Easy Access to (*n*+3)-Dimethylamino-1-ethenylbicyclo[*n*.1.0]alkanes and their Facile Conversion to Ring-annelated Cyclopentadienes[1]

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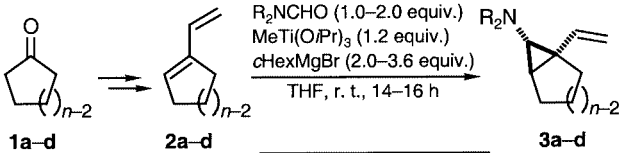
Abstract: Aminocyclopropanation of 1-ethenylcycloalkenes **2a**–**d** with *N*,*N*-dibenzyl- and *N*,*N*-dimethylformamide, respectively, by treatment with cyclohexylmagnesium bromide in the presence of methyltitanium triisopropoxide yielded the *exo*-(*n*+3)-*N*,*N*-dimethylamino-1-ethenylbicyclo[*n*.1.0]alkanes **3a**–**d** (58–72%). Compounds **7b**–**d** could be transformed by thermal vinylcyclopropane to cyclopentene rearrangement to the corresponding *exo*-4-dimethylaminobicyclo[*n*.3.0]alk-1-enes **7b**–**d** (84–90%). Elimination of the dimethylamino group led to the cyclopentadienes **11b**–**d** and **12b**–**d** (72–82%). The 5-dimethylamino-1-ethenylbicyclo[2.1.0]pentane did not undergo the typical vinylcyclopropane rearrangement, but ring-opening at the bridgehead-bridgehead bond to form 1-ethenyl-2-dimethylaminocyclopentene **8**.

Key words: cyclopentadiene derivatives, cyclopropane derivatives, organometallics, rearrangement, titanium chemistry

Ring-annelated cyclopentadienes, including chirally modified ones, play a significant role as ligands in transition-metal complexes,[2,3] several of which are valuable catalysts.[2] A number of five-membered ring-annelation methodologies that make such compounds available, have previously been published.[4] Utilizing our recently reported regioselective aminocyclopropanation of conjugated dienes,[5] we have developed an alternative five-membered ring-annelation protocol that may complement and in certain cases be superior to previous ones starting from cycloalkanones.

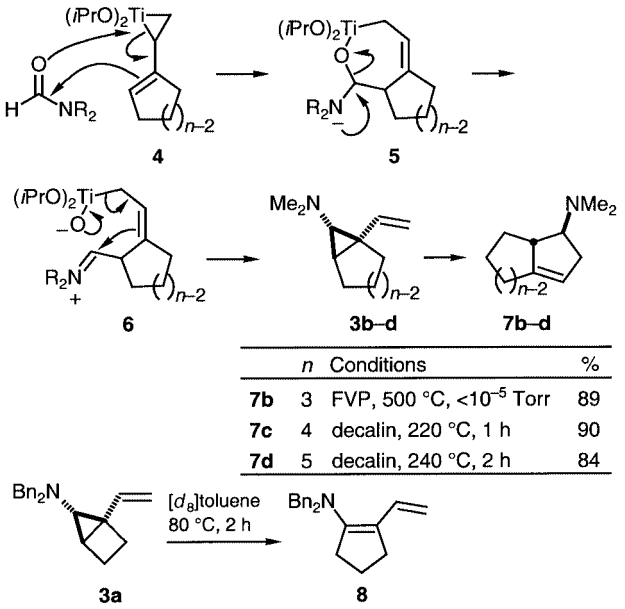
A series of 1-ethenylcycloalkenes **2a**–**d** was prepared from cycloalkanones **1a**–**d** via the corresponding 1-ethenylcycloalkanols according to published procedures (Scheme 1).[6–8] Titanium-mediated aminocyclopropanation of conjugated dienes has been found to occur at the more highly substituted double bond.[5] Thus, treatment of the dienes **2a**–**d** with cyclohexylmagnesium bromide in the presence of methyltitanium triisopropoxide and *N*,*N*-dibenzyl- or *N*,*N*-dimethylformamide, respectively, afforded the pure 1-ethenyl-*exo*-(*n*+3)-dialkylaminobicyclo[*n*.1.0]alkanes **3a**–**d**.[9,10] The outcome of the reactions of **2b**–**d** was rather sensitive to both the amounts of *N*,*N*-dimethylformamide as well as cyclohexylmagnesium bromide. After individual optimization of both these parameters acceptable yields (58–72%) of the desired products could be obtained. It is particularly remarkable that 1-ethenylcyclobutene **2a** is converted to *exo*-5-dibenzylaminobicyclo[2.1.0]pentane (**3a**) without any problems in 63% yield. This is the first example of a bicyclo[2.1.0]pentylamine.



	n	R	**3** (%)
a	2	Bn	63
b	3	Me	72
c	4	Me	63
d	5	Me	58

Scheme 1

The most likely mechanism of this transformation is that the formamide adds by way of an ene-reaction to the cycloalkenyltitanacyclopropane **4**, which reacts as an allyltitanium species, to yield the cycloalkyl-annelated oxatitanacycloheptene **5**. Subsequent ring opening gives the iminium titaniumoxide zwitterion **6**, which can cyclize to the dimethylaminoethenylcyclopropane **3** with liberation of diisopropyloxytitanium oxide (Scheme 2).



	n	Conditions	%
7b	3	FVP, 500 °C, <10^{-5} Torr	89
7c	4	decalin, 220 °C, 1 h	90
7d	5	decalin, 240 °C, 2 h	84

Scheme 2

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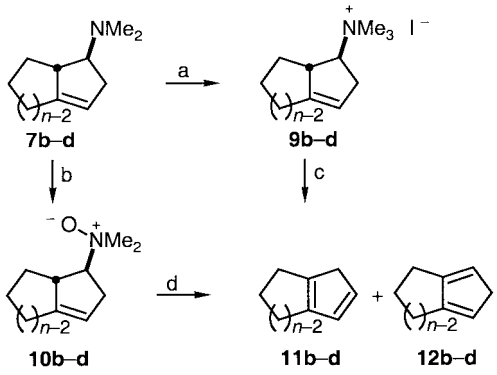
The well established vinylcylopropane to cyclopentene rearrangement[12] has previously also been applied to a number of 2-ethenylcyclopropylamines.[13] This rearrangement could be accomplished for **3b** by flash vacuum pyrolysis (FVP) at 500 °C/10^{-5} Torr, to provide the product **7b** in 89% yield. Surprisingly, when **3c** and **3d** were subjected to FVP under the same conditions, inseparable mixtures of the expected products **7c** and **7d** with 22 and 43%, respectively, of unidentified isomeric by-products were obtained.[14] At lower temperature (300 °C), incomplete conversion, and at higher temperature (600 °C), partial decomposition was observed. However, when **3c** and **3d** were heated in decalin in a sealed tube at 220–240 °C for 1–2 h,[15] the pure products **7c** and **7d** were isolated in 84 and 90% yield, respectively. The 1-ethenylbicyclo[2.1.0]pentane derivative **3a** did not undergo the same type of rearrangement as its higher homologues **3b**–**d**, but simple ring opening of the three-membered ring at its internal bond with subsequent hydrogen shift to quantitatively form dibenzyl-(2-ethenylcyclopentenyl)amine (**8**) upon heating in toluene at 80 °C for 2 h.

The conversion of the dimethylaminocyclopentenyl-**7b**–**d** to the cyclopentadienyl-annelated cycloalkanes **11b**–**d**/**12b**–**d** can be achieved by either a Hofmann or a Cope elimination. Quaternization of **7b**–**d** with methyl iodide, conversion of the ammonium iodides to the hydroxides with silver oxide and subsequent thermolysis gave inseparable mixtures of two isomeric cyclopentadienes **11b**–**d**/**12b**–**d** each in 64–76% yield. Oxidation of **7b**–**d** to the *N*-oxides **10b**–**d** and subsequent thermolysis afforded **11b**–**d** and **12b**–**d** in only 36–45% over two steps. The observed isomers **11** and **12** are known to interconvert into each other by a pericyclic 1,5-H shift which is rapid under the reaction conditions, and the observed ratios apparently depend on the size of the annelated ring.[16]



Scheme 3 (a) MeI, Et_2O, r.t., 5 h; (b) H_2O_2, r.t., 2 d; (c) Ag_2O, H_2O, 10 Torr, 180 °C, 30 min; (d) H_2O, 1 Torr, 150 °C. Details see Table.

In conclusion, ring-annelated cyclopentadienes can easily be obtained from cycloalkanones via 1-ethenylcycloalkenes, their titanium-mediated aminocyclopropanation, followed by thermal rearrangement and elimination.

Table Yields of Quaternary Ammonium Iodides **9**, *N*-Oxides **10** and Annelated Cyclopentadienes **11** and **12** (See Scheme 3)

		Yield (%)				
Entry	*n*	**9**	**10**	**11**/**12**[a]	(**11**/**12**[b])	Ratio
b	3	95	95	80	(47)	48:52 (49:51)
c	4	95	94	82	(40)	93:7 (88:12)
d	5	89	87	72	(41)	21:79 (24:76)

[a] From **9**.
[b] From **10**.

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(8) Alternatively, 1-ethenylcycloalkenes **2a**–**d** may be prepared from the corresponding cycloalkanones via the enol triflates by Stille cross coupling with tri-*n*-butylvinylstannane. Cf. ref.[6]
(9) **General Procedure (GP) for the Preparation of 1-ethenyl-*exo*-(*n*+3)-dialkylaminobicyclo[*n*.1.0]alkanes 3**: To a well-stirred solution of the corresponding 1-ethenylcycloalkene **2a**–**d** (10 mmol), MeTi(*i*-PrO)$_3$ (12 mmol) and *N*,*N*-dialkylformamide (10–20 mmol) in 30 mL of THF was added cyclohexylmagnesium bromide (13.3–24 mL, 20–36 mmol) as a 1.50 M solution in diethyl ether) over a period of 2 h, and the mixture was stirred at ambient

temperature overnight. The reaction was quenched by carefully adding 5 mL of water, the mixture was exposed to air until it had turned light yellow or colorless and then filtered. The solids on the filter were washed with diethyl ether (3 × 20 mL). The combined filtrates were concentrated in vacuo, and the light yellow residue was subjected to column chromatography (column 2 × 25 cm, 40 g of silica gel) eluting with pentane/diethyl ether/triethylamine 90:9.5:0.5.

***exo*-5-Dibenzylaminobicyclo[2.1.0]pentane (3a)**: According to GP, 962 mg (12 mmol) of 1-ethenylcyclobutene (**2a**) with *N*,*N*-dibenzylformamide (5.63 g, 25 mmol), methyltitanium triisopropoxide (2.88 g, 12 mmol) and 15.8 mL (30 mmol) of cyclohexylmagnesium bromide solution (1.90 M in diethyl ether) gave 2.20 g (63%) of **3a** as a light yellow oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.42 (ddd, ^2J = 11.0, ^3J = 6.5, ^3J = 3.9 Hz, 1 H, 3-H$_{endo}$), 1.55 (ddd, ^2J = 11.0, ^3J = 6.5, ^3J = 4.6 Hz, 1 H, 2-H$_{endo}$), 1.79 (d, ^3J = 4.6 Hz, 1 H, 4-H), 2.01 (dddd, ^2J = 11.0, ^3J = 11.0, ^3J = 4.6, ^3J = 4.6 Hz, 1 H, 3-H$_{exo}$), 2.31 (ddd, ^2J = 11.0, ^3J = 11.0, ^3J = 3.9 Hz, 1 H, 2-H$_{exo}$), 2.36 (s, 1 H, 5-H), 3.61 (AB, d, ^2J = 14.0 Hz, 2 H, NCH_2Ph), 3.80 (AB, d, ^2J = 14.0 Hz, 2 H, NCH_2Ph), 5.09 (dd, ^2J = 1.9, $^3J_{trans}$ = 17.5 Hz, 1 H, 7-H), 5.17 (dd, ^2J = 1.9, $^3J_{cis}$ = 10.8 Hz, 1 H, 7-H), 6.20 (dd, $^3J_{trans}$ = 17.5, $^3J_{cis}$ = 10.8 Hz, 1 H, 6-H), 7.25–7.47 (m, 10 H, Ph-H). ^{13}C NMR (62.9 MHz, $CDCl_3$, additionally DEPT): δ = 19.2 (–, C-3), 22.9 (–, C-2), 31.3 (+, C-4), 36.0 (C_{quat}, C-1), 56.9 (–, 2 C, NCH_2Ph), 57.7 (+, C-5), 112.3 (–, C-7), 126.9 (+, 2 C, Ph-C), 128.1 (+, 4 C, Ph-C), 129.3 (+, 4 C, Ph-C), 137.4 (+, C-6), 137.9 (C_{quat}, 2 C, Ph-C). MS (70 eV): *m/z* (%) = 289(16) [M^+], 288(12) [$M^+ - H$], 262(3) [$M^+ - C_2H_3$], 224(11), 198(29) [$M^+ - C_7H_7$], 170(5) [$M^+ - C_7H_7 - C_2H_4$], 144(20) [$M^+ - C_7H_7 - C_4H_6$], 106(8) [$HNC_7H_7^+$], 91(100) [$C_7H_7^+$]. $C_{21}H_{23}N$: 289.1830 (correct HRMS). Anal. Calcd for $C_{20}H_{23}N$ (289.4): C, 87.15; H, 8.01; N, 4.84. Found; C, 86.88; H, 7.90; N, 4.97.

(10) All new compounds were fully characterized by spectroscopic techniques (^{1}H and ^{13}C NMR, MS), and bulk purities – except for the quaternary ammonium salts **9** and *N*-oxides **10** – were established by elemental analyses. Spectroscopic data of representative examples: ***exo*-*N*,*N*-Dimethyl-(1-ethenylbicyclo[4.1.0]hept-7-yl)amine (3c)**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.03 (ddd, ^3J = 1.8, ^3J = 8.0 Hz, $^3J_{trans}$ = 4.3 Hz, 1 H, 6-H), 1.08–1.24 (m, 3 H, 3-H*, 4-H), 1.27–1.37 (m, 1 H, 4-H), 1.45 (d, $^3J_{trans}$ = 4.3 Hz, 1 H, 7-H), 1.52−1.63 (m, 2 H, 2-H, 5-H), 1.87−1.98 (m, 2 H, 2-H, 5-H), 2.20 (s, 6 H, CH_3), 4.99 (dd, ^2J = 1.6, ^3J = 10.8 Hz, 1 H, 2′-H), 5.03 (dd, ^2J = 1.6, ^3J = 17.6 Hz, 1 H, 2′-H), 5.82 (dd, ^3J = 10.8, ^3J = 17.6 Hz, 1 H, 1′-H). ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.1 (–, C-3*), 22.7 (–, C-4*), 22.1 (–, C-5**), 25.8 (–, C-2**), 27.7 (+, C-6), 28.5 (C_{quat}, C-1), 45.0 (+, 2 C, CH_3), 58.4 (+, C-7), 110.4 (–, C-2′), 143.7 (+, C-1′). MS (70 eV, EI): *m/z* (%) = 165 (100) [M^+], 150 (42), 136 (62), 122 (30), 108 (23), 84 (57), 70 (38), 58 (30), 42 (48). Anal. Calcd for $C_{11}H_{19}N$ (165.3): C, 79.94; H, 11.59; N, 8.47. Found: C, 79.66; H, 11.35; N, 8.53.

***exo*-*N*,*N*-Dimethyl-(1-ethenylbicyclo[5.1.0]oct-8-yl)amine (3d)**: ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.89−1.14 (m, 4 H, 2-H*, 6-H, 7-H), 1.20−1.31 (m, 1 H, 3-H*), 1.40 (d, $^3J_{trans}$ = 3.8 Hz, 1 H, 8-H), 1.48−1.56 (m, 1 H, 3-H*), 1.58−1.72 (m, 2 H, 4-H*), 1.74−1.83 (m, 1 H, 5-H*), 2.19 (s, 6 H, CH_3), 2.14−2.27 (m, 1 H, 6-H), 2.30−2.37 (m, 1 H, 5-H*), 5.01 (dd, ^2J = 1.6 Hz, ^3J = 17.4 Hz, 1 H, 2′-H), 5.02 (dd, ^2J = 1.6 Hz, ^3J = 11.1 Hz, 1 H, 2′-H), 5.67 (dd, ^3J = 11.1 Hz, ^3J = 17.4 Hz, 1 H, 1′-H). ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 27.0 (–, C-2*), 29.4 (–, C-3*), 30.8 (–, C-6), 32.4 (–, C-4*), 32.5 (–, C-5*), 33.8 (+, C-7), 34.7 (C_{quat}, C-1), 45.2 (+, 2 C, CH_3), 64.8 (+, C-8), 111.1 (–, C-2′), 142.4 (+, C-1′). MS (70 eV, EI): *m/z* (%) = 179 (30) [M^+], 164 (21), 150 (18), 136(100), 122 (39) [$M^+ - C_4H_9$], 108 (80) [$M^+ - C_5H_{11}$], 84 (62), 71(45), 42 (100), 41 (49). Anal. Calcd for $C_{12}H_{21}N$ (179.3): C, 80.38; H, 11.81; N, 7.81. Found: C,80.18; H, 11.74; N, 7.74.

(2,4,5,6,7,7a-Hexahydro-1*H*-inden-1-yl)dimethylamine (7c): ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.93−1.38 (m, 3 H, 4-H*, 5-H*), 1.69−1.80 (m, 2 H, 6-H*), 1.80−1.98 (m, 1 H, 7-H*), 1.98−2.17 (m, 1 H, 7-H*), 2.17−2.45 (m, 4 H, 1-H, 2-H, 4-H), 2.23 (s, 6 H, CH_3), 2.55−2.64 (m, 1 H, 7a-H), 5.15 (m_c, 1 H, 3-H). ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 26.1 (–, C-6), 26.9 (–, C-5), 29.2 (–, C-4), 35.4 (–, C-2), 35.5 (–, C-7), 43.3 (+, 2 C, CH_3), 48.5 (+, C-7a), 73.2 (+, C-1), 118.3 (+, C-3), 144.8 (C_{quat}, C-3a). MS (70 eV, EI): *m/z* (%) = 165 (100) [M^+], 150 (42), 136 (51), 122 (23), 108 (15), 91 (24), 84 (41), 70 (33), 58 (19), 42 (26). Anal. Calcd for $C_{11}H_{19}N$ (165.3): C, 79.94; H, 11.59; N, 8.47. Found: C, 79.85; H, 11.57; N, 8.35.

4,5,6,7-Tetrahydro-1*H*-indene(11c) and 4,5,6,7-Tetrahydro-2*H*-indene (12c): 11c: ^{1}H NMR see ref.[11]. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 23.1 (–, C-4*), 23.3 (–, C-5*), 24.4 (–, C-6*), 25.3 (–, C-7*), 34.1 (–, C-1), 129.8 (+, C-2), 134.5 (+, C-3), 137.9 (C_{quat}, C-3a*), 139.2 (C_{quat}, C-7a*). **12c**: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.58−1.80 [m, 4 H, 5(6)-H], 2.47−2.58 [m, 4 H, 4(7)-H], 2.72−2.80 (m, 2 H, 2-H), 5.97 [m_c, 2 H, 1(3)-H]. ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 24.4 [–, C-4(7)], 25.7 [–, C-5(6)], 39.7 (–, C-2), 125.1 [+, C-1(3)]. The signals of the quaternary carbon atoms C-3a and C-7a were not visible because of the low concentration of **12c**.

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(14) The structure of the by-products could not unambiguously be determined.

(15) (a) The necessity of relatively high temperatures for the rearrangement of **3b**–**d** is consistent with the fact that the dimethylamino and the ethenyl group in each of them are *cis*-oriented with respect to each other. It is known that the direct ring enlargement of a *cis*-2-donor-substituted ethenylcyclopropane to a cyclopentene is much slower than that of the *trans* isomer, and the *cis* to *trans* isomerization of **3b**–**d**, which would correspond to an *exo* to *endo* isomerization, is retarded due to the bulk of the dimethylamino group. (b) Cf. ref.[13] and ref.[14] and see also: McGaffin, G.; Grimm, B.; Heinecke, U.; Michaelsen, H.; de Meijere, A.; Walsh, R. *Eur. J. Org. Chem.* **2001**, 3559.

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