Acyclic Stereocontrol in Fischer Carbene Chemistry by *Syn*-Selective Michael Addition/Trapping Sequence

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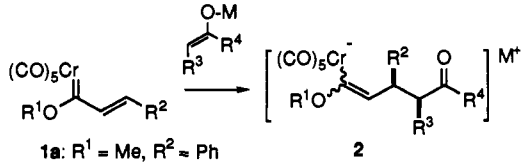
Abstract: Michael addition of a metal enolate to a Fischer vinyl carbene complex **1** takes place with *syn*-diastereoselectivity. The resulting anion **2** can be trapped stereoselectively to afford a carbene complex **3** with stereocontrol of three contiguous stereogenic centers. The *syn*-diastereoselectivity of the Michael addition was unaffected either by the geometry or the countercation of the enolate. Lewis acidic metal countercation slows down the Michael addition. Lewis-acid mediated Mukaiyama–Michael addition of enol silyl ethers also failed. ^1H and ^{13}C NMR studies indicated no complexation of $SnCl_4$ with the vinyl carbene complex **1a**. All these data strongly suggest that the vinyl carbene complex **1** is a unique electron-deficient olefin that is incapable of having interaction with Lewis acidic metals, and that the observed *syn*-diastereoselectivity may be the result of an open chain transition state.

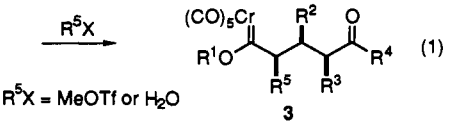
The origin of stereoselectivity in the addition of a metal enolate to an electron-deficient olefin (Michael addition) has been the subject of intensive discussion for the past decade. A crucial point of these discussions is whether the reaction proceeds through a chelated transition state. In a chelated transition state, the metal countercation of the enolate is coordinated to the heteroatom of the nucleophile and also activates the olefin of the electrophile.[2] Common electron-deficient olefins always possess an electronegative heteroatom which acts as an electron sink and serves as the site of coordination to the metal enolate. The stereoselectivity of the Michael addition is usually very sensitive to the basicity of the solvent or the additive present in the reaction mixture (e.g., HMPA).

We found that a Fischer vinylcarbene complex (**1**)[3] is a unique Michael acceptor because it is incapable of coordination to a Lewis acid. The Michael addition of an enolate to **1** is *syn*-selective irrespective of the enolate geometry or the nature of the countercation. This method provides a powerful new stereoselective entry to carbene complexes bearing several chiral centers upon trapping of the anion **2** (eq 1). This procedure permits the synthesis of aliphatic carbene complexes with acyclic stereogenic centers for which reliable synthetic methods are still very scarce.[4]



1a: R^1 = Me, R^2 = Ph
1b: R^1 = Et, R^2 = 2-furyl
1c: R^1 = Me, R^2 = *n*-Bu

2



R^5X = MeOTf or H_2O (1)

3

Results and Discussion

Although Fischer vinylcarbene complexes were previously utilized as Michael acceptors,[5] very little is known about the stereochemistry of the addition reaction. In the present studies, we have examined representative metal enolate structures and relate these to the observed stereochemistry of the reaction. In view of the mechanistic kinship between Michael and aldol reactions, we investigated four classes of enolates[6] that we have recently shown to be good mechanistic probes. Hence, we have investigated lithium (class I) and titanium (class II) enolates that have an intrinsic preference to react via a chelated transition state. A tetrabutylammonium enolate (class III) is expected to react only via an open transition state. The lithium enolate was also examined in the presence of 12-crown-4 and HMPA, both of which could significantly affect the enolate's coordination and aggregation state. Finally, we have investigated an enol silyl

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(1) (a) Tokyo Institute of Technology. (b) Brown University.

(2) (a) Oare, D. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 157. (b) Reviews: Oare, D. A.; Heathcock, C. H. *Topics Stereochem.* **1989**, *19*, 227. Yamaguchi, M. *J. Synth. Org. Chem. Soc. Jpn.* **1986**, *44*, 405.

(3) Reviews: (a) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissl, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complex*; VCH: Weinheim: 1984. (b) Aumann, R. In *Organometallics in Organic Synthesis*; de Meijere, A.,; tom Dieck, H., Eds.: Springer: Berlin, 1988, pp. 69–83. (c) Dötz, K. H. In *Organometallics in Organic Synthesis*; de Meijere, A., tom Dieck, H., Eds.: Springer: Berlin, 1988, pp 85–104. (d) Wulff, W. D. *Advance in Metallo-Organic Chemistry* **1989**, *1*, 209. (e) Review: Brown, F. J. *Prog. Inorg. Chem.* **1980**, *27*, 1. (f) For some recent references, see: Parker, K. A.; Cobum, C. A. *J. Org. Chem.* **1991**, *56*, 1667. Boger, D. L.; Jacobsen, I. C. *J. Org. Chem.* **1991**, *56*, 2115. (g) Söderberg, B. C.; Hegedus, L. S. *J. Org. Chem.* **1991**, *56*, 2209, and references therein. (h) Chemistry of metal-free vinylcarbenes, cf.: Tokuyama, H.; Isaka, M.; Nakamura *J. Am. Chem. Soc.* **1992**, *114*, 5523 references therein.

(4) (a) Aoki, S.; Fujimura, T.; Nakamura, E. *J. Am. Chem. Soc.* **1992**, *114*, 2985. (b) For some pertinent references, see: Casey, C. P.; Brunsvold, W. R. *J. Organomet. Chem.* **1974**, *77*, 345. Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1983**, *105*, 6726. Wulff, W. D.; Yang, D. C. *J. Am. Chem. Soc.* **1984**, *106*, 7565. Wulff, W. D.; Gilbertson, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 503. Chan, K.-S.; Wulff, W. D. *J. Am. Chem. Soc.* **1986**, *108*, 5229. Aumann, R.; Heinen, H. *Chem. Ber.* **1987**, *120*, 537. Xu, Y.-C.; Wulff, W. D. *J. Org. Chem.* **1987**, *52*, 3263. Macomber, D. W.; Hung, M.-H.; Verma, A. G. *Organometallics* **1988**, *7*, 2072. Lattuada, L.; Licandro, E.; Papagni, A.; Maiorana, S.; Villa, A. C.; Guastini, C. *J. Chem. Soc., Chem. Commun.* **1988**, 1092. Macomber, D. W.; Madhukar, P. *Organometallics* **1989**, *8*, 1275. Wulff, W. D.; Anderson, B. A.; Toole, A. J. *J. Am. Chem. Soc.* **1989**, *111*, 5485. Hegedus, L. W., *Pure Appl. Chem.* **1990**, *62*, 691.

(5) (a) Casey, C. P.; Brunsvold, W. R. *Inorg. Chem.* **1977**, *16*, 391. Casey, C. P.; Brunsvold, W R.; Scheck, D. M. *Inorg. Chem.* **1977**, *16*, 3059. (b) Wang, S. L. B.; Wulff, W. D. *J. Am. Chem. Soc.* **1990**, *112*, 4550. (c) Conjugate addition of alkyl radicals: Merlic, C. A.; Xu, D. *J. Am. Chem. Soc.* **1991**, *113*, 9856. (d) Macomber, D. W.; Hung, M.; Madhukar, P.; Liang, M.; Rogers, R. D. *Organometallics* **1991**, *10*, 737.

(6) Yamago, S.; Machii, D.; Nakamura, E. *J. Org. Chem.* **1991**, *56*, 2098. See, also: Denmark, S. E.; Henke, B. R. *J. Am. Chem. Soc.* **1991**, *113*, 2177.

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ether (under Mukaiyama conditions: i.e., class IV), which should act as a highly reactive donor when the Michael acceptor is activated by coordination to a strong Lewis acid.

The Michael addition to **1** was carried out utilizing Casey's protocol,[5a] i.e., by addition a THF/hexane solution of an enolate to **1** at −78 °C, followed by aqueous quenching at a temperature between −78 and 20 °C. Lithium enolates were generated either from enol silyl ethers or from the parent ketones (with LDA).[7] ZnCl-[8] and Ti(O-*i*-Pr)$_3$-enolates[9] were prepared by Li/metal exchange using an appropriate metal chloride. Generation of Bu_4N^+ enolates followed our original procedure taking advantage of the activation of an enol silyl ether with fluoride anion.[10] The $TiCl_4$- and $SnCl_4$-mediated Mukaiyama–Michael addition was carried out as previously described.[11] The results for the classes I-III enolates are summarized in Table I.[12] Details are discussed below.

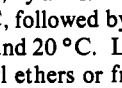
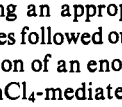
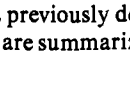
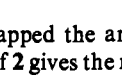
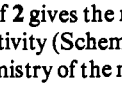
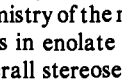
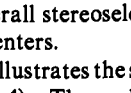
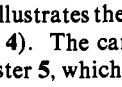
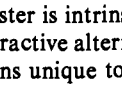
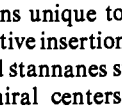
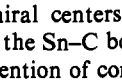
We also trapped the anion **2** with MeOTf[13] and found that methylation of **2** gives the methylated product **3** with ca. 90% net diastereoselectivity (Scheme I). We do not completely understand the stereochemistry of the methylation at this time,[14] but it follows the precedents in enolate chemistry.[15] This sequence proceeds with good overall stereoselectivity and creates three contiguous stereogenic centers.

Scheme II illustrates the synthetic use of the Michael/trapping product (e.g., **4**). The carbene moiety is oxidized readily with CAN to the ester **5**, which is further reduced stereoselectively to the lactol 6. Michael addition of a ketone enolate to an unsaturated ester is intrinsically difficult. The present route to **5** offers an attractive alternative. Especially noteworthy are the transformations unique to carbene complexes. For instance, a diastereoselective insertion reaction of **4** into Sn–H bonds affords functionalized stannanes such as **7**.[16] This sequence creates four contiguous chiral centers in two operations starting from **1**. Furthermore, the Sn–C bond in **7** can be converted into a C–C bond with retention of configuration.[17]

***syn*-Selective Michael Addition.** The data in Table I indicate some unusual features of the diastereoselectivity of the present Michael addition. *syn*-Stereoselectivity is observed for a variety of enolate structures and counterions. The diastereoselectivity is particularly high for the lithium enolates of cyclohexanones (entries 13 and 14) or those with a bulky R^4 groups (entries 1–11 and 19). Comparison of the entries 1–6 vs 12 and 16 suggests that the selectivity improves as the R^4 group and the metal environment become more sterically demanding. The same effect of the R^4 group is well-documented in the aldol chemistry.[6]

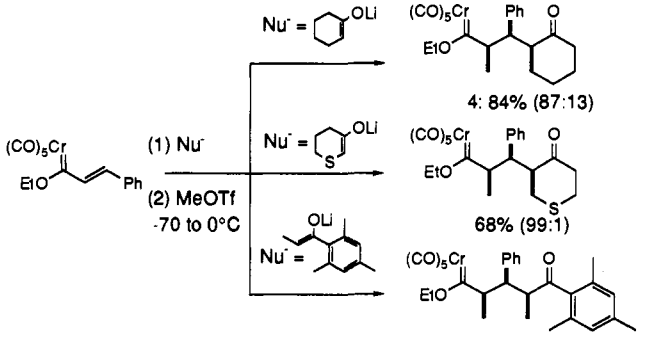
The Michael addition stereoselectivity of the *E*- and *Z*-enolates of ethyl mesityl ketone (entries 1–11) was examined for the four classes of metal enolate previously investigated for aldol reaction.[6] The most important observation is that both the *E*- and the *Z*-enolates show the same sense and level of the diastereoselectivity for each countercation (cf. entries 1–6 vs 7–11).[18] In the reaction of the less stable *E*-enolate, we confirmed that enolate equilibration does not take place by recovery of unreacted enolate as enol silyl

Table I. *syn*-Stereoselective Michael Addition to Vinylcarbene Complexes **1** (eq 1, $R^5X = H_2O$)[a]

entry	1	enolate	% yield	*syn* : *anti*
	1a	M =		
1		Bu_4N	19	71:29
2		Li/crown	8	81:19
3		Li/HMPA	40	99:1
4		Li	50	99.4:0.6
5	(*E*:*Z* = 3:97)	ZnCl	74	92:8
6		$Ti(OiPr)_3$	0	–
		M =		
7		Bu_4N	16	73:27
8		Li/crown	9	79:21
9		Li	40	99.6:0.4
10		ZnCl	70	82:18
11	(*E*:*Z* = 100:0)	$Ti(OiPr)_3$	0	–
12			96	78:22
13			90	98:2
14			87	>97:3
15			94	80:20
16		(*E*:*Z* = 0:100)	93	55:45
17		(*E*:*Z* = 89:11)	89	67:33
	1b			
18			71	87:13
	1c			
19			95	91:9
		M =		
20		Li	95	85:15
21		Li/HMPA	61	83:17

[a] The reactions were carried out using 1.1–1.5 equiv of an enolate except in entries 1, 2, and 5–10, 2.0–2.5 equiv of enolate was used. Enolates in entries 12, 14, 15, and 19 were prepared by the action of LDA on the corresponding carbonyl compound, and expected to be predominantly *Z* as indicated. Others were prepared from enol silyl ethers. In entries 1, 2, 7, and 8, insoluble, uncharacterizable solid accounts for the rest of the material. The reactions were carried out at −78 °C for 0.3–0.5 h in entries 1, 3, 7, 12, 13, 15–18, and 20–21, at −40 °C for 0.15–0.5 h in entries 2, 4, 8, 9, 14, and 19, and at 0 °C for 2 h in entries 5, 6, 10, and 11.

Scheme I



(7) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4462, 4464. House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361. House, H. O.; Czuba, L J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

(8) House, H. O.; Crumrine, D. S.; Teranishi, A. Y.; Olmstead, H. D. *J. Am. Chem. Soc.* **1973**, *95*, 3310.

(9) Reetz, M. R.; Peter, R. *Tetrahedron Lett.* **1981**, *22*, 4691.

(10) (a) Kuwajima, I.; Nakamura, E. *J. Am. Chem. Soc.* **1975**, *97*, 3257. Kuwajima, I.; Nakamura, E. *Acc. Chem. Res.* **1985**, *18*, 181. (b) Fluoride-mediated Michael addition: Nakamura, E.; Shimizu, M.; Kuwajima, I.; Sakata, J.; Yokoyama, K.; Noyori, R. *J. Org. Chem.* **1983**, *48*, 932. RajanBabu, T. V. *J. Org. Chem.* **1984**, *49*, 2083.

(11) Narasaka, K.; Soai, K.; Aikawa, Y.; Mukaiyama, T. *Bull. Soc. Chem. Jpn.* **1976**, *49*, 779. Stereochemical studies: Heathcock, C. H.; Uehling, D. E. *J. Org. Chem.* **1986**, *51*, 279.

(12) The stereochemistry was determined unequivocally for entries 12, 13, and 15 in Table I and for **4** and others assigned by analogy.

(13) Xu, Y.-C.; Wulff, W. D. *J. Org. Chem.* **1987**, *52*, 3263.

(14) This is in part due to the lack of information on the stereochemistry of the anion **2**.

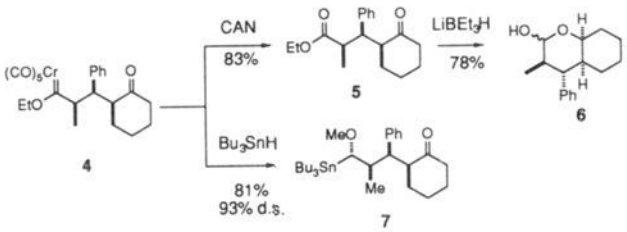
(15) Cf.: Kawasaki, H.; Tomioka, K.; Koga, K. *Tetrahedron Lett.* **1985**, *26*, 3031. Tomioka, K.; Kawasaki, K.; Koga, K. *Tetrahedron Lett.* **1985**, *26*, 3027. Yamamoto, Y.; Maruyama, K. *J. Chem. Soc., Chem. Commun.* **1984**, 904. Bernhard, W.; Fleming, I.; Waterson, D. *J. Chem. Soc., Chem. Commun.* **1984**, 28. Fleming, I.; Hill, J. H.; Parker, D.; Waterson, D. *J. Chem. Soc., Chem. Commun.* **1985**, 318.

(16) Nakamura, E.; Tanaka, K.; Aoki, S. *J. Am. Chem. Soc.* **1992**, *114*, 9715.

(17) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201.

(18) To the contrary for "organic" Michael acceptors: Yamaguchi, M.; Tsukamoto, M.; Tanaka, S.; Hirao, I. *Tetrahedron Lett.* **1984**, *25*, 5661. See also ref 2.

Scheme II



ether.[19] Hence we confirmed the kinetic nature of the enolate addition The absence of a correlation between the enolate geometry and the diastereoselectivity is surprising. We are pleased to report that the selectivity was maximum for the readily available lithium enolates in THF and HMPA/THF (entries 3, 4, and 9).

The highly dissociated Bu_4N^+ enolate was the most reactive. The rate drops dramatically as the countercation-oxygen bond becomes stronger: M = Bu_4N^+ ≃ Li/crown (reacting at –78 °C) > Li/HMPA (at –78 °C) > Li (at –40 °C) > ZnCl (at 0 °C) >> Ti(O-*i*-Pr)$_3$ (no reaction at 0 °C).[20] Thus, there is no indication that the Lewis acidic metal countercation assists the addition reaction. The magnitude of the *syn*-selectivity is cation-dependent (71–99.6% ds). Interestingly, the level of the selectivity of the highly dissociated Bu_4N^+ and Li/crown enolates (entries 1, 2, 7, and 8) is different from that of the lithium enolate in THF or in HMPA/THF (entries 3, 4, and 9) which we believe to react as an aggregates.[21] The Mukaiyama–Michael addition of enol silyl ethers in the presence of $TiCl_4$ or $SnCl_4$ (CH_2Cl_2, –78 to 0 °C) failed entirely for **1a**, which was recovered upon workup at –78 °C.

NMR Studies. The foregoing observations strongly suggest that the Michael addition of a metal enolate to a carbene complex proceeds without metal assistance. The mechanism by which the vinylcarbene complex is activated toward a nucleophile may be quite unique. In fact, NMR studies of the carbene complex **1a** in the presence and absence of $SnCl_4$ indicate that **1a** is incapable of complexing with the Lewis acid. The ^{1}H (500 MHz, at –40 and 20 °C) and ^{13}C NMR (125 MHz at –40 °C) spectra of **1a** remain unchanged either in the presence or absence of $SnCl_4$ (1 equiv) in CD_2Cl_2 (0.06 M) (observed changes within ±0.01 ppm for ^{1}H NMR and ±0.06 ppm for ^{13}C NMR for two independent runs at –40 °C). Especially noteworthy are the chemical shifts of the signals due to the basic carbonyl (^{13}C) and methoxy groups (^{13}C and ^{1}H). These do not change (see supplementary material for the spectra).

The ^{13}C NMR chemical shift values of the olefinic carbons of the parent vinylcarbene complex **8** are similar to those of electron-rich olefins (e.g., enol acetate) rather than those of electron-deficient olefins (e.g., acrylate) as shown below.[22] Notably, there is a significant *upfield* shift of the "electrophilic" β-carbon atom of **8**. This shift suggests an electron-rich nature of the β-carbon under the conditions of the NMR measurement.[23] A similar dilemma was noticed for the parent Fischer carbene complex.

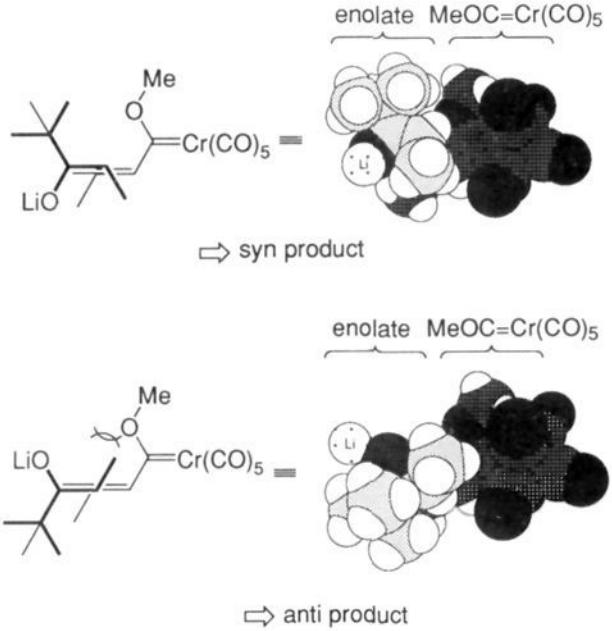
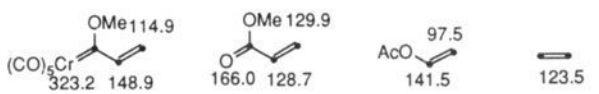


Figure 1. Schematic pictures of the approach of a (*Z*)-pinacolone enolate to a 1-propenylcarbene complex (the carbene complex is shown in dark).

Thus, *ab initio* calculations on $(CO)_5Cr{=}CH(OH)$[24] indicate that the strongly electrophilic carbene carbon is negatively charged. Hence, the electrophilicity of the carbene carbon originates from the low-lying LUMO rather than from the total electron density.[25] These calculations combined with the ^{13}H NMR spectra imply that the olefin activation toward the vinylcarbene complex **1** is entirely different from that of an unsaturated carbonyl compound.



8 (^{13}C NMR chemical shift values in δ)

The lack of Lewis basicity of the carbonyl groups in **1a** can arise for two reasons. The observed electrophilicity of the olefin may not be due to actual electron-withdrawal but due to lowering of the LUMO level. Alternatively, if the carbene group does indeed serve as an electron-withdrawing group, the excess negative charge may be equally dissipated to the five, intrinsically nonbasic sp-hybridized oxygen atoms. Theoretical studies could be useful to distinguish between these two possibilities.

The experimental and spectral observations define the Fischer vinylcarbene complex as a very unique electron-deficient olefin. The stereochemistry of Michael addition reaction to this unique complex suggests a rare example of an open transition state (**A**). The precise reasons for the *syn*-diastereoselectivity is unclear at this time, but this agrees with a working model depicted below that includes (1) an open transition state, (2) significant steric effects of the R^4 and O-metal groups, and (3) placement of the R^3 group away from the $(CO)_5Cr{=}C(OMe)$ moiety to avoid steric interactions between R^3 and the chromium moiety or the MeOC grouping. The space filling model shown in Figure 1 depicts this last effect.[26] Some of these issues can be verifiable

(19) We thank a referee for suggesting this possibility.

(20) Similar trend was also observed for allylic Grignard and zinc reagents, of which only the former was reactive at –70 to –40 °C: unpublished results.

(21) Cf.: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1624. Seebach, D.; Amstutz, R.; Dunitz, J. D. *Helv. Chim. Acta* **1981**, *64*, 2622.

(22) (a) The ^{13}C NMR chemical shift values (δ) of a carbene complex: Wilson, J. W.; Fischer, E. O. *J. Organomet. Chem.* **1973**, *57*, C63. The values for the reference olefins: Breitmaier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*; VCH: Weinheim, 1987. (b) For the related spectral characteristic for phenylcarbene complexes, see ref 4a.

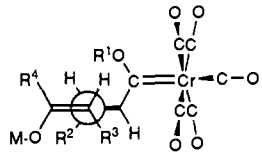
(23) It is likely that the conformation of the vinyl carbene complex may play an important role. A similar unsolvable puzzle has recently been reported in the studies of the Diels–Alder reaction of aminovinylcarbene complex, wherein single crystal X-ray structures and NMR spectra were examined in relation to the reactivity of the carbene complexes. Anderson, B. A.; Wulff, W. D.; Powers, T. S.; Tribbitt, S.; Rheingold, A. L. *J. Am. Chem. Soc.* **1992**, *114*, 10784.

(24) Nakatsuji, H.; Ushio, J.; Han, S.; Yonezawa, T. *J. Am. Chem. Soc.* **1983**, *95*, 426.

(25) Similar interpretation may also apply to the upfield shift of the ^{13}C NMR signals of the para carbon of arylcarbene complexes (ref 4a).

(26) Although an s-trans conformation is assumed here, it may be possible that an s-cis conformation of the vinylcarbene complex takes part in the reaction to give the same selectivity. In the s-cis conformation, severe steric interaction between the $Cr(CO)_5$ and the enolate methyl substituent does not seem to allow the reaction to give the anti product (cf. Figure 1) The s-cis conformation of vinyl carbene complex has been found in some crystal structures (ref 23).

by further experiments that are the subject of further studies.



A

In summary, we have demonstrated the previously unknown chemical properties of Fischer vinyl carbene complexes manifested as the *syn*-stereoselective Michael addition. We suggest that this stereochemistry stems from the intrinsic properties of vinylcarbene complexes.

Experimental Section

General Data. A description of the instrumentation was previously given.[4a] Throughout the present studies the minor diastereomers could only be characterized by ^1H and/or ^{13}C NMR (including decoupling experiments) as a minute component of a diastereomeric mixture of the carbene complex containing the major product (isolated by silica gel chromatography). The similar polarity of the diastereomers combined with their instability precluded extensive purification. Therefore, the diastereoselectivity of the reaction was determined either by ^1H and ^{13}C NMR analysis of the diastereomeric mixture of carbene complexes or alternatively by NMR or capillary GC analysis of their CAN oxidation product (vide infra). We have confirmed that the diastereomeric ratio does not change much during the CAN oxidation for three cases.

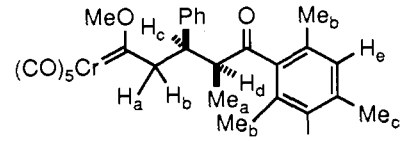
Typical Procedure for the Michael/Trapping Sequence. [Methoxy-[2-(2-oxocyclohexyl)-2-phenyl-1-methylethyl]carbene]pentacarbonylchromium (4). A 1.64 M solution of *n*-BuLi (0.64 mL, 1.05 mmol) was added at 0 °C to a 4.0 mL THF solution of 1-(trimethyl)siloxycyclohexene (228 μL, 1.10 mmol). After 30 mL, the mixture was cooled to −70 °C and was added slowly to a 10 mL THF solution of (methoxystyrylcarbene)pentacarbonylchromium (338 mg, 1.00 mmol) at −70 °C. After 20 min, MeOTf (124 μL, 1.10 mmol) was added and the mixture was warmed to 0 °C. After 30 min, the mixture was poured to a pH 7.2 phosphate buffer (10 mL). Extraction with pentane, drying over $MgSO_4$ concentration, and chromatography on silica gel (hexane) gave the title compound as yellow oil (378 mg, 84%): IR (neat) 2950, 2070, 1940, 1720, 1460, 1300, 1260, 1221, 970; ^1H NMR (500 MHz, $CDCl_3$) major isomer δ 0.73 (d, J = 6.6 Hz, 3 H), 1.54–1.77 (m, 5 H), 1.77–1.96 (m, 1 H), 2.30 (m, 1 H), 2.37–2.50(m, 1 H), 2.62 (dd, J = 6.0, 11.2 Hz, 1 H), 3.69 (dd, J = 6.0, 10.0 Hz, 1 H), 4.50 (dq, J = 6.6, 10.0 Hz, 1 H), 4.74 (s, 3 H), 7.15–7.36 (m, 5 H).

This compound was oxidized to the corresponding keto ester and then was fully characterized (vide infra). The diastereoselectivity of the reaction was determined to be 87:13 by GC analysis of this keto ester.

[Methoxy[2-[6-oxo-3-thiacyclohexyl]-2-phenyl-1-methylethyl]carbene]pentacarbonylchromium: IR (neat) 2900, 2800, 2050, 1880, 1700, 1450, 955; ^1H NMR (200 MHz, $CDCl_3$) δ 0.74 (d, J = 6.7 Hz, 3 H), 2.25 (dd, J = 7.6, 14.3 Hz, 1 H), 2.67 (dd, J = 4.8, 14.3 Hz, 2 H), 2.79–2.98 (m, 3 H), 3.06 (ddd, J = 3.8, 9.1, 12.9 Hz, 1 H), 3.73 (d, J = 9.12 Hz, 1 H), 4.40 (dq, J = 6.7, 9.1 Hz, 1 H), 4.63 (s, 3 H), 7.10–7.40 (m, 5 H). Anal. Calcd for $C_{21}H_{20}O_7SCr$: C, 53.84; H, 4.30. Found: C, 54.08; H, 4.45. The diastereoselectivity of the title compound (99:1) was determined by GC analysis of the oxidation product.

[Methoxy[4-oxo-4-mesityl-3-methyl-2-phenyl-1-methylbutyl]carbene]pentacarbonylchromium. IR (CCl_4) 2050 (w, trans CO), 1950 (s, cis CO), 1700 (carbonyl), 1460, 960, 700, 670, 650; ^1H NMR (200 MHz, $CDCl_3$) δ 0.82 (d, J = 7.2 Hz, 3 H, Cr=CCHCH_3), 1.13 (d, J = 7.6 Hz, 0.21 H, OCCHCH_3), 1.23 (d, J = 7.4 Hz, 2.79 H, OCCHCH_3), 1.89 (s, 5.58 H, o-C_6H_2CH$_3$), 2.00 (s, 0.42 H, o-C_6H_2CH$_3$), 2.20 (s, 2.79 H, p-C_6H_2CH$_3$), 2.23 (s, 0.21 H, p-C_6H_2CH$_3$), 3.44 (dq, J = 2.9, 7.2 Hz, 1 H, OCCHCH$_3$), 3.59 (dd, J = 7.2, 9.7 Hz, 1 H, PhCH), 4.51 (s, 3 H, OCH_3), 4.56 (m, 1 H, Cr=CCHCH$_3$), 6.68 (s, 1.86 H, $C_6H_2(CH_3)_3$), 6.76 (s, 0.14 H, $C_6H_2(CH_3)_3$), 7.06–7.20 (m, 5 H, Ph). Anal. Calcd for $C_{28}H_{28}O_7Cr$: C, 63.63; H, 5.34. Found: C, 63.64; H, 5.21. The diastereomeric ratio (93:7) was determined by integration of the methyl proton signals on ^1H NMR spectra (δ 1.13: major; δ 1.23: minor).

Michael Addition of Ethyl Mesityl Ketone Enolate. [Methoxy[4-oxo-4-mesityl-3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium from (*E*)-Zinc Enolate. To a solution of(*E*)-1-(trimethylsiloxy)-1-mesityl-1-propene (135 μL, 0.50 mmol) in 1.5 mL of THF was added 1.61 M *n*-BuLi in hexane (0.31 mL, 0.50 mmol) at 0 °C. After 30 min, a solution of $ZnCl_2$ (67.5 mg, 0.50 mmol) in 1.0 mL of THF was added to the lithium enolate solution at 0 °C. After 30 min, the mixture was cooled to −70 °C and was added slowly via a cannula to a solution of (methoxystyrylcarbene)pentacarbonylchromium (67.6 mg, 0.20 mmol) in 2.0 mL of THF at −70 °C, and the dark red reaction mixture was warmed to −50 °C for 30 min, then to −40 °C for 10 min, and finally to 0 °C for 2 h. Then the color of the solution changed to yellow from dark red. The mixture was poured to a 1/15 M pH 7.2 phosphate buffer solution (ca. 10 mL) and was extracted with pentane. The crude product was purified on silica gel (0–5% AcOEt in hexane) to obtain 75.7 mg of the title compound (75%) as a yellow solid (a 82:18 mixture of diastereomers). The diastereomeric ratio was determined by integration of the clearly identifiable methyne proton signals on decoupled ^1H NMR spectra (δ 1.15 Me irradiation): R_f 0.29 (5% AcOEt in hexane); mp 125 °C; IR (CCl_4) 2050 (w, CO), 1950 (s, CO), 1700 (s, CO), 1400, 1260, 665, 655 cm^{-1}; ^1H NMR (200 MHz $CDCl_3$) δ 1.15 (d, J = 7.6 Hz, 3 H, Me_a), 2.00 (s, 6 H, Me_b), 3.12 (dq, J = 5.9, 7.6 Hz, 1 H, H_d), 3.65 (dd, 1 H, J = 3.8, 17.1 Hz, 1 H, H_a), 3.91 (ddd, J = 3.8, 5.9, 10.5 Hz, 1 H, H_c), 4.32 (dd, J = 10.5, 17.1 Hz, 1 H, H_b), 4.59 (s, 3 H, OMe), 6.78 (s, 2 H, H_e), 7.10–7.30 (m, 5 H, Ph). For the labels of hydrogen, see below. ^{13}C NMR (62.5 MHz, $CDCl_3$) 12.7, 19.6, 21.0, 41.6, 52.7, 64.2, 67.7, 126.5, 128.1, 128.2, 128.8, 133.7, 137.9, 138.6, 142.6, 211.2, 216.2, 222.8, 360.3. Anal. Calcd for $C_{27}H_{26}O_7Cr$: C, 63.03; H,5.09. Found: C, 63.33; H, 5.11.



Stereochemical assignment was made by analogy to that of the Michael reaction of propiophenone enolate (see below for [ethoxy[4-oxo-4-phenyl-3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium).

[Methoxy[4-oxo-4-mesityl-3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium from (*Z*)-Zinc Enolate. Prepared from (methoxystyrylcarbene)pentacarbonylchromium (67.5 mg, 0.20 mmol) in the same manner by the use of (*Z*)-1-(trimethylsiloxy)-1-mesityl-1-propene (135 μL, 0.50 mmol) in 75% yield (76.4 mg, a 92:8 mixture of diastereomers).

[Methoxy[4-oxo-4-mesityl 3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium from (*E*)-Enol Silyl Ether and TBAF. Tetrabutylammonium fluoride trihydrate (161 mg, 0.51 mmol) was dried over P_2O_5 *in vacuo* (1 m Hg) at room temperature for 10 h and was stirred with molecular sieves 3A (0.1 g) and 2.0 mL of THF for 24 h. The solution was cooled to −70 °C, and (*E*)-1-(trimethylsiloxy)-1-mesityl-1-propene (136 μL, 0.50 mmol) and the mixture was added slowly via a cannula to a solution of (methoxystyrylcarbene)pentacarbonylchromium (67.6 mg, 0.20 mmol) in 1 mL of THF at −70 °C. After 30 min, the color of the reaction mixture was changed to yellow from dark red. The mixture was poured to a 1/15 M pH 7.2 phosphate buffer solution (ca. 10 mL) and extracted with pentane. The crude product was purified on silica gel to obtain 19.4 mg of the title compound (19%, a 71:29 mixture of diastereomers). The diastereomeric ratio of the title compound was determined in the same manner as described for the zinc enolate addition.

[Methoxy[4-oxo-4-mesityl-3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium from (*Z*)-Enol Silyl Ether and TBAF. Prepared from (methoxystyrylcarbene)pentacarbonylchromium (67.6 mg, 0.20 mmol) in the same manner by the use of (*Z*)-1-(trimethylsiloxy)-1-mesityl-1-propene (136 μL, 0.50 mmol) and tetrabutylammonium fluoride trihydrate (161 mg, 0.51 mmol) in 16% yield (16.0 mg, a 73:27 mixture of diastereomers).

[Methoxy[4-oxo-4-mesityl-3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium from (*Z*)-Li/Crown Enolate. 12-Crown-4 (130 mL, 0.80 mmol) and a small amount of bipyridine were heated *in vacuo* (10 mmHg) at 50 °C for 30 min to ensure dryness of the reagents. (*Z*)-1-(Trimethylsiloxy)-1-mesityl-1-propene (109 μL, 0.40 mmol), 1.0 mL of THF, and then 1.61 M *n*-BuLi in hexane (0.25 mL, 0.40 mmol) were added consecutively at 0 °C. After 30 min, the mixture was cooled to −70 °C and was added slowly via a cannula to a solution of (methoxystyrylcarbene)pentacarbonylchromium (67.6 mg, 0.20 mmol) in 2.0 mL of THF at −70 °C. After 2 h, the dark red reaction mixture was warmed to −40 to −45 °C during 10 min. The color of the solution changed to yellow. The mixture was poured to a 1/15 M pH 7.2 phosphate buffer

solution (ca. 10 mL) and extracted with pentane. The crude product containing a large amount of black insoluble material was purified on silica gel to obtain 8.0 mg of the title compound (8%, a 81:19 mixture of diastereomers). The diastereoselectivity of the title compound was determined in the same manner as described for the zinc enolate addition.

[Methoxy[4-oxo-4-mesityl-3-methyl-2-phenylbutyl]carbenepentacarbonylchromium from (*Z*)-Li/Crown Enolate. Prepared from (methoxystyrylcarbene)pentacarbonylchromium (67.6 mg, 0.20 mmol) in the same manner by the use of (*E*)-1-(trimethylsiloxy)-1-mesityl-1-propene (109 μL, 0.40 mmol) and 12-crown-4 (130 μL, 0.80 mmol) in 7% yield (7.3 mg, a 79:21 mixture of diastereomers).

[Methoxy[4-oxo-4-mesityl-2-phenylbutyl]carbene]pentacarbonylchromium from Li/HMPA Enolate. To a solution of (*Z*)-1-(trimethylsiloxy)-1-mesityl-1-propene (109 μL, 0.40 mmol) in 1.0 mL of THF was added 1.61 M *n*-BuLi in hexane (0.25 mL, 0.40 mmol) at 0 °C. After 30 min, hexamethylphosphoramide (279 μL, 1.20 mmol) was added to the lithium enolate solution at 0 °C. The mixture was cooled to −70 °C and was added to a solution of (methoxystyrylcarbene)pentacarbonylchromium (67.6 mg, 0.20 mmol) in 1.0 mL of THF at −70 °C. After 30 min, the color of the reaction mixture was changed to yellow from dark red. The mixture was poured to a 1/15 M pH 7.2 phosphate buffer solution (ca. 10 mL) and extracted with pentane. The crude product was purified on silica gel to obtain 40.2 mg of the title compound (39%) as a yellow solid (a >99:1 mixture of diastereomers). The diastereoselectivity of the title compound was determined in the same manner as described for the zinc enolate addition.

[Methoxy[4-oxo-4-mesityl-3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium from (*E*)-Lithium Enolate. To a solution of (*E*)-1-(trimethylsiloxy)-1-mesityl-1-propene (60.0 μL, 0.22 mmol) in 1.0 mL of THF was added 1.61 M *n*-BuLi in hexane (0.14 mL, 0.23 mmol) at 0 °C. After 30 min, the mixture was cooled to −70 °C and added slowly via a cannula to a solution of (methoxystyrylcarbene)pentacarbonylchromium (67.6 mg, 0.20 mmol) in 1.0 mL of THF at −70 °C, and after 15 min the dark red reaction mixture was warmed to −40 to −45 °C during 2 h. The color of the solution changed to yellow. The mixture was added to a 1/15 M pH 7.2 phosphate buffer solution (ca. 10 mL) and was extracted with pentane. The extract was dried over $MgSO_4$, and solvent was removed. The residue was purified on silica gel to obtain 56.0 mg of the title compound (55%) as a yellow solid (a 240:1 mixture of diastereomers). The diastereomeric ratio was determined in the same manner as described for the zinc enolate addition.

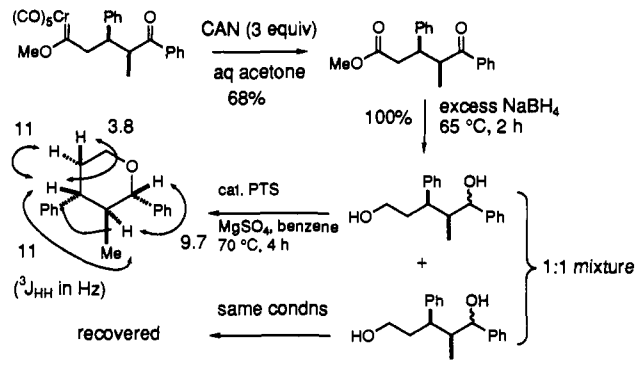
[Methoxy[4-oxo-4-mesityl-3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium from (*Z*)-Lithium Enolate. Prepared from (methoxystyrylcarbene)pentacarbonylchromium (67.6 mg, 0.20 mmol) in the same manner by the use of (*Z*)-1-(trimethylsiloxy)-1-mesityl-1-propene (60.0 μL, 0.22 mmol) in 37% yield (38.2 mg, a 170:1 mixture of diastereomers). The diastereomeric ratio was determined in the same manner as described for the zinc enolate addition.

[Methoxy[2-[2-oxo-cyclohexyl]-2-phenylethyl]carbene]pentacarbonylchromium. To a solution of 1-(trimethylsiloxy)-1-cyclohexene (87 μL, 0.35 mmol) in 2 mL of THF was added 1.66 M BuLi in hexane (0.27 mL, 0.35 mmol) at 0 °C. After 30 min the solution was cooled to −70 °C and transferred to a solution of (methoxystyrylcarbene)pentacarbonylchromium (78 mg, 0.23 mmol) in 3 mL of THF at −70 °C. After 10 min H_3PO_4 (20 μL, 0.23 mmol) was added to the reaction mixture, and solvent was removed. The residue was purified on silica gel (5% AcOEt in hexane) to obtain 89 mg of the title compound (89%) as a yellow oil (a 98:2 mixture of diastereomers). The diastereoselectivity of the title compound was determined by GC analysis of oxidation product.

The *syn*-diastereoselectivity was determined after methyl trapping of the anionic addition product (see below for [methoxy-[2-(2-oxocyclohexyl)-2-phenyl-1-methylethyl]carbene]pentacarbonylchromium).

[Methoxy[2-[6-oxo-3-thiacyclohexyl]-2-phenylethyl]carbene]pentacarbonylchromium. To a solution of diisopropylamine (71 μL, 0.50 mmol) in 1 mL of THF was added 1.57 M BuLi in hexane (0.32 mL, 0.50 mmol) at 0 °C. After 15 min a solution of tetrahydrothiopyran-4-one (61.6 mg, 0.53 mmol) in 1 mL of THF was added to LDA at 0 °C, and after 30 min the mixture was cooled to −70 °C and transferred to a solution of (methoxystyrylcarbene)pentacarbonylchromium (169 mg, 0.50 mmol) in 5 mL of THF at −70 °C. The reaction mixture was warmed to −40 to −45 °C, and after 30 min the mixture was added to a 1/15 M phosphate buffer solution (ca. 5 mL). The mixture was extracted by pentane and dried over $MgSO_4$. Solvent was removed. The crude product was purified on silica gel (0–10% AcOEt in hexane) to obtain 197 mg of the title compound (0.43 mmol, 87%) as a yellow solid (a >97:3 mixture of diastereomers): R_f 0.23 (10% AcOEt in hexane); mp 105 °C; IR (Nujol)

Scheme III



2920, 2850, 2050, 1930, 1700, 1460, 1380, 660; ^{1}H NMR (270 MHz, $CDCl_3$) δ 2.34 (dd, *J* = 8.8, 14.1 Hz, 1 H), 2.56 (dd, J = 4.0, 14.1 Hz, 1 H), 2.72–2.84 (m, 2 H), 2.86–3.03 (m, 3 H), 3.43 (dd,J = 4.0, 15.8 Hz, 1 H), 3.75 (dt, J = 4.0, 10.6 Hz, 1 H), 4.0 (dd, J = 10.6, 15.8 Hz, 1 H), 4.65 (s, 3 H), 7.10–7.44 (m, 5 H); ^{13}C NMR (125 MHz, $CDCl_3$) 31.8, 35.1, 41.9, 44.4, 57.6, 67.5, 127.1, 128.0, 128.8, 140.3, 210.4, 216.0, 222.9, 360.6. Anal. Calcd for $C_{20}H_{18}O_7SCr$: C, 52.86; H, 3.99. Found: C, 52.86; H, 3.85. The diastereoselectivity of the title compound (>98:2) was determined by ^{13}C NMR analysis of the isomeric signals (43.2 ppm).

Physical Properties of Michael Adducts. [Methoxy[2-[6-oxo-3-thiacyclohexyl]-3-(2-furyl)ethyl]carbene]pentacarbonylchromium. IR (neat) 2960, 2820, 2060, 1950, 1715, 1460, 1265, 740, 655; ^{1}H NMR (200 MHz $CDCl_3$) major isomer δ 2.40 (dd *J* = 9.5, 14.3 Hz, 1 H), 2.83–3.05 (m, 3 H), 3.33 (dd, *J* = 3.8, 15.2 Hz, 1 H), 3.89 (dt, *J* = 0.38, 2.9 Hz, 1 H), 4.03 (dd, *J* = 9.5, 15.2 Hz, 1 H), 4.73 (s, 3 H), 6.00 (dd, *J* = 0.38, 2.9 Hz, 1 H), 6.24 (dd, *J* = 1.9, 2.9, 1 H), 7.30 (dd, *J* = 0.38, 1.9 Hz, 1 H). The diastereomeric ratio (87:13) was determined by integration of the furyl proton signals on ^{1}H NMR spectra (δ 6.00, 6.24: major; δ 5.96, 6.13: minor).

[Ethoxy[4-oxo-4-phenyl-3-methyl-2-phenylbutyl]carbene]pentacarbonylchromium. Major isomer: IR (neat) 3053, 2980, 2940, 2060, 1920, 1683, 1455, 1375, 1270, 1245, 670; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.5 Hz, 3 H), 1.44 (t, *J* = 7.1 Hz, 3 H), 3.33 (dd, *J* = 3.8, 16.5 Hz, 1 H), 3.57–3.69 (m, 2 H), 4.11 (dd, *J* = 9.7, 16.5 Hz, 1 H), 4.80–4.95 (m, 2 H), 7.15–7.35 (m, 5 H), 7.45–7.65 (m, 3 H), 8.02 (distorted d, J = 6.9 Hz, 2 H). Minor isomer: IR (neat) 2980, 2025, 1945, 1688, 1455, 1378, 1270, 1242, 670, 660; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.27 (d, *J* = 6.5 Hz, 3 H), 1.36 (t, *J* = 7.0 Hz, 3 H), 3.65–3.85 (m, 3 H), 4.11 (dd, *J* = 11.5, 17.5 Hz, 1 H), 4.87 (q, *J* = 7.0 Hz, 2 H), 7.00–7.20 (m, 5 H), 7.30–7.55 (m, 3 H), 7.76 (distorted d, *J* = 7.0 Hz, 2 H). Anal. Calcd for $C_{25}H_{22}O_7Cr$: C, 61.73; H, 4.56. Found: C, 61.78; H, 4.63.

The stereochemistry was assigned as shown in Scheme III.

[Ethoxy[3-(ethoxycarbonyl)-1-methyl-2-phenylbutyl]carbene]pentacarbonylchromium: IR (CCl_4) 2980, 2050, 1940, 1735, 1375, 1260, 1240, 670, 600; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.90 (d, J = 6.7 Hz, 3 H), 1.31 (t, J = 6.7 Hz, 3 H), 1.40 (t, J = 6.7 Hz, 3 H), 2.60 (dq, J = 2.9, 6.7 Hz, 1 H), 3.24–3.50 (m, 2 H), 4.03–4.29 (m, 3 H), 4.94 (q, J = 6.7 Hz, 2 H), 7.03–7.28 (m, 5 H).

In order to assign the stereochemistry, the chromium carbene moiety was oxidized with CAN to the corresponding diester, which was found isomeric with the *anti*-diastereomer obtained by Michael addition of ethyl propionate to ethyl cinnamate.[18]

[Ethoxy[3,5,5-trimethyl-4-oxo-2-phenylhexyl]carbene]pentacarbonylchromium. ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.74 (d, *J* = 6.0 Hz, 3 H), 1.24 (s, 9 H), 1.42 (t, *J* = 7.1 Hz, 3 H), 3.00–3.20 (m, 2 H), 3.37 (dd, *J* = 3.8, 10.0 Hz, 1 H), 4.20 (dd, *J* ≈ 11.4, 16.8 Hz, 1 H), 4.75–4.95 (m, 2 H), 7.10–7.35 (m, 5 H). Anal. Calcd for $C_{23}H_{21}O_7Cr$: C, 59.22; H, 5.62. Found: C, 59.36; H, 5.65.

[Ethoxy[2-(oxocyclohexyl)hexyl]carbene]pentacarbonylchromium. IR (neat) 2940, 2060, 1945, 1715, 1373, 1255, 670, 660; ^{1}H NMR (200 MHz, $CDCl_3$) major isomer δ 0.86 (distorted t, *J* = 6.7 Hz, 3 H), 1.0–1.4 (m, 6 H), 1.61 (t, *J* = 7.0 Hz, 3 H), 1.85–2.40 (m, 9 H), 2.55–2.70 (m, 1 H), 3.29 (dd, *J* = 6.5, 17.0 Hz, 1 H), 3.45 (dd, *J* = 6.3, 17.0 Hz, 1 H), 5.14 (q, *J* = 7.0 Hz, 2 H). Anal. Calcd for $C_{20}H_{26}O_7Cr$: C, 55.81; H, 6.09. Found: C, 56.00; H, 6.17.

Typical Procedure for the CAN Oxidation of the Keto Carbene Complex. Methyl 3-(2-Oxocyclohexyl)-3-phenylpropionate. To a 3.0 mL ethereal solution of [methoxy-[2-(6-oxocyclohexyl)-2-phenylethyl]carbene]pen-

tacarbonylchromium (27.7 mg, 0.063 mmol) was added a 0.50 mL aqueous solution of ceric ammonium nitrate (0.22 g, 0.40 mmol), and the mixture was stirred vigorously at room temperature for 20 min. After extraction with ether followed by drying over $MgSO_4$, the crude product was chromatographed on silica gel (20% AcOEt/hexane) to obtain the title compound as white solid (12.0 mg, 73%): mp 98–100 °C; IR (Nujol) 1730, 1700, 1160, 700; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.46–1.85 (m, 5 H), 1.90–2.10 (m, 1 H), 2.27–2.50 (m, 3 H), 2.58 (dd, J = 9.5, 15.2 Hz, 1 H), 2.85 (dd, J = 4.8, 15.2 Hz, 1 H), 3.50 (s, 3 H), 3.40–3.58 (m, 1 H), 7.10–7.33 (m, 5 H). Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.54; H, 7.56.

The diastereomeric ratio was determined to be 98:2 by GC analysis: retention times (HR-1, 160 °C) of the major and the minor isomers were 18.1 and 19.5 min, respectively.

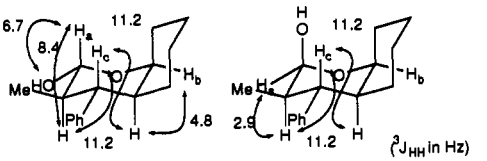
A parallel experiment carried out for the corresponding ethyl ester gave crystals suitable for X-ray structure determination to determine that the reaction proceeded in a *syn* fashion as described in the text. The structure and crystal data are shown at the end of the supplementary material.

Methyl 3-(2-Oxocyclohexyl)-3-phenyl-2-methylpropionate (5). IR (neat) 2950, 1740, 1715, 1455, 1200, 1170, 710; ^{1}H NMR (270 MHz, $CDCl_3$) major isomer δ 0.93 (d, J = 7.4 Hz, 3 H), 1.62–2.0 (m, 6 H), 2.20–2.59 (m, 2 H), 2.76 (dt, J = 3.8, 8.6 Hz, 1 H), 2.90 (dq, J = 7.4, 8.6 Hz, 1 H), 3.61 (t, J = 8.6 Hz, 1 H), 3.65 (s, 3 H), 7.12–7.40 (m, 5 H). Anal. Calcd for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.12; H, 8.00. The diastereomeric ratio was determined to be 87:13 by GC analysis: retention times (HR-1, 170 °C) of the major and the minor isomers were 14.1 and 13.0 min, respectively.

Methyl 3-(6-Oxo-3-thiacyclohexyl)-3-phenyl-1-methylpropionate. IR (CCl_4) 1740, 1710, 1170, 700; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.95 (d, J = 7.2 Hz, 3 H), 2.39 (dd, J = 7.6, 14.3 Hz, 1 H), 2.67–2.82 (m, 3 H), 2.90–3.00 (m, 3 H), 3.10 (m, 1 H), 3.62 (s, 3 H), 3.88 (dd, J = 7.8, 9.7, 1 H), 7.10–7.39 (m, 5 H). Anal. Calcd for $C_{16}H_{19}O_3S$: C, 65.95; H, 6.57; S, 11.00. Found: C, 65.69; H, 6.31; S, 11.17. The diastereomeric ratio was determined to be 99:1 by GC analysis: retention times (HR-1, 180 °C) of the major and the minor isomers were 16.9 and 17.5 min respectively.

Stereochemical Assignment of [Methoxy-[2-(2-oxocyclohexyl)-2-phenyl-1-methylethyl]carbene]pentacarbonylchromium. The keto ester **5** (60.4 mg, 0.22 mmol) in 1.0 mL of THF was cooled to −70 °C. A 1.0 M THF solution of lithium triethylborohydride (0.67 mL, 0.67 mol) was added, and, after 30 min, the reaction mixture was warmed to 0 °C. After 1 h, 12 mL of water and then a mixture of triethanolamine (0.25 mL), water (2.0 mL), and ether (7.0 mL) was added. The mixture was extracted with ether, and the crude product was purified on silica gel (20% AcOEt/hexane) to obtain the lactol **6** (42.2 mg, 78%) as a mixture of 85:15 diastereomers due to the hemiacetal moiety: IR (CCl_4) 3600, 3370, 2940, 1600, 1490, 1450, 1070, 700; ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.68 (d, J = 6.7 Hz, minor CH_3), 0.76 (d, J = 6.7 Hz, 3 H, CH_3), 1.24 (br s, 5 H, -(CH_2)-), 1.76–1.79 (m, 3 H,-(CH_2)-), 1.98–2.10 (m, 1 H, CH), 2.17–2.30 (m, 1 H, CH), 2.56 (t, J = 11.2 Hz, 1 H, H_c), 2.98 (t, J = 11.2 Hz, minor H_c), 3.26 (d, J = 6.7 Hz, 1 H, OH), 3.95–4.04 (m, minor H_b), 4.15 (dt, J = 4.8, 11.2 Hz, 1 H, H_b), 4.84 (dd, J = 6.7, 8.4 Hz, 1H, H_a), 5.25 (dd, J = 2.1, 2.9 Hz, minor H_a), 7.22–7.48 (m, 5 H, Ph). Anal. Calcd for $C_{16}H_{22}O_2$: C,78.01; H, 9.00. Found: C, 77.74; H, 8.76.

The isomeric ratio was determined by the relative area of the δ 4.84 and the δ 5.25 signals. The stereochemistry of the major and the minor isomers were determined on the basis of coupling constant (shown below) and NOE analyses. The coupling constants obtained with MM2 force field for the indicated conformer of the major isomer coincided with the observed ones within 1 Hz.



6: major isomer **6**: minor isomer

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Supplementary Material Available: The NMR spectra of a **1a**/$SnCl_4$ mixture and tables of bond lengths, bond angles, torsion angles, and temperature factors for ethyl 3-(2-oxycyclohexyl)-3-phenylpropionate (11 pages); listing of observed and calculated structure factors (11 pages). Ordering information is given on any current masthead page.