An Enantioselective Approach to Cytotoxic Norcalamenenes via Electron-Transfer-Driven Benzylic Umpolung of an Arene Tricarbonyl Chromium Complex

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Dedicated to Professor Wolfgang Steglich on the occasion of his 70th birthday.

Abstract: An efficient enantioselective total synthesis of (*R*)-1-isopropenyl-6-methoxy-7-methyl-1,2,3,4-tetrahydronaphthalene, the dehydro-analog of the cytotoxic norsesquiterpene (*R*)-7-demethyl-2-methoxycalamenene, was achieved in seven steps starting from 6-methoxytetralone. The synthesis exploits the specific reactivity and stereochemistry of planar chiral η^6-arene-$Cr(CO)_3$ complexes. In a key step, a $Cr(CO)_3$-complexed benzylic anion, regioselectively generated by means of electron- transfer-driven benzylic umpolung, is diastereoselectively alkylated with acetyl chloride.

Key words: arene complexes, asymmetric synthesis, chromium, electron-transfer, natural products

The demethyl calamenene **1** and some related norsesquiterpenes were isolated by Bohlmann et al. from the plant *Heterotheca grandiflora* in 1979.[1] Three syntheses of *rac*-**1** using standard methodology have been published.[2] The main challenge for synthetic chemistry posed by such compounds, however, is the control of the absolute configuration of the benzylic stereocenter. The only enantioselective synthesis of **1** and its dehydro analogue **2** (Figure 1) was reported in 1995 by Tietze and Raschke.[3] These authors also identified **1** as a potent cytotoxic agent against cells of the human bronchial adenocarcinoma A 549. The Tietze synthesis utilizes an elegant enantioselective (silane terminated) Heck reaction[4] as the key step and reaches the target molecule in eleven steps starting from 3-(3-methoxyphenyl)propanol.

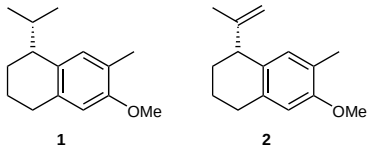
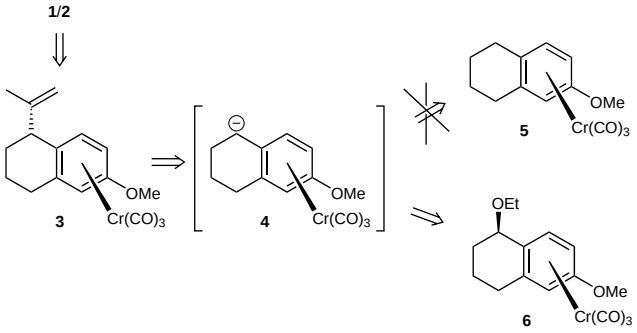


Figure 1 Structures of the cytotoxic *nor*-sequiterpene **1** and its dehydro-analog **2**

In the course of our program aimed at the use of planar chiral arene-$Cr(CO)_3$ complexes as synthetic building blocks,[5] we were interested in developing an efficient alternative access to **1** and related compounds in order to probe and demonstrate the power of arenechromium chemistry.[6] We disclose here a short and highly selective synthesis of **2**, which makes use of a methodology developed in this laboratory, i.e. the benzylic umpolung of arene-$Cr(CO)_3$ complexes.[7]

As a precursor for the synthesis of **1** and **2** we considered the chromium complex **3** as a suitable candidate, which would allow aromatic methylation in the position *ortho* to the methoxy group. The diastereoselective introduction of the isopropenyl side chain could then be imagined by benzylic alkylation of the planar chiral anionic complex **4** from the less hindered face of the ligand. This intermediate **4** represents a $Cr(CO)_3$-stabilized benzylic anion[8,9] which cannot be prepared by regioselective deprotonation of the substituted tetralin-$Cr(CO)_3$ derivative **5** (Scheme 1).[10] Nevertheless, it seemed feasible to generate **4** from the chiral (nonracemic) ethoxy substituted complex **6** by treating it with a single electron reducing agent according to our method for the benzylic umpolung of such complexes.[7]



Scheme 1 Retrosynthetic Analysis

Our synthesis (Scheme 2) started from the commercially available ketone **7**, which was first converted to the tetralol **8** by enantioselective borane reduction (CBS reduction)[11] in the presence of the oxazaborolidine catalyst **12** [prepared from (*S*)-α,α-diphenylprolinol and methylboronic acid]. Dichloromethane proved to be the solvent of choice in this case giving the product **8** in 96% yield and an enantiomeric purity of 94% ee.[12] Less satisfying results (89% ee, 85% yield) were obtained in THF as the solvent commonly used in such reactions. Diastereoselective complexation of **8** was achieved, even on multigram scale,

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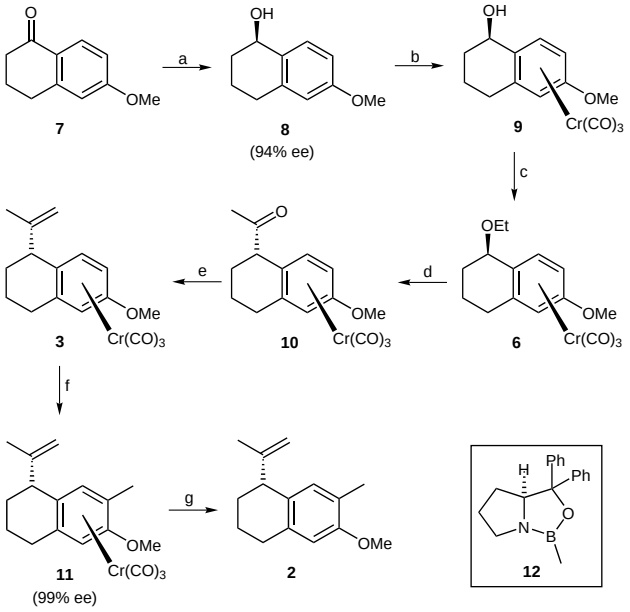
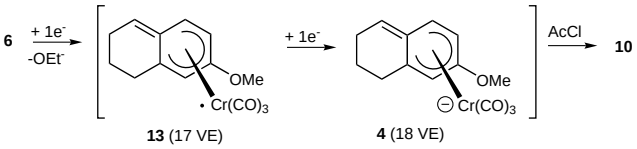
by refluxing it with $Cr(CO)_6$ in a 1:1 mixture of dibutyl ether and heptane containing small amounts of THF.[13] The diastereoselectivity was greater than 90% as determined by HPLC from the crude reaction mixture. After removing the significantly more polar (undesired) *exo*-diastereomer by flash chromatography, the pure crystalline *endo*-complex **9** was obtained in 84% yield. Reaction of **9** with ethyl iodide and powdered KOH in DMSO[14] afforded the desired ether **6**, the key intermediate for the planned benzylic alkylation.



Scheme 2 *Reagents and conditions*: (a) **12** (30 mol%), BH_3·DMS (1.5 equiv), CH_2Cl_2, r.t., 3 h, 96%; (b) $Cr(CO)_6$ (1.5 equiv), Bu_2O–*n*-heptane–THF (10:10:1), reflux, 42 h, 84%; (c) KOH (4 equiv), EtI (2 equiv), DMSO, r.t., 3 h, recryst., 74%; (d) LiDBB (excess), THF, –78 → –40 °C, 1 h, AcCl (3 equiv), –40 °C → r.t., 2.5 h, 61%; (e) $TiCl_4$, Zn, CH_2Br_2, THF, CH_2Cl_2, 0 °C, 15 min, → r.t., 4 h, 76%; (f) *n*-BuLi (1.2 equiv), –70 → –25 °C, 1.5 h, → –45 °C, MeI (2.2 equiv), → –20 °C, 40 min, r.t., 70 min, recryst., 71%; (g) sunlight, air, Et_2O, 6 h, 97%

Following the standard protocol developed before,[7] compound **6** was first reacted with an excess (4 equiv) of lithium 4,4′-di-*tert*-butylbiphenyl (LiDBB)[15] at –78 °C, and the resulting anion **4** was trapped with acetyl chloride to give exclusively the *exo*-acetylated product **10** in 61% yield.

The facile conversion of **6** under the conditions described can be understood in terms of the electron-transfer (ET)-driven process shown in Scheme 3. After the initial transfer of an electron from the single electron reducing agent LiDBB and loss of the ethoxy anion, a 17 VE (valence electron) radical intermediate **13** is formed. This is rapidly reduced by a second ET to the more stable anionic 18 VE species **4**, from which the product **10** arises by benzylic *exo*-acylation as a sole diastereomer.



Scheme 3 Electron-transfer-driven formation of the benzylic anion **4**

Having succeeded in preparing the benzylic acylated tetralin derivative **10** in a highly regio- and diastereoselective manner, methylenation of **10** employing the method of Lombardo (CH_2Br_2, Zn, $TiCl_4$)[16] afforded complex **3** in 76% yield. Remarkably, the time required for the preparation of the reagent was reduced considerably by using ultrasound (4 h at 0 °C versus 3 d at 5 °C in the original procedure). The regioselective introduction of the methyl group at C-3 was then achieved by *ortho*-lithiation of **3** with *n*-butyllithium and subsequent addition of methyl iodide. After chromatographic separation of the bis-methylated by-product **14** (ca. 15%) and recrystallization in order to remove small amounts (ca. 5%) of the undesired regioisomer **15** (Figure 2), the pure complex **11** was obtained in 71% yield.

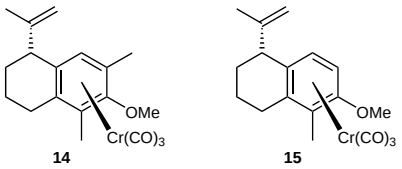


Figure 2 By-products **14** and **15** formed during the preparation of **11**

Complex **11** showed an enantiomeric purity of 99% ee as determined by HPLC.[12] Obviously, an enantiomeric enrichment had occurred during recrystallization at the stage of **6** or **11.** The relative and absolute configuration of complex **11** was confirmed by X-ray crystal structure analysis (Figure 3), which shows the molecule preferring a pseudochair conformation with the isopropenyl side chain in a pseudo-equatorial position.[17]

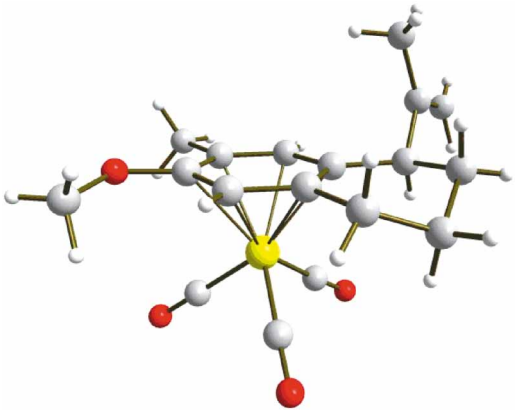


Figure 3 Structure of complex **11** in the crystalline state

Simple exposure of an etheral solution of **11** to sunlight and air finally led to compound **2** in 97% yield, which exhibited identical characteristic properties as the sample reported by Tietze and coworkers.

In conclusion, we have synthesized the target compound **2** in a short and efficient reaction sequence exploiting both chemical and stereochemical properties of arene-$Cr(CO)_3$ complexes. Starting from a central chiral compound **8** the absolute stereochemical information is transferred in the complexation step to the planar chiral metal complex substructure, from which it is transferred back during the benzylic alkylation to a lasting chiralilty center. Thus, this synthesis represents another example for the concept of *self-regeneration of a stereocenter*.[18] The synthesis requires only seven steps for the conversion of 6-methoxytetralone (**7**) to the target molecule **2** in ca. 20% overall yield. It demonstrates the usefulness of the electron-transfer-driven umpolung of $Cr(CO)_3$-complexed benzylic ethers for the regioselective generation of a $Cr(CO)_3$-complexed benzylic anion. As both carbon substituents at the tetralin core are introduced by alkylation, it should be possible to use the same strategy for the preparation of a broad range of structurally related compounds with different side chains.[19]

NMR spectra were recorded on Bruker AM 270, AM 400, AM 500 spectrometers. Proton chemical shifts are reported in ppm (δ) relative to the solvent reference ($CDCl_3$, δ = 7.24). Data are reported as follows: chemical shift (multiplicity [singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), broad (br) and pseudo (Ψ)], coupling constants [Hz], integration). Carbon chemical shifts are reported in ppm (δ) relative to the solvent resonance as the internal standard ($CDCl_3$, δ = 77.0). Multiplicities were determined via DEPT and are given as follows: q (CH_3), t (CH_2), d (CH), s (quaternary carbons). IR spectra were recorded on a Nicolet Magna FT-IR using the ATR technique (attenuated total reflectance). Mass spectra were obtained on a Finnigan MAT 95 ST spectrometer (70 eV). Enantiomeric purities were determined by analytical HPLC using Daicel Chiracel OJ column on a Merck-Hitachi HPLC system with pump L 6200 and UV detector L 4000. Optical rotations were measured on Perkin-Elmer 241 polarimeter at 20 °C, concentrations (*c*) are given in g/100 mL. Preparative thin layer chromatography (PTLC) was carried out using a chromatotron Harrison Research 7924 T on glass plates coated with 1–4 mm layers of silica gel containing gypsum (Merck PF 60F 254). The sonochemical transformation was carried out using a Branson Sonifier 250 apparatus.

(1*R*)-6-Methoxy-1,2,3,4-tetrahydronaphthalene-1-ol (8)

In a flame dried Schlenk flask equipped with a pressure equalizing dropping funnel (charged with 40 mL of 4 Å molecular sieves, and topped with a reflux condenser), a solution of (*S*)-diphenylprolinol (861 mg, 3.4 mmol) and methylboronic acid (204 mg, 2.00 mmol) in anhyd toluene (96 mL) was refluxed for 15 h under argon. After removal of the solvent, the residue (the oxazaborolidine **12**) was dried in vacuo and then dissolved in anhyd CH_2Cl_2 (10 mL). Then, a 2 M solution of $BH_3{\cdot}SMe_2$ (8.5 mL) was added and the mixture was stirred for 15 min before a solution of 6-methoxytetralone (**7**; 2.00 g, 11.35 mmol) in anhyd CH_2Cl_2 (9 mL) was added via a syringe pump over a period of 2 h. After stirring for 1 h at r.t., MeOH (ca. 15 mL) was added carefully (gas evolution) and all the solvents were evaporated in vacuo. The crude product was purified by flash chromatography (EtOAc– cyclohexane, 1:1) to yield 1.939 g (96%) of **8** as a colorless oil (94% ee as determined by HPLC). HPLC: isopropyl alcohol–hexane (20:80), UV-detection at 256 nm; t_r (*ent*-**8**) = 12.5 min, t_r (**8**) = 14.4 min; $[\alpha]_{589}$ –23.3, $[\alpha]_{578}$ –24.4, $[\alpha]_{546}$ –28.1, $[\alpha]_{436}$ –52.3.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.68–1.82 (1 H, m), 1.88–2.02 (3 H, m), 2.46–2.55 (1 H, m), 2.56–2.66 (1 H, m), 3.79 (3 H, s), 4.72 (1 H, br s), 6.63 (1 H, d, *J* = 3.0 Hz); 6.77 (1 H, dd, *J* = 3.0, 8.5 Hz); 7.33 (1 H, d, *J* = 8.5 Hz).

(1*R*,4a*S*)-Tricarbonyl-[η^6-(6-methoxy-1,2,3,4-tetrahydronaphthalene-1-ol)]chromium(0) (9)

A flame dried Schlenk flask equipped with a reflux condenser and a mercury bubbler was charged with 6-methoxytetralol (**8**; 1.99 g, 11.2 mmol), $Cr(CO)_6$ (3.70 g, 16.8 mmol), anhyd dibutyl ether (65 mL) and anhyd *n*-heptane (65 mL). The apparatus was evacuated and flushed with argon several times before adding anhyd THF (6.5 mL). The mixture was refluxed under stirring for 42 h and then allowed to cool to r.t. under argon. After filtration and concentration in vacuo, the crude product was purified by flash chromatography (CH_2Cl_2) to yield pure **9** as a yellow crystalline solid (2.97 g, 84%); mp 101 °C; $[\alpha]_{589}$ –20.9, $[\alpha]_{578}$ –23.9, $[\alpha]_{546}$ –35.1 (*c* = 0.33, $CHCl_3$).

IR: 3436, 3091, 2944, 2870, 1951, 1862, 1541, 1475, 1458, 1439, 1393, 1271, 1235, 1151, 1112, 1069, 1044, 1022, 999, 971, 845, 687, 671 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.65–1.74 (2 H, m), 1.92–2.02 (2 H, m), 2.60–2.68 (1 H, m), 2.76–2.86 (1 H, m), 3.74 (3 H, s), 4.83–4.44 (1 H, m), 4.94 (1 H, d, *J* = 2.5 Hz), 5.04 (1 H, dd, *J* = 2.5, 7.0 Hz), 5.91 (1 H, d, *J* = 7.0 Hz).

^{13}C NMR (67.7 MHz, $CDCl_3$): δ = 18.7 (t), 28.2 (t), 32.2 (t), 55.6 (q), 65.6 (d), 77.9 (d), 76.9 (d), 94.5 (d), 107.9 (s), 113.6 (s), 142.7 (s), 233.2 (s).

MS (DIPMS: 90 °C): *m*/*z* (%) = 314 ([M]$^+$, 28), 258 (9), 230 (28, [M]$^+$ – 3 CO), 228 (19), 212 (17), 210 (28), 162 (12), 161 (100), 149 (10), 148 (11), 111 (11), 109 (10), 97 (16).

HRMS: *m*/*z* calcd for $C_{14}H_{14}CrO_5$: 314.0246; found: 314.0241.

(1*R*,4a*S*)-Tricarbonyl[η^6-(1-ethoxy-6-methoxy-1,2,3,4-tetrahydronaphthalene)]chromium(0) (6)

Powdered KOH (1.45 g, 25.9 mmol) and complex **9** (2.0 g, 6.47 mmol) were suspended in anhyd DMSO (15 mL) and the mixture was stirred for 15 min at r.t. to give a brownish solution. The mixture was then cooled to 15 °C and EtI (1 mL, 12.9 mmol) was added. After 4 h at r.t., TLC control indicated complete conversion of **9**. The mixture was partitioned between H_2O and *t*-butyl methyl ether (MTBE) and the aqueous phase was extracted several times with MTBE. The combined organic layers were washed with H_2O and brine, dried ($MgSO_4$) and the solvent was removed under reduced pressure. The resulting yellow solid was recrystallized from MTBE–hexane. An additional crop of pure **6** was obtained from the mother liquor after PTLC (hexane–EtOAc, 5:1). Complex **6** was obtained as a yellow solid (combined yield: 1.64 g, 74%); mp 132 °C; $[\alpha]_{589}$ –25.9, $[\alpha]_{546}$ –39.5 (*c* = 0.495, $CHCl_3$).

IR: 2975, 2943, 2869, 1951, 1863, 1541, 1475, 1440, 1394, 1270, 1150, 1114, 1023, 671 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.29 (3 H, t, *J* = 7.0 Hz), 1.56–1.70 (2 H, m), 1.88–2.02 (2 H, m), 2.56–2.64 (1 H, m), 2.76–2.86 (1 H, m), 3.49 (1 H, m), 3.71 (3 H, s), 3.76 (1 H, m), 4.08 (1 H, br dd, *J* = 5.0, 7.0 Hz), 4.86 (1 H, d, *J* = 2.0), 5.01 (1 H, dd, *J* = 2.0, 7.5 Hz), 5.80 (1 H, d, *J* = 7.5 Hz).

^{13}C NMR (67.7 MHz, $CDCl_3$): δ = 15.3 (q), 18.8 (t), 27.7 (t), 28.1 (t), 55.5 (q), 64.6 (t), 72.5 (d), 76.2 (d), 76.4 (d), 94.2 (d), 105.2 (s), 112.1 (s), 142.9 (s), 233.9 (s).

MS: *m*/*z* (%) = 342 (45), 286 (20), 258 (58), 256 (39), 214 (100), 212 (98), 197 (12), 162 (10), 161 (85), 115 (10), 91 (10), 69 (14), 52 (96).

HRMS: *m*/*z* calcd for $C_{16}H_{18}CrO_5$: 342.0559; found: 342.0555.

(1*S*,4a*S*)-Tricarbonyl[η⁶-(1-acetyl-6-methoxy-1,2,3,4-tetrahydronaphthalene)]chromium(0) (10)

An argon flushed Schlenk flask was charged with di-*tert*-butylbiphenyl (309 mg, 1.16 mmol) in anhyd THF (15 mL). The stirred solution was cooled in an ice–water bath before lithium metal (16 mg, 2.32 mmol, freshly cleaned by immersing into acetone for a few seconds and subsequently polishing the surface under cyclohexane) were added. Within a few min a deep blue-green color appeared and rapid stirring was continued for another 3–4 h at 0 °C. The mixture was filtered under argon through a Schlenk frit and cooled to –78 °C. Then, a solution of **6** (100 mg, 0.29 mmol) in anhyd THF (5 mL) was added all at once by means of a gas-tight syringe. The resulting mixture was stirred for about 1 h while warming from –78 to –40 °C, before it was transferred through a cannula to a stirred solution of freshly distilled acetyl chloride (0.062 mL, 0.87 mmol) in THF (5 mL) cooled to –40 °C. After stirring for 30 min at the same temperature, the cooling bath was removed and stirring was continued for 2.5 h at r.t. The reaction mixture was partitioned between MTBE (20 mL) and H_2O (25 mL) and the aqueous layer was extracted with MTBE (2 × 30 mL). The combined organic layers were washed with brine and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash chromatography (hexane–EtOAc, 3:1) to yield **10** (60 mg, 61%) as a yellow solid; mp 128 °C (dec.); $[\alpha]_{589}$ +96.7, $[\alpha]_{546}$ +118.2 (*c* = 0.295, $CHCl_3$).

IR: 2945, 1951, 1859, 1711, 1544, 1480, 1359, 1267, 1155, 1023, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.65–1.76 (1 H, m), 1.82–1.92 (2 H, m), 2.08–2.16 (1 H, m), 2.26 (3 H, s), 2.63–2.79 (2 H, m), 3.59 (1 H, t, *J* = 6.5 Hz), 3.71 (3 H, s), 5.02 (1 H, d, *J* = 2.5 Hz), 5.13 (1 H, dd, *J* = 7.0, 2.5 Hz), 5.37 (1 H, d, *J* = 7.0 Hz).

^{13}C NMR (67.7 MHz, $CDCl_3$): δ = 19.3 (t), 25.6 (t), 28.0 (t), 28.5 (q), 51.1 (d), 55.6 (q), 78.0 (d), 78.2 (d), 96.3 (d), 99.3 (s), 111.2 (s), 142.8 (s), 208.8 (s), 233.9 (s).

MS: *m*/*z* (%) = 340 (24), 257 (32), 256 (100), 210 (10), 161 (73).

HRMS: *m*/*z* calcd for $C_{16}H_{16}CrO_5$: 340.0403; found: 340.0407.

(1*R*,4a*S*)-Tricarbonyl[η⁶-(1-isopropenyl-6-methoxy-1,2,3,4-tetrahydronaphthalene)]chromium(0) (3)

A suspension of activated zinc powder (2.90 g, 44.3 mmol) and CH_2Br_2 (2.477 g, 14.25 mmol) in anhyd THF (30 mL) was cooled to –40 °C and $TiCl_4$ (1.25 mL) was added slowly. After 5 min (the color had changed to grayish green), an ultrasound horn was introduced into the solution under a continuous stream of argon. The suspension was then sonicated for 4.5 h while being constantly cooled in an ice–water bath. The resulting suspension (Lombardo reagent) was ready for use, but it could be stored at –20 °C for at least several days. To a stirred mixture of the Lombardo reagent (4 mL) and anhyd CH_2Cl_2 (5 mL) was added slowly a solution of **10** (200 mg, 0.588 mmol) in anhyd CH_2Cl_2 (4 mL) at 0 °C via a syringe. After 5 min at 0 °C, the reaction mixture was warmed up to r.t., and stirring was continued for 4 h before sat. aq $NaHCO_3$ (4 mL) was added carefully. The aqueous layer was extracted with MTBE (2 × 10 mL), the combined organic layers were washed with brine (2 × 10 mL) and dried ($MgSO_4$). The solvents were removed under reduced pressure and the residue was purified by PTLC (hexane–EtOAc, 10:1) to yield **3** (152 mg, 76%) as a yellow oil; $[\alpha]_{589}$ +140.0, $[\alpha]_{546}$ +174.5 (*c* = 0.225, $CHCl_3$).

IR: 2942, 1952, 1862, 1541, 1474, 1261, 1150, 1023, 671 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.54–1.64 (1 H, m), 1.67 (3 H, s), 1.75–1.88 (3 H, m), 3.24 (1 H, dd, *J* = 9.0, 7.0 Hz), 3.69 (3 H, s), 4.70 (1 H, s), 4.92 (1 H, s), 4.99 (1 H, d, *J* = 2.0 Hz), 5.12 (1 H, dd, *J* = 7.0, 2.0 Hz), 5.58 (1 H, d, *J* = 7.0 Hz).

^{13}C NMR (67.7 MHz, $CDCl_3$): δ = 19.5 (q), 19.7 (t), 27.2 (t), 29.0 (t), 45.3 (d), 55.5 (q), 77.8 (d), 78.5 (d), 95.9 (d), 103.9 (s), 111.5 (s), 114.8 (t), 142.4 (s), 147.2 (s), 233.8 (s).

MS: *m*/*z* (%) = 338 ($[M]^+$, 16), 254 ($[M]^+$ – 3 CO, 100), 161 (17), 91 (16), 71 (13), 58 (22), 43 (65).

HRMS: *m*/*z* calcd for $C_{17}H_{18}CrO_4$: 338.0610; found: 338.0612.

(1*R*,4a*S*)-Tricarbonyl[η⁶-(1-isopropenyl-6-methoxy-7-methyl-1,2,3,4-tetrahydronaphthalene)]chromium(0) (11)

A solution of **3** (100 mg, 0.294 mmol) in anhyd THF (5 mL) was cooled to –70 °C before a 1.58 M solution of *n*-BuLi in hexane (0.225 mL, 0.355 mmol) was added by a syringe. The mixture was allowed to warm up to –25 °C over a period of 90 min before it was cooled to –45 °C and MeI was added. After allowing the mixture to warm up to –20 °C within 40 min, the cooling bath was removed and the stirring was continued for 70 min at r.t. After dilution with MTBE (30 mL), H_2O (10 mL) was added. The aqueous phase was extracted with MTBE (2 × 40 mL) and the combined organic phases were washed with brine (2 × 30 ml) and dried ($MgSO_4$). The solvent was distilled off under reduced pressure and the resulting yellow oil was purified by PTLC using hexane–CH_2Cl_2 (3:1) to yield a 93:7 mixture of **11** and its isomer **15** (detected by ^1H NMR spectroscopy). Recrystallization yielded pure **11** (88 mg, 71%) as a yellow solid; mp 104 °C; $[\alpha]_{589}$ +249.7, $[\alpha]_{546}^{20}$ +307.7, (*c* = 0.1, $CHCl_3$).

IR: 2941, 2863, 1949, 1862, 1644, 1545, 1481, 1264, 1104, 1023, 900, 673 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.55–1.64 (1 H, m), 1.68 (3 H, s), 1.70–1.86 (3 H, m), 2.10 (3 H, s), 2.63 (2 H, Ψt, *J* = 6.0 Hz), 3.29 (1 H, dd, *J* = 8.0, 5.0 Hz), 3.70 (3 H, s), 4.70 (1 H, d, *J* = 1.5 Hz), 4.94 (1 H, dd, *J* = 1.5, 1.5 Hz), 4.98 (1 H, s), 5.48 (1 H, s).

^{13}C NMR (67.7 MHz, $CDCl_3$): δ = 15.8 (q), 19.6 (q), 19.8 (t), 27.2 (t), 28.7 (t), 45.2 (d), 55.9 (q), 75.9 (d), 97.6 (s), 97.7 (d), 104.3 (s), 109.2 (s), 114.7 (t), 140.6 (s), 147.6 (s), 234.2 (s).

MS: *m*/*z* (%) = 352 ($[M]^+$, 12), 286 (100), 216 (19), 201 (16), 175 (38), 173 (17), 128 (14), 115 (17).

HRMS: *m*/*z* calcd for $C_{18}H_{20}CrO_4$: 352.0767; found: 352.0765.

(1*R*,4a*S*)-Tricarbonyl[η⁶-(1-isopropenyl-5,7-dimethyl-6-methoxy-1,2,3,4-tetrahydronaphthalene)]chromium(0) (14)

This compound was obtained as a by-product in the preparation of **11**.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.60–1.76 (2 H, m), 1.69 (3 H, s), 1.76–1.91 (2 H, m), 2.20 (3 H, s), 2.22 (3 H, s), 2.48 (1 H, dt, J_d = 17 Hz, J_t = 6.5 Hz), 2.63 (1 H, dt, J_d = 17 Hz, J_t = 6 Hz), 3.36 (1 H, t, *J* = 6.5 Hz), 3.72 (3 H, s), 4.63 (1 H, d, *J* = 1 Hz), 4.94 (1 H, dd, J_1 = 1 Hz, J_2 = 1 Hz), 5.09 (1 H, s).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.4 (q), 16.2 (q), 19.4 (t), 20.1 (q), 26.3 (t), 26.5 (t), 45.8 (d), 60.3 (q), 93.0 (d), 103.6 (s), 103.9 (s), 106.9 (s), 109.6 (s), 115.0 (t), 137.2 (s), 147.2 (s), 234.4 (s).

(1*R*)-1-Isopropenyl-6-methoxy-7-methyl-1,2,3,4-tetrahydronaphthalene (2)

A solution of **11** (100 mg, 0.284 mmol) in Et_2O was exposed to sunlight and air for 6 h. Filtration over Celite and removal of the solvent under reduced pressure yielded compound **2** (60 mg, 97%) in virtually pure form as a colorless oil; $[\alpha]_{589}$ –41.1, $[\alpha]_{578}$ –43.1, $[\alpha]_{546}$ –53.9, $[\alpha]_{436}$ –136.9, $[\alpha]_{356}$ –291.1 (*c* = 0.07, $CHCl_3$).

IR: 3071, 2927, 2856, 1731, 1643, 1617, 1581, 1506, 1465, 1455, 1402, 1373, 1323, 1303, 1250, 1201, 1154, 1108, 1031, 950, 895, 838, 800, 789 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.65 (3 H, s), 1.68–1.96 (4 H, m), 2.17 (3 H, s), 2.70–2.81 (2 H, m), 3.47 (1 H, dd, *J* = 6.0, 7.0 Hz), 3.82 (3 H, s), 4.70 (1 H, d, *J* = 1.5 Hz), 4.91 (1 H, d, *J* = 1.5 Hz), 6.55 (1 H, s), 6.87 (1 H, s).

^{13}C NMR (67.7 MHz, $CDCl_3$): δ = 15.8 (q), 19.5 (q), 21.5 (t), 28.8 (t), 30.0 (t), 46.8 (d), 55.3 (q), 110.1 (d), 114.0 (t), 124.0 (s), 129.6 (s), 131.1 (d), 135.7 (s), 149.4 (s), 155.9 (s).

MS: (DIPMS: 40 °C): *m/z* (%) = 216 ($[M]^+$, 61), 201 ($[M]^+ - CH_3$, 33), 185 (11), 176 (14), 175 ($[M]^+ - C_3H_5$, 100), 173 (38), 160 (12), 145 (11), 129 (15), 128 (16), 115 (17), 91 (12).

HRMS: *m/z* calcd for $C_{15}H_{20}O$: 216.1514; found: 216.1514.

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