N-(2-Methylinden-4-yl)pyrrole as a heterocyclic analog of 2-methyl-4-arylindene. Synthesis of [μ-$SiMe_2$(η^5-2-Me-4-(2,4-$Me_2C_4H_2N$)Ind)$_2$]$ZrCl_2$

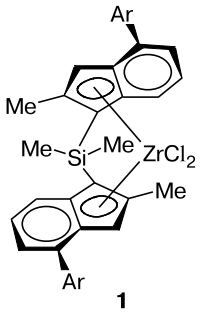
P. V. Ivchenko, N. B. Ivchenko, and I. E. Nifant´ev*

Department of Chemistry, M. V. Lomonosov Moscow State University, 1 Leninskie Gory, 119992 Moscow, Russian Federation. Fax: +7 (495) 939 4523. E-mail: inpv@org.chem.msu.ru

A unique strategy for the synthesis of 2-methyl-4-arylindenes was tested for 1-(4-indenyl)-pyrrole. The procedure includes the Paal—Knorr synthesis of a nonsymmetric arylhetaryl fragment followed by intramolecular acylation. The zirconium complex of the 2-methyl-4-arylindenyl type containing the 1-pyrrolyl substituent was synthesized.

Key words: Paal—Knorr pyrrole synthesis, Friedel—Crafts intramolecular reaction, indanones, 4-arylindenes, *ansa*-zirconocenes.

Zirconocenes **1** represent a structural type of efficient catalysis for propene polymerization (see Ref. 1). Presently, the synthesis of these compounds has sufficiently been developed and can be reduced to the preparation of corresponding substituted indenes **2**. 2-Methyl-4(7)-phenylindene is traditionally considered as a prototypical molecule. The variation of substituents in the indenyl ring allows one to efficiently affect the catalytic properties of zirconocenes and the properties of polymers formed.



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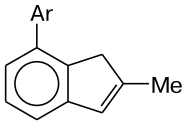

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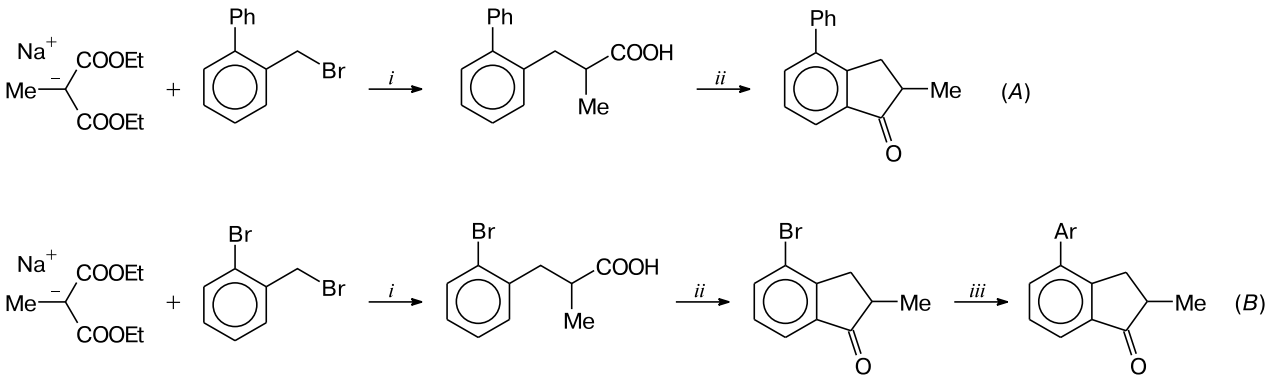
Two main synthetic approaches were developed for compounds of general formula **2**. The first approach, which provides, in particular, the synthesis of 2-methyl-7-phenylindene, is based on the substrate containing the biaryl fragment (2-bromomethylbiphenyl) and yields the target product through the stages of malonic synthesis and cyclization of substituted arylpropionic acid to 2-methyl-4-phenylindanone[1] (Scheme 1, route *A*). An alternative approach is based on the use of 2-bromobenzyl bromide, includes the Suzuki reaction[2] (Scheme 1, route *B*), and

Scheme 1



i. 1) EtOH, 2) NaOH, EtOH, Δ, 3) Δ; *ii*. 1) $SOCl_2$, CH_2Cl_2, 2) $AlCl_3$, CH_2Cl_2; *iii*. $ArB(OH)_2$, Pd(0)

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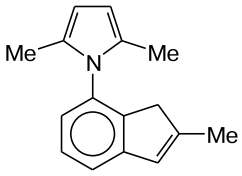
thus makes it possible to introduce various aryl (including heteroaromatic) substituents into the indene molecule. However, these substituents are bound to the indenyl fragment through the carbon atoms.

It seemed rather interesting to synthesize *ansa*-zirconocene containing in position 4 or 7 of the indenyl ring the hetaryl substituent bound to indene through the heteroatom of the cycle. Pyrrol-1-yl is the simplest substituent of this type. Molecule **3**, whose α-positions of the pyrrole ring are occupied by methyl groups, was chosen as the target compound to prevent possible difficulties at the stages of synthesis of the bisindenyl bridged compound and zirconocene including the reaction of substituted indene with alkyllithium.



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Results and Discussion

The Paal—Knorr reaction seems to be most attractive for the creation of a pyrrole system. Its use for the preparation of 4(7)-arylindene means, in fact, the application of the new synthetic approach to the biaryl fragment of the target molecule, namely, the creation of the heteroaromatic ring from functionalized arene. Two general routes that could give molecule **3** were designed.

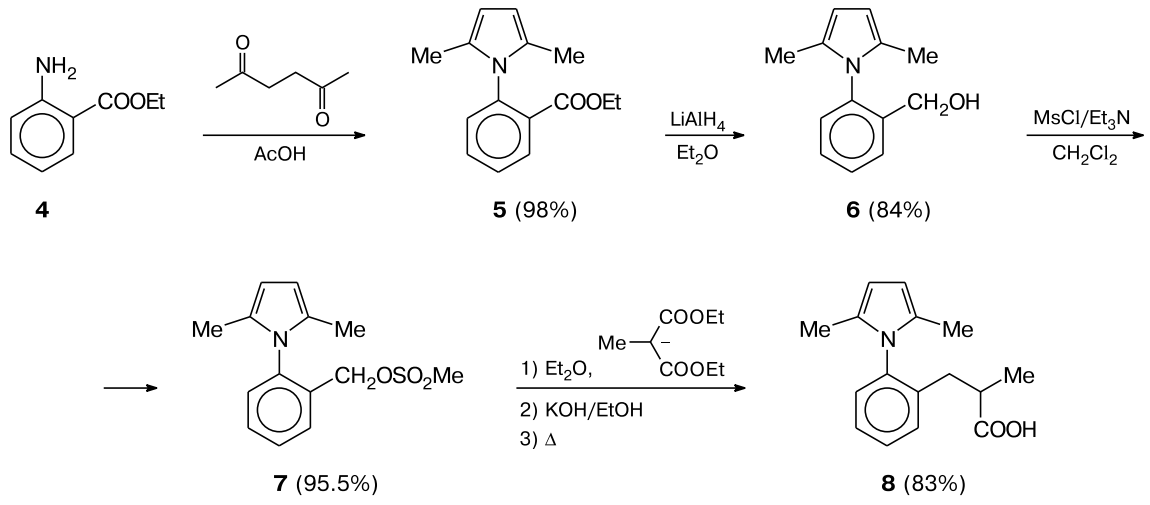
The first approach assumed the synthesis of 2-methylindene-4(7)-amine followed by its transformation into the corresponding indenylpyrrole *via* the Paal—Knorr reaction. The second route, whose success seemed first improbable because of possible side reactions, included the preparation of substituted 1-arylpyrrole and the synthesis from the latter of the five-membered indanone ring and target indene, and main difficulties were expected at the stage of indanone synthesis.

For the first route, *ortho*-amino-, *ortho*-acetylamino-, and *ortho*-nitroiodobenzenes were chosen as the starting compounds. We planned to obtain methacrylic acid derivatives by the Heck reaction, to synthesize 4-substituted indanone by the reduction of these derivatives followed by cyclization, and to prepare indenylpyrrole from 4-substituted indanone by the Paal—Knorr reaction. It turned out that the Heck reaction with methacrylic acid proceeds smoothly only in the case of *o*-iodonitrobenzene. However, we failed to reduce the product to the corresponding (2-aminophenyl)propionic acid in high yield.

For the second route, we chose accessible anthranylate **4** as the starting compound to synthesize functionalized 1-arylpyrrole. 2,5-Dimethylpyrrol-1-yl was chosen as the pyrrole fragment for the reasons presented above. Compound **5** can easily be obtained by the Paal—Knorr reaction of acetonylacetone and ester **4**. The reduction of pyrrolyl benzoate **5** yielded alcohol **6**, and the transformation of the latter into mesylate **7** and the malonic synthesis according to a standard procedure gave arylpropionic acid **8** (Scheme 2).

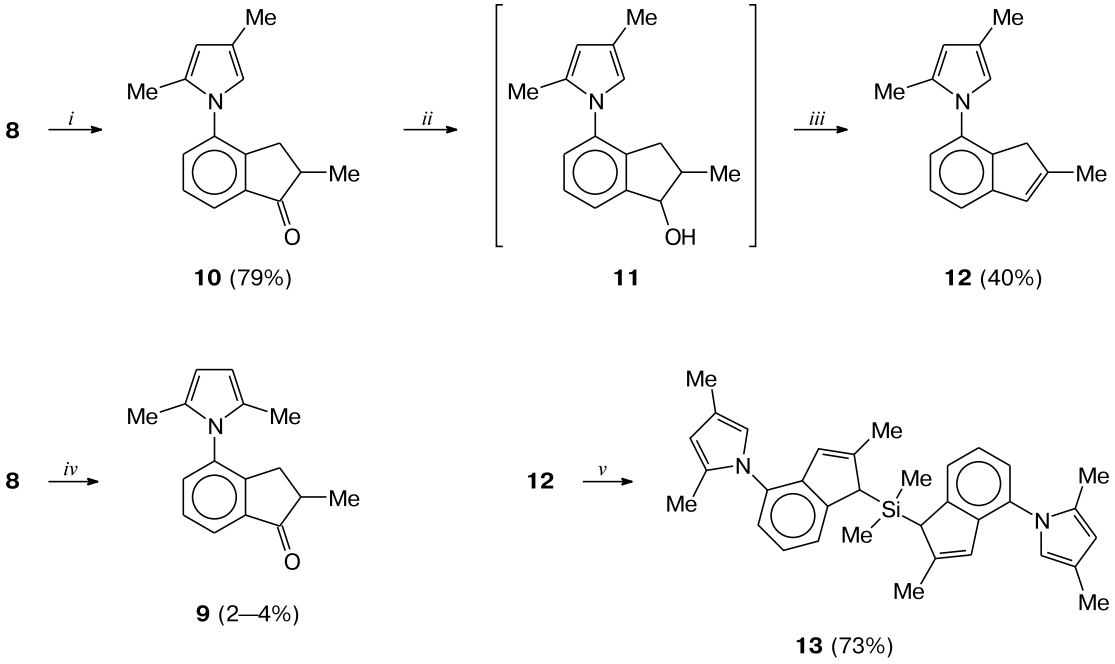
Acid chloride **8** was thermally unstable, and the attempts to prepare it *in situ* by the Fridel—Crafts intramolecular reaction in the presence of $AlCl_3$ were unsuccessful. An attempt to synthesize target indanone **9** directly from carboxylic acid **8** using the known[3] efficient method, *viz.*, cyclization in an $AlCl_3$—NaCl melt, showed

Scheme 2



4 **5** (98%) **6** (84%) **7** (95.5%) **8** (83%)

Scheme 3



i. $AlCl_3$/NaCl, 180—200 °C; *ii*. $LiAlH_4$, Et_2O; *iii*. *o*-TsOH, benzene, Δ; *iv*. PPA, 80 °C; *v*. 1) BuLi, toluene/THF, 2) $SiMe_2Cl_2$

that the cyclization was accompanied by the quantitative migration of one methyl group of the pyrrole ring to form isomeric indanone **10** in 79% yield (Scheme 3).

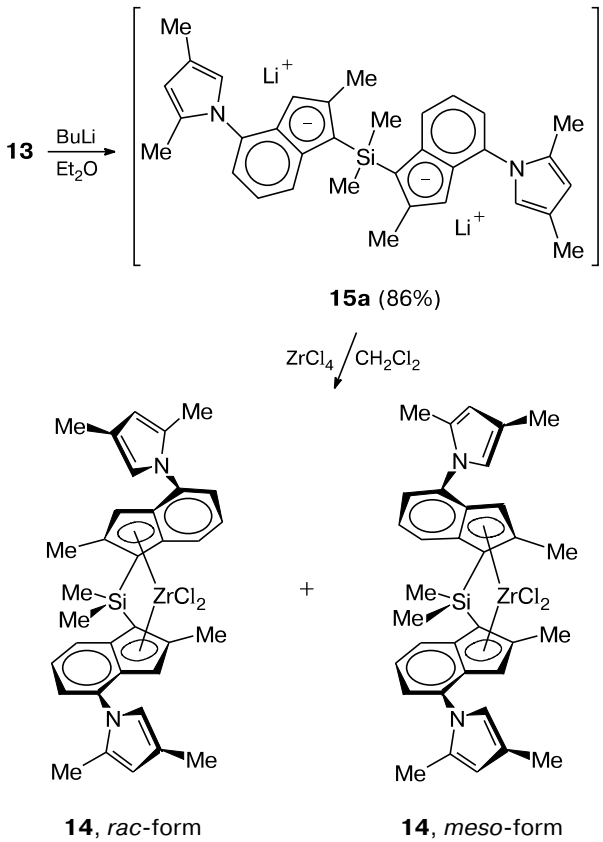
2,4-Dimethyl-1-(2-methyl-7-indenyl)pyrrole **12** was obtained from compound **10** by the reduction of the carbonyl group followed by the dehydration of intermediate alcohol **11**. The low yield of compound **12** is caused. most likely by the fact that one of the α-positions of the pyrrole substituent is free and accessible for the electrophilic attack. In this case, cationic intermediates formed upon the protonation of alcohol **11** with subsequent dehydration can act as electrophiles.

No indanone **10** was found in the reaction mixture for the cyclization of **8** in polyphosphoric acid (according to the NMR spectral data). However, the yield of **9** was 2—4% (Scheme 3) and, hence, the further synthesis of corresponding indenylpyrrole **3** had no sense.

Compound **12** was used as ligand for the synthesis of *ansa*-zirconocene. Compound **13** was synthesized in satisfactory yield by the reaction of the lithium derivative compound **12** with dimethyldichlorosilane in a toluene—THF mixture according to a known procedure[1] (see Scheme 3).

ansa-Zirconocene **14** was obtained by the direct reaction of the dilithium derivative of compound **13** with $ZrCl_4$ (**15**) in methylene chloride in almost quantitative yield as a mixture of diastereomers (Scheme 4). Recrystallization from ether gave 23% pure *rac*-form.

Scheme 4



Thus, a possibility to synthesize 4-hetarylindenyl zirconium complexes, *viz.*, structural analogs of bisindenyl complex **1**, was demonstrated using indenylpyrrole **12** and zirconocene **14** as an example. In addition, it was shown that the presence of the pyrrole fragment unsubstituted in the α-position in the molecule of an organic ligand does not principally prevent the synthesis of organoelement derivatives and metallocenes using standard procedures.

Experimental

All experiments were carried out in inert atmosphere (argon). Whole-sealed glass systems of the Schlenk type were used for crystallization of complex **14**. Ethyl anthranylate (2-aminobenzoate) was prepared according to a known procedure[4] in 60% yield. Ethereal solvents and toluene were distilled over sodium in the presence of benzophenone (dibenzo-18-crown-6 was added in the case of toluene). Methylene chloride was purified by distillation with CaH_2. ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 instrument in $CDCl_3$ at 20 °C. Elemental analyses for hydrogen and carbon were carried out on a Carlo Erba automated analyzer (model 1106). Samples for elemental analysis of oily compounds were preheated at 70—80 °C on a vacuum setup to a constant residual pressure (about 10^{-2} Torr).

Ethyl 2-(2,5-dimethyl-1*H*-pyrrol-1-yl)benzoate (5). A mixture of ester **4** (18.1 g, 110 mmol) and 2,5-hexanedione (20 mL, 165 mmol) in glacial acetic acid (100 mL) was refluxed for 1 h, cooled, and poured into water with ice (250 mL). After CH_2Cl_2 (100 mL) was added, the organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (5×50 mL). Joined organic phases were washed with a solution of Na_2CO_3, dried over $MgSO_4$, and concentrated by evaporation to obtain the product as a light brown oil in a yield of 26.3 g (98%). ^1H NMR, δ: 1.23 (t, 3 H, —O—CH_2—C$\underline{H}_3$, J = 7.2 Hz); 1.94 (s, 6 H, —CH_3); 4.1 (q, 2 H, —O—C$\underline{H}_2$—CH_3, J = 7.2 Hz); 5.88 (s, 2 H, H(3), H(4), pyrrolyl); 7.28 (dd, 1 H, J = 8 Hz, J = 2 Hz); 7.50 (ddd, 1 H, J = 8 Hz, J = 8 Hz, J = 2 Hz); 7.60 (ddd, 1 H, J = 8 Hz, J = 8 Hz, J = 2 Hz); 7.95 (dd, 1 H, J = 8 Hz, J = 2 Hz). Found (%): C, 73.99; H, 7.11. $C_{15}H_{17}NO_2$. Calculated (%): C, 74.05; H, 7.04.

[2-(2,5-Dimethyl-1*H*-pyrrol-1-yl)phenyl]methanol (6). A solution of **5** (26.3 g, 0.108 mol) in Et_2O (30 mL) was added dropwise to a suspension of $LiAlH_4$ (4.1 g, 0.108 mol) in Et_2O (120 mL) under argon with cooling to 0 °C. Then cooling was removed, and the reaction mixture was stirred at room temperature for 1 h. Then water was added by small portions to the reaction mixture until the end of gas evolution. The resulting mixture was washed with Et_2O (6×50 mL), and the joined organic phases were washed with water (2×100 mL), dried over $MgSO_4$, and evaporated to obtain a dark brown solid residue, which was recrystallized from boiling hexane. The yield was 18.12 g (83.5%) of **6** as light beige needle-like crystals (m.p. 107 °C). ^1H NMR, δ: 1.60 (s, 1 H, —CH_2—O$\underline{H}$); 1.90 (s, 6 H, —CH_3); 4.30 (s, 2 H, —C$\underline{H}_2$—OH); 5.90 (s, 2 H, H(3), H(4), pyrrolyl); 7.17 (dd, 1 H, J = 7.8 Hz, J = 1.9 Hz); 7.37—7.48 (m, 2 H); 7.59 (dd, 1 H, J = 8.1 Hz, J = 1.6 Hz). Found (%): C, 77.60; H, 7.56. $C_{13}H_{15}NO$. Calculated (%): C, 77.59; H, 7.51.

2-(2,5-Dimethyl-1*H*-pyrrol-1-yl)benzyl methanesulfonate (7). Triethylamine (68.4 mL, 0.494 mol) was added at room temperature to a solution of compound **6** (79.4 g, 0.395 mol) in CH_2Cl_2 (450 mL), after which methanesulfonyl chloride (33.9 mL, 0.435 mol) was added dropwise with cooling to −78 °C, and the mixture was stirred for 1 h. Then cooling was removed, and the reaction mixture was stirred at room temperature for 4 h. Then 3.5% HCl (100 mL) was added. The aqueous phase was extracted with CH_2Cl_2 (2×100 mL), and the joined organic phases were washed with a solution of Na_2CO_3, dried over $MgSO_4$, and concentrated by evaporation to obtain a blue oil, which further crystallized completely. The yield was 105.2 g (96%, dark blue crystals, the color is caused by admixtures), m.p. 118 °C (after recrystallization from benzene). ^1H NMR, δ: 1.90 (s, 6 H, 2 —CH_3); 2.80 (s, 3 H, —$OSO_2C\underline{H}_3$); 4.78 (s, 2 H, —C$\underline{H}_2$—O—); 5.90 (s, 2 H, H(3), H(4), pyrrolyl); 7.22—7.25 (m, 1 H); 7.46—7.50 (m, 2 H); 7.59—7.63 (m, 1 H). Found (%): C, 60.27; H, 6.18. $C_{14}H_{17}NO_3S$. Calculated (%): C, 60.19; H, 6.13.

3-[2-(2,5-Dimethyl-1*H*-pyrrol-1-yl)phenyl]-2-methylpropionic acid (8). A solution of diethyl 2-methylmalonate (6.8 mL, 0.039 mol) in Et_2O (20 mL) was added dropwise to a suspension of NaH (1.45 g of 60% suspension in oil, 36 mmol) in Et_2O (80 mL) under argon with cooling to 0 °C. Cooling was removed, and the reaction mixture was stirred for 1.5 h. Then a solution of compound **7** (8.46 g, 0.03 mol) in Et_2O (50 mL) was rapidly added by small portions to the reaction mixture with cooling to −40 °C. Cooling was removed, and the mixture was refluxed for 3 h and stirred at room temperature for 16 h. Then 3% HCl (100 mL) was added to the reaction mixture, the aqueous phase was extracted with CH_2Cl_2 (4×50 mL), and the joined organic phase was washed with a solution of Na_2CO_3, dried over $MgSO_4$, and evaporated. The obtained brown oil was dissolved in alcohol (45 mL), then mixed with an aqueous solution of KOH (12 g of KOH in 22.5 mL of H_2O), and the mixture was refluxed for 4 h. The reaction mixture was poured into water (100 mL), the solution formed was extracted with Et_2O (3×50 mL), and the aqueous phase was acidified with HCl to pH ≈ 1 and extracted with CH_2Cl_2 (4×80 mL). The joined organic phases were washed with a solution of Na_2CO_3, dried over $MgSO_4$, and evaporated to dryness. The resulting red-brown solid residue was heated in an oil bath (160 °C) until gas stopped evolving (about 25 min), and the product was obtained as a viscous brown oil, which further crystallized, in a yield of 5.46 g (70%). ^1H NMR, δ: 1.06 (d, 3 H, $CH_2CHC\underline{H}_3$, J = 7.6 Hz); 1.90 (s, 3 H); 1.94 (s, 3 H); 2.56 (sext, 1 H, —$CH_2C\underline{H}CH_3$—, J = 7.6 Hz); 2.75 (dd, 1 H, J = 14 Hz, J = 7.6 Hz), 2.32 (dd, 1 H, J = 14 Hz, J = 7.6 Hz) {—C$\underline{H}_2$—CHMe—}; 5.9 (s, 2 H, H(3), H(4), pyrrolyl); 7.14—7.17 (m, 1 H); 7.29—7.36 (m, 3 H). Found (%): C, 74.61; H, 7.39. $C_{16}H_{19}NO_2$. Calculated (%): C, 74.68; H, 7.44.

4-(2,5-Dimethyl-1*H*-pyrrol-1-yl)-2-methylindan-1-one (9). Compound **8** (2.57 g, 10 mmol) was added with stirring to polyphosphoric acid (prepared by dissolution of P_2O_5 (100 g) in 80 mL of H_3PO_4) and heated to 120 °C. After 1 h at this temperature the mixture was poured to water with ice (500 mL). The resulting mixture was extracted with methylene chloride (4×25 mL), and the joined organic phases were washed with a solution of Na_2CO_3 (2×50 mL), dried over $MgSO_4$, and concentrated by evaporation. A broad fraction (R_f in an interval of 0.8—0.4) was separated by column chromatography (silica gel, benzene—ethyl acetate (5 : 1) as eluent). After the solvent was removed, the weight of the fraction was 0.1 g. The isolated product was compound **9** insignificantly contaminated

with nonidentified impurities. No isomeric indanone **10** was observed in compound **9**. ^{1}H NMR, δ: 1.26 (d, 3 H, $CH_2CHC\underline{H}_3$, J = 8.1 Hz); 1.94 (br.s, 6 H); 2.32—2.38 (m, 1 H), 2.66—2.75 (m, 1 H), 2.98—3.05 (m, 1 H) {—C$\underline{H}_2$—C$\underline{H}$Me—}); 5.93 (s, 2 H, H(4), H(5), pyrrolyl); 7.44—7.52 (m, 2 H); 7.82 (m, 1 H).

4-(2,4-Dimethylpyrrol-1-yl)-2-methylindan-1-one (10). The synthesis was carried out according to a known procedure.[3] Melted compound **8** (5.46 g, 21 mmol) was rapidly poured into the melt of a mixture of $AlCl_3$ (38.5 g) and NaCl (7.7 g) at the temperature about 200 °C, the mixture was stirred for 3—4 min, and then the melt was poured into 5% hydrochloric acid with ice (300 mL). The resulting mixture was extracted with methylene chloride (5×80 mL), and the joined organic phases were washed with a solution of Na_2CO_3 (2×100 mL), dried over $MgSO_4$, and evaporated. Compound **10** (4.0 g (79%) was obtained as a brown-red oil, which further vitrified. ^{1}H NMR, δ: 1.32 (d, 3 H, $CH_2CHC\underline{H}_3$, J = 8.2 Hz); 2.06 (s, 3 H); 2.14 (s, 3 H); 2.58 (m, 1 H), 2.74 (m, 1 H), 3.22 (m, 1 H) {—C$\underline{H}_2$—C$\underline{H}$Me—}; 5.95; 6.48 (both s, 1 H each, H(3), H(5), pyrrolyl); 7.45—7.48 (m, 2 H); 7.79 (m, 1 H). Found (%): C, 80.34; H, 7.21. $C_{16}H_{17}NO$. Calculated (%): C, 80.30; H, 7.16.

2,4-Dimethyl-1-(2-methyl-7-1*H*-indenyl)-1*H*-pyrrole (12). A suspension of compound **10** (4.0 g, 0.034 mol) in ether (10 mL) was rapidly added to a suspension of $LiAlH_4$ (1.3 g, 0.017 mol) in Et_2O (30 mL) under argon with cooling to −78 °C, after which cooling was removed, the reaction mixture was stirred for 2 h, and then water was added slowly by small portions until gas stopped evolving. Then 5% HCl (30 mL) was added to the resulting mixture, the mixture was extracted with CH_2Cl_2 (4×40 mL), and the joined organic phases were washed with water (2×100 mL), dried over $MgSO_4$, and evaporated. Benzene (25 mL) and *para*-toluenesulfonic acid (0.2 g) were added to the residue, and the resulting mixture was refluxed for about 2 h monitoring the reaction by TLC. After the end of the reaction, the mixture was poured into water (70 mL), the aqueous phase was extracted with methylene chloride (3×40 mL), and the joined organic phases were washed with water, dried over $MgSO_4$, and evaporated. The residue was purified by column chromatography using hexane—methylene chloride (5 : 1) as eluent. Compound **12** (1.51 g, 40%) was obtained as a light yellow oil. ^{1}H NMR, δ: 2.07 (s, 3 H); 2.13 (s, 3 H); 2.15 (s, 3 H); 3.21 (br.s, 2 H); 5.91; 6.51 (both s, 1 H each, H(3), H(5), pyrrolyl); 6.53 (m, 1 H, =CH—); 6.95—6.98 (m, 1 H); 7.24—7.30 (m, 2 H). Found (%): C, 86.14; H, 7.75. $C_{16}H_{17}N$. Calculated (%): C, 86.06; H, 7.67.

Bis[4-(2,4-Dimethyl-1*H*-pyrrol-1-yl)-2-methyl-1*H*-inden-1-yl]dimethylsilane (13). A solution of butyllithium (1.6 *M* in hexane, 21 mL, 0.033 mol) was rapidly poured on cooling to −40 °C with stirring in a solution of compound **12** (7.45 g, 0.033 mol) in a mixture of toluene (200 mL) and THF (10 mL). Then cooling was removed, and the resulting mixture was let to warm up to room temperature with stirring. The reaction mixture was cooled to −40 °C, $SiMe_2Cl_2$ (2.01 mL, 0.017 mol) was rapidly poured in, cooling was removed, and the mixture was stirred at 60 °C for 6 h. A formed precipitate of LiCl was filtered off, the mother liquor was concentrated by evaporation, and compound **13** (6.24 g, 73%) as a yellow oil was isolated from the residue by column chromatography (benzene as eluent). ^{1}H NMR, δ: −0.26, −0.25, −0.20 (all s, 6 H, $Si(CH_3)_2$); 2.08 (s, 6 H); 2.18 (s, 6 H); 2.20 (s, 6 H); 3.83; 3.85 (both s, 2 H, C$\underline{H}$—Si); 5.92; 6.48 (both s, 2 H each, H(3), H(5), pyrrolyl); 6.55 (br.s, 2 H, =CH—); 7.13—7.17 (m, 2 H); 7.35—7.39 (m, 2 H); 7.44—7.48 (m, 2 H). Found (%): C, 81.28; H, 7.66. $C_{34}H_{38}N_2Si$. Calculated (%): C, 81.22; H, 7.62.

[μ-1-Dimethylsilylenebis(η^5-4-(2,4-dimethyl-1*H*-pyrrol-1-yl)-2-methylinden-1-yl)]dichlorozirconium(IV) (14). A solution of butyllithium in hexane (1.6 *M*, 10.32 mL, 16.5 mmol) was added to a solution of compound **13** (4.15 g, 8.25 mmol) in Et_2O (50 mL) cooled to −40 °C. The resulting suspension was washed with Et_2O (3×30 mL), and the precipitate was dried. Dilithium derivative **15a** was obtained (4.7 g, 86%). A portion of the product (3.18 g, 4.8 mmol) was suspended in CH_2Cl_2 (100 mL) cooled to −60 °C, and $ZrCl_4$ (1.12 g, 4.8 mmol) was added. The reaction mixture was let to warm up to room temperature and stirred for 20 min. The solution was separated by decantation and concentrated by evaporation. A mixture of *rac*- and *meso*-forms of **14** (6.12 g) was obtained in a ratio of 1 : 1 in 96% yield. The pure *rac*-form of **14** was isolated as an orange powder in a yield of 0.73 g (23%) by recrystallization from ether. ^{1}H NMR for ***rac*-14**, δ: 1.35 (s, 6 H, $Si(CH_3)_2$); 2.08 (s, 6 H); 2.12 (s, 6 H); 2.25 (s, 6 H); 5.88 (s, 2 H); 6.73; 6.75 (both s, 2 H each, H(3), H(5), pyrrolyl); 7.11 (dd, 2 H, J = 8.2 Hz, J = 7.5 Hz); 7.18 (d, 2 H, J = 7.5 Hz); 7.66 (d, 2 H, J = 8.2 Hz). We failed to isolate ***meso*-14** in the pure form, and the spectral data were obtained by the comparison of the spectrum of a mixture of the forms with that of the pure *rac*-form. ^{1}H NMR for ***meso*-14**, δ: 1.25, 1.48 (both s, 3 H each, $Si(CH_3)_2$); 2.02 (s, 6 H); 2.05 (s, 6 H); 2.45 (s, 6 H); 5.86 (s, 2 H); 6.64; 6.73 (both s, 2 H each, H(3), H(5), pyrrolyl); 6.80 (t, 2 H, J = 8.3 Hz, J = 7.5 Hz); 6.97 (d, 2 H, J = 7.5 Hz); 7.68 (d, 2 H, J = 8.3 Hz).

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