Organometallic Chemistry

Chromium arene complexes in synthesis of *trans*-resveratrol

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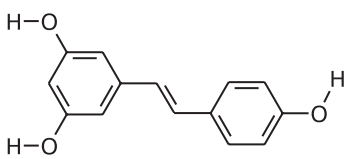
Two variants of synthesis of resveratrol (3,5,4′-*trans*-trihydroxystilbene) from dimethyl ether and anisaldehyde were performed using the chromium η^6-benzenetricarbonyl complex. The Wittig—Horner reactions or aldol condensation in four stages followed by demethylation by EtSLi were applied.

Key words: chromium(0) η^6-arenetricarbonyl complex, *trans*-resveratrol, phytoalexin, hydroxystilbenes, methoxystilbenes, aldol condensation, Wittig—Horner reaction, demethylation.

Chromium arene complexes find wide use in fine organic synthesis in recent years.[1—5] The employment of chromium η^6-arenetricarbonyl complexes as synthons provided the development of new competitive methods for the synthesis of complicated natural compounds, some of which can barely be prepared by any other method.[6—8] Such biologically active substances as helioporin, D(+)-ptilocaulin, olivetol, and other 5- and 2,5-substituted resorcinol derivatives were synthesized in high yields due to the use of Cr arenecarbonyl complexes, such as tricarbonyl-1,3-dimethoxybenzenechromium (**1**).[9—11]

In this work we pursued these studies and attempted to synthesize plant antibiotic phytoalexin (resveratrol) (**2**), which is contained in the vine bark, leaves, and grapes, in some species of pine-tree and acacia, in peanut, orchid, lilies, *etc*.[12—13] As found in the recent studies,[14—15] *trans*-isomer of **2** with the 3,4′,5-trihydroxystilbene structure is an antioxidant and an antimutagene; it retards the development and growth of human cancerous cells and prevents organism intoxication from the tumor development. It is the strongest antiviral medicine, which decomposes viruses of influenza, herpes, and even, presumably, acquired immunodeficiency.



trans-**2**

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Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 7, pp. 1219—1223, July, 2002.

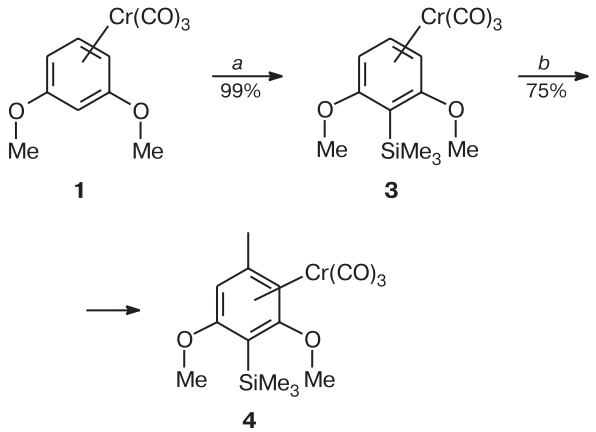
1066-5285/02/5107-1319 $27.00

The above properties of resveratrol (**2**) attracted great attention because it can serve as a polyfunctional drug without noxious side effect. Some other polyhydroxystilbenes also exhibit high biological activity.[16] However, stilbene-derived phytoalexins are not virtually used in official pharmacology because their biochemical properties are poorly studied and technological procedures for their isolation in the pure state from plants are difficult. Hydroxystilbenes manifest several other valuable physicochemical properties, due to which they can be used for the development of photoconductors, laser dyes, displays, data mapping devices, *etc*.[17]

Results and Discussion

We developed a method for the synthesis of compound **2** from fairly cheap, accessible, and preparatively convenient tricarbonyl-1,3-dimethoxybenzenechromium (**1**), whose preparation and properties were first described[18] in 1958. Compound **1** is usually prepared by heating the arene with $Cr(CO)_6$ in a high-boiling solvent.[19] In this complex the arene ligand can readily be modified by introducing various groups.[1,20—21] It has recently[11] been found that complex **1** can regiospecifically be alkylated in high yield to any position by variation of the reaction conditions. Its analog **3** is methylated by lithium tetramethylpiperidide only to the α-position.[11,20] The oxidative elimination of the tricarbonylchromium ligand and desilylation occur easily in ~100% yield.[1,11] These data enabled us to develop a synthetic scheme for the formation of the stilbene and diarylethanol frameworks, which was used as a basis for the synthesis of resveratrol **2**. This scheme is believed also to be used for the syntheses of other pharmacologically valuable hydroxystilbenes.

Scheme 1



Reagents and conditions: *a*. Bu^nLi, THF, TMSCl, −78 °C; *b*. LiTMP, THF, MeI, −50 °C.

Two variants of the synthesis of **2** were proposed. In both variants, the initial complex **1** was silylated in position 2 resulting in the protected complex **3**, which was methylated in position 5 (Scheme 1). The overall yield of complex **4** prepared in three stages from 1,3-dimethoxybenzene was 61%. Dimethoxymethyltrimethylsilyl derivative **4** that formed is the common intermediate for two routes of resveratrol synthesis (Scheme 2).

In the first variant, complex **4** was deprotonated at the benzyl position and then underwent aldol condensation with anisaldehyde to produce disubstituted ethanol **5**. After the chromium complex was decomposed and the silylic protection was removed, the trimethoxy derivative of ethanol **6** formed and transformed into stilbene **7** by dehydration.

The second variant of synthesis of **2** is based on the preparation of phosphonate **8** as a component of the subsequent Wittig—Horner reaction with anisaldehyde, which affords complex stilbene **9**. This compound is transformed into trimethoxystilbene **7** in high yield *via* two stages (removal of protection and decomposition of the complex). The reaction of complex **4** deprotonated at the benzyl position with diethyl chlorophosphate was not earlier studied.

The four stages in the first variant, including the aldol condensation (85%), occur in 51% yield based on complex **4**. The yield of trimethoxystilbene **7** synthesized from **4** by the Wittig—Horner reaction (80%) was 48%.

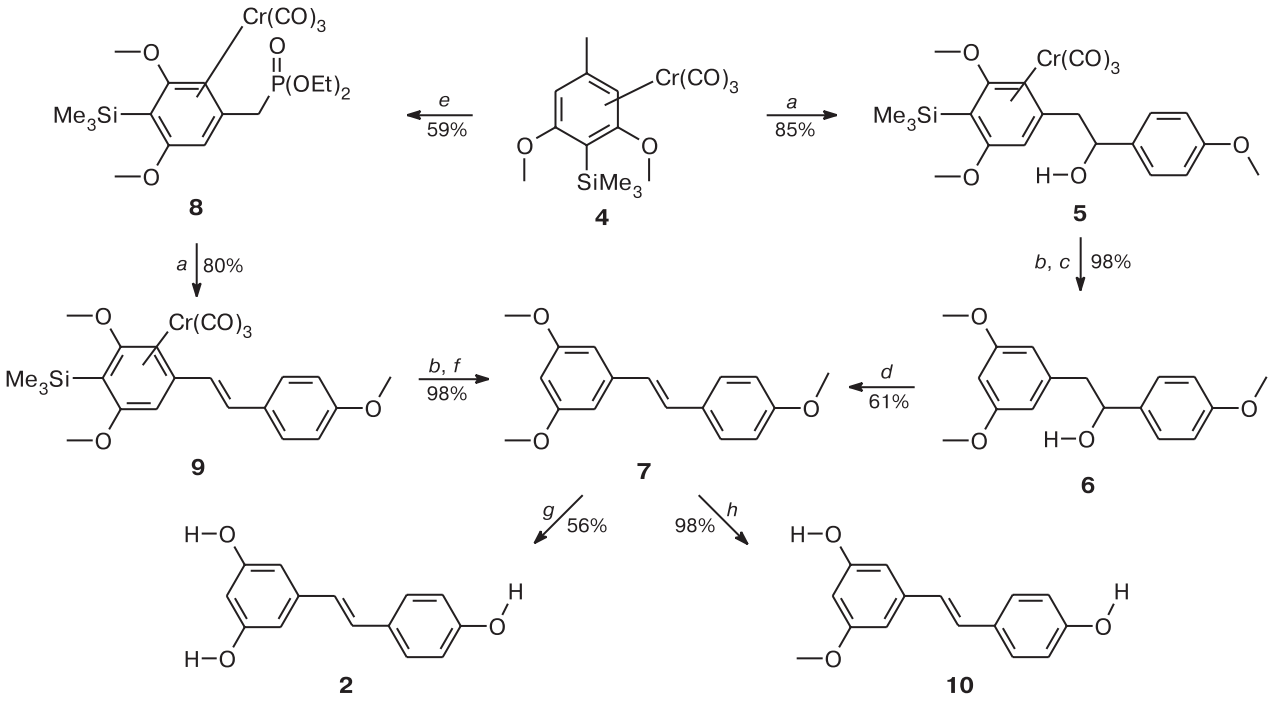
The final stage in both syntheses is the removal of the methyl protection of the hydroxy groups in compound **7**. The known procedures for this process (using BBr_3, MeMgI, or $LiPPh_2$ [21—24]) give moderate (30—60%) yields. We studied demethylation by lithium thioethoxide, whose application affords monomethoxystilbene **10** in 98% yield. An increase in the reaction time from 2 to 12 h provides only 30% yield of the target product **2**.

All synthesized compounds were characterized by IR, ^1H and ^{13}C NMR, and mass spectra, which entirely correspond to the proposed structures.

Note that the approach to synthesis of **2** using chromium arene complexes as reactants for regiospecific synthesis can be extended to other hydroxystilbenes, for example, piceatannol (3,5,4′,5′-tetrahydroxystilbene), pterostilbene (3,5-dimethoxy-4′-hydroxystilbene), pinostilbene (3,4′-dihydroxy-5-methoxystilbene), tunalbene (3,3′-dihydroxy-5-methoxystilbene), and others.

Thus, compared to other known methods for preparation of resveratrol,[23—27] the arene complexes of chromium(0) are promising for application in stoichiometric amounts because they exhibit high stereo- and regioselectivity, require mild reaction conditions, and afford target products in fairly high yields.

Scheme 2



Reagents and conditions: *a*. Bu^{n}Li, THF, −40 °C, anisaldehyde, −20 °C→0 °C, 1 h; *b*. Bu$^n_4$NF, H_2O, 2 h; *c*. *hν*, Et_2O, 2 days; *d*. TsOH, PhH, 80 °C, 13 h; *e*. Bu^{n}Li, THF, −40 °C, 15 min, $ClP(O)(OEt)_2$, −10 °C, 30 min; *f*. I_2, Et_2O, 20 °C, 12 h; *g*. MeMgI, 100 °C, 30 min; *h*. LiSEt, DMF, 160 °C, 2 h.

Experimental

^{1}H NMR spectra were recorded on Bruker AM-400 (400 MHz) and Bruker AM-270 (270 MHz) spectrometers in $CDCl_3$, using $CHCl_3$ for $CDCl_3$ and CH_3OD for CD_3OD as internal standards. ^{13}C NMR spectra were obtained using Bruker AM-400 (100.64 MHz) and Bruker AM-270 (67.7 MHz) instruments. Mass spectra were obtained on Varian MAT 711 and Varian MAT 44 mass spectrometers (electron impact, 70 eV, direct injection into an ion source). IR spectra were recorded on a Magna FT-IR 750 spectrometer (Nicolet) with KBr windows. Melting points were measured with a Buchi 510 instrument without correction. The reaction courses and purity of isolated products were monitored by TLC on the Kieselgel 60F_{254} plates (Merck) in an AcOEt—hexane system. Compounds were detected by UV absorption after irradiation with a Fluotest lamp (λ 254 or 365 nm).[11] Individual compounds were isolated from reaction products by preparative TLC on a Harrison Research 7924 T chromatotron using glass circular plates covered with Kieselgel PF-60F_{254} (Merck) (hexane—AcOEt as eluent) and by column chromatography (Kieselgel 60, Merck, 230—400 mesh) using AcOEt—petroleum ether as eluent. The yields of compounds were not optimized.

All reagents and solvents (Aldrich, Fluka, Acros, Merck) were 99% purity and used as received. Hexacarbonylchromium (Fluka) with 99% purity was used in synthesis of complex **1**.

All reactions involving complex **4** were carried out under a low pressure of the moisture- and oxygen-free highly purified argon in a Schlenk flask using a syringe technique. Reagents and solvents were dried using standard methods. Glassware was calcined before use and cooled in an argon flow.

Tricarbonyl-[η^6-1,3-dimethoxy-2-trimethylsilylbenzene]chromium(0) (3). A solution of complex **1** (2.00 g, 1.4 mmol) in anhydrous THF (50 mL) was placed in a 100-mL Schlenk flask and cooled to −78 °C. A 1.6 *M* solution of Bu^{n}Li (4.78 mL, 7.65 mmol) in hexane was added with stirring. After stirring for 0.5 h, trimethylchlorosilane ($SiMe_3Cl$) (2.3 mL, 18.3 mmol) was added. The solution was stirred for 15 min at −78 °C, after which the temperature was raised to 0 °C for 1 h. Ethyl acetate (50 mL) was added to the mixture, and the solution was washed with saturated solutions of $NaHCO_3$ (2×60 mL) and NaCl (50 mL), dried over $MgSO_4$, and evaporated *in vacuo*. Yellow crystals of compound **3** were obtained in 99% yield (2.50 g) with m.p. 150 °C (*cf*. Ref. 11: m.p. 150 °C) and R_f 0.3 (hexane—AcOEt, 5 : 1). IR, ν/cm^{-1}: 2975, 2957, 2903, 1943, 1871, 1843, 1524, 1505, 1453, 1442, 1415, 1285, 1238, 1096, 847, 669. ^{1}H NMR (270 MHz, $CDCl_3$), δ: 0.34 (s, 9 H, CH_3—Si); 3.68 (s, 6 H, OCH_3); 4.71 (d, 2 H, C(4)H/C(6)H, J = 7.0 Hz); 5.72 (t, 1 H, C(5′)H, J = 7.0 Hz). ^{13}C NMR (67.7 MHz, $CDCl_3$), δ: 1.6 (q, CH_3—Si); 55.4 (q, OCH_3); 73.2, 69.7 (d, C(4)/C(6)); 80.9 (s), 93.2 (d, C(5)); 148.4 (s); 234.2 (s, $Cr(CO)_3$). MS (EI, 70 eV), m/z (I_{rel} (%)): 346 [M]$^+$ (15), 334 (57), 290 (10), 262 (100), 217 (9), 190 (11), 135 (9), 52 (26).

Tricarbonyl-[η^6-1,3-dimethoxy-5-methyl-2-trimethylsilylbenzene]chromium(0) (4). A 1.5 *M* solution of Bu^{n}Li (0.2 mL, 0.32 mmol) in hexane was added at −78 °C to a solution of 2,2,6,6-tetramethylpiperidine (0.055 mL, 0.32 mmol) in an-

hydrous THF (1 mL) placed in a 25-mL Schlenk flask. The mixture was stirred for 40 min at −40 °C and cooled to −78 °C. Complex **3** (100 mg, 0.288 mmol) was added, and the mixture was stirred for 30 min at −78 °C. A solution of CH_3I (90 μL, 1.4 mmol) in anhydrous THF (4 mL) was placed into another 25-mL Schlenk flask and cooled to −50 °C. A solution of the anion of complex **3** from the first flask was rapidly added through a pumping pipe to a solution in the second flask. The mixture was stirred for 30 min at −50 °C and 1 h at 25 °C, then heptane (20 mL) was added, and ~50% solvent were evaporated *in vacuo*. Ethyl acetate (20 mL) was added to the residue, and the resulting solution was washed successively with 2 *N* HCl (2×20 mL) and saturated solutions of $NaHCO_3$ (20 mL) and NaCl (20 mL). The organic layer was dried with $MgSO_4$ and concentrated *in vacuo*. Complex **4** was obtained as yellow crystals in 75% yield (78 mg), m.p. 158 °C (*cf.* Ref. 11: m.p. 158 °C), R_f 0.27 (hexane—AcOEt, 5 : 1). IR, ν/cm^{-1}: 2950, 2901, 1937, 1863 (C=O, $Cr(CO)_3$), 1849, 1320, 1229, 1112, 839. ^{1}H NMR (270 MHz, $CDCl_3$), δ: 0.33 (s, 9 H, CH_3—Si); 2.35 (s, 3 H, CH_3); 3.68 (s, 6 H, OCH_3); 4.65 (s, 2 H, C(4)H/C(6)H). ^{13}C NMR (67.7 MHz, $CDCl_3$), δ: 1.5 (q, CH_3—Si); 21.3 (q, CH_3); 55.3 (q, C—OCH_3); 72.6 (d, C(4)/C(6)); 77.2 (s); 108.4 (s); 148.2 (s); 234.6 (s). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 360 $[M]^+$ (18), 304 (15), 276 (100), 261 (8), 201 (5), 149 (12), 52 (10).

Tricarbonyl-[2-(η^6-3,5-dimethoxy-4-trimethylsilyl-phenyl)-1-(4′-methoxyphenyl)ethanol]chromium(0) (5). A solution of complex **4** (500 mg, 1.38 mL) in anhydrous THF (10 mL) was placed in a 50-mL Schlenk flask and cooled to −40 °C, and a 1.6 *M* solution of Bu^{n}Li (0.95 mL, 1.53 mmol) in hexane was added with stirring. The mixture was stirred for 15 min at −40 °C and 30 min at 0 °C until the solution became dark red, after which it was cooled to −40 °C. Anisaldehyde (0.25 mg, 2.08 mmol) was added to the cooled solution, and the mixture was stirred for 30 min at −20 °C and for 1 h at 0 °C. Methyl *tert*-butyl ether (MTBE) (40 mL) was added to the reaction mixture. The organic layer was washed with water (2×40 mL) and a saturated solution of NaCl (30 mL), dried with $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (hexane—AcOEt (10 : 1) eluent). Compound **5** was obtained in 85% yield (584 mg) as yellow oil with R_f 0.06 (hexane—AcOEt, 5 : 1). IR, ν/cm^{-1}: 3586 (OH), 2954, 1950, 1865 (C=O, $Cr(CO)_3$), 1513, 1496, 1248, 1227. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.34 (s, 9 H, CH_3—Si); 2.04 (d, 1 H, OH, *J* = 3.0 Hz); 2.85 (dd, 1 H, CH_2, *J* = 14.0 Hz, *J* = 5.0 Hz); 2.93 (dd, 1 H, CH_2, *J* = 14.0 Hz, *J* = 8.0 Hz); 3.61, 3.64 (both s, 3 H, OCH_3); 3.82 (s, 3 H, OCH_3); 4.58, 4.65 (both s, 1 H, C(2)H/C(6)H); 4.93 (m, 1 H, C<u>H</u>—OH); 6.91 (d, 2 H, C(2′)H/C(6′)H, *J* = 9.0 Hz); 7.29 (d, 2 H, C(3′)H/C(5′)H, *J* = 9.0 Hz). ^{13}C NMR (67.7 MHz, $CDCl_3$), δ: 1.5 (q, CH_3—Si); 26.9 (d, C<u>H</u>—OH); 45.4 (t, CH_2); 55.4, 55.29, 55.27 (all q, OCH_3); 73.2, 74.6 (both d, C(2)/C(6)); 108.3 (s); 114.0 (d, C(3′)/C(5′)); 127.2 (d, C(2′)/C(6′)); 135.3 (s); 148.1 (s); 159.5 (s); 234.5 (s, $Cr(CO)_3$). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 496 $[M]^+$ (8), 412 (100), 394 (20), 224 (48), 137 (52), 52 (7).

2-(3,5-Dimethoxyphenyl)-1-(4′-methoxyphenyl)ethanol (6). <u>Desilylation</u>. One water droplet and 5.75 mL (5.75 mmol) of Bu$^n_4$NF (1 *M* solution in THF) were added with stirring to complex **5** (517 mg, 1.04 mmol) in THF (20 mL). After stirring for 2 h at 20 °C, AcOEt (30 mL) was added. The solution was washed with water (40 mL) and a saturated solution of NaCl (40 mL), dried with $MgSO_4$, and concentrated. Complex **5** was obtained in 99% yield (437 mg) with R_f 0.55 (hexane—MTBE, 1 : 1). <u>Decomposition of chromium arene complex **5**</u>. Desilylated complex **5** (450 mg, 0.9 mmol) was dissolved in an AcOH—Et_2O (1 : 10) mixture (60 mL), and the resulting solution was stored for 2 days in sunlight. Then the green residue was filtered through a zeolite layer 1 cm thick, and the colorless filtrate was concentrated *in vacuo*. Alcohol **6** was obtained as yellow viscous oil in 99% yield (285 mg), R_f 0.27 (hexane—MTBE, 1 : 1). IR, ν/cm^{-1}: 3450 (OH), 2927, 1596, 1512, 1246, 1149, 1066. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.94 (d, 1 H, OH, *J* = 3.0 Hz); 2.91 (dd, 1 H, CH_2, *J* = 14.0 Hz, *J* = 8.0 Hz); 2.96 (dd, 1 H, CH_2, *J* = 14.0 Hz, *J* = 5.0 Hz); 3.77 (s, 6 H, OCH_3); 3.81 (s, 3 H, OCH_3); 4.85 (m, 1 H, C<u>H</u>—OH); 6.36 (br.s, 3 H, C(2)H/C(6)H/C(4)H); 6.89 (d, 2 H, C(2′)H/C(6′)H, *J* = 9.0 Hz); 7.3 (d, 2 H, C(3′)H/C(5′)H, *J* = 9.0 Hz). ^{13}C NMR (67.7 MHz, $CDCl_3$), δ: 46.4 (t, CH_2); 55.2, 55.3 (both q, OCH_3); 74.7 (q, OCH_3); 98.6 (d, C<u>H</u>—OH); 107.4 (d, C(2)/C(6)); 113.7 (d, C(3′)/C(5′)); 127.1 (d, C(2′)/C(6′)); 135.9 (s); 143.5 (s); 140.4 (s), 159.0 (s), 160.8 (c). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 288 $[M]^+$ (1), 270 (4), 152 (100), 137 (98), 109 (18).

(*E*)-2-(3,5-Dimethoxy)-1-(4′-methoxyphenyl)ethylene (7). To a solution of alcohol **6** (250 mL, 0.59 mmol) TsOH (20 mg, 0.012 mmol) in benzene (10 mL) was added, and the mixture was refluxed for 13 h. Then AcOEt (20 mL) was added, and the solution was washed with a 10% solution of $NaHCO_3$ (3×30 mL) and a saturated solution of NaCl (30 mL), dried with $MgSO_4$, and concentrated *in vacuo*. After purification by preparative TLC (hexane—AcOEt (8 : 1) eluent), stilbene **7** (94 mg, 61% yield) was obtained with m.p. 47 °C and R_f 0.16 (hexane—AcOEt, 10 : 1). IR, ν/cm^{-1}: 3027, 2935, 1590, 1511, 1251, 1150, 1066. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 2.83 (s, 9 H, OCH_3); 6.37 (t, 1 H, C(2)H, *J* = 2.0 Hz); 6.65 (d, 2 H, C(2)H/C(4)H, *J* = 2.0 Hz); 6.99 (d, 2 H, C(2′)H/C(6′)H, *J* = 9.0 Hz); 7.01 (d, 1 H, olefin, *J* = 17.0 Hz); 7.03 (d, 2 H, C(3′)H/C(5′)H, *J* = 9.0 Hz); 7.45 (d, 1 H, olefin, *J* = 17.0 Hz). ^{13}C NMR (67.7 MHz, $CDCl_3$): 55.2, 55.3, 55.32 (all q, OCH_3); 99.6 (q, C(4)); 104.3 (d, C(2)/C(6)); 114.1 (d, C(3′)H/C(5′)H); 126.5 (d, olefin); 127.8 (d, C(2′)/C(6′)); 128.7 (d, olefin); 139.9 (s); 139.6 (s); 159.4 (c); 160.9 (c). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 270 $[M]^+$ (100), 239 (8), 196 (7), 115 (3).

Tricarbonyl-[1-(η^6-3,5-dimethoxy-4-trimethylsilyl-phenyl)methyldiethylphosphonate]chromium(0) (8). Complex **4** (200 mg, 0.554 mmol) in anhydrous THF (6 mL) was placed in a 25-mL Schlenk flask, and Bu^{n}Li (0.38 mL, 0.71 mmol) as a 1.6 *M* solution in hexane was added at −40 °C. The mixture was stirred for 15 min at −40 °C and 30 min at −10 °C (the dark red color appeared). Then the mixture was cooled to −30 °C, and diethyl chlorophosphate (104 μL, 0.72 mmol) was added. After stirring for 30 min at −10 °C and for 1 h at 0 °C, AcOEt (20 mL) was added. The solution was washed with a saturated solution of NaCl (2×30 mL), water (30 mL), and a saturated solution of NaCl (30 mL), dried with $MgSO_4$, and concentrated *in vacuo*. Purification on a column packed with silica gel (10 g) yielded phosphonate **8** (162 mg, 59% yield) as yellow crystals with m.p. 130 °C and initial compound **4** (75 mg, 37% yield) with R_f 0.18 (hexane—AcOEt, 1 : 1). The corrected yield of compound **4** was 94% (taking into account conversion). IR, ν/cm^{-1}: 2903, 1951, 1866 (C=O, $Cr(CO)_3$), 1230, 1104, 1054, 1026. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.32 (s, 9 H, CH_3—Si), 1.34 (t, 6 H, CH_3, *J* = 7.0 Hz); 2.96 (d, 2 H,

CH_2, $^3J_{P,H}$ = 20.5 Hz); 3.69 (s, 6 H, OCH_3); 4.13 (m, 4 H, OCH_2); 4.74 (s, 2 H, C(2)H/C(6)H). ^{13}C NMR (67.7 MHz, $CDCl_3$), δ: 1.5 (q, CH_3—Si); 16.4, 16.5 (both q, CH_3); 32.7, 34.9 (both t, OCH_2); 62.5 (t, CH_2P); 72.27, 72.31 (both d, C(2)/C(6)); 79.3 (s, C(1)); 102.3 (s, C(4)); 148.0 (s, C(3)/C(5′)); 234.2 (s, $Cr(CO)_3$. MS (EI, 70 eV), *m/z* (I_{rel} (%)): 496 $[M]^+$ (2), 412 (100), 360 (30), 345 (61), 315 (10), 285 (68), 52 (40).

Tricarbonyl-[1-(η^6-3,5-dimethoxy-4-trimethylsilylphenyl)-2-(4′-methoxyphenyl)ethylene]chromium(0) (9). Phosphonate **8** (265 mg, 0.735 mmol) in anhydrous THF (10 mL) was placed in a 25-mL Schlenk flask, and a 1.5 *M* solution of Bu^nLi (0.5 mL, 0.81 mmol) in hexane was added at −40 °C. The mixture was stirred for 15 min at −40 °C and 30 min at −10 °C (the red color appeared). Then anisaldehyde (0.25 mL, 2.08 mmol) was added. The mixture was heated during 1 h to boiling and cooled to 20 °C, and AcOEt (30 mL) was added. The solution was washed with water (2×40 mL), a saturated solution of $NaHCO_3$ (30 mL), and a saturated solution of NaCl (30 mL), dried with $MgSO_4$, and concentrated *in vacuo*. The crude product was purified on a column packed with kiesel gel (10 g) (hexane—AcOEt, 50 : 1). Stilbene **9** was obtained in 80% yield (280 mg) as red needles with m.p. 202 °C and R_f 0.57 (hexane—AcOEt, 1 : 1). IR, ν/cm^{-1}: 2978, 2956, 1935, 1843 (C=O, $Cr(CO)_3$), 1605, 1535, 1228, 839. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.45 (s, 9 H, CH_3—Si); 3.76 (s, 6 H, OCH_3); 3.83 (s, 3 H, OCH_3); 4.93 (s, 2 H, C(2)H/C(6)H); 6.72 (d, 1 H, olefin, *J* = 17.0 Hz); 6.91 (d, 2 H, C(2′)H/C(6′)H, *J* = 9.0 Hz); 6.98 (d, 1 H, olefin, *J* = 17.0 Hz); 7.44 (d, 2 H, C(3′)H/C(5′)H, *J* = 9.0 Hz). ^{13}C NMR (67.7 MHz, $CDCl_3$), δ: 1.5 (q, CH_3—Si); 55.2, 55.3, 55.4 (all q, OCH_3); 68.9 (d, C(2)/C(6)); 79.4 (s); 106.5 (s); 114.4 (d, C(3′)/C(5′)); 123.9 (d, olefin); 128.3 (d, C(2′)/C(6′)); 128.4 (s); 131.8 (d, olefin); 148.3 (s); 160.2 (s); 234.0 (s, $Cr(CO)_3$). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 478 $[M]^+$ (1), 394 $[M - 3\ CO]^+$ (8), 342 $[M - 3\ CO - Cr]^+$ (92), 327 (21), 267 (100), 223 (45).

Desilylation of stilbene **9** was similar to desilylation in the synthesis of alcohol **6**. The yield was 99%.

Synthesis of trimethoxystilbene **7** was carried out by the decomposition of its chromium complex. Desilylated complex **9** (115 mg) was dissolved in an AcOEt—Et_2O (1 : 10) mixture (50 mL), and diiodine (300 mg) was added. The mixture was stirred for 12 h at 20 °C, and Et_2O (50 mL) was added. The solution was washed with a saturated solution of NaCl (50 mL), dried with $MgSO_4$, and concentrated *in vacuo*. Stilbene **7** was obtained in 99% yield (76 mg) and exhibited the above described characteristics.

(*E*)-2-(3,5-Dihydroxyphenyl)-1-(4′-hydroxyphenyl)ethylene (resveratrol) (2). Trimethoxystilbene **7** (70 mg, 0.26 mmol) in Et_2O (2 mL) was added to a solution in Et_2O (10 mL) of MeMgI, prepared from Mg (148 mg, 6.08 mmol) and MeI (1.43 mL, 22.8 mmol). The ether was distilled off in an argon flow, and the residue was heated *in vacuo* for 30 min at 100 °C and then in an argon flow for 15 min, rising temperature to 160 °C. After the solution was cooled to 20 °C, 10% NH_4Cl (15 mL) and AcOEt (20 mL) were carefully added to the contents of the flask. The aqueous layer was extracted with AcOEt (3×30 mL), and the combined extracts were washed with a saturated solution of NaCl (30 mL), dried with $MgSO_4$, and concentrated *in vacuo*. The crude product was purified on a chromatotron (hexane—AcOEt, 1 : 1). Resveratrol **2** (32 mg, 54%) was obtained as solid white needles with m.p. 247 °C (*cf.* Ref. 23: m.p. 247 °C) and R_f 0.24 (hexane—AcOEt, 1 : 1). IR, ν/cm^{-1}: 3329, 3029, 1604, 1238, 1147, 836. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 6.13 (t, 1 H, C(4)H, *J* = 2.0 Hz); 6.42 (d, 2 H, C(2)H/C(6)H, *J* = 2.0 Hz); 6.74 (d, 2 H, C(2′)H/C(6′)H, *J* = 9.0 Hz); 6.78 (d, 1 H, olefin, *J* = 17.0 Hz); 6.93 (d, 1 H, olefin, *J* = 17.0 Hz); 7.33 (d, 2 H, C(3′)H/C(5′)H, *J* = 9.0 Hz). ^{13}C NMR (100.64 MHz, CD_3OD), δ: 102.6 (d, C(4)); 105.8 (d, C(2)/C(6)); 116.5 (d, C(3′)/C(5′)); 127 (d, olefin); 128.8 (d, C(2′)/C(6′)); 129.4 (d, olefin); 130.3 (s); 141.3 (s); 158.4 (s); 159.7 (s). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 228 $[M]^+$ (56), 165 (18), 107 (10), 85 (100), 57 (8).

(*E*)-2-(5-Hydroxy-3-methoxyphenyl)-1-(4′-hydroxyphenyl)ethylene (10). Trimethoxystilbene **7** (30 mg, 0.11 mmol) and lithium thioethoxide (135 mg, 1.33 mmol) in DMF (4 mL) were placed in a 25-mL Schlenk flask connected with a reflux condenser and a paraffinic bubble counter. After this apparatus was thoroughly degassed by tenfold evacuation and filling with argon, and the mixture was heated for 2 h at 160 °C. After cooling, 0.1 *M* HCl (15 mL) and AcOEt (20 mL) were slowly added to the solution, and the latter was washed with water (6×30 mL). The organic layer was washed with a saturated solution of NaCl (50 mL), dried with $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by preparative TLC (hexane—AcOEt (7 : 1) eluent). Stilbene **10** was obtained in 98% yield (26 mg) as colorless oil with R_f 0.4 (hexane—AcOEt, 1 : 1). IR, ν/cm^{-1}: 3365, 2960, 1604, 1589, 1343, 1148, 836. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.82 (s, 3 H, OCH_3); 4.86 (br.s, 1 H, OH); 4.91 (br.s, 1 H, OH); 6.32 (t, 1 H, C(4), *J* = 2.0 Hz); 6.58, 6.63 (both d, 2 H, C(2)H/C(6)H, *J* = 2.0 Hz); 6.83 (d, 2 H, C(2′)H/C(6′)H, *J* = 9.0 Hz); 6.85 (d, 1 H, olefin, *J* = 17.0 Hz); 7.00 (d, 1 H, olefin, *J* = 17.0 Hz); 7.39 (d, 2 H, C(3′)H/C(5′)H, *J* = 9.0 Hz). ^{13}C NMR (100.64 MHz, CD_3Cl_3), δ: 55.6 (q, OCH_3); 101.4 (d, C(4)); 104.4, 106.6 (both d, C(2)/C(6)); 116.5 (d, C(3′)/C(5′)); 129.9 (d, olefin); 128.9 (d, C(2′)/C(6′)); 129.8 (d, olefin); 130.3 (s); 141.3 (s); 158.4 (s); 159.7 (s); 162.5 (s). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 228 $[M]^+$ (56), 165 (18), 107 (10), 85 (100), 57 (8). According to the ^{1}H NMR data, the product contains ~3% *cis*-isomer.

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Received January 14, 2002