Tetrahedron Vol. 43, No. 13, pp. 2873–2889, 1987
Printed in Great Britain.

0040–4020/87 $5.00+.00
Pergamon Journals Ltd.

TETRAHEDRON REPORT NUMBER 220

ORTHOQUINODIMETHANES

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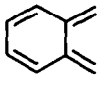
(*Received in USA* 9 *March* 1987)

CONTENTS

1. INTRODUCTION

o-Quinodimethane (*o*-QDM) **1**, also known as *o*-xylylene and *o*-quinododimethide, has been used extensively as a reactive intermediate in organic synthesis. Its discovery, characterization, reactivity



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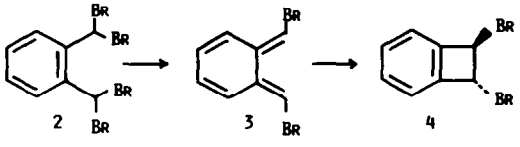
and use in synthesis will be the subject of this review. Aspects of *o*-QDM chemistry which have been treated, in part, in previous reviews[1–13] will receive less attention here and emphasis will be given to more recent work involving *o*-QDMs.

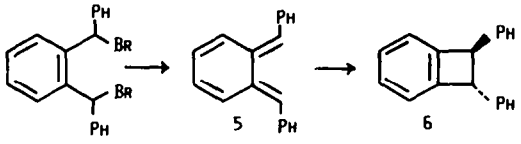
2. DISCOVERY AND CHARACTERIZATION OF *o*-QUINODIMETHANES

In 1957 Cava *et al.* first suggested the participation of an *o*-quinodimethane as a reaction intermediate.[14] They proposed the intermediacy of *o*-QDM **3** in the conversion of α,α,α′,α′-tetrabromo-*o*-xylene **2** to *trans*-α,α′-dibromobenzocyclobutene, **4**, a reaction earlier reported by

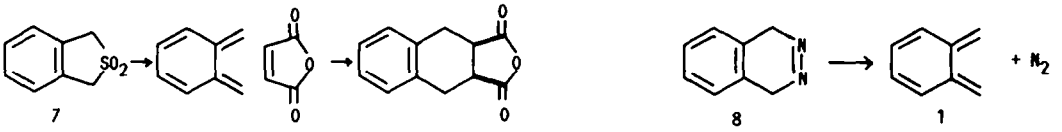


Finkelstein.[15] In 1958 Jensen and Coleman also reported the generation of the disubstituted *o*-

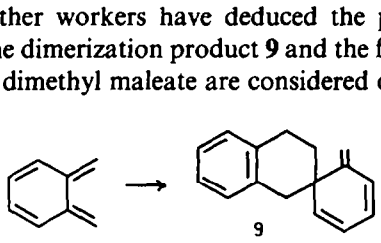
QDM **5** as an intermediate in the preparation of 1,2-diphenylbenzocyclobutene **6**.[16] Later, in 1959,



Cava *et al.* generated the unsubstituted *o*-QDM **1** by thermal decomposition of 1,3-dihydrobenzo[c]thiophene-2,2-dioxide, **7**, and trapped it with typical dienophiles in Diels–Alder cycloaddition reactions.[17] Direct observation of the unsubstituted *o*-QDM **1** was first made by Flynn and Michl in 1973 by irradiating the dihydrodiazanaphthalene **8** in a glassy matrix at −196°C.[18] They recorded the UV, fluorescence and excitation spectra of **1**. Better resolved spectra of **1** were obtained



by Migirdicyan and Baudet in 1975,[19] and in 1977 Tseng and Michl reported the measurement of the IR and Raman spectra of **1** isolated in an argon matrix.[20] The UV-photoelectron spectrum of **1** in the gas phase was reported in 1984[21] and very recently Trahanovsky and Macias have produced the *o*-QDM **1** in acetonitrile solution and estimated the ε at λ_{max} to be 3015.[22] They also found that **1** rapidly decayed in acetonitrile solution by dimerization with a rate constant of 9.9×10^{-3} L mol^{-1} s^{-1} (25°C). Hehre *et al.* have used cyclotron double resonance spectroscopy to determine the relative heats of formation of *p*-, *m*-, and *o*-QDM and found a value of 53 kcal mol^{-1} for *o*-QDM **1**.[23] References to direct observation of substituted *o*-QDMs and isoindenes can be found in papers by Michl[18] and McCullough.[5] Other workers have deduced the presence of *o*-QDMs by indirect methods. The observation of the dimerization product **9** and the formation of Diels–Alder cycloadducts with dienophiles such as dimethyl maleate are considered diagnostic.[17,18,22,24] Much interest



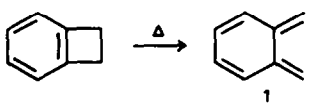
has been shown in theoretical considerations regarding the structure of **1**, spurred on by the possibility that it may have a triplet (biradicaloid) ground state.[5,18,19,25–29] In summary, the calculations indicated that (1) the ground state of *o*-QDM is a singlet, (2) that S_0 and S_1, the ground and first excited state are planar, (3) that S_1 is very nearly degenerate with S_2 and that (4) the double bonds in *o*-QDM **1** are *ca* 1.36 Å in length while the single bonds are 1.45–1.46 Å in length. Our own *ab initio* calculations using the STO-3G basis set with gradient optimization gave double bonds of 1.32 Å and single bonds of 1.48–1.49 Å.[30]

3. METHODS OF GENERATION OF *o*-QUINODIMETHANES

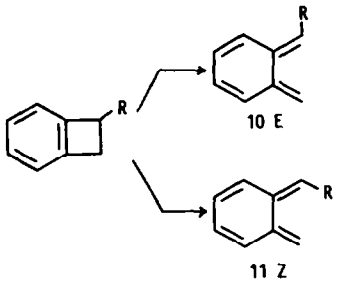
After the discovery and characterization of variously substituted and unsubstituted *o*-quinodimethanes, it was realized that *o*-quinodimethanes could have a great potential in organic synthesis when employed as Diels–Alder dienes. New ways of generating *o*-QDMs were quickly developed which are summarized below.

3.1. *Thermolysis of benzocyclobutenes*

The most frequent way of generating *o*-quinodimethanes is by the thermal ring opening of a benzocyclobutene. The transformation proceeds via a thermally allowed con-rotatory electrocyclic



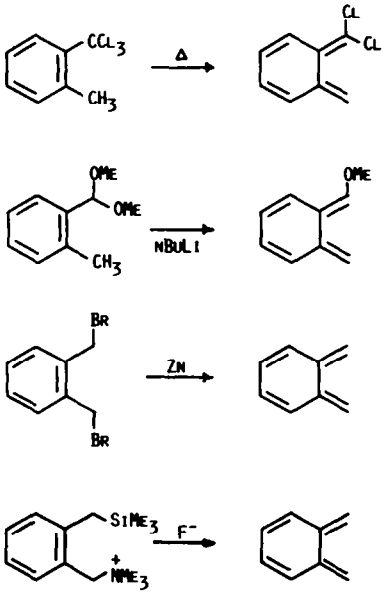
ring opening.[7,31] Benzocyclobutenes having a substituent on the 4-membered ring open outward to produce the sterically less hindered (*E*)-*o*-quinodimethanes **10** in preference to the (*Z*) form **11**[7] and they open at a lower temperature than does unsubstituted benzocyclobutene (alkoxy substituted 110°C, alkyl substituted 140°C, benzocyclobutene, 200°C).[4,7,32] The synthesis and chemistry of



benzocyclobutenes has been reviewed.[10,12,14,31,33] Jung *et al.* also reviewed current methods for benzocyclobutene synthesis in a report on an unsuccessful bid to prepare a *trans*-2-aryl-benzocyclobutenol.[34] MacDonald and Durst later reported a successful route to *trans*-2-aryl-benzocyclobutenols.[35] Other references to benzocyclobutenes and benzocyclobutenols can be found in a paper by Caubere *et al.* on the synthesis of benzocyclobutenols.[36]

3.2. 1,4-*Elimination process*

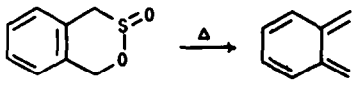
The 1,4-elimination process to generate *o*-quinodimethanes may involve thermal eliminations,[37–39] base catalysed eliminations,[40] reductive eliminations,[4,12,40–46] and fluoride ion catalysed elimination.[41,47,48] One example of each of these methods is shown.



3.3. *Thermal elimination of sulfur dioxide from sulfones and sultines*

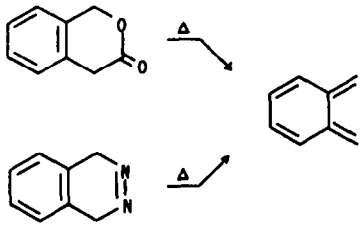
The cheletropic elimination of sulfur dioxide from benzodihydrothiophene-2,2-dioxide goes back to 1959, when Cava generated an *o*-quinodimethane and trapped it with dienophiles, i.e. **7** to **1**.[17,49] Oppolzer reviewed previous literature on this reaction,[6] which includes the work of Nicolaou *et al.*[50] Other papers on this source of *o*-QDMs have since appeared.[51–56]

Durst *et al.* were the first to generate *o*-quinodimethanes by thermal elimination of sulfur dioxide from a sultine.[57,58] Recently other papers on sultines as *o*-QDM precursors have appeared.[6,59–61]



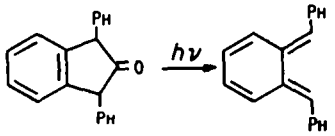
3.4. *Diels–Alder cycloreversion*

Diels–Alder cycloreversion processes can also lead to *o*-QDMs. Two such processes are the loss of carbon dioxide from isochromanone[6,62,63] and the loss of nitrogen from 3,4-dihydrodiazanaphthalene.[20,58,64] The loss of nitrogen can also be accomplished photochemically.[20]



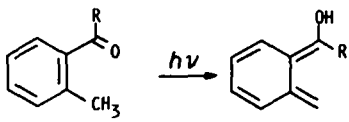
3.5. *Photochemical expulsion of carbon monoxide*

α,α-Disubstituted *o*-quinodomethanes can be generated photochemically from substituted 2-indanones by the loss of carbon monoxide.[2,5]



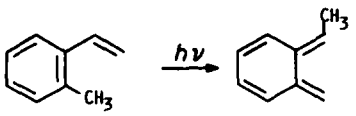
3.6. *Photoenolisation and photorearrangement*

A very effective route to α-hydroxy-*o*-QDMs can be achieved by irradiation of *o*-alkylbenzaldehydes or *o*-alkylbenzophenones.[2,7,8,54,65,66] Early work on this process has been reviewed by Sammes.[8] The process involves excitation to an $n\pi^*$ triplet state followed by intramolecular hydrogen abstraction to give a triplet diradical. This then decays to the *E* and *Z* hydroxy-*o*-quinodimethanes. It is thought that the *Z* isomer returns rapidly to the starting carbonyl compound by a [1,5] sigmatropic shift, while the *E* isomer is relatively longer lived.



It is notable that certain substituted tolualdehydes do not appear to give *o*-QDMs on irradiation. For instance 2-methyl-4-methoxybenzaldehyde did not produce a reactive *o*-QDM on irradiation presumably because of a change in the excited state character of the aldehyde due to the substituent methoxyl group.[67]

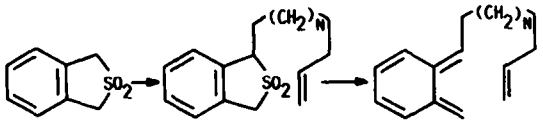
The photolysis of *o*-alkylstyrenes has also been reported to produce *o*-QDMs via a [1,5] sigmatropic shift.[68]



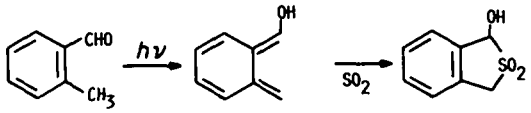
3.7. *Summary*

The choice of method for the preparation of an *o*-quinodimethane depends on the availability of starting materials, the overall yield of the process and the ease with which the method can be carried out. Among all the methods described above, the method most frequently used for producing *o*-quinodimethanes has been the thermolysis of benzocyclobutenes. However the most serious drawback to their use is the difficulty in their synthesis.[6,34] The photochemical preparation of *o*-quinodimethanes has the advantage of ease of accessibility of the necessary precursors but is limited by the possibility of photochemical side reactions. Oppolzer *et al.* found that sulfones were preferred precursors for the generation of *o*-quinodimethanes.[6,69] The readily available unsubstituted sulfone could be substituted with appropriate substituents and thermolysed to the *o*-quinodimethane. Similar

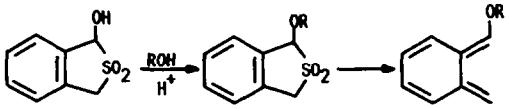
work was also carried out by Nicolaou *et al.*[50]



The reversible trapping of *o*-quinodimethanes by sulfur dioxide[70] was employed by Charlton and Durst to trap a photochemically generated α-hydroxy-*o*-quinodimethane to give an α-hydroxy sulfone.[51,54] This appears to be a very straightforward route to *o*-quinodimethane precursors from reasonably simple starting materials.



The α-hydroxy sulfones are quite stable and can be converted into α-alkoxy and α-acetoxy sulfones, which can be used as precursors for the generation of α-substituted *o*-quinodimethanes.[54]

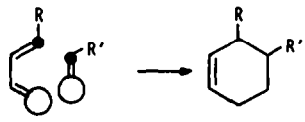


4. *o*-QUINODIMETHANE AS A DIENE IN THE DIELS-ALDER REACTION

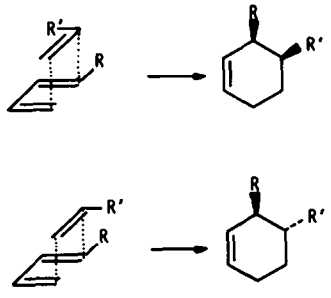
The synthetic utility of *o*-quinodimethanes comes from their propensity to undergo Diels–Alder cycloadditions with dienophiles to form aryl tetralins. An excellent article on the Diels–Alder

reaction has recently appeared and the reader is referred to that article for references on the Diels–Alder reaction.[71] From the earlier studies several generalizations regarding the reaction can be made. The reaction is considered to be concerted (pericyclic) with bonds being broken and formed simultaneously without the intervention of free radical or ionic intermediates. The reaction is stereospecifically *syn* (suprafacial) for both the diene and the dienophile with obvious stereochemical consequences for 1,2-disubstituted dienophiles and 1,4-disubstituted dienes. *Endo* products such as **12** are stereoselectively preferred over *exo* products and 1,2-disubstituted products, such as **13** are regioselectively preferred over 1,3-disubstituted products. Excellent qualitative predictions of

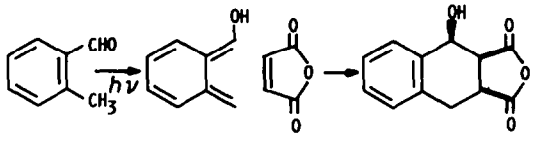
regioselectivity in Diels–Alder reactions have been made using frontier orbital theory (FMO),[72] although this theory has been questioned recently by Hehre *et al.*[71] According to FMO theory regioselectivity can be predicted on the basis of the most favourable interaction of the highest occupied molecular orbital (HOMO) on the diene with the lowest unoccupied orbital (LUMO) on the dienophile. The interaction energy for the HOMO and LUMO is dependent on the square of the overlap between HOMO and LUMO which in turn depends on the orbital coefficients for these orbitals.[71] In brief, the transition state leading to the predicted product has the larger HOMO coefficient of carbons 1 and 4 of the diene interacting with the larger LUMO coefficient of the dienophile. This generally means that dienes with electron donating groups add head to head with dienophiles having electron withdrawing groups. Several examples of regioselectivities can be found in Ref. 71. When the diene is substituted on carbon 1 or 4 and the dienophile also bears a substituent,



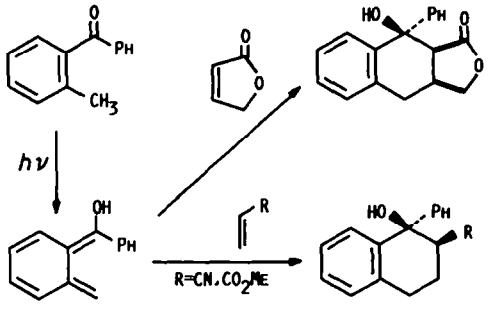
endo and *exo* addition leads to isomeric products. While primary orbital interactions (between atoms to which new bonds are forming) control the regioselectivity of the addition, secondary orbital



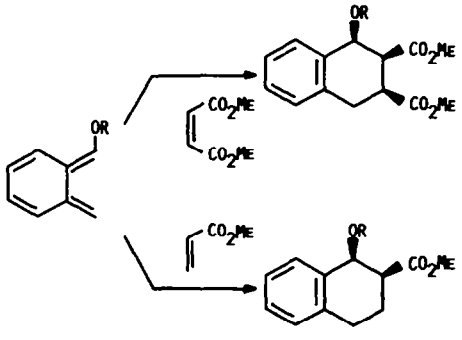
overlap of the group on the dienophile with carbon 2 of the diene can lead to predominantly *endo* products. Results from cycloaddition reactions of α-oxy and/or α-phenyl substituted *o*-QDM to dienophiles[4,25,51-55] indicated that the regio- and stereochemical course of the additions followed that expected for a Diels–Alder reaction of substituted dienes with substituted dienophiles. Thus the *E*-dienol, formed on irradiation of 2-methylbenzaldehyde, reacted with maleic anhydride to give only the all *cis* adduct by *endo* addition.[73] With unsymmetrical dienophiles the dienol from 2-



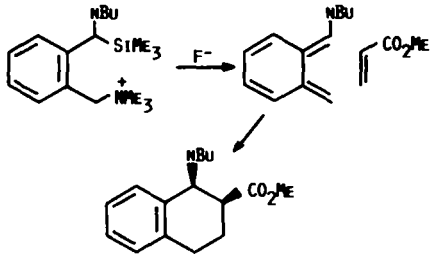
methylbenzophenone shows both regioselective and stereoselective addition.[66,74,75] α-Alkoxy and α-acetoxy *o*-QDMs also add dienophiles such as dimethyl maleate by *endo* addition[54] and add



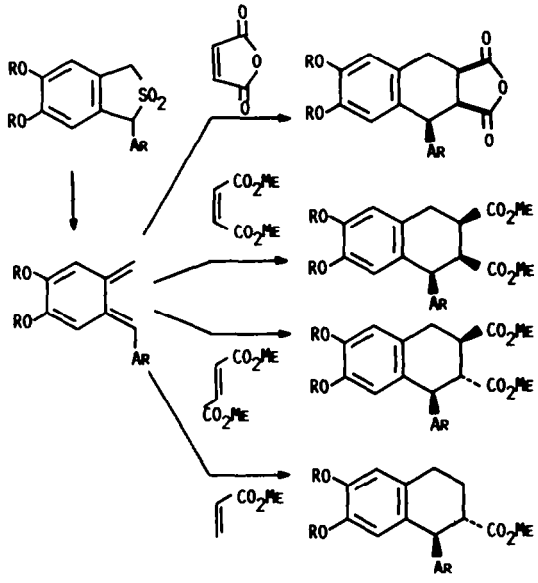
unsymmetrical dienophiles such as methyl acrylate to give the 1,2-disubstituted adducts.[48,76] When α-alkyl-*o*-QDMs react with unsymmetrical dienophiles, less stereoselectivity and regioselectivity is



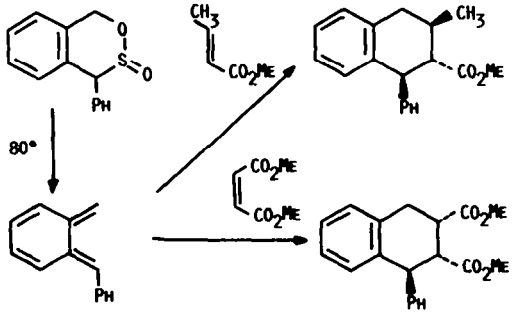
observed but the major product still appears to be the *endo*-1,2-adduct.[41] Mann and Piper have studied the regio- and stereoselectivity of addition reactions to α-aryl-*o*-QDMs.[52,53] Two series of



compounds were studied: (a) R,R = CH_2, Ar = 3,4,5-trimethoxyphenyl, (b) R = Me, Ar = 3,4-dimethoxyphenyl. The cycloaddition with maleic anhydride and dimethyl maleate gave mostly *endo*

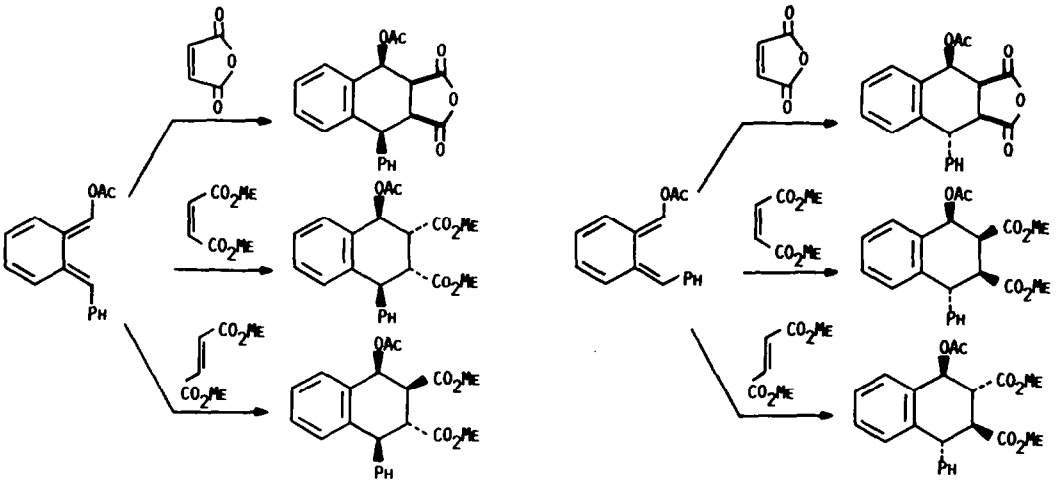


adduct, i.e. 1,2-*cis*, which was expected. However the reaction with dimethyl fumarate and methyl acrylate gave results consistent with *exo* addition, i.e. 1,2-*trans*, > 75%. The regioselectivity of the cycloaddition with methyl acrylate was that expected from FMO theory but the stereoselectivity was surprising. The authors suggested that the abnormal *exo* selectivity was due to a reversible Diels–Alder reaction that allowed equilibration between the *endo* (1,2-*cis*) and *exo* (1,2-*trans*) products and the eventual accumulation of the thermodynamically more stable *exo* configuration as the major product.[52] In a later study Durst *et al.* also added methyl acrylate to α-phenyl-*o*-QDM and found that addition was *exo*.[54] The lower temperature used in Durst's reaction as compared to



that of Mann and Piper above excludes the possibility of a reversible Diels–Alder reaction and one is left with the conclusion that at least in some cases *exo* addition to aryl substituted *o*-QDMs does occur.

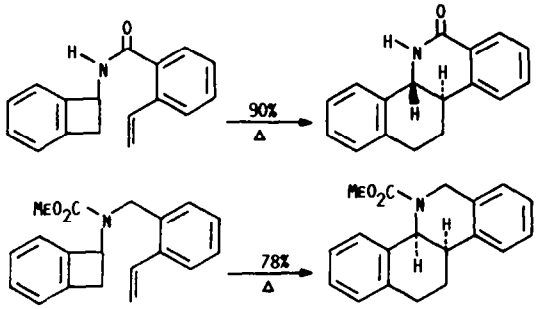
In a study of both *E,E* and *E,Z*-α-hydroxy-α′-phenyl-*o*-QDM it has been found that *endo* addition of maleic anhydride occurs to both isomers.[55] In contrast, dimethyl fumarate and dimethyl maleate yield major products which have the phenyl and neighboring carbomethoxy group *trans*. It would



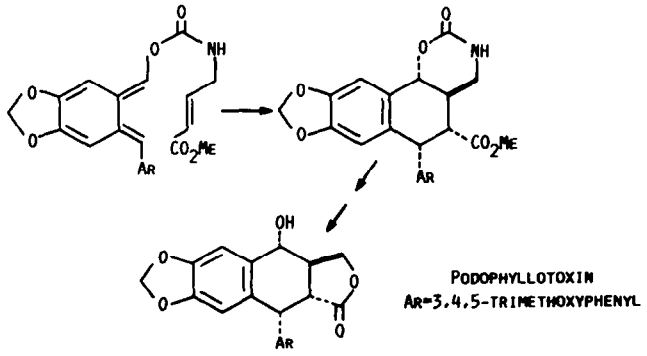
appear that some dienophiles, such as maleic anhydride, undergo *endo* addition due to secondary orbital effects and kinetic control. Addition of others (fumarate and maleate) appears to add *exo*, guided by product development control, possibly via steric repulsion between the phenyl and carbomethoxy group. This may also be the controlling factor in the formation of the *exo* products observed by Mann and Piper (see above).

Intramolecular cycloadditions have received considerable attention and many examples can be found in the earlier reviews.[1,2,4,6,7,9-13] The selectivity of the addition is variable[7] and is often different from that expected for an intermolecular addition due to the steric influence of the linking bridge. Thus, α-(6-hex-1-enyl)-*o*-QDM gives only the *trans* octahydrophenanthrene in 70% yield via *exo* addition.[41] That the stereoselectivity is highly dependent on the *o*-QDM-dienophile linkage is

illustrated by the following two examples.[7] Durst and Macdonald made use of the reversed stereoselectivity of the intramolecular addition to prepare podophyllotoxin.[77] Further discussion



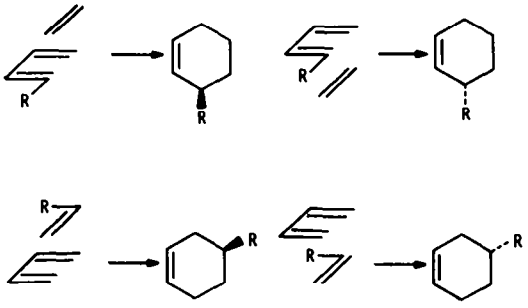
and examples of the stereoselectivity of the intramolecular cycloaddition reactions of *o*-QDMs can be found in reviews by Fallis[1] and Quinkert.[2]



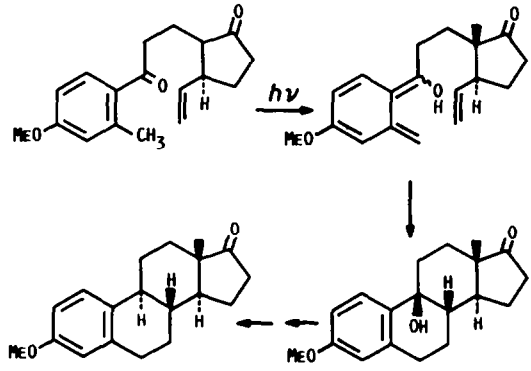
5. ASYMMETRIC INDUCTION IN REACTIONS OF *o*-QUINODIMETHANES

At the threshold of synthetic chemistry, one of the main challenges is to find routes which satisfy the demands of accessibility to enantiomerically pure compounds. The definition of an asymmetric reaction is any reaction in which an achiral substrate, or achiral unit within a molecule, is converted to a chiral substrate or unit with the resulting two chiral forms being produced in unequal amounts.

For the Diels–Alder reaction, asymmetric induction can occur if the reaction can be induced to take place preferentially on one face of the diene or dienophile. While there has been extensive

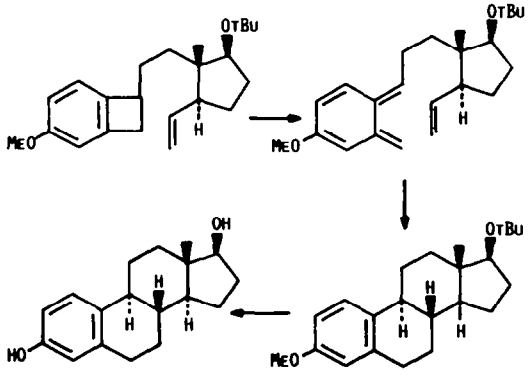


work carried out on asymmetric induction in Diels–Alder reactions of butadienes,[78–83] relatively fewer studies have been made of asymmetric induction in Diels–Alder reactions of *o*-quinodimethanes.[2,9,48,84,76,13] The stereoselectivity of the intramolecular Diels–Alder reaction of *o*-quinodimethanes have been exploited in the preparation of optically pure steroids. Quinkert *et al.* achieved an asymmetric synthesis of a steroid by photochemically generating an *o*-QDM having a chiral substituent which stereochemically controlled an intramolecular Diels–Alder reaction.[2]



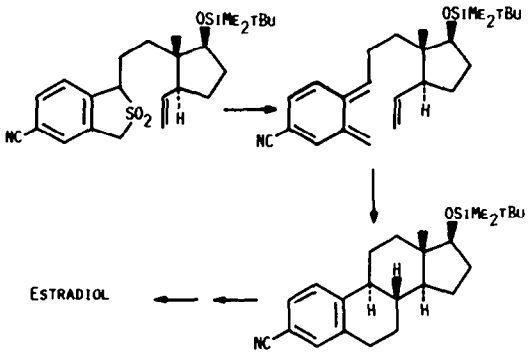
ESTRONE

Kametani *et al.* achieved stereoselectivity in the synthesis of estradiol from a benzocyclobutene by an intramolecular Diels–Alder reaction of a thermally generated chiral *o*-QDM.[9] Oppolzer *et*



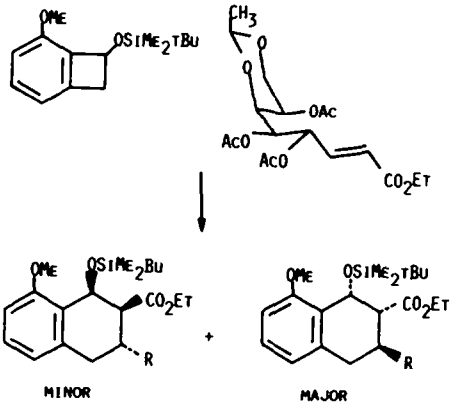
ESTRADIOL

al. also synthesized enantioselectively, (+)estradiol by the intramolecular cycloaddition of an *o*-quinodimethane generated by thermal extrusion of SO_2.[2,85,86] In all of these reactions described



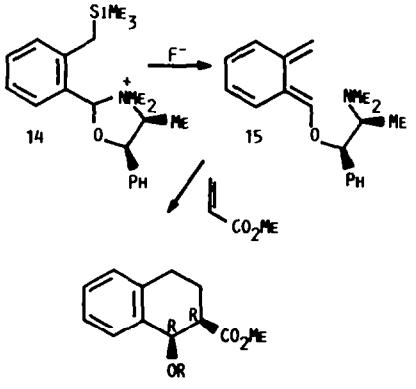
above, asymmetric induction was achieved by a chiral auxiliary which became a part of the product molecule. Due to the configuration of the chiral auxiliary, addition occurred stereoselectively to only one face of both the diene and the dienophile thereby ensuring asymmetric induction at the newly created chiral centres.

Franck *et al.* have studied the intermolecular reaction of an achiral *o*-quinodimethane with a chiral dienophile to determine the relative roles of steric and secondary orbital interactions on the asymmetric induction.[84] Two adducts were formed in the ratio 4:1. Both of the adducts were the



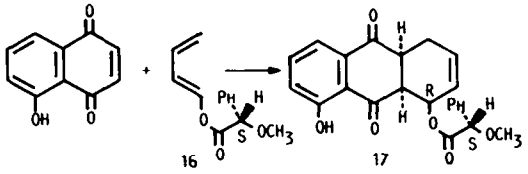
results of *endo* addition of the ester. The authors concluded that orbital interaction predominated over steric interactions in guiding the asymmetric addition.

More recently Ito *et al.* have reacted the oxazolidinium system **14** with fluoride ion to give *o*-quinodimethane **15** bearing a chiral auxiliary that partially controlled the stereochemistry of the subsequent addition of methyl acrylate. Two diastereomers were found in the ratio 2:1 with the *R,R* isomer being the major adduct.[48]



In each case cited so far the asymmetric induction was attributed to the ability of the chiral auxiliary to block one face of the *o*-quinodimethane or to specifically direct the dienophile to one

face of the *o*-quinodimethane. In the case of the work of Ito *et al.*,[48] the presence of an α-phenyl substituent at C-5 of the oxazolidinium ring in **14** markedly increased the asymmetric induction in the intramolecular Diels–Alder cycloaddition via **15**. The enantioselectivity was accounted for in accordance with Trost's and Daubin's observation that π-stacking interactions may serve as a steric factor to block the incoming dienophile from one of the two enantiotopic faces of the diene.[81,82] The π-stacking model had been developed earlier by Trost and used to explain the asymmetric formation of **17**, a key intermediate in the synthesis of tetracyclic natural products.[81] On the basis

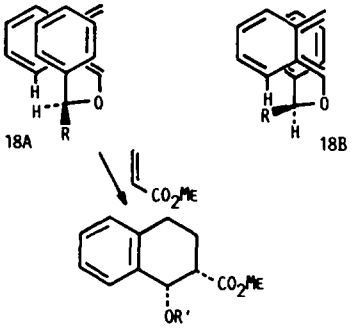


16 17

of the π-stacking model, two conformations can be envisioned for a diene such as **16**. In the folded form represented by **16A**, the large group L projects towards the diene producing a severe nonbonded interaction. Such a nonbonded interaction is much less between the small group S and the diene in

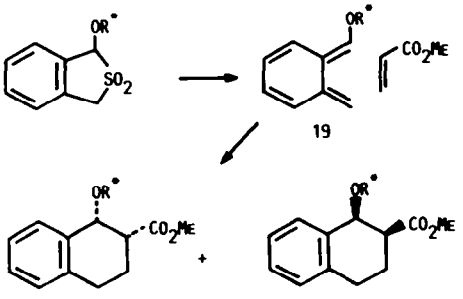
16A 16B

16B, and on this basis **16B** should be the favored conformation. The dienophile should preferentially attack from the bottom face. The aromatic ring serves as a steric control element to direct the incoming dienophile to one of the two enantiotopic faces of the diene. However, the contention that π-stacking could explain the asymmetric induction in the reaction of Ito *et al.* has been shown to be incorrect.[76] From the diagram of **18A** and **18B** it is observed that **18A** should be less hindered, because the nonbonded interaction between the aromatic hydrogen and the benzylic hydrogen adjacent to the ether oxygen is much less than the nonbonded interaction between the aromatic hydrogen and the much more bulky group, i.e. $—CHCH_3N(CH_3)_2$, in **18B**. Addition of the dienophile to the open face of **18A** would lead to a product having a stereochemistry opposite to that observed by Ito *et al.*



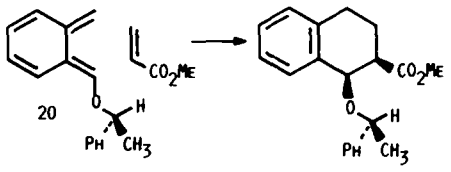
18A 18B

Charlton presented a different explanation for the asymmetric induction in the Diels–Alder reaction of *o*-quinodimethanes.[76] He generated the *o*-quinodimethane **19** by thermal extrusion of SO_2 from a sulfone and added it to the dienophiles, maleic anhydride, dimethyl fumarate and methyl

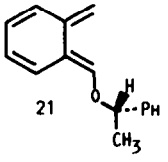


19

acrylate. Various chiral auxiliaries (*R*) were used and in all cases some asymmetric induction was observed. The 1-phenylethyl group yielded the greatest asymmetric induction. In the case of the (*S*)-phenylethyl chiral auxiliary cycloaddition of methyl acrylate to the upper face gave the 1′*S*,1*R*,2*R* cycloadduct similar to the results obtained by Ito *et al.* (see above). Schaefer *et al.* have shown that



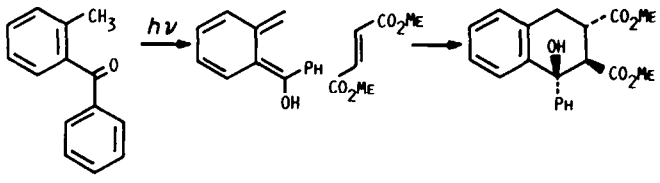
in alkyl phenyl ethers the most stable conformation is one in which the alkyl group lies in the plane of the aromatic ring allowing p–π overlap.[87] On the basis of this analogy Charlton suggested that the preferred conformation of the α-((*S*)-phenylethoxy)-*o*-quinodimethane is as in **20**. In this conformation the relative steric bulk of the phenyl and methyl groups serves to block the lower face of the *o*-quinodimethane and therefore dienophiles add to the upper face. This mechanism is also capable of explaining Ito's earlier results. Close examination of **20** suggests that other conformers such as **21** would be as probable in solution and could also explain the asymmetric induction. It would appear that further work is necessary before a definitive answer to the mechanism of the induction can be formulated.



6. USE OF *o*-QUINODIMETHANES IN ORGANIC SYNTHESIS

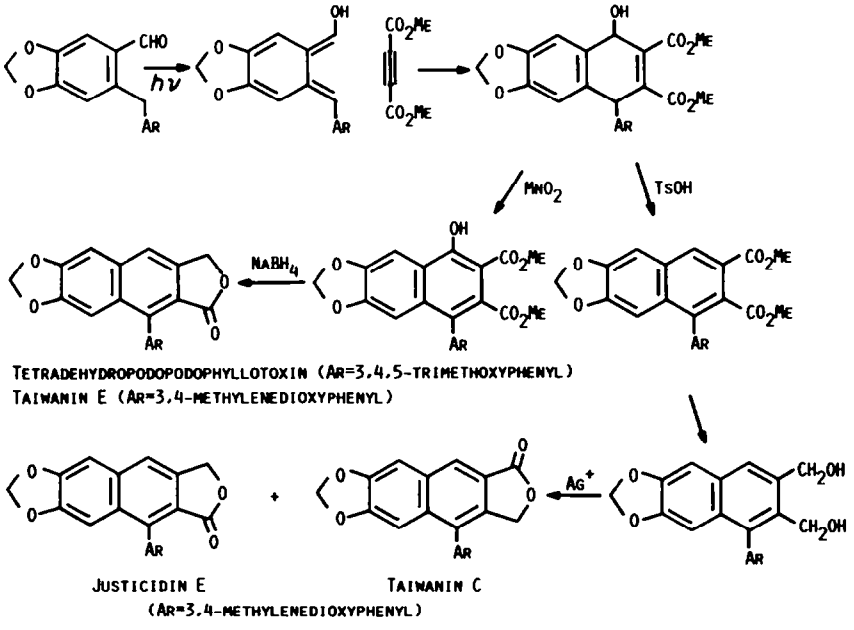
There has been considerable recent interest in the application of *o*-quinodimethanes in organic synthesis based on inter and intramolecular Diels–Alder reactions. In fact, the literature is so extensive that an exhaustive survey would be impractical. The reader is referred to several recent review articles that have appeared.[1-13] In particular Fallis has tabulated many of the intramolecular cycloaddition reactions in a review that covers the literature up to early 1983.[1] The very extensive work of Kametani's group on alkaloids, steroids, terpenes and anthracyclines can be best found in his reviews.[3,9,11,13] Two of the reviews deal specifically with steroid synthesis.[2,9] One area of interest to us is the use of *o*-QDMs in the synthesis of aryltetralin lignans (for a review of lignan and neolignan synthesis see Ref. 88). What follows is a short review of this particular synthetic application of *o*-QDMs.

In 1973, Block and Stevenson first prepared a few lignan analogs via an *o*-QDM by irradiation of 2-methylbenzophenone in the presence of various dienophiles.[74] About the same time, Sammes

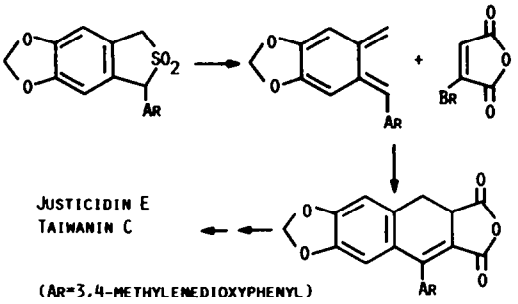


et al., also using photoenolization to produce an *o*-QDM, published syntheses of Taiwanin E and C, Justicidin E and tetradehydropodophyllotoxin.[89] Mann *et al.* have also synthesized Justicidin E and Taiwanin C via 1-(3,4-methylenedioxyphenyl)-1,3-dihydro-5,6-methylenedioxybenzo[c]thiophen-2,2-dioxide.[52,53] Mann used a similar sulphone intermediate to synthesize (+/−)phyltetralin and other lignan analogues.[53,90] (+/−)Deoxyisosikkimotoxin has been synthesized by

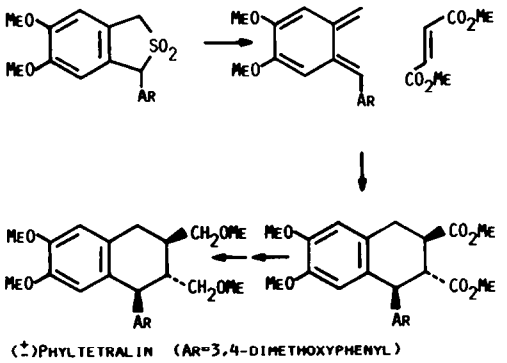
Das *et al.* via an *o*-QDM generated from an isochromanone.[63] Glinski and Durst prepared (+/−)epiisopodophyllotoxin via a photoenol.[91] Takano *et al.* used an unusual 1,4-elimi-

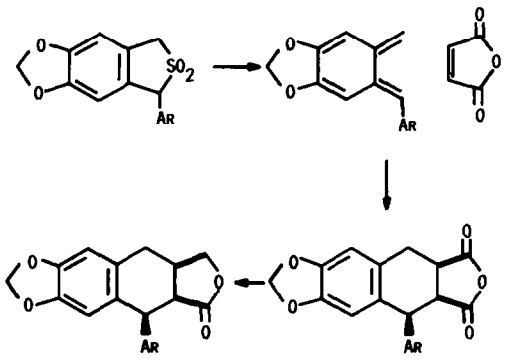


nation process to prepare an *o*-QDM precursor to (+/−)deoxypodophyllotoxin.[92] A key feature in their synthesis was the epimerization of the C-3 carbomethoxy group while protecting the C-2 configuration by forming the salt of the acid at C-2.



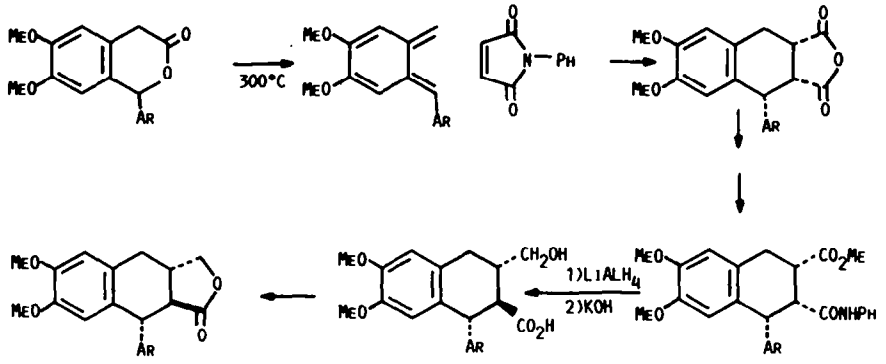
Charlton and Alauddin have recently published the first example of an asymmetric synthesis of an aryl tetralin lignan.[93] They used a chiral auxiliary on the *o*-QDM to control face selectivity of





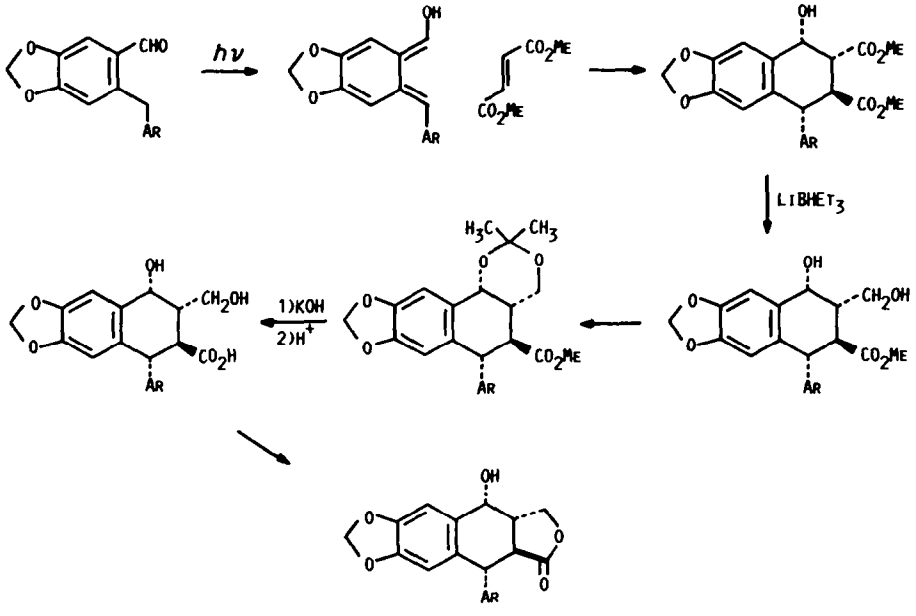
(±)ISODEOXYPICROPODOPHYLLOTOXIN
(AR=3,4,5-TRIMETHOXYPHENYL)

the Diels–Alder addition. Macdonald and Durst very recently published an account of their synthesis

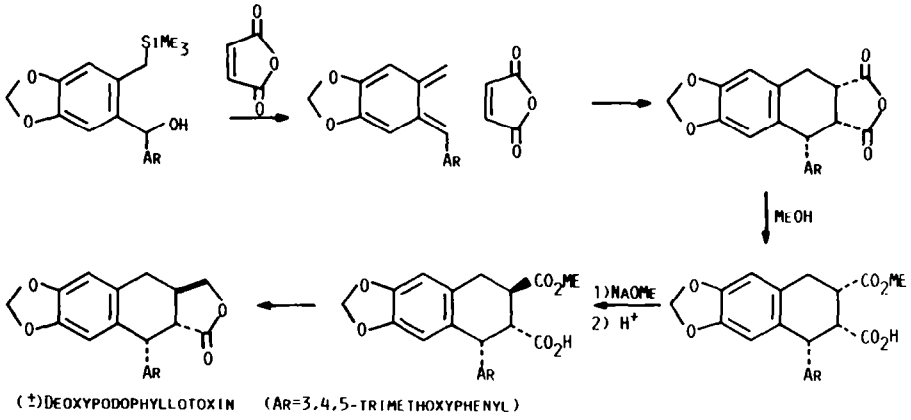


(±)DEOXYISOSIKKIMOTOXIN (AR=3,4,5-TRIMETHOXYPHENYL)

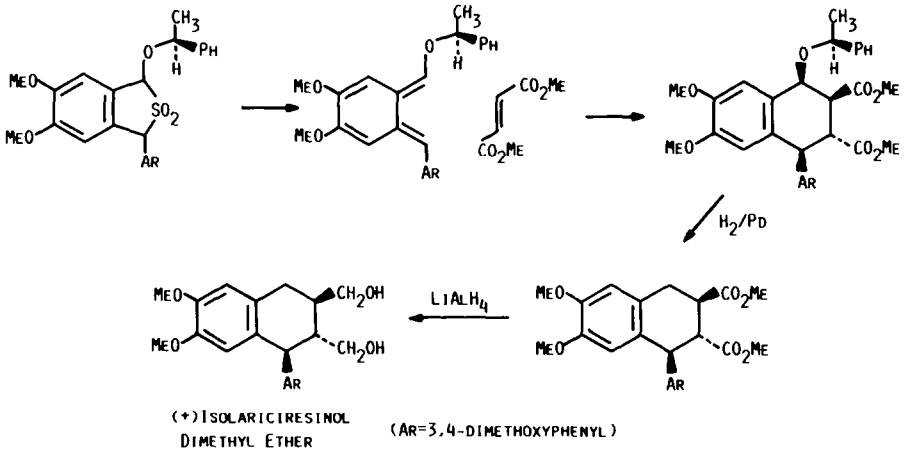
of the medicinally important podophyllotoxin.[77] This lignan, due to its unusual stereochemistry, cannot be synthesized by an intermolecular cycloaddition. By using an intramolecular cycloaddition



(±)EPIISOPODOPHYLLOTOXIN (AR=3,4,5-TRIMETHOXYPHENYL)



Macdonald and Durst were able to control the stereoselectivity of the cycloaddition to produce the podophyllotoxin geometry (see Section 4).



7. CONCLUSIONS

It appears that *o*-quinodimethanes will continue to be of both theoretical and synthetic interest for some time to come. For both intermolecular and intramolecular Diels–Alder reactions there is a high degree of stereoselectivity making *o*-QDMs very useful in synthesis. The addition of asymmetric control to these reaction will only enhance this utility.

Acknowledgement—The authors would like to acknowledge the financial assistance of the Natural Sciences and Engineering Research Council of Canada.

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