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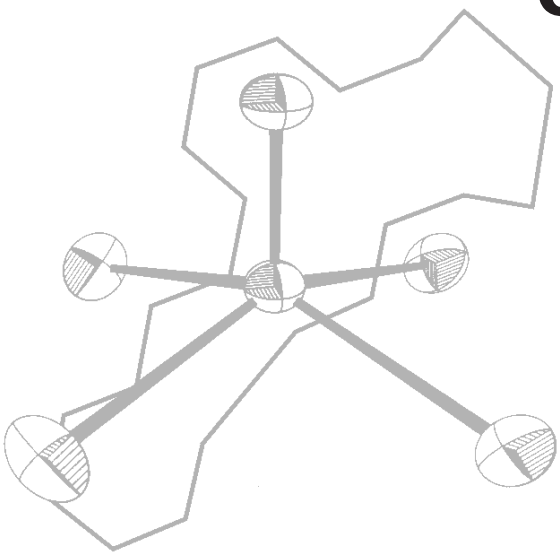

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Experiments Directed Towards the Synthesis of Anthracyclinones. XXXIV* Hetero-Diels–Alder Reactions Using Chiral Boron and Titanium Reagents

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Reactions between benzaldehyde or *o*-anisaldehyde and a series of silyloxy dienes catalysed by the chiral acyloxyborane (CAB) complex (4) give high yields of enantioselective products from a Mukaiyama aldol rather than a hetero-Diels–Alder reaction. Attempts to effect a similar catalytic reaction with anthraquinone aldehydes were unsuccessful but use of 2 equiv. of the CAB complex (1) followed by cyclization promotes a formal hetero-Diels–Alder reaction between the aldehyde (7) and the diene (12) to give the dihydropyrone (24) in 45% yield and with a 79% e.e. in favour of the 2′*R* enantiomer.

Hetero-Diels–Alder reactions between the aldehyde (7) and the diene (12) using the chiral titanium complexes Ti[(*R*)-BINOL]Cl_2, Ti[(*R*,*R*)-TADDOL]Cl_2 and Ti[(*R*)-BINOL]$_2$ have been investigated. The first two complexes promote the reaction at –30 and –78° respectively but with low induced enantioselectivities.

Introduction

In the previous paper[1] in this series we established that in many respects Togni's catalyst, (+)-bis[3-(heptafluorobutyryl)camphorato]vanadium(IV) [(+)-VO(hfc)$_2$],[2] was an effective catalyst for hetero-Diels–Alder reactions between several anthraquinone aldehydes and a variety of silyloxy dienes. However, the enantioselectivities of these reactions were smaller than those observed by Togni for simple aldehydes such as benzaldehyde. In a search for greater enantioselectivities the potential of several members of the chiral acyloxyborane (CAB) class of Lewis acids as catalysts for hetero-Diels–Alder reactions has also been examined. In addition, a brief investigation of the potential of three chiral titanium Lewis acids as hetero-Diels–Alder catalysts has been undertaken.

Yamamoto has demonstrated the potential of tartrate-derived chiral acyloxyboranes, such as (1)–(5), to serve as highly efficient enantioselective catalysts for a variety of Lewis acid mediated processes including the Diels–Alder,[3–7] Mukaiyama aldol,[8,9] Sakurai–Hosomi,[10,11] and hetero-Diels–Alder[12,13] reactions. The potential of CAB catalysis for a hetero-Diels–Alder reaction between the keto aldehyde (6) and the diene (9) was recognized by us in 1992.[14] In a brief investigation, a solution of (6), (9), and the CAB (1) (0.1 equiv.) in dichloromethane was stirred at –78° for 18 h. However, this resulted only in recovery (89%) of the keto aldehyde (6), while a similar reaction employing (1) (2.5 equiv.) afforded the hydroxy ketone (13) (63%) with an e.e. of 60% (Scheme 1). It was assumed that (13) arose from a Mukaiyama aldol-like reaction and the failure to observe any reaction with catalytic quantities of the CAB complex was rationalized by assuming that coordination of the complex to other basic sites of the anthraquinone molecule, such as the oxygens of the quinone carbonyl and the *peri* methoxy groups, was inhibiting the desired reaction between the C2 formyl group of (6) and the diene (9).

Subsequent to our initial investigations, Yamamoto reported the successful catalysis of hetero-Diels–Alder reactions between simple aldehydes and dienes using CAB complexes.[12,13] Yamamoto's procedure involved stirring a solution of the aldehyde, an excess of a diene, and 10 mole % of a CAB catalyst in propionitrile at –78° for 4–9 h, followed by workup and treatment of the crude reaction product with trifluoroacetic acid, with no attempt to isolate or characterize the initial adducts. The enantioselectivity of a reaction was dependent on both the aldehyde used and the nature of the substituent on the CAB catalyst. The best results were obtained with aromatic aldehydes, and with CAB complexes such as (5) with bulky groups attached to boron which generally led to higher enantioselectivities, but the yield of a product tended to decrease as the bulk of this group was increased. The reactions all favoured formation of a dihydropyrone with an *R* configuration at C2′, which was con-

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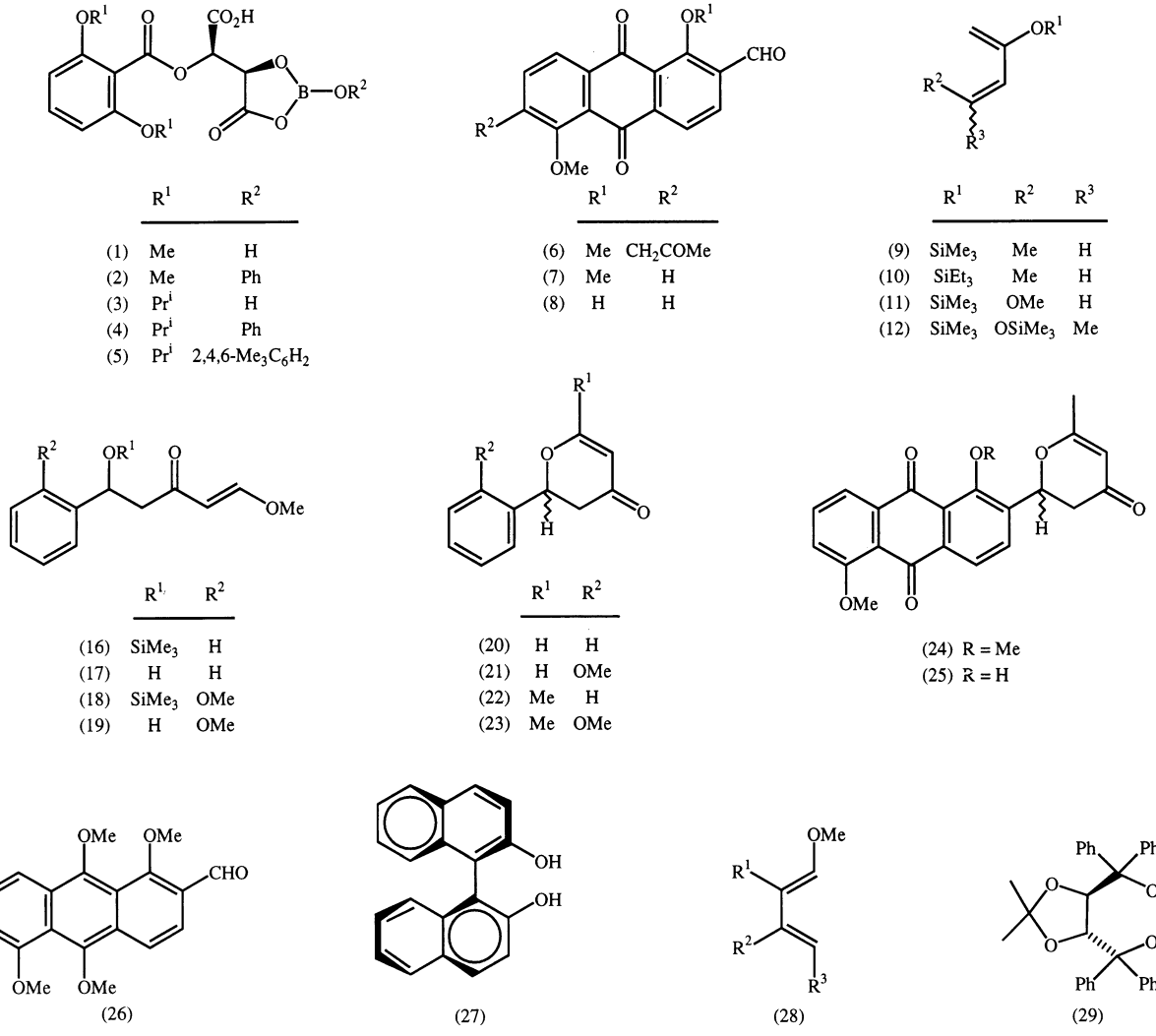
sistent with attack of the diene at the *re* face of the aldehyde carbonyl group, and implied a shielding of the *si* face by the catalyst. This observation was consistent with the enantiofacial selectivities in CAB catalysed Diels–Alder, Mukaiyama aldol, ene, and Sakurai–Hosomi reactions in which delivery of the nucleophile to the *re* face of the electrophile was also strongly favoured. To account for this *re* face selectivity, Yamamoto proposed the transition state assembly shown in Fig. 1. This model proposes coordination of the CAB catalyst by the lone pair of electrons on the carbonyl oxygen that is *anti* to the phenyl ring, and that π-stacking of the aryl rings of the catalyst and the substrate favours a transition state where the *si* face of the aldehyde is strongly shielded by the 2,6-diisopropoxybenzoyl moiety, forcing the diene to attack the less congested *re* face of the carbonyl group. Recently, however, an alternative model for explaining the enantiofacial selectivity of reactions mediated by chiral boron Lewis acids has been proposed by Corey,[15-17] who notes that complexes of formyl compounds with B–F or B–O containing Lewis acids show a conformational preference for an eclipsed geometry in which the formyl group and a B–F or B–O bond are coplanar (Fig. 2).[15] This preference, which results from a novel type of hydrogen bond between the aldehydic proton and either an oxygen or fluorine atom on boron, is supported by X-ray crystallographic studies of several complexes of formyl compounds with boron Lewis acids. Corey[16,17] has used his hypothesis to postulate that the favoured mode of coordination of benzaldehyde to the (*R,R*)-tartrate-derived CAB complexes (3)–(5) is that which allows a bifurcated hydrogen bond between the aldehydic proton



Scheme 1. CAB catalysed reaction of (6) and (9).

(2) Me Ph
(7) Me H
(10) SiEt$_3$ Me H

and the oxygens corresponding to the carbonyl oxygen of the C1 carboxy group and the C3 alcohol oxygen of the ligand of (3)–(5) (Fig. 3*a*). This mode of coordination in combination with a favourable π-stacking interaction between the aromatic rings of benzaldehyde and the 2,6-diisopropoxybenzoyl moiety on the ligand results in strong shielding of the *si* face of the benzaldehyde carbonyl group. Nucleophilic attack at the less hindered *re* face of this carbonyl group is therefore favoured by this arrangement. Corey argues that the alternative mode of coordination of benzaldehyde to (3)–(5) (Fig. 3*b*), in which the π-stacking interactions between the 2,6-diisopropoxybenzoyl moiety of the ligand and benzaldehyde would result in shielding of the *re* face of the aldehyde carbonyl group, is somewhat less favoured as this arrangement would allow only a single hydrogen bond between the aldehydic proton and a somewhat less basic carboxylate oxygen.

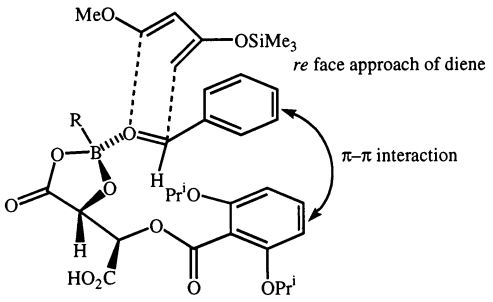


Fig. 1. Yamamoto's proposed transition state assembly.

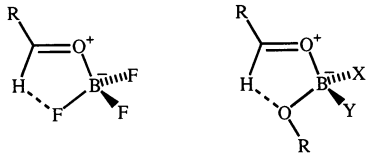


Fig. 2. Corey's formyl C---H---O hydrogen bond postulate.

Publication of Yamamoto's results, which suggested that CAB complexes bearing alkyl or aryl substituents directly attached to boron are efficient catalysts for the hetero-Diels–Alder reaction of simple aldehydes and dienes under mild conditions, prompted our renewed investigations.

Discussion

Chiral Acyloxyborane Complexes

Attempted hetero-Diels–Alder reactions of the keto aldehyde (6) and the diene (10) using the CAB catalyst (4) (0.5 or 1 equiv.) and following Yamamoto's procedure[13] were unsuccessful, returning only the starting keto aldehyde (6) after 24 h. Use of 2 equiv. of the CAB complex afforded the hydroxy ketone (13) (10%) along with recovered (6) (82%). The specific rotation of (13) was only –1.1° (cf. $[\alpha]_D$ –41.5° equivalent to 60% e.e. for the earlier reaction[14]) indicating that this reaction proceeded with a very small degree of enantioselection.

Further investigations were made to determine if the limited degree of reactivity, and the favouring of a Mukaiyama aldol-like reaction pathway, were a consequence of the structure of the anthraquinone aldehyde or of the dienes (9) and (10) which lack a C1 alkoxy substituent, or were due to a combination of these factors. Reaction of benzaldehyde and the diene (10) with the CAB complex (4) (0.25 equiv.) in propionitrile at –78° for 7 h and then warming to room temperature over 12 h afforded the triethylsilyl ether (14) (34%) and the hydroxy ketone (15) (58%). Formation of each of these products can be attributed to the operation of a Mukaiyama aldol-like reaction pathway. Presumably, transfer of the triethylsilyl group from the C2 oxygen of the diene to the C1 oxygen of the aldehyde occurs via a six-membered transition state (Scheme 2). The alcohol (15) could arise either from loss of the triethylsilyl group from (14) or from a nucleophilic displacement of this group during the Mukaiyama aldol reaction. However, the nature of the nucleophile responsible for this displacement is not clear.

A high-resolution mass spectrum of the ether (14) contained an ion at *m/z* 304.1856 consistent with the molecular formula $C_{18}H_{28}O_2Si$. The i.r. spectrum contained a band at 1670 cm^{-1} attributable to an α,β-unsaturated ketone carbonyl, but lacked any absorbance due to a hydroxy group. The ^1H n.m.r. spectrum contained a six-proton quartet at δ 0.48 and a nine-proton triplet at 0.83 indicative of the presence of a triethylsilyl group, as well as a five-proton multiplet centred at 7.29 corresponding to the protons of the aromatic ring. A spin system consisting of one-proton doublets of doublets at δ 2.62 and 3.09 corresponding to the diastereotopic methylene protons at C2, and a one-proton doublet of doublets at 5.22 corresponding to the benzylic proton at C1, along with a second spin system consisting of

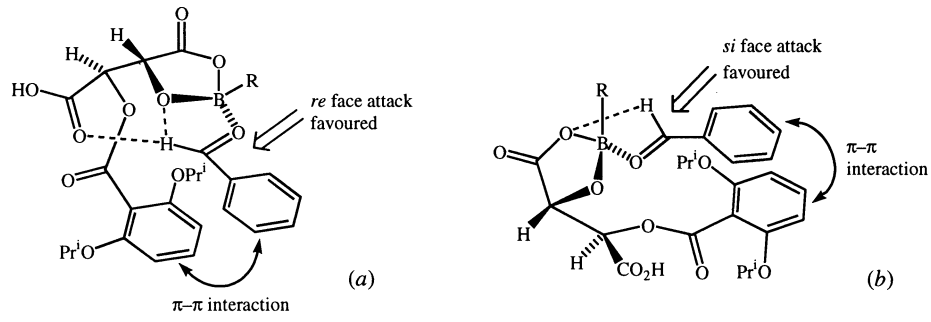
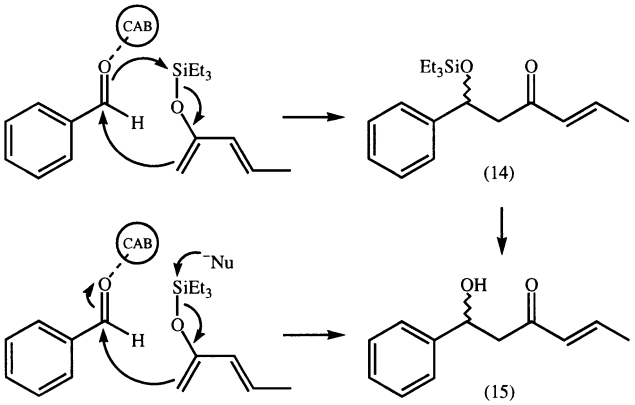


Fig. 3. Corey's proposed CAB–aldehyde transition state assemblies.

a three-proton doublet of doublets at 1.87 corresponding to the C6 methyl group, was only consistent with the triethylsilyloxy group being located at C1 and the carbonyl group at C3. A coupling constant of 15.8 Hz between the olefinic protons indicated an *E* geometry for the double bond. The ^{13}C n.m.r. spectrum contained the expected 12 resonances and included signals at δ 4.7 and 6.6 corresponding to the carbons of the triethylsilyl group, a signal at 198.1 corresponding to the C3 ketone carbon, as well as resonances for the aromatic carbons and the rest of the hex-4-en-3-one side chain.



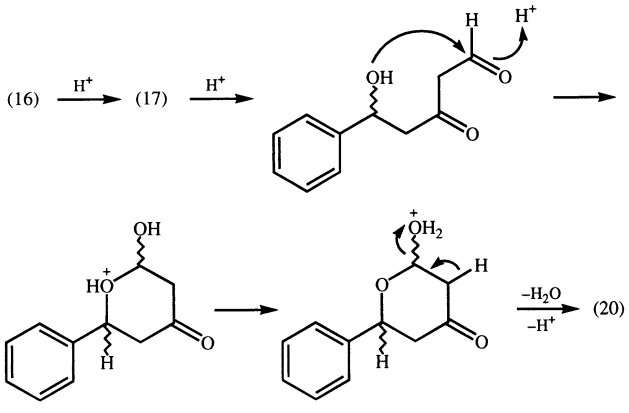
Scheme 2. Formation of (14) and (15) via a Mukaiyama aldol reaction.

A high-resolution mass spectrum for the alcohol (15) contained a molecular ion at *m/z* 190.0993 consistent with the molecular formula $C_{12}H_{14}O_2$. The i.r. spectrum contained strong bands at 3448 and 1654 cm^{-1} commensurate with the presence of alcohol and α,β-unsaturated ketone carbonyl functions. The ^1H n.m.r. spectrum contained a five-proton multiplet centred at δ 7.30 corresponding to the protons of the aromatic ring, and a broad one-proton singlet at 3.68 which exchanged with deuterium oxide, confirming the presence of a hydroxy group. The remaining signals in the spectrum were consistent with an (*E*)-1-hydroxy-hex-4-en-3-one side chain on the aromatic ring. The ^{13}C n.m.r. spectrum contained the expected 10 resonances including one at δ 200.1 attributable to the C3 ketone carbon.

The reaction between benzaldehyde and the diene (10) was clearly catalysed by the CAB (4) as it gave a 92% combined yield of (14) and (15), which indicated that for complex aldehyde substrates, such as anthraquinones that possess other Lewis-basic sites, it may be difficult to achieve a catalytic reaction with CAB complexes. The specific rotations of the products (14) and (15) were +64 and +60.7° respectively, indicating some degree of enantioselection. It was also clear that CAB catalysed or promoted reactions involving benzaldehyde or anthraquinone aldehydes and the diene (10) favoured the initial formation of Mukaiyama aldol products rather than the desired hetero-Diels–Alder cycloadducts. In contrast to the dienes used by Yamamoto, the diene (10) lacks a C1 alkoxy group and it was considered that this structural difference may account for the difference in reaction pathway. However, since Yamamoto never isolated any cycloadducts from his reported hetero-Diels–Alder reactions it is possible that these also gave Mukaiyama aldol products which were converted into the formal cycloaddition products by treatment of the crude reaction mixtures with trifluoroacetic acid.

In an attempt to decide between these two possibilities the CAB catalysed reaction between benzaldehyde and the diene (11) was investigated. This afforded the trimethylsilyl ether (16) (13%) and the alcohol (17) (56%), the structures of which were assigned by comparison with those of (14) and (15). This result demonstrated that the reaction favoured a Mukaiyama aldol-like reaction pathway rather than a pericyclic pathway, and that the formation of the dihydropyrone (20) reported by Yamamoto from this reaction was formed as a result of the acidic workup. This was verified when treatment of each of the compounds (16) and (17) with trifluoroacetic acid afforded the dihydropyrone (20) in high (94–98%) yield. In each case the dihydropyrone had a specific rotation of –89° which, when compared with that of the pure *R* enantiomer of (20)[13] corresponded to a 74% e.e. in favour of the *R* enantiomer and agreed well with the 75% e.e. reported by Yamamoto for his overall reaction. The enantiopurity of the alcohol (17) was also determined by using a chiral solvating agent—^1H n.m.r. methodology similar to that employed for measuring the enantiopurity of products from hetero-Diels–Alder reactions of 1-methoxyanthraquinone aldehydes.[1] However, in the case of (17) it was the C5 methoxy protons that were observed to be anisochronous in the presence of (*S*)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol (TFAE). A best separation (5.5 Hz) of the resonances due to these protons was obtained in the presence of 5 equiv. of (*S*)-(+)-TFAE, and integration of these signals also revealed an enantiomeric excess of 74%. The sense of the anisochrony created in the resonances of the C5 methoxy group of (17) was opposite to that observed for the resonances of the C5 methoxy groups of the anthraquinone hetero-Diels–Alder adducts with the resonance of the major *R* enantiomer being shifted downfield relative to that of the minor *S* enantiomer.

The acid-catalysed cyclizations of (16) and (17) to the dihydropyrone (20) presumably occur via processes similar to those outlined in Scheme 3.[18–20] Cleavage of the



Scheme 3. A mechanism for the cyclization of (16) and (17).

trimethylsilyl ether group of (16) would give the alcohol (17), the enol ether group of which could undergo facile acid cleavage to generate a hydroxy dicarbonyl compound. This could then undergo an intramolecular cyclization to give a β-hydroxy ketone which, under the acidic conditions, would readily eliminate water to give dihydropyrone (20). These pathways would preserve the stereochemistry at C 1 of (16) and (17) generated via the asymmetric CAB catalysed Mukaiyama aldol reaction.

The present results have important implications for the use of CAB complexes as catalysts in the asymmetric synthesis of olivose *C*-glycosides. As the CAB catalysed reaction favours an initial Mukaiyama aldol pathway rather than a pericyclic hetero-Diels–Alder route there is no cycloadduct that can be elaborated via hydroboration in the manner of Danishefsky to generate the olivose sugar.[21] Furthermore, the Mukaiyama aldol products from reactions involving dienes such as (10), which lack a C 1 oxygen, cannot be readily cyclized to the corresponding dihydropyrone. This limits the utility of CAB catalysts to reactions involving dienes with both the C 1 functionality necessary for cyclization to the dihydropyrone and a C 1 methyl group required to generate the olivose sugar.

Attempts were next made to establish why a catalytic reaction with anthraquinone aldehydes could not be achieved. It was considered that the methoxy group *ortho* to the formyl group in the keto aldehyde (6) may interact unfavourably with the CAB complex and prevent a catalytic reaction, and thus it was of interest to determine if a CAB catalysed reaction of *o*-anisaldehyde and the diene (11) could be achieved. In the event, reaction afforded the trimethylsilyl ether (18) (11%), the alcohol (19) (59%), and starting aldehyde (21%). The combined yield (70%) of the two Mukaiyama aldol products (18) and (19) showed that the presence of an *o*-methoxy group in the anthraquinone (6) may not be an important factor in preventing a CAB catalysed reaction between the substrate and the diene (10). Compounds (18) and (19) were each optically active and the enantiopurity of the alcohol (19) was readily determined from a ^{1}H n.m.r. spectrum in (D_6)benzene in the presence of (*R*)-(–)-TFAE, the addition of which induced detectable anisochrony in the signals of the C 5 and C 2′ methoxy groups which appeared in regions of the spectrum free from overlap with other signals. However, integration revealed an enantiomeric excess of only 5% in favour of the *R* enantiomer. No useful anisochrony was observed in the ^{1}H n.m.r. spectra of the ether (18) in the presence of (*R*)-(–)-TFAE following the sequential addition of up to 10 equivalents. Compounds (18) and (19) each cyclized to the dihydropyrone (21) in high yield (91–94%) when treated with trifluoroacetic acid. The specific rotations of the dihydropyrone (21) derived from the alcohol (19) and the trimethylsilyl ether (18) were –3.8 and –3.5° respectively, indicating that, within the limits of error, (18) and (19) were of similar enantiopurity.

Reaction of benzaldehyde with the diene (12) and 20 mole % of the CAB complex (4) followed by acid workup gave the dihydropyrone (22) (62%). No attempt was made to isolate the aldol products of this reaction since t.l.c. prior to acid workup indicated the formation of a multiplicity of products. The dihydropyrone (22) had a specific rotation of –52.2° revealing that the reaction proceeded with some degree of enantioselection. However, the lack of a methoxy group on (22) precluded use of the usual chiral solvating agent—^{1}H n.m.r. protocols to establish the enantiopurity of this compound. Togni[2] has obtained the same dihydropyrone (22) in 18% e.e. in favour of the (*R*)-(–) enantiomer from the (+)-$VO(hfc)_2$ catalysed hetero-Diels–Alder reaction of benzaldehyde and (12) but did not report the magnitude of the specific rotation. However, the observation of a negative sign of rotation in both cases indicates that the CAB catalysed reaction also favoured formation of the *R* enantiomer.

Reaction of *o*-anisaldehyde with the diene (12) was investigated to ascertain what effect the presence of an *ortho* methoxy group would have on the yield and enantioselectivity of the reaction. The reaction, catalysed by 20 mole % of the CAB complex (4) followed by acid workup, gave only 31% of the dihydropyrone (23) along with starting aldehyde (54%). The specific rotation of (23) was +4° which corresponded with a 7% e.e. for the reaction as determined by ^{1}H n.m.r. in the presence of (*S*)-(+)-TFAE. The reasons for reduced reactivity and enantioselectivity in reactions involving *o*-anisaldehyde are not clear, but they may result from a specific interaction between the *o*-methoxy group and the catalyst in the activated complex, or may simply be the result of increased steric congestion about the boron centre forcing the CAB–aldehyde complex to adopt a conformation in which the energy differential for attack of the diene at the prochiral faces of the aldehyde is smaller.

Attempts to achieve a CAB promoted reaction between the anthraquinone aldehyde (7) and the diene (12) at 0° or room temperature using the CAB complexes (1), (2), (3), or (4) were largely unsuccessful, with all returning high yields of starting material. A significant reaction was achieved only with the least sterically demanding CAB complex (1) and only when 2 equiv. of the complex were present. This reaction afforded the dihydropyrone (24)[1] (45%) with a 79% e.e. in favour of the *R* enantiomer. This result parallels that of the reaction between the keto aldehyde (6) and diene (9) in the presence of the same CAB complex (2.5 equiv.), which afforded a 63% yield of the product (13) in 60% e.e. The failure to observe any reaction between (7) and (12) when the analogous CAB complex (3) (2.5 equiv.) was used indicates that the extra steric bulk arising from replacement of the methoxy groups of (1) with isopropoxy groups is sufficient to inhibit reaction. This suggests that steric congestion about the formyl group in the aldehyde–CAB complex may be one of the factors responsible for the poor reactivity of anthraquinone aldehydes. It is also possible that the conformation of the anthraquinone aldehyde–CAB complexes differs from that postulated for complexes between CABs and simple aromatic aldehydes because of interactions between Lewis basic sites on the anthraquinone molecule and sites on the CAB such as the boron atom or the free carboxy group of the ligand. The observation that 1.1 equiv. of the CAB (1) was insufficient to promote any reaction indicates that reactions were occurring between this CAB and the aldehyde (7) at sites

other than the formyl group. It could also be expected that π–π interactions between the aromatic ring of the CAB ligand and the relatively electron-deficient aromatic rings of the anthraquinone would differ significantly in strength from the equivalent interactions proposed by Yamamoto and Corey for benzaldehyde–CAB complexes.

Reaction of the anthracene aldehyde (26) with the diene (12) in the presence of the CAB complex (4) was investigated in the hope that using a more electron-rich aldehyde, in which the quinone carbonyls had been masked as their methyl ethers, would result in greater reactivity than with the equivalent aldehyde (7). However, no reaction was observed with either 0.5 or 2.5 equiv. of the CAB complex (4) at 0° in propionitrile for 19 h.

Chiral Titanium Complexes

The use of chiral titanium complexes to catalyse or promote hetero-Diels–Alder reactions between aldehydes and silyloxy dienes has received little attention, despite the pioneering work of Danishefsky,[22,23] which showed that simple titanium Lewis acids such as titanium(IV) chloride are efficient catalysts of such reactions. Two reports have appeared which suggest that chiral titanium(IV) complexes have potential for the catalysis of enantioselective hetero-Diels–Alder reactions. Mikami[24] has demonstrated that 10 mole % of the complex Ti[(*R*)-BINOL]Cl_2, derived from the reaction of (*R*)-BINOL (27) (1 equiv.) and bis(chloro)bis(isopropoxy)titanium(IV), catalyses the reaction between methyl glyoxylate and dienes of the type (28) (R^1,R^2,R^3 = H or OMe) in dichloromethane at –30° to afford predominantly the *cis* cycloadducts indicative of the operation of an *endo*-selective pericyclic reaction. The enantioselectivities were typically greater than 90%, and reaction favoured formation of adducts having a 2′*R* configuration. Recently, Keck has reported that 10% of a complex derived from titanium(IV) tetraisopropoxide and BINOL (2 equiv.) catalyses the reaction between a variety of aldehydes and the diene (11) in dichloromethane at –20°.[25] The degree of enantioselection was dependent on the nature of the aldehyde although the reaction with benzaldehyde proceeded with lower enantioselectivity than reactions employing aliphatic aldehydes. Keck assumed, on the basis of previous studies which showed that this complex catalyses Mukaiyama aldol reactions, that these formal hetero-Diels–Alder reactions involved an aldol reaction followed by an acid-catalysed cyclization.

In the present study reaction of the aldehyde (7) with an excess of the diene (12) and Ti[(*R*)-BINOL]Cl_2 (1.5 equiv.) at –30° for 40 h followed by addition of trifluoroacetic acid afforded the dihydropyrone (24) (68%) along with starting aldehyde (20%). The specific rotation of (24) was +6.4° which corresponded to an enantiomeric excess of 26% in favour of the *R* enantiomer based on the use of ^{1}H n.m.r. spectroscopy in the presence of (*S*)-(+)-TFAE. A similar sequence using the titanium complex (1 equiv.) at –78° for 24 h and then at room temperature for 24 h gave only 28% of the dihydropyrone (24) with an e.e. of 31%, along with starting aldehyde (69%). While these two reactions demonstrated that Ti[(*R*)-BINOL]Cl_2 promoted a formal hetero-Diels–Alder reaction between (7) and (12) the combination of slow reaction rates at low temperatures and poor enantioselectivity indicated that the development of a synthetically useful catalytic reaction was unlikely.

The complex Ti[(*R,R*)-TADDOL]Cl_2 (1.2 equiv.), prepared from (*R,R*)-TADDOL (29),[26] also promoted the reaction between (7) and an excess of (12). Reactions employing this complex proceeded more readily at low temperature (–30 or –78° for *c*. 24 h) with the same facial selectivity but with lower enantioselectivities (17–20%) than the analogous reactions with Ti[(*R*)-BINOL]Cl_2. Like most Ti[BINOL]Cl_2 catalysed reactions[24] the enantioselectivity of Ti[TADDOL]Cl_2 reactions increased (28%) when the reaction was carried out in the absence of 4 Å molecular sieves used in the preparation of the complex. Reaction of the phenolic anthraquinone aldehyde (8) and the diene (12) in the presence of Ti[(*R,R*)-TADDOL]Cl_2 was also attempted since it was envisaged that chelation of the titanium complex by the formyl group and the *ortho* phenolic oxygen of (8) might alter both the enantioselectivity and facial selectivity of the hetero-Diels–Alder reaction. In the event, reaction with Ti[(*R,R*)-TADDOL]Cl_2 (2 equiv.) in the absence of molecular sieves at –78° for 24 h followed by addition of trifluoroacetic acid afforded the dihydropyrone (25) (82%). The specific rotation of (25) was –26.7°, and in order to assess the degree of enantioselectivity the phenolic group of (25) was methylated to give the dihydropyrone (24) (95%). The specific rotation of (24) was –3.8° which is opposite in sign to that observed previously for this compound resulting from the Ti[(*R,R*)-TADDOL]Cl_2 promoted reaction of the dimethoxy aldehyde (7) and the diene (12). Confirmation of this reversal of enantiofacial selectivity was provided by a reversal in the sense of anisochrony observed in the ^{1}H n.m.r. spectrum of this sample of (24) in the presence of (*S*)-(+)-TFAE. The enantiofacial selectivity of the formal hetero-Diels–Alder reaction was only 15% in favour of (*S*)-(25). The change in enantiofacial selectivity from attack of the diene at the *re* face of the aldehyde (7) to one of attack at the *si* face is considered to result from chelation of the Ti[(*R,R*)-TADDOL]Cl_2 to the phenolic and C2 formyl groups of (8).

Finally, several attempts were made to achieve a reaction between (7) and (12) by using the Ti[(*R*)-BINOL]$_2$ complex of Keck,[25] but use of 0.5, 1.2, and 2 equiv. of this complex returned only the starting aldehyde.

Experimental

For general experimental details see ref. 27.

CAB Promoted Reaction of 2-Formyl-1,5-dimethoxy-6-(2′-oxopropyl)anthraquinone (6) and 2-[(Triethylsilyl)oxy]penta-1,3-diene (10)

A solution of the keto aldehyde (6) (25 mg, 0.07 mmol) in propionitrile (4 ml) was added to a stirred solution of mono(2,6-diisopropoxybenzoyl)tartaric acid [CAB (4)][13] (58 mg, 0.16 mmol) and phenylboronic acid (19 mg, 0.07 mmol) in propionitrile (2 ml) under nitrogen, at room temperature. The mixture was stirred for 10 min, the diene (10) (31 mg, 0.16 mmol) was added and the mixture was stirred at room temperature for 24 h, poured into saturated aqueous sodium hydrogencarbonate (20 ml), and extracted with CH_2Cl_2. The extracts were washed with sat-

urated aqueous sodium hydrogencarbonate, and water, dried, and the solvent was removed under reduced pressure. P.l.c. of the residue gave starting material (20 mg, 82%) and (E)-*1-[1′,5′-dimethoxy-6′-(2″-oxopropyl)anthraquinon-2′-yl]-1-hydroxy-hex-4-en-3-one* (13) (3 mg, 10%) as an orange solid, m.p. 152–154°, $[\alpha]_D$ –1.1° (*c*, 0.29 in $CHCl_3$) (Found $M^{+\bullet}$, 436.1511. $C_{25}H_{42}O_7$ requires $M^{+\bullet}$, 436.1522). λ_{max} 236 (log ε 4.88), 261 (4.97), 345 (4.73). ν_{max} 3448br (OH), 2925, 1718 (CO), 1670 (quinone CO), 1384, 1260, 1076 cm^{-1}. δ_H 1.91, dd, $J_{6,5}$ 6.9, $J_{6,4}$ 1.6 Hz, H6; 2.29, s, H3″; 2.75, dd, $J_{2a,2b}$ 17.6, $J_{2a,1}$ 9.4 Hz, H2a; 3.24, dd, $J_{2b,2a}$ 17.6, $J_{2b,1}$ 2.3 Hz, H2b; 3.26, d, $J_{1a'',1b''}$ 16.5 Hz, H1a″; 3.32, d, $J_{1b'',1a''}$ 16.5 Hz, H1b″; 3.67, s, 1′-OCH_3; 3.70, s, 5′-OCH_3; 5.53, unresolved dd, $J_{1,2a}$ 9.4 Hz, H1; 6.16, dd, $J_{4,5}$ 15.8, $J_{4,6}$ 1.6 Hz, H4; 6.91, dq, $J_{5,4}$ 15.8, $J_{5,6}$ 5.9 Hz, H5; 7.56, d, $J_{7',8'}$ 7.9 Hz, H7′; 8.03, d, $J_{3',4'}$ 8.1 Hz, H 3′; 8.06, d, $J_{8',7'}$ 7.9 Hz, H8′; 8.12, d, $J_{4',3'}$ 8.1 Hz, H4′. *m/z* 436 (M), 418 (M–H_2O), 352, 310, 295, 267, 165, 69, 43.

A similar reaction using CH_2Cl_2 instead of propionitrile as solvent returned starting material (98%).

In an earlier (1992) experiment[14] the keto aldehyde (6) (20 mg, 0.06 mmol) in CH_2Cl_2 (1 ml) and the diene (9) (39 mg, 0.25 mmol) were added to a stirred solution of diborane (0.16 mmol) in tetrahydrofuran (1 ml) and the tartrate precursor of the CAB (1) (50 mg, 0.15 mmol) in CH_2Cl_2 (1 ml) under argon at –78°. The mixture was stirred for 18 h and worked up as above to give (6) (2 mg, 12%) and (13) (17 mg, 63%), $[\alpha]_D$ –41.5° (*c,* 0.05 in $CHCl_3$).

CAB Catalysed Reaction of Benzaldehyde and 2-[(Triethylsilyl)oxy]penta-1,3-diene (10)

Benzaldehyde (50 mg, 0.47 mmol) followed by the diene (10)[21] (0.19 g, 0.94 mmol) were added to a cooled (–78°) solution of the tartrate precursor of the CAB (4) (44 mg, 0.2 mmol) and phenylboronic acid (14 mg, 0.12 mmol) in dry, freshly distilled propionitrile (1 ml) which had been stirred at room temperature for 1 h. The mixture was stirred for 7 h, warmed to room temperature, stirred for a further 12 h, and then poured into saturated aqueous sodium hydrogencarbonate (10 ml). The mixture was extracted with ether and the solvent was removed from the dried extracts under reduced pressure to give a colourless oil, p.l.c. (hexanes/ether, 2:1) of which gave the following. (i) (E)-*1-Phenyl-1-[(triethylsilyl)oxy]hex-4-en-3-one* (14) (48 mg, 34%) was obtained as a colourless oil, $[\alpha]_D$ +64° (*c,* 4.25 in $CHCl_3$) (Found: $M^{+\bullet}$, 304.1856. $C_{18}H_{28}O_2Si$ requires $M^{+\bullet}$, 304.1859). ν_{max} (neat) 2954, 2876, 1670 (CO), 1631, 1454, 1070, 1006, 970, 802, 744, 700 cm^{-1}. δ_H 0.48, q, 6H, *J* 7.6 Hz, (Me**C**$\mathbf{H}_2$)$_3$; 0.83, t, 9H, *J* 7.6 Hz, (**C**$\mathbf{H}_3$$CH_2$)Si; 1.87, dd, $J_{6,5}$ 6.8, $J_{6,4}$ 1.3 Hz, H6; 2.62, dd, $J_{2a,2b}$ 14.9, $J_{2a,1}$ 4.2 Hz, H2a; 3.09, dd, $J_{2b,2a}$ 14.9, $J_{2b,1}$ 8.5 Hz, H2b; 5.22, dd, $J_{1,2'b}$ 8.5, $J_{1,2'a}$ 4.2 Hz, H1; 6.11, dq, $J_{4,5}$ 15.8, $J_{4,6}$ 1.3 Hz, H4; 6.81, dq, $J_{5,4}$ 15.8, $J_{5,6}$ 6.8 Hz, H5; 7.20–7.37, m, 5H, H2′,3′,4′. δ_C 4.65, (Me**C**H_2)$_3$; 6.63, (**C**$H_3$$CH_2$)$_3$Si; 18.2, C6; 50.8, C2; 71.7, C1; 125.7, C2′ or C3′; 127.2, C4′; 128.2, C2′ or C3′; 124.0, C4; 143.4, C5; 145.3, C1′; 198.1, C3. *m/z* 304 (M, 1%), 275 (65), 221 (10), 169 (100), 103 (18), 75 (26). (ii) (E)-*1-Hydroxy-1-phenylhex-4-en-3-one* (15) (52 mg, 58%) was obtained as a colourless oil, $[\alpha]_D$ +60.7° (*c,* 4.34 in $CHCl_3$) (Found: $M^{+\bullet}$, 190.0993. $C_{12}H_{14}O_2$ requires $M^{+\bullet}$, 190.0994). ν_{max} (neat) 3448 (OH), 1654 (CO), 1628, 1441, 1056, 969, 756, 701, 548 cm^{-1}. δ_H 1.89, dd, $J_{6,5}$ 6.8, $J_{6,4}$ 1.6 Hz, H6; 2.90–2.94, m, 2H, H2; 3.68, br s, 1-OH; 5.17, t, $J_{1,2}$ 5.9 Hz, H1; 6.11, dq, $J_{4,5}$ 15.8, $J_{4,6}$ 1.6 Hz, H4; 6.86, dq, $J_{5,4}$ 15.8, $J_{5,6}$ 6.8 Hz, H5; 7.21–7.38, m, 5H, H2′,3′,4′. δ_C 18.3, C6; 48.0, C2; 69.9, C1; 125.6, C2′ or 3′; 127.4, C4′; 128.4, C2′ or C3′; 132.0, C4; 143.0, C1′; 144.4, C5; 200.1, C3. *m/z* 190 (M, 10%), 171 (10), 162 (12), 120 (18), 105 (100), 84 (22), 77 (52), 69 (80).

CAB Catalysed Reaction of Benzaldehyde and 1-Methoxy-3-[(trimethylsilyl)oxy]buta-1,3-diene (11)

Benzaldehyde (50 mg, 0.47 mmol) and then the diene (11) (0.24 g, 1.41 mmol) were added to a cooled (–78°) solution of the tartrate precursor of the CAB (4) (35 mg, 0.09 mmol) and phenylboronic acid (12 mg, 0.09 mmol) in dry, freshly distilled propionitrile (1 ml) which had been stirred at 0° under argon for 1 h. The mixture was stirred at –78° for 19 h, poured into saturated aqueous sodium hydrogencarbonate (10 ml), and extracted with ether. The extracts were washed with water, dried, and concentrated under reduced pressure to give an oil, p.l.c. (hexanes/ether, 2:1) of which gave the following. (i) (E)-*5-Methoxy-1-phenyl-1-[(trimethylsilyl)oxy]pent-4-en-3-one* (16) (17 mg, 13%) was obtained as a colourless oil (Found: $M^{+\bullet}$, 278.4420. $C_{15}H_{22}O_3Si$ requires $M^{+\bullet}$, 278.4425). ν_{max} (neat) 2957, 1684 (CO), 1621, 1595, 1251, 1086, 948, 843, 701 cm^{-1}. δ_H 0.01, s, 9H, $(CH_3)_3Si$; 2.60, dd, $J_{2a,2b}$ 14.5, $J_{2a,1}$ 3.9 Hz, H2a; 2.96, dd, $J_{2b,2a}$ 14.5, $J_{2b,1}$ 8.8 Hz, H2b; 3.68, s, 5-OCH_3; 5.20, dd, $J_{1,2b}$ 8.8, $J_{1,2a}$ 3.9 Hz, H1; 5.89, d, $J_{4,5}$ 12.7 Hz, H4; 7.20–7.39, m, 5H, H2′,3′,4′; 7.58, d, $J_{5,4}$ 12.7 Hz, H5. δ_C –0.01, $(CH_3)_3Si$; 52.0, C2; 57.4, 5-OCH_3; 71.8, C1; 106.9, C4; 125.6, C2′ or C3′; 127.2, C4′; 128.2, C2′ or C3′; 144.6, C1′; 163.4, C5; 197.6, C3. *m/z* 278 (M, 12%), 206 (10), 188 (15), 179 (34), 173 (10), 157 (33), 142 (16), 120 (25), 105 (30), 100 (28), 85 (100). (ii) (E)-*1-Hydroxy-5-methoxy-1-phenylpent-4-en-3-one* (17) (55 mg, 56%) was obtained as a colourless oil, $[\alpha]_D$ +56° (*c,* 4.11 in CH_2Cl_2) (Found: $M^{+\bullet}$, 206.0945. $C_{12}H_{14}O_3$ requires $M^{+\bullet}$, 206.0943). ν_{max} (neat) 3451, 2951, 1669 (CO), 1653, 1457, 1073, 1001, 996, 970, 811, 741 cm^{-1}. δ_H 2.83–2.87, m, 2H, H2; 3.69, s, 5-OCH_3; 3.84, br s, 1-OH; 5.17, dd, $J_{1,2'b}$ 7.1, $J_{1,2'a}$ 5.2 Hz, H1; 5.58, d, $J_{4,5}$ 12.7 Hz, H4; 7.24–7.39, m, 5H, H2′,3′,4′; 7.60, d, $J_{5,4}$ 12.7 Hz, H5. δ_C 48.9, C2; 57.6, 5-OCH_3; 70.1, C1; 105.8, C4; 125.6, C2′ or C3′; 127.4, C4′; 128.4, C2′ or C3′; 143.0, C1′; 163.7, C5; 199.3, C3. *m/z* 206 (M, 8%), 174 (10), 120 (26), 105 (28), 100 (12), 87 (10), 85 (100).

Cyclization of (E)-*5-Methoxy-1-phenyl-1-[(trimethylsilyl)oxy]pent-4-en-3-one (16)*

Trifluoroacetic acid (2 drops) was added to a stirred solution of the pentenone (16) (15 mg, 0.06 mmol) in CH_2Cl_2 (2 ml) at 0° and the mixture was stirred at 0° for 30 min, diluted with CH_2Cl_2 (10 ml), and poured into saturated aqueous sodium hydrogencarbonate (20 ml). The organic layer was washed with water, dried, and the solvent was removed under reduced pressure. P.l.c. (hexanes/ether, 9:1) of the resulting oil gave 2-phenyl-2,3-dihydro-4*H*-pyran-4-one (20) (9 mg, 94%) as a colourless oil, $[\alpha]_D$ –89° (*c,* 0.82 in $CHCl_3$) (correct ^1H n.m.r. spectrum).[2]

Cyclization of (E)-*1-Hydroxy-5-methoxy-1-phenylpent-4-en-3-one (17)*

Trifluoroacetic acid (2 drops) was added to a solution of the pentenone (17) (24 mg, 0.12 mmol) in CH_2Cl_2 (2 ml) at 0° and the mixture was stirred at 0° for 30 min, diluted with CH_2Cl_2 (10 ml), and poured into saturated aqueous sodium hydrogencarbonate (20 ml). The organic layer was washed with water, dried, and the solvent was removed under reduced pressure to give an oil, p.l.c. (hexanes/ether, 1:1) of which yielded 2-phenyl-2,3-dihydro-4*H*-pyran-4-one (20) (20 mg, 98%) as a colourless oil, $[\alpha]_D$ –89° (*c*, 1.27 in $CHCl_3$) (expected ^1H n.m.r. spectrum).[2]

CAB Catalysed Reaction of o-*Anisaldehyde with 1-Methoxy-3-[(trimethylsilyl)oxy]buta-1,3-diene (11)*

A solution of *o*-anisaldehyde (50 mg, 0.37 mmol) in propionitrile (1 ml) followed by the diene (11) (0.19 g, 1.10 mmol) were added to a cooled (–78°) solution of the tartrate precursor of the CAB (4) (27 mg, 0.07 mmol) and phenylboronic acid (9 mg, 0.07 mmol) in dry, freshly distilled, propionitrile (1 ml) which had been stirred under argon for 1 h. The mixture was stirred at –78° for 17 h, poured into saturated aqueous sodium hydrogencarbonate (10 ml) and extracted with ether. The extracts were dried and concentrated under reduced pressure to give an oil, p.l.c. (hexanes/ether, 1:1) of which afforded the following. (i) *o*-Anisaldehyde (10 mg, 21%). (ii) (E)-*5-Methoxy-1-(2′-methoxyphenyl)-1-[(trimethylsilyl)oxy]pent-4-en-3-one* (18) (11 mg, 11%) was obtained as a colourless oil, $[\alpha]_D$ –5.8° (*c*, 0.97 in CH_2Cl_2) (Found: $M^{+\bullet}$, 308.1448. $C_{16}H_{24}O_4Si$ requires $M^{+\bullet}$, 308.1444). ν_{max} (neat) 2957, 1685 (CO), 1622, 1598, 1490, 1464, 1248, 1085, 843, 756 cm^{-1}. δ_H 0.01, s, 9H, $(CH)_3Si$; 2.73–2.76, m, 2H, H2; 3.70, s, 5-OCH_3; 3.84, s, 2′-OCH_3; 5.54, t, $J_{5',4'}$ 6.1 Hz, H5′; 5.62, d, $J_{4,5}$ 12.8 Hz, H4; 6.83, dd, $J_{6',5'}$ 8.2, $J_{6',4'}$ 1.1 Hz, H 6′; 6.96, ddd, $J_{4',3'} = J_{4',5'}$ 7.5, $J_{4',6'}$ 1.1 Hz, H4′; 7.22, ddd, $J_{5',6'}$ 8.2, $J_{5',4'}$ 7.5, $J_{5',3'}$ 1.8 Hz, H5′; 7.49, dd, $J_{3',4'}$ 7.5, $J_{3',5'}$ 1.8 Hz, H3′; 7.62, d, $J_{5,4}$ 12.8 Hz, H5. δ_C –0.07, $(CH_3)_3Si$; 50.0, C2; 55.2, 2′-OCH_3; 57.3, 5-OCH_3; 66.3, C1; 106.9, C4; 109.9, C3′; 120.5, C5′; 126.5, C4′; 127.9, C6′; 132.9, C1′; 155.2, C2′; 163.1, C5; 197.8, C3. *m/z* 308 (M,

20%), 209 (100), 187 (45), 157 (33), 142 (14), 135 (28), 119 (10), 100 (16). (iii) (E)-*1-Hydroxy-5-methoxy-1-(2′-methoxyphenyl)pent-4-en-3-one* (19) (51 mg, 59%) was obtained as a colourless oil, $[\alpha]_D$ –6.0° (*c*, 3.14 in CH_2Cl_2) (Found: $M^{+\bullet}$, 236.1043. $C_{13}H_{16}O_4$ requires $M^{+\bullet}$, 236.1049). ν_{max} (neat) 3444 (OH), 2939, 1674 (CO), 1620, 1589, 1492, 1241, 1049, 757 cm^{-1}. δ_H 2.74, dd, $J_{2a,2b}$ 16.5, $J_{2a,1}$ 9.1 Hz, H2a; 2.98, dd, $J_{2b,2a}$ 16.5, $J_{2b,1}$ 3.0 Hz, H2b; 3.69, s, 5-OCH_3; 3.82, s, 2′-OCH_3; 5.44, dd, $J_{1,2a}$ 9.1, $J_{1,2b}$ 3.0 Hz, H1; 5.58, d, $J_{4,5}$ 12.7 Hz, H4; 6.85 dd, $J_{6',5'}$ 8.2, $J_{6',4'}$ 1.0 Hz, H6′; 6.97, ddd, $J_{4',3'} = J_{4',5'}$ 7.5, $J_{4',6'}$ 1.0 Hz, H4′; 7.23, ddd, $J_{5',6'}$ 8.2, $J_{5',4'}$ 7.5, $J_{5',3'}$ 1.7 Hz, H5′; 7.48, dd, $J_{3',4'}$ 7.5, $J_{3',5'}$ 1.8 Hz, H 3′; 7.61, d, $J_{5,4}$ 12.7 Hz, H5. δ_C 47.3, C2; 55.2, 2′-OCH_3; 57.5, 1-OCH_3; 65.7, C1; 106.1, C4; 110.1, C3′; 120.8, C5′; 126.4, C4′; 128.2, C6′; 131.2, C1′; 155.7, C2′; 163.5, C5; 199.8, C3. *m/z* 236 (M, 12%), 187 (22), 150 (20), 135 (49), 119 (16), 107 (22), 100 (24), 85 (100).

Cyclization of (E)-*5-Methoxy-1-(2′-methoxyphenyl)-1-[(trimethylsilyl)oxy]pent-4-en-3-one (18)*

Trifluoroacetic acid (2 drops) was added to a stirred solution of the pentenone (18) (9 mg, 0.03 mmol) in CH_2Cl_2 (1 ml) at 0° and the mixture was stirred for 30 min, diluted with CH_2Cl_2 (10 ml), and poured into saturated aqueous sodium hydrogencarbonate (20 ml). The organic layer was washed with water, and concentrated under reduced pressure to give an oil, p.l.c. (hexanes/ether, 1:1) of which afforded *2-(2′-methoxyphenyl)-2,3-dihydro-4*H*-pyran-4-one* (21) (5 mg, 91%) as a colourless oil, $[\alpha]_D$ –3.5° (*c,* 0.51 in CH_2Cl_2) (Found: $M^{+\bullet}$, 204.0783. $C_{12}H_{12}O_3$ requires $M^{+\bullet}$, 204.0786). ν_{max} 1664 (CO), 1609, 1498, 1393, 1247, 1031, 1005, 944, 756 cm^{-1}. δ_H 2.72–2.76, m, 2H, H2*ax*,2*eq*; 3.84, s, 2′-OCH_3; 5.51, d, $J_{5,6}$ 6.5 Hz, H5; 5.80, dd, $J_{2,3ax}$ 10.7, $J_{2,3eq}$ 7.1 Hz, H2; 6.91, dd, $J_{6',5'}$ 8.1, $J_{6',4'}$ 1.0 Hz, H6′; 7.02, ddd, $J_{4',5'}$ 8.2, $J_{4',3'}$ 7.6, $J_{4',6'}$ 1.0 Hz, H4′; 7.34, ddd, $J_{5',4'}$ 8.2, $J_{5',6'}$ 8.1, $J_{5',3'}$ 1.7 Hz, H5′; 7.48, dd, $J_{3',4'}$ 7.6, $J_{3',5'}$ 1.5 Hz, H3′; 7.51, d, $J_{6,5}$ 6.5 Hz, H6. δ_C 42.3, C3; 55.3, 2′-OCH_3; 76.4, C2; 107.2, C5; 110.5, C3′; 120.8, C5′; 126.3, C4′; 126.5, C2′; 129.6, C6′; 155.8, C1′; 163.5, C6; 192.9, C 4. *m/z* 204 (M, 44%), 175 (12), 134 (100), 119 (99), 91 (98), 77 (18).

Cyclization of (E)-*1-Hydroxy-5-methoxy-1-(2′-methoxyphenyl)pent-4-en-3-one (19)*

Trifluoroacetic acid (2 drops) was added to a stirred solution of the pentenone (19) (23 mg, 0.1 mmol) in CH_2Cl_2 (1 ml) at 0°, and the mixture was stirred for 30 min at 0°, diluted with CH_2Cl_2 (10 ml), and poured into saturated aqueous sodium hydrogencarbonate (20 ml). The organic layer was washed with water, dried, and the solvent was removed under reduced pressure. P.l.c. (hexanes/ether, 1:1) of the residue afforded the dihydropyrone (21) (19 mg, 94%) as a colourless oil, $[\alpha]_D$ –3.8° (*c*, 1.03 in CH_2Cl_2) (correct ^{1}H n.m.r. spectrum).

CAB Catalysed Reaction of Benzaldehyde and 2,4-Bis[(trimethylsilyl)oxy]penta-1,3-diene (12) [1]

Benzaldehyde (75 mg, 0.71 mmol) and the diene (12) (0.26 g, 1.06 mmol) were added to a solution of the tartrate precursor of the CAB (4) (52 mg, 0.14 mmol) and phenylboronic acid (17 mg, 0.14 mmol) in propionitrile (1 ml) which had been stirred at 0°, under argon, for 30 min and then cooled to –78°. The mixture was stirred at –78° for 24 h, poured into 20% aqueous hydrochloric acid, stirred at room temperature for 30 min, and then extracted with ether. The extracts were washed with water, dried, and the solvent was removed under reduced pressure. P.l.c. (hexanes/ether, 2:1) of the residue afforded 6-methyl-2-phenyl-2,3-dihydro-4*H*-pyran-4-one (22) (83 mg, 62%) as a colourless oil, $[\alpha]_D$ –52.2° (*c*, 3.67 in CH_2Cl_2) (correct ^{1}H n.m.r. spectrum).[2]

CAB Catalysed Reaction of o-*Anisaldehyde and 2,4-Bis[(trimethylsilyl)oxy]penta-1,3-diene (12)*

A solution of *o*-anisaldehyde (50 mg, 0.37 mmol) in propionitrile (1 ml) was added to a cooled (–78°) solution of the tartrate precursor of the CAB (4) (27 mg, 0.07 mmol) and phenylboronic acid (9 mg, 0.07 mmol) in propionitrile (1 ml) which had been stirred at 0° under argon for 1 h. The mixture was stirred for 10 min, the diene (12) (27 mg, 1.1 mmol) was added, and the mixture was stirred at –78° for 25 h, and then poured into 20% aqueous hydrochloric acid (10 ml). The mixture was stirred at room temperature for 30 min, extracted with ether, and the extracts were washed with saturated aqueous sodium hydrogencarbonate, water, and brine. Solvent was removed from the dried solution under reduced pressure, and p.l.c. (hexanes/ether, 2:1) of the residue gave *o*-anisaldehyde (27 mg, 54%) and *2-(2′-methoxyphenyl)-6-methyl-2,3-dihydro-4*H*-pyran-4-one* (23) (25 mg, 31%) as a colourless oil, $[\alpha]_D$ +4° (*c*, 1.97 in CH_2Cl_2) (Found: $M^{+\bullet}$, 218.0943. $C_{13}H_{14}O_3$ requires $M^{+\bullet}$, 218.0943). ν_{max} 1667 (CO), 1612, 1495, 1396, 1247, 1027, 1006, 953, 766 cm^{-1}. δ_H ($CDCl_3$) 2.08, s, 6-CH_3; 2.62–2.67, m, 2H, H3*ax*,3*eq*; 3.83, s, 2′-OCH_3; 5.43, s, H5; 5.76, dd, $J_{2,3ax}$ 10.0, $J_{2,3eq}$ 7.7 Hz, H2; 6.91, dd, $J_{6',4'}$ 8.2, $J_{6',4'}$ 0.7 Hz, H6′; 7.02, ddd, $J_{4',5'}$ 8.1, $J_{4',3'}$ 7.6, $J_{4',6'}$ 0.7 Hz, H4′; 7.33, ddd, $J_{5',6'}$ 8.2, $J_{5',4'}$ 8.1, $J_{5',3'}$ 1.5 Hz, H5′; 7.50, dd, $J_{3',4'}$ 7.6, $J_{3',5'}$ 1.5 Hz, H 3′. δ_H (C_6D_6) 1.48, s, 6-CH_3; 2.51, dd, $J_{3ax,3eq}$ 16.6, $J_{2,3ax}$ 14.1 Hz, H3*ax*; 2.70, dd, $J_{3eq,3ax}$ 16.6, $J_{2,3eq}$ 3.4 Hz, H3*eq*; 3.09, s, 2′-OCH_3; 5.36, s, H5; 5.72, dd, $J_{2,3ax}$ 14.1, $J_{2,3eq}$ 3.4 Hz, H2; 6.40, dd, $J_{6',5'}$ 8.2, $J_{6',4'}$ 0.9 Hz, H6′; 6.85, ddd, $J_{4',5'}$ 8.1, $J_{4',3'}$ 7.5, $J_{4',6'}$ 0.9 Hz, H4′; 7.04, ddd, $J_{5',6'}$ 8.2, $J_{5',4'}$ 8.1, $J_{5',3'}$ 1.7 Hz, H5′; 7.37, dd, $J_{3',4'}$ 7.5, $J_{3',5'}$ 1.7 Hz, H3′. δ_C 21.1, 6-CH_3; 41.3, C3; 55.3, 2′-OCH_3; 76.0, C2; 105.0, C5; 110.5, C3′; 120.7, C5′; 126.3, C4′; 126.9, C2′; 129.5, C6′; 155.8, C1′; 174.8, C6; 193.2, C4. *m/z* 218 (M, 20%), 200 (12), 187 (10), 175 (38), 134 (78), 119 (100), 91 (70), 77 (14).

CAB Promoted Reaction of 2-Formyl-1,5-dimethoxyanthraquinone (7) and 2,4-Bis[(trimethylsilyl)oxy]penta-1,3-diene (12)

Borane–tetrahydrofuran complex (0.10 ml, 1 mol l^{-1} solution in tetrahydrofuran) was added to a stirred suspension of the tartrate precursor of the CAB (1) (32 mg, 0.10 mmol) in CH_2Cl_2 (1 ml) under argon at room temperature and the mixture was stirred for 1 h, cooled to –30°, and treated with a solution of the aldehyde (7) (15 mg, 0.06 mmol) in CH_2Cl_2 (2 ml) and the diene (12) (37 mg, 0.15 mmol). Stirring was continued for 24 h, trifluoroacetic acid (2 drops) was added, and the mixture was warmed slowly to room temperature. The mixture was stirred for 10 min, poured into saturated aqueous sodium hydrogencarbonate (20 ml), and the organic layer was washed with saturated aqueous sodium hydrogencarbonate, water, and dried. Solvent was removed under reduced pressure to give a solid, p.l.c. (CH_2Cl_2/ether) of which gave starting aldehyde (7) (6 mg, 37%) and 1,5-dimethoxy-2-(6′-methyl-4′-oxo-2′,3′-dihydro-4′*H*-pyran-2′-yl)anthraquinone (24) (9 mg, 45%) as a yellow solid, $[\alpha]_D$ +18° (*c*, 0.36 in CH_2Cl_2) (expected t.l.c. behaviour and ^{1}H n.m.r. spectrum).[1]

Similar reactions at room temperature or 0° returned starting material. An attempted reaction using phenylboronic acid instead of borane–tetrahydrofuran complex at room temperature also returned starting material (94%).

Ti[(R)-*BINOL]Cl_2 Promoted Reactions of 2-Formyl-1,5-dimethoxyanthraquinone (7) and 2,4-Bis[(trimethylsilyl)oxy]penta-1,3-diene (12)*

A solution of the aldehyde (7) (10 mg, 0.03 mmol) in CH_2Cl_2 (2 ml) was added to a mixture of (*R*)-(+)-BINOL (27) (15 mg, 0.05 mmol), $Ti(O^iPr)_2Cl_2$ (61 µl of a 0.83 mol l^{-1} solution in toluene, 0.05 mmol), crushed activated 4 Å molecular sieves (0.25 g), and CH_2Cl_2 (1 ml) which had been stirred under argon for 2 h. The mixture was cooled to –30°, stirred for 10 min, the diene (12) (25 mg, 0.10 mmol) was added, and the mixture was stirred for a further 40 h. Trifluoroacetic acid (2 drops) was added and the mixture was warmed to room temperature, stirred for 30 min, and then poured into saturated aqueous sodium hydrogencarbonate (10 ml). The organic layer was washed with water, dried, and the solvent was removed under reduced pressure. P.l.c. (CH_2Cl_2/ether, 49:1) of the residue gave starting aldehyde (2 mg, 20%) and the dihydropyrone (24) (9 mg, 68%) as a yellow solid, $[\alpha]_D$ +6.4° (*c*, 0.75 in CH_2Cl_2) (correct t.l.c. behaviour and ^{1}H n.m.r. spectrum).

In a similar experiment a solution of the aldehyde (7) (10 mg, 0.03 mmol) in CH_2Cl_2 (2 ml) was added to a mixture of (*R*)-(+)-BINOL (11 mg, 0.04 mmol), $Ti(O^iPr)_2Cl_2$ (41 µl) of a 0.83 mol l^{-1} solution in toluene, 0.03 mmol), crushed activated 4 Å molecular sieves (0.25 g), and CH_2Cl_2 (1 ml) which had been stirred, under argon, at room temperature for 2 h. The mixture was cooled to –78°, stirred for 10 min, and the diene (12) (25 mg, 0.10 mmol) was added. The mixture was stirred at –78° for

24 h and then at room temperature for 24 h before trifluoroacetic acid (2 drops) was added. Workup and p.l.c. yielded starting material (7 mg, 69%) and the dihydropyrone (24) (4 mg, 28%), $[\alpha]_D$ +7.4° (*c*, 0.34 in CH_2Cl_2) (correct t.l.c. behaviour and ^{1}H n.m.r. spectrum).

Ti[(R,R)-TADDOL*]Cl$_2$ Promoted Reactions of 2-Formyl-1,5-dimethoxyanthraquinone (7) and 2,4-Bis[(trimethylsilyl)oxy]penta-1,3-diene (12)*

A solution of the aldehyde (7) (10 mg, 0.03 mmol) in CH_2Cl_2 (2 ml) was added to a cooled (–78°) mixture of (*R,R*)-TADDOL (29) (19 mg, 0.04 mmol), $Ti(O^iPr)_2Cl_2$ (49 µl of a 0.83 mol l^{-1} solution in toluene, 0.04 mmol), crushed activated 4 Å molecular sieves (0.25 g), and CH_2Cl_2 (1 ml) under argon. Stirring was continued for 10 min, the diene (12) (25 mg, 0.10 mmol) was added, and the mixture was stirred at –78° for 20 h before trifluoroacetic acid (2 drops) was added. The mixture was warmed to room temperature, stirred for 30 min, and poured into saturated aqueous sodium hydrogencarbonate (10 ml). The organic layer was washed with water, dried, and the solvent was removed under reduced pressure. P.l.c. of the resulting solid gave the dihydropyrone (24) (11 mg, 86%) as a yellow solid, $[\alpha]_D$ +4.9° (*c*, 0.94 in CH_2Cl_2) (correct t.l.c. behaviour and ^{1}H n.m.r. spectrum).

In a similar experiment the molecular sieves were removed before the addition of the diene (12). Workup gave starting aldehyde (28%) and (24) (59%), $[\alpha]_D$ +6.8° (*c*, 0.72 in CH_2Cl_2).

Reactions in the presence of molecular sieves at higher temperature (–30°) or with less Lewis acid (0.5 equiv.) gave lower yields of (24) (74 and 37% respectively).

Ti[(R,R)-TADDOL*]Cl$_2$ Promoted Reaction of 2-Formyl-1-hydroxy-5-methoxyanthraquinone (8) and 2,4-Bis[(trimethylsilyl)oxy]penta-1,3-diene (12)*

A mixture of (*R,R*)-TADDOL (33 mg, 0.07 mmol), $Ti(O^iPr)_2Cl_2$ (85 µl of a 0.83 mol l^{-1} solution in toluene, 0.07 mmol), activated crushed 4 Å molecular sieves (0.25 g), and CH_2Cl_2 (1 ml) was stirred, under argon, at room temperature for 2 h. Stirring was discontinued and once the sieves had settled, the supernatant liquid and CH_2Cl_2 washings were centrifuged until the supernatant liquid was clear. This solution was added dropwise to a stirred solution of the aldehyde (8) (10 mg, 0.04 mmol) in CH_2Cl_2 (3 ml) under argon. The mixture was stirred at –78° for 10 min, the diene (12) (26 mg, 0.11 mmol) was added, the mixture was stirred at –78° for 24 h, and then trifluoroacetic acid (2 drops) was added. The mixture was warmed to room temperature, stirred for 10 min, poured into saturated aqueous sodium hydrogencarbonate (10 ml) and the organic layer was washed with water, dried, and concentrated under vacuum to give a solid. P.l.c. (CH_2Cl_2/ether, 49 : 1) afforded *1-hydroxy-5-methoxy-2-(6′-methyl-4′-oxo-2′,3′-dihydro-4′*H*-pyran-2′-yl)anthraquinone* (25) (11 mg, 82%) which crystallized from CH_2Cl_2/hexanes as small yellow needles, m.p. 210–212°, $[\alpha]_D$ –26.7° (*c*, 0.79 in CH_2Cl_2) (Found: $M^{+\bullet}$, 364.0938. $C_{21}H_{16}O_6$ requires $M^{+\bullet}$, 364.0937). λ_{max} 228 (log ε 4.43), 256 (4.37), 409 nm (3.86). ν_{max} 3446 (OH), 1670, 1629, 1607, 1397, 1268, 1004, 814 cm^{-1}. δ_H 2.13, s, 6′-CH_3; 2.62, dd, $J_{3'ax,3'eq}$ 16.8, $J_{2',3'ax}$ 13.8 Hz, H3′*ax*; 2.85, ddd, $J_{3'eq,3'ax}$ 16.8, $J_{2'3'eq}$ 3.8, $J_{3'eq,5'}$ 0.9 Hz, H3′*eq*; 4.06, s, 5-OCH_3; 5.48, br s, H5′; 5.86, dd, $J_{2',3'ax}$ 13.8, $J_{2',3'eq}$ 3.8 Hz, H2′; 7.39, dd, $J_{6,7}$ 8.5, $J_{6,8}$ 1.0 Hz, H6; 7.76, dd, $J_{7,6}$ 8.5, $J_{7,8}$ 7.7 Hz, H7; 7.85, d, $J_{3,4}$ 8.0 Hz, H3; 7.93, d, $J_{4,3}$ 8.0 Hz, H4; 7.99, dd, $J_{8,7}$ 7.7, $J_{8,6}$ 1.0 Hz, H8; 12.88, s, 1-OH. δ_C 21.5, 6′-CH_3; 41.1, C3′; 57.0, 5-OCH_3; 75.8, C2′; 106.0, C5′; 115.8, 119.2, 119.6, 120.0, 121.8, 133.0, 134.0, 135.0, 135.6, 135.7, 158.8, 161.0, 174.5, 181.8, 189.3, 189.3, 192.3. *m/z* 364 (M, 54%), 321, 306 (12), 293 (16), 280 (100), 265 (30), 251 (12), 165 (16), 148 (18).

*Methylation of 1-Hydroxy-5-methoxy-2-(6′-methyl-4′-oxo-2′,3′-dihydro-4′*H*-pyran-2′-yl)anthraquinone (25)*

A mixture of the hydroxyanthraquinone (25) (8 mg, 0.02 mmol), potassium carbonate (31 mg, 0.23 mmol), dimethyl sulfate (14 mg, 0.11 mmol), and acetone (5 ml) was heated at reflux, under argon, for 1.5 h, cooled, and poured onto ice. The solid was filtered off, washed with water, and dissolved in CH_2Cl_2 (20 ml). The organic solution was washed with water, dried, and the solvent was removed under reduced pressure to give (24) (8 mg, 95%), $[\alpha]_D$ –3.8° (*c*, 0.81 in CH_2Cl_2) as a yellow solid (expected t.l.c. behaviour and ^{1}H n.m.r. spectrum).

References

[1] Bercich, M. D., Cambie, R. C., and Rutledge, P. S., *Aust. J. Chem*., 1999, **52**, 303.
[2] Togni, A., *Organometallics*, 1990, **9**, 3106.
[3] Furuta, K., Miwa, Y., Iwanaga, K., and Yamamoto, H., *J. Am. Chem. Soc.*, 1988, **110**, 6254.
[4] Furuta, K., Shimizu, S., Miwa, Y., and Yamamoto, H., *J. Org. Chem*., 1989, **54**, 1481.
[5] Ishihara, K., Gao, Q., and Yamamoto, H., *J. Org. Chem*., 1993, **58**, 6917; *J. Am. Chem. Soc.*, 1993, **115**, 10412.
[6] Furuta, K., Kanematsu, A., Takaoka, S., and Yamamoto, H., *Tetrahedron Lett.*, 1989, **30**, 7231.
[7] Furuta, K., Gao, Q., and Yamamoto, H., *Org. Synth.*, 1995, **72**, 86.
[8] Furuta, K., Maruyama, T., and Yamamoto, H., *J. Am. Chem. Soc.*, 1991, **113**, 1041.
[9] Ishihara, K., Maruyama, T., Mouri, M., Gao, Q., Furuta, K., and Yamamoto, H., *Bull. Chem. Soc. Jpn*, 1993, **66**, 3483.
[10] Furuta, K., Mouri, M., and Yamamoto, H., *Synlett*, 1991, 561.
[11] Ishihara, K., Mouri, M., Gao, Q., Maruyama, T., Furuta, K., and Yamamoto, H., *J. Am. Chem. Soc.*, 1993, **115**, 11490.
[12] Gao, Q., Maruyama, T., Mouri, M., and Yamamoto, H., *J. Org. Chem*., 1992, **57**, 1951.
[13] Gao, Q., Ishihara, K., Maruyama, T., Mouri, M., and Yamamoto, H., *Tetrahedron*, 1994, **50**, 979.
[14] Bercich, M. D., M.Sc. Thesis, University of Auckland, 1992.
[15] Corey, E. J., Rohde, J. J., Fischer, A., and Azimioara, M. D., *Tetrahedron Lett.*, 1997, **38**, 33.
[16] Corey, E. J., Rohde, J. J., *Tetrahedron Lett.*, 1997, **38**, 37.
[17] Corey, E. J., Barnes-Seeman, D., and Lee, T. W., *Tetrahedron Lett.*, 1997, **38**, 1699.
[18] Corey, E. J., Cywin, C. L., and Roper, T. D., *Tetrahedron Lett.*, 1992, **38**, 6907.
[19] Oppolzer, W., and Rodriguez, I., *Helv. Chim. Acta*, 1993, **76**, 1282.
[20] Bednarski, M., Maring, C., and Danishefsky, S. J., *Tetrahedron Lett*., 1992, **33**, 6907.
[21] Danishefsky, S. J., Uang, B. J., and Quallich, G., *J. Am. Chem. Soc*., 1985, **107**, 1285.
[22] Danishefsky, S. J., Harvey, D. F., Pearson, W. H., Maring, C. J., and Springer, J. P., *J. Am. Chem. Soc.*, 1985, **107**, 1256.
[23] Danishefsky, S. J., Harvey, D. F., and Pearson, W. H., *J. Am. Chem. Soc.*, 1984, **106**, 2455, 2456.
[24] Mikami, K., Motoyama, Y., and Terada, M., *J. Am. Chem. Soc*., 1994, **116**, 2812.
[25] Keck, G. E., Krishnamurthy, D., and Xiang-Yi, L., *J. Org. Chem.*, 1995, **60**, 5998.
[26] Seebach, D., Hayakawa, M., Sakaki, J., and Schweizer, W. B., *Tetrahedron*, 1993, **49**, 1711.
[27] Cambie, R. C., Holroyd, S. E., Larsen, D. S., Rutledge, P. S., and Woodgate, P. D., *Aust. J. Chem*., 1992, **45**, 1589.