New strategy for the synthesis of ladybird beetle azaphenalene alkaloids using a combination of allylboration and intramolecular metathesis. Total synthesis of (±)-*Hippocasine* and (±)-*epi-Hippodamine**

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A new strategy for assembly a tricyclic skeleton of ladybirds azaphenalene alkaloids (coccinellides) was developed based on the combination of allylboration reaction and intramolecular metathesis. The first key step is the 1,2-organolithiation of 4-picoline with (4,4-diethoxybutyl)lithium with subsequent reductive allylation with triallylborane leading to *trans*-2-allyl-6-(4,4-diethoxybutyl)-4-methyl-1,2,3,6-tetrahydropyridine. The 4,4-diethoxybutyl substituent was further converted to 4-acetoxy-5-hexenyl in four steps, then, the product obtained was involved in the second key step, the intramolecular allylic amination upon treatment with a [Pd] or an [Ir] catalyst giving diastereomeric bicyclic terminal dienes (~1 : 1), which were separated by chromatography. The stereochemistry of one of the dienes is the same as that in alkaloid *Hippocasine*. The third key step (the intramolecular metathesis reaction) includes the final assembly of the azaphenalene system. The tricyclic derivative obtained contains two differently substituted C=C bonds, selective hydrogenation of one of which (Pd/C) leads to (±)-*Hippocasine*, whereas exhaustive hydrogenation gives (±)-*epi-Hippodamine*.

Key words: *Hippocasine*, *epi-Hippodamine*, allylboranes, allylboration, nitrogen heterocycles, cyclization, metathesis.

Ladybird beetles (*Coccinellidae*) is a large *Coleoptera* family with more than 5000 species worldwide,[1—3] about 100 of which live in Russia.[1] These beetles and their larvae are very voracious and play an important environmental role in the regulation of the population of crop pests, consuming a large amounts of aphids, psyllides, mealy and citrus coccids, scale insects, and mites. Many coccinellid species have bright coloration (red, yellow, rarely black), thus noticeably differing from most other insects. Despite the bright colour pattern, ladybirds have little enemies: apparently, only parasites,[4] ants, quails,[2] and amphibians.[5] Other insects and birds do not eat them. This is explained by a highly developed mechanism of chemical defence of coccinellids, known as reflex bleeding.[1] When disturbed or molested, these insects "throw away" small droplets of bitter and very toxic hemolymph from the tibio-femoral joints of their legs, thus repelling the potential predators. In 1970th, by alcoholic extraction of grounded adult coccinellids were isolated and characterized eight alkaloids, which were found to be differently joint isomers of 2-methylperhydro[9b]azaphenalene or its monodehydro analogs (hippocasine and hippocasine N-oxide)[1,2,6] (Fig. 1).

Apparently, coccinellids are the only natural source of these compounds, however, on a milligram scale.[1,2] To date, all the alkaloids[7,8] shown in Fig. 1 are synthesized, including methods using perhydro[9b]boraphenalene as the starting compounds.[7b,c]

There are data that some azaphenalene alkaloid derivatives, *viz.*, azaphenalene esters and amides of aromatic acids, are powerful antagonists of serotonin receptors,[9] thus attracting attention of researches who are dealing with the search of agents for treatment of diseases of the central nervous system, brain, and digestive tract.

In the present work, we describe a total synthesis of alkaloids (±)-*Hippocasine* and (±)-*epi-Hippodamine* (the isomer of *Hippodamine* alkaloid) from 4-picoline. We for the first time used allylboration reaction, palladium- and iridium-catalyzed intramolecular allylic amination, and metathesis reaction as the key steps of the synthesis.

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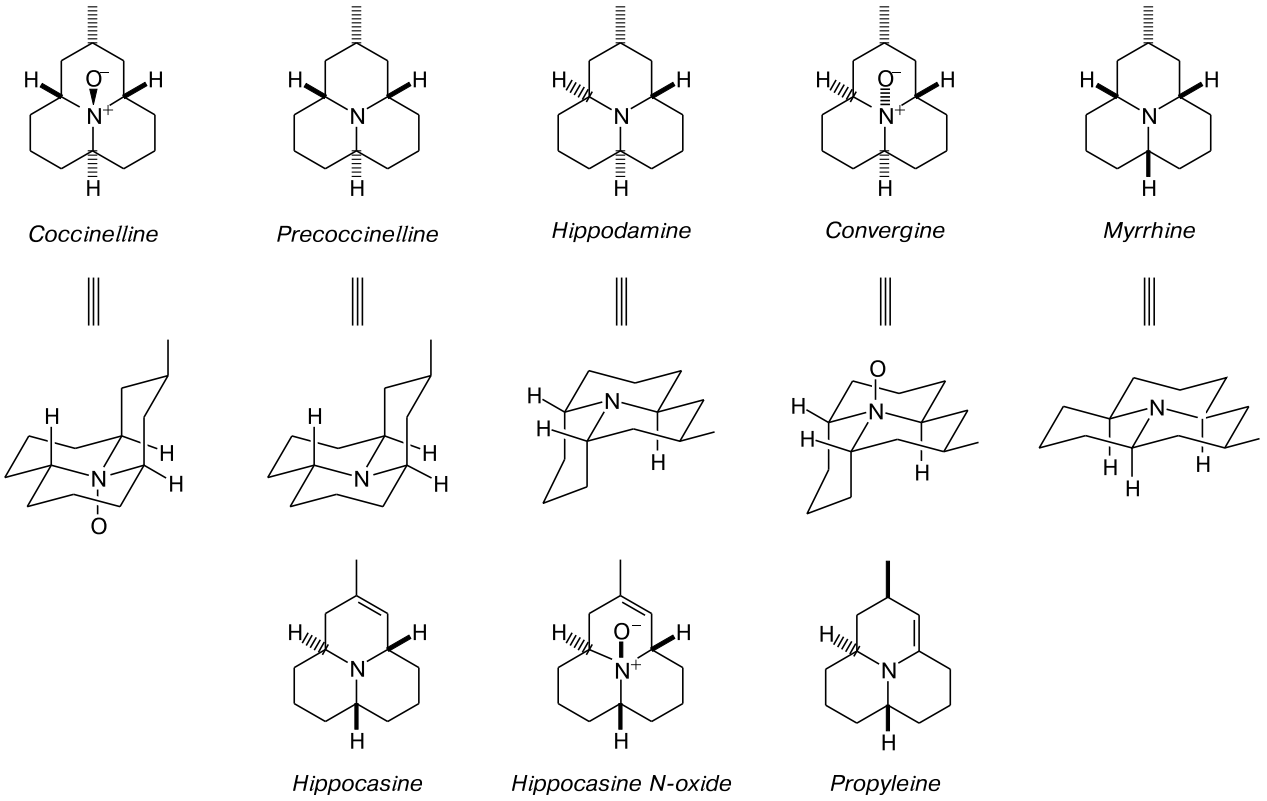
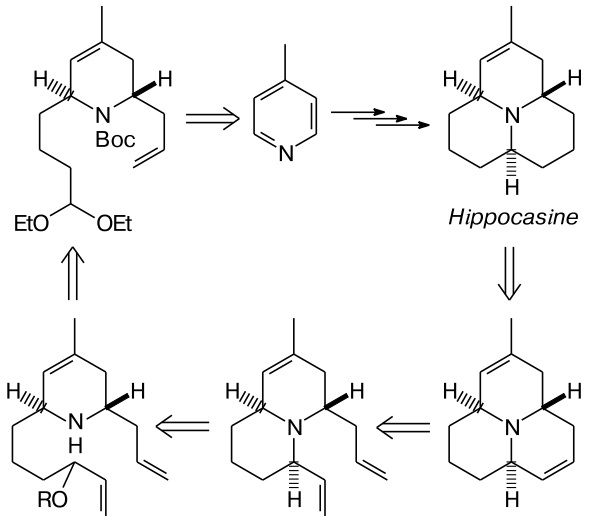


Fig. 1. Alkaloids of azaphenalene family produced by coccinellides.

Results and Discussion

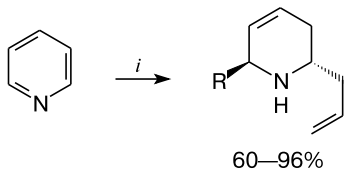
The retro-synthetic analysis (Scheme 1) shows that hippocasine and some other perhydro[9b]azaphenalene compounds can be obtained by the reductive *trans*-6-alkyl-2-allylation of 4-picoline and subsequent closure of second and third rings.

Scheme 1



Earlier, we have developed a general approach to the preparation of various *trans*-6-R-2-allyl-Δ^3-piperideines (tetrahydropyridines), based on the combination of the long known 1,2-organolithiation of pyridines[10] and subsequent *trans*-2-allylation with triallylborane in the presence of alcohols[11] (Scheme 2).

Scheme 2



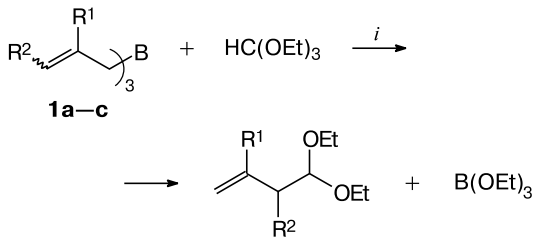
R = Alk, Ar

Reagents and conditions: *i*. 1) RLi, –70—0 °C; 2) All_3B, MeOH (4 equiv.), –15 °C; 3) NaOH, H_2O.

This approach was applied for the synthesis of a number of important piperidine[11c,d,12a,b] and indolizidine[11c,d,12c] alkaloids. The same combination of these two one-pot reactions was the first key step in our synthesis of azaphenalene compounds. To accomplish the synthesis according to the retro-synthetic Scheme 1, we started from the development of a convenient method for the prepara-

tion of 4,4-diethoxy-1-butenes **2** (Scheme 3), consisting in the monoallylation of triethyl orthoformate with triallyl-, trimethallyl-, or tricrotylborane in the presence of zinc trifluoromethanesulfonate as a catalyst (1 mol.%) at 70 °C. The preparative yields of acetals **2a—c** are 89—94% (Table 1).

Scheme 3



$R^1 = R^2 = H$ (**a**); R^1 = Me; $R^2 = H$ (**b**); $R^1 = H$; R^2 = Me (**c**)

Reagents and conditions: *i*. 1) $Zn(OTf)_2$, 1 mol.(%), 70 °C, 6 h; 2) NaOH, H_2O

It should be noted that these reactions are carried out without solvent. Their progress and completion were conveniently monitored using ^{1}H NMR spectra, that makes it possible to control consumption of triethyl formate and amount of the unreacted boronallylic fragments. Despite all three allylic groups in the starting boron derivative are involved in the reaction, we used a small excess of borane (R_3B : $HC(OEt)_3$ = 1 : 2.5—2.9) for the more rapid proceeding of the reaction. It appeared that other Lewis acids ($Et_2O \cdot BF_3$, $ZnCl_2$, $InCl_3$) also catalyzed the reaction, but less efficiently (see Table 1). Thus, on the addition of triallylborane to a mixture of orthoformate and $Et_2O \cdot BF_3$, a strong warming-up was observed accompanied by the formation of a considerable amount of polymeric products, while the yield of the target acetal **2a** was only 36%. The allylation of the orthoformate in the presence of $ZnCl_2$ and $InCl_3$ proceeded with higher yields (58 and 67%), but was also complicated by the formation of polymeric products. Moreover, in all the cases, the reaction resulted in a mixture of acetal and the starting orthoformate, which cannot be separated by distillation, that makes it impossible to use it for the synthetic purposes. It should be noted that the thermal reaction of triallylborane with $HC(OEt)_3$ (135—140 °C, without catalyst) follows an alternative pathway and leads to the formation of a mixture of diallylboronic acid ester (All_2BOEt) and triallylmethylboronic acid ester [$All_3C—B(OEt)_2$] (35%).[13]

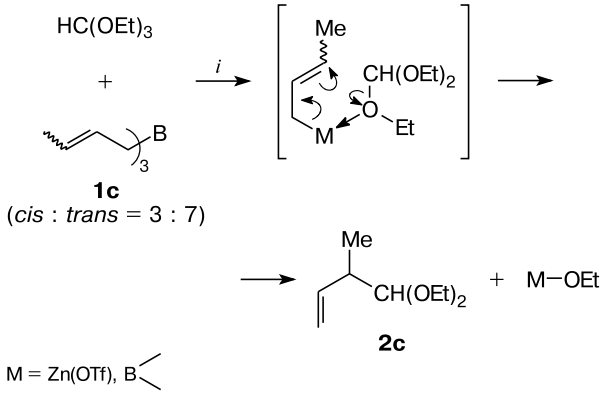
Table 1. Allylation of triethyl orthoformate with allylic boranes

R_3B	$(EtO)_3CH$ (equiv.)	*t*/ °C	Time/ h	Lewis acid (mol.%)	Yield (%)
1a	1.5	5—12	24	$Et_2O \cdot BF_3$ (10%)	36
1a	1.8	20—30	1.5	$ZnCl_2$ (5%)	58
1a	2.0	25	3	$InCl_3$ (5%)	67
1a	2.9	25[a], 75[b]	1[a], 6[b]	$Zn(OTf)_2$ (1%)	94
1b	2.9	25[a], 75[b]	1[a], 6[b]	$Zn(OTf)_2$ (1%)	89
1c	2.9	25[a], 85[b]	1[a], 10[b]	$Zn(OTf)_2$ (1%)	92

[a] Conditions for the initial exothermic reaction.
[b] Conditions for the subsequent process.

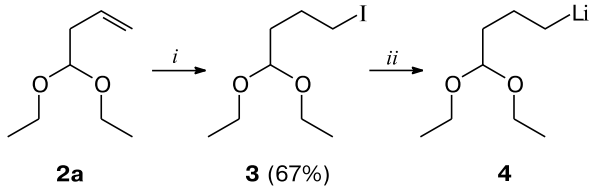
Substitution of the EtO group in orthoformate is accompanied by allylic rearrangement (Scheme 4), apparently, through the transition state with cyclic electron transfer. This is indicated by the formation from tricrotylborane **1c** of acetal **2c** with a terminal C=C bond and α-methyl group. The fragment M can be both boron and zinc derivative.[14]

Scheme 4



Acetal **2a** obtained according to Scheme 3 was further transformed to iodide **3** using a modified procedure[15] through the hydroboration and subsequent cleavage of the trialkylborane formed with iodine in the presence of the equimolar amount of potassium ethylate (obtained by the dissolution of Bu^tOK in anhydrous ethanol) (Scheme 5). Note a high synthetic potential of iodoacetal **3**, which was earlier used (as dimethyl acetal) in the synthesis of a taxol derivative for the expansion of one of the carbocycles by four carbon atoms at once.[16]

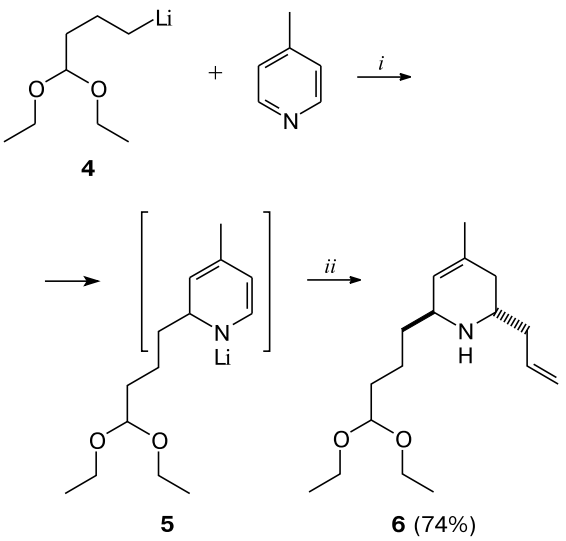
Scheme 5



Reagents and conditions: *i*. 1) $BH_3 \cdot Me_2S$; 2) $I_2/Bu^tOK/EtOH$); *ii*. 2 Bu^tLi, Et_2O, $-90 \rightarrow 20$ °C.

The reaction of iodoacetal **3** with *tert*-butyllithium (2 equiv.) led to the formation of the lithium derivative **4**, which was used for 1,2-organolithiation of 4-picoline[17] (Scheme 6). Subsequent treatment of the lithium amide **5** with triallylborane **1a** and methanol[11a,12a–c] gave *trans*-2-allyl-6-(4,4-diethoxybutyl)-4-methyl-1,2,3,6-tetrahydropyridine (**6**) (isolated by chromatography, 74%), which was a key compound in the synthesis of the target product.

Scheme 6



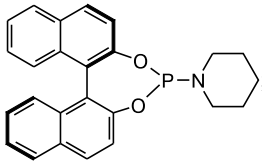
Reagents and conditions: *i*. 0 → 20 °C, Et_2O, 1 h; *ii*. 1) $(CH_2=CHCH_2)_3B$, –15 °C; 2) MeOH, NaOH.

Further, amine **6** was converted to the *N*-Boc-derivative **7**, which was hydrolyzed in aqueous acetic acid to aldehyde **8** (Scheme 7). The reaction of the latter with vinylmagnesium bromide at –90 °C furnished the allylic-type alcohol **9**. Here two moments should be noted: 1) vinylation of aldehyde **8** at temperatures above –70 °C is accompanied by the side processes, and the yield of carbinol **9** decreases; 2) the vinylation reaction proceeds diastereoselectively: only one diastereomer of alcohol **9** was obtained (confirmed by the NMR spectroscopic data), that can be explained by the formation of a cyclic structure in the coordination of the vinylmagnesium bromide with the C=O groups of the side chain and the Boc-protection, with the bulky *tert*-butyl group blocking one of the sides of the aldehyde group in the course of the vinylation. The subsequent acylation of carbinol **9** and removal of the Boc protecting group in compound **10** by treatment with trifluoroacetic acid resulted in the synthesis of amine **11**. Its intramolecular catalytic cyclization (allylic amination upon treatment with allylpalladium dichloride or an iridium catalyst) led to a mixture of diastereomeric bicyclic amines **12** and **13** in the ratio from ~1 : 3 to ~1 : 1 in 67—87% total yield (see Scheme 7, Table 2). It should be noted that

Table 2. Yields and ratios of amines **12** and **13***

Entry	Catalyst/ligand	**12 : 13**	Yield (%)
1	$[AllylPdCl]_2$/no ligand	23 : 77	67
2	$[AllylPdCl]_2$/(*S*)-Pipphos	42 : 58	87
3	$[Ir(COD)Cl]_2$/(*S*)-Pipphos/Pyrr	51 : 49	80

* The ratios of isomers were determined by GLC, 115 °C, carrier gas N_2 (1.8 bar); retention times for compounds **12** and **13** are 6.24 and 6.87 min, respectively.

(*S*)-Pipphos =  ; Pyrr =  .

such a diastereoselectivity is observed in the palladium-catalyzed (Pd/C, H_2) intramolecular reductive amination of related substrates.[18] As it is seen from Tables 2, the amination reaction with the Pd-catalyst is successful even without phosphorus ligands, leading to a mixture of dienes **12** and **13** (~1 : 3) in 67% yield (entry *1*). Both dienes were isolated in the individual states using chromatography on silica gel.

The relative configurations of the chiral centers in diene **13** were established based on the NMR spectra: initially we assigned all the signals in the proton spectrum of the compound ($^1H—^1H$ COSY experiment), then we determined steric interactions of hydrogen atoms (NOESY) (Fig. 2). As it is seen from Fig. 2, both substituents gave nuclear Overhauser effect (NOE) between each other and hydrogen at position 9a, besides, hydrogen atoms at positions 4 and 6 also interact.

Thus, atom C(4) has *R**-configuration in the major isomer **13** and, correspondingly, *S** in isomer **12**. From this it follows that the configuration of stereocenters in minor isomer **12** correspond to the configurations of the chiral centers in alkaloid hippocasine (see Fig. 1). To increase the amount of the required isomer **12**, the cyclization of diene **11** was carried out in the presence of the phosphite ligand (*S*)-Pipphos (see Table 2, entry *2*); In this case, the ratio of isomers **12** : **13** became 1 : 1.4. When an

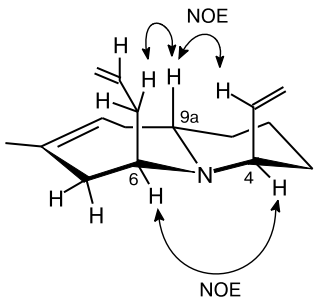
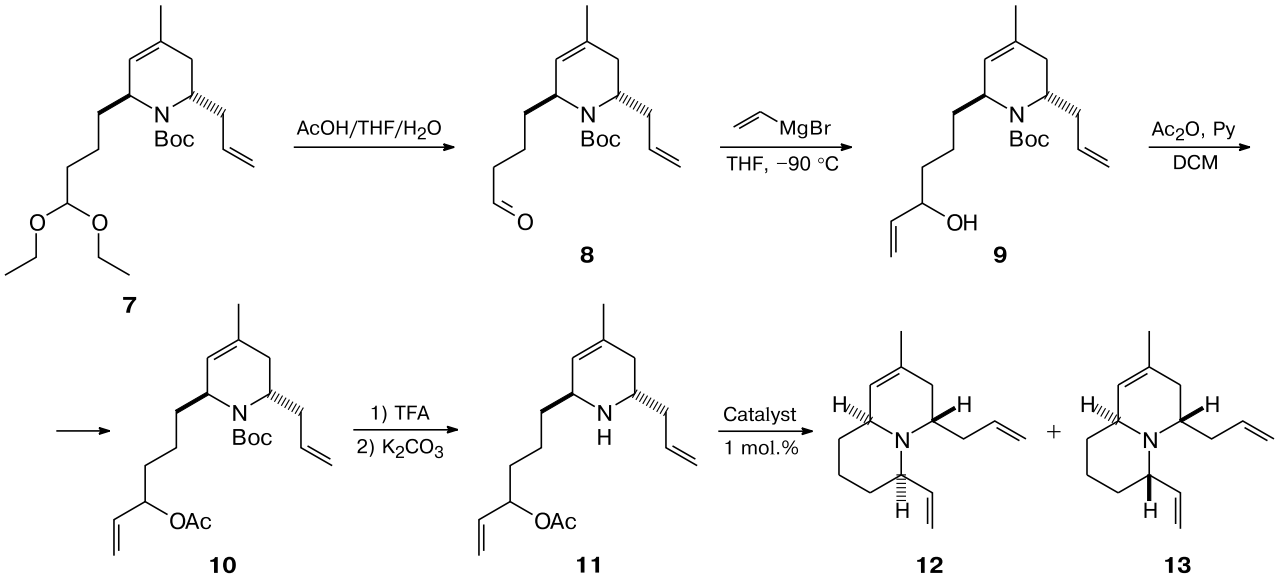


Fig. 2. NOE in determination of configurations of centers in compound **13**.

Scheme 7

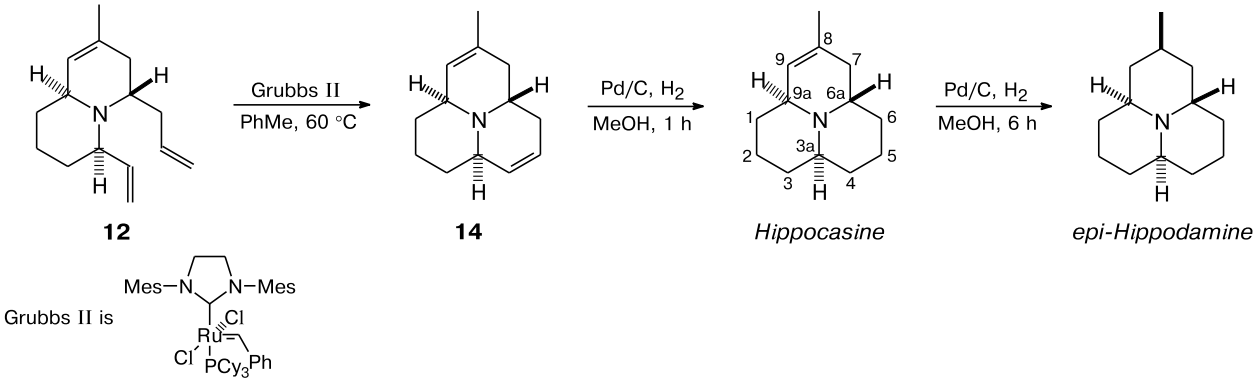


iridium catalyst $[Ir(COD)Cl]_2$ was used with (*S*)-Pipphos and pyrrolidine additive to accelerate the reaction,[19] dienes **12** and **13** were obtained in the ratio 1 : 1 (see Table 2, entry *3*). Treatment of diene **12** with the second generation Grubb´s catalyst (Scheme 8) gives the intramolecular metathesis reaction with the formation of hydroazaphenalene derivative **14** containing two different C=C bond, the structure of which was confirmed by mass spectrometry and NMR spectroscopy.

The presence of the differently substituted C=C bonds in diene **14** allowed us to selectively hydrogenate the disubstituted double bond and obtain alkaloid hippocasine (see Scheme 8), which was completely characterized by spectroscopy for the first time in the present work. Exhaustive hydrogenation of hippocasine gave *epi*-hippodamine,[8f] the level of the minor epimer at the methyl group (hippodamine alkaloid) was 6% (^{1}H NMR spectrum).

In conclusion, we developed a new strategy for the assembly of tricyclic skeleton of the azaphenalene alkaloids of coccinellids, which is based on the combination of allylboration reaction and intramolecular metathesis. This strategy was used for the synthesis of alkaloid hippocasine and an epimer of hippodamine alkaloid, *epi*-hippodamine. To accomplish this synthesis, we developed a new atom-saving method for the preparation of 4,4-diethoxy-1-butenes through the Zn-catalyzed allylation of triethyl orthoformate with allylic boranes. The second and third rings of the azaphenalene system were built-up by the catalytic reactions: allylic amination and intramolecular metathesis. We believe that the approach suggested can be used in the synthesis of other compounds of azaphenalene family.

Scheme 8



Experimental

Reactions were carried out under dry argon. All the solvents used were purified according to the standard procedures. NMR spectra were recorded on Bruker Avance (300, 400 and 600 MHz) spectrometers. Column chromatography was carried out using Merck silica gel (60—230 mesh). Mass spectra were recorded on a Finnigan Polaris Q Ion Trap instrument. Grubb´s ruthenium catalyst, benzylidene[1,3-*bis*(2,4,6-trimethylphenyl)-2-imidazolidinylidene]dichloro(tricyclohexylphosphine)ruthenium is a commercial reagent available from Aldrich. Complexes $[Ir(COD)Cl]_2$[20] and $[AllylPdCl]_2$[21] were obtained according to the described procedures.

4,4-Diethoxy-1-butene (2a). Triallylborane (11.6 g, 14.9 mL, 86 mmol) was added to a mixture of triethyl orthoformate (37 g, 41.6 mL, 0.25 mol) and $Zn(OTf)_2$ (0.91 g, 1 mol.%, 2.5 mmol) with cooling in a bath with a tap water (≤25 °C). After the exothermic reaction was completed (1 h), the reaction mixture was stirred for another 6 h at 75 °C. The reaction progress was monitored by ^{1}H NMR spectroscopy, following the disappearance of the signals for the allylic (CH_2=) and formate (CH) protons. Then, the cooled reaction mixture was poured into 20% aqueous NaOH (200 g) with vigorous stirring. The emulsion obtained was extracted with diethyl ether (3×100 mL), the combined extracts were dried with potassium carbonate, concentrated using a rotary evaporator. The residue was distilled *in vacuo* using a water-jet pump to isolate a fraction with b.p. 46—48 °C (10 Torr). The yield was 33.85 g (94%). ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 5.86 (ddt, 1 H, CH=, J = 17.2 Hz, J = 10.2 Hz, J = 7.0 Hz); 5.21—5.10 (m, 2 H, CH_2=); 4.57 (t, 1 H, OCH, J = 5.8 Hz); 3.73 (m, 2 H, OCH_2); 3.55 (m, 2 H, OCH_2); 2.45 (tt, 2 H, CH_2^{allyl}, J = 1.0 Hz, J = 5.8 Hz); 1.26 (t, 6 H, 2 Me, J = 7.1 Hz) (*cf.* Ref. 22a). ^{13}C NMR (DMSO-d_6, 75 MHz), δ: 133.76 (CH=), 116.94 (CH_2=), 101.55 (CHO_2); 60.44 (2 CH_2O); 38.07 (Me), 15.12 (Me). n^{18}_D 1.4075 (*cf.* Ref. 22b).

4,4-Diethoxy-3-methyl-1-butene (2b). The reaction and work-up were carried out similarly to those in the preparation of compound **2a**. Trimethallylborane (7.7 g, 44 mmol) was added to a mixture of triethyl orthoformate (18.8 g, 0.127 mol) and $Zn(OTf)_2$ (0.47 g, 1.3 mmol), the reaction mixture was allowed to stand for 1 h at 25 °C, then heated for 6 h at 70 °C. Distillation gave a fraction with b.p. 62—65 °C (10 Torr). The yield was: 18.46 g (92%). ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 4.80—4.78 (m, 1 H, C$\underline{H}_A$$H_B$=); 4.76—4.74 (m, 1 H, $CH_A$$\underline{H}_B$=); 4.61 (t, 1 H, OCH, J = 5.8 Hz); 3.64 (dq, 1 H, OCH_2, J = 9.3 Hz, J = 7.1 Hz); 3.49 (dq, 1 H, OCH_2, J = 9.3 Hz, J = 7.1 Hz); 2.33 (d, 1 H, $CH_2^{methallyl}$, J = 5.8 Hz); 1.76 (s, 2 H, Me), 1.18 (t, 3 H, 2 Me, J = 7.1 Hz) (*cf.* Ref. 22c). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 141.50, 112.73, 101.79, 60.93 (2 C), 41.88, 23.08, 15.25 (2 C). n^{18}_D 1.4113.

4,4-Diethoxy-2-methyl-1-butene (2c). The reaction and work-up were carried out similarly to those in the preparation of compound **2a**. Tricrotylborane (4.0 g, 22.7 mmol) was added to a mixture of triethyl orthoformate (9.74 g, 65.8 mmol) and $Zn(OTf)_2$ (0.24 g, 0.65 mmol), the solution was allowed to stand for 1 h at 25 °C, then heated for 10 h at 85 °C. Distillation led to the isolation of a fraction with b.p. 60—62 °C (10 Torr). The yield was 9.25 g (89%). ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 5.83 (ddd, 1 H, CH=, J = 7.3 Hz, 10.5 Hz, 17.1 Hz); 5.06—5.00 (m, 2 H, CH_2=); 4.19 (d, 1 H, $CH(OEt)_2$, J = 6.7 Hz); 3.69—3.60 (m, 2 H, OC$\underline{H}_a$$H_b$); 3.52—3.44 (m, 2 H, $OCH_a$$\underline{H}_b$); 2.49—2.41 (m, 1 H, C$\underline{H}$$CH_3$); 1.20—1.15 (m, 6 H, 2 $OCH_2C\underline{H}_3$); 1.01 (d, 3 H, Me, J = 6.6 Hz) (*cf.* Ref. 14). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 139.64, 114.47, 105.94, 62.07, 61.90, 41.11, 15.15 (2 C), 14.67. n^{18}_D 1.4122.

1,1-Diethoxy-4-iodobutane (3). The compound $BH_3 \cdot Me_2S$ (BMS) (3.87 g, 4.83 mL, 51 mmol) was added to a solution of 4,4-diethoxy-1-butene (**2a**) (21 g, 0.146 mol) in THF (60 mL) over 10 min at 0 °C with stirring. After the addition was completed, the cooling was removed, and the reaction mixture was stirred for 1 h at 20 °C. Anhydrous EtOH (1 mL) was added to neutralize excessive borohydride, then I_2 (38.1 g, 0.15 mol) was added in portions with stirring, maintaining temperature below 15 °C. A solution of Bu^tOK (18.8 g, 0.168 mol) in anhydrous EtOH (70 mL) was added dropwise to the mixture obtained, maintaining temperature within 15—25 °C, then, the suspension formed was stirred for 24 h. Excessive iodine was neutralized by addition of aqueous $Na_2S_2O_3$ and K_2CO_3 to adjust pH ~8 (to prevent hydrolysis of the acetal). The mixture was poured into brine (500 mL), the product was extracted with hexane (3 × 100 mL). The combined extracts were washed with brine, dried with K_2CO_3, concentrated, and distilled *in vacuo* to isolate iodoacetal **3** (26.6 g, 67%), b.p. 97—98 °C (0.5 Torr). ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 4.48 (t, 1 H, $CH(OEt)_2$, J = 5.6 Hz); 3.62 (dq, 2 H, OC$\underline{H}_a$$H_b$, J = 9.3 Hz, J = 7.1 Hz); 3.46 (dq, 2 H, $OCH_a$$\underline{H}_b$, J = 9.3 Hz, J = 7.1 Hz); 3.25 (t, 2 H, CH_2I, J = 6.9 Hz); 1.94—1.82 (m, 2 H, C$H\underline{H}_2$); 1.74—1.64 (m, 2 H, $C\underline{H}_2CH_2I$); 1.18 (t, 6 H, 2 $OCH_2C\underline{H}_3$, J = 7.1 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz), δ: 101.87, 61.19 (2 C), 34.46, 28.82, 15.32 (2 C), 6.74. Found (%): C, 35.36; H, 6.31; I, 46.59. $C_8H_{17}IO_2$. Calculated (%): C, 35.31; H, 6.30; I, 46.63.

***trans*-2-Allyl-6-(4,4-diethoxybutyl)-4-methyl-1,2,3,6-tetrahydropyridine (6).** A 1.5 *M* solution of Bu^tLi (102.7 mL, 0.154 mol) in pentane was added rapidly to a stirred solution of iodoacetal **3** (20.0 g, 73.5 mmol) in Et_2O (200 mL) at –90 °C, the mixture was stirred for another 20 min, then the cooling was removed. The mixture was allowed to warm-up to ~20 °C, which was accompanied by the formation of a white precipitate of organolithium compound **4**. The suspension obtained was cooled in a water-ice bath to 0—5 °C, followed by addition of 4-picoline (6.79 g, 7.11 mL, 73 mmol) and stirring for 1 h at 20 °C. Then, the mixture was cooled to –15 °C, followed by addition of triallylborane (9.78 g, 12.6 mL, 73 mmol). The yellow two-phase mixture was heated to 10 °C and MeOH (20 mL) was added, followed by a dropwise addition of a 20% aqueous NaOH (20 mL). The reaction mixture was deboronated by reflux for 30 min, the aqueous layer was saturated with K_2CO_3. The organic layer was separated, washed with brine, dried with K_2CO_3, concentrated, and purified by chromatography (eluent EtOAc—MeOH—NH_{3aq}, 50 : 1 : 0.1) to obtain compound **6** (15.2 g, 74%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 5.87—5.73 (m, 1 H, CH=^{allyl}); 5.40 (s, 1 H, CH=^{cycle}); 5.15—5.08 (m, 2 H, CH_2=); 4.49 (t, 1 H, $CH(OEt)_2$, J = 5.5 Hz); 3.70—3.60 (m, 2 H, OC$\underline{H}_a$$H_b$); 3.54—3.44 (m, 2 H, $OCH_a$$\underline{H}_b$); 3.32 (br.s, 1 H, CHN); 3.01—2.93 (m, 1 H, CHN); 2.75 (br.s, 1 H, NH); 2.21—2.17 (m, 2 H, CH_2^{allyl}); 1.96 (dd, 1 H, C$\underline{H}_A$$H_B^{cycle}$, J = 3.5 Hz, J = 17.3 Hz); 1.78 (dd, 1 H, $CH_A$$\underline{H}_B^{cycle}$, J = 8.1 Hz, J = 17.4 Hz); 1.68 (s, 3 H, Me); 1.67—1.62 (m, 2 H, C$H\underline{H}_2$); 1.45 (br.s, 4 H, 2 CH_2); 1.21 (t, 6 H, 2 $OCH_2C\underline{H}_3$, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz), δ: 135.31, 131.79, 123.44, 117.21, 102.58, 60.78, 60.75, 51.89, 46.94, 39.91, 35.99, 35.09, 33.43, 28.29, 23.30, 21.51, 15.18. MS (EI, 70 eV), m/z (I_{rel} (%)): 282 $[MH]^+$ (6), 252 (3), 236 (9), 206 (8), 194 (24), 192 (10), 190 (34), 164 (11), 150 (65), 148 (51), 146 (12), 136 (22), 107 (10), 95 (12), 94 (100), 93 (8), 79 (7). Found (%):

C, 72.46; H, 11.18; N, 4.79. $C_{17}H_{31}NO_2$. Calculated (%): C, 72.55; H, 11.10; N, 4.98.

***tert*-Butyl *trans*-2-allyl-6-(4,4-diethoxybutyl)-4-methyl-3,6-dihydro-1(*2H*)-pyridinecarboxylate (7).** To a solution of compound **6** (3.48 g, 12.36 mmol) in THF (10 mL), Boc_2O (3.67 g, 16.8 mmol) was added. The mixture was heated to reflux. The reaction progress was monitored by TLC (ethyl acetate—hexane, 1 : 15). Then, the solution was concentrated, the product was isolated by chromatography to obtain ester **7** (4.65 g, 99%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 5.84—5.70 (m, 1 H, $CH=^{allyl}$); 5.56 (br.s, 1 H, $CH=^{cycle}$); 5.04—5.00 (m, 2 H, $CH_2=$); 4.48 (t, 1 H, $CH(OEt)_2$, J = 5.6 Hz); 4.05—4.01 (m, 2 H, $OC\underline{H}_aH_b$); 3.70—3.60 (m, 2 H, $OCH_a\underline{H}_b$); 3.55—3.45 (m, 2 H, 2 CHN); 2.37—2.23 (m, 2 H, $C\underline{H}_AH_B^{cycle}$, $C\underline{H}_AH_B^{allyl}$); 2.16 (dd, 1 H, $CH_A\underline{H}_B^{allyl}$, J = 9.0 Hz, J = 13.3 Hz); 1.98 (d, 1 H, $CH_A\underline{H}_B^{cycle}$, J = 15.1 Hz); 1.76 (s, 3 H, Me); 1.74—1.60 (m, 4 H, 2 CH_2); 1.49 (s, 9 H, Bu^t); 1.39—1.28 (m, 2 H, $CHC\underline{H}_2$); 1.22 (t, 6 H, 2 $OCH_2C\underline{H}_3$, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz), δ: 155.17, 136.29, 131.71, 122.94, 116.71, 102.87, 79.22, 60.91, 60.84, 52.32, 51.47, 38.23 (br.), 35.64 (br.), 33.67, 31.34, 29.68, 28.49 (3 C), 23.67, 20.66, 15.32. MS (EI, 70 eV), m/z (I_{rel}(%)): 337/336 $[M—EtO]^+$ (3/11), 237 (5), 236 (32), 194 (50), 190 (15), 180 (36), 151 (14), 150 (100), 148 (48), 138 (16), 136 (6), 122 (6), 107 (9), 94 (46), 93 (23), 88 (12), 80 (7), 57 (8), 41 (10). Found (%): C, 70.06; H, 10.38; N, 3.57. $C_{22}H_{39}NO_4$. Calculated (%): C, 69.25; H, 10.30; N, 3.67.

***tert*-Butyl *trans*-2-allyl-4-methyl-6-(4-oxobutyl)-3,6-dihydro-1(*2H*)-pyridinecarboxylate (8).** A solution of ester **7** (3.10 g, 8.12 mmol) in a mixture of THF (4 mL), water (3 mL), and AcOH (5 mL) was heated for 14 h at 50 °C. The reaction progress was monitored by TLC (ethyl acetate—hexane, 1 : 4). The product was extracted with *n*-hexane, dried with K_2CO_3, concentrated on a rotary evaporator. Compound **8** (1.79 g, 72%) was isolated by chromatography as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 9.74 (t, 1 H, CH=O, J = 1.6 Hz); 5.73 (dddd, 1 H, $CH=^{allyl}$, J = 6.1 Hz, J = 8.6 Hz, J = 11.4 Hz, J = 17.7 Hz); 5.52 (m, 1 H, $CH=^{cycle}$); 5.00—4.97 (m, 2 H, $CH_2=$); 4.06 (m, 1 H, CHN); 3.99 (m, 1 H, CHN); 2.42 (tt, 2 H, $C\underline{H}_2CH$=O, J = 1.6 Hz, J = 7.5 Hz); 2.29—2.20 (m, 2 H, $C\underline{H}_AH_B^{cycle}$ and $C\underline{H}_AH_B^{allyl}$); 2.15 (dt, 2 H, $CH_A\underline{H}_B^{allyl}$, J = 8.8 Hz, J = 13.3 Hz); 1.96 (dd, 1 H, $CH_A\underline{H}_B^{cycle}$, J = 1.6 Hz, J = 15.9 Hz); 1.73 (s, 3 H, Me); 1.72—1.68 (m, 2 H, CH_2); 1.64—1.53 (m, 2 H, CH_2); 1.46 (s, 9 H, Bu^t). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 202.61, 155.22, 136.17, 132.19, 122.52, 116.83, 79.45, 52.02, 51.49, 43.90, 38.21 (br.), 35.00 (br.), 31.44, 28.48 (3 C), 23.67, 17.86. MS (EI, 70 eV), m/z (I_{rel}(%)): 308 $[MH]^+$ (5,8), 252 (5), 190 (8), 180 (25), 166 (100), 148 (38), 138 (17), 131 (15), 122 (22), 94 (54), 93 (32), 91 (17), 79 (10), 41 (9). Found (%): C, 70.26; H, 9.48; N, 4.60. $C_{18}H_{29}NO_3$. Calculated (%): C, 70.32; H, 9.51; N, 4.56.

***tert*-Butyl *trans*-2-allyl-6-(5-hexenyl-4-hydroxy)-4-methyl-3,6-dihydro-1(*2H*)-pyridinecarboxylate (9).** A 1.21 *M* solution of vinylmagnesium bromide (7.3 mL, 8.83 mmol) in THF was added dropwise to a solution of aldehyde **8** (2.71 g, 8.82 mmol) in THF (80 mL) at –90 °C under argon. The mixture was stirred for 1 h at –90 °C, then was allowed to warm-up to –40 °C. The reaction progress was monitored by TLC (ethyl acetate—hexane, 1 : 2). Then, the mixture was treated with aqueous NH_4Cl, extracted with *n*-hexane (3 × 50 mL), dried with K_2CO_3, and concentrated using a rotary evaporator. Compound **9** (2.57 g, 87%) was isolated by chromatography as a colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 5.87 (dddd, 1 H, $CH=^{vinyl}$, J = 2.3 Hz, J = 6.2 Hz, J = 10.4 Hz, J = 16.7 Hz); 5.80—5.70 (m, 1 H, $CH=^{allyl}$); 5.55 (s, 1 H, $CH=^{cycle}$); 5.24 (ddd, 1 H, $C\underline{H}_AH_B=^{vinyl}$, J = 1.5 Hz, J = 3.1 Hz, J = 17.2 Hz); 5.10 (dt, 1 H, $CH_A\underline{H}_B=^{vinyl}$, J = 1.4 Hz, J = 1.9 Hz, J = 10.4 Hz); 5.02—4.98 (m, 2 H, $CH_2=^{allyl}$); 4.16—4.06 (m, 2 H, C<u>H</u>OH, CHN); 4.02—3.95 (m, 1 H, CHN); 2.33 (dm, 1 H, $C\underline{H}_AH_B^{allyl}$, J = 13.3 Hz); 2.26 (dm, 1 H, $C\underline{H}_AH_B^{cycle}$, J = 15.9 Hz); 2.16 (dt, 1 H, $CH_A\underline{H}_B^{allyl}$, J = 8.9 Hz, J = 13.3 Hz); 1.97 (dd, 1 H $CH_A\underline{H}_B^{cycle}$, J = 2.3 Hz, J = 15.9 Hz); 1.74 (s, 3 H, Me); 1.73 (m, 1 H, $CHOHC\underline{H}_AH_B$); 1.69 (br.s, 1 H, $CHOHCH_A\underline{H}_B$); 1.56—1.50 (m, 2 H, CH_2); 1.48 (s, 9 H, Bu^t); 1.39—1.30 (m, 2 H, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 155.27, 141.28, 141.20, 136.31, 131.18, 122.96, 116.76, 114.49, 79.35, 73.21, 73.05, 52.26, 51.53, 38.26, 37.02, 36.95, 35.64, 31.41, 31.38, 28.53 (3 C), 23.71, 21.09. MS (EI, 70 eV), m/z (I_{rel}(%)): 336/335 $[M]^+$ (0.5/2.2), 243 (4), 236 (4), 195 (8), 194 (76), 192 (12), 180 (51), 177 (9), 176 (66), 174 (47), 138 (29), 136 (11), 134 (16), 120 (18), 107 (12), 96 (20), 95 (17), 94 (100), 93 (40), 88 (16), 80 (17), 78 (6), 77 (10), 41 (10). Found (%): C, 71.65; H, 9.85; N, 4.16. $C_{20}H_{33}NO_3$. Calculated (%): C, 71.60; H, 9.91; N, 4.18.

***tert*-Butyl *trans*-6-[4-(acetyloxy)-5-hexenyl]-2-allyl-4-methyl-3,6-dihydro-1(*2H*)-pyridinecarboxylate (10).** Allylic alcohol **9** (0.42 g, 1.26 mmol) was mixed with pyridine (0.64 mL) and Ac_2O (0.39 g, 0.37 mL, 3.84 mmol) and heated on a water bath. The reaction progress was monitored by TLC (ethyl acetate—*n*-hexane, 1 : 2). The product was extracted with *n*-hexane, the extracts were washed with water and aqueous sodium bicarbonate, dried with K_2CO_3, and concentrated using a rotary evaporator. Compound **10** (0.47 g, 99%) was isolated by chromatography as a dense colorless oil. ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 5.84—5.70 (m, 2 H, $2CH=^{vinyl,\ allyl}$); 5.55 (br.s, 1 H, $CH=^{cycle}$); 5.34—5.16 (m, 3 H, C<u>H</u>OAc and $CH_2=^{vinyl}$); 5.04—4.99 (m, 2 H, $CH_2=^{allyl}$); 4.06—4.00 (m, 2 H, 2 CHN); 2.37—2.12 (m, 3 H, CH_2^{allyl}, $C\underline{H}_AH_B^{cycle}$); 2.08 (s, 3 H, Ac); 1.98 (dd, 1 H, $CH_A\underline{H}_B^{cycle}$, J = 1.4 Hz, J = 15.9 Hz); 1.67 (s, 3 H, Me); 1.65—1.60 (m, 4 H, 2 CH_2); 1.50 (s, 9 H, Bu^t); 1.36—1.24 (m, 2 H, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 170.33, 155.16, 136.52, 136.47, 136.25, 131.92, 122.84, 116.76, 116.61, 116.50, 79.29, 74.83, 74.75, 52.18, 51.47, 38.22, 35.45; 34.20, 34.16, 31.37, 28.49 (3 C), 23.67, 21.20, 20.97. MS (EI, 70 eV), m/z (I_{rel}(%)): 379/378 $[MH]^+$ (0.2/1.5), 266 (5), 237 (10), 236 (63), 180 (38), 177 (14), 176 (100), 174 (47), 147 (5), 146 (5), 138 (20), 134 (11), 120 (12), 108 (8), 96 (17), 95 (12), 94 (75), 93 (31), 91 (11), 88 (13), 80 (12), 44 (6). Found (%): C, 70.15; H, 9.45; N, 3.66. $C_{22}H_{35}NO_4$. Calculated (%): C, 69.99; H, 9.34; N, 3.71.

1-{3-[(2*S,6*S**)-6-Allyl-4-methyl-1,2,5,6-tetrahydropyridin-2-yl]propyl}prop-2-en-1-yl acetate (11).** Trifluoroacetic acid (2 mL) was added to compound **10** (0.47 g, 1.24 mmol), and the mixture was stirred until the starting Boc-substituted compound disappeared. The reaction progress was monitored by TLC (ethyl acetate—*n*-hexane, 1 : 2). The acid was evaporated using a rotary evaporator, the residue was diluted with CH_2Cl_2, washed with aqueous K_2CO_3, dried with K_2CO_3, and concentrated using a rotary evaporator. Amine **11** (0.24 g, 70%) was isolated by chromatography (ethyl acetate—methanol, 100 : 1) as a yellow oil and used further without additional purification. ^{1}H NMR ($CDCl_3$, 400 MHz), δ: 5.86—5.74 (m, 2 H, 2 $CH=^{vinyl,\ allyl}$); 5.45 (s, 1 H, $CH=^{cycle}$); 5.32—5.19 (m, 5 H, C<u>H</u>OAc and 2 $CH_2=^{vinyl,allyl}$); 3.36 (br.s, 1 H, CHN); 3.04—3.01 (m, 1 H, CHN); 2.63—2.59 (m, 1 H, $C\underline{H}_AH_B^{allyl}$); 2.38 (dt, 1 H, $CH_A\underline{H}_B^{allyl}$, J = 7.9 Hz, J = 13.7 Hz); 2.26 (dd, 1 H, $C\underline{H}_AH_B^{cycle}$, J = 3.3 Hz,

J = 17.9 Hz); 2.15 (s, 3 H, Ac); 2.09—2.05 (m, 1 H, $CH_A\underline{H}_B^{cycle}$); 1.87—1.75 (m, 2 H, CH_2); 1.78 (s, 3 H, Me); 1.73—1.60 (m, 2 H, CH_2); 1.53—1.45 (m, 2 H, CH_2). MS (EI, 70 eV), m/z (I_{rel}(%)): 278 $[MH]^+$ (0.71), 266 (2); 236 (26), 214 (14), 176 (47), 174 (35), 149 (10), 147 (10), 136 (20), 134 (10), 132 (9), 131 (9), 120 (15), 107 (14), 105 (10), 96 (15), 95 (14), 94 (100), 91 (11), 77 (12), 43 (12), 41 (12). Found: m/z 278.2111 $[MH]^+$. $C_{17}H_{28}NO_2$. Calculated: (M + H) = 278.2115.

(4*R,6*S**,9a*S**)- and (4*S**,6*S**,9a*S**)-6-Allyl-8-methyl-4-vinyl-1,3,4,6,7,9a-hexahydro-*2H*-quinolizines (12) and (13).** The catalyst $[AllPdCl]_2$ (3.6 mg, 1 mol.%, 0,0097 mmol) was added to a solution of (*S*)-Pipphos (7.7 mg (2 mol.%, 0,019 mmol) in CH_2Cl_2 (0.5 mL) with stirring under argon. This solution of the catalyst and powdered K_2CO_3 (for the binding of forming AcOH) was added to a solution of compound **11** (0.27 g, 0.97 mmol) in CH_2Cl_2 (2 mL). The reaction progress was monitored by TLC (EtOAc—MeOH, 100 : 1). The mixture was diluted with CH_2Cl_2 (10 mL), washed with water, dried with K_2CO_3, and concentrated using a rotary evaporator. Two isomers were isolated by column chromatography in 0.183 g (87%) total yield as a yellow oil. Isomer **(4*S**,6*S**,9a*S**)-12**. $R_{f\,max}$ 0.52 (EtOAc—*n*-hexane, 1 : 4), a colorless oil. ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 5.80—5.75 (br.m, 1 H, $CH=^{vinyl}$); 5.68 (dddd, 1 H, $CH=^{allyl}$, J = 5.8 Hz, J = 8.5 Hz, J = 10.7 Hz, J = 16.2 Hz); 5.23—5.17 (m, 2 H, $CH_2=^{vinyl}$); 5.09 (br.d, 1 H, CH=, J = 9.5 Hz); 5.00—4.97 (m, 2 H, $CH_2=^{allyl}$); 3.24 (br.s, 1 H, C$\underline{H}$NCH=); 3.04 (br.s, 1 H, C$\underline{H}$NAll); 2.83 (br.s, 1 H, C$\underline{H}N^{vinyl}$); 2.35 (dd, 1 H, $C\underline{H}_A\underline{H}_B^{allyl}$, J = 5.4 Hz, J = 13.0 Hz); 2.31 (br.s, 1 H, $CH_A\underline{H}_B^{allyl}$); 1.95 (dd, 1 H, $C\underline{H}_A\underline{H}_BCCH_3$, J = 10.6 Hz, J = 17.9 Hz); 1.87 (d, 1 H, $CH_A\underline{H}_BCCH_3$, J = 17.4 Hz); 1.79—1.72 (m, 2 H, C$\underline{H}_2$CHNCH=); 1.68 (s, 3 H, Me); 1.66—1.58 (m, 3 H, C$\underline{H}_2CHN^{vinyl}$, $C\underline{H}_A\underline{H}_B$); 1.46—1.38 (m, 1 H, $CH_A\underline{H}_B$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 141.08 (br.), 136.81 (br.), 130.74, 123.68 (br.), 116.50, 115.77 (br.), 63.82, 54.65, 53.16, 33.55 (br.), 32.90 (br.), 32.43 (br.), 27.37, 24.26, 23.18. MS (EI, 70 eV), m/z (I_{rel}(%)): 217 $[M]^+$ (4), 216 (5), 199 (5), 183 (16), 177 (13), 176 (96), 175 (16), 174 (100), 172 (7), 163 (5), 152 (6), 149 (24), 146 (14), 134 (17), 132 (18), 120 (17), 107 (18), 94 (27), 83 (31), 67 (11), 57 (8), 41 (10). Found: m/z 218.1902 $[MH]^+$. $C_{15}H_{24}N$. Calculated: (M + H) = = 218.1903.

Isomer **(4*R**,6*S**,9a*S**)-13**. $R_{f\,min}$ 0.24 (EtOAc—*n*-hexane, 1 : 4), colorless oil. ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 5.90—5.84 (m, 1 H, $CH=^{vinyl}$); 5.80 (dddd, 1 H, $CH=^{allyl}$, J = 6.0 Hz, J = 7.9 Hz, J = 10.2 Hz, J = 16.9 Hz); 5.20—5.16 (m, 2 H, $CH_2=^{vinyl}$); 5.05 (d, 1 H, CH=, J = 11.1 Hz); 5.04—5.00 (m, 2 H, $CH_2=^{allyl}$); 3.63 (br.s, 1 H, C$\underline{H}$NCH=); 3.18—3.15 (m, 1H, C$\underline{H}$NAll); 3.05 (td, 1 H, C$\underline{H}N^{vinyl}$, J = 1.9 Hz, J = 9.2 Hz); 2.39 (br.s, 1 H, $C\underline{H}_A\underline{H}_B^{allyl}$); 2.17 (dt, 1 H, $CH_A\underline{H}_B^{allyl}$, J = 9.0 Hz, J = 13.5 Hz); 2.07 (dm, 1 H, $C\underline{H}_A\underline{H}_BCCH_3$, J = 19.0 Hz); 1.80—1.74 (m, 1 H, $C\underline{H}_A\underline{H}_B$CHNCH=); 1.70 (s, 3 H, CH_3); 1.65—1.62 (m, 1 H, $CH_A\underline{H}_B$CHNCH=); 1.58—1.48 (m, 4 H, $CH_A\underline{H}_BCCH_3$, C$\underline{H}_2CHN^{vinyl}$, $C\underline{H}_A\underline{H}_B$); 1.42—1.34 (m, 1 H, $CH_A\underline{H}_B$). ^{13}C NMR ($CDCl_3$, 150 MHz), δ: 142.21, 136.64, 132.48, 122.52, 116.20, 115.25, 59.62, 53.81, 48.49, 37.49, 33.16, 30.64, 26.43, 23.53, 19.84. Found: m/z 218.1902 $[MH]^+$. $C_{15}H_{24}N$. Calculated: (M + H) = 218.1903.

(3a*S,6a*S**,9a*R**)-5-Methyl-2,3,3a,6,6a,7,9a,9b-octahydro-9b-azaphenalene (14).** The second generation Grubb´s catalyst (8 mg, 5 mol.%, 0.009 mmol) was added to a degassed solution of diene **12** (40 mg, 0.18 mmol) in toluene (5 mL), and the solution obtained was heated for 20 min at 60 °C. A progress of the reaction was monitored by TLC (*n*-C_6H_{14}—EtOAc, 3 : 1). After the reaction reached completion, the solution was passed through a column with silica gel, the product was eluted by the mixture of EtOAc—Et_3N, 60 : 1 to obtain azaphenalene derivative **14** (29 mg (84%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz), δ: 5.78—5.67 (m, 2 H, C$\underline{H}$=C$\underline{H}$); 5.47—5.45 (m, 1 H, CH=); 3.52—3.43 (br.m, 2 H, 2 C$\underline{H}$NCH=); 3.43—3.33 (m, 1 H, C$\underline{H}N(CH_2)_2$); 2.39 (dt, 1 H, $C\underline{H}_A\underline{H}_B$CH=, J = 17.7 Hz, J = 5.0 Hz); 2.25 (dd, 1 H, $C\underline{H}_A\underline{H}_BCCH_3$, J = 5.0 Hz, J = 17.5 Hz); 2.08 (td, 1 H, $CH_A\underline{H}_B$CH=, J = 1.8 Hz, J = 9.4 Hz); 2.00 (dd, 1 H, $CH_A\underline{H}_BCCH_3$, J = 9.4 Hz, J = 17.7 Hz); 1.86—1.75 (m, 1 H, $CH_2C\underline{H}_A\underline{H}_BCH_2$); 1.71 (s, 3 H, CH_3); 1.56—1.36 (m, 5 H, $CH_2CH_A\underline{H}_BCH_2$, 2 CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 129.80 (C$\underline{H}$=CH), 129.40 (br., C=), 123.63 (br., C$\underline{H}$=C), 122.38 (CH=C$\underline{H}$), 57.12 (C$\underline{H}$NCH=), 56.82 (C$\underline{H}$NCH=), 41.83 (C$\underline{H}N(CH_2)_2$), 38.89 (C$\underline{H}_2CCH_3$), 34.27 (C$\underline{H}_2$CH=), 27.75 (CH_2), 27.69 (CH_2), 24.48 ($CH_2C\underline{H}_2CH_2$), 22.76 (Me). MS (EI, 70 eV), m/z (I_{rel}(%)): 189 $[M]^+$ (30), 188 (100), 186 (14), 184 (7), 174 (31), 160 (15), 149 (12), 146 (21), 144 (16), 132 (12), 131 (15), 120 (10), 94 (25), 81 (10), 67 (10), 57 (9), 41 (12). Found (%): C, 82.53; H, 10.15; N, 7.44. $C_{13}H_{19}N$. Calculated (%): C, 82.48; H, 10.12; N, 7.40.

(3a*S,6a*S**,9a*S**)-8-Methyl-1,2,3,3a,4,5,6,6a,7,9a-decahydropyrido[2,1,6-*de*]quinolizine ((±)-hippocasine).** A solution of tricycle **14** (0.1 g, 0.53 mmol) in MeOH (3 mL) was added to a suspension of 10% Pd/C (17 mg) in MeOH (7 mL). The mixture obtained was hydrogenated using a Parr apparatus for 1 h at 20 °C, hydrogen pressure 2 bar. A progress of the reaction was monitored by TLC (EtOAc—Et_3N, 60 : 1). After the starting compound disappeared, the reaction mixture was passed through the Super Cel layer on a filter funnel and concentrated *in vacuo* using a rotary evaporator. The residue was purified by chromatography on silica gel to obtain (±)-hippocasine (76 mg, 76%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 5.38 (sharp m, 1 H, CH=(9)); 3.24 (dm, 1 H, CHN^{allyl}(9a), J = 11.0 Hz); 3.10—3.07 (dm, 1 H, CHN(3a), J = 11.0 Hz); 3.04—2.99 (tt, 1 H, CHN(6a), J = 4.0 Hz, J = 10.3 Hz); 1.94 (dd, 1 H, $C\underline{H}_A\underline{H}_B$(7), J = 4.6 Hz, J = 17.4 Hz), 1.89—1.80 (m, 3 H, $CH_A\underline{H}_B$(7), $C\underline{H}_A\underline{H}_B$(2), $C\underline{H}_A\underline{H}_B$(5)); 1.83—1.78 (m, 2 H, $C\underline{H}_A\underline{H}_B$(3), $C\underline{H}_A\underline{H}_B$(6)); 1.64 (s, 3 H, Me); 1.57 (dm, 1 H, $C\underline{H}_A\underline{H}_B$(4), J = 13.3 Hz), 1.55—1.49 (m, 3 H, $CH_A\underline{H}_B$(2), $CH_A\underline{H}_B$(5), $CH_A\underline{H}_B$(4)), 1.38 (dtd, 1 H, $C\underline{H}_A\underline{H}_B$(1), J = 3.7 Hz, J = 11.9 Hz, J = 13.7 Hz); 1.32 (dm, 1 H, $CH_A\underline{H}_B$(1), J = 13.7 Hz); 1.21 (ddd, 1 H, $CH_A\underline{H}_B$(6), J = 5.0 Hz, J = 12.8 Hz, J = 24.2 Hz), 1.09 (dm, 1 H, $CH_A\underline{H}_B$(3), J = 12.4 Hz) (see Ref. 7c). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 130.61 (C(8)), 124.04 (C(9)H=), 58.31 (C(9a)HN), 57.15 (C(3a)), 44.99 (C(6a)), 39.08 (C(7)H_2), 34.42 (C(5)H_2), 31.83 (C(6)H_2), 26.47 (C(1)H_2), 25.58 (C(2)H_2), 23.46 (C(3)H_2), 22.82 (Me), 19.21 (C(4)H_2). Found: m/z 192.1756 $[MH]^+$. $C_{13}H_{22}N$. Calculated: (M + H) = 192.1747.

The longer reaction time (6 h) gave the product of exhaustive hydrogenation (±)-*epi*-hippodamine. ^{1}H NMR ($CDCl_3$, 600 MHz), δ: 2.99—2.92 (m, 3 H, 3 CHN); 2.12 (dt, 1 H, J = 6.4 Hz, J = 13.7 Hz); 2.00—1.94 (m, 1 H, CHMe); 1.93—1.81 (m, 4 H); 1.59—1.44 (m, 6 H); 1.39 (ddd, 1 H, J = 2.3 Hz, J = 4.5 Hz, J = 13.3 Hz); 1.36 (ddd, 1 H, J = 2.3 Hz, J = 4.1 Hz, J = 13.7 Hz); 1.24—1.18 (m, 2 H); 1.11 (d, 3 H, Me, J = 7.7 Hz); 1.04 (dm, 1 H, J = 12.8 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz), δ: 58.46, 58.33, 43.20, 40.37, 36.53, 34.64, 31.44, 27.04, 26.64, 25.63, 23.43, 22.03, 19.73 (see Ref. 8f). Found: m/z 194.1898 $[MH]^+$. $C_{13}H_{24}N$. Calculated: (M + H) = 194.1903.

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