutral alumina, the black gum being triturated in dry ether. The solution was concentrated to give 6.04 g (77%) of the title compound as a pale yellow fragrant liquid: IR (film): 2950, 2870, 2820, 2720, 1720 cm^{-1}; ^{13}C NMR (22.4 MHz): δ 200.7 (CHO), 43.9, 40.7, 24.8.

6-Choro-1-hexen-3-ol (4)
A solution of **3** (10.3 g, 96.7 mmol) in dry THF (50 ml) was cooled to -20°C as vinylmagnesium chloride (75.5 ml, 1.6M in THF, 1.25 equiv) was added slowly. The reaction mixture was stirred for further 20 minutes at -20°C and was then carefully hydrolyzed with saturated NH_4Cl. It was then extracted with ether and the extracts were dried over $MgSO_4$, concentrated to give 13g (100%) of the title compound as a pale yellow liquid which was found to be pure by ^1H and ^{13}C NMR analysis: IR(film): 3350, 3070, 2940, 2920, 2870, 2870, 1640, 1110, 1055, 990, 920, 880 cm^{-1}; ^1H NMR (200 MHz): δ 5.85 (ddd, J= 17.1, 10.5, 6.53 Hz, 1H, CH_2=CH), 5.19 (d, J= 17.1 Hz, 1H, =CH), 5.10 (d, J= 10.5 Hz, 1H, =CH), 4.15 (m, 1H, CHOH), 3.55 (t, J= 6.38 Hz, 2H, CH_2Cl), 2.15 (bs, OH), 1.85 (m, 2H), 1.65 (m, 2H); ^{13}C NMR (22.4 MHz): δ 140.7 (=CH), 114.7 (=CH_2), 72.2 (CHOH), 44.9 (CH_2Cl), 34.0, 28.4.

3-Acetoxy-6-chloro-1-hexene (5a)
A solution of **4** (6.5 g, 48.3 mmol) and 4-dimethylaminopyridine (600 mg) in dry dichloromethane (30ml) was cooled to 0°C as freshly distilled acetic anhydride (9.1 ml, 2 equiv) was added dropwise. The reaction mixture was stirred for 20 minutes at room temperature, quenched at 0°C with methanol (10 ml). The resultant solution was poured into 1M hydrochloric acid and extracted with dichloromethane. The combined extracts

were washed with saturated $NaHCO_3$, dried over $MgSO_4$ and concentrated to give 8.5 g (99%) of the title compound which was pure enough for the next step: ^1H NMR (200 MHz): δ 5.75 (ddd, J= 16.7, 10.7, 6 Hz, 1H, =CH), 5.23 (m, 3H, $=CH_2$ and CHOAc), 3.55 (m, 2H, CH_2Cl), 2.08 (s, 3H, CH_3CO), 1.83-1.70 (m, 4H); ^{13}C NMR (50 MHz): δ 169.8 (C=O), 136.1 (=CH), 117.0 ($=CH_2$), 74.1 (CHOAc), 44.6 (CH_2Cl), 31.3 (2 carbons), 28.2 (CH_3CO).

3-Acetoxy-6-iodo-1-hexene (6a)
5a (6.5 g, 36.8 mmol) was added to a solution of sodium iodide (11.6 g, 2 equiv), in acetone (60 ml), and the resultant mixture was refluxed for 24 hours. Aqueous sodium thiosulfate was added to the reaction mixture which was then extracted with ether. The extracts were washed with saturated brine, dried over $MgSO_4$ and evaporated. The crude material was distilled under reduced pressure, bp= 76-78°C (0.1 mmHg), to give 7.8 g (79%) of the title compound as a pale yellow oil: IR (film): 3080, 2940, 1730, 1645, 1425, 1365, 1230, 1170, 1020, 710 cm^{-1}; ^1H NMR (400 MHz): δ 5.77 (ddd, J= 17.04, 10.44, 6.04 Hz, 1H, =CH), 5.23 (m, 1H, $=CH_2$ and CHOAc), 3.19 (t, J= 6.6 Hz, 2H, CH_2I), 2.05 (s, 3H, CH_3CO), 1.85 (m, 2H), 1.7 (m, 2H); ^{13}C NMR (50 MHz): δ 169.6 (C=O), 135.8 (=CH), 116.6 ($=CH_2$), 73.1(CHOAc), 34.7, 28.7, 20.8, 5.50 (CH_2I).

3-Pivaloyloxy-6-chloro-1-hexene (5b)
To a solution of **4** (7.6 g, 56.4 mmol) and 4-dimethylaminopyridine (690 mg, 5.6 mmol) in dry dichloromethane (30ml) was added dropwise pivaloic anhydride (11.4 ml, 1 equiv), and the resultant mixture was stirred overnight at room temperature. Methanol (10 ml) was added dropwise and strirring was maintained for further 2 hours. The reaction mixture was then hydrolyzed with 1M hydrochloric acid, and extracted with ether (100 ml). The organic extracts were washed with saturated $NaHCO_3$, dried over $MgSO_4$ and concentrated to give a crude material (9.7 g) still containing a small amount of trimethyl acetic anhydride. It was then directly used in the next step without further purification:
^1H NMR (200 MHz): δ 6.30 (ddd, J=17.2, 10.65, 5.80 Hz, 1H, =CH), 5.35 (m, 3H, $=CH_2$ and CHOPiv), 3.55 (t, J=6.29 Hz, 2H, CH_2Cl), 1.8 (m, 4H), 1.25 (s, 9H, $(CH_3)_3$); ^{13}C NMR (50 MHz): δ 177.7 (C=O), 136.1 (=CH), 116.2 ($=CH_2$), 73.4 (CHOPiv), 44.3 (CH_2Cl), 38.3 ($C(CH_3)_3$), 31.3, 28.0, 26.9 ($(CH_3)_3$).

6-Iodo-3-pivaloyloxy-1-hexene (6b)
The crude material **5b** (9.7 g) was added to a solution of sodium iodide (12.3 g, 82.3 mmol) in acetone, and the reaction was carried out as described for the preparation of **6a**. Distillation of the residue under reduced pressure, bp= 107°C (0.6 mmHg), afforded 9.5 g (74% from **4**) of the title compound as a colorless oil: IR (film): 3080, 2960, 2860, 1750, 1645, 1475, 1275, 1150, 930, 765 cm^{-1}; ^1H NMR (200 MHz): δ 5.77 (ddd, J=17.04, 10.44, 5.5 Hz, 1H, =CH), 5.22 (m, 3H, $=CH_2$ and CHOPiv), 3.19 (t, J=6.29 Hz, 2H, CH_2Cl), 1.86 (m, 2H), 1.75 (m, 2H), 1.21 (s, 9H, $(CH_3)_3$); ^{13}C NMR (100 MHz): δ 177.4 (C=O), 136.0 (=CH), 116.4 ($=CH_2$), 72.8 (COPiv), 38.7 ($C(CH_3)_3$), 34.8, 28.9, 27.05, 3.00 (CH_2I).

3-(N,N-Diethyl)carbamoyloxy-6-chloro-1-hexene (5c)
A solution of **4** (6 g, 44.1 mmol) in dry THF (25 ml) was cooled to -20°C as n-butyllithium (26.3 ml, 1.7M in hexanes, 1 equiv) was added dropwise. The temperature was then allowed to rise to -10°C and N,N-diethylcarbamoyl chloride (6.2 ml, 1.1 equiv) was added. The cooling bath was removed and the resultant mixture was stirred for 48 hours at room temperature. It was then quenched with saturated $NaHCO_3$, extracted with ether and the combined extracts were dried over $MgSO_4$, evaporated. The residual oil was distilled under reduced pressure, bp= 80°C (0.1mmHg), to give 3.5 g (34%) of the title compound as a colorless oil: ^1H NMR (200 MHz): δ 5.80 (m, 1H, =CH), 5.28-5.10 (m, 3H, $=CH_2$ and OCH-CH=), 3.56 (m, 2H, CH_2Cl), 3.27 (q, J= 7.1 Hz, 4H, CH_2N), 1.80 (m, 4H), 1.13 (t, J= 7.1 Hz, 6H, CH_3CH_2N); ^{13}C NMR (50 MHz): δ

155.9 (C=O), 136.9 (=CH), 115.8 ($=CH_2$), 74.0 (OCH), 45.6, 44.5 and 44.3 (CH_2N), 41.3, 31.7, 28.1, 13.5 (CH_3).

3-(N,N-Diethyl)carbamoyloxy-6-iodo-1-hexene (6c)
5c (3.5 g, 14.9 mmol) was added to a solution of sodium iodide (4.5 g, 2equiv) in dry acetone (30 ml) and the reaction was carried out as described for the preparation of **6a**. The crude material was purified by flash chromatography (eluent, cyclohexane / ethyl acetate : 4/1) to give 2.45 g (51%) of the title compound as a colorless oil: IR (film): 3070, 1690, 1640, 1530, 1480, 1420, 1265, 1165, 985, 720 cm^{-1}; ^1H NMR (200 MHz): δ 5.80 (ddd, J=16.7, 10.47, 6.10 Hz, 1H, $CH_2=CH$), 5.25 (m, 1H, $=CH_2$ and OCH-CH=), 3.28 (q, J=7.11 Hz, 4H, CH_2N), 3.21 (t, J=6.81 Hz, 2H, CH_2I), 1.83 (m, 4H), 1.13 (t, J=7.11 Hz, 6H, CH_3CH_2N); ^{13}C NMR (50 MHz): δ 155.2 (C=O), 137.1 (=CH), 116.1 ($=CH_2$), 73.9 (CHO), 41.5, 35.4 (CH_2N), 29.2, 13.9 (CH_3), 6.26 (CH_2I).

General procedure for the cyclization involving Rieke's activated zinc
A 50 ml flask, fitted with a magnetical stirrer, an inert gas inlet and a septum cap was charged with naphthalene (1.62 g, 12.66 mmol) and freshly cut lithium (84.9 mg, 12.23 mmol). Dry THF (5 ml), was added and the colour of the reaction mixture immediately turned dark green. It was stirred for 2 hours at room temperature, and then cooled by mean of an ice-water bath, as zinc bromide (6.15 ml, 1M in ether, 6.15 mmol) was added dropwise (2 drops per second). The black suspension was stirred for ten minutes at room temperature and dry ether (20 ml) was added. Magnetical stirring was stopped and the active zinc was allowed to settle . The supernatant was removed by mean of a cannula and dry ether (20 ml) was added, the suspension being stirred for 5 min and allowed to settle: this washing process was repeated twice and finally dry ether (15 ml) was added to the active zinc slurry, which was ready for use. The iodide (2 to 3.5 mmol) was added neat to the vigorously stirred suspension of the active zinc. The disappearance of the iodide as well as the formation of the cyclic products were followed by G.C. analysis of hydrolyzed aliquots.

Functionalization of the cyclic organozinc reagent
- Hydrolysis: the reaction mixture was cooled with an ice-water bath as 1M hydrochloric acid (10 ml) was added slowly. Stirring was maintained until all the zinc had disappeared. Ether was added and the layers were separated, the aqueous one being extracted with ether. The combined extracts were washed with saturated $NaHCO_3$, and stirred for at least 3 hours with a few $Na_2S.9H_2O$ crystals that enabled the removal of all zinc salts before purification (otherwise isolated yields are lower than those reported). These were then removed by filtration and the organic solution was washed with brine, dried over $MgSO_4$ and concentrated.
- Iodinolysis: the reaction mixture was cooled with an ice-water bath as an excess of solid iodine (3 g, 11.8 mmol) was added. After stirring for 20 minutes at room temperature, 1M hydrochloric acid (10 ml) and ether (10 ml) were added. The layers were separated, the aqueous one being extracted with ether. The combined extracts were washed with saturated $NaHCO_3$, and dilute $Na_2S_2O_3$. They were then stirred for at least 3 hours with a few $Na_2S.9H_2O$ crystals. These were then removed by filtration and the organic solution was washed with brine, dried over $MgSO_4$ and concentrated.

1-Acetoxy-2-methylcyclopentane (8a)
6a (750 mg, 2.8 mmol) was subjected to the cyclization procedure, and after one hour at room temperature, the reaction mixture was hydrolyzed. The crude material was purified by chromatography (eluent, cyclohexane / ethyl acetate gradient: 100/0 to 4/1) to give 358 mg (90%) of the title compound as a colorless oil (59/41 mixture of cis/trans diastereoisomers): IR (film): 2950, 2820, 1730, 1440, 1420, 1370, 1235, 1175, 1020 cm^{-1}; ^1H NMR (200 MHz): δ 5.12 (m, 0.59 H, CHOAC cis), 4.70 (m, 0.41 H, CHOAc trans), 2.05 (s, 3H, CH_3CO), 1.80-1.20 (m, 7H), 0.99 (d, J= 6.6 Hz, 1.23 H, CH_3 trans), 0.95 (d, J= 7.15 Hz, 1.77 H, CH_3 cis); major diastereoisomer (cis) ^{13}C NMR (50 MHz): δ 170.9 (C=O), 78.8 (CHOAc), 38.5 ($CHCH_3$), 32.3, 31.8, 22.3, 21.2,

13.9 (CH_3); minor diastereoisomer (trans) ^{13}C NMR (50 MHz): δ 170.9 (C=O), 82.7 (CHOAc), 40.1 ($CHCH_3$), 32.0, 31.5, 22.5, 21.3, 18.3 (CH_3); Anal. Calcd. for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found C, 67.81; H, 10.01.

1-Acetoxy-2-(iodomethyl)cyclopentane (9a)
6a (750 mg, 2.8 mmol) was subjected to the cyclization procedure, and after one hour at room temperature, the reaction mixture was iodinolyzed. The crude material was purified by chromatography (eluent, cyclohexane / ethyl acetate gradient: 100/0 to 4/1) to give 532 mg (74%) of the title compound as a colorless oil (59/41 mixture of cis/trans diastereoisomers): IR (film): 2950, 2820, 1730, 1440, 1420, 1370, 1235, 1175, 1020 cm^{-1}; ^1H NMR (400 MHz): δ 5.19 (m, 0.59 H, CHOAC cis), 4.80 (m, 0.41 H, CHOAc trans), 3.33 (dd, J= 9.34, 4.95 Hz, 0.41H, CHI trans), 3.26-3.13 (m, 1.59H, CHI cis and trans), 2.32 (m, 0.59H, $CHCH_2I$ cis), 2.20 (m, 0.41H,$CHCH_2I$ trans), 2.05 (s, 1.77H, CH_3CO cis), 2.02 (s, 1.23H, CH_3CO trans), 2.00-1.30 (m, 6H); ^{13}C NMR (50 MHz): δ 170.1 (C=O), 80.1 (CHOAc trans), 77.3 (CHOAc cis), 47.7 ($CHCH_2I$ trans), 47.3 ($CHCH_2I$ cis), 32.5 (cis), 32.4 (trans), 31.7 (cis), 30.6 (cis), 22.5 (CH_3CO cis,trans and another carbon), 21.1, 10.3 (CH_2I trans), 4.68 (CH_2I cis); Anal. Calcd. for $C_8H_{13}O_2I$: C, 35.84; H, 4.88. Found C, 36.11; H, 4.97.

2-Methyl-1-(pivaloyloxy)cyclopentane (8b)
6b (1 g, 3.22 mmol) was subjected to the cyclization process and after three hours at room temperature, the reaction mixture was hydrolyzed. The crude material was purified by chromatography (eluent, cyclohexane / ethyl acetate gradient: 100/0 to 4/1) to give 516 mg (87%) of the title compound as a colorless oil (55/45 mixture of cis/trans diastereoisomers): IR (film): 2950, 2920, 2900, 2860, 1720, 1475, 1455, 1390, 1360, 1280, 1155, 1030 cm^{-1}; ^1H NMR (200 MHz): δ 5.07 (m, 0.55 H, CHOPiv cis), 4.66 (m, 0.45 H, CHOPiv trans), 2.10-1.30 (m, 7H), 1.19 (s, 4.95H, $(CH_3)_3C$ cis), 1.18 (s, 4.05 H, $(CH_3)_3C$ trans), 0.98 (d, J= 6.78 Hz, 1.35H, CH_3 trans), 0.97 (d, J= 6.80 Hz, 1.65 H, CH_3cis); major diastereoisomer (cis) ^{13}C NMR (50 MHz): δ 178.1 (C=O), 78.3 (COPiv), 38.6 ($CHCH_3$), 38.9 ($C(CH_3)_3$), 32.4, 31.8, 27.3 (($CH_3)_3C$), 22.3, 13.9 (CH_3); minor diastereoisomer (trans) ^{13}C NMR (50 MHz): δ 178.1 (C=O), 82.2 (COPiv), 40.0 ($CHCH_3$), 38.9 ($C(CH_3)_3$), 31.9, 31.2, 27.3 (($CH_3)_3$), 22.3, 18.2 (CH_3); Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found C, 71.87; H, 10.81.

2-Iodomethyl-1-(pivaloyloxy)cyclopentane (9b)
6b (1 g, 3.22 mmol) was subjected to the cyclization procedure, and after two hours at room temperature, the reaction mixture was iodinolyzed. The crude material was purified by chromatography (eluent, cyclohexane / ethyl acetate gradient: 100/0 to 4/1) to give 730 mg (73%) of the title compound as a colorless oil (55/45 mixture of cis/trans diastereoisomers): IR (film): 2950, 2860, 1735, 1470, 1455, 1275, 1150, 1025 cm^{-1}; ^1H NMR (200 MHz): δ 5.16 (m, 0.55 H, CHOPiv cis), 4.70 (m, 0.45 H, CHOPiv trans), 3.34 (dd, J= 9.4, 5.13 Hz, 0.45H, CHI trans), 3.27-3.10 (m, 1.55H, CHI cis and trans), 2.43-1.50 (m, 7H), 1.21 (s, 4.95 H, $(CH_3)_3C$ cis), 1.19 (s, 4.05 H, $(CH_3)_3C$ trans); major diastereoisomer (cis) ^{13}C NMR (50 MHz): δ 177.5 (C=O), 77.25 (COPiv), 47.9 ($CHCH_2I$), 39.1 ($C(CH_3)_3$), 32.7, 32.5, 30.9, 27.3 (($CH_3)_3C$), 22.3, 4.41 (CH_2I); minor diastereoisomer (trans) ^{13}C NMR (50 MHz): δ 177.5 (C=O), 80.2 (COPiv), 48.0 ($CHCH_2I$), 38.6 ($C(CH_3)_3$), 31.9, 27.3 (($CH_3)_3$), 22.7, 10.0 (CH_2I); Anal. Calcd. for $C_{11}H_{19}O_2I$: C, 42.59; H, 6.17. Found C, 42.88; H, 6.23.

1-(N,N-Diethylcarbamoyloxy)-2methylcyclopentane (8c)
6c (500 mg, 1.54 mmol), was subjected to the cyclization process using the general procedure, and after one hour at room temperature, the reaction mixture was hydrolyzed. The crude material was purified by chromatography (eluent, cyclohexane / ethyl acetate gradient: 9/1 to 4/1) to give 245 mg (80%) of the title compound as a colorless oil (59/41 mixture of cis/trans diastereoisomers): ^1H NMR (200 MHz): δ 5.04 (m, 0.59 H, OCH cis), 4.64 (m, 0.41 H, OCH trans), 3.35 (m, 4H, CH_2N), 2.06-1.30 (m, 7H), 1.12 (t,

J= 7.1 Hz, 3.54 H, CH_3CH_2 cis), 1.11 (t, J= 7.09 Hz, 2.46 H, CH_3CH_2 trans), 0.99 (d, J= 6.49 Hz, 3H, CH_3). ^{13}C NMR (50 MHz): δ 156.2 (C=O), 83.1 (CHO trans), 79.3 (CHO cis), 41.5 (CH_2N), 40.1 ($CHCH_3$ trans), 38.7 ($CHCH_3$ cis), 32.6, 31.9, 31.6, 22.4, 22.3, 18.4, 14.2, 13.9; Anal. Calcd. for $C_{11}H_{21}O_2N$: C, 62.29; H, 10.62. Found C, 62.41; H, 10.53.

Preparation of the authentic samples

2-methylcyclopentanol
A solution of 2-methylcyclopentanone (1 g, 10.2 mmol) in methanol (20 ml) was cooled between -10°C and 0°C (external temperature) as sodium borohydride (3 .5 g, 9.1 equiv) was added per small portions. After stirring for 5 minutes, the reaction mixture was quenched with saturated NH_4Cl and extracted several times with ether. The combined extracts were dried over K_2CO_3 and evaporated to give 991 mg (96%) of the title compound as a colorless liquid (70/30 mixture of trans/cis diastereoisomers): ^1H NMR (400 MHz): δ 4.07 (m, 0.3H, CHOH cis), 3.73 (m, 0.7H, CHOH trans), 1.97-1.10 (m, 8H), 1.02 (d, J= 6.6 Hz, 0.9H, CH_3 cis), 0.99 (d, J= 6.6 Hz, 2.1H, CH_3 trans)

1-Acetoxy-2-methylcyclopentane
2-methylcyclopentanol (950 mg, 9.48 mmol) was converted into the title compound, 922 mg (68%, 70/30 mixture of trans/cis diastereoisomers) using the procedure described for the preparation of **5a**. It was purified by flash chromatography (eluent, cyclohexane / ethyl acetate: 4/1).

2-Methyl-1-(pivaloyloxy)cyclopentane
2-methylcyclopentanol (990 mg, 9.9 mmol) was converted into the title compound 1.25 g (69%, 70/30 mixture of trans/cis diastereoisomers) using the procedure described for the preparation of **5b**. It was purified by flash chromatography (eluent, cyclohexane / ethyl acetate: 4/1).

1-(N,N-Diethylcarbamoyloxy)-2-methylcyclopentane
A solution of 2-methylcyclopentanol (1.5 g, 15 mmol) in dry THF (20 ml) was cooled to 0°C as sodium hydride (1.2 g, 50% in grease, 25 mmol) was added. After the evolution of hydrogen has ceassed, N,N-diethylcarbamoyl chloride (2.5 ml, 1.16 equiv) was injected into the flask at 5°C, and the resultant mixture was stirred overnight at room temperature. It was then cooled to -20°C and carefully quenched with saturated NH_4Cl. It was extracted with ether and the combined extracts were dried over $MgSO_4$, concentrated to give an oil which was purified by flash chromatography (eluent, cyclohexane / ethyl acetate: 4/1), to give 1.94 g (65%, 70/30 mixture of trans/cis diastereoisomers) of the title compound as a pale yellow oil.

6-Chloro-3-methyl-1-trimethylsilyl-1-hexyne (10)
1-Butyne (4.5 l, 0.2 mol) was dissolved in dry THF (300ml) at -10°C. The solution was cooled between -30°C and -10°C as n-butyllithium (310 ml, 1.6M in hexanes, 0.5 mol) was added slowly. The cooling bath was removed and the reaction mixture was heated at 20°C. At this point, a slightly exothermic reaction started and the temperature rose to 30°C. The resultant yellow-orange suspension of 1,3-dilithio-1-butyne was heated at 30-35°C for further 2 hours. It was then cooled to -40°C as 1-bromo-3-chloropropane (31.5 g, 0.2 mol) was added rapidly. The cooling bath was removed immediately. Above -20°C, the temperature began to rise more rapidly. After stirring for 30 minutes, dry HMPA (40 ml) was added and the orange suspension has almost completely turned to a greenish solution, which was further heated for 1 hour at 40-50°C. It was then cooled to -20°C as trimethylchlorosilane (25.3 ml, 0.2 mol) was added. The resultant mixture was heated again for one hour at 50°C, cooled to 0°C, and poured into 1M hydrochloric acid. It was extracted twice with ether, the combined extracts were washed again with 1M hydrochloric acid, dried over $MgSO_4$, and evaporated. The crude material was distilled under reduced pressure, bp= 95-97°C (10 mmHg), to give 18 g (44%) of the title compound as a colorless oil: ^1H NMR (200 MHz): δ 3.57 (t, J= 6.56 Hz, 2H, CH_2Cl),

2.49 (m, 1H, ≡CH-CH), 1.98-1.86 (m, 2H), 1.63-1.47 (m, 2H), 1.18 (d, J= 6.91 Hz, 3H, CH_3CH), 0.15 (s, 9H, $(CH_3)_3Si$).

6-Iodo-3-methyl-1-trimethylsilyl-1-hexyne (11)
10 (11.5 g, 56.7 mmol), was added to a solution of sodium iodide (17 g, 0.11 mol) in acetone (100 ml), and the resultant mixture was refluxed for 12 hours. It was then concentrated in vacuo and dry pentane (200 ml) was added to the solid residue. The insoluble inorganic material was filtered off. Concentration afforded an oil which was distilled under reduced pressure, bp= 70-74°C (0.5 mmHg), to give 11.2 g (67%) of the title compound as a colorless oil: ^{13}C NMR (22.4 MHz): δ 111.0 (C≡CSi), 84.9 (SiC≡C), 37.6, 31.4, 26.1, 21.3, 6.5 (CH_2I), 0.50 (($CH_3)_3Si$).

(Z)-6-Iodo-3-methyl-1-trimethylsilyl-1-hexene (12)
A solution of **11** (11.2 g, 38.1 mmol) in dry ether (40 ml) was cooled between 0 and 10°C as DIBAL-H (39 ml, 1M in hexane, 39 mmol) was added slowly. The cooling bath was removed and the temperature rose to 25-28°C. The reaction mixture was heated at 30-35°C for further two hours. It was then cooled to -60°C as methanol (20 ml) was added, allowed to warm to -10°C and hydrolyzed with 1M hydrochloric acid (100 ml). The layers were separated and the aqueous one was extracted with ether. The combined exrtacts were washed with water, dried over $MgSO_4$ and concentrated. The crude material was first purified by passage through a short column packed with silica and eluted with a 1/1 mixture of cyclohexane and ether. Evaporation of the solvents and distillation under reduced pressure, bp= 79-81°C (0.6 mmHg), afforded 9.6 g (85%) of the title compound as a colorless liquid: ^1H NMR (200MHz): δ 6.02 (dd, J= 13.9, 10.1 Hz, 1H, =CH), 5.42 (d, J= 13.9 Hz, 1H, =CHSi), 3.17 (t, J=6.9 Hz, 2H, CH_2I), 2.3 (m, 1H, =CH-CH(CH_3)-), 1.8 (m, 2H), 1.45 (m, 2H), 0.97 (d, J= 6.51 Hz, 3H, CH(CH_3)), 0.15 (s, 9H, $(CH_3)_3Si$); ^{13}C NMR (22.4 MHz) δ 154.4 (C=CSi), 127.9 (C=CH), 38.2, 37.4, 31.9, 21.5, 6.9 (CH_2I), 0.75 (($CH_3)_3Si$).

6-Iodo-3-methyl-1-hexene (13)
APTS monohydrate (8 g, 4 6.8 mmol) was added to a solution of **12** (10.9 g, 36.8 mmol) in dry acetonitrile (30 ml) and the resultant mixture was stirred overnight at room temperature. It was then hydrolyzed with saturated $NaHCO_3$, extracted with pentane (3*60 ml) and ether (40 ml). The combined extracts were washed with brine, dried over $MgSO_4$ and concentrated The crude material was distilled under reduced pressure, bp= 78-80°C (16 mmHg), to give 6.2 g (75%) of the title compound as a colorless oil: ^1H NMR (200 MHz): δ 5.66 (ddd, J= 17.7, 10.24, 7.76 Hz, 1H, =CH), 4.95 (m, 2H, $=CH_2$), 3.18 (t, J= 6.94 Hz, 2H, CH_2I), 2.15 (m, 1H, $CHCH_3$), 1.85 (m, 2H), 1.40 (m, 2H), 1.40 (m, 2H), 1.00 (d, J= 6.99 Hz, 3H, CH_3); ^{13}C NMR (22.4 MHz): δ 143.9 (=CH), 113.2 ($=CH_2$), 37.5, 37.1, 31.5, 20.4, 7.1 (CH_2I).

trans-1-Iodomethyl-2-methylcyclopentane trans-(14)
Cyclization of the organolithium reagent
A solution of **13** (0.5 g, 2.24 mmol) in dry ether (20 ml) was cooled to -78°C as tertbutyllithium (2.7 ml, 1.7M in pentane, 2.05 equiv) was added dropwise. The cooling bath was removed and the resultant mixture was stirred for 5 minutes at 20°C, cooled again to -20°C as iodine (1 g, 4 mmol) was added. After stirring for 20 minutes at 20°C, the reaction mixture was quenched with 1M hydrochloric acid. The aqueous layer was extracted with ether. The combined extracts were washed with saturated $NaHCO_3$ and dilute $Na_2S_2O_3$, dried over $MgSO_4$ and concentrated. The crude material was purified by passage through a short column packed with silica and eluted with pentane, to afford after concentration 410 mg (82 %) of the title compound as a colorless liquid (93/7 mixture of trans/cis diastereoisomers).

Cyclization of the organozinc reagent
13 (0.5 g, 2.24 mmol) was added to a suspension of Rieke's activated zinc in ether according to the general procedure. After stirring for 12 hours at room temperature, the

reaction mixture was iodinolyzed. After usual work-up, the crude material was purified by chromatography (eluent, pentane) to give 398 mg (80%) of the title compound as a slightly pale yellow liquid (93/7 mixture of trans/cis diastereoisomers): ^{1}H NMR (200MHz): δ 3.38 (A part of ABX, J_{AB}= 9.54 Hz, J_{AX}= 3.86 Hz, 1H, CHI), 3.12 (B part of ABX, J_{AB}= 9.5 Hz, J_{BX}= 7.3 Hz, 1H, CHI), 1.90 (X part of ABX, 1H, $CHCH_2I$), 1.67-1.45 (m, 7H), 0.99 (d, J= 6.24 Hz, 3H, CH_3CH); ^{13}C NMR (50 MHz): δ 49.6 ($CHCH_2I$), 40.9, 35.4, 33.9, 23.2, 19.3 (CH_3), 13.7 (CH_2I).

General procedure for the cyclization reactions involving diethylzinc
Exchange procedure in hexane
To **6a** (268 mg, 1 mmol) was added diethylzinc (2 to 3 ml, 1M in hexane, 2 to 3 mmol), and the resultant mixture was refluxed for three hours. GC analysis of an hydrolyzed aliquot indicated a 80-85% conversion to the linear organozinc species.
Cyclization procedure in ether
Hexane was removed under reduced pressure (15 mmHg) from the preceeding solution. After complete evacuation of the solvent, the content of the flask was put under argon, and dry ether (10 ml) was slowly injected into the flask via syringue. After stirring overnight at room temperature, the solution of the cyclic organozinc reagent was ready for further conversions.
Exchange and cyclization in ether
To **6a** (0.5 g, 1.86 mmol) was added diethylzinc (3.73 ml, 1M in hexane, 2 equiv). Hexane was removed under reduced pressure (15 mmHg) and after complete evacuation of the solvent, the content of the flask was put under argon, and dry ether (10 ml) was slowly injected into the flask via syringue. The resultant mixture was stirred for 36 to 48 hours.

1-Acetoxy-2-methylcyclopentane (8a)
249 mg (94%, 55/45 mixture of cis/trans diastereoisomers) of the title compound have been obtained using the exchange / cyclization procedure in ether, followed after 48 hours by hydrolysis with 1M hydrochloric acid. After usual work-up, the crude material was purified by flash chromatography (eluent, cyclohexane / ethyl acetate: 9/1)

1-Acetoxy-2-(iodomethyl)cyclopentane (9a)
6a (270 mg, 1.01 mmol) was subjected to the general exchange / cyclization procedure in ether followed after 48 hours by iodinolysis. The crude material was purified by flash-chromatography (eluent, cyclohexane / ethyl acetate: 4/1) to give 216 mg (80%) of the title compound as a slightly pale yellow oil (55/45 mixture of cis/trans diastereoisomers).

(Z)-1-Chloro-5-decene
A suspension of $CuBr.Me_2S$ (2.82 g, 13.75 mmol) in dry ether (30 ml) was cooled to -40°C as n-butyllithium (14 ml, 1.96M in ether, 27.4 mmol) was added slowly. The reaction mixture was allowed to warm to -35°C and stirred for 20 minutes at that temperature. Acetylene (620 ml, 27.7 mmol) was bubbled into this clear grey solution of the organocuprate reagent at -55°C. After stirring for 30 minutes at -30°C, a green solution of the (Z)-dihexenyl cuprate was obtained. Dry HMPA (5 ml) and dry THF (5 ml) were then added at -30°C, followed by 4-chloro-1-iodobutane (6 g, 27.5 mmol) dissolved in dry THF (5 ml) and finally triethylphosphite (7 ml). The cooling bath was removed and the reaction mixture was stirred overnight at room temperature. It was then cooled to -20°C and quenched with 6M hydrochloric acid (80 ml). After stirring for 20 minutes at room temperature, a white precipitate formed and was filtered off. The layers were separated and the aqueous one was extracted with ether (10 ml) and pentane (100 ml). The combined extracts were washed with a saturated NH_4Cl / 32% NH_4OH, 2/1 solution, brine, dried over $MgSO_4$ and concentrated. The crude material was purified by chromatography (eluent, pentane) to give 1.78 g (37%) of the title compound as a colorless liquid: ^{1}H NMR (400 MHz): δ 5.36 (m, 2H, =CH), 3.54 (t, J= 6.59 Hz, 2H, CH_2Cl), 2.04 (m, 4H, =CH-CH_2), 1.79 (m, 2H), 1.50 (m,2H), 1.32 (m, 2H), 0.90 (t, J= 7.15 Hz, 3H, CH_3).

(Z)-1-Iodo-5-decene (15)
(Z)-chloro-5-decene (946 mg, 5.42 mmol) was added to a solution of sodium iodide (1.61 g, 2 equiv) in acetone (20 ml). The resultant mixture was refluxed for 24 hours and worked-up as described for the preparation of **6a**. The crude material was purified by chromatography (eluent, pentane) to give 1 g (77%) of the title compound as a colorless liquid: ^{1}H NMR (400 MHz): δ 5.36 (m, 2H, =CH), 3.20 (t, J= 6.92 Hz, 2H, CH_2I), 2.11-2,01 (m, 4H, =CH-CH_2), 1.88-1.77 (m, 2H), 1.54-1.26 (m, 2H), 0.90 (m, 3H, CH_3); ^{13}C NMR (50 MHz) δ 130.8, 128.9, 33.3, 32.1, 30.7, 27.1, 26.2, 22.5, 14.1 (CH_3), 6.7 (CH_2I).

Attempt to cyclize (15)
(Z)-5-decene
15 (343 mg, 1.3 mmol) was added to a suspension of Rieke's activated zinc in ether according to the general procedure. After stirring for 12 hours at room temperature, the reaction mixture was hydrolyzed. The crude material was analyzed by G.C. and N.M.R. indicating the formation of the title compound, 112mg (62%): ^{1}H NMR (400 MHz): δ 5.33 (t, J= 4.5 Hz, 2H, =CH), 2.1-1.9 (m, 4H), 1.5-1.1 (m, 8H), 1.05-0.80 (m, 6H, CH_3); ^{13}C NMR (100 MHz): δ 130.1 (=CH), 32.2, 27.1, 22.5, 14.2.

Transmetalation of the organozinc reagent with CuCN.2LiCl and reaction with ethyl propiolate:
(E)-1-Acetoxy-2-(3-carboethoxy-2-propen-1-yl)cyclopentane (17)
- cyclization using Rieke's activated zinc
6a (400 mg, 1.5 mmol) was subjected to the cyclization process using the general procedure. After 2 hours, magnetical stirring was stopped and the excess zinc was allowed to settle. The clear solution of the cyclic organozinc reagent was transferred via cannula into another flask, and it was then cooled to 0°C as dry THF (10ml) and CuCN.2LiCl (1.6 ml, 1M in THF, 1.6 mmol) were subsequently added. The greenish solution of corresponding organozinccopper reagent was stirred for 10 minutes at 0°C. It was then cooled to -40°C as freshly distilled ethyl propiolate (191 mg, 1.95 mmol) was added via syringue. The reaction mixture was allowed to warm to room temperature overnight and it was then quenched with a saturated NH_4Cl / 32% NH_4OH, 2/1 solution. After usual work-up, the crude material was purified by flash chromatography (eluent, cyclohexane / ethyl acetate, 4/1) to give 226 mg (66%) of the title compound as a pale yellow oil (59/41 mixture of cis / trans diastereoisomers): ^{1}H NMR (400 MHz): δ 6.94-6.89 (m, 2H, CH=CH-COOEt), 5.83 (d, J= 15.94 Hz, 0.41H, =CH-COOEt cis), 5.14 (d, J= 15.39 Hz, 0.59H, =CH-COOEt trans), 5.14 (m, 0.59H, CHOAC cis), 4.77 (m, 0.41H, CHOAc trans), 4.18 (q, J= 7.15 Hz, 2H, OCH_2), 2.36 (m, 2H, =CH-CH_2), 2.20-1.21 (m, 13H, including 2.04 (s, 1.23H, CH_3CO trans), 2.02 (s, 1.77H, CH_3CO cis), 1.28 (t, J= 7.15 Hz, 3H, OCH_2CH_3); ^{13}C NMR (50 MHz): δ 171.2 (COOEt trans), 171.1 (COOEt cis), 166.7 (CH_3CO), 147.9 (CH=CH-COOEt trans), 147.2 (CH=CH-COOEt cis), 122.6 (=CH-COOEt trans), 122.3 (=CH-COOEt cis), 80.3 (CHOAc trans), 77.7 (CHOAc cis), 60.4 (OCH_2), 43.4, 43.2, 36.1, 32.5, 32.3, 31.8, 29.8, 29.6, 22.6, 22.1, 21.4, 14.5 (OCH_2CH_3); Anal. Calcd. for $C_{12}H_{20}O_4$: C, 67.57; H, 9.92. Found C, 67.40; H, 9.83.

- cyclization using Et_2Zn
6a (500 mg, 1.86 mmol) was subjected to the general exchange / cyclization procedure in ether. After stirring for 40 hours, ether and excess diethylzinc were removed under reduced pressure (0.01 mmHg). Dry THF (5 ml) was then slowly injected into the flask, and the resultant solution was cooled to 0°C as CuCN.2LiCl (2 ml, 1M in THF, 2 mmol) was added. After stirring for 10 minutes at 0°C, the reaction mixture was cooled to -40°C as freshly distilled ethyl propiolate (196 mg, 2 mmol) was added. After stirring overnight at room temperature, the reaction mixture was worked-up as described previously. The crude material was purified by flash chromatography (eluent, cyclohexane / ethyl acetate: 4/1) to give 265 mg (72%) of the title compound as a slightly pale yellow oil (55/45 mixture of cis/trans diastereoisomers).

Cyclization of secondary organozinc reagents

5-Bromo-1-pentene

1,5-Dibromopentane (48.8 ml, 0.21 mol) was heated to 195°C (external temperature of an oil bath) as HMPA (72 ml) was added at a slow rate (2 or 3 drops per second). After the addition the temperature of the oil bath was raised to 220°C until no more product distilled into a single receiver cooled in liquid nitrogen. The distillate was then dissolved into pentane (50 ml) and treated with 1M hydrochloric acid (10 ml). The organic layer was dried over $MgSO_4$, and both solvent and product, bp= 124-126°C, were distilled, to give 24.5 g (46%) of the title compound as a colorless liquid: ^1H NMR (200 MHz): δ 5.76 (ddt, J= 17.0, 10.1, 6.9 Hz, 1H, =CH), 5.06 (d, J= 17.0 Hz, 1H, $=CH_2$), 5.00 (d, J= 10.1 Hz, 1H, $=CH_2$), 3.39 (t, J= 6.74 Hz, 2H, CH_2Br), 2.19 (m, 2H, $=CH-CH_2$), 1.93 (m, 2H); ^{13}C NMR (22.4 MHz): δ 136.7 (=CH), 115.8 ($=CH_2$), 32.9, 32.1, 31.9

Preparation of the secondary alcohols

4-penten-1-yllithium

A solution of 5-bromo-1-pentene (29 .8 g, 0.2 mol) in dry ether was slowly added to freshly cut lithium pieces (2.3 g, 2.2 equiv) covered with dry ether (30 ml) at -10°C over 45-60 minutes. After the addition, the cooling bath was removed and the reaction mixture was stirred for 10 minutes at room temperature. The solution of the organolithium reagent was transferred via cannula into a bottle purged with argon. Titration of the solution indicated a 1M concentration (90%).

2-methyl-7-octen-3-ol

A solution of freshly distilled isobutyraldehyde (5.04 g, 70 mmol) in dry ether (30 ml) was cooled to -20°C, as 4-penten-1-yllithium (70 ml, 1M in ether, 70 mmol) was added slowly. After the addition, the cooling bath was removed and the reaction mixture was warmed to room temperature. It was then quenched with saturated NH_4Cl, extracted with ether and the extracts dried over $MgSO_4$. The crude material was distilled under reduced pressure, bp= 48-50°C (0.5 mmHg), to give 7.2 g (72%) of the title compound as a colorless oil: IR (film): 3350, 3060, 2930, 2860, 1640, 1460, 990, 905 cm^{-1}; ^1H NMR (400 MHz): δ 5.83 (ddt, J= 17.05, 9.9, 6.6 Hz, 1H, =CH), 5.01 (d, J= 17.05 Hz, 1H, $=CH_2$), 4.95 (d, J= 9.9 Hz, 1H, $=CH_2$), 3.2 (m, 1H, CHOH), 2.05 (m, 2H, $=CH-CH_2$), 1.70-1.35 (m, 5H), 0.98 (d, J= 6.4 Hz, 3H, CH_3CH), 0.94 (d, J= 6.3 Hz, 3H, CH_3CH); ^{13}C NMR (100 MHz): δ 138.8 (=CH), 114.3 (=CH2), 76.2 (CHOH), 33.7, 33.5, 25.3, 18.7, 17.2.

2,2-dimethyl-7-octen-3-ol

This compound has been prepared in 60 % yield starting from pivaladehyde (2.58 g, 30 mmol) according to the procedure described for the preparation of the preceeding alcohol The crude product was directly used in the next step without purification: IR (film): 3380, 3070, 2940, 2860, 1640, 1470, 1360, 1015, 1000, 905 cm^{-1};^1H NMR (400 MHz): δ 5.82 (m, 1H, =CH), 5.01 (d, J= 15.4Hz, 1H, $=CH_2$), 4.95 (d, J= 9.9 Hz, 1H, $=CH_2$), 3.47 (m, 1H, CHOH), 2.10-2.07 (m, 2H), 1.67-1.20 (m, 4H), 0.88 (s, 9H, $(CH_3)_3C$); ^{13}C NMR (22.4 MHz): δ 138.8 (=CH), 114.4 ($=CH_2$), 79.7 (CHOH), 35.0, 33.8, 31.0, 26.8, 26.4, 25.8.

9-Decen-5-ol

Valeraldehyde (3.87 g, 45 mmol) was added at -40°C to an etheral solution (20 ml) of the Grignard reagent prepared from 5-bromo-1-pentene (4.47 g, 30 mmol) and magnesium turnings (1.1 g, 45 mmol). After the addition, the reaction mixture was warmed to 0°C and poured into 1M hydrochloric acid. The aqueous layer was extracted with ether and the combined extracts were dried over $MgSO_4$, evaporated to give an oil which was purified by flash chromatography (eluent, cyclohexane / ethyl acetate, 85/15) to give 2.64 g (56%) of the title compound as a colorless oil: ^1H NMR (200 MHz): δ

5.80 (ddt, J= 17.0, 10.45, 6.7 Hz, 1H, =CH), 5.00 (m, 2H, $=CH_2$), 3.6 (m, 1H, CHOH), 2.05 (m, 2H), 1.60-1.20 (m, 10H), 0.9 (m, 3H, CH_3); ^{13}C NMR (100 MHz): δ 138.8 (=CH), 114.6 ($=CH_2$), 71.9 (CHOH), 37.2 ($=CH-CH_2$), 36.9, 33.8, 27.9, 24.9, 22.8, 14.1.

5-Hexen-1-al

To a suspension of pyridinium chlorochromate (19.4 g, 90 mmol) in dry dichloromethane (150 ml) was added all at once 5-hexen-1-ol (6 g, 60 mmol) and the resultant mixture was stirred for three hours at room temperature. It was then diluted with ether (200 ml), the black gum being triturated again in dry ether (3*50 ml). The insoluble material was removed by filtration through a pad of silica. The solvents were then distilled off and the crude material was distilled under reduced pressure, bp= 62°C (60mmHg), to give 5 g (85%) of the title compound as a colorless fragrant oil: ^1H NMR (200 MHz): δ 9.77 (t, J= 1.4 Hz, 1H, CHO), 5.77 (ddt, J= 17.0, 10.3, 6.65 Hz, 1H, =CH), 5.03 (m, 2H, $=CH_2$), 2.45 (t, J= 7.3, 1.4 Hz, 2H, $CHOCH_2$), 2.10 (m, 2H, $=CH-CH_2$), 1.74 (m, 2H); ^{13}C NMR (50 MHz): δ 202.3 (CHO), 137.6 (=CH), 115.5 ($=CH_2$), 43.1, 33.0, 21.3.

Typical procedure for the preparation of the secondary iodides from the corresponding secondary alcohols

Triphenylphosphine (1.5 equiv) and imidazole (1.5 equiv) were subsequently dissolved in dry dichloromethane (100 ml). This solution was cooled with an ice-water bath as iodine (1.5 equiv) was added per small portions. The cooling bath was removed, and the resultant suspension was stirred for 5 minutes at room temperature, before the alcohol in dry dichloromethane (20 ml) was added. After stirring for three hours at room temperature, water was added (30ml). The layers were separated and the aqueous one was extracted with dichloromethane. The combined extracts were washed with dilute $Na_2S_2O_3$, dried over $MgSO_4$ and evaporated to give a solid residue which was vigorously stirred overnight in dry pentane (200 ml). The insoluble triphenylphosphine oxyde was filtered off, and pentane was evaporated to give the crude iodide.

6-Iodo-1-heptene (18)

A solution of 5-hexenal (3 g, 30.6 mmol) in dry ether (20 ml) was cooled to - 30°C as methylmagnesiumbromide (25.5 ml, 1.2M in ether, 1 equiv) was added slowly. After the addition, the cooling bath was removed, and the reaction mixture was stirred for 5 minutes at room temperature. It was then cooled to -20°C, and poured into a saturated NH_4Cl solution. The layers were separated and the aqueous one was extracted with ether (3x25ml). The combined extracts were dried over $MgSO_4$ and evaporated to give crude 6-hepten-2-ol which was directly converted into the corresponding iodide using the general procedure. The crude material was distilled under reduced pressure, bp= 73-74°C (13 mmHg), to give 3.9 g (55 %) of the title compound as a colorless oil: ^1H NMR (200 MHz): δ 5.77 (ddt, J= 17.01, 10.22, 6.79 Hz, 1H, =CH), 4.96 (m, 2H, $=CH_2$), 4.17 (m, 1H, CHI), 2.06 (m, 2H, $=CH-CH_2$), 1.89 (d, J= 6.83 Hz, 3H, CH_3CHI), 1.79-1.45 (m, 4H); ^{13}C NMR (100 MHz): δ 138.4 (=CH), 115.1 ($=CH_2$), 42.4, 32.9, 30.5, 29.1 (2 carbons).

4-Iodo-2,8-nonadiene (19)

A solution of 5-hexenal (3 g, 30.6 mmol) in dry ether (15 ml) was cooled to - 30°C as allylmagnesiumbromide (14.1 ml, 2.18M in ether, 1 equiv) was added slowly. After the addition, the cooling bath was removed, and the reaction mixture was stirred for 5 minutes at room temperature. It was then cooled to -20°C, and poured into saturated NH_4Cl (10 ml). The layers were separated and the aqueous one was extracted with ether (3x25ml). The combined extracts were dried over K_2CO_3 and evaporated to give crude 2,8-nonadien-4-ol which was directly converted into the corresponding iodide using the general procedure. The crude material was purified by passage through a short column packed with neutral alumina and eluted with pentane, to give 4.1 g (53%) as a slightly pale yellow oil: ^1H NMR (400 MHz): δ 5.80-5.65 (m, 2H, =CH), 5.10-5.00 (m, 2H,

=CH_2), 4.97-4.85 (m, 2H, =CH_2), 4.03 (m, 1H, CHI), 2.56 (m, 2H, =CH-CH_2-CHI), 2.01 (m, 2H, =CH-CH_2), 1.90-1.40 (m, 4H); ^{13}C NMR (100 MHz): δ 138.3 (=CH), 136.4 (=CH), 117.8 (=CH_2), 115.1 (=CH_2), 44.9, 39.3, 37.0, 32.9, 28.8.

6-Iodo-1-decene (20)
This compound has been prepared in 67% yield from the corresponding alcohol (2.64 g, 17 mmol) and purified by chromatography (eluent, pentane): ^1H NMR (400 MHz): δ 5.80 (ddt, J= 16.98, 10.25, 6.72 Hz, 1H, =CH), 5.00 (m, 2H, =CH_2), 4.12 (m, 1H, CHI), 2.2-2.12 (m, 12H), 0.91 (t, J= 6.9 Hz, 3H, CH_3); ^{13}C NMR (22.4 MHz): δ 138.4 (=CH), 115.0 (=CH_2), 40.7, 40.5, 40.3, 33.0, 31.8, 28.9, 22.0, 14.2 (CH_3).

6-Iodo-7-methyl-1-octene (21)
This compound has been prepared in 61% yield from the corresponding alcohol (7.3 g, 51.4 mmol) and purified by chromatography (eluent, pentane): ^1H NMR (200 MHz): δ 5.80 (ddt, J= 17.06, 10.32, 6.43 Hz, 1H, =CH), 4.95 (m, 2H, =CH_2), 4.16 (m, 1H, CHI), 2.10-1.87 (m, 2H), 1.65-1.15 (m, 5H), 0.98 (d, J= 6.39Hz, 3H, CH3CH), 0.93 (d, J= 6.33 Hz, 3H, CH_3CH); ^{13}C NMR (50 MHz): δ 138.8 (=CH), 114.8 (=CH_2), 51.6, 38.0, 34.8, 32.8, 29.0, 23.0, 20.0.

6-Iodo-7,7-dimethyl-1-octene (22)
This compound has been prepared in 43% yield from the corresponding alcohol (3.1 g, 19.9 mmol) and purified by chromatography (eluent, pentane): ^1H NMR (400 MHz): δ 5.80 (ddt, J= 17.05, 10.45, 6.6 Hz, 1H, =CH), 5.04 (dq, J= 17.05, 1.65 Hz, 1H, =CH_2), 4.97 (dd, J= 11.55, 2.2 Hz, 1H, CHI), 2.12-2.04 (m, 3H), 1.84-1.64 (m, 2H), 1.43 (m, 1H), 1.09 (s, 9H, $(CH_3)_3$); ^{13}C NMR (100 MHz): δ 138.5 (=CH), 115.0 (=CH_2), 58.7 (CHI), 36.1, 35.2, 32.9, 30.3, 28.7 ($(CH_3)_3$).

General procedure for the cyclization of secondary organozinc reagents
Rieke's activated zinc was generated by addition of zinc bromide (4.7 ml, 1M in ether, 4.7 mmol) to a solution of lithium-naphthalenide (9.38 mmol) prepared from lithium (65.1 mg, 9.38 mmol) and naphthalene (1.24 g, 9.69 mmol) in dry THF (5 ml). It was then washed several times with dry ether as described previously. Then, the secondary iodide (1 or 2 mmol) was added neat to the suspension of the active zinc in ether at the required temperature. The fomation of the organozinc reagent as well as its cyclization can easily be followed by G.C. analysis of hydrolyzed aliquots.

cis-1-Iodomethyl-2-methylcyclopentane cis-(14)
18 (300 mg, 1.33 mmol) was added at -20°C to Rieke's activated zinc according to the general procedure. After stirring for 40 minutes, GC analysis of both hydrolyzed and iodinolyzed aliquots indicated a complete conversion to the corresponding linear organozinc reagent and that cyclization has only occured to an extent of 5%. The reaction mixture was slowly warmed to room temperature, the amount of cyclic products reached 50% at -5°C and 100% at 10°C (cis/trans= 81/19). The reaction mixture was then iodinolyzed. The crude product was purified by chromatography (eluent, pentane) to give 209 mg (70%) of the title compound, the major diastereoisomer being isolated (cis/trans= 98/2) as a colorless oil: ^1H NMR (200 MHz): δ 3.12 (dd, J= 7.80, 1.46 Hz, 2H, CH_2I), 2.25 (m, 1H, $CHCH_2I$), 2.15 (m, 2H), 1.85-1.25 (m, 5H), 0.80 (d, J= 6.93 Hz, 3H, CH_3); Anal. Calcd. for $C_7H_{13}I$: C, 37.52; H, 5.85. Found: C, 37.69; H, 5.97.

1-Butyl-2-methylcyclopentane (25)
20 (532 mg, 2 mmol) was added to Rieke's activated zinc in ether following the general procedure. After stirring for 20 minutes at room temperature (25°C), the reaction mixture was hydrolyzed. The crude material was purified by chromatography (eluent, pentane) to give 160 mg (57%) of the title compound as a colorless liquid (73/27 mixture of cis/trans diastereoisomers): ^1H NMR (400 MHz): δ 2.00-1.00 (m, 14H), 0.95 (d, J= 6.42 Hz, 0.81H, CH_3CH trans), 0.89 (t, J= 6.26 Hz, 2.19H, CH_3CH cis); cis diastereoisomer

^{13}C NMR (50 MHz): δ 43.6, 36.2, 33.8, 31.3, 30.4, 29.9 (2 carbons), 23.3, 22.7, 15.0 trans diastereoisomer (also synthetized by an independent way) ^{13}C NMR (50 MHz): δ 47.9, 40.9, 35.0, 34.7, 32.7, 31.1, 23.7, 23.3, 19.7, 14.3. Anal. Calcd. for $C_{10}H_{20}$: C, 85.63; H, 14.37. Found: C, 85.77; H, 14.48.

2-Butyl-1-(iodomethyl)cyclopentane (26)
20 (532 mg, 2 mmol) was added to Rieke's activated zinc in ether according to the general procedure. After stirring for 20 minutes at room temperature (25°C), the reaction mixture was hydrolyzed. The crude material was purified by chromatography (eluent, pentane) to give 360 mg (67%) of the title compound as a colorless oil (73/27 mixture of cis/trans diastereoisomers): ^1H NMR (400 MHz): δ 3.38 (A part of ABX, J_{AB}= 9.5 Hz, J_{AX}= 4.2 HZ, 0.27H, CHI trans),3.27 (A part of ABX, J_{AB}= 9.4 Hz, J_{AX}= 6.2 HZ, 1H, CHI cis), 3.12 (B part of ABX, J_{AB}= J_{BX}= 9.5 Hz, 0.27H, CHI trans) 3.05 (B part of ABX, J_{AB}= J_{BX}= 9.4 Hz, 0.73H, CHI cis), 2.39-2.31 (m, X part of ABX, 0.73H, $CHCH_2I$ cis), 2.00-1.05 (m, 7.27H), 0.91 (m, 3H, CH_3); ^{13}C NMR (50 MHz): δ 48.1, 46.4, 46.2, 43.3, 34.8, 33.9, 33.1, 32.1, 30.8, 30.2, 28.7, 23.6, 23.1, 22.7, 14.3 (CH_2I trans), 14.25 (CH_3), 10.1 (CH_2I cis); Anal. Calcd. for $C_{10}H_{19}I$: C, 45.13; H, 7.19. Found: C, 45.39, H, 7.21.

1-Iodomethyl-2-isopropylcyclopentane (27)
21 (300 mg, 1.2 mmol) was added to a suspension of Rieke's activated zinc in ether according to the general procedure. After stirring for 2 hours at 20-25°C, the reaction mixture was iodinolyzed. After usual work-up, the crude material was purified by chromatography (eluent, pentane) to give 234 mg (78%) of the title compound as a colorless oil (70/30 mixture of cis/trans diastereoisomers). ^1H NMR (200 MHz): δ 3.36 (m, 1H, CHI), 3.09 (dd=t, J= 8.8 Hz, 0.3H, CHI trans), 2.87 (dd, J= 12.2, 9.4 Hz, 0.7 H, CHI cis), 2.42 (m, 0.7 H, $CHCH_2I$ cis), 1.83-1.20 (m, 8.3H), 0.95 (d, J= 5.58 Hz, 3H, CH_3CH), 0.89 (d, J= 5.24 Hz, 3H, CH_3CH); ^{13}C NMR (50 MHz): δ 53.0, 52.8, 45.3, 44.8, 34.4, 32.7, 31.0, 29.8, 29.3, 27.8, 24.3, 22.4, 22.3, 21.9, 21.6, 19.2, 15.5 (CH_2I trans), 10.2 (CH_2I cis); Anal. Calcd. for $C_9H_{17}I$: C, 42.87; H, 6.80. Found: C, 43.04; H, 6.85.

1-Iodomethyl-2-tertbutylcyclopentane (28)
22 (375 mg, 1.41 mmol) was added to a suspension of Rieke's activated zinc in ether according to the general procedure. After stirring overnight at 20-25°C, the reaction mixture was iodinolyzed. After usual work-up, the crude material was purified by chromatography (eluent, pentane) to give 225 mg (60%) of the title compound as a colorless oil (67/33 mixture of cis/trans diastereoisomers): ^1H NMR (200 MHz): δ 3.31 (A part of ABX, J_{AB}= 9.5 Hz, J_{AX}= 4.3 Hz, 0.33H, CHI trans), 3.26 (A part of ABX, J_{AB}= 9.6 Hz, J_{AX}= 6.3 Hz, 0.67H, CHI cis), 3.05 (B part of ABX, J_{AB}=J_{AX}= 9.6 Hz, 0.67H, CHI cis), 2.93 (B part of ABX, J_{BX}= 11.8 Hz, J_{AB}= 9.5 Hz, 0.33H, CHI trans), 2.4 (X part of ABX, 0.33H, $CHCH_2I$ trans), 2.05 (X part of ABX, $CHCH_2I$ cis), 1.97-1.00 (m, 6H), 0.95 (s, 3H), 0.86 (s, 6H); ^{13}C NMR (50 MHz): δ 57.0, 56.2, 51.4, 45.5, 43.7, 35.3, 34.8, 33.6, 30.1, 29.65, 27.9, 25.6, 25.4, 23.6, 23.2, 21.2, 21.0, 17.1, 16.9; Anal. Calcd. for $C_{10}H_{19}I$: C, 45.13; H, 7.19. Found C, 45.37; H, 7.24.

3-Iodomethyl-bicyclo[3.3.0]octane (29)
19 (250 mg, 1 mmol) was added to a suspension of Rieke's activated zinc in ether. After stirring for 4 hours at room temperature, the reaction mixture was iodinolyzed and worked-up as usual. The crude product was purified by chromatography (eluent, pentane) to give 182 mg (73%) of the title compound as a pale brown oil (64/36 mixture of exo/endo diastereoisomers): ^1H NMR (200 MHz): δ 3.18 (d, 2H, J= 6.33 Hz, CH_2I exo), 3.17 (d, 2H, J= 6.91 Hz, CH_2I endo), 2.55-0.75 (m, 13H); major diastereoisomer (exo) ^{13}C NMR (100 MHz): δ 42.85, 42.05, 40.86, 35.01, 27.11,

12.91; minor diastereoisomer (endo) ^{13}C NMR (100 MHz): δ 44.63, 43.37,0 41.83, 33.45, 24.86, 12.31.

trans-1-Iodomethyl-2-(2-propenyl)cyclopentane (30)
This compound has been characterized in the preceeding crude reaction mixture (15%) ^1H NMR (200 MHz): δ 5.78 (m, 1H, =CH), 5.01 (m, 2H, $=CH_2$), 3.37 (A part of ABX, J_{AB}= 9.46 Hz, J_{AX}= 4.23 Hz, 1H, CHI), 3.13 (B part of ABX, JAB= 9.46 Hz, JBX= 7.46 Hz, 1H, CHI), 2.55-1.1 (m, 10H); 13C NMR (100 MHz): δ 137.30 (=CH), 115.9 ($=CH_2$), 47.31, 45.49, 39.11, 33.91, 32.705, 23.54, 14.47 (CH_2I).

1-Butyl-2-methylcyclopentane by cyclization of (31)
20 (300 mg, 1.13 mmol) was added to suspensio of Rieke's activated zinc in ether. After stirring overnight at room temperature, the reaction mixture was hydrolyzed. After usual work-up, the crude material was purified by chromatography (eluent, pentane) and carrefully concentrated to give 127 mg (80%) of the title compound **25** as a colorless liquid.(68/32 mixture of cis/trans diastereoisomers).

1-Acetoxy-1-bromo-5-hexene (33)
A solution of freshly distilled acetyl bromide (4.5 ml, 60 mmol) and dry zinc chloride (100 mg) in dry dichloromethane (15 ml) was cooled to -10°C as 5-hexen-1-al (3.9 g, 40 mmol) was added dropwise. After stirring for 2 hours at -5°C the cold reaction mixture was filtered through a short column packed with neutral alumina (30 g) and eluted with dichloromethane. Concentration afforded an oil which was distilled under reduced pressure, bp= 40°C (0.1 mmHg), to give 5.7 g (43%) of the title compound as a pale yellow oil which was immediately stored at -20°C: ^1H NMR (400 MHz): δ 6.61 (t, J= 6.05 Hz, 1H, CHOAcBr), 5.77 (ddt, J= 16.5, 9.9, 6.6 Hz, 1H, =CH), 5.06-4.98 (m, 2H, $=CH_2$), 2.20-2.04 (m, 5H, including 2.11 (s, 3H)), 1.85-1.56 (m, 4H); ^{13}C NMR (100 MHz): δ 168.4 (C=O), 137.7 (=CH), 115.5 ($=CH_2$), 76.2 (CHOAcBr), 38.7 (CH_3CO), 32.7, 25.0, 21.0.

1-Acetoxy-2-methylcyclopentane (8a) by cyclization of (33)
33 (400 mg, 1.81 mmol) was added to a suspension of Rieke's activated zinc in ether at room temperature. After stirring for 3 to 12 hours, the reaction mixture was hydrolyzed and worked-up as usual. The crude material was purified by flash-chromatography (eluent, pentane / ether, 4/1- to give 257 mg (50%) of the title compound as a pale yellow oil (86/14 mixture of cis/trans diastereoisomers).

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