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Synthesis of Arylcycloalkanes from ω-Alkenyl Benzylselenides

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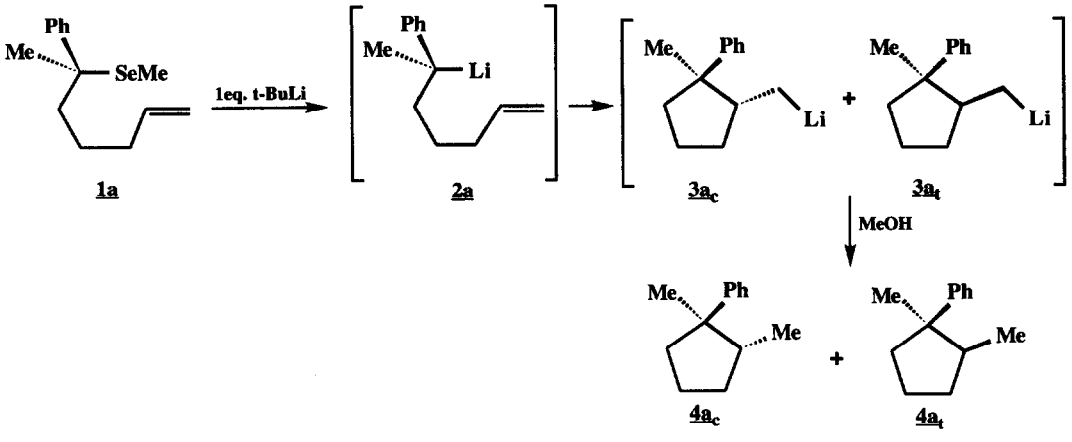
Abstract: Arylcycloalkanes are produced from ω-alkenyl benzylselenides on reaction with alkyllithiums or on Lewis acid mediated electrophilic cyclisation.

We recently disclosed [1,2] that 6-phenyl-6-methylseleno-1-heptene **1a** bearing a terminal double bond is transformed to 1,2-dimethyl-2-phenyl-cyclopentanes **4a** in high yields on reaction with butyllithiums and methanolysis of the intermediates **3a** (Scheme 1). The reaction is highly regio- and stereoselective and produces the stereoisomeric phenylcyclopentanes **4a$_c$** or **4a$_t$** depending upon both the solvent and the temperature used.[1]

Scheme 1

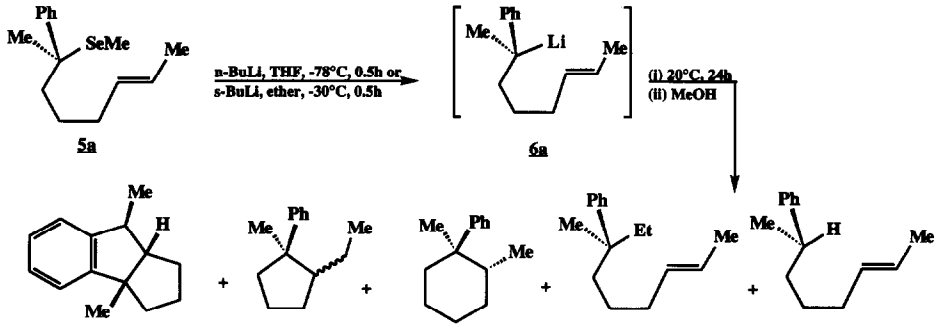


THF, -78°C, 0.5h	**85%**	98	02
Ether, -30°C, 0.5h	**85%**	02	98
Pentane, 20°C, 0.8h	**90%**	02	98

We now report that homologous *(E)*-7-methylseleno-7-phenyl-2-octene **5a$_E$** also cyclises to the corresponding arylcycloalkanes **9a-11a$_c$** in THF or ether but the reaction requires more drastic conditions (20°C, 24 h for **5a$_E$** instead of -78°C or -30°C, 0.5 h for **1a**) and leads to substantial amounts of olefinic products resulting from the protonation **7a$_E$** and ethylation **8a$_E$** of the intermediate benzyllithium **6a$_E$** (Scheme 2). The reaction is again solvent dependent but it now produces stereoselectively the six membered cycle **9a$_t$** if it is carried out in THF and a stereoisomeric mixture of 2-ethyl-1-methyl-1-phenyl cyclopentanes **10a$_c$** and **10a$_t$** as well as the tricyclic derivative **11a** if it is instead performed in ether (Scheme 2).

Dedicated to Professor L. Ghosez at the occasion of his 60th birthday.

Scheme 2

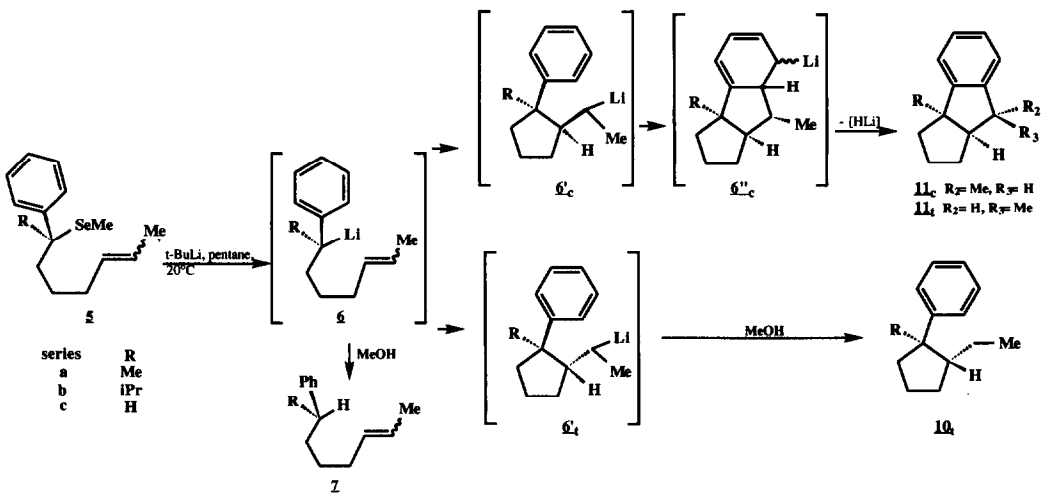


	11a$_c$	10a$_c$/10a$_t$	9a$_t$	8a	7a
THF	07	01/05	27	20	40
Ether	37	12/12	00	24	15

The formation of the cyclised products **11a**, **10a** and **9a** is particularly unusual since it implies the intramolecular addition of the benzyllithium compound **6a**$_E$ onto an α,β-dialkyl substituted C=C double bond. This type of reaction has been only described previously in the case of strained olefins.[3] Furthermore, the formation in ether of the tricyclic derivative **11a**$_c$ requires the intramolecular addition of the secondary alkyllithium **6'a**$_c$ to the benzene ring leading to **6"a**$_c$ which further aromatizes by lost of lithium hydride (Scheme 3).[4,5]

We further found that, if the reaction is carried out in pentane (this requires the use of t-butyllithium instead of n-butyllithium), the cyclopent(a)indene derivative **11a**$_c$ can be obtained almost quantitatively besides small amounts of partially cyclised product **10a**$_t$ and olefinic products **7a**$_E$ (Scheme 3, entry a). In such solvent the yield in pure product is nevertheless rather low due to the difficulty encountered in removing **7a**$_E$. We have observed that, under the above mentioned conditions, (i) both *(E)*- and *(Z)*-**5a** cyclise, at a closely related rate leading to the same derivative **11a**$_c$ and (ii) the *(Z)*-derivative **5a**$_Z$ is slightly more reactive than its *(E)*-stereoisomer **5a**$_E$ (Scheme 3, entries a and b).

Scheme 3



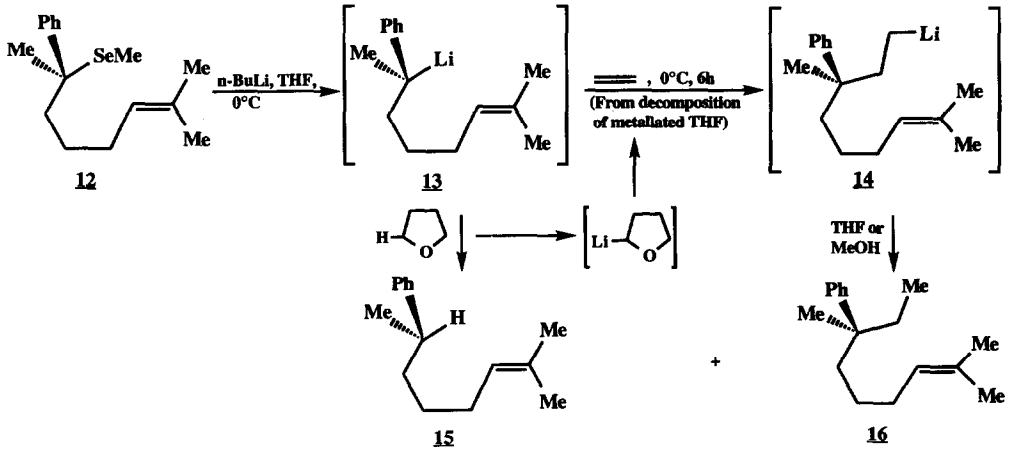
Entry	R	Selenide	Olefin stereochemistry	Reaction time (days)	**11c/11t/10t/7** [a]
a	Me	**5aE**	E	1	88/5/3/4
b	Me	**5aZ**	Z	1	88/5/3/4
c	H	**5cE**	E	9	84 [b]/2/-- [c]
d	iPr	**5bE**	E	15	71/19//0/10

a. Obtained by /GC/[2] on a SE 30 column in the crude mixture. b. Relative stereochemistry not yet determined. c. Another compound whose structure has not been yet identified, has been also isolated in 14% yield. **7** not quantified.

This reaction is not limited to **5a** and has been extended to the benzyl selenides **5bE** and **5cE** bearing an isopropyl or a hydrogen in place of the methyl group on the benzylic carbon (Scheme 3 entries c and d). A complete stereocontrol is observed for the formation of **11cc** from **5cE** whereas a mixture of diastereoisomers, in which **11bc** greatly prevails (**11bc/11bt** : 86/14), is formed from **5bE** (Scheme 3, entries c and d). In the case of **5cE** another compound, whose structure has not yet been assigned, is also observed.

We have also reacted 2-methyl-7-methylseleno-7-phenyl-2-octene **12**, which bears a trialkyl substituted C=C double bond with alkyllithiums in different solvents but have been unable to find conditions which allow the cyclisation of the intermediate benzyllithium **13** (THF, 0°C, 6h or pentane, 20°C, 5h). In THF metallation occurs leading to **15** and 2-lithio-THF. Decomposition of this metallated species [6] produces ethylene which adds to **13** producing **14** [2] and then **16** (**15**/**16**: 1/1, Scheme 4).

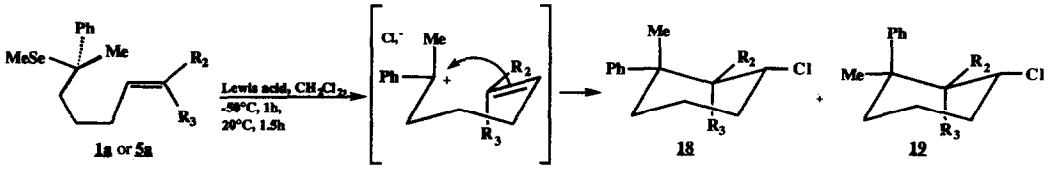
Scheme 4



We then turned our attention towards the synthesis of arylcycloalkanes from the benzylselenides **1a**, **5a**, **12** using Lewis acid promoted C-Se bond cleavage, expecting a different behaviour depending upon (i) the substitution at C-6 and C-7 (i.e. the aptitude of these carbon atoms to stabilise the intermediate carbenium ion) and (ii) the stereochemistry of the olefin. This type of reaction has been used in (i) the pinacolic-type rearrangement of β-hydroxyalkyl selenides to carbonyl compounds [7] (ii) the cyclisation of δ- and ε-hydroxyalkyl selenides to furans [8] and pyrans [9] and in (iii) the transformation [10] of selenoacetals to α-seleno carbenium ions. This last reaction has been recently used to promote the intramolecular cyclisation of ε-alkenyl phenylselenoacetals to 3-chloro-1-phenylseleno-cyclohexane derivatives.[11]

We have thus reacted unsaturated benzylselenides **1a**, **5a**, **12** with Lewis acids (2 equiv. $TiCl_4$ or $SnCl_4$, CH_2Cl_2, -50°C, 1.5h then 20°C, 1.5h, Scheme 5 and 6) and found that the unsaturated selenides bearing a terminal **1a** or a α,β-dialkyl substituted C=C double bond **5aE** and **5aZ** produce 3-chloro-1-methyl-1-phenylcyclohexane derivatives **18** or/and **19** in reasonably good yields and with reasonably good stereocontrol (Scheme 5). A mixture of **18a** and **19a** (R_2, R_3= H, 57% yield, **18a/19a** = 87/13) is obtained from **1a** whereas the stereoisomers **18bt** (R_2= Me, R_3= H, 78% oyield) or **18bc** (R_2= H, R_3= Me, 61%) resulting from an antiperiplanar addition of the benzylic carbon and the chlorine ion across the C=C double bond are stereoselectively produced from **5aE** and **5aZ** respectively. The higher interactions in the transition states between the phenyl and the methyl group from **5a** or the hydrogen from **1a** should be responsible for the different levels of stereocontrol observed.

Scheme 5

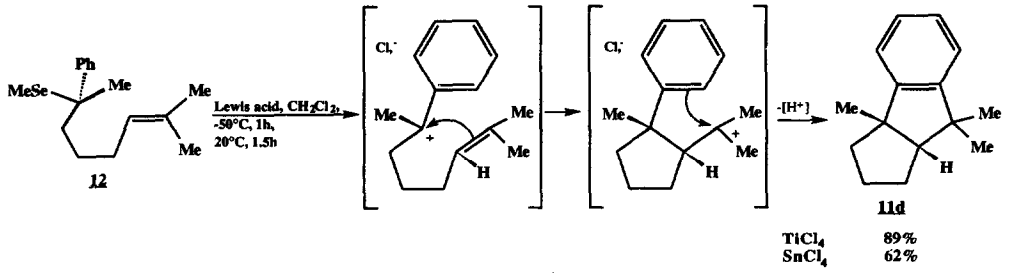


Entry	R_2	R_3	Selenide	E/Z ratio	Lewis acid	Overall yield	Products	ratio [a]
a	H	H	**1a**	-	$TiCl_4$	57	**18a/19a**	87/13
b	H	H	**1a**	-	$SnCl_4$	53	**18a/19a**	83/17
c	Me	H	**5aE**	96/4	$TiCl_4$	78	**18bt/18bc**	97/3 [b]
d	Me	H	**5aE**	96/4	$SnCl_4$	73	**18bt/18bc**	96/4 [b]
e	H	Me	**5aZ**	4/96	$TiCl_4$	61	**18bc/18bt**	4 [b]/96

a. The relative ratio of stereoisomers has been determined by /GC/[2] on a methylsilicone (SE 30) column. b. This refers to a mixture of two compounds in a 1/1 ratio which seem to be isomeric at the carbon bearing the chlorine atom.

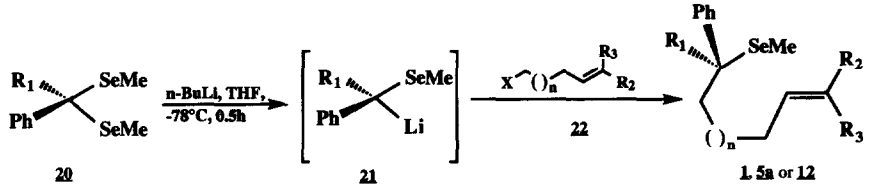
Under the same conditions 2-methyl-7-methylseleno-7-phenyl-2-octene **12** behaves differently and leads, via a 5-exo-trig process, to the tricyclic derivative **11d** with high stereocontrol.[12] This implies a *cis*-arrangement between the phenyl group and the isopropyl cation in the intermediate prior to Friedel-Craft cyclisation (Scheme 6). This is a particularly efficient route to such compound unavailable from **12** *via* the organolithium mediated cyclisation (compare the results disclosed in Scheme 6 to the one disclosed in Scheme 4) and therefore the whole set of tricyclic derivatives **11** is available from the unsaturated selenides using, depending upon the substitution pattern of the C=C double bond, the appropriate reaction conditions (BuLi or Lewis acids).

Scheme 6



All the alkenyl selenides described in this paper have been synthesised from benzaldehyde or acetophenone *via* a two step sequence which involves the formation of their methylselenoacetals **20** (2 equiv. MeSeH, 0.35 equiv. $TiCl_4$, CH_2Cl_2, -50°C, 1h, 89% for **20'** and 70% for **20"**).[13,15] The synthesis of **1a**, **1b**, **5a**, **5c** and **12** involves the cleavage of the C-Se bond of the selenoacetal **20** (n-BuLi, THF, -78°C, 0.5h) followed by alkylation of the resulting α-selenobenzyllithium **21** with the appropriate alkenyl halide **22** (Scheme 7).[14]

Scheme 7

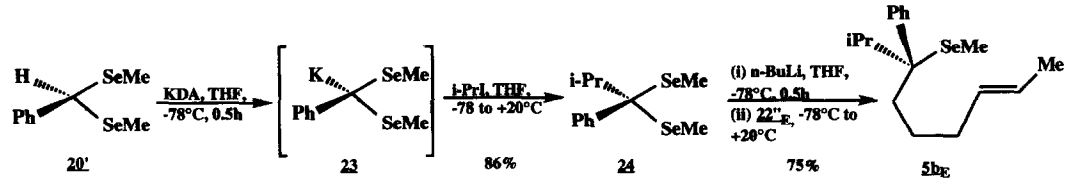


Entry	Selenoacetal	R_1	halide	X	n	R_2	R_3	Selenides	Yield (%)
a	**20'**	H	**22''$_E$**	I	1	Me	H	**5c$_E$** [a]	55
b	**20"**	Me	**22''$_E$**	I	1	Me	H	**5a$_E$** [a]	81
c	**20"**	Me	**22''$_Z$**	I	1	H	Me	**5a$_Z$** [a]	86
d	**20"**	Me	**22'''**	I	1	Me	Me	**12**	82
e	**20"**	Me	**22'**	Br	1	H	H	**1a**	96
f	**20"**	Me	**22''''**	Br	2	H	H	**1b**	87

[a] Obtained as a 96/04 mixture of stereoisomers

The synthesis of the benzylselenide **5b$_E$** has been achieved in a different manner (Scheme 8) due to the impossible selenoacetalisation of isobutyrophenone.[13] The required selenoacetal **24** has been obtained by metallation of the selenoacetal **20'** (KDA, -78°C, 0.5h) [15] and alkylation of the resulting bis(methylseleno)benzylpotassium **23** with isopropyl iodide (iPrI, -78°C to 20°C, 0.5h, 86%). Sequential reaction with n-butyllithium and *(E)*-6-iodo-2-hexene **22''$_E$** under the conditions described above (n-BuLi, THF, -78°C, 0.5h then **22''$_E$** (1.1 equiv.), -78°C to 20°C, 0.5h) leads to the desired benzylselenide **5b$_E$** in good yield (75%, Scheme 8).

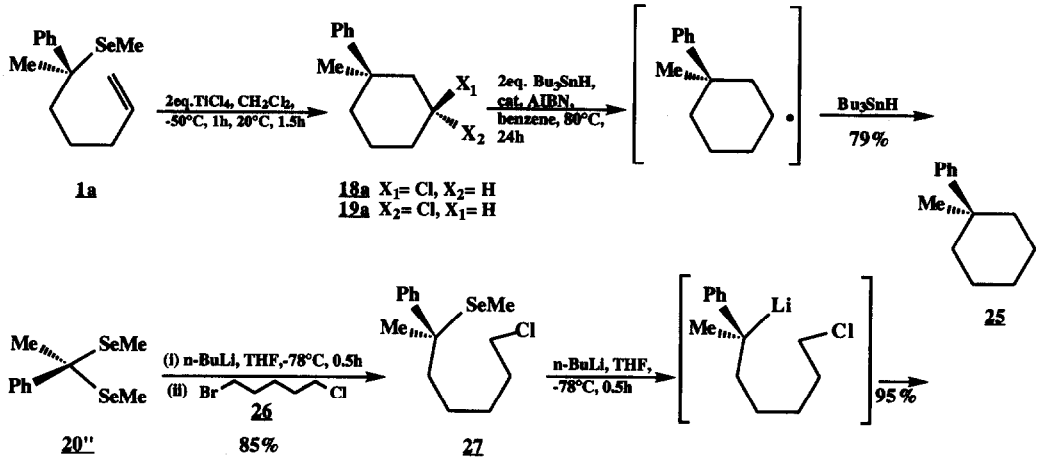
Scheme 8



Most of the structures determinations and stereochemical assignments have been made by ^1H and ^{13}C NMR including 2D NMR and, in some cases, by comparison of the phenylcycloalkanes, obtained by reduction of **18** and/or **19** with tributyl tin hydride, with authentic samples prepared as described below.

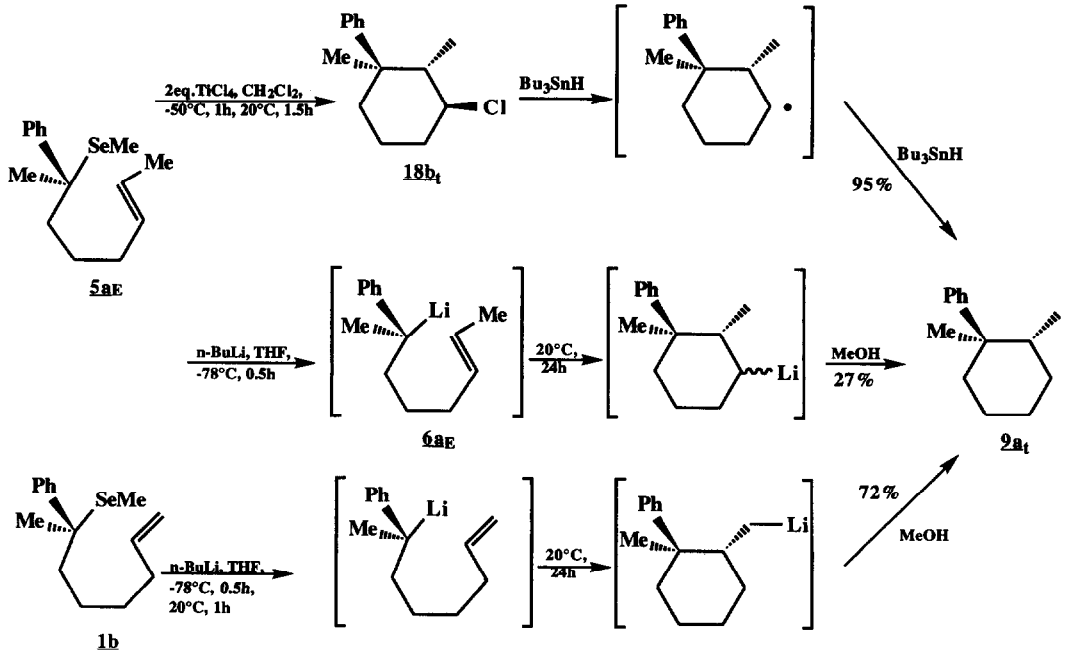
Thus, 1-methyl-1-phenyl cylohexane **25**, obtained by reduction of the stereoisomeric mixture of compounds **18a**/**19a** (87/13), proved to be identical to the one synthesised from acetophenone *via* 7-chloro-2-methylseleno-2-phenyl heptane **27** (by sequential treatment of 1,1-bis(methylseleno)-1-phenyl-ethane **20"** with n-butyllithium, 1-bromo-5-chloropentane **26** and n-butyllithium again, Scheme 9).

Scheme 9



Similarly, the reduction of **18b$_t$** and **18b$_c$** with tin hydride (Bu_3SnH, C_6H_6, 80°C, 24-48h) produces respectively 1,2-dimethyl-1-phenyl-cyclohexanes **9a$_t$** (80%) possessing a *trans*-relationship between the phenyl and methyl group and **9a$_c$** (95%) possessing a *cis*-relationship instead (Scheme 10). The stereoisomer **9a$_t$** has been identified by comparison with authentic samples derived from anionic cyclisation of (i) *(E)*-7-methylseleno-7-phenyl-2-octene **5a$_E$** in THF (see scheme 2) or of (ii) 7-phenyl-7-methylseleno-1-octene **1b** in the same solvent (nBuLi, THF, -78°C, 0.5h then 20°C, 0.5h, 72%).

Scheme 10



In conclusion we have described that benzyllithiums are able to add, under mild conditions, to an α,β-dialkyl substituted C=C double bond. This type of carbolithiation reaction is very rare and has to our knowledge never been published in the literature [16] except in the case of a strained olefin.[3] Although several examples of addition of an organometallics to terminal C=C double bonds have been published[16], they are only very few reports on related reactions involving α,β-dialkyl substituted olefins.[5,17-23] Several authors have even recently quoted the impossibility to do so with organolithium compounds.[24-26] Recently however Normant and his team [27] have disclosed the first efficient cyclisation of an organozinc compound across an α,β-dialkyl substituted C=C double bond. Much earlier Pines described a reaction related to the one disclosed in Scheme 3 but involving aryl alkene and molten potassium. The conditions were very harsh (>220°C) and the yield in cyclised product very poor.[4]

We have also described several synthetic routes to arylcycloalkanes from benzylselenides which involve anionic or cationic intermediates. We have observed that the nature of the cyclised product is highly dependent in both cases upon the substitution around the C=C double bond and that, in the case of the anionic route, upon the nature of the solvent. Work is now in progress to generalise such finding.

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Experimental Section

1. General

^{1}H-NMR spectra have been performed on JEOL EX 400 (400 MHz for ^{1}H or 100.4 MHz for ^{13}C), JEOL JNM 60 Si (60 MHz) and JEOL FX 90 Q (90 MHz) spectrometers. The spectra were measured in CCl_4 or $CDCl_3$ with TMS as an internal standard (δ : 0.00). IR data reported in cm^{-1} were obtained using a Perkin-Elmer model 337 spectrophotometer. The spectra were performed on neat liquids. Mass spectra were obtained on AEI MS30 or HP 5995 A GC / MS spectrometers. In the discussion M refers to $M^{+\circ}$ and only a few characteristics are reported. Microanalyses were performed in the Microanalysis Laboratory of the Paris VI University (Paris, France). Layer chromatography : Analytical thin-layer chromatography (TLC) was performed on pre-made, glass-backed plate SiO_2, 60PF254, 250 microns (Merck 5719). Compounds were visualised by UV illumination and by heating to 150°C after spraying phosphomolybdic acid in ethanol. Preparative layer chromatography (PLC) was performed on SiO_2 (Merck 7747, 1.5 mm thickness) prepared as described previously.[13] Preparative HPLC have been performed on Prochrom LC.50 stainless steel column (Diam.: 50mm, Length : 350 mm filled with 400 g of SiO_2 (Merck 15.111 (15-40 μm)) using a flow rate of 100 ml/min and the detection was performed using UV detector (λ= 254 nm). GC analyses have been performed on HP 5890 chromatograph mounted with FID detectors ($T_{det.}$= 250°C) using glass coated, crosslinked methylsilicone (SE 30) column (HP-1, fused silica, 30 m x 0.2 mm x 0.33 μm film thickness) or OV17 (RSL, fused silica, 30 m x 0.32 mm x 0.3 μm film thickness) and He as a carrier gas (1ml/min). Injection have been performed *via* a spliter (split ratio : 1/40, $T_{inj.}$= 250°C). The temperature of the column used for GC analysis, as well as other changing parameters will be described for each specific cases.

All the reactions were performed in two necked round bottomed flasks equipped with a rubber septum and an argon filled balloon or in sealed tubes filled with argon and closed by a rubber septum, except some reactions involving organometallics and long reaction time which have been carried out, under argon, in a 25 ml tube closed by a rubber septum (method A).

All the glassware was flame heated prior use and degassed at 0.1 mm Hg. All transfer of reagents were performed *via* syringes. When the reactions needed to be cooled, the flasks were immersed in a Dewar filled with a dry-ice/acetone mixture (-78°C) or in an acetonitrile/dry-ice mixture (-50°C).

2. Reagents and solvents.

Unless otherwise noted, the reagents and solvents used in this work have been purchased from Janssen Chimica (Beerse, Belgium) or Aldrich (Bornem, Belgium). 4-Penten-1-ol (Aldrich), 5-bromo-1-pentene **22'** (Aldrich), 6-bromo-1-hexene **22"'** (Aldrich), 5-chloro-1-pentyne (Aldrich) were distilled prior to use. Anhydrous THF or ether were distilled from sodium benzophenone ketyl just prior to use and anhydrous dichloromethane was distilled from phosphorous pentoxyde. n-BuLi (1.6 M in hexane, Aldrich), s-BuLi (1.0 M in cyclohexane, Janssen) and t-BuLi (1.7 M in cyclopentane, Aldrich) have been titrated prior to use using the Gilman's procedure.[28]

3. Synthesis of ***22"$_Z$*** *and* ***22"$_E$***

Synthesis of *(E)-6-iodo-2-hexene* 22"$_E$

Mesylchloride (9.06 g, 79 mmol) was added dropwise to a solution of *(E)*-4-hexen-1-ol (Aldrich; 7.13 g, 72 mmol) and Et_3N (10.90 g, 108 mmol) in 150ml of dichloromethane stirred, under argon, at 0°C. The solution was stirred at 0°C for an additionnal 0.25h, then at room temperature for 0.25h and was hydrolysed with ice-water. The solution was diluted with dichloromethane, washed successively with HCl 10% w/w, saturated solution of aqueous $NaHCO_3$, water (2x 10 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mm Hg) to give the crude mesylate as an oil. It was used in the next reaction without purification.

The crude mesylate was dissolved at room temperature in a 1.2 M solution of NaI (Janssen Chimica ; 26.82 g, 180 mmol) in acetone and was refluxed for 17h. It was then cooled to room temperature and diluted with pentane, washed with water (2x10 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mm Hg) to give the crude alkyl iodide. The residue was distilled *in vacuo* (b.p. 78-80°C/20 mm Hg) to provide 13.20 g of *(E)*-6-iodo-2-hexene **22"$_E$** (63 mmol, 87%).[29]

Synthesis of *(Z)-6-iodo-2-hexene* 22"$_Z$

Synthesis of 6-iodo-2-hexyne:. A solution of 5-chloro-1-pentyne (Aldrich; 3.08 g, 30 mmol) in 30 ml of dry tetrahydrofuran was cooled under argon to -78°C with stirring and n-butyllithium (18.75 ml, 30 mmol) was added dropwise. The resulting pale yellow solution was stirred for 0.4h at this temperature and methyl iodide (Janssen Chimica; 4.65 g, 33 mmol) in 10 ml of hexamethylphopshotriamide was added dropwise. The stirring was continued at -78°C for 0.2h and at room temperature for 2.5 h. The solution was diluted with 30 ml of ether, washed with water (2x10 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* (400 mm Hg) to approximately 10 ml. This crude mixture was dissolved at room temperature in a 1.2 M solution of NaI (Janssen Chimica ; 6.70 g, 45 mmol) in acetone. The yellow solution was refluxed for 24h, cooled to room temperature, diluted with pentane and washed with water (2x10 ml). The organic layer was dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mm Hg) to give the crude alkynyl iodide. This was distilled *in vacuo* (b.p. 76°C/20 mm Hg, lit., [30]: b.p. 86°C/90 mm Hg) to provide 5.41 g of 6-iodo-2-hexyne (28 mmol, 94%).

Semi-hydrogenation of 6-iodo-2-hexyne [31] To a solution of 6-iodo-2-hexyne (2.76 g, 13 mmol) in 13 ml of methanol was added 10% Pd-on-barium sulfate (Merck, 0.138 g) and quinoleine (Merck, 0.150 g). The reaction slowed down after the uptake of 26 ml of hydrogen. The reaction mixture was filtered through a short path of celite (Janssen Chimica) and the solvent removed *in vacuo* (20 mm Hg). Distillation (b.p. 80°C/20 mm Hg) afforded 1.80 g of *(Z)*-6-iodo-2-hexene **22"$_Z$** as a colourless oil (8.6 mmol, 70%). TLC: Rf= 0.9 (pentane).

^{1}H NMR ($CDCl_3$/90 MHz): δ (ppm) : 1.55-2.34 (m, 7H, -C<u>H</u>$_2$-C<u>H</u>$_2$-CH=CH-C<u>H</u>$_3$), 3.17 (t, J= 6.59 Hz, 2H, I-C<u>H</u>$_2$-), 5.17-5.69 (m, 2H,-C<u>H</u>=C<u>H</u>-). ^{13}C NMR ($CDCl_3$/22.5 MHz): δ (ppm) : 5.79, 12.78, 27.78, 33.32, 125.31 and 128.13. MS (C.I.(CH_4^+)): m/z: 210, 196, 182, 168, 154. IR (neat): cm^{-1}: 3011, 2956, 2933, 2857, 1718, 1654, 1648, 1442, 1425, 1403, 1369, 1343, 1316, 1264, 1218, 1167, 977 and 760. Elemental analysis for $C_6H_{11}I$: Calc.: C, 34.30%; H, 5.27%; Found: C, 34.29%; H, 5.19%.

4. Synthesis of benzylselenides **1**, **5** *and* **12**

General procedure I : A 1.0 M solution of the selenoacetal [13] in anhydrous tetrahydrofuran was cooled to -78°C, under argon, with stirring and exactly 1.0 molar equivalent of n-butyllithium was added dropwise. The resulting dark red (for selenoacetals **20"** and **20'''**) or green (for selenoacetal **20'**) solution was stirred at this temperature for 0.5h and a solution of the ω-alkenyl-halide (1.1 equiv., 1.0 M in THF) was added dropwise. The pale yellow solution was stirred at -78°C for 0.5h then at room temperature for an additional 0.5h, quenched with water (10 ml) and diluted with ether. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water (10 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mm Hg). The residual yellow liquid was purified by distillation or by SiO_2 preparative thin layer chromatography (PLC) to afford the benzylselenides **5**, **12** or **1b** as pale yellow liquids. Specific details as well as spectroscopic and analytical data are described bellow.

Synthesis of 7-methylseleno-7-phenyl-2-octene 1a

Following the general procedure I, 1,1-bis(methylseleno)-1-phenyl-ethane **20"** [13] (7.66 g, 26.25 mmol) reacts successively with n-butyllithium (15.6 ml, 25 mmol) and 5-bromo-1-pentene **22'** (4.09 g, 27.5 mmol) to afford, after purification by distillation (b.p. 103°C/0.1 mm Hg), 6.40 g of the benzylselenide **1a** (24 mmol, 96%). For the success of this reaction, the 1/0.95 stoechiometry described above must be strictly used (for a complete discussion of such problem see ref.[1]). TLC: Rf= 0.47 (pentane/benzene (9:1,v/v). ^{1}H NMR (CCl_4/60 MHz): δ (ppm) : 0.66-2.50 (m, 12H, -(C<u>H</u>$_2$)$_3$-CH=C<u>H</u>$_2$, SeC<u>H</u>$_3$ at 1.63 ppm (s) and PhCC<u>H</u>$_3$ at 1.82 ppm (s)), 4.70-5.20 (m, 2H, -CH=C<u>H</u>$_2$), 5.30-6.10 (m, 1H, -C<u>H</u>=CH$_2$) and 6.70-7.66 (m, 5H, ArH). IR (neat): cm^{-1}: 3050, 2920, 1640, 1600, 1490, 1440, 1375, 1030, 990, 910, 760, 700. MS (E.I.): m/z: 268 (M), 173 (M-SeCH$_3$), 131, 117, 105 and 91(tropylium ion). Elemental analysis for $C_{14}H_{20}Se$: Calc.: C, 62.91%; H, 7.54%; Found: C, 63.16%; H, 7.57%.

Synthesis of 7-methylseleno-7-phenyl-2-octene 1b

Following the general procedure I, 1,1-bis(methylseleno)-1-phenyl-ethane **20"** [13] (0.292 g, 1 mmol) reacts successively with n-butyllithium (0.63 ml, 1 mmol) and 6-bromo-1-hexene **22''''** (0.179 g, 1.1 mmol) to afford, after purification by PLC (eluent: pentane/benzene (9:1,v/v)), 0.245 g of the benzylselenide **1b** (0.87 mmol, 87%). TLC: Rf= 0.56 (pentane/benzene (9:1,v/v). ^{1}H NMR (CCl_4/60 MHz): δ (ppm) : 0.85-2.30 (m, 14H, -(C<u>H</u>$_2$)$_4$-CH=C<u>H</u>$_2$, SeC<u>H</u>$_3$ at 1.59 ppm (s) and PhCC<u>H</u>$_3$ at 1.79 ppm (s)), 4.70-5.20 (m, 2H, -CH=C<u>H</u>$_2$), 5.30-6.10 (m, 1H, -C<u>H</u>=CH$_2$) and 6.85-7.60 (m, 5H, ArH). IR (neat): cm^{-1}: 2905, 1490, 1370, 1140, 900, 760 and 695. MS (E.I.): m/z: 186 (M-SeCH$_3$), 171 (M-CH$_3$), 158, 143, 131, 128, 117, 115, 105, 103 and 91(tropylium ion). Elemental analysis for $C_{15}H_{22}Se$: Calc.: C, 64.08%; H, 7.86%; Found: C, 63.62%; H, 7.87%.

Synthesis of *(E)*-7-methylseleno-7-phenyl-2-octene 5a$_E$

Following the general procedure I, 1,1-bis(methylseleno)-1-phenyl-ethane **20"** [13] (8.76 g, 30 mmol) reacts successively with n-butyllithium (18.75 ml, 30 mmol) and *(E)*-6-iodo-2-hexene **22"$_E$** (6.93 g, 33 mmol) to afford, after purification by distillation (b.p. 123°C/0.1 mm Hg), 7.126 g of the benzylselenide **5a$_E$** (25.5 mmol,

85%). TLC: Rf= 0.20 (pentane). ^{1}H NMR ($CDCl_3$/60 MHz): δ (ppm): 1.0-2.26 (m, 15H, -(CH_2)3-CH=CH-CH_3, SeCH_3 at 1.66 ppm (s) and PhCCH_3 at 1.83 ppm (s)), 5.2-5.4 (m, 2H,-CH=CH-), 7.0-7.5 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$/22.5 MHz): δ (ppm) : 3.47 (q, SeCH_3), 17.66 (q, =CHCH_3), 25.23 (t, -CH_2-), 26.50 (q, PhCCH_3), 32.81 (t, -CH_2-) 42.27 (t, -CH_2-), 47.00 (s, PhC), 121.77 (d, -CH=CH-CH_3), 123.04, 123.6 et 123.98 (d, Ar), 126.19 (d, -CH=CH-CH_3), 145.12 (s, C_{Ar}ipso). IR (neat): cm^{-1}: 3084, 3055, 3020, 2933, 2861, 1940, 1870, 1801, 1740, 1668, 1598, 1442, 1270, 965, 697 and 612. MS (E.I.): m/z: 186 (M-SeCH_3), 157, 144, 131 (M-SeCH_3 - (CH_2)-CH=CH-CH_3), 118, 115, 91 (tropylium), 77 and 55.

Synthesis of *(E)*-8-methyl-7-methylseleno-7-phenyl-2-nonene 5b$_E$

Following the general procedure I, 1,1-bis(methylseleno)-2-methyl-1-phenyl-propane **20'''** [15] (3.09 g, 10 mmol) reacts successively with n-butyllithium (6.55 ml, 10 mmol) and *(E)*-6-iodo-2-hexene **22''$_E$** (2.37 g, 11 mmol) to afford, after purification by distillation (b.p. 128-130°C/0.1 mm Hg), 2.23 g of the benzylselenide **5b$_E$** (7.5 mmol, 75%). TLC: Rf= 0.31 (pentane). ^{1}H NMR ($CDCl_3$/60 MHz): δ (ppm): 0.96 et 0.88 (2d, J= 6.95 Hz, 6H (CH_3)$_2$CH-), 1.36-2.53 (m, 13H, (CH_3)$_2$CH-, -(CH_2)3-CH=CH-CH_3, SeCH_3 (s) at 1.66 ppm), 5.26-5.40 (m, 2H,-CH=CH-), 7.0-7.6 (m, 5H, ArH). IR (neat): cm^{-1}: 3085, 3054, 3020, 2959, 2932, 1944, 1900, 1850, 1717, 1654, 1598, 1545, 1442, 965, 787, 762 and 702. MS (E.I.): m/z: 214 (M-SeCH_3), 159, 146, 131, 117 (PhC=CHCH_3^+), 105, 91(tropylium), 77 and 55. Elemental analysis for $C_{17}H_{26}Se$: Calc.: C, 66.00%; H, 8.47%; Found: C, 65.29%; H, 8.52%.

Synthesis of *(E)*-7-methylseleno-7-phenyl-2-heptene 5c$_E$

Following the general procedure I, bis(methylseleno)-phenyl-methane **20'** [13] (2.67 g, 9.6 mmol) reacts successively with n-butyllithium (1.5 M in hexanes, 6.7 ml, 9.6 mmol) and *(E)*-6-iodo-2-hexene **22''$_E$** (2.10 g, 10 mmol) to afford, after purification by distillation, 1.37 g of the benzylselenide **5c$_E$** (5.2 mmol, 55%). TLC: Rf= 0.22 (pentane). ^{1}H NMR ($CDCl_3$/90 MHz): δ (ppm): 1.21-2.09 (m, 12H, -(CH_2)3-CH=CH-CH_3, SeCH_3 (s) at 1.66 ppm), 3.84 (t, J= 7 Hz, 1H, -CHPh), 5.21-5.42 (m, 2H,-CH=CH), 7.0-7.2 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$/22.5 MHz): δ (ppm) : 3.79(SeCH_3), 17.71 (=CHCH_3), 28.17, 32.02 and 35.48 (3x-CH_2-), 43.94 (PhC), 124.88 (-CH=CH-CH_3), 126.45, 127.99 et 128.08 (Ar), 130.62 (-CH=CH-CH_3), 142.82 (Ar ipso). IR (neat): cm^{-1}: 3058, 3024, 2924, 1942, 1796, 1734, 1684, 1600, 1543, 1492, 1451, 966, 901, 760 and 698. MS (E.I.): m/z: 268 (M), 173 (M-SeCH_3), 143, 117, 91(tropylium), 77 and 55. Elemental analysis for $C_{14}H_{20}Se$: Calc.: C, 62.91%; H, 7.54%; Found: C, 62.35%; H,7.51%.

Synthesis of *(Z)*-7-methylseleno-7-phenyl-2-octene 5a$_Z$

Following the general procedure I, 1,1-bis(methylseleno)-1-phenyl-ethane **20''** [13] (8.88 g, 30 mmol) reacts successively with n-butyllithium (18.75 ml, 30 mmol) and *(Z)*-6-iodo-2-hexene **22''$_Z$** (6.93 g, 33 mmol) to afford, after purification by distillation (b.p. 120-123°C/0.1 mm Hg), 7.22 g of the benzylselenide **5a$_Z$** (25.6 mmol, 86%). TLC: Rf= 0.23 (pentane). ^{1}H NMR ($CDCl_3$/400 MHz): δ (ppm): 1.20 (m, 1H, -CHH-CH_2-CH=CH-), 1.40 (m, 1H, -CHH-CH_2-CH=CH-), 1.57 (d, J=6.4 Hz, 3H, -CH=CH-CH_3), 1.69 (s, 3H, PhCCH_3), 1.95-2.10 (m, 3H, -CH_2-CH_2-CHH-CH=CH-), 2.20 (m, 1H, -CH_2-CH_2-CHH-CH=CH-), 5.2-5.4 (m, 2H,-CH=CH-), 7.00-7.46 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$/100 MHz): δ (ppm) : 3.24 (SeCH_3), 12.80 (=CHCH_3), 24.98 (t, -CH_2-), 26.21 (PhCCH_3), 26.96 (-CH_2-), 42.39 (-CH_2-), 46.67 (PhC), 124.22 (-CH=CH-CH_3), 126.08, 126.8 et 127.9 (Ar), 130.1 (-CH=CH-CH_3), 145.26 (Ar ipso). IR (neat): cm^{-1}: 3084, 3055, 3020, 2925, 2863, 1653, 1598, 1942, 1869, 1793, 1494, 1458, 1444, 1424, 1403, 1375, 1270, 1082, 1060, 1030, 900, 697 and 653. MS (E.I.): m/z: 186 (M-SeCH_3), 157, 144, 131 (M-SeCH_3 - (CH_2)-CH=CH-CH_3), 118, 115, 105, 91 (tropylium), 77 and 55.

Synthesis of 2-methyl-7-methylseleno-7-phenyl-2-octene 12

Following the general procedure I, 1,1-bis(methylseleno)-1-phenyl-ethane **20"** [13] (7.30 g, 25 mmol) reacts successively with n-butyllithium (15.62 ml, 25 mmol) and 6-iodo-2-methyl-2-hexene **22""** [32] (6.16 g, 27.5 mmol) to afford, after purification by distillation (b.p. 138-140°C/0.1 mm Hg), 6.05 g of the benzylselenide **12** (21 mmol, 82%). TLC: Rf= 0.11 (pentane). ^{1}H NMR ($CDCl_3$/90 MHz): δ (ppm): 1.0-2.09 (m, 18H, -(CH_2)3-CH=CH-(CH_3)2, SeCH_3, PhCCH_3 at 1.81 ppm), 4.99 (m, 1H,-C**H**=C-), 7.09-7.4 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$/22.5 MHz): δ (ppm) : 3.25 (q, Se**C**H3), 17.71 (q, C=C**C**H3), 25.35 (t, -**C**H2-), 25.68 (q, C=C**C**H3-) 26.22 (q, PhC**C**H3), 28.22 (t, -**C**H2-), 42.42 (t, -**C**H2-), 46.81 (s, Ph**C**), 124.23, 126.25, 126.83 and 127.91 (d, Ar and -**C**H=C-), 131.71 (s, -CH=**C**-), 145.30 (Ar ipso). IR (neat): cm^{-1}: 3084, 3056, 3023, 2962, 1942, 1868, 1796, 1734, 1671, 1631, 1599, 1493, 1444, 1375, 1309, 859, 769 and 733. MS (E.I.): m/z: 200 (M-SeCH_3), 157, 131 (M-SeCH_3 - -(CH_2)-CH=C(CH_3)2), 115, 91(tropylium), 82, 77 and 55. Elemental analysis for $C_{16}H_{24}Se$: Calc.: C, 65.07%; H, 8.19%; Found: C, 65.20%; H, 8.20%.

Synthesis of 7-chloro-2-methylseleno-2-phenyl-heptane 27

Following the general procedure I, 1,1-bis(methylseleno)-1-phenyl-ethane **20"** [13](0.876 g, 3 mmol) reacts with n-butyllithium (1.94 ml, 3 mmol) and is then transferred into a 2 M solution of 1-bromo-5-chloro-pentane in THF pre-cooled at -78°C (1.12 g, 6 mmol) to afford, after purification by PLC (Eluent: ether/pentane 2/98 (v/v)), 0.81 g of the benzylselenide **27** (24 mmol, 96%). TLC: Rf= 0.52 (ether/pentane (2:98,v/v). ^{1}H NMR (CCl_4/60 MHz): δ (ppm) : 0.90-2.40 (m, 14H, -(CH_2)4-Cl, SeCH_3 at 1.63 ppm (s) and PhCCH_3), 3.4 (t, J= 7 Hz, 2H,-C**H**2Cl) and 6.90-7.56 (m, 5H, ArH). IR (neat): cm^{-1}: 2920, 2850, 1595, 1490, 1460, 1440, 1370, 1265, 1075, 1025, 900, 760, 730 and 695. MS (E.I.): m/z: 306 et 304 (M), 209 (M-SeCH_3), 118, 115, 105 and 91(tropylium ion). Elemental analysis for $C_{14}H_{21}ClSe$: Calc.: C, 55.36%; H, 6.97%; Found: C, 55.16%; H, 6.96%.

5. Synthesis of arylcycloalkanes by anionic cyclisation of benzylselenides

General procedure II : In a two necked flask fitted with a rubber septum or in a 25 ml sealed tube closed by a rubber septum (method A), a 0.5 M solution of the benzylselenide in dry solvent (tetrahydrofuran, ether or pentane) was stirred under argon and n-butyllithium (1.0 molar equivalent) was added dropwise at the given temperature. The dark red solution was stirred at a temperature for the time disclosed below and was quenched with methanol at this temperature when it turned to pale yellow. It was then diluted with ether and poured into water (10 ml). The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layers were washed with water (10 ml), dried over $MgSO_4$, filtered and concentrated *in vacuo* (20 mm Hg). The residual liquid was purified either by PLC or directly subjected to the reaction of bromine (0.3 M in CCl_4, 20°C, until persistant brown color, method B) in order to transform the olefinc products into dibromides derivatives, concentration of the solution *in vacuo* (20 mm Hg) purification by PLC. Specific details as well as spectroscopic and analytical data are described bellow for each specific cases. The composition was determined by GC analysis using Se 30 capillary column (T_{oven}: 100 to 220°C (10°C/min)) and by GC/MS analysis.

Synthesis of *rel*(1R,2R)-1,2-dimethyl-1-phenyl-cyclohexane 9a$_t$

Following the general procedure II, the benzylselenide **1b** (0.281 g, 1 mmol) dissolved in dry tetrahydrofuran reacts with n-butyllithium (0.65 ml, 1 mmol) at -78°C for 0.5h follow by 0.5h at room temperature and afford, after purification by method B followed by PLC (Eluent: pentane), 0.135 g of cyclohexane **9a$_t$** (0.72 mmol, 72%). TLC: Rf= 0.77 (pentane). ^{1}H NMR ($CDCl_3$/400 MHz): δ (ppm): 0.53 (d, J= 7.3 Hz, 3H, CH-C**H**3), 1.25 (s, 3H, PhCC**H**3), 1.30-1.85 (m, 8H, -(C**H**2)4-), 1.90-2.05 (m, 1H, -C**H**-

CH_3), 7.08-7.53 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$/100 MHz): δ (ppm) : 15.86, 16.86, 22.61, 26.61, 30.78, 39.36, 41.28, 41.99, 125.29, 125.93, 127.95 and 150.81. IR (neat): cm^{-1}: 3070, 3040, 3010, 2900, 1595, 1490, 1440, 1375, 1178, 1030, 750, 700 and 690. MS (E.I.): m/z: 188 (M), 131 $(PhCH_3C{=}CCH_3)^+$, 118 $(PhCCH_3{=}CH)^+$, 115, 105, 91(tropylium), 77 and 55. Elemental analysis for $C_{14}H_{20}$: Calc.: C, 89.29%; H, 10.71%; Found: C, 89.13%; H, 10.73%.

Synthesis of *rel*(8R, 8aS, 3aS)-3a,5-dimethyl-1:2:3:3a:8:8a-hexahydro-cyclopent(a)indene 11a

A. From the selenide **5a**$_E$: Following the general procedure II (method A), the benzylselenide **5a**$_E$ (0.562 g, 1 mmol) dissolved in dry pentane reacts with t-butyllithium (1.2 ml, 2 mmol) at 20°C for 24h and afford, after purification by method B followed by PLC (Eluent: pentane), 0.183 g of tricyclic derivative **11a**$_C$ (0.98 mmol, 49%) as a mixture of two diastereoisomers (95/05) contaminated by 4% of 2-ethyl-1-methyl-1-phenyl-cyclopentane **10a**$_t$ (compared with an authentic sample by GC). TLC: Rf= 0.80 (pentane). ^1H NMR ($CDCl_3$/90 MHz of the major diastereoisomer): δ (ppm): 1.25 (d, J= 7 Hz, 3H, CH-C<u>H</u>$_3$), 1.39 (s, 3H, ArCC<u>H</u>$_3$), 1.42-2.15 (m, 7H, -(C<u>H</u>$_2$)$_3$-C<u>H</u>-), 2.82 (dq, J= 4 and 7 Hz, 1H, -C<u>H</u>-CH$_3$), 7.16 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$/22.5 MHz): δ (ppm) : 22.64 (CH-<u>C</u>H$_3$), 28.33 (-<u>C</u>H$_2$-), 29.58 (PhC<u>C</u>H$_3$), 34.07 and 41.93 (-(<u>C</u>H$_2$)$_2$-), 46.43 (<u>C</u>HCH$_3$), 55.34 (Ph<u>C</u>CH$_3$), 59.88 (-<u>C</u>HCH$_2$-), 122.8, 123.3, 126.29, 126.78 (Ar), 147.58 and 151.32 (Ar ipso). IR (neat): cm^{-1}: 3065, 3016, 2951, 1901, 1795, 1685, 1602, 1479, 1447, 1372, 760 and 750. MS (E.I. of the major diastereoisomer : 96%): m/z: 186 (M), 157, 144, 129, 115, 91(tropylium), 77 and 55. MS (E.I. of the minor diastereoisomer : 04%) m/z: 186 (M), 157, 144, 129, 115, 91(tropylium), 77 and 55.

B. From the selenide **5a**$_Z$: Following the general procedure II (method A), the benzylselenide **5a**$_Z$ (0.281 g, 1 mmol) dissolved in dry pentane reacts with t-butyllithium (0.58 ml, 1 mmol) at 20°C for 24h and afford, after purification by method B followed by PLC (Eluent: pentane), 0.125 g of tricyclic derivative **11a**$_C$ (0.66 mmol, 66%) as a mixture of two diastereoisomers (95/05) contaminated by 4% of 2-ethyl-1-methyl-1-phenyl-cyclopentane **10a**$_t$ (compared to an authentic sample in GC). Spectroscopic and analytical data were identical with the tricyclic derivative **11a**$_C$ obtained from the benzylselenide **5a**$_E$.

Synthesis of 3a-isopropyl-5-methyl-1:2:3:3a:8:8a-hexahydro-cyclopent(a)indene 11b

Following the general procedure II (method A), the benzylselenide **5b**$_E$(0.160 g, 0.5 mmol) dissolved in dry pentane reacts with t-butyllithium (0.29 ml, 0.5 mmol) at 20°C for 15 days and afford, after purification by method B followed by PLC (Eluent: pentane), 0.062 g of tricyclic derivative **11b**$_C$ (0.28 mmol, 57%) as a mixture of two diastereoisomers (86/14)(GC analysis). TLC: Rf= 0.82 (pentane).^1H NMR ($CDCl_3$/90 MHz): δ (ppm): 0.75 et 0.87 (2d, J= 6.79 Hz, (C<u>H</u>$_3$)$_2$CH-), 1.30 (major diastereoisomer) and 1.24 (minor diastereoisomer.) (2x d, J= 7.26 Hz (major diastereoisomer) and 7.03 Hz (minor diastereoisomer), 3H, CH-C<u>H</u>$_3$), 1.36-2.27 (m, 7H, -(C<u>H</u>$_2$)$_3$-C<u>H</u>-), 2.7 (m, 1H, -C<u>H</u>-CH$_3$), 6.90-7.0 (m, 4H, ArH).MS (E.I. of the major diastereoisomer : 86%): m/z: 241 (M), 171, 149, 129, 105, 91(tropylium), 77 and 55. MS (E.I. of the minor diastereoisomer : 14%) m/z: 241 (M), 171, 149, 129, 105, 91(tropylium), 77 and 55. IR (neat): cm^{-1}: 3065, 3017, 2952, 1904, 1850, 1734, 1600, 1584, 1479, 1450 and 757. The relative stereochemistry of this product has not yet been determined.

Synthesis of 5-methyl-1:2:3:3a:8:8a-hexahydro-cyclopent(a)indene 11c

Following the general procedure II (method A), the benzylselenide **5c**$_E$ (0.267 g, 1 mmol) dissolved in dry pentane reacts with t-butyllithium (0.58 ml, 1 mmol) at 20°C for 9 days and afford, after purification by method B followed by PLC (Eluent: pentane), 0.083 g of tricyclic derivative **11c** (0.49 mmol, 49%) as a mixture of two

diastereoisomers (98/02) contaminated by 14% (GC analysis) of cycloalkane of unknown structure that could not be purified . TLC: Rf= 0.80 (pentane).^{1}H NMR ($CDCl_3$/90 MHz): δ (ppm): 1.25 (d, J= 7.03 Hz, 3H, CH-C<u>H</u>3), 1.30-2.03 (m, 6H, -(C<u>H</u>2)3-), 2.42 (m, 1H, CH3-C<u>H</u>-CH2-), 3.62 (dt, J= 8.43, 3.6 Hz, 1H, Ar-C<u>H</u>-CH2-) 7.0 (m, 4H, ArH). IR (neat): cm^{-1}: 3065, 3017, 2949, 2862, 1940, 1904, 1795, 1684, 1602, 1584, 1478, 1449, 787, 751, and 699. MS (E.I. of the major diastereoisomer): m/z: 172 (M), 157, 143, 129, 115, 102, 91(tropylium), 77 and 51. MS (E.I. of the minor diastereoisomer) m/z: 172 (M), 157, 143, 129, 115, 91(tropylium), 77 and 51. MS (E.I. of the impuritiy : 14%) m/z: 174, 145, 131, 117, 104, 91, 77 and 51. Elemental analysis for $C_{13}H_{16}$: Calc.: C, 90.69%; H, 9.37%; Found: C, 89.75%; H, 9.85%. The relative stereochemistry of this product has not yet been determined.

Cyclisation of the benzylselenide <u>5a</u>$_E$ in tetrahydrofuran

Following the general procedure II (method A), the benzylselenide <u>5a</u>$_E$ (0.281 g, 1 mmol) dissolved in dry tetrahydrofuran reacts with n-butyllithium (0.63 ml, 1 mmol) at -78°C for 0.5h and at 20°C for 24h and afford 0.285 g of crude mixture. The GC, GC/MS analysis and comparison with authentic materials gave the following composition : the tricyclic derivative <u>11a</u>$_C$ (10.3%), the arylalkene <u>7a</u> (15%),the arylalkene <u>8a</u> (39%), 2-ethyl-1-methyl-1-phenyl-cyclopentane <u>10a</u> (7%) and 1,2-dimethyl-phenylcyclohexane <u>9a</u>$_t$ (32%). The yield of <u>9a</u>$_t$ based on internal standard (t-butyl-benzene) is 18%. After purification by method B followed by PLC (Eluent: pentane), we obtained 0.04 g (23%, 0.2 mmol) of a mixture with the following composition: the tricyclic derivative <u>11a</u>$_C$ (16%), 2-ethyl-1-methyl-1-phenyl-cyclopentane <u>10a</u> (7%) and 1,2-dimethyl-phenylcyclohexane <u>9a</u>$_t$ (72%) (compared with an authentic sample) and unknown compounds (5%)(GC analysis).

Cyclisation of the benzylselenide <u>5a</u>$_E$ in ether

Following the general procedure II (method A), the benzylselenide <u>5a</u>$_E$ (0.281 g, 1 mmol) dissolved in dry ether reacts with s-butyllithium (0.77 ml, 1 mmol) at -30°C for 0.5h and at 20°C for 24h and affords 0.292 g of crude mixture. The GC (Se 30 methylsilicone column), GC/MS analysis and comparison with authentic materials gave the following composition : tricyclic <u>11a</u>$_C$ (34.6%), arylalkene <u>7a</u> (14.6%), arylalkene <u>8a</u> (22.8%), 2-ethyl-1-methyl-1-phenyl-cyclopentane <u>10a</u>$_C$ (12%), 2-ethyl-1-methyl-1-phenyl-cyclopentane <u>10a</u>$_t$ (12%) and unknown products (4%).The yield of <u>11a</u>$_C$ based on internal standard (t-butyl benzene) is 28%. After purification by PLC (Eluent: pentane), we obtained 0.170 g (approximately 91% of the material balance) with an identical composition.

Cyclisation of the benzylselenide <u>12</u> in tetrahydrofuran

Following the general procedure II (method A), the benzylselenide <u>12</u> (0.295 g, 1 mmol) dissolved in dry tetrahydrofuran reacts with n-butyllithium (0.69 ml, 1.1 mmol) at 0°C for 6 h affords after purification by PLC (Eluent: pentane), 0.17 g of a mixture composed (GC and GC/MS analysis) of the 2-methyl-7-phenyl-2-octene <u>15</u> (50%) and 2,7-dimethyl-7-phenyl-2-nonene <u>16</u> (50%).

Synthesis of 1-methyl-1-phenyl-cyclohexane <u>25</u>

Following the general procedure II, the benzylselenide <u>27</u> (0.303 g, 1 mmol) dissolved in dry tetrahydrofuran reacts with t-butyllithium (0.59 ml, 1 mmol) at -78°C for 0.1h and affords, after purification by PLC (Eluent: pentane), 0.150 g of cyclohexane <u>25</u> (0.95 mmol, 95%). TLC: Rf= 0.80 (pentane).

^{1}H NMR (CCl_4/60 MHz): δ (ppm): 1.05-2.4 0 (m, 13H, -(C<u>H</u>2)5- and PhCC<u>H</u>3 (s) at 1.15 ppm), 6.90-7.5 (m, 5H, ArH). IR (neat): cm^{-1}: 3040, 3010, 2910, 1595, 1490, 1460, 1440, 1370, 1300, 1020, 760, and 700. MS (E.I.): m/z: 174 (M), 159 (M-CH3), 91(tropylium). Elemental analysis for $C_{13}H_{18}$: Calc.: C, 89.59%; H, 10.51%; Found: C, 89.57%; H, 10.53%.

6. Synthesis of arylcycloalkanes ***18bt, 18bc, 18a, 19a and 11d*** *by Lewis acid mediated cyclisation.*

General procedure III : A 1.0 M solution of titanium tetrachloride or tin tetrachloride (2 equiv.) in dry dichloromethane was cooled under argon to -50°C with stirring and a solution of the benzylselenide (1 M in the same solvent) was added dropwise. The resulting dark brown solution was stirred at -50°C for 1h, at room temperature for 1.5h and the reaction mixture was filtered through a short path of basic alumina (Janssen Chimica). The solvent was removed *in vacuo* (20 mm Hg) and the residual yellow liquid was purified by PLC or preparative HPLC to afford the arylcycloalkanes **18bt**, **18bc**, **18a**, **19a** and **11d** as clear oils. The stereochemical purity was determined by GC analysis using SE 30 capillary column (T_{oven} : 100 to 220°C (path of 10°C/min)). Specific details as well as spectroscopic and analytical data are described bellow only in the case of titanium tetrachloride but exactly the same experimental procedure can be used with tin tetrachloride (see table for diastereoisomeric excess and yields).

Synthesis of *rel*(8aS,3aS)3a,8,8-trimethyl-1:2:3:3a:8:8a-hexahydro-cyclopent(a)indene 11d

Following the general procedure III, the benzylselenide **12** (0.148 g, 0.5 mmol) reacts with titanium tetrachloride (0.189 g, 1 mmol) to afford, after purification by PLC (Eluent: pentane), 0.089 g of tricyclic derivative **11d** (0.44 mmol, 89%). TLC: Rf= 0.92 (pentane). ^{1}H NMR ($CDCl_3$/90 MHz): δ (ppm): 1.15-2.18 (m, 16H, -(CH_2)3-CH-, ArCCH_3 at 1.81 ppm, ArC(CH_3)2- at 1.18 ppm), 6.81-7.15 (m, 4H, ArH). ^{13}C NMR ($CDCl_3$/22.5 MHz): δ (ppm) : 24.81 and 26.49 (t, 2x -CH_2-), 34.67, 30.55 and 30.34 (q, 3x PhCCH_3), 42.91 (t, -CH_2-), 44.37 and 54.72 (s, 2xArC), 62.68 (d, CH), 122.23, 122.99, 126.51, 126.86, (d, Ar) 151.27 and 150.84 (s, 2xAr ipso). IR (neat): cm^{-1}: 3064, 3015, 2949, 1950, 1800, 1849, 1707, 1600, 1479, 1446, 910 and 754. MS (E.I.): m/z: 200 (M),185 (M-CH_3), 157, 143, 129, 115, 91(tropylium), 77 and 55. Elemental analysis for $C_{15}H_{20}$: Calc.: C, 89.93%; H,10.07%; Found: C, 89.91%; H, 10.00%.

Synthesis of *rel*(1S,2R,3S)-3-chloro-1,2-dimethyl-1-phenyl-cyclohexane 18bt

Following the general procedure III, the benzylselenide **5aE** (0.281 g, 1 mmol) reacts with titanium tetrachloride (0.378 g, 2 mmol) to afford, after purification by PLC (Eluent: pentane), 0.172 g of chlorocyclohexane **18bt** (0.78 mmol, 78%) as a mixture 97/02/01 of three diastereoisomers (GC analysis). TLC: Rf= 0.35 (pentane). ^{1}H NMR ($CDCl_3$/90 MHz): δ (ppm): 0.78 (d, J= 6.56 Hz, 3H, CH-CH_3), 1.27 (s, 3H, PhCCH_3), 1.36-2.48 (m, 7H, -(CH_2)3-CH-CH_3), 3.75-4.09 (dt, J= 11.2 and 4.1 Hz, 1H, CHCl), 7.12-7.42 (m, 5H, ArH). 1D DIF NOE experiment ($CDCl_3$/400 MHz) : pre-irradiation at 0.78 ppm caused enhancement of the CHCl at 3.75-4.09 ppm. ^{13}C NMR ($CDCl_3$/22.5 MHz): δ (ppm) : 14.24 and 16.63 (q, 2x CH_3), 22.59, 38.25 and 41.61 (t, -(CH_2)3), 43.61 (s, PhC), 47.73 (d, $CHCH_3$), 65.12 (d, $CHCl$), 128.08, 125.75, 125.53 (d, Ar) 148.99 (s, Ar ipso). IR (neat): cm^{-1}: 3086, 3056, 3030, 2975, 1946, 1900, 1850, 1598, 1552, 1495, 1444, 977, 941, 758 and 700. MS (E.I. of the major diastereoisomer **18bt**): m/z: 222 (M), 186 (M-Cl), 171, 143, 131 ($PhCH_3C{=}CCH_3)^+$, 118 ($PhCCH_3{=}CH)^+$, 105, 91(tropylium), 77 and 55. The other diastereoisomers (respectively 02 and 01%) present essentially the same fragmentation. Elemental analysis for $C_{14}H_{19}Cl$: Calc.: C, 75.48%; H, 8.59%; Found: C, 74.79%; H, 8.45%.

Synthesis of *rel*(1S,2S,3S)-3-chloro-1,2-dimethyl-1-phenyl-cyclohexane 18bc

Following the general procedure III, the benzylselenide **5aZ** (2.81 g, 10 mmol) reacts with titanium tetrachloride (3.78 g, 20 mmol) to afford, after purification by HPLC (Eluent: pentane), 1.35 g of chlorocyclohexane **18bc** (6.1 mmol, 61%) as a mixture 96/02/02 of three diastereoisomers (GC analysis). TLC:

Rf= 0.21 (pentane). ^{1}H NMR ($CDCl_3$/400 MHz): δ (ppm): 0.67 (d, J= 7.03 Hz, 3H, CH-C**H**$_3$), 1.33 (s, 3H, PhCC**H**$_3$), 1.46-2.11 (m, 6H, -(C**H**$_2$)$_3$-), 2.38 (dq, J= 4.4 et 7.0 Hz, 1H, C**H**CH$_3$) 4.62 (ddq, J= 11.72, 4.4 and 3.9 Hz (determined by spin decoupling experiment)), 1H, C**H**Cl), 7.13-7.45 (m, 5H, ArH). 1D DIF NOE experiment ($CDCl_3$/400 MHz) : pre-irradiation at 0.67 ppm caused enhancement of the C**H**Cl at 4.62 ppm and C**H**CH$_3$ at 2.38 ppm. ^{13}C NMR ($CDCl_3$/100 MHz): δ (ppm) : 9.65 (CH$_3$), 22.00 (-**C**H$_2$-), 26.81 (**C**H$_3$), 27.50 and 30.26 (-(**C**H$_2$)$_2$-), 42.66 (Ph**C**), 45.31 (**C**HCH$_3$), 61.90 (**C**HCl), 127.97, 125.63, 125.07 (Ar), 150.01 (Ar ipso). IR (neat): cm^{-1}: 3087, 3057, 3027, 2977, 2945, 1946, 1900, 1850, 1800, 1599, 743 and 700. MS (E.I. of the major diastereoisomer **18b$_c$**): m/z: 222 (M), 186 (M-Cl), 171, 157, 143, 131 (PhCH$_3$C=CCH$_3$)$^+$, 118 (PhCCH$_3$=CH)$^+$, 115, 105, 91(tropylium), 77 and 55. Elemental analysis for $C_{14}H_{19}Cl$: Calc.: C, 75.48%; H, 8.59%; Found: C, 74.30%; H, 8.73%.

Synthesis of the*rel*(1S,3S)-3-chloro-1-methyl-1-phenyl-cyclohexanes 18a and 19a as a 87/13 mixture of stereoisomers

Following the general procedure III, the benzylselenide **1a** (0.267 g, 1 mmol) reacts with titanium tetrachloride (0.378 g, 2 mmol) to afford, after purification by PLC (Eluent: pentane), 0.114 g of the chlorocyclohexanes **18a** and **19a** (0.57 mmol, 57%) as a mixture 87/13 of two diastereoisomers (GC analysis). TLC: Rf= 0.55 (pentane). ^{1}H NMR ($CDCl_3$/90 MHz): δ (ppm): 1.15 (minor diastereoisomer) and 1.27 (major diastereoisomer) (s, 3H, PhCC**H**$_3$), 1.48-2.48 (m, 8H, -(C**H**$_2$)3-CHCl-C**H**$_2$), 3.82-4.12 (m, 1H, C**H**Cl), 7.00-7.42 (m, 5H, ArH). IR (neat): cm^{-1}: 3058, 2936, 1599,1496, 1444, 1378, 1366, 1240, 1079, 1031, 909, 844, 763, 742 and 699. MS (E.I. of the major diastereoisomer **18a**): m/z: 208 (M), 193 (M-CH$_3$), 172 (M-Cl), 157, 131, 118 (PhCCH$_3$=CH)$^+$, 105, 91(tropylium), 77 and 55; of the minor diastereoisomer **19a** : m/z: 208 (M), 193 (M-CH$_3$), 172 (M-Cl), 157, 131, 118 (PhCCH$_3$=CH$_2$), 105, 91(tropylium), 77 and 55. Elemental analysis for $C_{13}H_{17}Cl$: Calc.: C, 74.81%; H, 8.21%; Found: C, 74.82%; H, 8.14%.

7. Synthesis of arylcycloalkanes **25**, **9a$_t$** *and* **9a$_c$** *by reduction of the chlorocyclohexane derivatives* **18b$_t$**, **18b$_c$**, **18a** *or* **19a** .

General procedure IV : A 0.3 M of the chlorocyclohexane **18b$_t$**, **18b$_c$**, **18a** or **19a** (1 mmol) in dry benzene containing tri-butyltin hydride (1.5-2 equiv., 0.435-0.540 g) and AIBN (0.01 equiv., 0.02 g) was refluxed under argon for 24-48h and cooled to room temperature. The benzene was removed *in vacuo* (20 mm Hg) and the residual yellow liquid was purified by SiO_2 preparative thin layer chromatography to afford the arylcycloalkanes **9a** as clear oil. The stereochemical purity was determined by GC analysis using OV17 column (T_{oven}: 100°C for 11 min and warm to 220°C (10°C/min)). Specific details as well as spectroscopic and analytical data are described bellow.

Synthesis of 1-methyl-1-phenyl-cyclohexane 25

Following the general procedure IV, the diastereoisomeric mixture of chlorocyclohexane **18a** and **19a** (0.195 g, 0.95 mmol) afford 0.130 g of cyclohexane **25** (0.79 mmol, 80%).Spectroscopic and analytical data were identical to a sample synthesised by anionic cyclisation of the benzylselenide **27** (*vide infra*).

Synthesis of *rel*(1R,2R)-1,2-dimethyl-1-phenyl-cyclohexane 9a$_t$

Following the general procedure IV, chlorocyclohexane **18b$_t$** afford 0.156 g of cyclohexane **9a$_t$** (0.83 mmol, 83%). Spectroscopic and analytical data were identical to a sample synthesised by anionic cyclisation of the benzylselenide **1b** *(vide infra)*

Synthesis of *rel*(1R,2S)-1,2-dimethyl-1-phenyl-cyclohexane 9a$_c$

Following the general procedure IV, chlorocyclohexane 18b$_c$ afford 0.180 g of cyclohexane 9a$_c$ (0.95 mmol, 95%) as a mixture 96/04 of two diastereoisomers (GC analysis).TLC: Rf= 0.77 (pentane). ^{1}H NMR ($CDCl_3$/400 MHz): δ (ppm): 0.61 (d, J= 7.3 Hz, 3H, CH-C$\underline{H}_3$), 1.33 (s, 3H, PhCC$\underline{H}_3$), 1.40-1.70 (m, 6H, -(C$\underline{H}_2$)$_3$-), 1.86-2.10 (m, 3H, -C$\underline{H}_2$-C$\underline{H}$-CH$_3$), 7.1-7.4 (m, 5H, ArH). ^{13}C NMR ($CDCl_3$/100 MHz): δ (ppm) : 15.80, 20.33, 22.14, 27.85, 28.78, 30.17, 38.13, 39.79, 127.92, 125.63, 125.05 and 151.18 .MS (E.I.): m/z: 188 (M), 145, 131 $(PhCH_3C{=}CCH_3)^+$, 118 $(PhCCH_3{=}CH)^+$, 115, 105, 91(tropylium), 77 and 55. IR (neat): cm^{-1}: 3084, 3055, 3021, 2928, 1937, 1869, 1794, 1653, 1599, 1579, 1495, 1465, 1444, 1400, 1374, 1178, 1032, 982, 846, 792, 760 and 699.

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