Asymmetric Hetero Diels–Alder Reactions Catalyzed by Novel Chiral Vanadium(IV) Bis(1,3-diketonato) Complexes†

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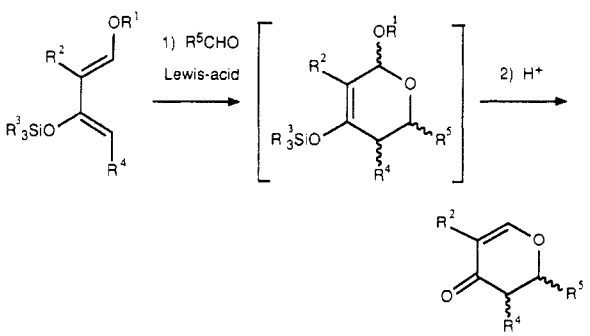
Novel optically active oxovanadium(IV) complexes bearing camphor-derived 1,3-diketonato ligands have been prepared, either by starting from $VOSO_4 \cdot 5H_2O$ and the 1,3-diketone in an aqueous medium or by a metathesis reaction of $VO(acac)_2$ in an inert solvent at elevated temperature. The complex bis(3-(heptafluorobutyryl)camphorato)oxovanadium (**5a**) was found to be a very efficient catalyst for the cycloaddition of aldehydes to activated dienes to give pyrone derivatives. Thus, the reaction of benzaldehyde with 1-methoxy-2,4-dimethyl-3-((triethylsilyl)oxy)butadiene (**6h**) in the presence of 5 mol % of **5a** at −78 °C gave, after protolytic workup, *cis*-3,5-dimethyl-6-phenyl-5,6-dihydro-4*H*-pyran-4-one (**7b**) with 98.5% diastereoselectivity and 85% enantiomeric excess. The influence of the substituents attached to the diene moiety was studied. The reaction of (*R*)-2,3-*O*-isopropylidene-D-glyceraldehyde (**13**) with 1-methoxy-2,4-dimethyl-3-((trimethylsilyl)oxy)butadiene (**6g**), catalyzed by (+)-**5a** and (−)-**5a**, respectively, was found to involve a high degree of double stereodifferentiation. Thus, the matched combination of (−)-**5a** with (*R*)-**13** gave one of the four possible diastereomeric pyrone products in 93.1% selectivity (**14a**). On the other hand, the mismatched pair showed almost no selectivity. When the heptafluoropropyl side chain in the ligands of complex **5a** was replaced by trifluoromethyl, or by an aromatic substituent, the corresponding vanadium(IV) complexes were both much less active and selective catalysts, compared to **5a**.

Among the synthetic methodologies that preferentially lead to the formation of a specific enantiomer of a targeted chiral compound, reactions in which the chiral information is conveyed by an optically active transition-metal catalyst constitute today a topic of fundamental importance. Whereas catalysts for asymmetric hydrogenation have been known for two decades,[1] the use of transition-metal complexes as catalysts for C–C and C–O bond-forming reactions is still a fast-growing field.[2]

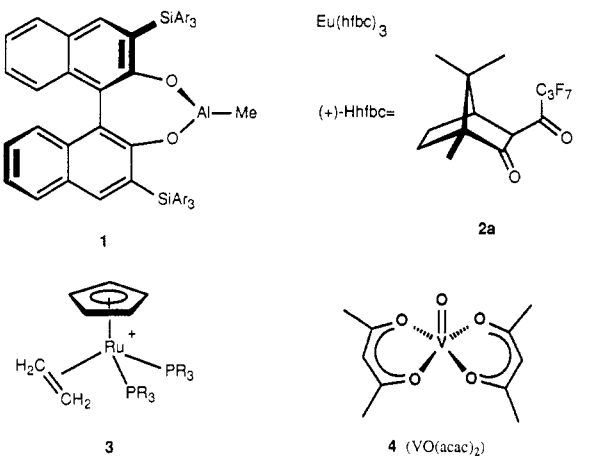
Lewis acids are some of the most important synthetic tools used in organic chemistry. They are used to assist or catalyze a wide variety of organic transformations (we use this terminology depending on whether they are used in stoichiometric or substoichiometric amounts, respectively).[3] In recent years chiral Lewis acids have been shown to impart high enantioselectivities to, for example, aldol,[4] Diels–Alder,[5] and ene reactions.[6] The Lewis-acid-catalyzed [2 + 4] cycloaddition of an aldehyde with an activated diene (usually a 1-alkoxy-3-(silyloxy)butadiene) is an example of the so-called hetero Diels–Alder reaction (eq 1).[7] The 5,6-dihydro-γ-pyrone derivatives



(1)

obtained after protolytic workup are useful synthons for the preparation of a variety of highly oxygenated products, in particular carbohydrates. The aforementioned reaction has mainly been developed and described in a very elegant series of papers by Danishefsky and co-workers,[8] who also investigated the influence of different types of Lewis acids upon diastereoselectivity. The role of the Lewis acid in hetero Diels–Alder reactions is recognized to be the lowering of the LUMO of the carbonyl moiety (dienophile), via interaction with the anti oxygen lone pair, thus lowering the activation energy for cycloaddition.[9] The most successful chiral catalyst to date was reported by Yamamoto

Chart I



† Dedicated to the memory of Professor John K. Stille.

(1) (a) Horner, L.; Siegel, H.; Buthe, H. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 942. (b) Knowles, W. S.; Sabacky, M. J. *J. Chem. Soc., Chem. Commun.* **1968**, 1445. For reviews, see: (c) Knowles, W. S. *Acc. Chem. Res.* **1983**, *16*, 106. (d) Koenig, K. E. In ref 2a, pp 71–101.

(2) (a) Morrison, J. D., Ed. *Asymmetric Synthesis*; Academic Press: Orlando, FL, 1985; Vol. 5. (b) Bosnich, B. *Asymmetric Catalysis*; NATO Series; Martinus Nijhoff: Dordrecht, The Netherlands, 1986. (c) Nógrádi, M. *Stereoselective Synthesis*; VCH: Weinheim, FRG, 1987. (d) Brunner, H. *Top. Stereochem.* **1988**, *18*, 129–247. (e) Noyori, R.; Kitamura, M. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1989; Vol. 5, pp 155–198. (f) Ojima, I.; Clos, N.; Bastos, C. *Tetrahedron* **1989**, *45*, 6901.

(3) Schinzer, D., Ed. *Selectivities in Lewis Acid Promoted Reactions*; NATO Series; Kluwer: Dordrecht, The Netherlands, 1989.

(4) See e.g.: Mukaiyama, T.; Uchiro, H.; Kobayashi, S. *Chem. Lett.* **1989**, 1001 and references cited therein.

(5) See e.g.: Furuta, K.; Shimizu, S.; Miwa, Y.; Yamamoto, H. *J. Org. Chem.* **1989**, *54*, 1483 and references cited therein.

(6) See e.g.: Mikami, K.; Terada, M.; Nakai, T. *J. Am. Chem. Soc.* **1990**, *112*, 3949 and references cited therein.

(7) Boger, D. L.; Weinreb, S. N. *Hetero Diels-Alder Methodology in Organic Synthesis*; Academic Press: San Diego, CA, 1987.

(8) For a personal account, see: Danishefsky, S. *Chemtracts: Org. Chem.* **1989**, *2*, 273 and references cited therein.

(9) (a) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: Chichester, England, 1976. (b) Reetz, M. T. In ref 3, pp 107–125.

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Table I. Novel Bis(3-acylcamphorato)oxovanadium Complexes Prepared[a]

ligand HL, R	method	product	yield, %	EPR,[b] $a(^{51}V)$, mT	$[\alpha]_D$,[c] deg	IR, ν(V=O)[d], cm^{-1}
(+)-**2a**, C_3F_7	A	(+)-**5a**	41	11.11	+225	1020
(−)-**2a**, C_3F_7	B	(−)-**5a**	44	11.11	−225	1020
(+)-**2b**, CF_3	A	(+)-**5b**	42	11.10	+144	1005
(+)-**2c**, Ph	A	(+)-**5c**	50	10.78	+114	1005
(+)-**2d**, 4-(F_3C)Ph	B	(+)-**5d**	97	10.75	+96	1005
(+)-**2e**, 3,5-(F_3C)$_2$Ph	B	(+)-**5e**	62	10.79	+228	973

[a] See also Scheme I. [b] See ref 18. [c] c = 0.05, CH_2Cl_2). [d] KBr pellets.

et al., who used aluminum complexes of type **1**, bearing a bulky binaphthol-derived ligand (see Chart I).[10] Lanthanide complexes of the type Eu(hfbc)$_3$ (Hhfbc = 3-(heptafluorobutyryl)camphor (**2a**)),[11] also known as chiral paramagnetic NMR shift reagents,[12] have been reported as the first complexes of non-main-group elements to catalyze this reaction. Despite the potential wealth of chiral Lewis acidic transition-metal complexes, their use as catalysts for the title reaction has been so far neglected. Faller et al. reported cationic Ru complexes of type **3** as the only examples known so far.[13] When chiral chelating diphosphines were introduced in **3**, only modest enantioselectivities could be obtained.

Our approach consisted of using chiral derivatives of the coordinatively unsaturated vanadium(IV) complex VO(acac)$_2$ (**4**) for the following reasons. (a) It is known that **4** can form weakly to moderately strongly bonded Lewis acid–base adducts (strictly 1:1) mainly with nitrogen donors,[14] but also with oxygen bases (e.g. dioxane)[15] or tertiary amine oxides.[16] These neutral molecules will usually occupy the unique vacant coordination site trans to the oxo ligand, thus preserving the geometrical features of the parent compound.[17] (b) Chiral bis(1,3-diketonato)oxovanadium(IV) complexes should be readily accessible, and easy to modify, thus allowing a fine tuning of the Lewis acidity. (c) These complexes should be easy to handle due to their expected low sensitivity toward moisture and oxygen.

For the synthesis of chiral VO(acac)$_2$ derivatives we chose the same type of camphor ligands previously described. These are in part commercially available or are readily obtained by acylation of camphor at the secondary carbon atom adjacent to the carbonyl moiety (position 3). We report the synthesis of novel bis(3-acylcamphorato)-oxovanadium(IV) complexes and their successful use as catalysts for the title reaction.

Results and Discussion

Synthesis of Complexes. The results are summarized in Scheme I and Table I. The preparation of the novel bis(3-acylcamphorato)oxovanadium(IV) complexes was achieved in two different ways. Starting from vanadyl sulfate, $VOSO_4 \cdot 5H_2O$, the ligand **2**, and 1 equiv of NEt_3 in EtOH/H_2O, the product was isolated by extraction with pentane or CH_2Cl_2 (method A). Alternatively, a metathesis reaction in a high-boiling inert solvent (toluene, xylene, or mesitylene) at 100–180 °C, starting from a 1:2 mixture of **4** and **2**, was used in particular for the less volatile ligands (method B). Both methods gave analytically pure materials, which were used without further purification. They were isolated as green to brown powders and could be kept in air for extended periods of time without deterioration. Complex **5a** proved very soluble in virtually any organic solvent, such that a recrystallization, even from pentane or CH_2Cl_2/pentane mixtures, both was invariably affected by relevant loss of material and did not improve the catalytic properties of the complex.

Scheme I

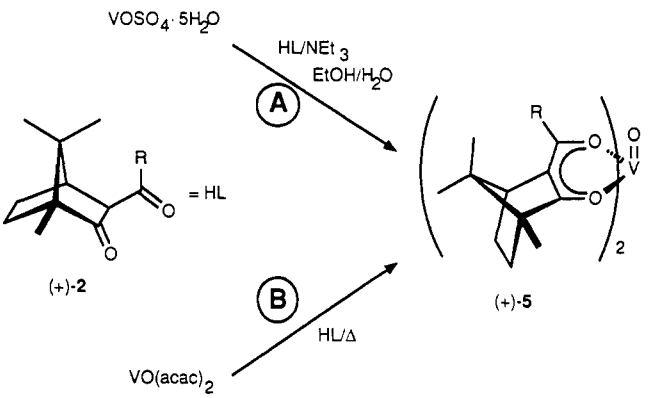
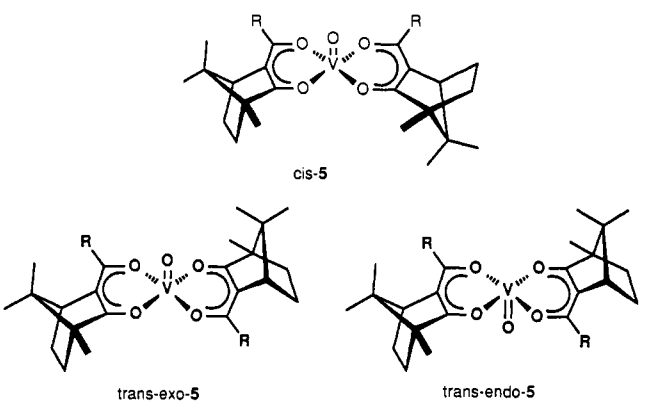


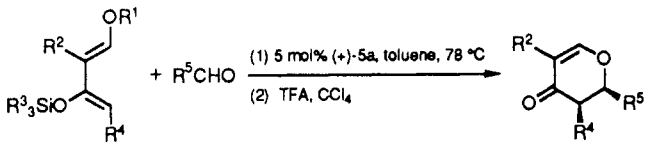
Chart II



If one reasonably assumes a square-pyramidal coordination geometry around vanadium, as in the parent compound,[17] then, due to the asymmetric nature of the ligands, three possible diastereomeric forms of the complexes exist. These are illustrated in Chart II. The nomenclature cis/trans refers to the orientation of the side chain R with respect to the main coordination plane of vanadium, whereas endo/exo indicates the position of the oxo ligand relative to the camphor moiety. We have not succeeded so far in growing crystals suitable for X-ray diffraction.[51] Thus, the exact geometry of these paramagnetic d^1 systems is still unknown. However, samples from different prep-

(10) Maruoka, K.; Itoh, T.; Shirasaka, T.; Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310.
(11) (a) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 3716. (b) Bednarski, M.; Maring, C.; Danishefsky, S. *Tetrahedron Lett.* **1983**, *24*, 3451.
(12) Sullivan, G. R. *Top. Stereochem.* **1978**, *10*, 287.
(13) Faller, J. W.; Smart, C. J. *Tetrahedron Lett.* **1989**, *30*, 1189.
(14) Vilas Boas, L.; Costa Pessoa, J. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon: Oxford, England, 1987; Vol. 3, p 453.
(15) Dichmann, K.; Hamer, G.; Nyburg, S. C.; Reynolds, W. F. *J. Chem. Soc. D* **1970**, 1295.
(16) Popp, C. J.; Nelson, J. H.; Ragsdale, R. O. *J. Am. Chem. Soc.* **1969**, *91*, 610.
(17) Nitrogen Lewis bases may lead to isomerization upon complexation; i.e., they will occupy the cis position relative to the oxo ligand. The adduct of 4-phenylpyridine with VO(acac)$_2$ was characterized by X-ray diffraction; see: Caira, M. R.; Haigh, J. M.; Nassimbeni, L. R. *Inorg. Nucl. Chem. Lett.* **1972**, *8*, 109. For the structure of VO(acac)$_2$, see: (a) Dodge, R. P.; Templeton, D. H.; Zalkin, A. *J. Chem. Phys.* **1961**, *35*, 55. (b) Hon, P. K.; Belford, R. L.; Pfluger, C. E. *J. Chem. Phys.* **1965**, *43*, 3111.

Table II. Stereoselectivities in the Hetero Diels–Alder Reaction Catalyzed by Complex (+)-5a[a]



entry no.		diene R1	diene R2	diene R3	diene R4	aldehyde R5	yield,[b] %	product, % ee (% ds)[c]
1	**6a**	Me	H	Me_3	H	Ph	82	**7a**, 68
2	**6b**	Me	H	Et_3	H	Ph	85	**7a**, 76
3	**6c**	*t*-Bu	H	Et_3	H	Ph	84	**7a**, 70
4	**6d**	*t*-Bu	H	Me_3	H	Ph	80	**7a**, 73
5	**6e**	(−)-Men[d]	H	Me_3	H	Ph	95	**7a**, 73
6	**6f**	(+)-Men[e]	H	Me_3	H	Ph	90	**7a**, 71
7	**6g**	Me	Me	Me_3	Me	Ph	94	**7b**, 82 (98.5)
8	**6h**	Me	Me	Et_3	Me	Ph	90	**7b**, 85 (99)
9	**6i**	Me	Me	*t*-$BuMe_2$	Me	Ph	90	**7b**, 84 (98)
10	**6j**	*t*-Bu	Me	Me_3	Me	Ph	89	**7b**, 71 (99)
11	**6k**	Me	OAc	Me_3	H	Ph	58	**7c**, 58
12	**6g**	Me	Me	Me_3	Me	2-furyl	95	**7d**, 63 (>99)
13	**6g**	Me	Me	Me_3	Me	2-Anisyl[f]	80	**7e**, 73[g] (90)
14	**6g**	Me	Me	Me_3	Me	*c*-C_6H_{11}	63	**7f**, 44 (>99)
15	**6g**	Me	Me	Me_3	Me	$-CH^E{=}CHPh$	90	**7g**, 68 (>99)
16	**6g**	Me	Me	Me_3	Me	$-CH_2OBn$	70	**7h**, 53 (95)
17	**6g**	Me	Me	Me_3	Me	−COOMe	27	**7i**, 42 (66)
18[h]	6a	Me	H	Me_3	H	Ph	95	**7a**, 39
19[i]	6a	Me	H	Me_3	H	Ph	91	**7a**, 39
20[i]	**6g**	Me	Me	Me_3	Me	Ph	88	**7b**, 48 (98.5)
21[j]	**6g**	Me	Me	Me_3	Me	Ph	*k*	**7b**, 50 (81)

[a] Only one stereoisomeric product is shown. The absolute configuration given is correct for **7a** (6*R*) and **7b** (5*R*,6*R*)[11] and tentative for all others and is based on a comparison of the elution times on a Chirasil-L-Val GLC column (see Table V). [b] Chromatographed product. [c] Determined in the crude mixture. [d] (1*R*,2*S*,5*R*)-Menthyl. [e] (1*S*,2*R*,5*S*)-Menthyl. [f] 2-(OMe)-Ph. [g] Determined by NMR spectroscopy with the chiral shift reagent (+)-TAE. [h] Reaction carried out at room temperature. [i] Reaction carried out at room temperature with 0.1 mol % catalyst. [j] Reaction carried out at −100 °C. [k] Not determined.

arations showed identical EPR patterns[18] and reproducible $[\alpha]_D$ values. We conclude that these materials are either a specific constant-equilibrium mixture of two/three of the stereoisomers illustrated in Chart II or, what seems more likely, a single isomer. There are very few bis(1,3-diketonato)oxovanadium complexes bearing different substituents adjacent to the carbonyl moieties and very few whose exact geometry is known. Among those, the complex derived from 1-phenylbuta-1,3-dione is known to exist exclusively in a cis arrangement of the ligands.[19] This can be rationalized on the basis of trans effects[20] within the main coordination plane of the vanadium ion. The different donor capabilities of the two carbonyl fragments, due to the electronically different substituents attached to them (Me and Ph, respectively), would preferentially induce a cis geometry, when the complex is formed under kinetic control. The same types of arguments should apply to complexes **5a–e**, as well. The two carbonyls in a 3-acylcamphor complex should be electronically very different from one another, in particular for derivatives bearing a perfluorinated side chain (**2a,b**). We therefore tentatively assign the cis geometry to complexes **5a–e**.

Catalytic Reactions with Bis(3-(heptafluorobutyryl)camphorato)oxovanadium. The first, and most readily available, complex prepared during this study, **5a**, proved to be a very efficient catalyst for the hetero Diels–Alder reaction of aldehydes with dienes of the Danishefsky type (**6a**). **5a** (5 mol % relative to the aldehyde; a slight excess of the diene was used throughout), in toluene at −78 °C, was found to ensure complete conversion to the cycloadduct within 10–30 h. After exposure of the reaction mixture to a catalytic amount of CF_3COOH in toluene/CCl_4 for 10 min, the product was isolated and purified by column chromatography. The determination of the enantiomeric excess (ee) was performed by capillary GLC, with a Chirasil-L-Val column (see Figure 1 and

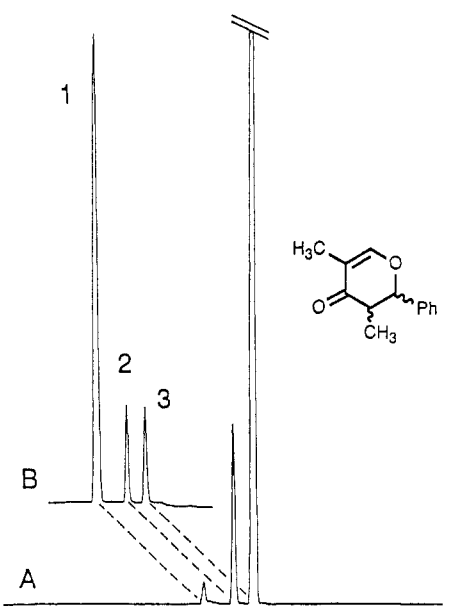


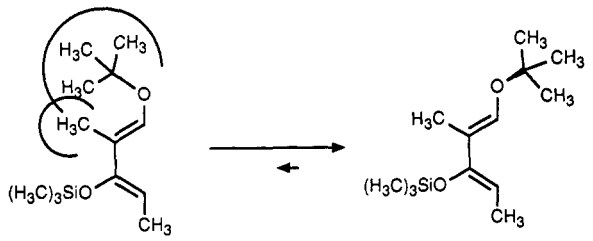
Figure 1. GLC traces (Chirasil-L-Val) of a typical mixture of pyrones **7b** obtained after workup with TFA: (A) catalysis by complex **5a**; (B) BF_3 catalysis (peak 1, trans isomers; peak 2, 5*S*,6*S* enantiomer; peak 3, 5*R*,6*R* enantiomer (trace A: cis/trans = 98.5/1.5; cis 82% ee)).

(18) The complexes **5a–e** and their adducts with substrates are currently being investigated by EPR, paramagnetic NMR, and ENDOR spectroscopy. The results from this study will be the subject of a future report from our laboratory.

(19) Hon, P. K.; Belford, R. L.; Pfluger, C. E. *J. Chem. Phys.* **1965**, *43*, 1323.

(20) Basolo, F.; Pearson, R. G. *Prog. Inorg. Chem.* **1963**, *4*, 381.

Scheme II



A (Z, s-cis) B (gauche)

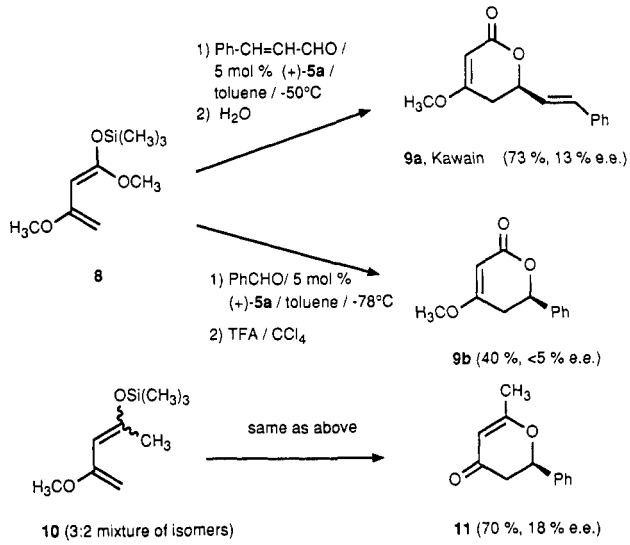
Experimental Section). For comparison and peak assignment, a racemic sample of every γ-pyrone derivative was prepared under $ZnCl_2$-assisted conditions, by following a protocol reported by Danishefsky.[21] Every reaction was carried out at least twice, and the error margin on the given optical purity of the products is less than 1%. A collection of the results obtained with catalyst **5a** is given in Table II.

Moderate to good enantioselectivities were observed if the reactions were carried out at low temperature only. A qualitatively similar reaction rate could be obtained at room temperature with 0.1 mol % catalyst, but with a reduction of the optical yield by a factor of ca. 2 (Table II, entries 18–20). It is important to note that the enantioselectivity of the reaction at a given temperature is independent of the catalyst concentration. This is likely to imply a first-order rate dependence on the catalyst.

For 4-substituted dienes the reaction leads to products containing two contiguous stereogenic centers. In all cases the diastereoselectivity found is very high, and unprecedented, leading to the preferred formation of cis-configurated γ-pyrone derivatives (entries 7–10, 12–16). Even the best known catalyst system, **1**,[10] does not afford such a high diastereoselection. According to Danishefsky,[22] the formation of cis-configurated products is indicative of a pericyclic, as opposed to a two-step, Mukaiyama aldol-like mechanism of the reaction. In our system there is no relevant change in diastereoselectivity when the reaction is carried out at room temperature (vs −78 °C). On the other hand, it is interesting to note that, when the reaction of diene **6g** with benzaldehyde was carried out at −100 °C in the presence of 10 mol % of **5a**, both diastereo- and enantioselectivity dropped from 98.5 to 81% and from 82 to 50%, respectively (entry 21). Thus, with the present vanadium catalyst the aldol-like pathway becomes operative at very low temperature only.

With the model substrate benzaldehyde, the dependence of the stereoselectivity on the structure of the diene was studied. The nature of the substituents in the butadiene unit was found to affect in a very relevant manner the stereoselection of the reaction. The bulkiness one can introduce at all four positions seems to have an influence, although the overall effects observed are invariably a combination of the effects due to each single substituent. Thus, *tert*-butoxy instead of methoxy at the butadiene terminus, for instance, is beneficial as long as R^2 = H (entries 1 and 4). **7a** was thus formed in 73 vs 68% ee. The same strategy for improving selectivity fails when applied to 2,4-disubstituted butadienes (entries 7 and 10). A drop of ee from 82 to 71% was obtained for **7b**. This observation possibly indicates that the conformation of the diene in the transition state also plays a very important

Scheme III



role. Durig and Compton[23] have shown that methyl vinyl ether has two energetically low-lying conformations in equilibrium: *Z* (s-cis, sp^2 hybridization at oxygen) and gauche (anticlinal, sp^3 hybridization). Analogous conformations can be formulated for diene **6j**, as shown in Scheme II. Due to steric repulsion between the *t*-Bu and methyl groups the *Z* conformation A will be seriously disfavored. Assuming that conformations A and/or B are relevant also in the transition state of the reaction, we conclude from our observations that only dienes which preferentially exist in, or can adopt, the conformation A will lead to high enantioselectivities.

The silyloxy group at position 3 was found to affect the selectivity in a similar way. Thus, the highest enantioface discriminations were obtained with the triethylsilyl group. Starting from dienes **6b** and **6h**, the products **7a** and **7b**, respectively, were formed in 76 and 85% ee (entries 2 and 8).

With chiral lanthanide catalysts of the type shown in Chart I, Danishefsky and co-workers observed double stereoselection[24] upon introduction of a menthoxy group at the diene terminus 1.[25] Pursuing the same strategy, we accordingly modified diene **6a**, formally replacing the methoxy by a (+)- and (−)-menthoxy group, respectively. The results (entries 5 and 6) indicate that with our vanadium catalyst the menthyl substituent just behaves as a bulky group, similar in consequences to *t*-Bu, practically in disregard of its absolute configuration. Although there is a slight double stereodifferentiation involved (73 vs 71% ee), this does not seem to be relevant for synthetic purposes.

The use of dienes of type **6** leads exclusively to the formation of γ-pyrone derivatives. A number of naturally occurring compounds contain a six-membered lactone ring; i.e., they are α-pyrone derivatives.[26] Such a class of compounds is easily accessible via a hetero Diels–Alder addition of an aldehyde to a 1-alkoxy-1-(silyloxy)butadiene, i.e. a γ,δ-unsaturated silylketene acetal. A representative of such compounds is the so-called Brassard diene,[27] **8**.

(21) Danishefsky, S.; Larson, E.; Askin, D.; Kato, N. *J. Am. Chem. Soc.* **1985**, *107*, 1246.

(22) (a) Larson, E. R.; Danishefsky, S. *J. Am. Chem. Soc.* **1982**, *104*, 6458. (b) Larson, E. R.; Danishefsky, S. *Tetrahedron Lett.* **1982**, *23*, 1975.

(23) Durig, J. R.; Compton, D. A. C. *J. Chem. Phys.* **1978**, *69*, 2028.

(24) (a) Masamune, S.; Choy, W.; Petersen, J. R.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1. For earlier reports, see: (b) Heathcock, C. H.; White, C. T. *J. Am. Chem. Soc.* **1979**, *101*, 7076. (c) Horeau, A.; Kagan, H.-B.; Vigneron, J.-P. *Bull. Soc. Chim. Fr.* **1968**, 3795.

(25) Bednarski, M.; Danishefsky, S. *J. Am. Chem. Soc.* **1983**, *105*, 6968.

(26) Davies-Coleman, M. T.; Rivett, D. E. A. In *Progress in the Chemistry of Organic Natural Products*; Herz, W., Grisebach, H., Kirby, G. W., Tamm, C., Eds.; Springer-Verlag: Vienna, 1989; Vol. 55, pp 1–35.

Table III. Distribution of Diastereomeric Products from the Reaction of Aldehyde 13 with Diene 6g Depending on the Catalyst Used[a]

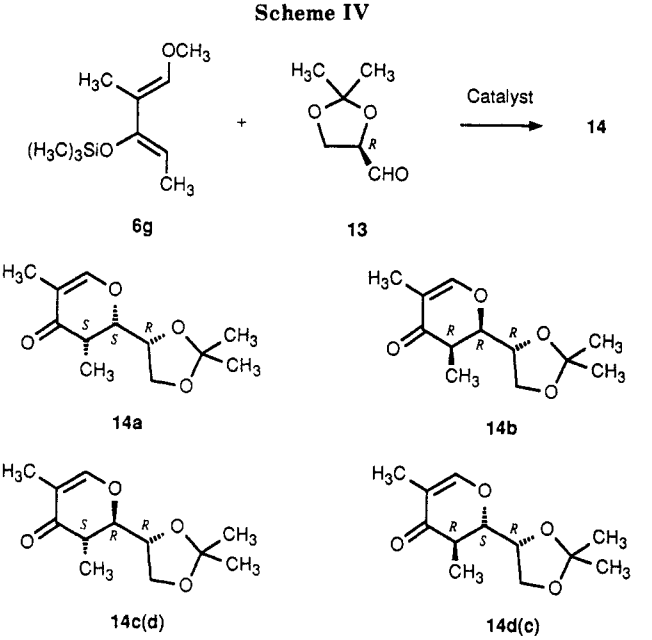
catalyst	amt of **14a**, %	amt of **14b**, %	**14a/14b**	amt of **14c(d)**, %	amt of **14d(c)**, %	**14c/14d**	yield, %[b]
5 mol % (−)-**5a**[c]	93.1	3.7	25.2	2.7	0.5	5.4	49
5 mol % (+)-**5a**[c]	45.7	47.5	0.96	6.6	0.2	33	48
1 equiv BF_3·Et_2O[d]	24.0	4.5	5.3	42.8	28.7	1.5	*e*
1 equiv $ZnCl_2$[f]	69.7	7.0	10.0	21.9	1.4	15.6	*e*
t_R, min[g]	10.47	11.69		10.62	11.08		
$[\alpha]_D$, deg (CH_2Cl_2, c = 1)	−70.4	+86.2		+107.1	−91.2		

[a] Determined by GLC in the crude mixture with a 25-m capillary fused-silicon DB 17/30 W column (HP 5890A gas chromatograph). Temperature program: 1 min at 100 °C, 10 °C/min, 200 °C final temperature. [b] Sum of yields of analytically pure diastereomers **14a** and **14b** after flash-chromatographic purification. [c] Reaction carried out at −78 °C in toluene. [d] Reaction carried out at −78 °C in CH_2Cl_2. [e] Not determined. [f] Reaction carried out at room temperature in THF. [g] Retention time.

Cycloaddition of 8 with cinnamaldehyde catalyzed by the vanadium(IV) complex (+)-**5a**, followed by aqueous workup, gave in good yield the natural product kawain[28] (**9a**; Scheme III). However, the optical yield of this reaction turned out to be rather modest. The *R* enantiomer of **9a** was isolated in 13% ee (determined by NMR spectroscopy with the diamagnetic chiral shift reagent TAE).[29] The reaction of **8** with benzaldehyde was even more disappointing; thus, compound **9b** was obtained essentially as a racemic mixture and in low yield. A 3:2 isomeric mixture of the diene **10** when reacted with benzaldehyde in the presence of the catalyst **5a** gave similar results. The optical purity of the 2-methyl-γ-pyrone **11** was found to be 18%. These experiments indicate that double substitution at the butadiene terminus has deleterious consequences upon the enantioselectivity of the cycloaddition reaction. A comparison with the results discussed above, concerning the effect of conformational constraints of the alkoxy group at C(1), seems to support the idea that, in order to achieve high selectivities, one hemispherical portion of space around C(1) should be free of substituents.

Double Stereodifferentiation with a Chiral Aldehyde. Masamune et al. advocated the powerful strategy of double stereoselection (double asymmetric induction) for the predictable formation of new stereogenic centers.[24] The utilization of this stratagem with the present vanadium(IV) catalyst seems to be unsuccessful by introducing further chiral information into the diene component (see Table II, entries 5 and 6). This is in contrast to the results obtained by Danishefsky using the chiral lanthanide catalyst Eu(hfbc)$_3$.[25] We previously showed that the chiral, and in optically pure form easily accessible, aldehyde **13**[30] shows a peculiar effect of double stereodifferentiation in the asymmetric gold(I)-catalyzed aldol condensation with isocyanoacetates.[31] In order to test the influence of its chirality in the vanadium-catalyzed hetero Diels–Alder reaction, **13** was reacted with the diene **6g** under the catalytic action of (+)-**5a** and (−)-**5a**, respectively. For comparison and in order to judge to what extent the chiral induction in this reaction is due to the aldehyde, the reaction was also carried out in the presence of 1 equiv of BF_3·Et_2O and of $ZnCl_2$, respectively. The four diastereomeric products **14a–d** were separated and isolated by column chromatography. The assignment of the absolute stereochemistry of **14a,b** is based on the following observations. (1) According to Danishefsky,[32] the $MgCl_2$- or $ZnCl_2$-assisted reaction of **13** with an activated diene is consistent with a Cram formulation[33] and no chelation control. Thus, the major stereoisomer formed in the $ZnCl_2$-assisted reaction of **13** with **6g** has to be formulated as **14a**. (2) (−)-**5a** leads to the preferred formation of 5*S*,6*S*-configurated γ-pyrone derivatives. The absolute configuration of the minor trans diastereomers **14c,d** is unknown. The results clearly indicate the existence of a matched and of a mismatched case (see Scheme IV and Table III). Thus, (−)-**5a** matches *R*-**13**, giving rise to the formation of **14a** with 93.1% diastereoselectivity (**14a/14b** = 25.2). On the other hand, the combination of (+)-**5a** with *R*-**13** constitutes the mismatched case, with almost no differentiation between the two major cis-diastereomeric products (**14a/14b** = 0.96). As expected,[21] the strong Lewis acid BF_3 showed a high trans selectivity (**14c** + **14d** = 71.5%) and a ratio of the two cis diastereomers of 5.3, whereas $ZnCl_2$ favors the formation of the cis diastereomers **14a** and **14b** (**14a/14b** = 10). The present results clearly indicate that in this reaction the extent of chiral induction is dominated by the aldehyde. Whether this is a general

Scheme IV



(27) (a) Brassard, P.; Savard, J. *Tetrahedron Lett.* **1979**, 4911. (b) Midland, M. M.; Graham, R. S. *J. Am. Chem. Soc.* **1984**, *106*, 4294.
(28) Aschenbach, H.; Theobald, N. *Chem. Ber.* **1974**, *107*, 735 and references cited therein.
(29) (+)-2,2,2-Trifluoro-1-(9-anthryl)ethyl alcohol; for leading references, see: (a) Pirkle, W. H.; Beare, S. D.; Muntz, R. L. *Tetrahedron Lett.* **1974**, 2295. (b) Pirkle, W. H.; Hoekstra, M. S. *J. Am. Chem. Soc.* **1976**, *98*, 1832. (c) Pirkle, W. H.; Sikkenga, D. L.; Pavlin, M. S. *J. Org. Chem.* **1977**, *42*, 384. (d) Pirkle, W. H.; Rinaldi, P. L. *J. Org. Chem.* **1977**, *42*, 3217. (e) Pirkle, W. H.; Beare, S. D.; Muntz, R. L. *J. Am. Chem. Soc.* **1969**, *91*, 4575.
(30) Häfele, B.; Jäger, V. *Liebigs Ann. Chem.* **1987**, 85.
(31) Togni, A.; Pastor, S. D. *Helv. Chim. Acta* **1989**, *72*, 1038.
(32) Danishefsky, S.; Pearson, W. H.; Harvey, D. F.; Maring, C. J.; Springer, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1256.
(33) Cram, D. J.; Wilson, D. R. *J. Am. Chem. Soc.* **1963**, *85*, 1245 and references cited therein.

Table IV. Dependence of the Enantioselectivity of 7a on the Catalyst Used

catalyst	conversn after 20 h at −78 °C, %[a]	ee, %	catalyst	conversn after 20 h at −78 °C, %[a]	ee, %
(+)-**5a**	100	68	(+)-**5d**	<10	<5
(+)-**5b**	40	29	(+)-**5e**	<10	<5
(+)-**5c**	<10	<5			

[a] As determined by GLC methods.

feature for the vanadium-catalyzed cycloaddition is still an open question. It was previously observed in the aforementioned gold(I)-catalyzed aldol condensation that the stereochemical behavior of the aldehyde **13** is somewhat unique and is likely to be due to the presence of heteroatom(s) attached and/or adjacent to the stereogenic center.[31,34] Of course, some caution in comparing two mechanistically completely different reactions has to be exercised.[35]

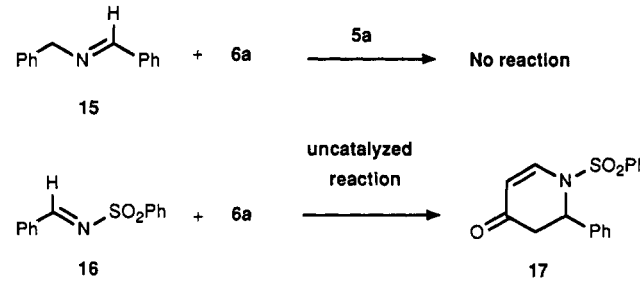
Catalysts with Varied Side Chains. Because of the easy accessibility of 3-acylcamphor derivatives of type **2** (see Scheme I), it was obvious to study the influence of the ligand side chain R upon both the activity and the selectivity of the corresponding vanadium(IV) complexes as catalysts for the hetero Diels–Alder reaction. We reasoned that, by replacement of the perfluoroalkyl side chain contained in the commercially available ligands **2a** and **2b** by an aromatic group, it would be possible to fine tune the Lewis acidity of the corresponding complexes by introducing electron-withdrawing or -donating substituents onto the aromatic moiety. Although we had anticipated a dependence of the catalytic properties of complexes **5** upon the nature of the group R, due to both its steric requirements and electronic effects, the results were most striking (see Table IV). **5a** was by far superior to all other complexes prepared. Thus, only **5b**, bearing a trifluoromethyl instead of a heptafluoropropyl group, gave a qualitatively somewhat comparable catalytic activity. On the other hand, the enantioselectivity in the formation of pyrone derivative **7a** dropped from 68% (**5a**) to 29% (**5b**). The other complexes, bearing an aromatic substituent (**5c–e**), showed a very low activity and gave essentially racemic products.

The dramatic specificity of the C_3F_7 side chain, needed in order to obtain both high activity and enantioselectivity, is, at the present time, not understood.

Attempted Catalysis of Imine Cycloaddition. The imino functionality is known to participate as a dienophile in various [2 + 4] cycloadditions.[36] Most of these reactions described in the literature involve activated imines, i.e. with electron-withdrawing groups attached to the C=N unit. Danishefsky and co-workers have shown that it is possible to achieve cycloaddition of an unactivated imine by activation with a Lewis acid.[37] It was therefore of interest to attempt the same type of reaction with the present vanadium(IV) system.

When imines **15** and **16** were exposed to diene **6a** in the presence of 5 mol % of complex **5a** at room temperature, no catalytic reaction could be observed (see Scheme V).

Scheme V



Cycloadduct **17**[38] formed slowly under these conditions by following the thermal pathway, as was proved by carrying out the reaction in the absence of the catalyst. A possible explanation for the lack of activity in this type of Diels–Alder reaction is the better ligation property of the imine (vs that for the aldehyde) toward the vanadyl system at hand. On the other hand, in analogy to, for example, pyridine derivatives,[17] coordination of the imine to vanadium could lead to rearranged species, which could possibly be both thermodynamically stable and kinetically inert. Although we were not able to isolate any of the adducts of complex **5a** with imines, the interaction of the catalyst with the substrates is currently being studied in solution by EPR spectroscopy.[18]

Conclusions. We have shown in the present study that complexes of type **4** can be modified to obtain novel derivatives active as catalysts for the asymmetric hetero Diels–Alder reaction. We believe that this is a still rare example of how a very well-known class of coordination compounds of a transition metal can find new potential applications in synthesis. As a catalyst for the title reaction, **5a** is superior to all previously described non-main-group Lewis acids, in terms of both activity and selectivity, and is second in terms of selectivity only to Yamamoto's aluminum complex **1**.[10] The peculiarities of our bis(3-acylcamphorato)oxovanadium system can be summarized as follows. (a) Among the derivatives described, only **5a** shows both high catalytic activities and enantioselectivities, thus constituting a dramatic example of the specificity of the ligand nature for a given catalytic reaction. This observation identifies at the same time the difficulties connected with a further improvement of the catalyst's properties. (b) Despite the fact that Lewis acids containing main-group elements or transition metals in their d^0 electronic configuration are able to catalyze various types of cycloaddition reactions,[3] the vanadium(IV) Lewis acid at hand gives satisfactory results in the hetero Diels–Alder condensation of aldehydes with 1-alkoxy-3-(silyloxy)butadienes only.

Experimental Section

General Considerations. $VOSO_4 \cdot 5H_2O$, Danishefsky's diene (**6a**), and the ligands (+)-**2a**, (−)-**2a**, and (+)-**2b** were purchased from commercial supply houses and used as received. $VO(acac)_2$ (Fluka) was recrystallized from $CHCl_3$ before use. The dienes **6b–e**,[39] **6f**,[39] **6g**,[40] **6h**,[41] **6i,j**,[41] **6k**,[42] **8**,[27] and **10**[43] were prepared either

(34) Togni, A.; Pastor, S. D. *J. Org. Chem.* **1990**, *55*, 1649.

(35) In the gold(I)-catalyzed aldol reaction the role of the catalyst consists of activating the reaction partner of the aldehyde, exclusively.[34] On the other hand, it is reasonably assumed that, in the vanadium-catalyzed hetero Diels–Alder reaction, the addition of the aldehyde to the complex is the relevant activating interaction.

(36) For a recent review, see ref 7, Chapter 2, and references cited therein.

(37) (a) Kerwin, J. F., Jr.; Danishefsky, S. *Tetrahedron Lett.* **1982**, *23*, 3739. (b) Danishefsky, S.; Langer, M. E.; Vogel, C. *Tetrahedron Lett.* **1985**, *26*, 5983. (c) Danishefsky, S.; Vogel, C. *J. Org. Chem.* **1986**, *51*, 3915.

(38) Abramovich, R. A.; Stovers, J. R. *Heterocycles* **1984**, *22*, 671.

(39) Danishefsky, S.; Bednarski, M.; Izawa, T.; Maring, C. *J. Org. Chem.* **1984**, *49*, 2290.

(40) Danishefsky, S.; Yan, C.-F.; Singh, R. K.; Gammill, R. B.; McMurry, P. M., Jr.; Fritsch, N.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 7001.

(41) Danishefsky, S.; Harvey, D. F. *J. Am. Chem. Soc.* **1985**, *107*, 6647.

(42) Danishefsky, S.; Craig, T. A. *Tetrahedron Lett.* **1981**, *37*, 4081.

(43) Emde, H.; Damsch, D.; Feger, H.; Frick, U.; Götz, A.; Hergott, H.; Hoffmann, K.; Kober, W.; Krageloh, K.; Oesterle, T.; Steppan, W.; West, W.; Simchen, G. *Synthesis* **1982**, 1.

Table V. GLC Retention Times of Pyrone Derivatives on Chirasil-L-Val[a]

compd	t_R, min			carrier,[c] kPa	T, °C
		cis enantiomers	trans enantiomers[b]		
7a	29.2	29.6		50	140
7b	35.7	36.7	33.5	50	140
7c	27.7	28.3		60	170
7d	23.8	24.2	*d*	40	120
7f	19.5	19.9	17.0	50	150
7g	31.2	32.0	30.0	50	170
7h	28.0	28.4	26.7	70	170
7i	13.0	13.3	10.9	50	130
11	31.2	31.9		50	150

[a] See ref 48. [b] In all cases no separation was observed. [c] Pressure of the carrier gas. [d] Not detected.

by reported procedures or by an adaptation thereof and stored at 4 °C under Ar. The aldehydes $PhCH_2OCH_2CHO$,[44] $H_3COC-OCHO$,[45] and **13**[30] and the imines **15**[46] and **16**[47] were prepared as previously described. All reactions with air- or moisture-sensitive materials were carried out under Ar with use of standard Schlenk techniques. Freshly distilled, dry, and oxygen-free solvents were used throughout. ^1H (250.133 MHz) and ^{13}C (62.896 MHz) NMR spectra were recorded with a Bruker AC 250 spectrometer. Chemical shifts are given in ppm relative to internal TMS, and coupling constants (J) are given in Hz. EPR spectra were recorded with a Varian X-band E-9 spectrometer (toluene solutions at room temperature). Optical rotations were measured with a Perkin-Elmer 241 polarimeter using 10-cm cells. Capillary GLC analyses were done on a Carlo Erba HRGC 5300 instrument using a 50-m Chirasil-L-Val column (a collection of the retention times of the different enantiomeric products is given in Table V)[48] or on a HP 5890A chromatograph equipped with a 25-m fused-silicon DB 17/30W column. Merck silica gel 60 (70–230 mesh) was used for flash column chromatography. Elemental analyses were performed by Analytical Research Services, CIBA-GEIGY AG.

(+)-(1*R*)-3-Benzoylcamphor ((+)-2c). To a suspension of 1.85 g (77.1 mmol) of NaH in 50 mL of 1,2-dimethoxyethane (DME) was added 5.0 g (32.8 mmol) of (+)-camphor, and the mixture was refluxed for 1 h. At reflux temperature 4.5 mL (36.1 mmol) of methyl benzoate, dissolved in 20 mL of DME, was then added dropwise over 1.5 h. The solution was refluxed overnight, quenched by 10 mL of EtOH with cooling, and added to 100 mL of H_2O and the mixture acidified with concentrated HCl to pH 1. After extraction with pentane (3 × 100 mL), washing of the organic layer with 100 mL of 5% aqueous $NaHCO_3$ solution, and drying over Na_2SO_4, the product was isolated as an oil (7.95 g) upon evaporation of the solvent. The oil was dissolved in 40 mL of pentane, and the solution was left overnight at 4 °C. The crystalline material formed was filtered off, washed with cold pentane, and dried in vacuo. Another crop of crystals was obtained by concentration of the mother liquor: total yield 7.0 g (83%); $[\alpha]^{22}_D$ = +131.0° (c = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.99 (s, 3 H), 1.03 (s, 3 H), 1.06 (s, 3 H), 1.30–1.43 (m, 1 H), 1.64–1.84 (m, 3 H), 2.52 (br t, J = 4, 1 H), 4.24 (br dd, J = 5, 1, 1 H), 7.42–7.52 (m, 2 H), 7.55–7.63 (m, 1 H), 7.91 (m, 2 H), diketo form; MS m/z 257, 256 (M^+), 241, 228, 213, 147, 105. Anal. Calcd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found: C, 79.60; H, 8.00.

(+)-(1*R*)-3-(4-(Trifluoromethyl)benzoyl)camphor ((+)-2d). This compound was obtained in an analogous way from 5.0 g (32.8 mmol) of (+)-camphor, 1.85 g (77.1 mmol) of NaH, and 7.9 g (36.1 mmol) of ethyl 4-(trifluoromethyl)benzoate, in 50 mL of DME: yield 3.91 g (37%) of yellowish needles (hexane); $[\alpha]^{22}_D$ = +178.6° (c = 1.08, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.83 (s, 3 H), 0.96 (s, 3 H), 1.04 (s, 3 H), 1.47–1.90 (m, 3 H), 2.06–2.25 (m, 1 H), 2.81 (d, J = 5, 1 H), 7.66–7.80 (m, 4 H), 12.33 (br s, 1 H), enol form; MS m/z 325, 324 (M^+), 309, 296, 281, 215, 211, 174, 173, 145, 123. Anal. Calcd for $C_{18}H_{19}F_3O_2$: C, 66.66; H, 5.91; F, 17.58. Found: C, 66.85; H, 5.88; F, 17.49.

(+)-(1*R*)-3-(3,5-Bis(trifluoromethyl)benzoyl)camphor ((+)-2e). This compound was obtained in an analogous way from 1.26 g (8.3 mmol) of (+)-camphor, 0.465 g (19.4 mmol) of NaH, and 2.6 g (9.1 mmol) of ethyl 3,5-bis(trifluoromethyl)benzoate, in 25 mL of DME: yield 1.77 g (54%) of brownish crystals (toluene); $[\alpha]^{22}_D$ = +157.8° (c = 0.995, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.76 (s, 3 H), 0.91 (s, 3 H), 0.97 (s, 3 H), 1.45–1.63 (m, 2 H), 1.72–1.86 (m, 1 H), 2.06–2.24 (m, 1 H), 2.70 (br d, J = 5, 1 H), 7.86 (br s, 1 H), 8.03 (br s, 2 H), 12.29 (br s, 1 H), enol form; MS m/z 393, 392 (M^+), 377, 364, 349, 348, 242, 241, 213. Anal. Calcd for $C_{19}H_{18}F_6O_2$: C, 58.17; H, 4.63; F, 29.06. Found: C, 58.42; H, 4.63; F, 29.05.

(+)-Bis(3-(heptafluorobutyryl)camphorato)oxovanadium(IV) ((+)-5a). This procedure is illustrative of method A (see Scheme I). To a solution of 2.45 g (9.68 mmol) of $VOSO_4 \cdot 5H_2O$ in 15 mL of H_2O was added 6.80 g (19.53 mmol) of (+)-**2a**, dissolved in 15 mL of EtOH. After the mixture was stirred for 0.5 h at room temperature, a green oil separated. NEt_3 (2.7 mL) was added dropwise, and stirring was continued for 15 min. The mixture was then diluted with 50 mL of H_2O, and the product was extracted with pentane (2 × 100 mL). The brown-green organic phase was washed with H_2O (3 × 100 mL). Upon concentration in vacuo and cooling to 0 °C, the product precipitated as a microcrystalline, dark brown material. This was filtered off, washed with a small amount of cold pentane, and dried in vacuo; yield 2.99 g (41%). Further concentration of the mother liquor afforded an oily material that did not crystallize. Anal. Calcd for $C_{28}H_{28}F_{14}O_5V$: C, 44.17; H, 3.71; F, 34.93. Found: C, 44.33; H, 3.64; F, 35.18.

(+)-Bis(3-(trifluoroacetyl)camphorato)oxovanadium(IV) ((+)-5b). This complex was prepared analogously to (+)-**5a**, by starting from 2.91 g (11.5 mmol) of $VOSO_4 \cdot 5H_2O$ and 5.95 g (23.9 mmol) of (+)-**2b**; yield 2.70 g (42%). Anal. Calcd for $C_{24}H_{28}F_6O_5V$: C, 51.35; H, 5.03; F, 20.30. Found: C, 51.34; H, 5.64; F, 19.97.

(+)-Bis(3-benzoylcamphorato)oxovanadium(IV) ((+)-5c). This complex was prepared analogously to (+)-**5a**, by starting from 1.01 g (4.0 mmol) of $VOSO_4 \cdot 5H_2O$ and 1.76 g (6.87 mmol) of (+)-**2c**; yield 0.99 g (50%). Anal. Calcd for $C_{34}H_{38}O_5V$: C, 70.70; H, 6.63. Found: C, 71.01; H, 6.77.

(−)-Bis(3-(heptafluorobutyryl)camphorato)oxovanadium ((−)-5a). This procedure is illustrative of method B (see Scheme I). A mixture of 4.88 g (14.0 mmol) of (−)-**2a** and 1.86 g (7.0 mmol) of **4** in 60 mL of toluene was refluxed for 18 h, giving a dark brown homogeneous solution. The solvent was evaporated under reduced pressure at 80–90 °C, leaving a viscous oily residue. The latter was taken up in 25 mL of pentane, and the solution was cooled to 0 °C. The product precipitated as a microcrystalline material, which was filtered off, washed with cold pentane, and dried in vacuo; yield 2.32 g (44%). Anal. Calcd for $C_{28}H_{28}F_{14}O_5V$: C, 44.17; H, 3.71; F, 34.93. Found: C, 44.55; H, 4.01; F, 34.45.

(+)-Bis(3-(4-(trifluoromethyl)benzoyl)camphorato)oxovanadium(IV) ((+)-5d). This complex was obtained analogously, by starting from 417 mg (1.57 mmol) of **4** and 1.019 g (3.14 mmol) of (+)-**2d** in 15 mL of mesitylene at 180 °C for 2 h; yield 1.09 g (97%). Anal. Calcd for $C_{36}H_{36}F_6O_5V$: C, 60.59; H, 5.09; F, 15.97. Found: C, 60.61; H, 5.42; F, 15.73.

(+)-Bis(3-(3,5-bis(trifluoromethyl)benzoyl)camphorato)oxovanadium(IV) ((+)-5e). This complex was obtained analogously, by starting from 170 mg (0.64 mmol) of **4** and 500 mg (1.27 mmol) of (+)-**2e** in 10 mL of mesitylene at 180 °C for 2 h; yield 340 mg (62%). Anal. Calcd for $C_{38}H_{34}F_{12}O_5V$: C, 53.72; H, 4.03; F, 26.83. Found: C, 53.50; H, 4.10; F, 25.95.

General Procedure for the Vanadium(IV)-Catalyzed Hetero Diels–Alder Reaction. The cycloaddition of benzaldehyde with diene **6a** catalyzed by complex **5a** is illustrative of the general methods for all catalytic reactions described in this study. Chemical and optical yields are given in Tables II and III and in Scheme III. All reactions were carried out by external cooling with a dry ice/2-propanol bath (−78 °C), unless otherwise stated. All enantiomerically enriched products were isolated after chromatography as yellowish, oily materials. Spectral data for

(44) Garner, P.; Park, J. M. *Synth. Commun.* **1987**, *17*, 189.
(45) Hook, J. M. *Synth. Commun.* **1984**, *14*, 83.
(46) For a standard procedure, see: Dayazi, S.; Degani, Y. In *The Chemistry of the Carbon-Nitrogen Double Bond*; Patai, S., Ed.; Interscience: New York, 1970.
(47) Albrecht, R.; Kresze, G.; Mlakar, B. *Chem. Ber.* **1964**, *97*, 483.
(48) (a) Frank, H.; Nicholson, G. J.; Bayer, E. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 363. (b) König, W. H.; Benecke, I.; Lucht, N.; Schmidt, E.; Schulze, J.; Sievers, S. *J. Chromatogr.* **1983**, *279*, 555.

pyrones **7a**,[49] **7b**,[11a,21] **7h**,[21] **9a**,[28] **9b**,[27b] and **11**[50] have been previously reported. Spectral and analytical data for new compounds follow the general procedure.

To a deep green solution of 79 mg (0.104 mmol) of **5a** in 5 mL of toluene were successively added 0.21 mL (2.08 mmol) of benzaldehyde (a slight color change to olive green was observed) and 0.44 mL (2.3 mmol) of **6a**. After the reaction mixture was stirred for 15 h, 0.2 mL of TFA in 10 mL of CCl_4 was added and the solution was warmed to room temperature and evaporated under reduced pressure. The dark brown, oily residue was chromatographed on 50 g of silica gel with hexane/diethyl ether (3/2 v/v) as eluent.

3-Acetoxy-6-phenyl-5,6-dihydro-4*H*-pyran-4-one (7c): ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 3 H), 2.66 (dd, J = 3.5, 17, 1 H), 3.07 (dd, J = 15, 17, 1 H), 5.54 (dd, J = 3.5, 15, 1 H), 7.41 (m, 5 H), 7.50 (s, 1 H); MS m/z 232 (M^+), 191, 190, 161, 144, 143, 104. Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.94; H, 5.66.

***cis*-3,5-Dimethyl-6-(2-furyl)-5,6-dihydro-4*H*-pyran-4-one (7d)**: ^{1}H NMR ($CDCl_3$) δ 1.09 (d, J = 6.5, 3 H), 1.70 (d, J = 1, 3 H), 2.88 (dq, J = 5, 7, 1 H), 5.45 (d, J = 5, 1 H), 6.26 (m, 2 H), 7.20 (q, J = 1, 1 H), 7.41 (m, 1 H); MS m/z 192 (M^+), 174, 163, 136, 109, 108, 107. Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.74; H, 6.29. Found: C, 68.73; H, 6.36.

***cis*-3,5-Dimethyl-6-(2-methoxyphenyl)-5,6-dihydro-4*H*-pyran-4-one (7e)**: ^{1}H NMR ($CDCl_3$) δ 0.88 (d, J = 7, 3 H), 1.74 (d, J = 1, 3 H), 2.76 (dq, J = 3, 7, 1 H), 3.80 (s, 3 H), 5.75 (d, J = 3, 1 H), 6.88 (dd, J = 8, 1, 1 H), 7.02 (td, J = 8, 1, 1 H), 7.30 (m, 1 H), 7.39 (q, J = 1, 1 H), 7.50 (m, 1 H). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.64; H, 6.94.

***cis*-3,5-Dimethyl-6-(cyclohexyl)-5,6-dihydro-4*H*-pyran-4-one (7f)**: ^{1}H NMR ($CDCl_3$) δ 0.78-1.00 (m, 2 H), 1.04 (d, J = 7, 3 H), 1.05-1.37 (m, 3 H), 1.53-1.84 (m, 5 H), 1.66 (d, partially overlapping with previous m, J = 1, 3 H), 2.14 (m, 1 H), 2.42 (dq, J = 2, 7, 1 H), 3.88 (dd, J = 2, 10, 1 H), 7.24 (q, J = 1, 1 H); MS m/z 208 (M^+), 190, 179, 165, 125, 124, 112, 95. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.67; H, 9.55.

***cis*-3,5-Dimethyl-6-(methoxycarbonyl)-5,6-dihydro-4*H*-pyran-4-one (7i)**: ^{1}H NMR ($CDCl_3$) δ 1.13 (d, J = 7, 3 H), 1.70 (d, J = 1, 3 H), 2.84 (dq, J = 3.5, 8, 1 H), 3.85 (s, 3 H), 4.95 (d, J = 3.5, 1 H), 7.26 (q, J = 1, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.5, 11.1, 41.9, 52.6, 79.5, 113.4, 157.0, 167.9, 195.0; MS m/z 184 (M^+), 125, 101. Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.46; H, 6.64. Trans isomer: ^{1}H NMR ($CDCl_3$) δ 1.23 (d, J = 7, 3 H), 1.67 (d, J = 1, 3 H), 2.88 (m, 1 H), 3.82 (s, 3 H), 4.66 (d, J = 9, 1 H), 7.23 (q, J = 1, 1 H).

Pyrone 14a: ^{1}H NMR ($CDCl_3$) δ 1.13 (d, J = 7, 3 H), 1.42 (s, 3 H), 1.46 (s, 3 H), 1.67 (d, J = 1, 3 H), 2.30 (dq, J = 3, 7, 1 H), 3.66 (dd, J = 8, 8, 1 H), 4.10 (dd, J = 6, 8, 1 H), 4.28 (dd, J = 3, 8, 1 H), 4.43 (td, J = 6, 8, 1 H), 7.29 (q, J = 1, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.5, 10.6, 25.6, 26.5, 41.6, 65.2, 75.0, 82.7, 110.4, 112.6, 158.6, 196.2; MS m/z 226 (M^+), 211, 169, 141, 126, 111, 101. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.36; H, 7.84.

Pyrone 14b: ^{1}H NMR ($CDCl_3$) δ 1.14 (d, J = 8, 3 H), 1.45 (s, 3 H), 1.40 (s, 3 H), 1.66 (d, J = 1, 3 H), 2.63 (dq, J = 3, 8, 1 H), 4.01 (dd, J = 4, 9, 1 H), 4.11-4.18 (m, 2 H), 4.28 (ddd, J = 4, 6, 9, 1 H), 7.16 (q, J = 1, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.2, 10.6, 25.1, 26.9, 40.9, 67.1, 72.9, 81.7, 109.8, 113.0, 157.9, 197.2. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.99; H, 8.08.

Pyrone 14c: ^{1}H NMR ($CDCl_3$) δ 1.26 (d, J = 7, 3 H), 1.37 (s, 3 H), 1.44 (s, 3 H), 1.67 (d, J = 1, 3 H), 2.56 (dq, J = 7, 9, 1 H), 4.02 (dd, J = 6, 9, 1 H), 4.06-4.15 (m, 2 H), 4.31 (q, J = 6, 1 H), 7.17 (q, J = 1, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.6, 12.4, 25.3, 26.4, 41.5, 66.1, 74.9, 83.3, 110.0, 112.8, 157.4, 194.6. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.56; H, 7.99.

Pyrone 14d: ^{1}H NMR ($CDCl_3$) δ 1.22 (d, J = 8, 3 H), 1.38 (s, 3 H), 1.47 (s, 3 H), 1.67 (d, J = 1, 3 H), 2.74 (dq, J = 8, 12, 1 H), 3.96 (dd, J = 3, 12, 1 H), 4.05 (dd, J = 6, 8, 1 H), 4.09 (dd, J = 6, 8, 1 H), 4.36 (td, J = 3, 6, 1 H), 7.25 (q, J = 1, 1 H); ^{13}C NMR ($CDCl_3$) δ 10.5, 10.6, 25.3, 26.2, 40.9, 64.8, 74.3, 82.6, 109.9, 112.9, 158.1, 195.2. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.30; H, 7.94.

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(49) Danishefsky, S.; Kerwin, J. F., Jr.; Kobayashi, S. *J. Am. Chem. Soc.* **1982**, *104*, 358.

(50) Danishefsky, S.; Harvey, D. F.; Quallich, G.; Uang, B. J. *J. Org. Chem.* **1984**, *49*, 393.

(51) Note Added in Proof: After the submission of this paper, we succeeded in growing crystals of complex **5a** suitable for X-ray diffraction. This was done by slow evaporation of a CH_2Cl_2 solution. **5a** was found to be *trimeric* in the solid state, with the oxo ligands in bridging positions and with a cis arrangement at each distorted-octahedral V(IV) center. According to Sloan (Sloan, T. E. *Top. Stereochem.* **1981**, *12*, 1) the observed absolute configuration at vanadium is [*OC*-6-33-Δ]. In contrast, **5a** was found to be *monomeric* in toluene or CH_2Cl_2 solution. Thus, the geometry of the complex in solution still remains unknown. The results of our structural studies will be reported at a later date.

Intramolecular Cyclopropanation Reactions of Chromium (Alkenyloxy)carbene Complexes

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Chromium (aryl)(alkenyloxy)carbene complexes underwent intramolecular cyclopropanation reactions under mild conditions. Evidence for the intervention of metathesis/readdition and for "twist" addition followed by β-hydride elimination/reductive elimination was obtained. Carbenes of this class, sufficiently stable to isolate, underwent facile photochemical intramolecular cyclobutanone formation.

Introduction

The thermal reaction of heteroatom-stabilized Fischer carbene complexes with electron-rich and electron-poor olefins to produce cyclopropanes was one of the earliest synthetically significant reactions of this class of complexes developed (eq 1).[1] The intermolecular version usually

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