Stereoselective Syntheses of Spirane Bridged Semi-titanocenes

Vidar Bjørnstad, Kjell Undheim*
Department of Chemistry, University of Oslo, 0315 Oslo, Norway
Fax +47(22)855507; E-mail: kjell.undheim@kjemi.uio.no
Received 8 November 2007

Abstract: The synthesis of bidentate cyclopentadienyl-alkoxide ligands and their complexation to titanium are described. The focus has been on methodology for stereoselective synthesis of ansa half-sandwich titanocenes with rigid C2- and C3-bridges which are embedded in a spirane scaffold. Intermediate reactions involve tandem acylation-alkylation in the conversion of a carbonyl carbon into a quaternary carbon and rhodium(I)-effected spiroannulations. Titanocene formation involved reaction between the dilithiated ligand and titanium(III) chloride, and subsequent oxidation of the trivalent titanium with lead(II) chloride whereby the semi-metallocene was formed.

Key words: spirane scaffold, ansa semi-titanocenes, C2- and C3-spirane bridges, geminal acylation-allylation, rhodium(I)-catalyzed spiroannulation

A large number of ligands have been developed in the search for specific catalysts for asymmetric synthesis and alkene polymerization. In this connection, the cyclopentadienyl group has assumed a dominant role as a six-electron ligand for metalocene formation. In metalocenes of group IV metals, the bent bis(cyclopentadienyl)ligand system causes substantial steric blocking of the metal-centered reaction site. Hence enhancement of reactivity is observed when the two ligand rings are tied back, and the ligand flexibility is restricted by a common backbone as in Brintzinger-type ansa-metalocene complexes. A common backbone will also reduce the tendency for irreversible dissociation of a ligand in a metal complex and thereby affect reactivity and stereoselectivity. Small-ring spiranes provide a potentially useful scaffold for attachment of configurationally highly oriented coordinating functions for metal complexations. The two rings in spirane are interconnected through a common ring atom and have an orthogonal relationship. Functionalities in the same relative positions in the two rings will have a pseudo-orthogonal relationship. Replacement of one of the cyclopentadienyl moieties in a bridged bis(cyclopentadienyl) ligand with a two-electron ligand may deshield the reactive metal center and increase the catalyst activity. Ansa-amido-ligated half-sandwich metalocenes show high productivity and have the ability to produce unique architecture in polymers with desirable properties because of the more open nature at the active site on the metal. Bridged alkoxy-half-sandwich complexes, however, have received little attention. We wanted to establish a synthetic route for the preparation of rigidly bridged bidentate cyclopentadienyl-alkoxide complexes of titanium. The synthetic targets were half-sandwich metalocenes as shown in Figure 1. The bidentate ligands were to have an annulated η3-indenyl moiety with a pendant oxido-κO-alkyl unit. Metal complexation requires a cis-relationship between the pendant oxidoalkyl and the cyclopentadienyl functionalities. The latter is part of a tetrahydrofluorene system where the C1 carbon will also become the spiro carbon in the final ligand scaffold.

The starting material for spiroannulation was tetrahydrofluoren-1-one. We have modified the literature procedure so that the fluorene 3 has become readily available. The starting material was indene which, under basic conditions, was alkylated in the 3-position with 1-iodobutane to furnish 4-(1H-inden-3-yl)butanenitrile (2). Subsequent cyclization was effected by polyphosphoric acid treatment, which yielded the cyclic ketone 3 in 74% overall yield (Scheme 1). The procedure is well suited for large-scale synthesis, and has repeatedly performed well with 100–200 g preparations.

For the spiroannulation, the initial operation was to convert the fluorene C1 ketone into a spiro-carbon by way of Martin’s efficient tandem acylation-alkylation, and subsequent rhodium(I)-catalyzed hydroacylation. The Martin methodology seemed very attractive, but appears to have enjoyed limited applications. The co-solvent originally used in the tandem acylation-alkylation was the carcinogenic hexamethyphosphoramide. We recommend the use of 1,3-dimethyl-3,4,5,6-tetrahydropyrimidin-2(1H)-one as an equally useful co-solvent for this reaction. The target molecule was the 1-allyl-1-formyl derivative 7 (Scheme 1). The initial reaction of ketone 3 with lithiated diethyl (benzylideneamino)methylphosphonate furnished an 2-azadiene 4. The diethyl (benzylideneamino)methylphosphonate reagent was prepared as described. Treatment with one molar equivalent of butyllithium furnished a lithiated enamine adduct 5 that subsequently was C-alkylated with allyl bromide. Hydrolysis showed that the 9-allyl-1-formyl derivative 6 had been formed in preference to the gem-disubstituted target.
Scheme 1

7. With excess butyllithium, the final product was the diallylated derivative 8. Presumably the initial metalation in substrate 4 is at the indenyl carbon with subsequent C1 alkylation. With excess butyllithium, an adduct-like structure 5 is an intermediate in the reaction towards diallylation and structure 8. In further work, the acidity of the indenyl proton was to be reduced, which was effected by saturation of the 4a,9a-double bond. Once the desired constructions had been completed, the double bond was to be reintroduced later in the reaction sequence.

Diastereoselective saturation of the 4a,9a-double bond with ammonium formate over 10% palladium on charcoal provided compound 9 with a cis-ring junction (Scheme 2). The actual product in the reaction was a mixture of the desired ketone 9 and its reduction product, the alcohol 10. Oxidation of the crude product mixture under Swern conditions provided the ketone 9 in an overall yield of 86%. One-pot acylation-alkylation of the ketone 9 furnished the enal 14, after hydrolysis of the imine 13, in high overall yield (87%) under excellent stereocontrol (de >95%) (Scheme 2). The stereochemistry of the product 14 indicates that the cis-fused ring system is an effective shield for the intermediate lithiated enamine 12 towards the incoming electrophile.

As an alternative to the reduction-reoxidation route hitherto described, we subsequently constructed a less elaborate synthetic pathway (Scheme 3). The carbaldehyde 15 became available in 84% overall yield from fluorenone 3.

Scheme 2
using the Martin conditions and acid cleavage of the intermediate azadiene 4. As the enamine 16 of pyrrolidine, the fluorene was regioselectively allylated in the 1-position and the alkylated product subsequently hydrolyzed to the enal 7 in good yield.

Scheme 3

Cyclopentanones can be prepared from pent-4-enals by intramolecular hydroacylation catalyzed by rhodium(I)–diphosphine complexes. Chloro(η4-cycloocta-1,5-diene)[1,2-bis(diphenylphosphino)ethane]rhodium(I) was an excellent catalyst system,9 which we previously have applied to spirane annulations,10 and this catalyst provided the spiroketone 17 in 93% yield (Scheme 4).

Scheme 4

For the 4a,9a-dehydrogenation in the spiroketone 17, a series of oxidation conditions were investigated and dimethyldioxirane,13 although not a very effective reagent, was by far the best reagent (Scheme 4). The reaction was run in a mixture of acetone and dichloromethane. The product was a stereochemical mixture of alcohols 18, which was dehydrated by 4-toluenesulfonic acid catalysis and heating in tetrahydrofuran and in this process was isomerized to the indene 19 in 79% yield.

The rhodium(I)-catalyzed hydroformylation reaction of substrate 7 resulted in formation of an anomalous product 20 in competition with the desired spiroketone 19 (Scheme 5); reactions were run in benzonitrile. The relative formation of the anomalous product 20 was favored

Scheme 5

Synthesis 2008, No. 6, 962–970 © Thieme Stuttgart · New York
by an increase in temperature. In the absence of a solvent, however, only the spiroketone 19 was obtained in high yield (90%). It was clear that the anomalous product 20 did not originate from ketone 19 since the latter was stable when subjected to the conditions of the reaction. The reaction is initiated by rhodium insertion into the formyl group with formation of a common intermediate (A) and the reaction presumably proceeds through a species B to the ketone 19. An alternatively pathway may involve formation of the rhodium(III) species C followed by rapid β-hydride migration to give D and reductive elimination to the carbaldehyde E, which serves as a substrate for cyclization. Water elimination from the alcohol F and a cationic rearrangement lead to the aromatic structure 20.

Attempts to methylenate the ketone 19 under Wittig conditions were thwarted because of the acidic indene proton. As an alternative, we turned to titanium(IV)-promoted methylenation with bis(iodozincio)methane.14,15 The procedure successfully furnished the methylenated product 21 in 56% yield (Scheme 6). With 9-borabicyclo[3.3.1]nonane, selective addition occurred at the less sterically shielded face of the spirane, reaction of the ad-
duct with hydrogen peroxide under alkaline conditions yielded 92% of the proligand 23.

The second proligand 22 would provide a C2-bridged semi-sandwich metallocene 29 in Scheme 7. Lithium aluminum hydride reduction of the ketone 19 in Scheme 6 provided the desired alcohol 22 as well as its epimeric alcohol in almost equimolar amounts. A modest selectivity was observed with 9-borabicyclo[3.3.1]nonane (de 34%) and Superhydride (de 54%) in tetrahydrofuran at reduced temperature. On the other hand, excellent stereocntrol (de >95%) was achieved with L-Selectride, and the proligand 22 was isolated in 87%.

For the metallocene formation, the proligands 22 and 23 were dilithiated by treatment with two equivalents of butyllithium in diethyl ether at 0 °C (Scheme 7). The respective dilithiated species 24 and 27 were precipitated from the diethyl ether solution. Attempts to produce the semimetallocenes 26 and 29 by reaction between titanium(IV) chloride and the lithium salts 24 and 27 following standard literature procedures failed. However, the corresponding titanium(III) complexes 25 and 28 could be generated from the dianionic salts in reactions with titanium(III) chloride. No attempts were made to isolate the highly reactive titanium(III) complexes. Instead, the titanium(III) complexes were converted in situ into the more stable titanium(IV) complexes 26 and 29. Lead(II) chloride was a good oxidation agent for this purpose.16 The yields of pure semi-metallocenes were low, however, due to the imposed limitations presented by the necessity of inert conditions during workup.

1H NMR and 13C NMR spectra were recorded in CDCl3, respectively at 200 or 300 MHz and 50 or 75 MHz with a Bruker DPX 200 or 300 instrument; residual CHCl3 (δ =7.24) and CDCl3 (δ = 77) were used as internal reference. MS spectra were recorded at 70 eV ionizing potential. IR spectra were measured on a Nicolet Magma 550 spectrophotometer using ATR.

THF was dried by distillation from Na/benzophenone under N2. CH2Cl2 was dried by distillation from CaH2. Anhyd ZnCl2 was heated at 200 °C under 0.013 mbar for 20 h shortly before use. Reactions
requiring dry and/or O₂-free conditions were run under a slight positive pressure of argon gas.

4-(1H-Inden-3-yl)butanenitrile (2) and 2,3,4,9-Tetrahydro-1H-fluoren-1-one (3)

A 1.6 M soln of BuLi in hexane (219 mL, 0.35 mol) was added over 10 min to a soln of freshly distilled indene (40.7 g, 0.35 mol) in anhyd THF (500 mL) at –75 °C under a slight positive pressure of argon gas. The cooling bath was removed, and the mixture left to reach r.t. overnight, cooled to –75 °C and 4-iodobutanenitrile (68.5 g, 0.35 mol) in THF (100 mL) under argon at –75 °C. The mixture was stirred at this temperature for 1 h, before the cooling bath was removed, and the mixture was stirred at r.t. for 20 h. It was then added to a mixture of sat. brine (300 mL) and sat. NH₄Cl (150 mL) and the two phases were separated, the aqueous phase was extracted with Et₂O (3 × 100 mL). The combined Et₂O extracts were dried (MgSO₄) and the solvents distilled off. The residual tanned colored oily material was 4-(1H-inden-3-yl)butanenitrile (2); yield: 63 g (98%).¹¹ H and ¹³C NMR spectra of the crude product were in accordance with the literature.¹¹

The product (2) (63 g, 0.34 mol) and PPA (1 kg) were heated together at 120 °C for 30 min with manual stirring. The viscous mixture was added with stirring to H₂O (4 L) and the mixture heated under reflux for 30 min. The mixture was cooled to r.t. and the solid material was extracted into CH₂Cl₂ (400 mL). The extracts were shaken with sat. NaHCO₃ (10 mL), dried (MgSO₄), and concentrated under vacuum. The residual powder; yield: 47.7 g (74%).¹¹ H and ¹³C NMR spectra were in accordance with the literature.¹¹

N-Benzylidene[1,2,3,4-tetrahydro-9H-fluoren-1-ylidene)methylamine (4)

Diethyl (benzylideneamino)methylphosphonate (0.61 g, 2.4 mmol) was added over 10 min to a soln of 1.6 M BuLi in hexane (15.7 mL, 0.12 mmol) in anhyd THF (40 mL) under argon at –75 °C. The mixture was stirred at this temperature for 1 h before 3 (1.84 g, 10 mmol) was added in one portion. The mixture was kept at 50 °C overnight, hexane (50 mL) was added, and the soln was washed with sat. NH₄Cl (30 mL), dried (MgSO₄), and the filtrate evaporated to dryness. Flash chromatography (silica gel 60, EtOAc–hexane, 1:6) furnished 4 as a yellow oil; yield: 2.44 g (85%).²

¹¹ H NMR (200 MHz, CDCl₃): δ = 2.03 (t, J = 5.7 Hz, 2 H, H₄), 2.6–2.8 (m, 2 H, H₃), 3.07 (t, J = 5.3 Hz, 2 H, H₂), 3.60 (s, 2 H, H₉), 7.12 (s, 1 H, =CHN), 7.2–7.4 (m, 7 H, H-Ar), 7.5–7.6 (m, 2 H, H-Ar), 8.24 (s, 1 H, CH=).²

¹¹C NMR (50 MHz, CDCl₃): δ = 22.8 (C₃), 23.1 (C₄), 25.6 (C₂), 36.1 (C₉), 119.4 (=CHN), 123.8 (CH=), 125.7 (CH₂), 126.2 (CH₂), 128.5 (CH₂), 129.0 (CH₂), 130.6 (CH₂), 135.0 (C=Ar), 135.3 (C=Ar), 137.2 (C₉a), 139.2 (C=Ar), 142.8 (C=Ar), 143.0 (C₄a), 157.4 (CH=N).²

MS (EI, 70 eV): m/z (%) = 385 (5) [M⁺], 354 (18), 338 (100).²

MS (EI, 70 eV): m/z (%) = 385 (5) [M⁺], 354 (18), 338 (100).²


1-Allyl-2,3,4,9-tetrahydro-1H-fluoren-1-one (7)

A soln of 15 (23.0 g, 116 mmol) and pyrrolidine (12 g, 169 mmol) in benzene (100 mL) was refluxed with constant removal of H₂O with a Dean–Stark trap for 6 h under a slight positive pressure of argon gas. The soln was evaporated and the residual pyrrolidine enamine dissolved in MeCN (80 mL). Allyl bromide (28.0 g, 231 mmol) was added to the enamine soln and the mixture heated at gentle reflux under argon for 40 h. 2 M HCl (100 mL) was added to the cold mixture, which was stirred under argon (r.t. overnight. The mixture was extracted with hexane (3 × 100 mL) and the combined extracts were washed with H₂O (100 mL) and NaHCO₃ (100 mL), dried (MgSO₄), the filtrate evaporated, and the residual material subjected to flash chromatography (silica gel 60, EtOAc–hexane, 1:20) giving a yellow oil; yield: 21.1 g (77%).

¹¹ H NMR (300 MHz, CDCl₃): δ = 1.7–1.9 (m, 3 H, H₂H₃), 2.0–2.1 (1 H, H₂β), 2.4–2.6 (m, 4 H, H₄, CH₂=CH₂=CH₂), 3.0–3.4 (m, 2 H, H₉), 5.0–5.1 (m, 2 H, CH=CH₂), 5.6–5.7 (m, 1 H, CH=CH₂), 7.2–7.4 (m, 4 H, H₅–H₆), 9.61 (s, 1 H, CHO).

¹¹C NMR (75 MHz, CDCl₃): δ = 19.2 (CH₃), 22.1 (CH₂), 28.4 (CH₂), 37.1 (CH₂=CH₂), 39.3 (C₉), 52.1 (C₁₁), 118.5 (CH₂=CH₂), 118.6 (CH=Ar), 123.6 (CH=Ar), 124.9 (CH=Ar), 126.3 (CH=Ar), 133.3 (CH=CH₂), 137.2, 141.7, 143.2, 144.8, 201.9 (CHO).

MS (EI, 70 eV): m/z [M⁺] calcd for C₁₇H₁₈O: 238 (41) [M⁺], 223 (50), 209 (100), 197 (39), 167 (40).


19R,9S*)-1-Diallyl-2,3,4,9-tetrahydro-1H-fluorene-1-carbaldehyde (8)

Diethyl (benzylideneamino)methylphosphonate (0.61 g, 2.4 mmol) was added over 5 min to a soln of 1.6 M BuLi in hexane (1.5 mL, 2.4 mmol) in anhyd THF (10 mL) under argon at –78 °C. The mixture was stirred at this temperature for 1 h before 3 (0.37 g, 2.0 mmol) was added in one portion. The mixture was heated under reflux for 2 h, cooled to –78 °C and 1.6 M BuLi in hexane (2.5 mL, 4.0 mmol) was added over 10 min. The mixture was stirred at –78 °C for 2 h and then allyl bromide (1.2 g, 10 mmol) was added over 10 min and the mixture stirred at r.t. for 10 h. 3 M HCl (10 mL) was added and the mixture stirred vigorously under argon at r.t. for 10 h. Sat. aq brine (5 mL) was added and the two phases of the cold mixture were separated, the aqueous phase was extracted with Et₂O (3 × 10 mL); the combined organic solns were washed with aq sat. NaHCO₃ (10 mL), dried (MgSO₄), and concentrated under vacuum. The residual oil was subjected to flash chromatography (silica gel 60, EtOAc–hexane, 1:4) to give a yellow oil; yield: 0.29 g (52%).
The mixture of the ketone 9 from above and its alcohol epimers 10 (129 mg) was subjected to flash chromatography (silica gel 60, EtOAc–hexane, 1:10) for analytical purposes. Separation yielded 2,3,4,9-tetrahydro-1H-fluoren-1-ol (61 mg) and an inseparable mixture of the alcohol epimers 2,3,4,4a,9,9a-hexahydro-1H-fluoren-1-ol (10) (51 mg).

IR (film): 3333 (s), 3040 (w), 2995 (w), 2904 (s), 2830 (s), 1420 (m) cm⁻¹.

1H NMR (300 MHz, CDCl₃): δ = 1.5–1.9 (m, 4 H, H₃, H₄), 2.1–2.8 (m, 6 H, H₂, CH₂CH=CH₂), 3.4–3.5 (m, 1 H, H9), 4.8–5.1 (m, 4 H, CH=CH₂), 5.2–5.4 (m, 1 H, H-9-allyl-CH=CH₂), 5.5–5.7 (m, 1 H, H-1-allyl-CH=CH₂), 7.1–7.4 (m, 4 H, H₅–H₈), 9.6 (s, 1 H, CHO).

13C NMR (75 MHz, CDCl₃): δ = 18.7 (C3), 22.2 (C2), 30.1 (C4), 34.0 (9-allyl-CH₃), 38.9 (1-allyl-CH₃), 48.2 (C9), 51.4 (C1), 117.3 (CH=CH₂), 118.4 (CH₂), 118.4 (CH-5, Ar), 121.3 (CH-5, Ar), 125.0 (CH-7, Ar), 133.7 (9-allyl-CH₃CH₂), 139.4, 142.3, 143.5, 146.6, 202.7 (CHO).

MS (EI, 70 eV): m/z (%) = 278 (38) [M⁺], 249 (50), 237 (91), 208 (52), 179 (48), 165 (100).


Et₄N (21.0 g, 0.21 mol), HCO₂H (8.28 g, 0.18 mol), and 10% Pd/C (2.65 g, 2.5 mmol Pd) were added to a solution of 3 (8.4 g, 0.1 mol) in DMF (60 mL). The mixture was stirred at 60 °C for 1 h, filtered through a bed of Celite and the filtrate poured into H₂O (500 mL). The cold mixture was extracted with Et₂O (4 × 150 mL), and the combined extracts were washed with H₂O (2 × 150 mL), dried (MgSO₄), and evaporated to dryness. The residual material was further dried under vacuum overnight to give 17.5 g of a 1:1 mixture of 9/10.

The mixture of the ketone 9 and an inseparable mixture of volatile impurities 10 was resolved over 10 min, the two layers separated and the aqueous phase extracted with Et₂O (3 × 50 mL). The combined ether extracts were dried (MgSO₄), evaporated to dryness, and the residual material (MeOH, 2.5 mL/g) to give a solid product; yield: 12.8 g (69%). The mother liquor from the chloroform extraction was stirred at room temperature for 1 h before allyl bromide (16.9 g, 140 mmol) was added over 10 min, and the mixture stirred at r.t. for 30 h. The mixture was filtered, and the filtrate evaporated. The residue was dried at 50 °C under vacuum overnight for removal of residual solvent.

The residual brown oil was subjected to flash chromatography (silica gel 60, EtOAc–hexane, 1:5) to give a yellow oil; yield: 7.3 g (87%).

1H NMR (300 MHz, CDCl₃): δ = 1.0–1.2 (m, 1 H, H₄α), 1.5–2.0 (m, 5 H, H₂, H₃, H₄β), 2.3–2.9 (m, 5 H, H₉, H₉α, CH₃CH₂CH₃), 3.16 (dt, J = 6.0, 12.1 Hz, 1 H, H₄α), 5.1–5.2 (m, 2 H, CH₂CH₃), 5.6–5.8 (m, 1 H, CH=CH₂), 7.2–7.3 (m, 4 H, H₅–H₈), 9.63 (s, 1 H, CHO).

13C NMR (75 MHz, CDCl₃): δ = 18.8 (C13), 23.1 (CH₂), 29.5 (C4), 31.5 (C9), 37.8 (CH₂CH₂), 41.8 (C4a), 44.7 (C9a), 50.5 (C1), 118.2 (CH=CH₂), 122.9 (CH-5, Ar), 126.3 (CH-7, Ar), 126.35 (CH-7, Ar), 132.9 (CH=CH₂), 141.2 (C-4), 147.9 (C-5), 205.7 (CHO).

MS (EI, 70 eV): m/z (%) = 240 (40) [M⁺], 222 (42), 211 (17), 199 (22), 169 (56), 143 (95), 130 (100).


A solution of the ketone 10 (129 mg) was subjected to flash chromatography (silica gel 60, EtOAc–hexane, 1:10) for analytical purposes. Separation yielded 2,3,4,9-tetrahydro-1H-fluoren-1-ol (61 mg) and an inseparable mixture of the alcohol epimers 2,3,4,4a,9,9a-hexahydro-1H-fluoren-1-ol (10) (51 mg).
chromatography (silica gel 60, EtOAc–hexane, 1:4) furnished a yellow oil; yield: 16.6 g (84%).

1H NMR (300 MHz, CDCl3): δ = 1.8–2.2 (m, 4 H, H2, H3), 2.3–2.6 (m, 3 H, H1, H4), 3.3–3.4 (m, 2 H, H9), 7.2–7.4 (m, 4 H, H5–H8), 9.71 (d, J = 1.9 Hz, 1 H, CHO).

13C NMR (75 MHz, CDCl3): δ = 20.8 (CH2), 22.0 (CH2), 23.3 (CH3), 39.2 (C2), 50.1 (C1), 118.5 (CH=Ar), 123.5 (CH=Ar), 125.0 (CH=Ar), 127.4 (CH=Ar), 134.7, 140.9, 143.4, 145.6, 202.1 (CHO).

IR (film): 3035 (m), 3016 (m), 2992 (m), 2907 (s), 2863 (s), 1720 (m), 1458 (m), 1380 (m), 1180 (m), 1152 (m), 1090 (s), 1020 (m), 988 (m), 918 (m).

Synthesis 2008, No. 6, 962–970 © Thieme Stuttgart · New York
dropwise. The mixture was allowed to reach r.t. over 45 min then 19 (0.762 g, 3.20 mmol) in THF (3 mL) was added over 5 min. The mixture was stirred for 1 h, hexane (25 mL) was added, and the soln was washed with sat. brine–sat. NaHCO3 (1:1, 20 mL) and subsequently with sat. brine (20 mL). The brine washings were extracted with hexane (2 × 10 mL) and the combined extracts were dried (MgSO4), evaporated, and the residual material subjected to flash chromatography (silica gel 60, hexane). The product was a pale yellow oil; yield: 0.42 g (56%).

**1H NMR (300 MHz, CDCl3):** δ = 1.7–2.0 (m, 6 H, CH3), 2.5–2.7 (m, 4 H, CH2), 3.30 (dt, J = 19.0 Hz, 1 H, H9a), 3.08 (dt, J = 18.9 Hz, 1 H, H9β), 5.72 (2H, =CH2), 7.3–7.6 (m, 4 H, H5–H8).

**13C NMR (75 MHz, CDCl3):** δ = 13.5 (CH3), 20.6 (CH2), 22.3 (CH2), 29.9 (CH2), 33.4 (CH2), 37.0 (C=C), 38.6 (C3), 52.3 (C1), 117.8 (s=CH2), 123.3 (CH- Ar), 123.8 (CH- Ar), 125.5 (CH- Ar), 126.0 (CH-Ar), 136.6, 142.8, 145.5, 145.9, 146.5.

**MS (EI, 70 eV):** m/z (%) = 236 (100) [M]+, 221 (12), 193 (12), 165 (57), 141 (49).

**HRMS (EI, 70 eV):** m/z [M]+ calcld for C18H22S: 254.1693; found: 254.1693.

(1R*,2R*)-2,3',4',9'-Tetrahydrospirop[cyclopentane-1,1'-[1H]-fluoren]-2-ol (22)

A 1 M soln of L-Selectride in THF (8.0 mL, 8 mmol) was added to a so1n of 19 (1.60 g, 6.7 mmol) in anhyd THF (5 mL) in an ice bath and the mixture stirred at this temperature overnight. NaOH (1.3 g, 33 mmol) in H2O (10 mL) was added followed by 30% H2O2 (3.7 g, 33 mmol). The mixture was stirred vigorously at r.t. for 2 h. Hexane (10 mL) was added, the two phases were separated and the aqueous phase was extracted with Et2O (2 × 5 mL). The combined organic solns were washed with sat. brine (10 mL), dried (MgSO4), and the mixture stirred at this temperature overnight. NaOH (1.3 g, 33 mmol) in H2O (10 mL) was added followed by 30% H2O2 (3.7 g, 33 mmol). The mixture was stirred vigorously at r.t. for 7 h. Most of the H2O2 (3 × 10 mL) was added and the mixture extracted with Et2O (3 × 5 mL). The combined organic extracts were dried (MgSO4), the solvent distilled off, and the residual material subjected to flash chromatography (silica gel 60, EtOAc–hexane, 1:2) which yielded a white solid; yield: 92%; mp 76–78 °C.

**1H NMR (200 MHz, CDCl3):** δ = 1.4–1.8 (m, 4 H, CH2), 1.9–2.3 (m, 4 H, CH2), 2.4–2.7 (m, 4 H, CH2), 3.3–3.4 (m, 2 H, H9), 3.7–3.8 (m, 1 H, OH), 4.17 (t, J = 4.6 Hz, 1 H, H2), 7.2–7.5 (m, 4 H, H5–H8).

**13C NMR (50 MHz, CDCl3):** δ = 25.5 (CH3), 25.9 (CH2), 27.4 (CH3), 33.0 (CH4), 34.1 (CH4), 39.4 (CH4), 44.6 (C9), 53.6 (C1), 78.9 (C2), 117.4 (CH- Ar), 123.1 (CH- Ar), 123.3 (CH- Ar), 125.8 (CH- Ar), 138.5, 142.1, 145.4, 146.7.

**MS (EI, 70 eV):** m/z (%) = 240 (100) [M]+, 222 (23), 194 (28), 169 (46), 153 (17).

**HRMS (EI, 70 eV):** m/z [M]+ calcld for C18H22O: 254.1516; found: 254.1516.

(1R*,2R*)-2,3',4',9'-Tetrahydrospirop[cyclopentane-1,1'-[1H]-fluoren]-2-ol (23)

A 0.5 M soln of 9-BBN in THF (4.4 mL, 2.2 mmol) and 21 (0.42 g, 1.8 mmol) under argon was stirred at r.t. for 20 h. A mixture of EtOH (1 mL), H2O (2 mL), NaOH (0.40 g, 10 mmol), and 30% H2O2 (1.2 g, 10 mmol) was added and the mixture stirred vigorously at 50 °C for 3 h. H2O (20 mL) was added and the mixture extracted with Et2O (3 × 10 mL). The combined organic extracts were dried (MgSO4), the solvent distilled off, and the residual material subjected to flash chromatography (silica gel 60, EtOAc–hexane, 1:2) which yielded a white solid; yield: 92%; mp 76–78 °C.

**1H NMR (300 MHz, CDCl3):** δ = 1.6–2.0 (m, 10 H, CH2), 2.1–2.3 (m, 2 H, H2, OH), 2.4–2.5 (m, 2 H, H6), 3.2–3.3 (m, 2 H, H9), 4.0–4.2 (2 H, CH2-OH), 7.1–7.4 (m, 4 H, H5–H8).

**13C NMR (75 MHz, CDCl3):** δ = 13.9 (CH3), 20.1 (CH3), 22.5 (CH2), 33.0 (CH4), 36.8 (C4), 39.5 (C9), 39.6 (CH3), 45.8 (C2), 53.8 (C1), 79.9 (CH-CH2), 117.8 (CH- Ar), 123.1 (CH- Ar), 123.9 (CH- Ar), 126.1 (CH- Ar), 137.2, 142.5, 145.3, 145.6.

**MS (EI, 70 eV):** m/z (%) = 254 (39) [M]+, 236 (100), 223 (27), 193 (14), 167 (65).

**HRMS (EI, 70 eV):** m/z [M]+ calcld for C18H22O: 254.1671; found: 254.1693.

**Semi-titanocene Formation; General Procedure**

Compound 23 or 22 (2.00 mmol) was dissolved in anhyd Et2O (10 mL), the soln cooled in an ice-water bath and 1.6 M BuLi (2.8 mL, 4.5 mmol) in hexane added dropwise under argon. The mixture was stirred overnight at r.t. and anhyd pentane (20 mL) added to precipitate the salt. Most of the supernatant was removed from the precipitated diltium salt which was dissolved in anhyd THF (15 mL). A syringe was used to transfer the soln into a stirred suspension of TiCl4 (0.308 g, 2.00 mmol) in anhyd THF (75 mL) at 0 °C. The mixture was left to reach r.t. overnight. Dried PbCl2 (0.278 g, 1.00 mmol) was added and the mixture stirred at r.t. for 7 h. Most of the solvents were removed at reduced pressure and the precipitate triturated with anhyd CH2Cl2 (30 mL). Filtration under argon and precipitation from CH2Cl2 yielded a dark colored solid which was ground to a powder with a spatula under argon, triturated with anhyd pentane (20 mL) with stirring and the solvent decanted off. Re-
moval of the remaining volatiles under high vacuum furnished the crude semi-titanocenes.

**Dichloro{(1R*,2R*)-2-(oxido-κ-O-methyl)-1',2',3',4'-tetrahydro-spirocyclopentane-1,1'-(4a,4b,8a,9a-η)-fluorenyl}titanium** (26)
The crude product, obtained as above, was subjected to sublimation at 140 °C at 0.067 mbar to give a red amorphous solid; yield: 0.120 g (16%); mp 210 °C (dec).

1H NMR (300 MHz, CDCl3): δ = 1.8–2.3 (m, 9 H, CH2), 2.6–2.8 (m, 2 H, CH2), 3.2–3.3 (m, 1 H, CH3), 5.3–5.5 (m, 2 H, CH OTi), 7.00 (s, 1 H, H9), 7.4–7.5 (m, 2 H, H6), 7.6–7.8 (m, 2 H, H7, H9) ppm.

13C NMR (75 MHz, CDCl3): δ = 24.7, 7.2 Hz, 1 H, H4 ppm.

HRMS (EI, 70 eV): \[m/z \text{ [M]}^+ \text{ calcd for C}_{18}\text{H}_{20}\text{Cl}_{2}\text{OTi: 370.0371; found: 356.0214, 370.0371} \]

---

**References**


---

Synthesis 2008, No. 6, 962–970 © Thieme Stuttgart - New York