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Zirconocene mediated cyclization and isomerization of 1,3,6-heptatriene

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Dedicated to Professor Pascual Royo on the occasion of his 65th birthday

Abstract

Cyclization of 1,3,6-heptatrienes **1** with Cp_2ZrBu_2 (Negishi reagent) furnished a mixture of *trans*- and *cis*-zirconacyclopentanes that after hydrolysis afforded a mixture of isomeric dimethylcyclopentenes **2** and **3** in ca. 5:1 ratio. An attempt to isomerize the mixture of zirconacyclopentanes by stirring the reaction for 48 h resulted, after hydrolysis, in rather surprising formation of *cis*-dimethylcyclopentenes **3** with high selectivity. This is the first example of *trans* to *cis* isomerization of zirconacyclopentanes. Further reaction of the intermediate zirconacyclopentanes with various electrophiles and a plausible reaction mechanism of the *trans* to *cis* isomerization are presented.

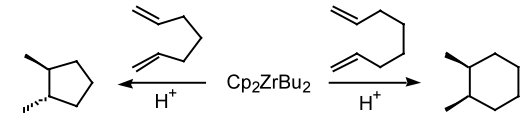
Keywords: 1,3,6-Heptatriene; Zirconacyclopentanes; Dimethylcyclopentenes

1. Introduction

Zirconocene mediated or catalyzed cyclization of 1,6-heptadienes and 1,7-octadienes has been in the center of synthetic interest for a number of years. Although the cyclization proceeds usually quantitatively, one of the concerns is the stereochemistry of the formed products. Already the first experiments concerning cyclization of 1,7-octadiene carried out by Schwartz with $Cp_2Zr(PMePh_2)_2$ complex indicated, that stereochemistry control may not be so simple. The product was a 1:1 mixture of *cis*- and *trans*-dimethylcyclohexanes [1]. Fortunately, the use of Cp_2ZrBu_2 for the cyclization of the above mentioned dienes gave products with better stereoselectivity [2]. The cyclization of 1,6-heptadiene affords predominantly *trans* product and the *trans*–*cis* ratio is ca. 20:1. On the other hand the cyclization of 1,7-octadiene proceeds with opposite stereoselectivity giving mainly *cis* product with *trans*–*cis* ratio of ca. 5:1 (Scheme 1). The same stereoselectivity was observed also for zirconocene-catalyzed cyclizations [3,4].

Nonetheless, certain stereoselectivity control of the cyclization can be exerted by suitable substitution pattern of the starting diene. Recently, we have shown that 4,5-substituted 1,4,7-octatrienes were cyclized stereospecifically to *cis*-dimethylcyclopentenes under both stoichiometric and catalytic conditions [5]. It has been shown that 1,6-heptadienes can be selectively cyclized to the *cis*-dimethylcyclopentanes with $CpZrCl_3$/Na–Hg system [6].

Nakamura and his co-workers showed that *cis*-zirconacyclopentanes could be isomerized into thermodynamically more stable *trans*-zirconacyclopentanes. In this case *cis*-zirconacyclopentane, prepared from 1,7-



Scheme 1.

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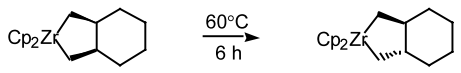
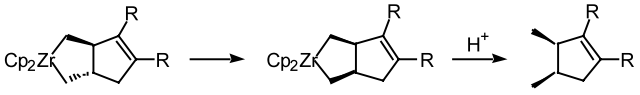


Scheme 2.



Scheme 3.

octadiene, was quantitatively isomerized into the *trans* isomer simply by heating the reaction mixture at 60 °C for 6 h (Scheme 2) [7].

Later, it was also shown that isomerization of variously substituted zirconacyclopentanes can be affected not only by temperature but also by solvent used [8,9]. Generally speaking, the isomerization of zirconacyclopentanes can be influenced by a combination of various factors. However, to the best of our knowledge, only isomerization of *cis*-zirconacyclopentanes to *trans*-zirconacyclopentanes has been reported. The opposite process, isomerization from *trans*- to *cis*-zirconacyclopentanes was not observed. Herein, we would like to report the first example of selective isomerization of *trans*-zirconacyclopentanes to *cis*-zirconacyclopentanes (Scheme 3).

2. Results and discussion

2.1. Cyclization of 1,3,6-heptatriene and isomerization of the formed zirconacyclopentanes

When 1,3,6-heptatrienes such as **1** were treated with Cp_2ZrBu_2 (Negishi reagent) under standard conditions [2], cyclization proceeded to give bicyclic zirconacyclopentanes, which after acidic hydrolysis afforded the corresponding dimethylcyclopentenes **2** and **3** (Scheme 4). Usually after 1 h at 20 °C dimethylcyclopentenes were obtained as a mixture of *trans* **2** and *cis* **3** isomers in high yields (ca. 90%). *cis*- and *trans*-Dimethylcyclopentenes were assigned by two methyl signals in their ^{13}C-NMR spectra. Two methyl groups appear in the range of 13–15 ppm for *cis* compounds and 18–21 ppm for *trans* isomers. This is consistent with the chemical shift of dimethylcyclopentane reported in the ^{13}C-NMR textbook [10]. Regardless of the substituents in the starting heptatriene, the predominant isomer was always the *trans* one (Table 1). For alkyl substituted heptatrienes **1a**–**c** the *trans*–*cis* ratio varied in between 4.5–5.5:1 after 1 h. For phenyl substituted heptatriene **1d**, it was somewhat lower at 2.5:1 after 3 h. The predominant formation of *trans* isomer is in accordance with the cyclization of unsubstituted heptadiene, which under the same conditions affords a 20:1 mixture of *trans*–*cis*-dimethylcyclopentanes [2].

Surprisingly, we found that, when the formed zirconacyclopentanes were stirred at 50 °C for 48 h, *trans* to *cis* isomerization occurred. The corresponding *cis* substituted dimethylcyclopentenes **3** were isolated after hydrolysis in both high yield (> 70%) as well as with high isomeric purity (Table 1). In the case of alkyl substituted heptatrienes *cis*–*trans* ratio was ca. 20:1. Much better isomeric ratio was, however, obtained for phenyl substituted one. The ratio was according to the NMR analysis as high as 65:1.

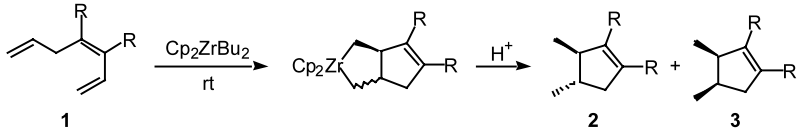
These results were rather puzzling, because according to the reported data, there had been so far observed only isomerization of *cis* into *trans*.

3. Reaction of zirconacyclopentanes with electrophiles

In a further step, reactions of zirconacyclopentanes with various electrophiles were carried out [11]. In all instances both Zr–C bonds reacted and bisfunctionalized products were obtained and their stereoselectivity was related to the stereoselectivity of the simply cyclized one (Scheme 5).

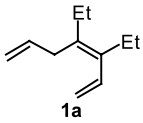
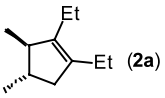
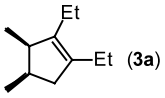
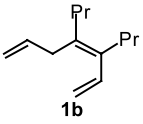
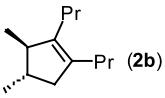
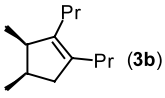
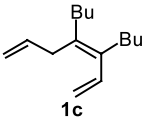
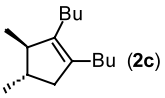
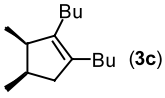
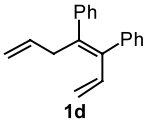
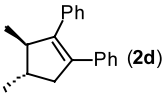
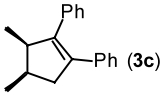
All the reactions with various electrophiles proceeded uneventfully to give disubstituted products, as expected (Table 2). The reaction with benzoyl chloride in the presence of CuCl afforded diketone **4a**. This is in sharp contrast to the observed data for 2-zirconahexahydroindenes that under the same conditions afford tetrahydroindenes [11b]. Moreover, the product was isolated as a single stereoisomer. The reaction with iodine proceeded to give diiodide **4b**, as well as the reaction with allyl chloride affording diallylated products.

All these results were also consistent with those obtained by deuterolysis of the reaction mixture with DCl, which afforded a mixture of dideuterated ***d*-4** and ***d*-5** (Scheme 6). Surprisingly, deuterolysis of the reaction mixture, after isomerization for 48 h, afforded a mixture of regioisomeric *monodeuterated cis*-products ***d*-6** and ***d*-7** in 1:1 ratio (Scheme 6).



Scheme 4.

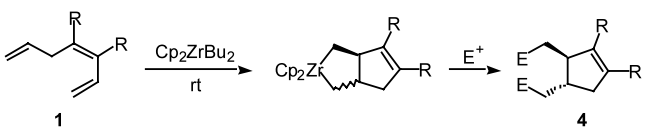
Table 1
Cyclization and isomerization of 1,3,6-heptatrienes

Heptatriene	T (h)	Major Product	Trans/Cis (2/3)	Yield (%)[a] (2 + 3)
 1a	1	 (2a)	4.7:1	90 (70)
	48	 (3a)	1:19	80 (61)
 1b	1	 (2b)	5.5:1	92 (73)
	48	 (3b)	1:25	78 (58)
 1c	1	 (2c)	5.0:1	97 (71)
	48	 (3c)	1:20	82(64)
 1d	3	 (2d)	2.5:1	(87)
	48	 (3c)	1:65	(70)

[a] GC yields. Isolated yields are in parentheses.

In comparison with the above mentioned results, the reaction of zirconacyclopentanes (after 48 h isomerization) with electrophiles afforded only *monosubstituted* products (Scheme 7).

In accordance with the deuterolysis experiment, all reactions of zirconacyclopentanes (after 48 h isomerization) with electrophiles such as PhCOCl–CuCl, I_2 or allyl chloride–CuCl afforded only regioisomeric mixtures of *monosubstituted* products **6** and **7** (Table 3). These results indicate that one of the Zr–C bonds in *cis*-zirconacyclopentane has been already cleaved before the reaction with electrophiles.



Scheme 5.

3.1. Reaction mechanism of the isomerization

Isomerization of zirconacyclopentanes is known and well documented. It is generally assumed that the whole process proceeds through η^2–η^2-bis(olefin)metal intermediate [7]. Initially, the two Zr–C bonds and the one C–C bond of the zirconacyclopentane ring are cleaved to give the η^2–η^2-bis(olefin)zirconium intermediate that cyclizes again into the zirconacyclopentane. However, at this stage it is not clear what factors influence the *trans*–*cis* isomerization. Usually *trans* isomers are thermodynamically more stable than *cis* ones. However, this phenomenon may be directly connected with the observed Zr–C bond cleavage and concomitant hydrogen transfer to the carbon atom.

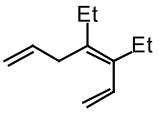
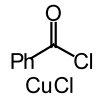
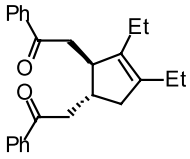
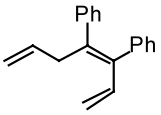
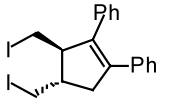
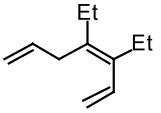
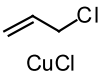
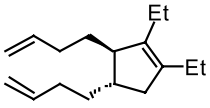
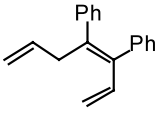
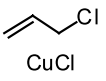
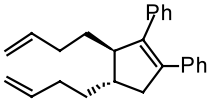
In order to clarify this point the reaction of **1c** was monitored by ^{1}H- and ^{13}C-NMR. After 1 h, both Cp rings gave two sharp peaks (^{1}H-NMR: δ 5.75 (s, 5H), 5.79 (s, 5H); ^{13}C-NMR: δ 109.29, 109.31) in the region of typical Cp signals. However, after 48 h, the overall pictures changed: ^{1}H-NMR showed a complex set of signals instead of previous sharp peaks and ^{13}C-NMR showed 11 peaks indicating magnetic inequivalency of carbon atoms belonging to the Cp-rings (^{1}H-NMR: δ 5.75–5.95 (m, 9H); ^{13}C-NMR: δ 109.85, 110.01, 110.21, 110.30, 110.34, 110.37, 110.46, 110.59, 110.63, 110.71, 110.79). Although it is difficult to make a clear conclusion from these observations, it is reasonable to assume that there was a loss of the hydrogen atom from the Cp ring and eventually a new bond was formed. In such a way magnetic equivalency of hydrogen and carbon atoms belonging to the Cp ring would be destroyed. A possible loss of the hydrogen atom is supported by the fact that zirconocene–diphosphine complex is known to lose a molecule of H_2 to give η^1–η^5 Cp ring bridged bimetal complex [1b,12]. Therefore, it is reasonable to assume that one of the two Zr–C bonds in a *cis*-zirconacyclopentane is cleaved because of ring strain or steric hindrance, with a concomitant abstraction of a proton from the Cp ring.

The overall reaction mechanism (Scheme 8) is assumed to proceed as follows: (i) formation of *trans*-zirconacyclopentane; (ii) its equilibrium with *cis*-zirconacyclopentane via bis(olefin)zirconium complex; (iii) cleavage of one of the Zr–C bonds in *cis*-zirconacyclopentane disrupts the equilibrium. In such a way *trans*-zirconacyclopentane is slowly consumed and after the reaction with an electrophile *cis*-product is isolated.

4. Experimental

Unless otherwise noted, all starting materials were commercially available and were used without further purification. The starting trienes were prepared by a combination of previously published method for vinyl-

Table 2
Cyclization and reaction with electrophiles of 1,3,6-heptatrienes

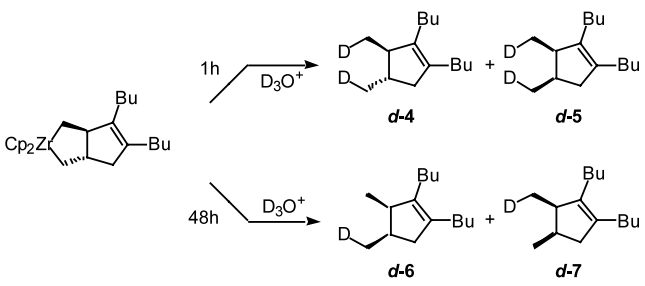
Heptatriene	Electrophile	t(°C) T (h)	Major Product	Trans/Cis (4/5)	Yield (%)[a] (4 + 5)
	 CuCl	20°C 3 h	 (**4a**)	-[b]	(57)
	I_2	0°C 12 h	 (**4b**)	3:1	(68)
	 CuCl	50°C 1 h	 (**4c**)	4.7:1	92 (80)
	 CuCl	50°C 1 h	 (**4d**)	3:1	(88)

[a] GC yields. Isolated yields are in parentheses.
[b] Only *trans*-isomer was isolated.

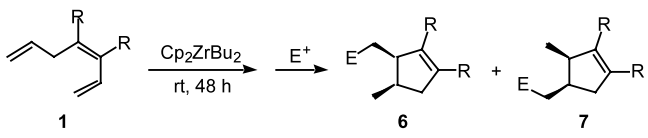
zirconation of alkynes [13a] followed by copper catalyzed allylation [13b]. Cp_2ZrCl_2 was purchased from Nichia Corporation. *n*-BuLi (1.6 M, C_6H_{14} solution) was purchased from Kanto Chemicals Co. Ltd. All the reactions were carried out under a positive dry nitrogen atmosphere. THF was distilled over Na and benzophenone under a nitrogen atmosphere. ^{1}H- and ^{13}C-NMR spectra were recorded for $CDCl_3$ (containing 1% Me_4Si) solution on a Bruker ARX-400 NMR spectrometer. GC analyses were performed on Shimadzu GC-14A equipped with fused silica capillary column CBP1-M25-025 and Shimadzu C-R6A Chromatopac integrator. GC yields were determined using suitable hydrocarbons as internal standards.

4.1. A typical procedure for the cyclization of 1,3,6-heptatrienes: formation of (3R*,4S*)-1,2-diethyl-3,4-dimethylcyclopentene (2a)

To a solution of Cp_2ZrBu_2, prepared by the reaction of Cp_2ZrCl_2 (1.0 mmol, 292 mg) with *n*-BuLi (1.25 ml, 2.0 mmol) at −78 °C in THF (5 ml) was added 3,4-diethyl-1,3,6-heptatriene (**1a**) (150 mg, 1.0 mmol) at −78 °C and the reaction mixture was warmed to 20 °C within 1 h. After that it was quenched with 3 N HCl and extracted with C_6H_{14}. Combined extracts were washed with sat. $NaHCO_3$, brine, dried over $MgSO_4$, and concentrated in vacuo. Column chromatography on silica gel (C_6H_{14}) afforded 106 mg (70%) of a mixture of **2a**–**3a** (4.7:1). ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.90 (t, $J = 7.6$ Hz, 3H), 0.94 (t, $J = 7.5$ Hz, 3H), 0.97 (d, $J = 7.0$ Hz, 3H), 1.02 (d, $J = 6.8$ Hz, 3H), 1.61–1.69 (m, 1H), 1.81–2.22 (m, 6H), 2.35–2.43 (m, 1H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 13.16, 13.19, 18.25, 19.12, 19.93, 21.49, 39.99, 42.07, 49.10, 134.96, 139.70. HRMS Calc. for $C_{11}H_{20}$: 152.1564. Found: 152.1554.

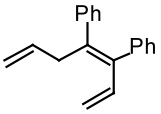
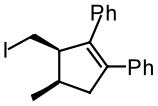
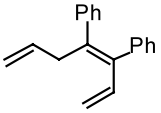
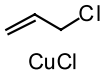
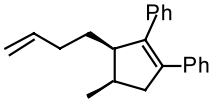
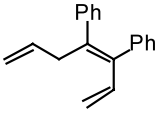
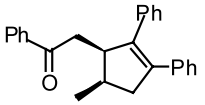


Scheme 6.



Scheme 7.

Table 3
Cyclization, isomerization, and reaction with electrophiles of 1,3,6-heptatrienes

Heptatriene	Electrophile	Conditions	Product		(6/7)	Yield (%)[a] (6 + 7)
	I_2	0°C 12 h		(**6a**)	1:1	61
	 CuCl	50°C 1 h		(**6b**)	1.2:1	83
	 CuCl	20°C 3 h		(**6c**)	1.2:1	72

[a] Isolated yields.

4.2. (3R*,4S*)-1,2-Dipropyl-3,4-dimethylcyclopentene (**2b**)

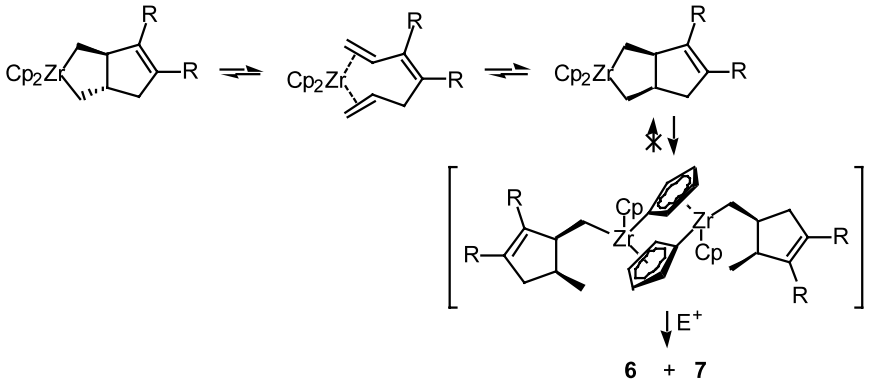
Isolated 132 mg (73%). ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.86 (t, $J = 7.4$ Hz, 6H), 0.96 (d, $J = 6.8$ Hz, 3H), 1.01 (d, $J = 6.7$ Hz, 3H), 1.21–1.45 (m, 4H), 1.61–1.69 (m, 1H), 1.80–2.25 (m, 6H), 2.35–2.43 (m, 1H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 14.03, 14.16, 18.32, 20.14, 21.33, 21.39, 28.19, 30.60, 39.92, 42.42, 49.30, 134.09, 138.96. HRMS Calc. for $C_{13}H_{24}$: 180.1877. Found: 180.1872.

4.3. (3R*,4S*)-1,2-Dibutyl-3,4-dimethylcyclopentene (**2c**)

Isolated 148 mg (71%). ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.89 (t, $J = 6.3$ Hz, 6H), 0.96 (d, $J = 6.8$ Hz, 3H), 1.01 (d, $J = 6.8$ Hz, 3H), 1.20–1.34 (m, 8H), 1.60–1.71 (m, 1H), 1.82–1.91 (m, 2H), 1.99–2.18 (m, 4H), 2.35–2.42 (m, 1H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 14.10, 18.33, 20.10, 22.69, 22.81, 25.83, 28.27, 30.54, 30.56, 39.97, 42.50, 49.31, 134.05, 138.91. HRMS Calc. for $C_{15}H_{28}$: 208.2191. Found: 208.2173.

4.4. (3R*,4S*)-1,2-Diphenyl-3,4-dimethylcyclopentene (**2d**)

Isolated 216 mg (87%). ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 1.00 (d, $J = 7.0$ Hz, 3H), 1.19 (d, $J = 6.9$ Hz, 3H), 1.97–2.07 (m, 1H), 2.35 (dd, $J = 15.9$, 6.2 Hz, 1H), 2.73–2.77 (m, 1H), 3.17 (ddd, $J = 15.9$, 8.1, 1.5 Hz, 1H), 7.07–7.21 (m, 10H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 18.51, 20.25, 39.65, 44.48, 52.94, 126.31, 126.36, 127.80, 128.08, 128.14, 128.16, 128.70, 135.29, 138.00, 138.49, 142.68. Anal. Calc. for $C_{19}H_{20}$: C, 91.88; H, 8.37. Found: C, 92.02; H, 8.37%.



Scheme 8.

4.5. A typical procedure for the cyclization and isomerization of 1,3,6-heptatrienes: formation of (3R*,4R*)-1,2-diethyl-3,4-dimethylcyclopentene (**3a**)

To a solution of Cp_2ZrBu_2, prepared by the reaction of Cp_2ZrCl_2 (1.0 mmol, 292 mg) with *n*-BuLi (1.25 ml, 2.0 mmol) at −78 °C in THF (5 ml), was added 3,4-diethyl-1,3,6-heptatriene (**1a**) (150 mg, 1.0 mmol) at −78 °C and the reaction mixture warmed to 20 °C within 1 h and stirred at the same temperature for 48 h. After that it was quenched with 3 N HCl and extracted with C_6H_{14}. Combined extracts were washed with sat. $NaHCO_3$, brine, dried over $MgSO_4$, and concentrated in vacuo. Column chromatography on silica gel (C_6H_{14}) afforded 93 mg (61%) of a mixture of 2a–3a (1:19). ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.82 (d, $J = 7.1$ Hz, 3H), 0.92 (d, $J = 7.2$ Hz, 3H), 0.93 (t, $J = 7.5$ Hz, 6H), 1.90 (q, $J = 7.5$ Hz, 2H), 2.01 (q, $J = 7.5$ Hz, 2H), 2.10–2.30, (m, 3H), 2.50–2.60 (m, 1H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.90, 13.12, 13.44, 15.69, 19.36, 21.42, 35.05, 41.56, 43.67, 135.26, 140.92. HRMS Calc. for $C_{11}H_{20}$: 152.1564. Found: 152.1554.

4.6. (3R*,4R*)-1,2-Dipropyl-3,4-dimethylcyclopentene (**3b**)

Isolated 105 mg (58%). ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.82 (d, $J = 7.1$ Hz, 3H), 0.85 (d, $J = 7.5$ Hz, 3H), 0.86 (t, $J = 7.4$ Hz, 3H), 0.92 (d, $J = 6.8$ Hz, 3H), 1.22–1.47 (m, 4H), 1.83–2.10 (m, 5H), 2.17–2.26 (m, 2H), 2.47–2.54 (m, 1H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.88, 13.92, 14.16, 15.67, 21.35, 21.63, 28.44, 30.46, 35.16, 41.91, 43.94, 134.43, 140.39. HRMS Calc. for $C_{13}H_{24}$: 180.1877. Found: 180.1870.

4.7. (3R*,4R*)-1,2-Dibutyl-3,4-dimethylcyclopentene (**3c**)

Isolated 133 mg (64%). ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.81 (d, $J = 7.1$ Hz, 3H), 0.88 (d, $J = 7.1$ Hz, 3H), 0.91 (t, $J = 6.8$ Hz, 6H), 1.22–1.34 (m, 8H), 1.85–1.90 (m, 2H), 1.98–2.05 (m, 2H), 2.10–2.25 (m, 3H), 2.51 (dq, $J = 7.2$, 7.2 Hz, 1H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.91, 14.10, 14.11, 15.71, 22.62, 22.82, 26.08, 28.17, 30.54, 30.79, 35.16, 41.99, 43.93, 134.39, 140.29. HRMS Calc. for $C_{15}H_{28}$: 208.2191. Found: 208.2198.

4.8. (3R*,4R*)-1,2-Diphenyl-3,4-dimethylcyclopentene (**3d**)

Isolated 174 mg (70%). ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.88 (d, $J = 7.1$ Hz, 3H), 1.10 (d, $J = 6.7$ Hz, 3H), 2.58–2.66 (m, 1H), 2.70–2.73 (m, 2H), 3.07–3.11 (m, 1H), 7.09–7.17 (m, 10H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.73, 15.54, 35.32, 44.04, 48.06, 126.25, 126.48, 127.79, 128.32, 128.79, 128.80, 135.68, 138.17, 138.46, 144.04. Anal. Calc. for $C_{19}H_{20}$: C, 91.88; H, 8.37. Found: C, 91.78; H, 8.28%.

4.9. A typical experimental procedure for the reaction of zirconacyclopentanes with electrophiles: formation of (3R*,4R*)-1,2-diethyl-3,4-bis(benzoylmethyl) cyclopentene (**4a**)

To a solution zirconacyclopentane (1 mmol) were added benzoyl chloride (295 mg, 2 mmol) and CuCl chloride (99 mg, 1 mmol) and the reaction mixture was stirred for 3 h. After that the reaction mixture was quenched with 3 N HCl and extracted with Et_2O. The combined extracts were washed with sat. $NaHCO_3$, brine, dried over $MgSO_4$, and concentrated in vacuo. Column chromatography on silica gel (30:1 C_6H_{14}–Et_2O) afforded 205 mg (57%) of the title compound. ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.95 (t, $J = 7.6$ Hz, 3H), 0.97 (t, $J = 7.6$ Hz, 3H), 1.80–1.89 (m, 1H), 1.95 (dd, $J = 16.3$, 2.7 Hz, 1H), 2.04 (q, $J = 7.5$ Hz, 2H), 2.18–2.28 (m, 1H), 2.38–2.44 (m, 1H), 2.66 (dd, $J = 16.4$, 8.0 Hz, 1H), 2.91–2.97 (m, 2H), 3.08 (d, $J = 10.2$ Hz, 1H), 3.15 (dd, $J = 16.4$, 3.6 Hz, 1H), 3.32 (dd, $J = 16.2$, 4.1 Hz, 1H), 7.26–7.53 (m, 6H), 7.96 (d, $J = 7.9$ Hz, 4H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.93, 13.31, 19.13, 21.34, 37.47, 39.65, 42.51, 45.24, 48.93, 127.94, 128.08, 128.38, 128.48, 132.70, 132.88, 136.47, 136.73, 137.00, 137.18, 200.21; ν(CO) 1680.2, 1687.9 cm^{-1}. HRMS Calc. for $C_{25}H_{28}O_2$: 360.2088. Found: 360.2073.

4.10. (3R*,4R*)-1,2-Diphenyl-3,4-di(iodomethyl)cyclopentene (**4b**) and (3R*,4S*)-1,2-diphenyl-3,4-di(iodomethyl)cyclopentene (**5b**)

Isolated 340 mg (68%). Compound **4b**: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 2.40 (dd, $J = 16.9$, 3.3 Hz, 1H), 2.50–2.57 (m, 1H), 3.12–3.20 (m, 2H), 3.33–3.44 (m, 4H), 7.11–7.25 (m, 10H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 13.49, 14.51, 43.37, 43.82, 58.69, 127.13, 127.26, 127.93, 127.97, 128.52, 128.81, 136.18, 136.60, 137.37, 138.08. Compound **5b**: ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 5.69, 6.65, 43.29, 43.49, 51.76, 127.05, 127.33, 127.78, 127.92, 128.53, 128.99, 136.32, 136.79, 138.40, 139.40. HRMS Calc. for $C_{19}H_{18}I_2$: 499.9497. Found: 499.9508.

4.11. (3R*,4R*)-1,2-Diethyl-3,4-di(3-butenyl)cyclopentene (**4c**) and (3R*,4S*)-1,2-diethyl-3,4-di(3-butenyl)cyclopentene (**5c**)

Isolated 185 mg (80%). Compound **4c**: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.91 (t, $J = 7.6$ Hz, 3H), 0.94 (t, $J = 7.5$ Hz, 3H), 1.25–1.56 (m, 4H), 1.80–2.30 (m, 11H), 2.45–2.51 (m, 1H), 4.93 (dd, $J = 10.1$, 1.5 Hz, 2H), 5.00 (dd, $J = 17.2$, 1.5 Hz, 2H), 5.79–5.88 (m, 2H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 13.16, 13.24, 19.15, 21.41, 31.18, 32.04, 32.22, 36.16, 39.98, 40.23, 52.49, 113.94, 114.05,

135.34, 137.75, 139.34, 139.52. Compound **5c**: ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 13.16, 13.34, 19.71, 21.46, 27.73, 29.58, 31.63, 33.06, 39.76, 40.55, 47.38, 113.80, 114.11, 136.34, 137.74, 139.39, 139.61. Anal. Calc. for $C_{17}H_{28}$: C, 87.86; H, 12.14. Found: C, 87.81; H, 12.32%.

4.12. (3R,4R*)-1,2-Diphenyl-3,4-di(3-butenyl)cyclopentene (**4d**) and (3R*,4S*)-1,2-diphenyl-3,4-di(3-butenyl)cyclopentene (**5d**)*

Isolated 288 mg (88%). Compound **4d**: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 1.38–1.67 (m, 4H), 2.01–2.18 (m, 5H), 2.37 (dd, $J = 16.4$, 3.0 Hz, 1H), 2.86 (dd, $J = 8.3$, 2.9 Hz, 1H), 3.28 (ddd, $J = 16.3$, 7.9, 2.6 Hz, 1H), 4.85 (d, $J = 16.8$ Hz, 1H), 4.90–4.99 (m, 2H), 5.05 (dd, $J =$ 17.1, 1.6 Hz, 1H), 5.72 (ddt, $J = 16.9$, 10.3, 6.6 Hz, 1H), 5.87 (ddt, $J = 16.9$, 10.3, 6.7 Hz, 1H), 7.09–7.24 (m, 10H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 31.37, 31.87, 32.00, 36.05, 39.81, 42.86, 56.64, 114.25, 114.43, 126.40, 126.54, 127.82, 127.95, 128.21, 128.73, 135.35, 137.98, 138.17, 138.98, 140.90. Compound **5d**: ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 27.88, 29.62, 31.67, 32.88, 41.01, 42.57, 51.44, 114.05, 114.50, 126.32, 126.59, 127.77, 127.79, 128.21, 128.81, 136.60, 138.14, 138.48, 139.15, 142.62. Anal. Calc. for $C_{25}H_{28}$: C, 91.41; H, 8.59. Found: C, 91.60; H: 8.76%.

4.13. (3R,4S*)-1,2-Dibutyl-3,4-bis(deuteromethyl)cyclopentene (**d-4**) and (3R*,4R*)-1,2-dibutyl-3,4-bis(deuteromethyl)cyclopentene (**d-5**)*

Isolated 164 mg (78%). Compound ***d*-4**: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.89 (t, $J = 6.2$ Hz, 6H), 0.94 (d, $J =$ 7.0 Hz, 2H), 0.99 (d, $J = 6.9$ Hz, 2H), 1.20–1.35 (m, 8H), 1.60–1.71 (m, 1H), 1.82–1.91 (m, 2H), 1.98–2.18 (m, 4H), 2.35–2.42 (m, 1H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 14.06, 18.01 (t, $J = 19$ Hz), 19.78 (t, $J = 19$ Hz), 22.68, 22.80, 25.83, 28.26, 30.53, 30.55, 39.85, 42.47, 49.20, 134.03, 138.89. Compound ***d*-5**: ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.60 (t, $J = 19$ Hz), 14.08, 15.40 (t, $J = 19$ Hz), 22.59, 22.79, 26.06, 28.15, 30.52, 30.77, 35.04, 41.96, 43.83, 134.36, 140.25. HRMS Calc. for $C_{15}H_{26}D_2$: 210.2314. Found: 210.2315.

4.14. (3R,4R*)-1,2-Dibutyl-3-deuteromethyl-4-methylcyclopentene (**d-6**) and (3R*,4R*)-1,2-dibutyl-4-deuteromethyl-3-methylcyclopentene (**d-7**)*

Isolated 272 mg (65%). Isomer 1: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.91 (d, $J = 7.1$ Hz, 2H), 0.88 (d, $J = 7.0$ Hz, 3H), 0.81 (t, $J = 7.0$ Hz, 6H), 1.22–1.34 (m, 8H), 1.85–1.90 (m, 2H), 1.98–2.05 (m, 2H), 2.10–2.25 (m, 3H), 2.48–2.54 (m, 1H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.60 (t, $J = 19$ Hz), 14.08, 15.69, 22.59, 22.79, 26.05, 28.13, 30.51, 30.76, 35.11, 41.97, 43.83, 134.36, 140.25. Isomer 2: ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.91, 14.09, 15.40 (t, $J = 19$ Hz), 22.59, 22.79, 26.05, 28.14, 30.51, 30.76, 35.04, 41.94, 43.89, 134.36, 140.25. HRMS Calc. for $C_{15}H_{27}D$: 209.2253. Found: 209.2258.

4.15. (3R,4R*)-1,2-Diphenyl-3-iodomethyl-4-methylcyclopentene (**6a**) and (3R*,4R*)-1,2-diphenyl-4-iodomethyl-3-methylcyclopentene (**7a**)*

Isolated 228 mg (61%). Isomer 1: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 1.28 (d, $J = 6.7$ Hz, 3H), 2.74–2.93 (m, 3H), 3.06 (dd, $J = 10.1$, 7.3 Hz, 1H), 3.28 (dd, $J = 10.2$, 2.7 Hz, 1H), 3.41–3.50 (m, 1H), 7.11–7.26 (m, 10H). ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 7.51, 14.40, 34.51, 44.02, 53.85, 126.75, 126.98, 127.85, 127.87, 128.43, 128.99, 137.14, 137.42, 139.03, 139.61. Isomer 2: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.92 (d, $J = 7.1$ Hz, 3H), 2.78–2.84 (m, 2H), 2.93–3.00 (m, 1H), 3.30–3.40 (m, 3H), 7.10–7.24 (m, 10H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 7.90, 11.68, 42.38, 44.34, 47.13, 126.60, 126.87, 127.68, 127.89, 128.27, 128.70, 134.84, 137.46, 137.55, 143.68. HRMS Calc. for $C_{19}H_{19}I$: 374.0532. Found: 374.0529.

4.16. (3R,4R*)-1,2-Diphenyl-3-(3-butenyl)-4-methylcyclopentene (**6b**) and (3R*,4R*)-1,2-diphenyl-4-(3-butenyl)-3-methylcyclopentene (**7b**)*

Isolated 240 mg (83%). Isomer 1: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.89 (d, $J = 7.1$ Hz, 3H), 1.45–1.73 (m, 2H), 1.90–2.17 (m, 2H), 2.63–2.77 (m, 3H), 3.08–3.12 (m, 1H), 4.98 (dd, $J = 10.1$, 1.8 Hz, 1H), 5.06 (dd, $J = 17.1$, 1.8 Hz, 1H), 5.88 (ddt, $J = 17.1$, 10.1, 6.8 Hz, 1H), 7.08–7.22 (m, 10H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 12.14.47, 29.93, 32.80, 40.74, 41.80, 47.14, 114.37, 126.31, 126.58, 127.73, 127.86, 128.19, 128.79, 135.42, 138.19, 138.21, 139.04, 144.36. Isomer 2: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 1.11 (d, $J = 6.6$ Hz, 3H), 4.86 (dd, $J = 10.1$, 1.8 Hz, 1H), 4.89 (dd, $J = 17.1$, 1.8 Hz, 1H), 5.70 (ddt, $J = 17.1$, 10.1, 6.7 Hz, 1H), others were overlapped by isomer 1; ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 15.54, 27.47, 31.98, 34.86, 44.80, 52.33, 114.10, 126.26, 126.48, 127.76, 127.86, 128.19, 128.84, 136.51, 138.07, 138.66, 139.11, 142.10. Anal. Calc. for $C_{22}H_{24}$: C, 91.61; H, 8.39. Found: C, 91.98; H, 8.59%.

4.17. (3R,4R*)-1,2-Diphenyl-3-benzoylmethyl-4-methylcyclopentene (**6c**) and (3R*,4R*)-1,2-diphenyl-4-benzoylmethyl-3-methylcyclopentene (**7c**)*

Isolated 255 mg (72%). Isomer 1: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.98 (d, $J = 6.4$ Hz, 3H), 2.65–2.85 (m, 3H), 3.19–3.27 (m, 3H), 7.11–7.85 (m, 15H); ^{13}C-NMR ($CDCl_3$, Me_4Si): δ 16.21, 34.26, 36.69, 44.65, 48.62, 126.52, 126.85, 127.85, 127.88, 128.36, 128.45, 128.96, 132.77, 136.88, 137.12, 137.51, 137.74, 137.78, 200.34. Isomer 2: ^{1}H-NMR ($CDCl_3$, Me_4Si): δ 0.89 (d, $J = 7.1$, 3H), other signals were overlapped by isomer 1; ^{13}C-

NMR ($CDCl_3$, Me_4Si): δ 12.99, 36.56, 39.69, 41.76, 46.78, 126.42, 126.69, 127.75, 127.82, 128.02, 128.22, 128.60, 128.81, 132.99, 135.09, 137.07, 137.78, 137.90, 143.85, 199.96. HRMS Calc. for $C_{26}H_{24}O$: 352.1826. Found: 352.1803. IR: ν(CO) 1691.7 cm^{-1}.

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