Construction of Bi- and Tricyclic Skeletons by Domino-*Heck*–*Diels*–*Alder* Reactions

by **Stefanie Körbe** and **Armin de Meijere***

Institut für Organische Chemie, Georg-August-Universität Göttingen, Tammannstrasse 2, D-37077 Göttingen (fax: +49-551-399475; e-mail: Armin.deMeijere@chemie.uni-goettingen.de)

and

Thomas Labahn

Institut für Anorganische Chemie, Georg-August-Universität Göttingen, Tammannstrasse 4, D-37077 Göttingen

Dedicated to Professor *Dieter Seebach* on the occasion of his 65th birthday

Palladium-catalyzed intramolecular reactions of 2-bromo 1,6-dienes followed by intermolecular [4+2] cycloaddition with suitable dienophiles in one-pot operations gave hexahydroindenes **8** and **9** in yields of 40–78%, an hexahydro-*s*-indacene derivative **13** could be obtained in up to 25% yield with cyclopent-2-en-1-one (**10**) as a dienophile in the presence of different *Lewis* acids, and a spirocyclopentane-hexahydroindenone **18** could be isolated in 72% yield. When *in-situ*-formed iminium salts were used as heterodienophiles, hexahydro-1*H*-[2]pyrindinols **31** could be obtained in a one-pot two-step operation in 29–46% yield.

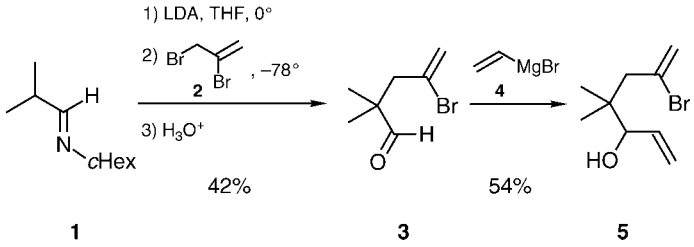
Introduction. – Domino reactions have emerged as a particularly versatile method for the construction of bi- and tricyclic systems, as they achieve the stereocontrolled formation of more than two new bonds in a single operational step [1]. Among the many new transition-metal-catalyzed reactions, the Pd-catalyzed *Heck* cross-coupling reaction has become one of the most important methods for C–C bond-formation [2]. Hexahydroindenes are easily prepared in a one-pot procedure starting from 2-bromo 1,6-dienes, which, by an intramolecular *Heck* reaction, first afford a 1,2-dimethylidenylcyclopentane[1]) that, in the presence of a dienophile, immediately undergoes an intermolecular *Diels*–*Alder* reaction. The reaction has been thoroughly studied for 2-bromo 1,6-dienes containing a dialkyl malonate unit at the 4-position, simply because the starting materials can easily be prepared by twofold alkylation of dialkyl malonates [4]. Geminal disubstitution in the open-chain precursor does play a role in the intramolecular *Heck* reaction because of the *Thorpe-Ingold* effect [5], but it is not essential for the success of the intramolecular coupling [4a]. With regard to the synthesis of natural products, the geminal ester groups would have to be replaced by geminal dimethyl groups. Therefore, in this paper, we report a study of the synthesis and Pd-catalyzed cyclization of 2-bromo 1,6-dienes with geminal dimethyl groups with respect to various Pd catalysts, solvents, bases, and ligands.

---

[1]) Dimethylidenylcycloalkanes can also be formed by cyclization of acetylenic vinyllithiums generated from the corresponding acetylenic vinyl bromides by Li/Br exchange [3].

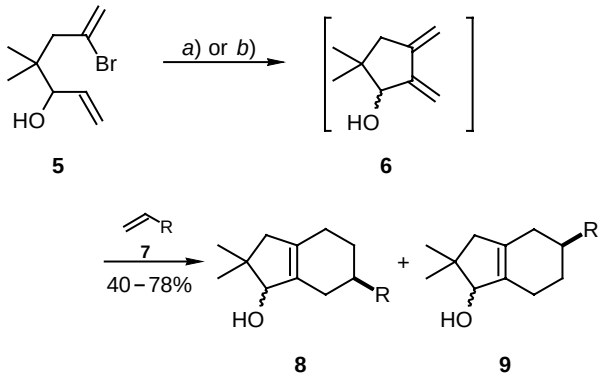
Results and Discussion. – *Formation of Carbocyclic Systems.* The synthesis of 2-bromo 1,6-dienes with geminal dimethyl groups is not as straightforward as that with geminal diester groups, which are disubstituted dialkyl malonates [4a]. However, the imine **1**, prepared from isobutyraldehyde and cyclohexylamine, can be deprotonated with lithium diisopropylamide (LDA) [6], and alkylation of the azaenolate with 2,3-dibromopropene (**2**) followed by acid-catalyzed hydrolysis furnishes the bromo aldehyde **3** in 42% isolated yield. Because of its instability, **3** has to be immediately converted further, *e.g.*, by reaction with vinylmagnesium bromide (**4**) to give 2-bromo-4,4-dimethylhepta-1,6-dien-5-ol (**5**) in 54% yield (*Scheme 1*).

Scheme 1. *Preparation of 2-Bromo-4,4-dimethylhepta-1,6-dien-5-ol* (**5**)



2-Bromo 1,6-dienes of type **5** have been shown to cyclize in the presence of $Pd(OAc)_2$, Ph_3P, and K_2CO_3 or Ag_2CO_3 to afford 1,2-bis(exomethylene)cyclopentanes of type **6**, which can subsequently undergo *Diels–Alder* reactions to give hexahydroindene derivatives **8** and **9**. As previous studies have revealed that the yields without isolation of intermediate **6** are consistently higher than those obtained in two steps, the reactions of **5** with acrylates and methyl vinyl ketone were carried out as single one-pot operations (*Scheme 2*) [4][7].

Scheme 2. *Cyclization of* **5** *and Diels–Alder Reaction*



a) $Pd(OAc)_2$ (5 mol-%), Ph_3P (10 mol-%), Ag_2CO_3 (1.2 equiv.), MeCN, 80°, 18 h. *b*) $Pd(OAc)_2$ (5 mol-%), Ph_3P (10 mol-%), K_2CO_3 (2 equiv.), MeCN, 80°, 18 h. For details, see *Table 1*.

In a typical experiment, a solution of the bromo diene **5** (1 mmol), the dienophile **7** (3 mmol), a base (1.2–2 mmol), $Pd(OAc)_2$ (5 mol%), and Ph_3P (10 mol%) was heated in anhydrous MeCN at 80° for 18 h.

In an effort to elucidate the conditions for this transformation, the 2-bromo 1,6-diene **5** in the presence of various dienophiles and different bases was subjected to such conditions. The products, mixtures of regioisomers and diastereoisomers **8** and **9**, were obtained in higher yields when K_2CO_3 instead of Ag_2CO_3 was used as a base. The latter is known to suppress not only double-bond migration but also the *Heck* reaction (*Table 1*, *Entries 1*, *3*, and *5*). The best yields resulted with methyl acrylate (*Entries 1* and *2*), but the regioisomeric excess was low, even when the sterically more-demanding *tert*-butyl acrylate was used (*Entries 3* and *4*). Each regioisomer was a mixture of diastereoisomers. The diastereoisomeric ratios could not be determined from the ^{1}H-NMR spectra of the mixtures since the peaks were not well-resolved.

Table 1. Heck–Diels–Alder *Reaction of* **5** *with Different Dienophiles under Various Conditions*

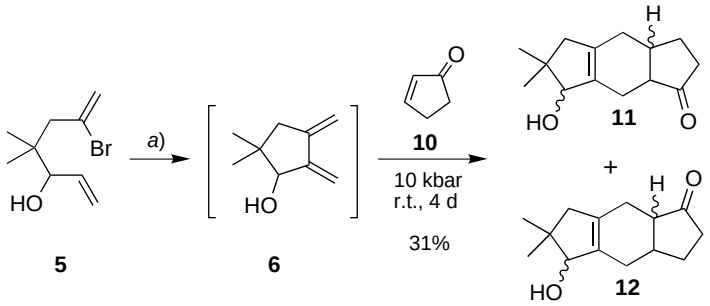
Entry	Base	R	Product	Yield [%]	Ratio **8**/**9**[a])
1	Ag_2CO_3	CO_2Me	**8a**, **9a**	41	1.5 : 1
2	K_2CO_3	CO_2Me	**8a**, **9a**	78	1.5 : 1
3	Ag_2CO_3	CO_2(*t*-Bu)	**8b**, **9b**	40	1.9 : 1
4	K_2CO_3	CO_2(*t*-Bu)	**8b**, **9b**	62	1.9 : 1
5	Ag_2CO_3	COMe	**8c**, **9c**	56	1.9 : 1
6	K_2CO_3	COMe	**8c**, **9c**	70	1.9 : 1

[a]) The ratios of the regioisomers were determined by integration of the relevant peaks in the ^{1}H-NMR spectra after oxidation of **8** and **9** to the corresponding ketones.

With cyclopent-2-en-1-one (**10**) as a dienophile, this *Heck–Diels–Alder* reaction should allow easy access to decahydro-*s*-indacene derivatives [8]. Because of the low reactivity of **10** under the established conditions described above, only decomposition could be detected after 14 days of heating. Carrying out the reaction as a one-pot two-step operation, in which the *Diels–Alder* reaction was performed at 10 kbar [9], gave the regioisomeric decahydro-*s*-indacene derivatives **11** and **12** after 4 d in 31% yield as a mixture of diastereoisomers (*Scheme 3*).

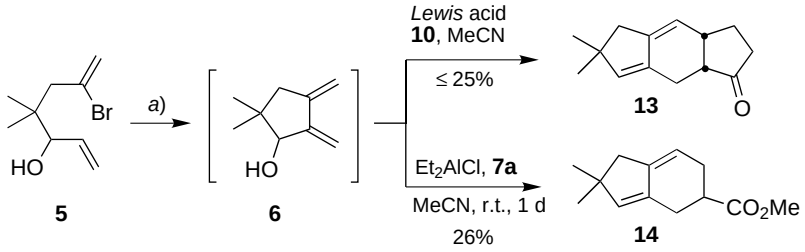
Diels–Alder reactions can be accelerated not only by high pressure (for recent reviews on high-pressure chemistry, see [9]), but also by addition of *Lewis* acids such as $LiBF_4$ [10], $BF_3 \cdot OEt_2$, dialkylaluminum chlorides, trialkylaluminum, or alkoxytitanium halides. With $LiBF_4$ added to the mixture of **5**, **10**, and the catalyst cocktail, the hexahydro-*s*-indacene derivative **13** was obtained as the only product, which must be formed from **11** by *Lewis* acid promoted elimination of H_2O. The reaction time of 14 d was very long, and even the best yield was only 25% (*Table 2*, *Entry 1*). Apparently, the dimethylidenylcyclopentanol **6** is not stable enough under these conditions for extended times. Therefore, Et_2AlCl was tested as a *Lewis* acid. After only 18 h, the product **13** could be isolated in 22% yield, but a large number of unidentified side products were also formed (*Entry 2*). In our search for a *Lewis* acid that is not as strong as Et_2AlCl but strong enough to catalyze the reaction, $AlMe_3$ and $Ti(O^iPr)_4$ were also tested (*Entries 4* and *5*). With these, however, no hexahydro-*s*-indacene derivative was observed; only the starting material could be recovered. With only 1.5 equiv. of

Scheme 3. Heck–Diels–Alder *Reaction of* **5** *with Cyclopentenone* **10** *as a Dienophile*



a) $Pd(OAc)_2$ (5 mol-%), Ph_3P (10 mol-%), K_2CO_3 (1 equiv.), MeCN, 80°, 18 h.

Scheme 4. *Reaction of* **5** *with* **10** *in the Presence of a* Lewis *Acid*



a) $Pd(OAc)_2$ (5 mol-%), Ph_3P (10 mol-%), K_2CO_3 (1 equiv.), MeCN, 80°, 18 h. For details, see *Table 2*.

Table 2. Heck–Diels–Alder *Domino Reaction of* **5** *with Cyclopentenone* **10** *in the Presence of Different* Lewis *Acids*

Entry	*Lewis* acid (equiv.), time	Product	Yield [%]
1	$LiBF_4$ (3), 14 d	**13**	25
2	Et_2AlCl (3), 18 h	**13**	22
3	Et_2AlCl (1.5), 18 h	**13**	6[a])
4	Me_3Al (3), 72 h	**5**	–[b])
5	$Ti(O^iPr)_4$ (3), 72 h	**5**	–[b])

[a]) Additionally, 17% of diene **6** was recovered. [b]) Only decomposition was observed.

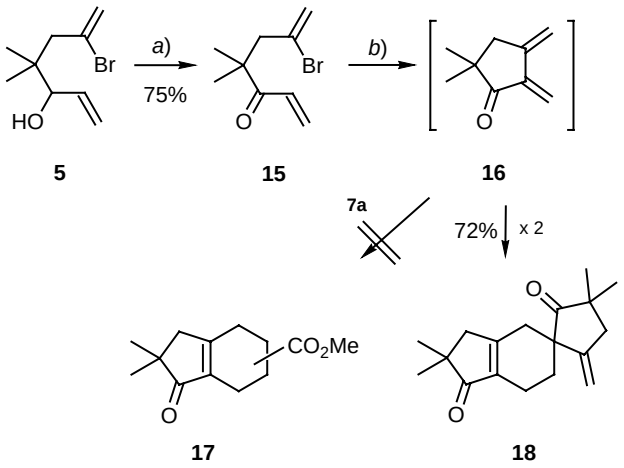
Et_2AlCl, only 6% of **13** and 17% of the dimethylidenylcycloalkane could be isolated (*Entry 3*).

After this partial success with an added *Lewis* acid, the *Diels–Alder* reaction of the preformed intermediate **6** with methyl acrylate (**7a**) was also tested in the presence of Et_2AlCl.

Towards that end, a solution of Et_2AlCl (3 equiv.) and **7a** (3 equiv.) in MeCN, which had been stirred for 15 min, was added to the mixture containing **6**, and stirring was continued at ambient temperature for 1 d. The expected tetrahydroindene **14** could be isolated in 26% yield, along with a considerable amount of decomposition product.

To avoid the formation of diastereoisomeric mixtures, the bromoheptadienol **5** was oxidized to the ketone **15** according to the *Swern* protocol [11]. Surprisingly, when the bromodienone **15** was treated with the Pd catalyst in the presence of **7a**, the expected product **17** was not observed, but the hexahydrospiro(cyclopentaneinden)one **18** was isolated as a single product in 72% yield (*Scheme 5*). Even in the presence of a large excess of **7a** (10 equiv.), only **18** was formed. Apparently, the α,β-unsaturated enone moiety in the 5,5-dimethyl-2,3-dimethylenecyclopentanone **16** first formed is a far better dienophile than **7a**. It is remarkable that the hexahydroindenone **18** was formed as a single regio- as well as diastereoisomer, the structure of which was established by X-ray-analysis (*Fig.*)[2]).

Scheme 5. Swern *Oxidation of the Bromodiene* **5** *and Palladium-Catalyzed Reaction of* **15**



a) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, r.t., 18 h. *b*) $Pd(OAc)_2$ (5 mol-%), Ph_3P (10 mol-%), Ag_2CO_3 (1.25 equiv.), MeCN, 80°, 18 h.

The mono- and dimethyl-substituted bromodienes **25** and **27** could be prepared from the *t*-Bu-substituted isobutyraldehyde imine in close analogy to the synthesis of **5** with (*E*)-1,2-dibromobut-2-ene (**22**) and 1,2-dibromo-3-methylbut-2-ene (**23**) instead of 2,3-dibromopropene in the alkylation of the azoenolate. In view of the illudine sesquiterpenes with their tetrahydroindene skeleton, the synthesis of such compounds

---

[2]) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-185854. Copies of this data can be obtained, free of charge, on application to the CCDC, 12 Union Rd., Cambridge CB2 1EZ, UK (fax: +44(1223)336-033; e-mail: deposit@ccdc.cam.ac.uk).

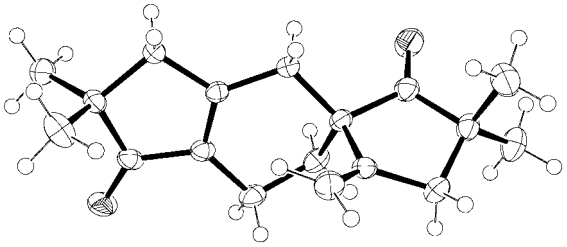


Figure. *Structure of* **18** *in the crystal*[2])

with a Me group at C(4) of the hexahydroindene derivative was of interest in this context [12].

Deprotonation of **21** with LDA, alkylation with **22** or **23**, and acidic workup gave the aldehydes **24** and **26** in moderate yields of 54 and 48%, respectively. Addition of vinylmagnesium bromide (**4**) yielded the bromodienes **25** and **27** in 45 and 47% yields, respectively (*Scheme 6*).

When the bromodiene **25** was subjected to the usual conditions of the domino *Heck–Diels–Alder* reaction, the exocyclic diene **20** could be isolated in 45% yield, but only a trace of the hexahydroindenes **19** could be detected. It is a bit surprising that the *Diels–Alder* reaction of **20** did not occur easily in spite of the s-*cis* conformation of its 1,3-diene unit.

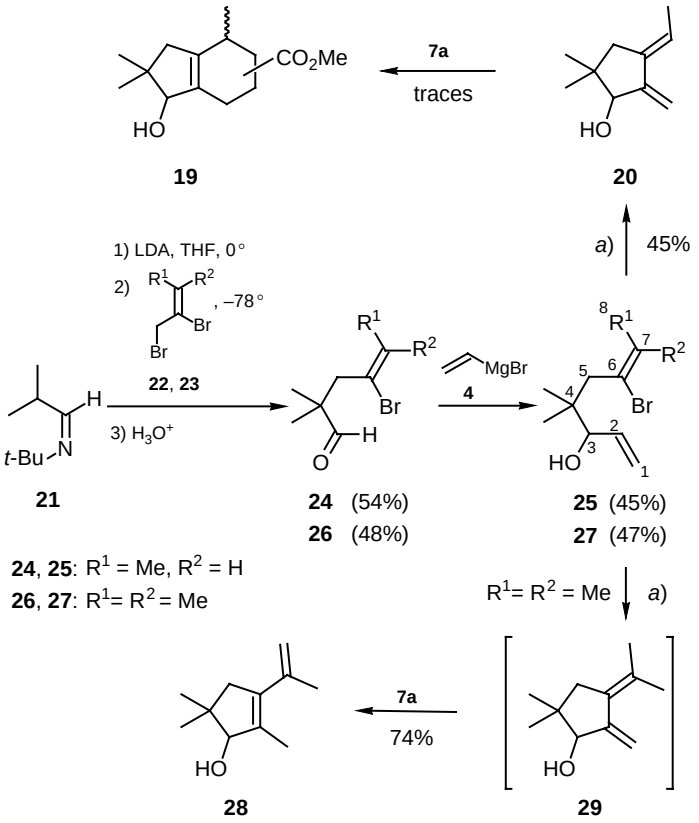
Under the same conditions, the dimethyl-substituted bromodiene **27** gave no bicyclic compound at all. Only the isopropenylcyclopentenol **28** was isolated in 74% yield; **28** probably results from the exocyclic diene **29** first formed by isomerization, which can occur either by re-addition with reversed regioselectivity of the eliminated hydridopalladium bromide and subsequent elimination of hydridopalladium bromide [13], or by a concerted suprafacial 1,5-H-shift. Cyclopentadienes are known to undergo such 1,5-H-shifts rapidly at room temperature; for this rearrangement to occur in acyclic or exocyclic dienes, higher temperatures ($>250°$) are usually required [14], although the s-*cis* conformation of **29** should facilitate such a 1,5-H-shift. The substitution pattern in the resulting diene **28** does not favor a conformation that would allow a *Diels–Alder* reaction to occur.

Formation of Heterocyclic Systems. Since N-containing heterocyclic systems are of particular interest because of their potential biological activities, the domino *Heck–Diels–Alder* sequence was also applied to the preparation of azabicycles. This can be achieved by incorporation of the N-atom in the cyclization precursor, as described in an earlier publication [15].

Another possibility is to use N-atom-containing dienophiles, such as imines and nitroso compounds [16]. For such hetero-*Diels–Alder* reactions, either the imines have to be electron deficient or the dienes particularly electron rich. Activation by added *Lewis* acids has also been used in many cases. *Larsen* and *Grieco* reported that imines formed *in situ* from formaldehyde and an amine hydrochloride react with unactivated dienes without added *Lewis* acids [17]. This approach has been adopted for the use with formaldehyde and amino acid ester hydrochlorides by *Waldmann* [18].

Since formaldehyde would immediately reduce the $Pd(OAc)_2$ precatalyst to inactive Pd black, the domino *Heck–Diels–Alder* reaction of the 2-bromo 1,6-diene

Scheme 6. *Preparation of the Bromodienes* **25** *and* **27**

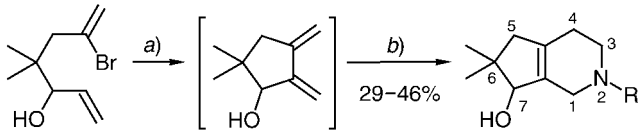


a) $Pd(OAc)_2$ (5 mol-%), Ph_3P (10 mol-%), K_2CO_3 (2 equiv.), MeCN, 80°, 18 h.

5 with such iminium hydrochlorides had to be carried out by the one-pot two-step variant [15]. Thus, a mixture of **5**, $Pd(OAc)_2$ (5 mol%), Ph_3P (10 mol%), and K_2CO_3 (1 equiv.) in MeCN was first heated at 80° for 18 h. After cooling to room temperature, formaldehyde, glycine methyl ester hydrochloride (**30a**), and H_2O were added. After an additional 18 h at ambient temperature, the hexahydro-1*H*-[2]pyrindene derivative **31a** could be isolated in 26% yield as a single regioisomer (*Table 3*, *Entry 1*). This yield could be improved to 38% by reducing the amount of K_2CO_3 from 1 equiv. to 0.5 equiv. (*Entry 2*) [15]. In an effort to evaluate the scope and limitations of this transformation, **5** was subjected to various conditions (*Entries 3–6*). With Ag_2CO_3 as the base, the yield was only 11% (*Entry 3*). Neither using MeOH instead of water nor heating to 50° increased the yield (*Entries 4* and *5*). In a reaction with the *in-situ*-formed iminium salt from cyclopentylamine (**30d**), the change from MeCN to THF for the first step led to incomplete reaction; 45% of the exocyclic diene **6** could be recovered (*Entry 11*). In an attempt to carry out the *Diels–Alder* reaction under a pressure of 10 kbar, only

decomposition was observed (*Entry 6*). The best yields were obtained when only 0.5 equiv. of K_2CO_3 was used. Under these optimized conditions, different amines were tested. The use of NH_4Cl led only to decomposition (*Entry 8*). Benzylamine hydrochloride (**30b**) gave **31b** in 46% yield (*Entry 7*); cyclopropylamine hydrochloride (**30c**) led to **31c** in only 36% yield (*Entry 9*). Cyclopentylamine hydrochloride (**30d**) and cyclohexylamine hydrochloride (**30e**) also gave low yields of 31 and 29% of **31d** and **31e**, respectively (*Entries 10* and *12*). In all cases, the iminium salts formed *in situ* gave only a single isolated regioisomer, in contrast to the reactions with most all-C dienophiles (see above).

Scheme 7. *One-Pot Two-Step Domino* Heck–Diels–Alder *Reactions of* **5** *and* In-Situ-*Formed Iminium Salts*



5 **6** **31**

a) $Pd(OAc)_2$ (5 mol-%), Ph_3P (10 mol-%), K_2CO_3 (0.5–1 equiv.), MeCN, 80°, 18 h. *b*) Formaldehyde, amine hydrochloride, R–NH_3Cl (**30**, 3 equiv.), H_2O, r.t., 18 h. For details, see *Table 3*.

Table 3. *Reaction of* **5** *with Amine Salts* **30** *as Heterodienophiles*

Entry	Amine salt **30**	Base (equiv.)	Product	Yield [%]
1	**a**: R = CH_2CO_2Me	K_2CO_3 (1)	**31a**	26
2	**a**: R = CH_2CO_2Me	K_2CO_3 (0.5)	**31a**	38
3	**a**: R = CH_2CO_2Me	Ag_2CO_3 (0.5)	**31a**	11
4	**a**: R = CH_2CO_2Me	K_2CO_3 (0.5)	**31a**	4[a])
5	**a**: R = CH_2CO_2Me	K_2CO_3 (0.5)	**31a**	4[b])
6	**a**: R = CH_2CO_2Me	K_2CO_3 (0.5)	**31a**	–[c])
7	**b**: R = Bn	K_2CO_3 (0.5)	**31b**	46
8	NH_4Cl	K_2CO_3 (0.5)	–	–
9	**c**: R = cyclopropyl	K_2CO_3 (0.5)	**31c**	36
10	**d**: R = cyclopentyl	K_2CO_3 (0.5)	**31d**	31
11	**d**: R = cyclopentyl	K_2CO_3 (0.5)	**31d**	10[d])
12	**e**: R = cyclohexyl	K_2CO_3 (0.5)	**31e**	29

[a]) MeOH instead of H_2O was used. [b]) Cycloaddition at 50°. [c]) 10 kbar, 3 d, decomposition. [d]) In THF instead of MeCN, 45% of **6** could also be isolated.

Conclusions. – A one-step synthesis of bicyclic and tricyclic compounds starting from 2-bromohepta-1,6-dienes with geminal dimethyl groups has been accomplished. Although, with all-C dienophiles, the regioselectivities are not very high, this approach is noteworthy in view of its simplicity. With *in-situ*-generated iminium hydrochlorides, azabicycles are formed in low-to-moderate yields, but with complete regioselectivity.

This work was supported by the *Fonds der Chemischen Industrie*. We are grateful to *BASF AG*, *Bayer AG*, *Chemetall GmbH*, and *Degussa AG* for generous gifts of chemicals. The authors are indebted to Dr. *Burkhard Knieriem* for his careful proofreading of the final manuscript.

Experimental Part

General. ^{1}H-NMR Spectra: *Bruker AM-250* spectrometer (250 MHz) at ambient temp. in $CDCl_3$ with $CHCl_3$ ($\delta = 7.26$) or $SiMe_4$ ($\delta = 0.00$) as int. standard; chemical shifts δ in ppm, coupling constants J as abs. values to the nearest 0.1 Hz. ^{13}C-NMR Spectra: *Bruker AM-250* (62.9 MHz) at ambient temp. in $CDCl_3$ with δ ($CDCl_3$) = 77.0 as int. standard; multiplicities determined by the DEPT pulse sequence unless otherwise indicated; signals that could not be unambiguously assigned, are marked with asterisks (*–***) IR Spectra: *Bruker IFS-66* FT-IR spectrometer ν in cm^{-1}. MS: *Varian MAT-CH-7* or *MAT-731*; electron-impact (EI) ionization at 70 eV or direct chemical ionization with NH_3 as reactant gas. HR-MS: *Varian MAT-311*, *INCOS 50* with *Varian 34000* (GC/MS); preselected ion peak-matching at $R \approx 10000$ within ± 2 ppm. Elemental analyses were performed by the Mikroanalytisches Labor des Instituts für Organische Chemie der Universität Göttingen, Germany. All solvents were distilled before use. Column chromatography (CC): *Merck* silica gel *60* (230–400 mesh, 0.063–0.200 mm); TLC plates: *Macherey-Nagel Alugram Sil G/UV*, detection under UV at 254 or 366 nm. For substances that were not UV active, the plates were developed with anisaldehyde soln. Unless specified otherwise, NH_4Cl, $NaHCO_3$, and NaCl were used as sat. aq. solns. Anh. solvents were prepared according to standard laboratory techniques [19]. All reactions with organometallic substances were performed under N_2 and exclusion of H_2O. In these cases, the glassware used was heated *in vacuo* to remove all H_2O. Reactions under high pressure were performed in sealed *Teflon* tubes in a commercial high-pressure apparatus from *Andreas Hofer GmbH* (Mülheim a.d. Ruhr, Germany). All chemicals were used as commercially available, unless otherwise noted. The substances N-*(cyclohexyl)*-N-*[(1*E*)-2-methylpropylidene]amine* (**1**) and N-*(*tert*-butyl)*-N-*[(1*E*)-2-methylpropylidene]amine* (**21**) were prepared according to literature procedures [6].

6-Bromo-4,4-dimethylhepta-1,6-dien-3-ol (**5**). To a soln. of LDA (60.0 mmol) in anh. THF (25 ml) was added **1** (7.67 g, 50.0 mmol) and *2,3-dibromoprop-1-ene* (**2**) (10.0 g, 50.0 mmol), and the mixture was stirred at –78° for 2 h. To the resulting mixture was added a mixture of AcOH/H_2O/NaOAc (1:4:1, 50 ml), the aq. layer was extracted with Et_2O (3 × 50 ml), and the combined org. layers were dried ($MgSO_4$). The solvent was removed under reduced pressure to yield 4.01 g (42%) *of 4-bromo-2,2-dimethylpent-4-enal* (**3**), which was immediately dissolved in anh. THF (25 ml), and 30 mmol vinylmagnesium bromide (30 ml, 1.0M in THF) was added at –78°. After warming to r.t., H_2O (50 ml) was added, and the aq. layer was extracted with Et_2O (3 × 30 ml). The combined org. layers were dried (Na_2SO_4), and the solvent was removed under reduced pressure. CC of the crude product (80 g SiO_2, 3.5 × 20 cm, pentane/Et_2O, 4:1) yielded 2.48 g (54%) of **5**. Colorless oil. R_f (pentane/Et_2O, 4:1) 0.34. IR (film): 3429 (OH), 2965, 2932, 2874, 1623 (C=C), 1471, 1427, 1389, 1368, 1190, 1124, 1090, 1041, 996, 930, 893. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.97 (*s*, Me–C(4)); 1.01 (*s*, Me–C(4)); 1.61 (*s*, OH); 2.42 (*d*, $^2J_{AB}$ = 14.2 Hz, H–C(5)); 2.69 (*d*, $^2J_{AB}$ = 14.2 Hz, H–C(5)); 3.95 (*d*, ^3J = 6.6 Hz, H–C(3)); 5.19–5.31 (*m*, 2 H–C(1)); 5.58–5.59 (*m*, 2 H–C(7)); 5.94 (*ddd*, ^3J = 6.6, ^3J = 10.5, ^3J = 17.1 Hz, H–C(2)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 22.4 (*Me*–C(4)); 23.6 (*Me*–C(4)); 38.4 (C(4)); 49.0 (C(5)); 78.9 (C(3)); 117.1 (C(7)*); 120.9 (C(1)*); 129.9 (C(6)); 137.3 (C(2)). EI-MS: 163/161 (98/100, $[M - C_3H_5O]^+$), 139 (44, $[M - Br]^+$), 135/133 (26/26), 121 (17, $[M - HBr - OH]^+$), 98 (16, $[M - C_2H_2Br - Me]^+$), 81 (16, $[M - C_2H_2Br - Me - OH]^+$), 67 (15, $[M - C_3H_5O - Br - Me]^+$), 58 (36), 57 (32, $[C_3H_5O]^+$). MS (DCI, NH_3): 255/253 (25/27, $[M + NH_4 + NH_3]^+$), 238/236 (98/100, $[M + NH_4]^+$), 220/218 (25/25, $[(M - H_2O) + NH_4)^+$). Anal. calc. for $C_9H_{15}BrO$ (219.1): C 49.33, H 6.90; found: C 50.56, H 7.01.

General Procedure for the One-Pot Heck *and Subsequent* Diels–Alder *Reaction* (*GP 1*). To a soln. of 1 mmol of the respective bromo diene and 3 mmol of a dienophile in 10 ml anh. MeCN in a screw-cap *Pyrex* bottle were added 5 mol-% of $Pd(OAc)_2$, 10 mol-% of Ph_3P, and 1.25–2 mmol of base. N_2 was bubbled through the mixture for 5 min, then the bottle was closed and heated at 80° for the given time. The mixture was filtered through a bed of *Celite* and charcoal and washed with Et_2O. The crude product was purified by CC (pentane/Et_2O mixtures).

*Methyl 2,3,4,5,6,7-Hexahydro-1-hydroxy-2,2-dimethyl-1*H*-indene-6-carboxylate* (**8a**) *and Methyl 2,3,4,5,6,7-Hexahydro-1-hydroxy-2,2-dimethyl-1*H*-indene-5-carboxylate* (**9a**). *Method A*. According to *GP 1*, **5** (219 mg, 1.00 mmol) and methyl acrylate (**7a**, 258 mg, 3.00 mmol) in anh. MeCN (10 ml) were treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and Ag_2CO_3 (345 mg, 1.25 mmol) at 80° for 18 h. CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O, 3:1) yielded 93 mg (41%) of a 1.5:1 mixture of **8a** and **9a**. Colorless oil. R_f (pentane/Et_2O, 3:1) 0.13. IR (film): 3425, 2952, 2840, 1735 (C=O), 1653 (C=C), 1437, 1363, 1169, 1033, 998. ^{1}H-NMR (250 MHz, $CDCl_3$, mixture): 1.03 (br. *s*, 2 Me–C(2)); 1.27 (br. *s*, OH); 1.63–2.67 (*m*, 9 H, H–C(3), H–C(4), H–C(5), H–C(6), H–C(7)); 3.68 (*s*, CO_2Me); 3.97 (br. *s*, H–C(1)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): **8a**: 22.4 and 22.7 (C(4)*); 22.9 (*Me*–C(2)); 25.5, 25.8 (C(5)*); 28.4, (C(7)*); 28.7 (*Me*–C(2)); 39.8, 39.9 (C(6)); 41.1 (C(2)); 48.8 (C(3)); 51.7 (CO_2*Me*); 86.2, 86.3 (C(1)); 134.9, 135.0 (C(3a)**);

136.1, 136.6 (C(7a)**); 176.2 (CO_2Me); **9a**: 22.9 (*Me*–C(2)); 25.0, 25.1 (C(4)*); 26.0 (C(6)*); 28.3 (C(7)*); 28.8 (*Me*–C(2)); 39.6, 39.7 (C(5)); 41.0 (C(2)); 48.9 (C(3)); 51.7 (CO_2*Me*); 87.0 (C(1)); 133.7 (C(3a)**); 137.6, 137.9 (C(7a)**); 176.3 (CO_2Me). EI-MS (mixture): 224 (11, M^+), 206 (33, $[M - H_2O]^+$), 191 (56, $[M - H_2O - Me]^+$), 164 (21, $[M - MeCO_2H]^+$), 149 (48, $[M - MeCO_2H - Me]^+$), 147 (100, $[M - CO_2Me - H_2O]^+$), 131 (63), 121 (16), 105 (15), 93 (21), 91 (33), 79 (25), 77 (17), 41 (21). Anal. calc. for $C_{13}H_{20}O_3$ (224.3): C 69.91, H 8.99; found: C 69.82, H 9.24.

Method B. According to *GP 1*, a soln. of **5** (110 mg, 0.500 mmol) and **7a** (129 mg, 1.50 mmol) was treated with $Pd(OAc)_2$, (5.6 mg, 0.025 mmol), Ph_3P (13 mg, 0.050 mmol), and K_2CO_3 (138 mg, 1.00 mmol) in anh. MeCN (10 ml) for 18 h at 80°. A mixture of **8a** and **9a** in the same ratio as described above was isolated in a yield of 88 mg (78%).

tert-*Butyl 2,3,4,5,6,7-Hexahydro-1-hydroxy-2,2-dimethyl-1*H-*indene-6-carboxylate* (**8b**) *and* tert-*Butyl 2,3,4,5,6,7-Hexahydro-1-Hydroxy-2,2-dimethyl-1*H-*indene-5-carboxylate* (**9b**). *Method A*. According to *GP 1*, **5** (219 mg, 1.00 mmol) and *tert*-butyl acrylate (**7b**) (385 mg, 3.00 mmol) in anh. MeCN (10 ml) were treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol%), and Ag_2CO_3 (345 mg, 1.25 mmol) at 80° for 18 h. CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O, 3:1) yielded 107 mg (40%) of a 1.9:1 mixture of **8b** and **9b**. Colorless oil. R_f (pentane/Et_2O, 3:1) 0.13. IR (film, mixture): 3423, 2955, 2840, 1727 (C=O), 1461, 1392, 1368, 1288, 1255, 1154, 1105, 1031, 997, 897, 850. ^{1}H-NMR (250 MHz, $CDCl_3$, mixture): 1.02 (*s*, Me–C(2)); 1.03 (*s*, Me–C(2)); 1.44 (*s*, C(Me)$_3$); 1.68–2.47 (*m*, 10 H, H–C(3), H–C(4), H–C(5), H–C(6), H–C(7), OH); 3.96 (br. *s*, H–C(1)). ^{13}C-NMR (62.9 MHz, $CDCl_3$). **8b**: 22.4, 22.7 (C(4)*); 22.9 (*Me*–C(2)); 25.8 (C(5)*); 28.1 (C(*Me*)$_3$); 28.4, 28.5 (C(7)*); 28.8 (*Me*–C(2)); 40.8, 40.9 (C(6)); 41.0 (C(2)); 48.9 (C(3)); 80.0 (*C*(Me)$_3$); 86.3, 86.4 (C(1)); 134.8, 134.9 (C(3a)**); 136.4, 136.8 (C(7a)**); 175.2 (CO_2C(Me)$_3$); **9b**: 22.9 (*Me*–C(2)); 25.0, 25.1 (C(4)*); 25.4, 25.5 (C(6)*); 25.9, 26.2 (C(7)*); 28.1 (C(*Me*)$_3$), 28.7 (*Me*–C(2)); 40.6, 40.7 (C(5)); 41.0 (C(2)); 48.8 (C(3)); 80.0 (*C*(Me)$_3$), 87.0, 87.1 (C(1)); 133.9 (C(3a)**); 137.6, 137.8 (C(7a)**); 175.1 (CO_2C(Me)$_3$). EI-MS (mixture): 266 (3, $[M]^+$), 248 (6, $[M - H_2O]^+$), 210 (24), 193 (29, $[M - OC_4H_9]^+$), 192 (100, $[M - C_4H_9OH]^+$), 177 (43, $[M - C_4H_9OH - Me]^+$), 165 (9, $[M - CO_2C_4H_9]^+$), 164 (9, $[M - C_4H_9CO_2H]^+$), 149 (13, $[M - C_4H_9CO_2H - Me]^+$), 147 (71, $[M - CO_2C_4H_9 - H_2O]^+$), 131 (9), 91 (9), 57 (29, $C_4H_9^+$), 41 (10). Anal. calc. for $C_{16}H_{26}O_3$ (266.4): C 72.14, H 9.84; found: C 72.06, H 9.57.

Method B. The use of K_2CO_3 (276 mg, 2.00 mmol) instead of Ag_2CO_3 yielded 165 mg (62%) **8b** and **9b**.

*6-Acetyl-2,3,4,5,6,7-hexahydro-1-hydroxy-2,2-dimethyl-1*H-*indene* (**8c**) *and 5-Acetyl-2,3,4,5,6,7-hexahydro-1-hydroxy-2,2-dimethyl-1*H-*indene* (**9c**). *Method A*. According to *GP 1*, to a soln. of **5** (219 mg, 1.00 mmol) and methyl vinyl ketone (210 mg, 3.00 mmol) in anh. MeCN (10 ml) was added $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and Ag_2CO_3 (345 mg, 1.25 mmol). The mixture was stirred for 18 h at 80°. CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O, 1:1) of the crude product yielded 116 mg (56%) of a 1.9:1 mixture of **8c** and **9c**. Colorless oil. R_f (pentane/Et_2O, 1:1) 0.18. IR (film, mixture): 3433, 2925, 2838, 1706 (C=O), 1649 (C=C), 1438, 1363, 1167, 1034, 997. ^{1}H-NMR (250 MHz, $CDCl_3$): **8c**: 1.03 (*s*, 2 Me–C(2)); 1.41 (br. *s*, OH); 1.53–2.43 (*m*, 8 H, H–C(3), H–C(4), H–C(5), H–C(7)); 2.18 (*s*, COMe); 2.55–2.62 (*m*, H–C(6)); 3.97 (br. *s*, H–C(1)); **9c**: 1.01 (*s*, Me–C(2)); 1.05 (*s*, Me–C(2)); 1.41 (br. *s*, OH); 1.53–2.43 (*m*, 8 H, H–C(3), H–C(4), H–C(6), H–C(7)); 2.18 (*s*, COMe); 2.55–2.62 (*m*, H–C(5)); 3.97 (br. *s*, H–C(1)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): **8c**: 22.6, 23.0 (C(4)*); 22.9 (Me–C(2)); 25.3 (C(5)*); 27.5 (C(7)*); 28.1 (CO*Me*); 28.8 (*Me*–C(2)); 41.0 (C(2)); 47.9 (C(6)); 48.8, 48.9 (C(3)); 86.1 (C(1)); 134.9, 135.0 (C(3a)**); 136.2, 136.7 (C(7a)**); 211.5 (COMe). **9c**: 22.9 (*Me*–C(2)); 24.8, 24.9 (C(4)*); 25.0 (C(6)*); 25.1 (C(7)*); 27.9, 28.2 (CO*Me*); 28.8 (*Me*–C(2)); 47.6, 47.8 (C(5)); 41.0 (C(2)); 48.7, 48.8 (C(3)); 86.9, 87.0 (C(1)); 133.8 (C(3a)**); 137.8 (C(7a)**); 211.5 (*C*OMe). EI-MS (mixture): 208 (9, M^+), 191 (13, $[M - OH]^+$), 190 (13, $[M - H_2O]^+$), 175 (10, $[M - H_2O - Me]^+$), 163 (20, $[M - OH - CO]^+$), 147 (100, $[M - COMe - H_2O]^+$), 131 (15), 105 (13), 91 (18). HR-MS: 208.1463 (M^+, $C_{13}H_{20}O_2$; calc. 208.1463).

Method B. When K_2CO_3 (276 mg, 2.00 mmol) was used as the base, 145 mg (70%) of a mixture of **8c** and **9c** was isolated.

*1,2,3,3a,5,6,8,8a-Octahydro-6,6-dimethyl-*s*-indacene-1-one* (**13**). *Method A*. According to *GP 1*, **5** (219 mg, 1.00 mmol) in anh. MeCN (10 ml) was treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and K_2CO_3 (138 mg, 1.00 mmol) at 80° for 18 h. After cooling to ambient temp., *cyclopentenone* (**10**) (410 mg, 4.99 mmol) and $LiBF_4$ (94 mg, 1.0 mmol) were added. After the mixture had been stirred at ambient temp. for 14 d, the solvent and dienophile were removed under reduced pressure. CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O, 4:1) gave 51 mg (25%) of **13** as a colorless oil. R_f (pentane/Et_2O, 4:1) 0.46. IR (film): 3058, 2961, 1737 (C=O), 1650, 1434, 1406, 1267, 1172, 1034, 919, 737, 703. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.99 (*s*, Me–C(6)); 1.04 (*s*, Me–C(6)); 1.84–1.91 (*m*, H–C(3)); 2.01–2.40 (*m*, 7 H, H–C(2), H–C(3), H–C(5), H–C(8), H–C(8a)); 2.83 (*d*, ^3J = 12.8 Hz, H–C(8)); 3.07 (br. *s*, H–C(3a)); 5.19 (br. *s*, H–C(4));

5.51 (br. *s*, H–C(7)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 21.8 (C(8)); 27.5 (C(3)); 29.0 (*Me*–C(6)); 34.8 (C(2)); 43.0 (C(6)); 44.2 (C(5)); 48.0 (C(8a)); 117.0 (C(4)); 133.8 (C(4a)); 141.3 (C(7)); 147.4 (C(7a)); 219.8 (C(1)). EI-MS: 202 (46, $[M]^+$), 187 (52, $[M-Me]^+$), 143 (100); 131 (37), 115 (16), 91 (23), 77 (9), 41 (10).

Method B. Et_2AlCl (3.0 ml, 3.0 mmol, 1.0M in hexane) was added instead of $LiBF_4$, and the resulting mixture was stirred at ambient temp. for 18 h. The Et_2AlCl was hydrolyzed with H_2O (15 ml) and the aq. layer was extracted with Et_2O (3 × 20 ml). The org. phases were dried ($MgSO_4$), and the solvent was removed under reduced pressure. CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O 4:1) gave 45 mg (22%) of **13** as a colorless oil. R_f (pentane/Et_2O, 4:1) 0.46.

Method C. The use of a soln. of Me_3Al (1.50 ml, 3.00 mmol, 2M in toluene) instead of Et_2AlCl did not give any cycloaddition product within 72 h.

Method D. When $Ti(O^iPr)_4$ (853 mg, 3.00 mmol) was used as a *Lewis* acid, only decomposition was observed within 72 h.

Method E. When the reaction was carried out with a smaller amount of Et_2AlCl (1.5 ml, 1.5 mmol, 1.0M in hexane) within 12 h, only 13 mg (6%) of **13** and 24 mg (17%) of **6** (for spectroscopic data, see **31d**) could be isolated.

*Methyl 2,4,5,6-Tetrahydro-2,2-dimethyl-1*H*-indene-5-carboxylate* (**14**). According to *GP 1*, **5** (219 mg, 1.00 mmol) in anh. MeCN (10 ml) was treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and K_2CO_3 (138 mg, 1.00 mmol) at 80° for 18 h. After cooling to r.t., **7a** (258 mg, 3.00 mmol) and Et_2AlCl (3.0 ml, 3.0 mmol, 1.0M in hexane) were added, and stirring was continued for 1 d at ambient temp. H_2O was added (5 ml), the aq. layer was extracted with Et_2O (2 × 10 ml), and the combined org. phases were dried ($MgSO_4$). After evaporation of the solvent *in vacuo*, the resulting crude product was purified by CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O, 4:1) to give 53 mg (26%) of **14** as a colorless oil[3]. R_f (pentane/Et_2O 4:1) 0.64. IR (film): 3055, 2956, 1734 (C=O), 1437, 1367, 1267, 1199, 1106, 1027, 919, 737. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.06 (*s*, 2 Me–C(2)); 2.26–2.78 (*m*, 7 H, H–C(1), H–C(4), H–C(5), H–C(6)); 3.68 (*s*, CO_2Me); 5.35–5.37 (*m*, H–C(3)*); 5.45 (br. *s*, H–C(7)*). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 27.5 (C(4)*); 27.9 (C(6)*); 29.2 (*Me*–C(2)); 39.8 (C(5)); 43.5 (C(2)); 43.7 (C(1)); 51.7 (CO_2*Me*); 113.2 (C(3)*); 136.3 (C(3a)**); 139.9 (C(7)*); 144.8 (C(7a)**); 176.0 (*C*O_2Me). CI-MS: 224 (96, $[M+NH_4]^+$), 207 (100, $[M+H]^+$). Anal. calc. for $C_{13}H_{18}O_2$ (206.3): C 75.69, H 8.80; found: C 75.81, H 8.98.

6-Bromo-4,4-dimethylhepta-1,6-dien-3-one (**15**). To a soln. of oxalyl chloride (1.39 g, 0.94 ml, 11.0 mmol) in anh. CH_2Cl_2 (30 ml), DMSO (1.72 g, 1.57 ml, 22.0 mmol) was added at −60°, and stirring was continued for 20 min at ambient temp. A soln. of **5** (2.19 g, 10.0 mmol) in anh. CH_2Cl_2 (10 ml) was added, and the soln. was stirred for 1 h at −60°. After addition of Et_3N (5.06 g, 6.93 ml, 50.0 mmol), the mixture was allowed to warm to r.t. The mixture was quenched with 30 ml of H_2O and the aq. layer was extracted with CH_2Cl_2 (3 × 30 ml). The combined org. layers were neutralized with sat. aq. NH_4Cl, washed with sat. aq. NaCl soln. (30 ml), and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product was purified by CC (50 g SiO_2; 2.5 × 20 cm; pentane/Et_2O 20:1) to give 1.62 g (75%) of **15**. Colorless oil. R_f (pentane/Et_2O 20:1) 0.34. IR (film): 2971, 2933, 1695 (C=O), 1624 (C=C), 1610 (C=C), 1468, 1401, 1368, 1164, 1103, 1054, 1006, 982, 893. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.24 (*s*, 3 Me–C(4)); 2.81 (*s*, 2 H–C(5)); 5.50–5.54 (*m*, 2 H–C(7)); 5.70 (*dd*, ^2J = 2.0, ^3J = 10.3 Hz, H–C(1)); 6.37 (*dd*, ^2J = 2.0, ^3J = 16.9 Hz, H–C(1)); 6.84 (*dd*, ^3J = 10.3, ^3J = 16.9 Hz, H–C(2)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 24.1 (*Me*–C(4)); 46.5 (C(4)); 49.8 (C(5)); 120.6 (C(1)*); 128.9 (C(7)*); 129.1 (C(6)); 130.8 (C(2)); 202.8 (C(3)). EI-MS: 163/161 (5/5, $[M-C_3H_3O]^+$), 137 (100, $[M-Br]^+$), 81 (47, $[M-C_3H_3O-HBr]^+$), 67 (13, $[M-C_3H_3O-Br-Me]^+$), 55 (50, $[C_3H_3O]^+$), 41 (29). DCI-MS (NH_3): 270/268 (11/14, $[M+NH_4+2\,NH_3]^+$), 253/251 (100/99, $[M+NH_4+NH_3]^+$), 236/234 (44/45, $[M+NH_4]^+$). Anal. calc. for $C_9H_{13}BrO$ (217.1): C 49.79, H 6.04; found: C 50.03, H 6.06.

*2′,3′,4′,5′,6′,7′-Hexahydro-2′,2′,3,3-tetramethyl-5-methylenespiro[cyclopentane-1,5′(1′*H*)-indene]-1′,2-dione* (**18**). According to *GP 1*, a soln. of **15** (217 mg, 1.00 mmol) in anh. MeCN (10 ml) was treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol), Ph_3P (26 mg, 0.10 mmol), Ag_2CO_3 (345 mg, 1.25 mmol), and **7a** (258 mg, 3.00 mmol) for 18 h at 80°. CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O, 8:1) yielded 195 mg (72%) of **18**. Colorless crystals; m.p. 108–110°. R_f (pentane/Et_2O, 8:1) 0.23. IR (KBr): 2962, 2929, 2865, 1736 (C=O), 1697 (C=O), 1654 (C=C), 1462, 1437, 1376, 1359, 1268, 1047, 986, 899. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.98 (*s*, Me–C(3)); 1.11 (*s*, 2 Me–C(2′)); 1.21 (*s*, Me–C(3)); 1.41–1.52 (*m*, 1 H); 1.62–1.71 (*m*, 1 H); 2.00–2.16 (*m*, 2 H); 2.27–2.82 (*m*, 6 H, H–C(4), H–C(3′), H–C(4′), H–C(6′), H–C(7′)); 4.62 (*d*, ^2J = 2.3 Hz, 1 H, CH_2=C(5)); 5.05 (*d*, ^2J = 2.3 Hz, 1 H, CH_2=C(5)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 16.9 (C(7′)); 24.2 (*Me*–C(3)); 24.8 (*Me*–C(3)); 25.2

---

[3]) A second fraction contained 61 mg (28%) of the starting material.

(*Me*–C(2′)); 25.3 (*Me*–C(2′)); 28.1 (C(4′)*); 35.0 (C(6′)*); 43.5 (C(2′)); 44.2 (C(4)); 46.5 (C(3)); 46.8 (C(3′)); 52.9 (C(5′)); 108.8 (CH_2=C(5)); 134.8 (C(3′a)); 150.2 (C(5)); 168.3 (C(7′a)); 211.9 (C(1′)); 223.0 (C(2)). EI-MS: 272 (37, M^+), 257 (37, $[M-Me]^+$), 244 (100, $[M-C_2H_4]^+$), 229 (19, $[M-C_3H_7]^+$), 201 (14, $[M-C_3H_7-CO]^+$), 173 (11, $[M-C_3H_7-2\,CO]^+$), 145 (7), 107 (8), 91 (12), 77 (6), 41 (6). Anal. calc. for $C_{18}H_{24}O_2$ (272.4): C 79.37, H 8.88; found: C 79.64, H 8.87.

*(*E*)-6-Bromo-4,4-dimethylocta-1,6-dien-3-ol* (**25**). To a soln. of 50.0 mmol of LDA in anh. THF (25 ml), **21** (4.71 g, 37.0 mmol) and *(*E*)-1,2-dibromobut-2-ene* (**22**) (7.91 g, 37.0 mmol) were added and stirred for 2 h at −78°. The resulting mixture was quenched with AcOH/H_2O/NaOAc (1:4:1), and the aq. layer was extracted with Et_2O (3 × 50 ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure to yield 4.12 g (54%) of *4-bromo-2,2-dimethylhex-4-enal* (**24**), which was immediately dissolved in anh. THF (25 ml), and vinylmagnesium bromide (30 ml, 30 mmol, 1.0M in THF) was added at −78°. After warming to r.t., H_2O (50 ml) was added, the aq. layer was extracted with Et_2O (3 × 30 ml), the combined org. layers were dried (Na_2SO_4), and the solvent was removed under reduced pressure. CC of the crude product (80 g SiO_2; 3.5 × 20 cm; CH_2Cl_2) yielded 2.13 g (45%) of **25** as a colorless oil. R_f (CH_2Cl_2) 0.48. IR (film): 3433, 2965, 2932, 2873, 1653 (C=C), 1470, 1427, 1389, 1368, 1309, 1259, 1153, 1123, 1040, 996, 931. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.93 (*s*, Me–C(4)); 0.94 (*s*, Me–C(4)); 1.65 (*d*, ^3J = 4.4 Hz, OH); 1.75 (*d*, ^3J = 6.5 Hz, Me–C(7)); 2.42 (*d*, $^2J_{AB}$ = 14.4 Hz, H–C(5)); 2.68 (*d*, $^2J_{AB}$ = 14.4 Hz, H–C(5)); 3.92 (*dd*, ^3J = 3.8, ^3J = 4.4 Hz, H–C(3)); 5.17–5.29 (*m*, 2 H–C(1)); 5.74 (*q*, ^3J = 6.5 Hz, H–C(7)); 5.93 (*ddd*, ^3J = 3.8, ^3J = 7.1, ^3J = 10.5 Hz, H–C(2)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 17.4 (C(8)); 22.5 (*Me*–C(4)); 22.7 (*Me*–C(4)); 38.6 (C(4)); 49.2 (C(5)); 78.9 (C(3)); 116.9 (C(1)); 124.5 (C(6)); 127.5 (C(7)); 137.4 (C(2)). EI-MS (70 eV): 177/175 (17/17, $[M-C_3H_5O]^+$), 153 (13, $[M-Br]^+$), 135/133 (7/7), 113 (12, $[M-C_3H_4Br]^+$), 95 (81), 81 (17, $[M-C_3H_4Br-Me-OH]^+$), 67 (33), 55 (44, $[M-C_3H_5O-C_3H_4Br-H]^+$), 43 (100), 41 (37). CI-MS: 269/267 (100/94, $[M+NH_4+NH_3]^+$), 252/250 (53/57, $[M+NH_4]^+$). Anal. calc. for $C_{10}H_{17}BrO$ (233.1): C 51.52, H 7.35; found: C 52.81, H 7.31.

4-Ethylidene-2,2-dimethyl-5-methylidenecyclopentan-1-ol (**20**). According to *GP 1*, a soln. of **25** (233 mg, 1.00 mmol) in anh. MeCN (10 ml) was treated with $Pd(OAc)_2$ (22 mg, 0.10 mmol), Ph_3P (52 mg, 0.20 mmol), K_2CO_3 (276 mg, 2.00 mmol), and **7a** (258 mg, 3.00 mmol) for 18 h at 80°. CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O 4:1 → 2:1) yielded 68 mg (45%) of **20** as a colorless oil. R_f (pentane/Et_2O, 4:1) 0.41. IR (film): 3395, 2956, 2867, 1695 (C=C), 1467, 1367, 1116, 1057, 999, 921, 736. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.80 (*s*, Me–C(2)); 1.05 (*s*, Me–C(2)); 1.51 (br. *s*, OH); 1.86 (*d*, ^3J = 7.3 Hz, *Me*–CH=C(4)); 2.15–2.17 (*m*, 2 H–C(3)); 4.00 (br. *s*, H–C(1)); 5.31–5.38 (*m*, CH_2=C(5)); 5.60 (*q*, ^3J = 7.3 Hz, H–C(1′)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 15.3 (C(2′)); 19.6 (*Me*–C(2)); 25.8 (*Me*–C(2)); 39.7 (C(2)); 45.4 (C(3)); 83.6 (C(1)); 110.2 (CH_2=C(5)); 122.2 (C(1′)); 135.3 (C(4)*); 150.8 (C(5)*). EI-MS: 152 (83, M^+), 137 (100, $[M-Me]^+$), 123 (33), 109 (56), 95 (31), 81 (31), 43 (26). HR-MS: 152.1201 (M^+, $C_{10}H_{16}O$; calc. 152.1201).

6-Bromo-4,4,7-trimethylocta-1,6-dien-3-ol (**27**). To a soln. of 60.0 mmol of LDA in anh. THF (25 ml), **21** (6.36 g, 50.0 mmol) and *1,2-dibromo-3-methylbut-2-ene* (**23**) (11.4 g, 50.0 mmol) were added and stirred for 2 h at −78°. The resulting mixture was quenched with AcOH/H_2O/NaOAc (1:4:1), the aq. layer was extracted with Et_2O (3 × 50 ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure to yield 5.21 g (48%) of *4-bromo-2,2,5-trimethylhex-4-enal* (**26**), which was immediately dissolved in anh. THF (25 ml), and vinylmagnesium bromide (30 ml, 30 mmol, 1.0M in THF) was added at −78°. After warming to r.t., H_2O (50 ml) was added, the aq. layer was extracted with Et_2O (3 × 30 ml). The combined org. layers were dried (Na_2SO_4), and the solvent was removed under reduced pressure. CC of the crude product (80 g SiO_2; 3.5 × 20 cm; pentane/Et_2O 10:1) yielded 2.74 g (47%) of **27** as a colorless oil. R_f (pentane/Et_2O 10:1) 0.27. IR (film): 3445 (OH), 2966, 2932, 2873, 1644 (C=C), 1470, 1425, 1387, 1367, 1218, 1110, 1041, 994, 926, 905, 865, 798. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.97 (*s*, Me–C(4)); 0.98 (*s*, Me–C(4)); 1.72 (*d*, ^3J = 4.3 Hz, OH); 1.79 (*s*, Me–C(7)*); 1.91 (*s*, H–C(8)*); 2.62 (*d*, $^2J_{AB}$ = 14.9 Hz, H–C(5)); 2.73 (*d*, $^2J_{AB}$ = 14.9 Hz, H–C(5)); 3.94 (*dd*, ^3J = 4.3, ^3J = 6.6 Hz, H–C(3)); 5.18–5.30 (*m*, 2 H–C(1)); 5.95 (*ddd*, ^3J = 6.6, ^3J = 10.5, ^3J = 17.2 Hz, H–C(2)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 21.7 (C(8)*); 22.7 (*Me*–C(4)); 23.9 (*Me*–C(4)); 25.9 (*Me*–C(7)*); 40.1 (C(4)); 44.7 (C(5)); 79.7 (C(3)); 116.9 (C(1)); 117.9 (C(7)*); 133.8 (C(6)*); 137.4 (C(2)). EI-MS: 248/246 (1/1, M^+),191/189 (38/39, $[M-C_3H_5O]^+$), 167 (34, $[M-Br]^+$), 166 (54, $[M-HBr]^+$), 149 (29, $[M-HBr-OH]^+$), 110 (63, $[M-C_3H_5O-Br]^+$), 109 (100, $[M-C_3H_5O-HBr]^+$), 95 (27, $[M-C_3H_5O-Br-Me]^+$), 81 (20, $[M-C_4H_6Br-Me-OH]^+$), 67 (63), 55 (32, $[M-C_3H_5O-C_4H_6Br-H]^+$), 43 (83). Anal. calc. for $C_{11}H_{19}BrO$ (247.2): C 53.45, H 7.75; found: C 53.69, H 7.65.

3-Isopropenyl-2,5,5-trimethylcyclopent-2-en-1-ol (**28**). To a soln. of **27** (247 mg, 1.00 mmol) in anh. MeCN (10 ml) was added, as described in *GP 1*, $Pd(OAc)_2$ (11 mg, 0.050 mmol), Ph_3P (26 mg, 0.10 mmol), K_2CO_3 (276 mg, 2.00 mmol), and **7a** (258 mg, 3.00 mmol). Stirring was continued for 18 h at 80°. CC (18 g SiO_2; 2.0 × 15 cm; pentane/Et_2O, 5:1) of the crude product gave 123 g (74%) of **28** as a colorless oil. R_f (pentane/Et_2O 5:1)

0.37. IR (film): 3354, 2951, 2923, 2862, 1652 (C=C); 1466, 1366, 1126, 1086, 1061, 999, 891, 798. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.81 (*s*, Me–C(5)); 1.07 (*s*, Me–C(5)); 1.47 (br. *s*, OH); 1.73 (*s*, Me–C(2)*); 1.94 (*s*, Me–C(1′)*); 2.09 (*d*, $^2J_{AB}$ = 16.1 Hz, H–C(4)); 2.24 (*d*, $^2J_{AB}$ = 16.1 Hz, H–C(4)); 3.95 (br. *s*, H–C(1)); 5.18 (*m*, 2 H–C(2′)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 20.3 (*Me*–C(5)); 22.4 (*Me*–C(1′)*); 23.2 (*Me*–C(2)*); 26.3 (*Me*–C(5)); 39.0 (C(5)); 43.1 (C(4)); 83.4 (C(1)); 107.7 (C(2′)); 128.7 (C(2)**); 131.1 (C(3)**); 151.6 (C(1′)). EI-MS: 166 (79, M^+), 151 (100, $[M - Me]^+$), 133 (25, $[M - Me - H_2O]^+$), 109 (27), 95 (33), 81 (19), 67 (14), 41 (13, $C_3H_5^+$). HR-MS: 166.1357 (M^+, $C_{11}H_{18}O$; calc. 166.1357).

General Procedure for the Heck–*Hetero*-Diels–Alder *Reaction as a Two-Step One-Pot Operation* (*GP 2*). In a screw-cap *Pyrex* bottle was placed the bromo diene (1 mmol) dissolved in anh. MeCN (10 ml). To the resulting soln. were added $Pd(OAc)_2$ (5 mol-%), Ph_3P (10 mol-%), and K_2CO_3 (50 mol-%). N_2 was bubbled through the mixture for 5 min, then the bottle was closed and heated to 80° for the given time. After cooling to r.t., formaldehyde (1 ml, 37% in H_2O), amine hydrochloride (2 mmol), and H_2O (8 ml) was added and stirring was continued for the given time at ambient temp. The mixture was filtered through *Celite* and washed with H_2O. The combined filtrates were extracted with Et_2O (20 ml), and NaOH (2M) was added to the aq. layer until pH 13. The aq. layer was extracted with Et_2O (3 × 20 ml). The combined org. layers were washed with sat. NaCl soln. (20 ml), dried (Na_2SO_4), and the solvent was removed under reduced pressure. The crude product was purified by CC.

*Methyl (2,3,4,5,6,7-Hexahydro-7-hydroxy-6,6-dimethyl-1*H*-[2]pyrinden-2-yl)acetate* (**31a**). *Method A*. As described in *GP 2*, a soln. of **5** (219 mg, 1.00 mmol) in anh. MeCN (10 ml) was treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5.0 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and K_2CO_3 (69 mg, 0.50 mmol) and stirred for 18 h at 80°. After cooling to r.t., a soln. of HCHO (1.0 ml, 12 mmol, 37% in H_2O), methyl glycinate hydrochloride (**30a**, 251 mg, 2.00 mmol), and H_2O (8 ml) were added, and stirring was continued for 18 h at r.t. After workup, the crude product was purified by CC (18 g SiO_2; 2.0 × 15 cm; CH_2Cl_2/MeOH 20:1 → 10:1) to yield 92 mg (38%) of **31a** as a colorless oil. R_f (CH_2Cl_2/MeOH 10:1) 0.21. IR (film): 3340 (OH), 2955, 1749 (C=O), 1646, 1437, 1364, 1205, 1122, 1004, 701, 677, 669. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.03 (*s*, Me–C(6)); 1.06 (*s*, Me–C(6)); 1.95–2.21 (*m*, 2 H–C(4), 2 H–C(5)); 2.71 (m_c, 2 H–C(1)*); 3.14–3.22 (*m*, 2 H–C(3)); 3.37 (*s*, NCH_2); 3.73 (*s*, CO_2Me); 4.03 (br. *s*, H–C(7)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 23.0 (*Me*–C(6)); 26.5 (C(4)*); 28.9 (*Me*–C(6)); 41.4 (C(6)); 48.7 (C(5)*); 49.9 (C(3)**); 50.9 (C(1)**); 51.7 (CO_2*Me*); 58.8 (CH_2CO_2Me*); 85.7 (C(7)); 133.5 (C(4a)***); 136.7 (C(7a)***); 171.0 (CO_2Me). EI-MS: 239 (2, M^+), 221 (8, $[M - H_2O]^+$), 206 (3, $[M - H_2O - Me]^+$), 180 (29, $[M - CO_2Me]^+$), 165 (100, $[M - CO_2Me - Me]^+$), 150 (6, $[M - CO_2Me - 2\ Me]^+$), 132 (5, $[M - CO_2Me - 2\ Me - H_2O]^+$), 107 (7), 91 (4), 77 (5), 42 (10). HR-MS: 239.1521 (M^+, $C_{13}H_{21}NO_3$; calc. 239.1521).

Method B. The use of K_2CO_3 (138 mg, 1.00 mmol) decreased the yield of **31a** to 63 mg (26%).

Method C. When Ag_2CO_3 (138 mg, 0.500 mmol) was added instead of K_2CO_3, only 27 mg (11%) of **31a** could be isolated.

Method D. The addition of MeOH (8 ml) instead of H_2O lowered the yield of **31a** to only 10 mg (4%).

Method E. When the hetero-*Diels–Alder* reaction was carried out at 10 kbar, only a decomposition product and oligomeric material was obtained.

Method F. When the *Diels–Alder* reaction was performed at 50°, an unidentified side product was formed, and the yield of **31a** decreased to 9 mg (4%).

*2-Benzyl-2,3,4,5,6,7-hexahydro-6,6-dimethyl-1*H*-[2]pyrinden-7-ol* (**31b**). According to *GP 2*, to a soln. of **5** (219 mg, 1.00 mmol) in anh. MeCN (10 ml) was added $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5.0 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and K_2CO_3 (69 mg, 0.50 mmol). The resulting mixture was stirred for 18 h at 80°. After cooling to r.t., a soln. of HCHO (1.0 ml, 12 mmol, 37% in H_2O), benzylamine hydrochloride (**30b**, 287 mg, 2 mmol), and H_2O (8 ml) was added and stirred for 18 h at r.t. CC (18 g SiO_2; 2.0 × 15 cm; CH_2Cl_2/MeOH, 20:1) yielded 118 mg (46%) of **31b** as a colorless oil. R_f (CH_2Cl_2/MeOH 20:1) 0.15. IR (film): 3358 (OH), 3062, 3028, 2953, 2900, 2838, 1667, 1602, 1454, 1362, 1265, 1199, 1065, 1028, 1004, 738, 699. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.04 (*s*, Me–C(6)); 1.06 (*s*, Me–C(6)); 1.95–2.22 (*m*, 2 H–C(4), 2 H–C(5)); 2.60 (*m*, 2 H–C(1)); 2.92–3.02 (*m*, H–C(3)); 3.12–3.19 (*m*, H–C(3)); 3.65 (*s*, 1 H, $PhCH_2$); 3.66 (*s*, 1 H, $PhCH_2$); 4.02 (br. *s*, H–C(7)); 7.24–7.37 (*m*, 5 arom. H). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 23.0 (*Me*–C(6)); 26.6 (C(4)*); 28.9 (*Me*–C(6)); 41.4 (C(6)); 48.7 (C(5)*); 49.7 (C(3)**); 51.4 (C(1)**); 62.7 (CH_2Ph); 85.7 (C(7)); 127.2 (arom. C); 128.3 (arom. C); 129.3 (C(4a)); 129.4 (arom. C); 133.8 (arom. C); 136.7 (C(7a)). EI-MS: 257 (7, M^+), 240 (9, $[M - OH]^+$), 224 (12, $[M - H_2O - Me]^+$), 201 (21), 185 (35), 172 (4), 132 (3), 120 (4), 91 (4, $C_7H_7^+$), 65 (6), 41 (3).

*2-Cyclopropyl-2,3,4,5,6,7-hexahydro-6,6-dimethyl-1*H*-[2]pyrindin-7-ol* (**31c**). As described in *GP 2*, a soln. of **5** (219 mg, 1.00 mmol) in anh. MeCN (10 ml) was heated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5.0 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and K_2CO_3 (69 mg, 0.50 mmol) to 80° for 18 h. The mixture was cooled to

r.t., and HCHO (1.0 ml, 12 mmol, 37% in H_2O), cyclopropylamine hydrochloride (**30c**, 187 mg, 2.00 mmol) and H_2O (8 ml) were added. Stirring was continued for 18 h at r.t. The crude product was purified by CC (18 g SiO_2; 2.0 × 15 cm; CH_2Cl_2/MeOH 10:1) to give 74 mg (36%) of **31c** as a colorless oil. R_f (CH_2Cl_2/MeOH 10:1) 0.31. IR (film): 3368 (OH), 3087, 2953, 2908, 2839, 1669, 1459, 1362, 1265, 1219, 1057, 1018, 1002, 869, 826, 737, 702. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.46–0.50 (*m*, 4 H, cyclopropyl); 1.02 (*s*, Me–C(6)); 1.06 (*s*, Me–C(6)); 1.69–1.77 (*m*, 1 H, cyclopropyl); 1.93–2.20 (*m*, 2 H–C(4), 2 H–C(5)); 2.75 (*m*, 2 H–C(1)*); 3.06–3.25 (*m*, 2 H–C(3)*); 4.03 (br. *s*, H–C(7)). ^{13}C-NMR (75.5 MHz, $CDCl_3$): 5.9 (CH_2, cyclopropyl); 23.0 (*Me*–C(6)); 26.7 (C(4)*); 28.9 (*Me*–C(6)); 38.2 (CH, cyclopropyl); 41.4 (C(6)); 48.8 (C(5)*); 50.5 (C(3)**); 51.3 (C(1)**); 85.8 (C(7)); 134.1 (C(4a)***); 136.4 (C(2)***). EI-MS: 207 (64, M^+), 192 (100, $[M-Me]^+$), 174 (9, $[M-H_2O-Me]^+$), 151 (4, $[M-Me-C_3H_5]^+$), 135 (10), 121 (6), 107 (5), 91 (6), 84 (26), 70 (14), 56 (15), 41 (22, $C_3H_5^+$).

*2-Cyclopentyl-2,3,4,5,6,7-hexahydro-6,6-dimethyl-1*H*-[2]pyrinden-7-ol* (**31d**). *Method A*. As described in *GP 2*, a soln. of **5** (219 mg, 1.00 mmol) in anh. MeCN (10 ml) was heated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5.0 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and K_2CO_3 (69 mg, 0.50 mmol) to 80° for 18 h. The mixture was cooled to r.t. and HCHO (1.0 ml, 12 mmol, 37% in H_2O), cyclopentylamine hydrochloride (**30d**, 243 mg, 2.00 mmol), and H_2O (8 ml) were added. Stirring was continued for 18 h at r.t. The crude product was purified by CC (18 g SiO_2; 2.0 × 15 cm; CH_2Cl_2/MeOH 10:1) to give 72 mg (31%) of **31d** as a colorless oil. R_f (CH_2Cl_2/MeOH 10:1) 0.13. IR (film): 3437 (OH), 3053, 2956, 2864, 2806, 1696, 1464, 1381, 1361, 1265, 1053, 894, 868, 736, 703. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.02 (*s*, Me–C(6)); 1.06 (*s*, Me–C(6)); 1.48–1.76 (*m*, 6 cyclopentyl H, OH); 1.88–2.07 (*m*, 1 cyclopentyl H, H–C(4), H–C(5)); 2.15–2.27 (*m*, 1 cyclopentyl H, H–C(4), H–C(5)); 2.58–2.82 (*m*, 1 cyclopentyl H, 2 H–C(1)); 2.97–3.13 (*m*, H–C(3)); 3.22–3.38 (*m*, H–C(3)); 4.00 (br. *s*, H–C(7)). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 23.0 (*Me*–C(6)); 24.0 (cyclopentyl CH_2); 26.1 (C(4)*); 28.9 (*Me*–C(6)); 30.2 (cyclopentyl CH_2); 41.5 (C(6)); 48.5 (C(5)*); 49.1 (C(1)**); 50.2 (C(3)**); 67.1 (cyclopentyl CH); 85.5 (C(7)); 133.0 (C(4a)***); 137.0 (C(7a)***). EI-MS: 235 (62, M^+), 218 (15, $[M-OH]^+$), 206 (70), 192 (28, $[M-C_2H_5N]^+$), 179 (45, $[M-C_3H_6N]^+$), 163 (100, $[M-C_4H_{10}N]^+$), 150 (6), 123 (7), 98 (10), 84 (8), 68 (14), 41 (22, $C_3H_5^+$).

Method B: When the reaction was carried out in anh. THF (10 ml) instead of MeCN, in addition to 23 mg (10%) of **31d**, 62 mg (45%) of *2,2-dimethyl-4,5-dimethylidenecyclopentan-1-ol* (**6**) could be isolated as a colorless oil[4]). R_f (pentane/Et_2O 4:1) 0.45. ^{1}H-NMR (250 MHz, $CDCl_3$): 0.82 (*s*, Me–C(2)); 1.07 (*s*, Me–C(2)); 1.49 (*d*, ^3J = 7.9 Hz, OH); 2.22 (m_c, 2 H–C(3)); 4.06 (*ddd*, ^3J = 7.9, ^4J = 2.3, ^4J = 2.3 Hz, H–C(1)); 4.90 (m_c, 1 H, C=CH_2); 5.10 (*d*, ^2J = 2.2 Hz, 1 H, C=CH_2); 5.43 (m_c, 1 H, C=CH_2); 5.48 (*d*, ^2J = 2.2 Hz, 1 H, C=CH_2). ^{13}C-NMR (62.9 MHz, $CDCl_3$): 19.6 (*Me*–C(2)); 25.7 (*Me*–C(2)); 39.8 (C(2)); 44.3 (C(3)); 82.6 (C(1)); 105.4 (C=*C*H_2); 105.9 (C=*C*H_2); 144.0 (C(5)*); 151.0 (C(4)*). EI-MS (70 eV): 138 (33, M^+), 123 (100, $[M-Me]^+$), 109 (12), 105 (20, $[M-Me-H_2O]^+$), 95 (73), 91 (11), 79 (16), 67 (30), 55 (16), 43 (16), 41 (13, $C_3H_5^+$).

*2-Cyclohexyl-2,3,4,5,6,7-hexahydro-6,6-dimethyl-1*H*-[2]pyrinden-7-ol* (**31e**). According to *GP 2*, to a soln. of **5** (219 mg, 1.00 mmol) in anh. MeCN (10 ml) was added $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5.0 mol-%), Ph_3P (26 mg, 0.10 mmol, 10 mol-%), and K_2CO_3 (69 mg, 0.50 mmol). The resulting mixture was stirred for 18 h at 80°. After cooling to r.t., a soln. of HCHO (1.0 ml, 12 mmol, 37% in H_2O), cyclohexylamine hydrochloride (**30e**, 271 mg, 2 mmol), and H_2O (8 ml) was added and stirring was continued for 18 h at r.t. CC (18 g SiO_2; 2.0 × 15 cm; CH_2Cl_2/MeOH 10:1) yielded 73 mg (29%) of **31e** as a colorless oil. R_f (CH_2Cl_2/MeOH, 10:1) 0.23. IR (film): 3352 (OH), 2930, 2856, 1668, 1451, 1380, 1264, 1205, 1135, 1069, 1036, 1003, 894, 737, 702. ^{1}H-NMR (250 MHz, $CDCl_3$): 1.03 (*s*, Me–C(6)); 1.06 (*s*, Me–C(6)); 1.14–1.36 (*m*, 6 cyclohexyl H); 1.62–2.21 (*m*, 4 cyclohexyl H, 2 H–C(4), 2 H–C(5), OH); 2.41–2.48 (*m*, 1 cyclohexyl H); 2.69 (m_c, 2 H–C(1)*); 3.06–3.34 (*m*, 2 H–C(3)*); 4.02 (br. *s*, H–C(7)). ^{13}C-NMR (75.5 MHz, $CDCl_3$, APT): 23.08 (*Me*–C(6)); 25.95 (cyclohexyl CH_2*); 26.25 (C(4)*); 27.08 (cyclohexyl CH_2*); 28.80 (cyclohexyl CH_2*); 28.92 (*Me*–C(6)); 41.48 (C(6)); 46.17 (C(5)*); 46.86 (C(1)**); 48.70 (C(3)**); 63.44 (cyclohexyl CH); 85.85 (C(7)); 134.14 (C(4a)***); 137.08 (C(7a)***). EI-MS: 249 (33, M^+), 206 (100, $[M-C_2H_5N]^+$), 193 (18, $[M-C_3H_6N]^+$), 177 (28, $[M-C_4H_{10}N]^+$), 165 (4), 133 (5), 26 (6), 84 (13), 68 (11), 53 (14), 49 (18), 41 (15, $C_3H_5^+$).

REFERENCES

[1] L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115; H. Waldmann, 'Domino Reactions', in 'Organic Synthesis Highlights II', Ed. H. Waldmann, VCH, Weinheim, 1995, p. 193; L. F. Tietze, U. Beifuss, *Angew. Chem.* **1993**, *105*,

[4]) Compound **6** has been previously reported [20].

137–170; *Angew. Chem., Int. Ed.* **1993**, *32*, 131; D. P. Curran, in 'Comprehensive Organic Synthesis', Eds. B. M. Trost, I. Fleming, Vol. 4, Pergamon Press, Oxford, 1991, p. 779–831.

[2] S. Bräse, A. de Meijere, in 'Metal-catalyzed Cross-Coupling Reactions', Ed. F. Diederich, P. J. Stang, Wiley-VCH, Weinheim, 1997, pp. 99–166; A. de Meijere, F. E. Meyer, *Angew. Chem*. **1994**, *106*, 2473; *Angew. Chem., Int. Ed*. **1994**, *33*, 2379; R. F. Heck, in 'Comprehensive Organic Synthesis', Ed. B. M. Trost, I. Fleming, Vol. 4, Pergamon Press, Oxford, 1991, pp. 833–863; R. F. Heck, in 'Palladium Reagents in Organic Synthesis', Academic Press, New York, 1985; A. de Meijere, S. Bräse, in 'Transition Metal Catalyzed Reactions', IUPAC Monographs 'Chemistry for the 21st Century', Eds. S. Murahashi, S. G. Davies, Blackwell Science, Oxford, 1999, pp. 99–131; A. de Meijere, S. Bräse, *J. Organomet. Chem*. **1999**, *576*, 88; I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009; S. Bräse, A. de Meijere, in ' Handbook of Organopalladium Chemistry', Ed. E.-I. Negishi, Wiley, New York, 2002, in press.

[3] W. F. Bailey, N. M. Wachter-Jurcsak, M. R. Pineau, T. V. Ovaska, R. R. Warren, C. E. Lewis, *J. Org. Chem*. **1996**, *61*, 8216.

[4] K. H. Ang, S. Bräse, A. G. Steinig, F. E. Meyer, A. Llebaria, K. Voigt, A. de Meijere, *Tetrahedron* **1996**, *52*, 11503; b) F. E. Meyer, K. H. Ang, A. G. Steinig, A. de Meijere, *Synlett* **1994**, 191.

[5] E. L. Eliel, 'Stereochemistry of Organic Compounds', Wiley & Sons, New York, 1994; D. F. Detar, N. P. Luthra, *J. Am. Chem. Soc*. **1980**, *102*, 4505.

[6] M. R. Tiollais, *Bull. Soc. Chim. Fr.* **1947**, *14*, 708.

[7] S. Körbe, A. G. Steinig, A. de Meijere, '10th IUPAC Symposium on Organo-Metallic Chemistry Directed Towards Organic Synthesis', Versailles 1999; S. Körbe, A. de Meijere, '4th International Symposium Transition Metals in Organic Synthesis', Leeds, 2000.

[8] F. Fringuelli, L. Minuti, L. Radics, A. Taticchi, E. Wenkert, *J. Org. Chem*. **1988**, *53*, 4607.

[9] F.-G. Klärner, F. Wurche, *J. Prakt. Chem*. **2000**, 342; A. Dijca, C. D. Hubbard, R. van Eldik, T. Assano, M. V. Basilevsky, W. J. Le Noble, *Chem. Rev.* **1998**, *98*, 2167; G. Jenner, *Tetrahedron* **1997**, *53*, 2669.

[10] J. W. Barton, A. Coop, J. W. Lewis, *Tetrahedron Lett*. **1993**, *34*, 6777; D. A. Smith, *Tetrahedron Lett*. **1991**, *32*, 1549.

[11] A. J. Mancuso, S. L. Huang, D. Swern, *J. Org. Chem*. **1978**, *43*, 2480.

[12] T. C. McMorris, M. Anchel, *J. Am. Chem. Soc*. **1965**, *87*, 1594; M. J. Kelner, T. C. McMorris, W. T. Beck, G. M. Zamora, R. Taetle, *Cancer Res.* **1987**, *47*, 3186; T. C. McMorris, M. J. Kelner, W. Wang, L. A. Estes, M. A. Montoya, R. Taetle, *J. Org. Chem*. **1992**, *57*, 6876.

[13] B. M. Trost, G. T. Tanoury, *J. Am. Chem. Soc*. **1988**, *110*, 1636.

[14] R. B. Woodward, R. Hoffmann, in 'The Conservation of Orbital Symmetry', Verlag Chemie, Weinheim, 1970.

[15] L. Bhat, A. G. Steinig, R. Appelbe, A. de Meijere, *Eur. J. Org. Chem*. **2001**, 1673.

[16] S. Weinreb, R. R. Staib, *Tetrahedron* **1982**, *38*, 3087; H. Waldmann, *Synthesis* **1994**, 535; J. F. Kerwin, S. Danishefsky, *Tetrahedron Lett*. **1982**, *23*, 3739; J. Streith, A. Defoin, *Synthesis* **1994**, 1107; F. Reichel, X. M. Fang, S. L. Yao, M. Ricci, K. A. Jorgensen, *Chem. Commun*. **1999**, 1505.

[17] S. D. Larsen, P. A. Grieco, *J. Am. Chem. Soc*. **1985**, *107*, 1768.

[18] K. Waldmann, *Liebigs Ann. Chem*. **1989**, 231.

[19] D. D. Perrin, W. L. F. Armarengo, 'Purification of Laboratory Chemicals', Pergamon Press, Oxford, 1987.

[20] B. M. Trost, J. M. Tour, *J. Am. Chem. Soc*. **1987**, *109*, 5268.

Received May 29, 2002