Asymmetric *syn*-Selective Michael Addition of Enolates to Chiral 8-Phenylmenthyloxy Vinyl Chromium Carbene Complexes

José Barluenga,* Javier M. Montserrat, Josefa Flórez, Santiago García-Granda, and Eduardo Martín

Abstract: The Michael addition reactions of ketone and ester lithium enolates to optically active Fischer vinylcarbene complexes derived from (−)-8-phenylmenthol take place with high *syn* selectivity and high levels of asymmetric induction. The initial Michael adducts can be further elaborated through diastereoselective addition of organometallic reagents to ketones and aldol reactions. Removal of the metal fragment and chiral auxiliary group leads to cyclic enol ethers with three or five contiguous stereogenic centers and of high enantiomeric purity.

Keywords: asymmetric syntheses · enol ethers · Fischer carbenes · Michael additions · *syn* diastereoselectivity

Introduction

The diastereoselectivity of the conventional Michael addition of metal enolates to electron-deficient alkenes[1] is usually very sensitive to the nature of the solvent[2] and highly dependent on the ketone, ester, or dithioester enolate geometry,[3] the geometry of the acceptor,[4] and the enolate counterion.[5] In contrast, it is largely unaffected by the configuration of amide enolates,[6] enol silanes, and silyl ketene acetals.[7] Although there are some Michael reactions that afford essentially the *syn* diastereoisomer,[8] in general, this 1,4-conjugate addition takes place preferentially with *anti* diastereoselectivity.[9] On the other hand, it has been demonstrated previously that Michael addition of an enolate to alkoxy-stabilized Fischer vinylcarbene complexes occurs with *syn* diastereoselectivity[10] irrespective of the enolate geometry or the nature of the counterion. High *syn* selectivity in the addition of ketone (*E*) enolates to nitrogen-stabilized (*O*-chelated imidazolidinone) Fischer vinylcarbene complexes has also recently been found;[11] hence, the transition metal carbene route is complementary to the former conventional Michael methodology. Recently, we reported the first asymmetric Michael additions of various organolithium compounds to enantiomerically pure alkenyl (−)-8-phenylmenthyloxy chromium carbene complexes, which proceed with uniformly high levels of asymmetric induction.[12] In this report, we wish to describe a highly *syn* diastereoselective Michael addition of ketone and ester lithium enolates to the chiral Fischer carbene complexes mentioned above and its successful application to the enantioselective synthesis of compounds with three or five contiguous stereogenic centers.

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Results and Discussions

Ketone enolates **3** were generated from the previously prepared (*E*) trimethylsilyl enol ether[13] of cyclohexanone and cyclopentanone and from the (*Z*) trimethylsilyl enol ether of propiophenone[13] and 4-heptanone[14] by cleavage with butyllithium.[15] The (*Z*) enolate of *p*-chloropropiophenone was prepared by treatment with lithium diisopropylamide (LDA).[16, 17] The results obtained in the Michael reactions of these lithium enolates with chirally modified Fischer vinylcarbene complexes **1** and **2** are summarized in Scheme 1 and Table 1.

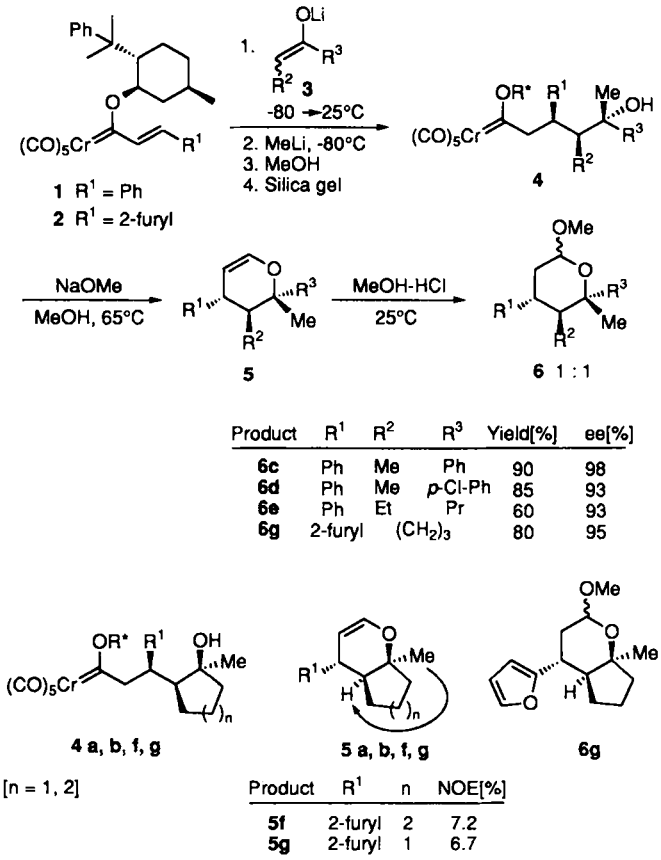
Addition of a solution of chiral carbene complex **1** or **2** in THF to a THF/hexane solution of the corresponding ketone lithium enolate **3** (1.1 equiv) followed by treatment with 2 equiv of methyllithium led, after quenching with methanol at low temperature and standard purification by silica gel column chromatography, to *syn*[18] Michael adducts **4** as single diastereoisomers, as judged by ^{13}C and ^{1}H NMR studies of the products; an exception to this was compound **4e** (only the *syn* isomer is depicted), derived from enolate of 4-heptanone, which was isolated as a 80:20 mixture of *syn* and *anti* isomers.[19] While not particularly good, this *syn* selectivity is much higher than that observed for the comparable addition of (*Z*) lithium enolate of 3-pentanone to alkoxy[10b] and imidazolidinone[11] carbene complexes (10% *de*). In the synthesis of compounds **4d**, **4e**, and **4g** the addition of MeLi was carried out in the presence of cerium(III) chloride; this clearly increased the chemical yield.[20] The pentacarbonylchromium fragment and the (−)-8-phenylmenthyl chiral auxiliary were removed by treatment with base: dropwise addition of the carbenes **4** to a sodium methoxide solution in methanol at reflux afforded the corresponding optically active cyclic enol ethers **5** with consistently high enan-

0570-0833/95/0404-0236 $ 40.00+.25/0

Table 1. Asymmetric Michael additions of ketone enolates to optically active carbene complexes **1** and **2**.

Entry	R^1	R^2	R^3	Enolate geometry	4	Yield [%] [a]	*de* [%] [b]	5	Yield [%] [c]	*ee* [%] [d]
1	Ph	$(CH_2)_4$		*E*	**4a**	40	99	**5a**	71	95
2	Ph	$(CH_2)_3$		*E*	**4b**	64	99	**5b**	40	93
3	Ph	Me	Ph	*Z*	**4c**	89	99	**5c**	61	-
4	Ph	Me	*p*-Cl-Ph	*Z*	**4d**	83 [e]	99	**5d**	65	-
5	Ph	Et	Pr	*Z*	**4e**	75	60	**5e**	67	-
6	2-furyl	$(CH_2)_4$		*E*	**4f**	67	99	**5f**	40	93
7	2-furyl	$(CH_2)_3$		*E*	**4g**	60	99	**5g**	45	-
8	2-furyl	Me	Ph	*Z*	**4h**	75	99	**5h**	58	97

[a] Yield of isolated product after flash chromatography based on **1** or **2**. [b] Determined by ^{1}H NMR spectroscopy (300 MHz) and qualitatively confirmed by their ^{13}C NMR spectra. [c] Isolated yield based on **4**. [d] Determined by chiral HPLC analysis. [e] Overall yield for a two step reaction; the corresponding δ-keto carbene generated in the addition of the enolate was isolated.



Scheme 1. Asymmetric *syn*-diastereoselective Michael additions of ketone enolates (for complete list of substituents R^1, R^2, and R^3, see Table 1).

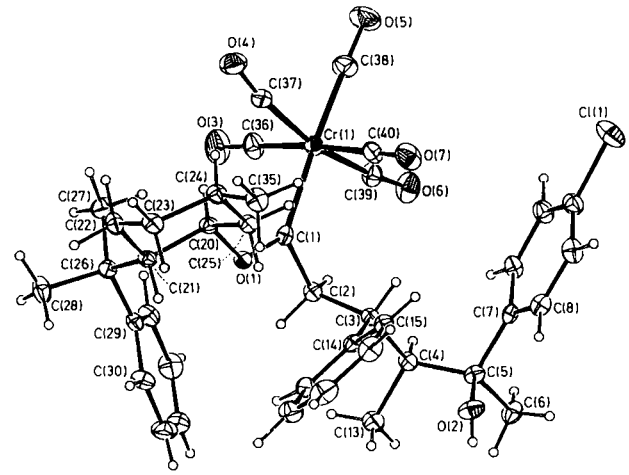
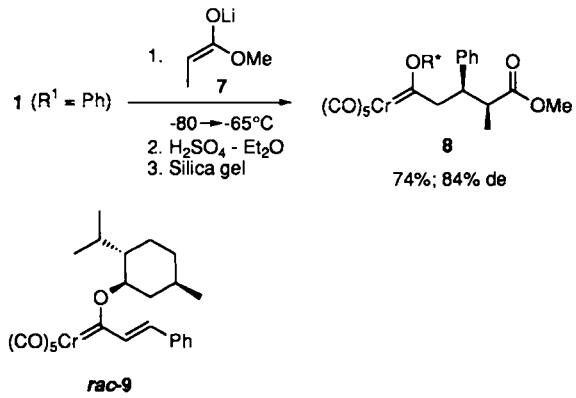


Fig. 1. Molecular structure of **4d** (EUCLID plot).

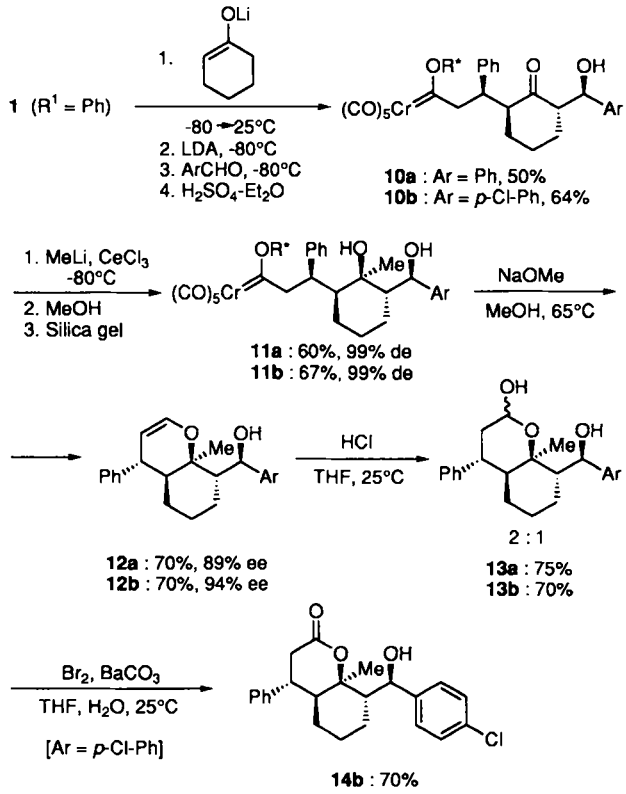
tiomeric excesses. This transformation presumably involves intramolecular alkoxide exchange[21] followed by elimination of the "$(CO)_5Cr$" moiety.[12] The enantiomeric purities of compounds **5c–e** and **5g**, which could not be resolved in the chiral HPLC column used, were determined by chiral HPLC analysis after conversion to the acetals **6c–e** and **6g**, respectively, by treatment with a solution of methanol saturated with hydrogen chloride. These acetals were obtained as an equimolar mixture of epimers at the acetal moiety, which could be partially separated by flash column chromatography in the case of compounds **6c** and **6d**. A single crystal X-ray structure determination of compounds **4d**[22] (Fig. 1) and **5c**[23] proved the relative and absolute configuration as depicted in Scheme 1. The observed stereochemistry corresponds to a *syn*-selective Michael addition.[10] The sense of facial selectivity is in agreement with our earlier results[12] and with a Felkin–Anh version of Cram's rule for 1,2-asymmetric induction in nucleophilic additions to acyclic chiral carbonyl compounds.[24] According to previous results[10a] and to difference NOE experiments on compounds **5f** and **5g** (Scheme 1), the stereochemistry of the third generated stereogenic center in the cyclic ketones (**4a, b, f, g**) is opposite to the one observed with acyclic substrates. This stereochemistry indicates that the addition to the carbonyl group took place from the less hindered side of the cyclic ketone: equatorial attack in the case of cyclohexanones and *trans* attack in the case of cyclopentanones; this is in accordance with predictions based on steric approach control.[25]

Similarly, the (*E*)[26] ester enolate **7**, prepared by deprotonation of methyl propionate with LDA,[16] reacted selectively with chiral carbene **1** (R^1 = Ph) to give the *syn* 1,4-adduct **8** as a 92:8 mixture of diastereoisomers (ratio determined from the ^{1}H NMR spectrum); this ratio corresponds to the diastereofacial selectivity.[27] The stereochemistry shown in Scheme 2 for compound **8** has been assumed by analogy.

In order to show the utility of the present asymmetric synthesis in the generation of up to five contiguous stereogenic centers, the transformations shown in Scheme 3 were carried out. Thus, the anionic derivative, obtained as described above by reaction of carbene complex **1** with cyclohexanone lithium enolate, was treated with LDA (1 equiv) and then with the corresponding aromatic aldehyde (5 equiv); this resulted in the formation of a single aldol product **10**, which was established to be the *anti*[28] (*u*[29] aldol adduct) isomer by correlation of the ^{1}H NMR coupling constants.[30] The diastereoselectivity of the aldol reaction



Scheme 2. Asymmetric *syn*-diastereoselective Michael addition of ester enolate 7. R*OH = (−)-8-phenylmenthol. Compound *rac*-**9** is racemic; only one enantiomer is shown.



Scheme 3. Asymmetric generation of five contiguous stereogenic centers.

is in agreement with the precedents.[31] The relative configuration in the cyclohexane ring was established by X-ray analysis (see below) to be opposite to that reported previously for similar reactions with racemic products.[10a] Addition was found to occur exclusively from the stereoelectronically favored axial direction.[30, 32] Addition of MeLi to **10** in the presence of $CeCl_3$[20] presumably also took place from the sterically favored equatorial direction[25] to give compounds **11** as single diastereoisomers. Elimination under basic conditions of the metal fragment and chiral auxiliary group as previously described afforded the bicyclic enol ethers **12** as compounds of high enantiomeric purity. Further synthetic uses of this sequence are illustrated by the transformations of enol ethers **12** via the hemiacetals **13** to the corresponding lactones. Thus, **14b** was obtained by oxidation of lactol **13b** with bromine. An X-ray crystal structure determination of racemic compound **12b** (*rac*-**12b**, Ar = *p*-Cl-Ph),[23] prepared in an analogous synthetic sequence starting from racemic carbene complex *rac*-**9**, confirmed the relative configuration in the cyclohexane ring and all the stereochemical assignment. The absolute configuration has been assumed from above and previous results.[12] Recrystallization from hexane or pentane of the corresponding optically active compound **12b**, isolated as a waxy oil, did not lead to suitable single crystals for X-ray studies.

Conclusion

The chiral (−)-8-phenylmenthyloxy Fischer vinylcarbenes described above are highly enantioselective and synthetically useful Michael acceptors. In addition they show better *syn* diastereoselectivity than the corresponding methoxy and ethoxy derivatives[10, 33] or the *O*-chelated imidazolidinone carbene complexes[11] in the reactions with lithium enolates. This is presumably because they are more sterically encumbered and therefore discriminate more effectively between the diastereomeric transition states, regardless of whether these chiral complexes undergo Michael addition in an *s-trans* conformation[10b] or an *s-cis* conformation of the vinylcarbene moiety.[11]

Experimental Procedure

General: All reactions involving organometallic species were carried out under an atmosphere of dry N_2 using oven-dried glassware and syringes. All common reagents and solvents were obtained from commercial suppliers and used without further purification unless otherwise indicated. THF and Et_2O were distilled from sodium benzophenone ketyl under N_2 immediately prior to use, and CH_2Cl_2 from P_2O_5 under N_2. Hexane, ethyl acetate, benzaldehyde, and *p*-chlorobenzaldehyde were distilled before use. The sodium methoxide solution in methanol was prepared by slow addition under N_2 of small pieces of surface-clean Na (2.3 g, 100 mmol) to reagent grade MeOH (100 mL). The resulting solution was stored at room temperature under N_2. The enantiomeric purities were determined by chiral HPLC analysis, by comparison with the corresponding racemic products prepared through analogous synthetic steps employing the appropriate vinylcarbene complex derived from (±)-menthol. TLC was performed on aluminum-backed plates coated with silica gel 60 with F_{254} indicator (Scharlau). Flash column chromatography was carried out on silica gel 60, 230–240 mesh (Sds). Melting points were obtained on a Büchi-Tottoli apparatus with open capillary tubes and are uncorrected. ^{1}H NMR (200, 300 MHz) and ^{13}C NMR (50.5, 75.5 MHz) spectra were measured on a Bruker AC-200 and AC-300 instruments, respectively, with tetramethylsilane ($\delta = 0.0$, ^{1}H NMR) or $CDCl_3$ ($\delta = 76.95$, ^{13}C NMR) as internal standard. Homonuclear decoupling experiments served to assign coupling constants. Carbon multiplicities were assigned by DEPT techniques. Low-resolution electron impact mass spectra (EI-LRMS) were obtained at 70 eV on a HP 5987A instrument, and the intensities are reported as a percentage relative to the base peak after the corresponding *m/z* value. High-resolution mass spectra (HRMS) were determined on a Finnigan MAT 95 spectrometer. Optical rotations were determined with a Perkin Elmer 241 polarimeter using a Na lamp; concentrations are reported in g per 100 mL of solvent. Chiral HPLC analysis were carried out with a Shimadzu instrument on a Chiralcel OD-H (Daicel Chem. Ind.) column (25 × 0.46 cm) with 120–240:1 hexane:2-propanol mixtures as eluant, at a flow rate of 0.9 mL min^{-1} and detection with photodiode array UV/Vis detector.

General Procedure for the Preparation of Chiral Chromium Complexes 1 and 2: Acetyl bromide (3.5 mL, 47.30 mmol) was added dropwise to a solution of freshly prepared [methyl[(tetramethylammonio)oxy]methylene]pentacarbonylchromium [34] (14.75 g, 47.73 mmol) in dichloromethane (200 mL) cooled to −45 °C. The reaction mixture was stirred at −45 °C for 45 min, after which (−)-8-phenylmenthol (10.0 g, 43.03 mmol) dissolved in CH_2Cl_2 (30 mL) was added [35]. The solution was stirred for 10 h and allowed to warm slowly to room temperature without removing the cold bath. The reaction was quenched with water (30 mL), stirred for 5 min, and extracted with CH_2Cl_2. Silica gel (ca. 25 g) was added to the organic layer, and the solvent removed under reduced pressure. The residue was loaded onto a silica gel column under N_2. Elution with hexane gave 14.50 g (31.84 mmol, 74%) of [[(1*R*,3*R*,4*S*)-8-phenylmenthyloxy](methyl)methylene]pentacarbonylchromium as an orange oil; $R_f = 0.73$ (hexane). This product was dissolved in diethyl ether (160 mL), and the aldehyde (90 mmol), triethylamine (80 mL, 57.39 mmol), and chlorotrimethylsilane (60 mL, 47.27 mmol) were added to the solution [36]. The

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resulting mixture was stirred at room temperature for 15 d when furfural was used and 30 d in the case of benzaldehyde. After removal of the volatiles, the residue was purified by chromatography on silica gel under N_2, eluting with hexane to give 14.56 g (27.06 mmol, 85%) of **1** or 12.95 g (25.51 mmol, 77%) of **2**, both as red oils.

1: $R_f = 0.27$ (hexane); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.70-2.40$ (m, 16H), 2.55 (s, 1H), 5.24 (s, 1H), 6.10 (d, $^3J(H,H) = 16$ Hz, 1H), 6.80–7.50 (m, 10H), 7.64 (d, $^3J(H,H) = 16$ Hz, 1H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 21.69$, 24.98, 26.56, 28.19, 31.20, 34.50, 39.61, 43.43, 52.53, 91.71, 125.03, 125.39, 127.90, 128.05, 128.77, 129.45, 130.31, 134.56, 140.81, 150.97, 216.87, 223.90, 327.70.

2: $R_f = 0.35$ (hexane); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.70-2.70$ (m, 17H), 5.10–5.30 (m, 1H), 5.65 (d, $^3J(H,H) = 15.0$ Hz, 1H), 6.42 (s, 1H), 6.57 (s, 1H), 6.80–7.45 (m, 6H), 7.64 (d, $^3J(H,H) = 15.0$ Hz, 1H); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): $\delta = 21.62$, 24.58, 26.50, 28.56, 31.10, 34.50, 39.47, 43.52, 52.52, 91.28, 112.85, 114.06, 119.04, 124.95, 125.32, 128.04, 137.91, 145.65, 151.05, 151.13, 216.89, 224.12, 324.74.

General Procedure for the Synthesis of Carbene Complexes 4: Ketone lithium enolates **3** were generated from the corresponding trimethylsilyl enol ethers prepared according to literature procedures [13,14]. To a solution of the appropriate trimethylsilyl enol ether (3.3 mmol) in THF (30 mL) was added BuLi (2.5 M in hexane, 1.3 mL, 3.3 mmol) at −45 °C. After the mixture had been stirred at −45 °C for 30 min and at room temperature for 10 min, it was cooled at −80 °C, and a solution of the vinylcarbene complex **1** or **2** (3.0 mmol) in THF (20 mL) was added. The reaction mixture was stirred at −80 °C for 30 min. The cold bath was then removed, and the reaction was stirred at room temperature for 10 min. The resulting solution was cooled to −80 °C again, and methyllithium (1.5 M in Et_2O, 4.0 mL, 6.0 mmol) was added. After the reaction had been stirred at −80 °C for 1 h, it was quenched at −80 °C with methanol (2 mL), and silica gel (ca. 5 g) was then added. The mixture was warmed to room temperature. Upon removal of solvent, the residue was transferred to a silica gel column under N_2. Elution with hexane/ethyl acetate mixtures gave the corresponding carbene complexes **4** as yellow oils, except for **4d**, which was isolated as a yellow solid. Yields are listed in Table 1.

The (*Z*) enolate of *p*-chloropropiophenone **3** (R^2 = Me, R^3 = Ph) was prepared as follows [16]: BuLi (2.5 M in hexane, 1.3 mL, 3.25 mmol) was added to a solution of diisopropylamine (0.33 g, 3.26 mmol) in THF (30 mL) at −40 °C. After 30 min stirring at −40 °C, a solution of *p*-chloropropiophenone (0.50 g, 2.97 mmol) in THF (30 mL) was added, and the mixture stirred at −40 °C for 30 min.

When the addition of MeLi was carried out in the presence of $CeCl_3$, the reagent system was prepared as follows [20]: a mixture of anhydrous $CeCl_3$ (1.11 g, 4.5 mmol) and THF (30 mL) was stirred at room temperature for 10 h. The resulting suspension was cooled to −65 °C, MeLi (1.5 M in Et_2O, 3.0 mL, 4.5 mmol) was added, and the mixture stirred at −65 °C for 1 h. The reaction was cooled to −80 °C and the appropriate reaction mixture, generated after the addition of the enolate as described above, was added.

4a: $R_f = 0.31$ (hexane:ethyl acetate, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.50-0.95$ (m, 5H), 1.00–2.30 (m, 25H), 3.17 (d, $^3J(H,H) = 10.7$ Hz, 1H), 3.60 (d, $^3J(H,H) = 11.1$ Hz, 1H), 4.80–4.90 (m, 1H), 6.87 (d, $^3J(H,H) = 6.0$ Hz, 2H), 7.05–7.30 (m, 6H), 7.32 (d, $^3J(H,H) = 7.3$ Hz, 2H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 21.32$, 21.48, 21.56, 22.52, 25.55, 26.66, 29.33, 30.36, 30.58, 33.86, 38.97, 40.76, 41.17, 42.66, 50.47, 52.70, 67.68, 72.17, 91.75, 124.96, 125.31, 126.89, 127.99, 128.06, 130.03, 139.61, 151.50, 216.68, 222.38, 355.64; $C_{37}H_{44}CrO_7$ (652.75): calcd C 68.08, H 6.79; found C 68.38, H 6.92.

4b: $R_f = 0.25$ (hexane:ethyl acetate, 20:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.60-2.50$ (m, 30H), 3.30–3.75 (m, 1H), 4.85–5.15 (m, 1H), 6.80–7.55 (m, 10H); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): $\delta = 20.24$, 21.26, 21.55, 25.55, 27.64, 27.71, 30.48, 30.60, 33.87, 38.97, 40.25, 41.10, 43.87, 50.48, 55.07, 67.54, 79.40, 91.67, 125.05, 125.36, 126.53, 127.81, 127.98, 129.39, 140.86, 151.63, 216.64, 222.46, 356.10; $C_{36}H_{42}CrO_7$ (638.7): calcd C 67.70, H 6.63; found C 67.76, H 6.54.

4c: $R_f = 0.29$ (hexane:ethyl acetate, 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.40-2.40$ (m, 26H), 3.16 (s, 2H), 4.76 (s, 1H), 6.51 (s, 2H), 6.80–7.60 (m, 13H; Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 9.06$, 21.17, 22.46, 25.36, 29.46, 30.23, 31.38, 33.70, 38.80, 40.34, 42.78, 47.96, 50.12, 68.15, 77.71, 91.15, 124.88, 125.33, 126.36, 126.92, 127.61, 127.70, 127.93, 128.25, 130.27, 138.59, 148.06, 151.43, 216.26, 222.40, 355.40; $C_{40}H_{44}CrO_7$ (688.8): calcd C 69.75, H 6.44; found C 69.43, H 6.32.

4d: M.p. 152–154 °C; $R_f = 0.28$ (hexane:ethyl acetate, 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.65-2.50$ (m, 27H), 3.27 (d, $^3J(H,H) = 8.60$ Hz, 1H), 4.80–4.90 (m, 1H), 6.63 (s, 1H), 7.10–7.60 (m, 13H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 9.06$, 21.20, 25.42, 29.31, 29.41, 30.27, 33.72, 36.44, 38.85, 40.50, 42.75, 47.85, 50.20, 68.08, 77.61, 91.29, 125.36, 126.31, 126.52, 127.76, 127.83, 127.96, 128.03, 130.23, 132.19, 138.33, 146.70, 151.47, 216.30, 222.25, 355.26; $C_{40}H_{43}ClCrO_7$ (723.2): calcd C 66.43, H 5.99; found C 66.39, H 6.00.

4e: Data on the 4:1 *syn*:*anti* mixture of isomers: $R_f = 0.25$ (hexane:ethyl acetate, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.65-2.50$ (m, 35H), 3.30–3.60 (m, 1H), 3.70–4.05 (m, 1H), 4.90–5.15 (m, 1H), 6.90–7.65 (m, 10H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): *syn* isomer: $\delta = 13.90$, 14.42, 16.49, 16.58, 18.95, 21.19, 22.43, 23.97, 25.45, 30.42, 33.81, 38.86, 40.51, 42.89, 44.06, 50.31, 55.90, 68.51, 75.72, 91.65, 125.04, 125.31, 126.44, 127.88, 129.06, 130.37, 140.36, 151.49, 216.68, 222.35, 355.61; *anti* isomer: $\delta = 13.48$, 15.51, 15.93, 16.99, 19.93, 20.92, 21.20, 23.46, 25.69, 28.31, 31.40, 39.21, 40.94, 43.55, 44.35, 50.43, 55.63, 66.82, 76.21, 92.10, 126.14, 126.24, 126.76, 127.46, 128.78, 129.21, 143.30, 151.04, 216.68, 222.35, 357.17; $C_{38}H_{46}CrO_7$ (668.8): calcd C 68.25, H 7.23; found C 68.43, H 7.18.

4f: $R_f = 0.28$ (hexane:ethyl acetate, 20:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.30-2.40$ (m, 30H), 3.05–3.45 (m, 2H), 3.90–4.20 (m, 1H), 4.75–5.20 (m, 1H), 5.50–5.80 (m, 1H), 5.90–6.20 (m, 1H), 6.60–7.40 (m, 6H); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): $\delta = 21.38$, 21.55, 22.33, 22.64, 25.84, 26.26, 28.87, 29.84, 30.71, 34.04, 35.23, 39.15, 40.81, 41.97, 50.56, 50.97, 65.74, 71.25, 92.50, 107.54, 110.16, 125.10, 125.27, 128.06, 140.84, 151.05, 154.37, 216.25, 222.33, 354.60; $C_{35}H_{42}CrO_8$ (642.7): calcd C 65.41, H 6.59; found C 65.71, H 6.31.

4g: $R_f = 0.29$ (hexane:ethyl acetate, 15:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.40-2.60$ (m, 30H), 3.30–3.75 (m, 1H), 5.00–5.35 (m, 1H), 5.75–6.05 (m, 1H), 6.10–6.45 (m, 1H), 6.90–7.80 (m, 6H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 20.03$, 21.38, 22.53, 25.52, 25.76, 26.75, 29.46, 30.62, 33.97, 35.48, 39.11, 40.97, 41.80, 50.81, 52.86, 66.16, 79.10, 92.27, 107.24, 110.08, 125.06, 125.32, 127.92, 140.57, 150.97, 154.55, 216.38, 222.32, 354.74; $C_{34}H_{40}CrO_8$ (628.7): calcd C 64.96, H 6.41; found C 64.83, H 6.55.

4h: $R_f = 0.28$ (hexane:ethyl acetate, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.65-2.20$ (m, 26H), 3.10–3.15 (m, 2H), 4.85–5.00 (m, 1H), 5.60 (s, 1H), 6.20 (s, 1H), 6.95–7.50 (m, 11H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 9.61$, 21.52, 23.11, 25.78, 28.15, 28.81, 30.53, 33.91, 36.27, 39.20, 41.45, 47.69, 50.36, 66.49, 77.41, 91.97, 109.92, 124.80, 125.04, 125.17, 126.44, 127.77, 128.02, 128.32, 141.33, 147.76, 150.87, 154.07, 216.19, 222.48, 354.67; $C_{38}H_{42}CrO_8$ (678.7): calcd C 67.25, H 6.24; found C 67.21, H 6.20.

General Procedure for the Synthesis of Enol Ethers 5: A given carbene complex **4** (2.0 mmol) dissolved in MeOH (20 mL) was added dropwise to a solution of NaOMe in MeOH (ca. 1 M, 30 mL) heated at reflux. The mixture was heated at reflux for 30 min and was then cooled to room temperature and filtered through a plug of Celite. After addition of silica gel (ca. 5 g), the solvent was removed and the residue was purified by column chromatography on silica gel with mixtures of hexane/ethyl acetate to give compounds **5** as colorless oils, except for **5c** and **5d**, which were obtained as white crystalline solids. The oily enol ethers were relatively unstable; slow decomposition was observed within 24–48 h of their preparation even when they were stored at −15 °C. Yields are reported in Table 1.

5a: $R_f = 0.63$ (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = -88.0$ ($c = 1$, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.17$ (s, 3H; CH_3), 1.30–1.95 (m, 9H; $4 \times CH_2$ and $CHCMe$), 3.28 (ddd, $^3J(H,H) = 6.7$, 3.0 Hz, $^4J(H,H) = 2.3$ Hz, 1H; $CHPh$), 4.71 (dd, $^3J(H,H) = 6.4$, 3.0 Hz, 1H; CH=CHO), 6.44 (dd, $^3J(H,H) = 6.4$ Hz, $^4J(H,H) = 2.3$ Hz, 1H; CH=CHO), 7.15–7.40 (m, 5H; Ph); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): $\delta = 22.04$, 22.84, 25.79, 27.17, 34.31, 39.11, 45.39, 76.31, 101.10, 125.96, 127.91, 128.11, 141.48, 145.30; LRMS (70 eV, EI): *m*/*z* (%): 228 (6.3) [M^+], 133 (52.8), 96 (38.8), 81 (100); HRMS (70 eV, EI): calcd for $C_{16}H_{20}O$ [M^+] 228.1514, found 228.1507.

5b: $R_f = 0.53$ (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = -101.3$ ($c = 0.39$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.00$ (s, 3H; CH_3), 1.50–1.90 (m, 7H; $3 \times CH_2$ and $CHCMe$), 3.18 (brs, 1H; $CHPh$), 4.72 (dd, $^3J(H,H) = 6.5$, 3.9 Hz, 1H; CH=CHO), 6.43 (dd, $^3J(H,H) = 6.5$ Hz, $^4J(H,H) = 2.1$ Hz, 1H; CH=CHO), 7.05–7.30 (m, 5H; Ph); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): $\delta = 19.50$, 23.76, 30.69, 38.27, 38.81, 49.14, 82.25, 99.52, 125.82, 127.87, 128.09, 142.41, 145.20; LRMS (70 eV, EI): *m*/*z* (%): 214 (66.2) [M^+], 171 (51.5), 133 (86.0), 28 (100); HRMS (70 eV, EI): calcd for $C_{15}H_{18}O$ [M^+] 214.1358, found 214.1362.

5c: M.p. 125–127 °C; $R_f = 0.60$ (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = -210.3$ ($c = 0.39$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.39$ (d, $^3J(H,H) = 6.9$ Hz, 3H; CH_3CH), 1.55 (s, 3H; CH_3C), 1.85 (dq, $^3J(H,H) = 10.7$, 6.9 Hz, 1H; $CHCH_3$), 2.89 (ddd, $^3J(H,H) = 10.7$, 1.7 Hz, $^4J(H,H) = 2.15$ Hz, 1H; $CHPh$), 4.65 (dd, $^3J(H,H) = 6.4$, 1.7 Hz, 1H; CH=CHO), 6.45 (dd, $^3J(H,H) = 6.40$, 2.15 Hz, 1H; CH=CHO), 7.05–7.40 (m, 10H; $2 \times$ Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 14.33$, 15.61, 43.98, 45.23, 81.32, 104.49, 125.88, 126.36, 127.14, 127.79, 128.17, 128.26, 142.04, 144.09, 144.95; LRMS (70 eV, EI): *m*/*z* (%): 264 (2.8) [M^+], 132 (100), 117 (57), 91 (11); HRMS (70 eV, EI): calcd for $C_{19}H_{20}O$ [M^+] 264.1514, found 264.1516.

5d: M.p. 129–131 °C; $R_f = 0.53$ (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = -125.4$ ($c = 0.86$, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.50$ (d, $^3J(H,H) = 6.9$ Hz, 3H; CH_3CH), 1.63 (s, 3H; CH_3C), 1.88 (dq, $^3J(H,H) = 10.4$, 6.9 Hz, 1H; $CHCH_3$), 3.00 (ddd, $^3J(H,H) = 10.7$, 1.7 Hz, $^4J(H,H) = 2.10$ Hz, 1H; $CHPh$), 4.76 (dd, $^3J(H,H) = 6.25$, 1.7 Hz, 1H; CH=CHO), 6.53 (dd, $^3J(H,H) = 6.2$ Hz, $^4J(H,H) = 2.1$ Hz, 1H; CH=CHO), 7.15–7.45 (m, 9H; ArH); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): $\delta = 14.32$, 15.76, 43.91, 45.22, 80.99, 104.68, 126.48, 127.45, 127.95, 128.26 (two carbons), 132.95, 141.88, 143.61, 143.87; LRMS (70 eV, EI): *m*/*z* (%): 300 (0.6) [$M^+ + 2$], 298 (1.8) [M^+], 166 (100), 131 (39.8), 115 (13.7).

5e: Data on the 15:1 *syn*:*anti* mixture of isomers; $R_f = 0.73$ (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = -125.6$ ($c = 0.60$, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): *syn* isomer: $\delta = 0.40$ (t, $^3J(H,H) = 7.65$ Hz, 3H; CH_3CH_2), 0.83 (t, $^3J(H,H) = 7.0$ Hz, 3H; CH_3CH_2), 1.11 (s, 3H; CH_3C), 1.15–1.60 (m, 7H), 2.94 (dt, $^3J(H,H) = 10.3$, 2.15 Hz; 1H; $CHPh$), 4.47 (dd, $^3J(H,H) = 6.2$, 1.75 Hz, 1H; CH=CHO), 6.25 (dd, $^3J(H,H) = 6.6$ Hz, $^4J(H,H) = 2.2$ Hz, 1H; CH=CHO),

7.05–7.25 (m, 5H; Ph); resolvable resonances of *anti* isomer: δ = 3.70 (m, 1H; C*H*Ph), 4.71 (d, ^3J(H,H) = 6.4 Hz, 1H; C*H*=CHO), 6.31 (d, ^3J(H,H) = 3.8 Hz, 1H; CH=C*H*O); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): *syn* isomer: δ = 14.12, 14.48, 15.97, 18.64, 23.58, 42.25, 43.41, 47.68, 79.77, 104.63, 126.27, 128.18, 128.37, 141.34, 144.89; LRMS (70 eV, EI): *m/z* (%): 244 (11.4) [M^+], 201 (11.1), 132 (100), 117 (9.2).

5f: R_f = 0.58 (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = -122.9$ (*c* = 0.35, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.97 (s, 3H; CH_3), 1.10–1.85 (m, 8H; 4 × CH_2), 2.00 (dt, ^3J(H,H) = 9.7, 4.3 Hz, 1H; C*H*CH_3), 3.07 (brs, 1H; C*H*Fu), 4.73 (ddd, ^3J(H,H) = 6.35, 4.15 Hz, ^4J(H,H) = 0.95 Hz, 1H; C*H*=CHO), 5.96 (dd, ^3J(H,H) = 1.3, 0.95 Hz, 1H; Fu), 6.20 (m, 1H; Fu), 6.31 (dd, ^3J(H,H) = 6.35 Hz, ^4J(H,H) = 1.9 Hz, 1H; CH=C*H*O), 7.20–7.25 (m, 1H; Fu); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 21.82, 24.33, 24.99, 28.99, 35.78, 37.37, 41.34, 75.12, 97.51, 104.55, 110.14, 140.48, 142.04, 158.11; LRMS (70 eV, EI): *m/z* (%): 177 (18.2) [M^+ − 41], 133 (61), 119 (100), 95 (80); HRMS (70 eV, EI): calcd for $C_{14}H_{18}O_2$ [M^+] 218.1307, found 218.1305.

5g: R_f = 0.60 (hexane:ethyl acetate, 15:1); $[\alpha]_D^{20} = -102.8$ (*c* = 1.1, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.02 (s, 3H; CH_3C), 1.45–1.95 (m, 6H; 3 × CH_2), 2.10–2.18 (m, 1H; C*H*CH_2), 3.15–3.25 (m, 1H; C*H*Fu), 4.72 (ddd, ^3J(H,H) = 6.35, 4.45 Hz, ^4J(H,H) = 0.95 Hz, 1H; C*H*=CHO), 5.97 (dd, ^3J(H,H) = 3.2, 0.65 Hz, 1H; Fu), 6.19 (dd, ^3J(H,H) = 3.2, 1.9 Hz, 1H; Fu), 6.33 (dd, ^3J(H,H) = 6.35 Hz, ^4J(H,H) = 1.9 Hz, 1H; CH=C*H*O), 7.20–7.25 (m, 1H; Fu); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): δ = 19.88, 22.27, 30.35, 32.06, 39.67, 44.84, 82.09, 96.59, 105.05, 109.99, 140.75, 142.61, 157.80; LRMS (70 eV, EI): *m/z* (%): 204 (41.4) [M^+], 161 (35.5), 119 (100), 94 (48.4); HRMS (70 eV, EI): calcd for $C_{13}H_{16}O_2$ [M^+] 204.1150, found 204.1155.

5h: R_f = 0.53 (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = -81.0$ (*c* = 0.60, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.56 (d, ^3J(H,H) = 6.75 Hz, 3H; CH_3CH), 1.52 (s, 3H; CH_3C), 2.09 (dq, ^3J(H,H) = 10.4, 6.75 Hz, 1H; C*H*CH_3), 3.13 (dt, ^3J(H,H) = 10.4, 2.3 Hz, 1H; C*H*Fu), 4.69 (dd, ^3J(H,H) = 6.2, 2.2, 1H; C*H*=CHO), 5.85–5.95 (m, 1H; Fu), 6.10–6.20 (m, 1H; Fu), 6.44 (dd, ^3J(H,H) = 6.2 Hz, ^4J(H,H) = 2.3 Hz, 1H; CH=C*H*O), 7.05–7.40 (m, 6H; Fu and Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 14.82, 16.04, 37.44, 42.14, 81.14, 101.38, 105.53, 110.03, 125.82, 127.17, 127.85, 140.99, 142.45, 144.67, 156.73; LRMS (70 eV, EI): *m/z* (%): 254 (2.6) [M^+], 132 (100), 117 (78), 91 (11); HRMS (70 eV, EI): calcd for $C_{17}H_{18}O_2$ [M^+] 254.1307, found 254.1312.

General Procedure for the Preparation of Acetals 6: A given enol ether **5** (1.0 mmol) was dissolved in a solution of anhydrous methanol (20 mL) saturated with hydrogen chloride. The solution was stirred at room temperature for 10 h, then neutralized with NaOH (3 M), and extracted with CH_2Cl_2. The organic solution was dried over anhydrous Na_2SO_4, concentrated, and the residue purified by column chromatography on silica gel with mixtures of hexane/ethyl acetate to yield products **6** as an equimolar mixture of isomers. Under these conditions the diastereoisomers of **6c** and **6d** were partially separated, but not the isomers of **6e** and **6g**. In the case of **6e**, the epimeric acetals corresponding to the minor *anti* isomer were removed in the column chromatography purification. All the acetals were isolated as colorless oils. Yields are reported in Scheme 1.

6c: less polar isomer: R_f = 0.51 (hexane:ethyl acetate, 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.36 (d, ^3J(H,H) = 6.9 Hz, 3H; CH_3CH), 1.75 (s, 3H; CH_3C), 1.90–2.15 (m, 3H), 3.00 (dt, ^3J(H,H) = 12.1, 3.5 Hz, 1H; C*H*Ph), 3.35 (s, 3H; CH_3O), 4.95 (d, ^3J(H,H) = 3.9 Hz, 1H; C*H*OMe), 7.05–7.35 (m, 8H; ArH), 7.50–7.55 (m, 2H; ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 14.30, 18.75, 39.26, 39.50, 46.15, 55.25, 80.03, 99.70, 126.04, 126.28, 126.88, 127.45, 127.82, 128.40, 144.09, 147.25; LRMS (70 eV, EI): *m/z* (%): 265 (1) [M^+ − 31], 144 (6.8), 118 (100), 91 (6.1); HRMS (70 eV, EI): calcd for $C_{20}H_{24}O_2$ [M^+] 296.1776, found 296.1774. More polar isomer: R_f = 0.50 (hexane:ethyl acetate, 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.32 (d, ^3J(H,H) = 6.9 Hz, 3H; CH_3CH), 1.55 (s, 3H; CH_3C), 1.70–1.80 (m, 2H; CH_2), 1.98 (m, 1H; C*H*CH_3), 2.63 (dt, ^3J(H,H) = 12.0, 3.9 Hz, 1H; C*H*Ph), 3.33 (s, 3H; CH_3O), 4.78 (dd, ^3J(H,H) = 9.6, 2.3 Hz, 1H; C*H*OMe), 7.05–7.30 (m, 8H; ArH), 7.50–7.60 (m, 2H; ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 13.80, 15.80, 39.75, 44.80, 45.61, 55.67, 80.25, 97.62, 125.91, 126.36, 126.86, 127.33, 127.67, 128.38, 143.72, 146.36.

6d: less polar isomer: R_f = 0.45 (hexane:ethyl acetate, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.43 (d, ^3J(H,H) = 6.9 Hz, 3H; CH_3CH), 1.80 (s, 3H; CH_3C), 1.95–2.20 (m, 3H), 3.06 (dt, ^3J(H,H) = 12.05, 3.9 Hz, 1H; C*H*Ph), 3.44 (s, 3H; CH_3O), 5.01 (d, ^3J(H,H) = 3.0 Hz, 1H; C*H*OMe), 7.15–7.35 (m, 7H; ArH), 7.50–7.55 (m, 2H; ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 14.24, 18.80, 39.23, 39.47, 46.25, 55.32, 79.75, 99.77, 126.41, 127.47, 127.62, 127.90, 128.48, 132.69, 143.90, 145.93; LRMS (70 eV, EI): *m/z* (%): 299 (1) [M^+ − 1], 118 (100), 91 (4.3); HRMS (70 eV, EI): calcd for $C_{14}H_{17}ClO_2$ [M^+] 330.1387, found 330.1404. More polar isomer: R_f = 0.35 (hexane:ethyl acetate, 20:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.41 (d, ^3J(H,H) = 6.9 Hz, 3H; CH_3CH), 1.64 (s, 3H; CH_3C), 1.85–2.10 (m, 3H), 2.65 (dt, ^3J(H,H) = 12.05, 3.9 Hz, 1H; C*H*Ph), 3.46 (s, 3H; CH_3O), 4.79 (dd, ^3J(H,H) = 9.9, 2.6 Hz, 1H; C*H*OMe), 7.00–7.30 (m, 7H; ArH), 7.55–7.60 (d, ^3J(H,H) = 8.6 Hz, 2H; ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 13.80, 15.90, 39.78, 44.83, 45.73, 55.81, 80.09, 97.79, 126.56, 127.42, 127.54, 127.85, 128.54, 132.75, 143.60, 145.06.

6e: data assigned with the assistance of the corresponding racemic products, which were partially separable by chromatography on silica gel; less polar isomer: R_f = 0.36 (hexane:ethyl acetate, 20:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.28 (t, ^3J(H,H) = 7.4 Hz, 3H; CH_3CH$_2$), 0.86 (m, 3H), 0.95–1.20 (m, 3H), 1.26 (s, 3H; CH_3C), 1.35–1.65 (m, 6H), 1.75–1.95 (m, 2H), 2.92 (dt, ^3J(H,H) = 11.1, 4.8 Hz, 1H; C*H*Ph), 3.34 (s, 3H, CH_3O), 4.73 (m, 1H; C*H*OMe), 7.05–7.30 (m, 5H; Ph); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): δ = 14.44, 14.59, 16.21, 21.40, 23.12, 38.71, 39.16, 44.67, 49.58, 55.11, 78.34, 98.96, 126.23, 128.07, 128.2, 144.53; LRMS (70 eV, EI): *m/z* (%): 261 (1) [M^+ − 15], 147 (14.9), 132 (100), 117 (36.2); HRMS (70 eV, EI): calcd for $C_{18}H_{28}O_2$ [M^+] 276.2089, found 276.2102. More polar isomer: R_f = 0.34 (hexane:ethyl acetate, 20:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.27 (t, ^3J(H,H) = 7.4 Hz, 3H; CH_3CH$_2$), 0.85 (m, 3H), 0.90–1.10 (m, 2H), 1.13 (s, 3H; CH_3C), 1.30–1.70 (m, 6H), 1.75–1.90 (m, 1H), 2.63 (dt, ^3J(H,H) = 12.0, 3.5 Hz, 1H; C*H*Ph), 3.38 (s, 3H; CH_3O), 4.51 (dd, ^3J(H,H) = 9.7, 2.4 Hz, 1H; C*H*OMe), 7.05–7.25 (m, 5H, Ph); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): δ = 14.44, 14.52, 15.81, 17.68, 22.70, 39.84, 44.23, 44.27, 50.50, 55.44, 78.47, 97.14, 126.36, 127.93, 128.29, 144.05.

6g: the following data were taken from the nearly 1:1 mixture of isomers. R_f = 0.33 (hexane:ethyl acetate, 20:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.22 (s, 3H; CH_3C), 1.43 (s, 3H; CH_3C), 1.45–2.00 (m, 17H), 2.18 (ddd, ^3J(H,H) = 13.0, 5.85, 3.0 Hz, 1H; C*H*CMe), 2.50–2.60 (m, 1H; C*H*Fu), 3.05–3.15 (m, 1H; C*H*Fu), 3.41 (s, 3H; CH_3O), 3.43 (s, 3H; CH_3O), 4.80–4.90 (m, 2H; C*H*OMe), 5.95–6.05 (m, 2H; Fu), 6.25–6.35 (m, 2H; Fu), 7.30–7.35 (m, 2H; Fu); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): δ = 19.37, 22.12, 27.20, 27.30, 29.85, 31.21, 32.16, 33.23, 33.73, 35.94, 36.68, 40.63, 45.53, 48.51, 54.41, 54.64, 81.22, 82.65, 97.63, 99.21, 104.18, 104.67, 109.62, 140.69, 140.77, 157.64 (two aromatic carbon not found); LRMS (70 eV, EI): *m/z* (%): 236 (3) [M^+], 204 (8.4), 178 (6.6), 137 (29.4), 120 (100), 94 (67.6), HRMS (70 eV, EI): calcd for $C_{14}H_{20}O_3$ [M^+] 236.1417, found 236.1417.

[[(1*R*,3*R*,4*S*)-8-Phenylmenthyloxy][(2*R*,3*S*)-3-methoxycarbonyl-2-phenylbutyl]methylene]pentacarbonylchromium (8): A solution of LDA, prepared from diisopropylamine (0.14 g, 1.4 mmol) and BuLi (2.5 M in hexane, 0.55 mL, 1.4 mmol) in THF (20 mL), was added dropwise to a solution of methyl propionate (0.13 g, 1.4 mmol) in THF (20 mL) cooled to −80 °C [16]. After stirring at −80 °C for 30 min, the carbene complex **1** (0.70 g, 1.3 mmol) dissolved in THF (20 mL) was added. The mixture was stirred at −80 °C for 1 h and allowed to warm to −65 °C slowly for 1 h. The reaction was quenched with a solution of concentrated sulfuric acid (0.3 mL) in Et_2O (5 mL) at −65 °C. After warming to room temperature, silica gel (ca. 5 g) was added, the solvents were removed under reduced pressure and the residue was loaded onto a silica gel column under N_2. Elution with a 20:1 mixture of hexane:ethyl acetate gave 0.70 g (1.12 mmol, 74%) of carbene complex **8** as a yellow oil. R_f = 0.25 (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = +54.0$ (*c* = 2.7, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.50–1.40 (m, 19H), 1.55–1.90 (m, 2H), 1.90–2.45 (m, 2H), 3.05–3.75 (m, 5H), 4.75–5.10 (m, 1H), 6.65–7.50 (m, 10H, 2 × Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 14.85, 21.36, 22.50, 25.75, 29.68, 30.55, 33.91, 39.20, 40.60, 46.75, 46.90, 50.61, 51.30, 64.40, 92.04, 125.43, 126.80, 127.63, 128.09, 128.88, 128.99, 139.72, 151.53, 174.68, 216.49, 222.46, 355.61; LRMS (70 eV, EI): *m/z* (%): 626 (7) [M^+], 542 (85), 454 (30), 214 (18), 119 (100); HRMS (70 eV, EI): calcd for $C_{34}H_{38}CrO_8$ [M^+] 626.1972, found 626.1965.

[[(1*R,3*R**,4*S**)-Menthyloxy][(*E*)-2-phenylethenyl]methylene] pentacarbonylchromium (*rac*-9)**: To a solution of [methyl[(tetramethylammonio)oxy]methylene]-pentacarbonylchromium [34] (20.02 g, 64.78 mmol) in CH_2Cl_2 (200 mL) cooled to −45 °C was added dropwise acetyl bromide (4.8 mL, 64.92 mmol). The resulting solution was stirred at −45 °C for 45 min. This was followed by addition of (±)-menthol (10.03 g, 64.29 mmol) dissolved in CH_2Cl_2 (30 mL) [35]. The mixture was stirred for 10 h and allowed to warm slowly to room temperature. It was then quenched with water (30 mL), stirred for 5 min, and extracted with CH_2Cl_2. Silica gel (ca. 15 g) was added to the organic layer, and the solvent was removed under reduced pressure. The residue was loaded onto a silica gel column under N_2. Elution with hexane gave 19.56 g (52.31 mmol, 81%) of [[(1*R**,3*R**,4*S**)-menthyloxy]-(methyl)methylene]pentacarbonylchromium [37] as a yellow oil; R_f = 0.68 (hexane). This product was dissolved in ether (150 mL), and BuLi (2.5 M in hexane, 20.90 mL, 52.25 mmol) added to this solution cooled to −80 °C. After 30 min, a solution of benzaldehyde (11.1 mL, 109 mmol) in Et_2O (30 mL) was added [38]. The reaction mixture was stirred at −80 °C for 30 min and allowed to warm to room temperature for 2 h. Silica gel (ca. 15 g) was added to the resulting solution, and, after removal of the solvents, the residue was transferred onto a silica gel column under N_2. Elution with hexane gave 18.85 g (40.80 mmol, 78%) of carbene complex *rac*-**9** as a red oil. R_f = 0.43 (hexane); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.50–2.30 (m, 17H), 4.90–5.20 (m, 1H), 6.80–8.00 (m, 7H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): δ = 16.97, 21.49, 21.88, 23.81, 26.50, 31.05, 33.95, 42.03, 48.19, 90.99, 128.98, 130.63, 134.52, 140.05, 216.84, 224.25, 324.05 (two aromatic carbons not found).

General Procedure for the Synthesis of Carbene Complexes 10. To a solution of 1-trimethylsilyloxycyclohexene [13] (0.69 g, 4.06 mmol) in THF (30 mL) cooled to −40 °C was added BuLi (2.5 M in hexane, 1.6 mL, 4.0 mmol) [15]. After the mixture had been stirred at −40 °C for 30 min and at room temperature for 15 min, it was cooled to −80 °C and a solution of **1** (1.94 g, 3.6 mmol) in THF (20 mL) was added.

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The reaction mixture was stirred at −80 °C for 30 min and at room temperature for 10 min and then cooled to −80 °C again. A solution of LDA, prepared from diisopropylamine (0.36 g, 3.6 mmol), BuLi (2.5 M in hexane, 1.45 mL, 3.6 mmol), and THF (20 mL) was added, and after 30 min at −80 °C a solution of the appropriate aldehyde (18 mmol) in THF (20 mL) was added. The reaction was stirred at −80 °C for 1 h and then quenched with a solution of concentrated H_2SO_4 (0.8 mL) in Et_2O (5 mL). After the mixture had warmed to room temperature, silica gel (ca. 2 g) was added. This was followed by removal of solvents and purification by column chromatography on silica gel under N_2. Elution with a 10:1 mixture of hexane:ethyl acetate gave the corresponding carbene complexes **10** as yellow solids. Yields are listed in Scheme 3.

10a: M.p. 103–105 °C; $R_f = 0.15$ (hexane:ethyl acetate, 20:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.55-2.40$ (m, 27H), 2.75–3.00 (m, 1H), 3.30–3.70 (m, 2H), 4.75–5.00 (m, 1H), 6.80–7.40 (m, 15H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 19.88$, 21.23, 22.74, 25.70, 29.12, 29.24, 30.09, 30.45, 33.82, 39.06, 40.30, 43.40, 50.70, 55.14, 56.79, 65.67, 74.45, 92.11, 125.24, 125.34, 125.49, 126.84, 127.60, 127.69, 128.01, 128.15, 128.83, 139.04, 140.94, 151.10, 216.13, 216.37, 222.22, 355.67; $C_{43}H_{46}CrO_8$ (742.8): calcd C 69.53, H 6.24; found C 69.25, H 6.02.

10b: M.p. 96–98 °C; $R_f = 0.23$ (hexane:ethyl acetate, 20:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.55-2.40$ (m, 27H), 2.70–2.90 (m, 1H), 3.25–3.70 (m, 1H), 4.75–4.95 (m, 2H), 6.60–7.45 (m, 14H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 19.75$, 21.14, 22.42, 25.60, 28.88, 29.38, 29.94, 30.40, 33.77, 38.94, 40.18, 43.38, 50.63, 54.85, 56.82, 65.55, 73.65, 92.09, 125.17, 125.44, 126.87, 127.96, 128.16, 128.76, 129.10, 133.17, 138.80, 139.58, 139.99, 151.05, 215.74, 216.32, 222.07, 355.45; $C_{43}H_{45}ClCrO_8$ (777.3): calcd C 66.45, H 5.84; found C 66.17, H 5.74.

General Procedure for the Preparation of Chromium Carbenes 11: A mixture of anhydrous $CeCl_3$ (1.36 g, 5.51 mmol) and THF (20 mL) was stirred at room temperature for 10 h. Methyllithium (1.5 M in Et_2O, 3.7 mL, 5.55 mmol) was added to this suspension, cooled to −80 °C. After the mixture had been stirred at −80 °C for 1 h, the complex **10** (2.0 mmol) dissolved in THF (20 mL) was added, and the mixture was stirred at −80 °C for 1 h [20]. The reaction was treated with MeOH (2 mL) and silica gel (ca. 2 g), and then warmed to room temperature. Solvents were removed and the residue was purified by column chromatography on silica gel under N_2. Elution with a 10:1 mixture of hexane:ethyl acetate gave the corresponding complexes **11** as yellow solids. Yields are reported in Scheme 3.

11a: M.p. 108–110 °C; $R_f = 0.38$ (hexane:ethyl acetate, 5:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.50-2.40$ (m, 31H), 3.75–3.90 (m, 1H), 4.35–4.70 (m, 2H), 4.75–5.00 (m, 1H), 6.70–7.40 (m, 15H); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): $\delta = 19.78$, 21.31, 22.54, 24.63, 25.12, 25.50, 25.96, 26.42, 27.78, 30.50, 33.92, 39.38, 40.59, 42.87, 45.76, 50.80, 51.60, 70.30, 78,52, 91.87, 125.05, 125.36, 125.94, 127.09, 127.33, 127.62, 128.03, 128.15, 129.85, 142.30, 143.43, 151.17, 216.78, 222.90, 357.85; HRMS (FAB): calcd for $C_{39}H_{50}CrO_3$ [$M^+ - 5CO$] 618.3165, found 618.3207.

11b: M.p. 107–109 °C; $R_f = 0.30$ (hexane:ethyl acetate, 10:1); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.50-2.45$ (m, 31H), 3.65–3.85 (m, 1H), 4.00–4.20 (m, 1H), 4.30–4.55 (m, 1H), 4.70–4.95 (m, 1H), 6.70–7.50 (m, 14H); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 19.79$, 21.33, 22.20, 24.18, 25.00, 25.51, 25.95, 26.39, 28.24, 30.53, 33.97, 39.37, 40.56, 42.81, 45.83, 50.81, 51.91, 69.96, 77.53, 91.88, 125.01, 125.33, 125.45, 126.11, 127.40, 128.08, 128.31, 128.47, 128.90, 129.94, 142.01, 151.36, 216.82, 222.80, 357.63; HRMS (FAB): calcd for $C_{39}H_{49}ClCrO_3$ [$M^+ - 5CO$] 652.2775, found 652.2781.

General Procedure for the Preparation of Bicyclic Enol Ethers 12: Compounds **12** were prepared from the appropriate carbene complex **11** (1.5 mmol) and a solution of NaOMe in MeOH (ca. 1 M, 30 mL) in the same manner as described above for **5**. In this case (−)-8-phenylmenthol eluted off the column at the same time as compounds **12** when different mixtures of hexane/ethyl acetate were used. The chiral auxiliary was removed by evaporation under reduced pressure (7×10^{-5} mmHg) at 50 °C. Compounds **12** were isolated as colorless oils.

12a: $R_f = 0.50$ (hexane:ethyl acetate, 5:1); $[\alpha]_D^{20} = -117.9$ ($c = 15$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.95-1.55$ (m, 6H; $3 \times CH_2$), 1.60 (s, 3H; CH_3), 1.83 (d, ^3J(H,H) = 10.8 Hz, 1H; C*H*CHC=), 2.30 (ddd, ^3J(H,H) = 11.8, 9.55, 4.9 Hz, 1H; C*H*CHOH), 3.47 (d, ^3J(H,H) = 10.8 Hz, 1H; C*H*C=), 4.64 (d, ^3J(H,H) = 9.55 Hz, 1H; C*H*OH), 4.77 (dd, ^3J(H,H) = 6.35 Hz, ^4J(H,H) = 1.90 Hz, 1H; C*H*=CHO), 4.87 (s, 1H; OH), 6.48 (dd, ^3J(H,H) = 6.35, 2.5 Hz, 1H; CH=C*H*O), 7.10–7.45 (m, 10H; 2 × Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 19.12$, 21.55, 23.89, 27.25, 36.43, 42.91, 46.87, 77.80, 82.38, 105.53, 126.54, 127.39, 127.53, 128.05, 128.13, 128.27, 139.65, 143.02, 144.04; LRMS (70 eV, EI): *m/z* (%): 334 (30) [M^+], 317 (40), 133 (100), 107 (70), 79 (68); HRMS (70 eV, EI): calcd for $C_{23}H_{26}O_2$ [M^+] 334.1931, found 334.1931.

12b: $R_f = 0.20$ (hexane:ethyl acetate, 20:1); $[\alpha]_D^{20} = -138.7$ ($c = 1.20$, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.85-1.55$ (m, 6H; $3 \times CH_2$), 1.59 (s, 3H; CH_3), 1.84 (d, ^3J(H,H) = 10.8 Hz, 1H; C*H*CHC=), 2.25 (ddd, ^3J(H,H) = 11.8, 9.55, 4.9 Hz, 1H; C*H*CHOH), 3.46 (d, ^3J(H,H) = 10.8 Hz, 1H; C*H*C=), 4.62 (d, ^3J(H,H) = 9.55 Hz, 1H; C*H*OH), 4.85 (dd, ^3J(H,H) = 6.35, 1.9 Hz, 1H; C*H*=CHO), 4.92 (s, 1H; OH), 6.48 (dd, ^3J(H,H) = 6.35 Hz, ^4J(H,H) = 2.5 Hz, 1H; CH=C*H*O), 7.10–7.45 (m, 9H; ArH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C): $\delta = 19.12$, 21.57, 23.90, 27.23, 36.43, 43.01, 46.87, 77.23, 82.34, 105.69, 126.64, 128.18, 128.28, 128.39, 128.80, 133.19, 139.63, 141.60, 143.98; LRMS (70 eV, EI): *m/z* (%): 368 (7) [M^+], 214 (9), 133 (38), 119 (100), 91 (37); HRMS (70 eV, EI): calcd for $C_{23}H_{25}ClO_2$ [M^+] 368.1543, found 368.1551. *rac*-**12b**: M.p. 200–201 °C.

General Procedure for the Preparation of Hemiacetals 13: HCl (1 M in H_2O, 3 mL) was added to a solution of the appropriate enol ether **12** (0.3 mmol) in THF (20 mL), and the mixture was stirred at room temperature for 10 h. Addition of silica gel (ca. 2 g), concentration, and chromatography on silica gel (elution with a 2:1 mixture of hexane:ethyl acetate) gave a 2:1 mixture of epimers (due to the hemiacetal moiety) of the title compounds **13** as colorless oils. Yields are listed in Scheme 3. The following data were collected in both cases on the 2:1 mixture of diastereoisomers.

13a: $R_f = 0.40$ (hexane:ethyl acetate, 2:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.65-2.10$ (m), 2.30–2.40 (m), 2.80–3.15 (m), 3.25–3.50 (m), 4.50–4.65 (m), 5.20–5.45 (m), 5.76 (s), 5.85 (d, ^3J(H,H) = 5.1 Hz), 6.36 (s), 7.0–7.45 (m); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): major isomer: $\delta = 19.37$, 23.08, 24.51, 27.06, 27.57, 39.05, 41.49, 47.52, 78.38, 82.06, 89.92, 142.66, 143.21; minor isomer: $\delta = 19.70$, 23.15, 25.23, 28.37, 33.23, 40.50, 45.24, 48.66, 78.65, 81.31, 92.69,143.03, 143.68; the following resonances were not assignable: $\delta = 125.63$, 126.27, 126.48, 127.10, 127.43, 127.57, 127.68, 127.79, 128.11, 128.47, 128.53.

13b: $R_f = 0.25$ (hexane:ethyl acetate, 2:1); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.80-2.10$ (m), 2.15–2.45 (m), 2.90–3.20 (m), 3.30–3.50 (m), 4.45–4.70 (m), 5.30–5.50 (m), 6.35 (s), 7.00–7.40 (m); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): major isomer: $\delta = 19.33$, 23.08, 24.48, 27.02, 33.21, 39.00, 41.71, 47.51, 77.76, 82.17, 90.10, 133.41, 141.18, 143.02; minor isomer: $\delta = 19.63$, 23.08, 25.19, 27.49, 33.21, 40.64, 45.26, 48.62, 78.08, 81.36, 92.72, 133.23, 141.56, 143.52; the following resonances were not assignable: 126.36, 126.58, 127.09, 127.31, 128.26, 128.34, 128.51, 128.59, 128.71, 129.04.

Preparation of Bicyclic Lactone 14b: A saturated aqueous solution of $BaCO_3$ (2 mL) and a solution of Br_2 (0.085 g, 0.54 mmol) in THF (2 mL) were successively added to a solution of **13b** (0.070 g, 0.18 mmol) in THF (10 mL). The mixture was stirred at room temperature for 1 h and then washed with a saturated aqueous solution of $NaHSO_3$ and extracted with CH_2Cl_2. The organic phase was filtered through a plug of silica gel and concentrated to yield 0.050 g (0.13 mmol, 70%) of **14b** as a colorless oil. $R_f = 0.30$ (hexane:ethyl acetate, 2:1); $[\alpha]_D^{20} = +11.2$ ($c = 0.45$, CH_2Cl_2); ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 0.80-1.50$ (m, 6H; $3 \times CH_2$), 1.64 (ddd, ^3J(H,H) = 12.7, 9.05, 3.0 Hz, 1H; C*H*COMe), 1.78 (s, 3H; CH_3), 2.12 (m, 1H; C*H*CHOH), 2.67 (dd, ^2J(H,H) = 17.8 Hz, ^3J(H,H) = 12.7 Hz, 1H; CHCOO axial), 2.95 (dd, ^2J(H,H) = 17.8 Hz, ^3J(H,H) = 5.1 Hz, 1H; CHCOO equatorial), 3.43 (dt, ^3J(H,H) = 12.7, 5.1 Hz, 1H; C*H*CH_2CO), 4.77 (d, ^3J(H,H) = 8.9 Hz, 1H; C*H*OH), 7.10–7.45 (m, 9H; ArH); ^{13}C NMR (50.5 MHz, $CDCl_3$, 25 °C): $\delta = 19.12$, 22.92, 24.56, 27.78, 37.38, 38.32, 46.39, 49.07, 76.11, 90.17, 127.06, 127.42, 128.37, 128.73, 129.10, 133.37, 140.64, 141.00, 169.02. LRMS (70 eV, EI): *m/z* (%): 384 (0.1) [$M^+ + 2$], 382 (0.2) [M^+], 244 (9.4), 119 (42.5), 95 (100); HRMS (70 eV, EI): calcd for $C_{23}H_{25}ClO_3$ [M^+] 384.1492, found 384.1483.

Acknowledgements: This work was supported by DGICYT (Grant PB92-1005). J. M. Montserrat thanks the Instituto de Cooperación con Iberoamérica (Ministerio de Asuntos Exteriores de España) for a MUTIS doctoral fellowship.

Received: November 8, 1994 [F17]

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