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o-QUINONE METHIDES 2.[1] STEREOSELECTIVITY IN CYCLOADDITION REACTIONS OF o-QUINONE METHIDES WITH VINYL ETHERS

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Abstract - Cycloaddition reactions between vinyl ethers **3** and o-quinone methides **2**, thermally generated from 2-hydroxybenzyl alcohols **1**, have been studied. The structure and conformational preferences of the 4-substituted 2-ethoxy-(2,3)-dihydro-2H-benzopyrans **4-9** obtained, which show new interesting features, are discussed together with competitive kinetic data. The cycloaddition process is concerted and involves o-quinone methides in the E-configuration. The OEt-endo transition state seems to be preferred with ethyl vinyl ether and Z-1-propenyl ethyl ether, whereas with E-1-propenyl ethyl ether the stereoselectivity of the cycloaddition process depends on substituents on the methylene group of the starting alcohol **1**. These results are discussed in terms of endo and exo preference of the propenyl ether methyl group.

In the previous paper of this series[1] we reported evidence on the key role played by the configuration (E or Z) of o-quinone methide intermediates in determining the course of reactions between aldehydes and phenol salts in low polarity media.

Useful information on the geometry of these intermediates were obtained by trapping them with ethyl vinyl ether and studying structure and conformation of the cycloaddition products[1].

Several data are available in literature on the reactivity of simple o-quinone methides with ethylenic compounds,[2] but very little is known on the stereochemistry of the cycloaddition process, expecially with o-quinone methides bearing substituents on the methylene group.

On the other hand, some new interest has been recently shown on intramolecular Diels-Alder reactions of o-quinone methides and ethylenic double bonds, as a way to perform the asymmetric synthesis of cannabinol derivatives.[3]

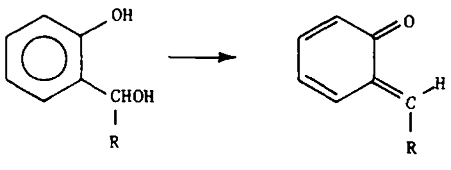
For these reasons we have undertaken a more systematic study of the stereochemistry of intermolecular cycloaddition reactions between o-quinone methides and vinyl ethers and report in this paper the results obtained.

RESULTS

Reactions between o-quinone methides 2 and ethyl vinyl ether 3a

In order to obtain preliminary data on these processes and on the conformational preferences of 4-substituted 2-ethoxy-2,3-dihydro-2H-benzopyrans, the reactions of ethyl vinyl ether with several o-quinone methides were first studied.

These intermediates have been generated by thermal dehydration of the corresponding 2-hydroxybenzyl alcohols **1**. The structure of the cycloaddition products has been established by 200 MHz ^1H NMR, using decoupling experiments for signal assigments.



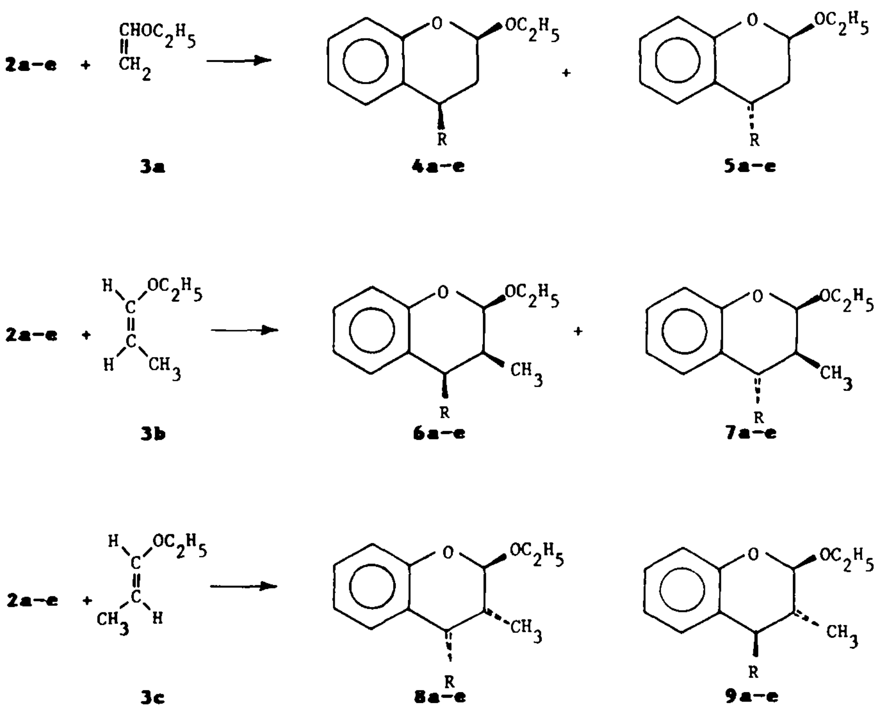
1a-e **2a-e**

a R = C_6H_5
b CH_3
c nC_3H_7
d iC_3H_7
e $C_6H_5CH_2$

Table 1. Reactions of *o*-quinone methides **2a–e** with vinyl ethers **3a–c**

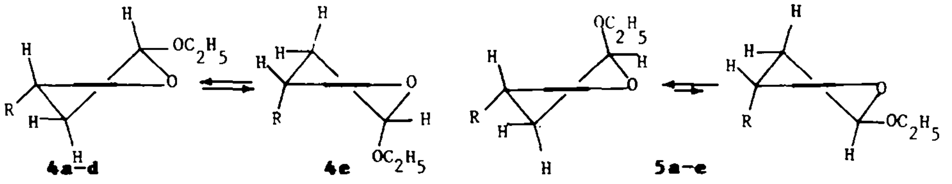
o-quinone methide **2** (R)	ether	cycloaddition products $^+$ total yield (%)	relative yield (%)	
2a (C_6H_5)	**3a** (vinyl)	100	**4a**(75)	**5a**(25)
	3b (propenyl-*Z* isomer)	100	**6a**(70)	**7a**(30)
	3c (propenyl-*E* isomer)	100	**8a**(30)	**9a**(70)
2b (CH_3)	**3a** (vinyl)	50	**4b**(80)	**5b**(20)
	3b (propenyl-*Z* isomer)	35	**6b**(90)	**7b**(10)
	3c (propenyl-*E* isomer)	60	**8b**(45)	**9b**(55)
2c (nC_3H_7)	**3a** (vinyl)	45	**4c**(80)	**5c**(20)
	3b (propenyl-*Z* isomer)	40	**6c**(95)	**7c**(5)
	3c (propenyl-*E* isomer)	45	**8c**(55)	**9c**(45)
2d (iC_3H_7)	**3a** (vinyl)	45	**4d**(90)	**5d**(10)
	3b (propenyl-*Z* isomer)	35	**6d**(90)	**7d**(10)
	3c (propenyl-*E* isomer)	45	**8d**(100)	--
2e ($C_6H_5CH_2$)	**3a** (vinyl)	50	**4e**(60)	**5e**(40)
	3b (propenyl-*Z* isomer)	40	**6e**(95)	**7e**(5)
	3c (propenyl-*E* isomer)	40	**8e**(60)	**9e**(40)

$^+$ yields established by g.l.c.



o-Quinone methide **2a** derived from 2-hydroxybenzhydrol (R = C_6H_5) gives a main reaction product with ethyl vinyl ether **3a** (see Table 1) which shows the same pattern of coupling constants observed previously with R = iC_3H_7[1].

In particular two coupling constants, $J_{2,3'}$ = 8.40 Hz (axial-axial) and $J_{3',4}$ = 10.50 Hz (axial-pseudoaxial), indicate an equatorial position for the 4-phenyl group and a pseudoequatorial one for the 2-ethoxy group in the cycloaddition product, which is therefore "cis" (**4a**).



$$\mathbf{4a{-}e} \xrightarrow[\text{Toluene, 80°C}]{\text{2,4,6-TMPOMgBr}} \mathbf{5a{-}e}$$

A similar behaviour is also shown by o-quinone methides **2b** and **2c** having R = CH_3 and R = nC_3H_7, where a slight decrease in $J_{2,3'}$ and $J_{3',4}$ (6.83 Hz and 8.30 Hz for R = CH_3; 6.59 and 8.40 for R = nC_3H_7) indicates a significant contribution, in product **4b** and **4c**, of the conformer having the 2-ethoxy group in axial and the 4-alkyl in pseudoaxial position.

It is noteworthy that with R = $C_6H_5CH_2$ this last conformer becomes predominant as inferred from the low values of $J_{2,3}$ (3.42 Hz), $J_{2,3'}$ (4.15 Hz), $J_{3,4}$ (5.62) Hz and $J_{3',4}$ (5.37 Hz) observed in compound **4e**.

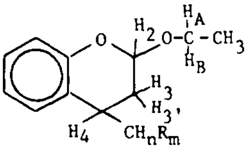


Table 2. Relevant ^1H NMR data for cycloaddition products **4-5**

	Chemical shifts δ(ppm)								Coupling Constants (Hz)					
Comp.	H(2)	H(3)	H(3')	H(4)	H_A	H_B	CH_3	$C(4)-CH_n$	$J_{2,3}$	$J_{2,3'}$	$J_{3,3'}$	$J_{3,4}$	$J_{3',4}$	$J_{H(4),CH_n}$
4a	5.23	2.37	2.17	4.15	4.06	3.64	1.26		2.80	8.40	13.00	6.50	10.50	
5a	5.25	2.22	2.10	4.26	3.90	3.64	1.20		2.80	2.80	13.00	6.30	11.30	
4b	5.18	2.13	1.72	2.91	3.98	3.58	1.22	1.35^a	2.93	6.83	13.43	6.35	8.30	6.80
5b	5.22	2.05	1.69	3.13	3.90	3.63	1.18	1.33^a	2.85	2.85	13.18	5.86	11.23	7.53
4c	5.14	2.15	1.80	2.87	4.00	3.62	1.24	^{b}	2.69	6.59	13.43	6.35	8.40	
5c	5.24	2.06	1.76	3.01	3.91	3.66	1.20	^{b}	2.69	4.15	13.06	5.70	9.50	
5d	5.22	1.87	1.79	2.95	3.82	3.57	1.16	2.36^c	3.30	3.30	12.95	5.80	10.60	4.60
4e	5.17	1.85	1.85	3.08	3.98	3.60	1.25	3.22^c 2.98^c	3.42	4.15	--	5.62	5.37	2.44^d 10.50^e
5e	5.10	1.77	1.62	3.22	3.80	3.52	1.07	3.30^c 2.54^c	2.93	3.91	13.50	5.73	9.40	5.12^d 9.52^e

[a] 3H [b] overlapped signals [c] 1H [d] J with the low field diastereotopic proton [e] J with the high field diastereotopic proton

The definitive proof of the cycloaddition product structure comes from epimerization experiments, using 2,4,6-trimethylphenoxymagnesium bromide (2,4,6-TMPOMgBr) as catalyst which transforms the cis product in the corresponding trans.[4]

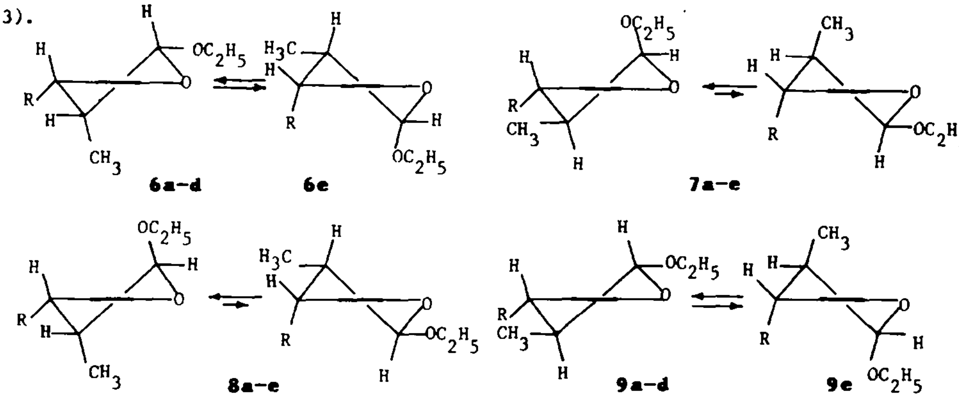
The latter shows in most cases (**5a–d**; R = C_6H_5, CH_3, nC_3H_7 and iC_3H_7) a strong decrease in the $J_{2,3'}$ which ranges between 2.80 Hz (R = C_6H_5) and 4.15 Hz (R = nC_3H_7), while the $J_{3',4}$ experiences a significant change only in **5e** and ranges between 9.40 Hz (R = $C_6H_5CH_2$) and 11,30 Hz (R = C_6H_5).

These data support the trans configuration for all the epimerized products **5a–e** with the 2-ethoxy group in the more stable axial position and the 4-substituent in the pseudoequatorial one.

Reactions of o-quinone methides with 1-propenyl ethyl ethers (E and Z)

Also in the series of reactions with the vinyl ethers **3b** and **3c** our reference point has been the o-quinone methide derived from 2-hydroxybenzhydrol **1a**. In fact it was expected that some benefit in establishing the structure of reaction products could derive from existing data on cycloaddition reactions of β-aryl-α,β-unsaturated carbonyl compounds and vinyl ethers[5] and from reported conformational studies on 2-alkoxy-4-aryl-2,3-dihydropyrans[6].

As observed with α,β-unsaturated carbonyl compounds, two cycloaddition products **6a** and **7a** are obtained in good yields in the reaction of o-quinone methide **2a** with Z ether **3b**, whereas the other two diastereoisomeric 2,3-dihydropyrans **8a** and **9a** are produced with E isomer **3c** (see Tab.3).

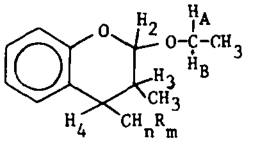


6a–d **6e** **7a–e**

8a–e **9a–d** **9e**

$$\mathbf{6a–e} \xrightarrow[\text{Toluene, 80°C}]{\text{2,4,6-TMPOMgBr}} \mathbf{8a–e} \qquad \mathbf{9a–e} \xrightarrow[\text{Toluene, 80°C}]{\text{2,4,6-TMPOMgBr}} \mathbf{7a–e}$$

Table 3. Relevant ^1H NMR data for cycloaddition products **6-9**



	Chemical shifts δ (ppm)								Coupling Constants (Hz)			
Comp.	H(2)	H(3)	H(4)	$CH_3(3)$	H_A	H_B	CH_3	$C(4)-CH_n$	$J_{2,3}$	$J_{3,4}$	J_{3,CH_3}	$J_{H(4),CH_n}$
6a	5.16	2.36	4.34	0.84	4.02	3.61	1.21		2.20	6.60	6.83	
7a	5.13	2.26	3.88	0.89	3.90	3.66	1.20		2.20	10.50	6.84	
8a	4.93	2.11	4.39	0.72	3.81	3.61	1.13		3.66	7.32	7.08	
9a	4.77	2.11	3.60	0.87	4.00	3.61	1.20		8.06	9.76	6.60	
6b	5.06	2.17	2.97	1.01	3.96	3.58	1.21	1.32[a]	2.20	5.85	7.10	7.08
7b	4.98	1.75	2.74	1.07	3.85	3.60	1.15	1.31[a]	2.20	10.01	6.84	6.84
8b	4.92	1.99	3.23	0.84	3.90	3.60	1.16	1.25[a]	2.93	5.13	7.08	7.32
9b	4.78	1.79	2.51	1.04	3.90	3.60	1.19	1.33[a]	5.37	6.10	7.08	7.08
6c	5.08	2.44	2.94	0.92	4.07	3.65	1.30	[b]	2.20	4.78	6.83	
7c	5.00	2.01	2.69	1.01	3.93	3.62	1.22	[b]	2.44	7.56	6.83	
8c	4.96	2.06	2.97	0.77	3.82	3.57	1.11	[b]	2.93	4.88	7.08	
9c	4.83	2.10	2.45	1.01	3.92	3.56	1.18	[b]	3.90	4.15	7.10	
6d	5.03	2.27	2.74	0.98	4.04	3.62	1.30	2.37[c]	2.94	4.90	6.80	4.70
8d	4.88	2.12	2.85	0.95	3.93	3.60	1.20	2.30[c]	4.30	4.90	6.60	4.80
6e	5.05	2.06	3.23	1.01	4.02	3.58	1.29	3.24[c] 2.89[c]	2.20	5.84	6.83	6.83[d] 10.50[e]
8e	4.92	1.88	3.56	0.88	3.87	3.60	1.16	3.39[c] 2.69[c]	2.93	4.64	6.80	6.47[d] 9.77[e]
9e	4.93	2.13	2.77	0.87	3.93	3.57	1.26	3.30[c] 3.00[c]	2.19	1.71	7.08	10.80[d] 5.25[e]

[a] 3H [b] overlapped signals [c] 1H [d] J with the low field diastereotopic proton [e] J with high field diastereotopic proton

The configuration and the conformational preferences of cycloaddition products have been assigned on the basis of ^1H NMR data (J and δ) compared with similar ones reported in literature. In particular the $J_{3,4}$ values (10.50 and 10.01 Hz) observed in products **7a** and **7b** indicate the equatorial position of the 3-methyl group and the pseudoequatorial for substituent in position 4. Similarly for compound **9a** the $J_{2,3}$ = 8.06 Hz and $J_{3,4}$ = 9.76 Hz indicate an equatorial position for substituents in 2 and 3 and pseudoequatorial for substituent in 4. Other useful stereochemical informations on products **6a**-**9a** can be obtained by looking at the chemical shift of H-2, H-4 and diastereotopic methylene protons of ethoxy groups of substituted dihydropyrans of known structure, having the 4-aryl group in the pseudoequatorial position[5,6].

In fact, some empirical rules (a-c), which can be useful for establishing the configuration and the preferred conformation, have been deduced by the critical examination of a complete set of ^1H NMR spectra of cycloaddition products from both literature and our data.

a) The H-2 chemical shifts (δ) are in the order **6**>**7**>**8**>**9**;

b) the H-4 chemical shifts (δ) are in the order **8**>**6**>**7**>**9**;

c) a $\Delta\delta$ = 0.2-0.3 ppm between the chemical shift of the two diastereotopic methylene protons of the ethoxy group is diagnostic for an axial position, whereas a $\Delta\delta$ = 0.35-0.45 ppm suggests an equatorial position for this group.

The first two rules (a-b) can be ractionalized considering that i) an axial proton is more shielded than its equatorial counterpart,[7] ii) a 3-methyl group in axial position exerts a deshielding effect on the vicinal axial proton, whereas in all other relative conformations causes a shielding effect,[8] iii) an axial 2-ethoxy group causes a deshielding effect on the axial proton in 4-position (1,3-diaxial interaction).[9] The last rule c) can be understood considering the effect of a phenyl over the ethoxy group.

So the main cycloaddition product of o-quinone methide derived from 2-hydroxybenzhydrol **1a** (R = C_6H_5) with **3b** (Z isomer) results to be **6a** (cis-cis product) with **7a** as a minor component, whereas with the **3c** (E isomer) the main reaction product is **9a** (trans-trans) with **8a** present as a byproduct. The more stable cis-trans products **7a** and **8a** can be obtained in a pure form through epimerization experiments, by treating respectively **9a** and **6a** with 2,4,6,-TMPOMgBr in toluene.

o-Quinone methides derived from 2-hydroxybenzyl alcohols **1b** and **1c** (R = CH_3 and nC_3H_7) give with **3b** (Z isomer) pratically one cycloaddition product **6b** and **6c** (90%) whereas with the E isomer **3c** two products **8b** and **9b** or **8c** and **9c** are obtained in almost equal amount.

Other two products **7b** and **7c** could be obtained by epimerization experiments respectively from **9b** and **9c** and their ^1H NMR spectra could be therefore registered and analyzed.

2-Hydroxybenzyl alcohol **1d** (R = iC_3H_7) gives a mayor product **6d** in the reaction with Z-1-propenyl ethyl ether **3b** with very little amount of the other stereoisomer **7d**, whose H-2 chemical shift (4.99 ppm) and $J_{2,3}$ coupling constant (2.44 Hz) can be easily detected in the ^1H NMR spectrum of the major component **6d**. Only one cycloaddition product **8d** is obtained in the reaction with the E isomer **3c**. A definitive proof of these structural assignments has been obtained by epimerization experiments in the presence of 2,4,6-TMPOMgBr, which converts **6d** in **8d** as expected.

Finally the reaction of alcohol **1e** (R = $C_6H_5CH_2$) with the vinyl ether **3b** (Z isomer) produces only **6e** whereas with **3c** (E isomer) gives **8e** and **9e** in almost equal amount.

As observed previously for compound **4e**, compound **9e** (trans-trans) has the 4-benzyl group in pseudoaxial and 2- and 3-substituents in axial position. This is inferred from the observed coupling constants $J_{2,3}$ = 2.19 Hz, $J_{3,4}$ = 1.71 Hz and $J_{2,4}$ = 1.0 Hz.[10]

It has been more difficult to establish the conformational preference of compound **6e** due to the absence of an axial-axial coupling constant in the two conformers. Looking at the $\Delta\delta$ between the two diastereotopic methylene protons of the benzyl group, which is 0.35 ppm, it is possible to hypothesize that the predominant conformer has the benzyl group in pseudoaxial position. In fact $\Delta\delta$ is usually $\simeq$ 0.3 ppm in compounds having the benzyl group in pseudoaxial and $\simeq$ 0.7 ppm when it is in pseudoequatorial position (see compds **4e**, **5e**, **8e**,**9e** in Table 3).

DISCUSSION

Conformational preferences of 4-substituted 2-ethoxy-2,3-dihydro-2H-benzopyrans.

The spectral and chemical evidences which led us to establish the structure of the numerous cycloaddition products obtained in this study allow also to draw some general conclusions on the conformational preferences of substituted 2,3-dihydrobenzopyran rings.

Some data obtained are in agreement with observations already put forward,[6] some other reveal new interesting conformational features.

2,3-Dihydrobenzopyran derivatives exist in rapidly inverting half chair forms and the conformational equilibrium seems to be determined by two main factors:

1) the anomeric effect which justifies the observed axial preference of the ethoxy group;

2) the strong tendency of a substituent in position 4 of dihydrobenzopyran ring to occupy the pseudoequatorial position if the steric interaction with the fused aromatic ring ("peri" position) is neglegible.

These two factors are in competition and our results indicate that the latter is usually more important since all 4-substituents (except benzyl) occupy the pseudoequatorial position.

As a consequence, we deduce that even in the case of a bulky group like isopropyl the steric interaction between the 4-substituent and the fused aryl ring is small.

When benzyl group is present in the 4-position of the ring, a new conformational effect seems to operate since this group shows a strong tendency to occupy the axial position.

In fact, the "cis" cycloaddition product **4e**, the "cis-cis" **6e** and the "trans-trans" **9e** have the benzyl group in pseudoaxial position. This effect does not seem to be due to steric interactions with the fused aromatic ring since, as pointed out before, this interaction in our systems is neglegible even for iC_3H_7 group which is bulkier than $C_6H_5CH_2$.

The exact nature of this new conformational effect is not clear at the moment and we are currently investigating the hypothesis that some secondary attractive interactions could stabilize the benzyl group in pseudoaxial position.

Cycloaddition Mechanism

On the basis of recent X-ray studies of stable *o*-quinone methide intermediates[11] and on the reported very low reactivity in cycloaddition processes of *Z*-α,β-unsaturated carbonyl compounds[5] we reasonably assume an *E* configuration for our reacting *o*-quinone methides.

Moreover it has been verified that the ratio between stereoisomeric cycloaddition products remains constant during the reaction and that the stereochemistry of the starting vinyl ethers is retained in the products.

These data suggest a kinetically controlled and concerted[12] cycloaddition process between *E* *o*-quinone methides and vinyl ethers.

Therefore other useful informations have been obtained by performing competitive kinetic experiments on these cycloaddition processes (Table 4).

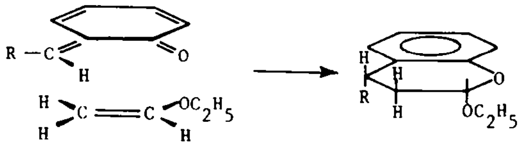
Table 4. Competitive reactions between *o*-quinone methides **2a–d** and ethyl vinyl ethers **3a–c**

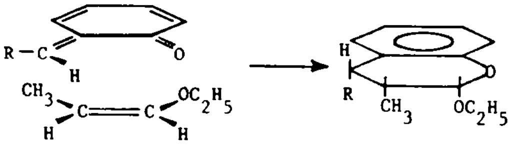
	Vinyl ethers relative reactivity				
o-quinone methide	vinyl	*E*-propenyl		*Z*-propenyl	
	(4+5)	**6**	**7**	**8**	**9**
2a	1	0.09	0.02	0.35	0.65
2b	1	0.54	--	0.49	0.33
2c	1	0.43	--	0.55	0.49
2d	1	0.39	--	0.82	--

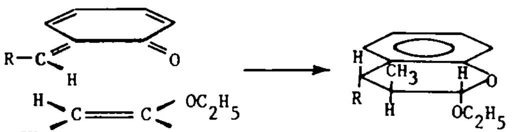
They show that reactivity generally follows the order: ethyl vinyl ether **3a** > E-1-propenyl ethyl ether **3b** > Z-1-propenylethyl ether **3c**[13], calling for a negative steric effect of the methyl group on the dienophile.

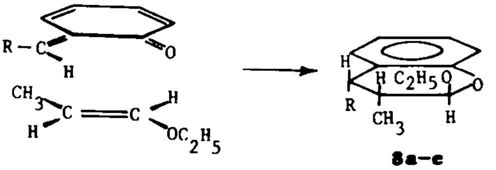
Usually the "endo"/"exo" selectivity in cycloaddition processes involving vinyl ethers is explained in terms of secondary attractive interations between the ethereal oxygen and the diene moiety. Our data show that the situation is more complex and also the effect of other substituents on both diene and dienophile have to be taken into account.

The reactions of ethyl vinyl ether **3a** and Z-1-propenyl ethyl ether **3b** can be ractionalized as a "normal" endo attack (respect to OEt) through a transition state stabilized by secondary attractive interactions between the oxygen of the ethoxy group and the carbonyl of the o-quinone methide.[14]


4a-e


6a-e


9a-e


8a-e

The behaviour of E-1-propenyl ethyl ether **3c** is more complex since the stereoselectivity of the cycloaddition process is strongly dependent on the substituent R on the methylene of the o-quinone methide. A normal endo selectivity is observed with R = C_6H_5, in agreement with the general trend shown by β-aryl-α,β-unsaturated carbonyl compounds in analogous cycloaddition reactions,[14] whereas with R = CH_3, nC_3H_7 and $C_6H_5CH_2$ an almost equal proportion of endo and exo processes is observed and the latter becomes the sole reaction pathway with R = iC_3H_7.

It appears from both kinetic and stereochemical data that selectivity in these processes depends not only on the OEt but also on the methyl group of the vinyl ether, which shows a certain degree of "directing effect". So a strong tendency to have this group exo appears in the case of phenyl-substituted o-quinone methides, whereas a methyl-endo selectvity is observed with alkyl substituents.[15]

CONCLUSIONS

The results obtained in this study, which refer to several cycloaddition reaction of methylene-substituted o-quinone methides and vinyl ethers and to the ^1H NMR stereochemical analysis of a quite large number of products allow us to reach some general conclusions on the conformational preferences of 4-substituted 2-ethoxy-2,3-dihydro-2H-benzopyrans, most of which are new products, and on the cycloaddition mechanism.

The conformational equilibrium in the cycloaddition products **4-9** is mainly determined by the preference of the 4-alkyl-substituent to occupy the pseudoequatorial position. This tendency is more important than the anomeric effect which is usually invoked to explain the conformational preferences in similar systems. An exception to this general trend is represented by the benzyl group for which a new conformational effect, forcing the substituent in pseudoaxial position, seems to operate. The cycloaddition mechanism appears to be concerted and the *o*-quinone methides react in the *E*-configuration, as previously suggested for other reactions of these intermediates.[1]

The data indicate a strong influence of the methyl group on the vinyl ether on both reactivity and stereoselectivity of cycloaddition.

The observed reactivity sequence indicates a negative steric influence of the methyl substituent on the vinyl ether dienophile. This group changes also the stereoselectivity of the process, which is usually *endo* respect to OEt, toward a CH_3-*endo* reaction with α-alkyl-substituted *o*-quinone methides and a CH_3-*exo* in the case of a phenyl substituted intermediate.

EXPERIMENTAL SECTION

Mass spectra were recorded by a 1020 Finnigan quadrupole instrument at 70 e.V. ^1H NMR spectra were measured at 200 MHz (CXP 200-Brucker) in $CDCl_3$ with TMS as internal standard. Chemical shift (δ) are expressed in ppm. G.L.C. analyses were performed on a DANI 3900 instrument with a capillary coloumn (SE 52).

Chemicals. Ethyl vinyl ether (Fluka) was purified by distillation. *Z*- and *E*-1-propenyl ethyl ether (Fluka) were purchased as a 70/30 mixture and separated by spinning-band coloumn distillation.[16] α-Phenyl-,[17] α-methyl-,[17] α-propyl-,[18] α-i-propyl-[19] and α-benzyl[20]-2-hydroxybenzylalcohols were prepared from 2-hydroxybenzaldehyde as previously reported.[19]

Reactions of o-quinone methides 2a-e with vinyl ethers 3a-c.

The 2-hydroxybenzylalcohols **1** (1 mmol) are suspended in hexane (15 ml) in a thick-wall glass tube, previously purged with nitrogen, and the vinyl ethers **3** (2 mmol) are added. The tube is closed under N_2 with a teflon valve and kept at 170°C in an oil bath for 24 h. The reaction products are purified by preparative TLC using hexane/ethylacetate (99/1) as eluent and are oily or low melting compounds.

Table 5. MS data, m/e (%), for compounds **4-9** at 70 eV

4a	254(15); 208(100); 181(78); 152(11)	**6b**	206(18); 191(11); 160(25); 145(100)
5a	254(19); 208(100); 181(79); 152(21)	**7b**	206(16); 191(10); 160(28); 145(100)
4b	192(48); 177(57); 146(51); 131(100)	**8b**	206(30); 191(16); 160(33); 145(100)
5b	192(30); 177(38); 146(41); 131(100)	**9b**	206(32); 191(16); 160(34); 145(100)
4c	220(21); 177(100); 149(28); 131(97)	**6c**	234(19); 191(74); 147(33); 145(100)
5c	220(11); 177(100); 149(15); 131(98)	**7c**	234(18); 191(100); 147(20); 145(71)
5d	220(4); 177(52); 149(11); 131(100)	**8c**	234(16); 191(93); 147(33); 145(100)
4e	286(3); 177(100); 149(21); 133(33)	**9c**	234(10); 191(87); 147(35); 145(100)
5e	286(5); 177(100); 149(20); 133(30)	**6d**	234(7); 191(100); 147(32); 145(57)
6a	268(10); 181(100); 222(48); 207(67)	**8d**	234(8); 191(100); 147(31); 145(52)
7a	268(11); 181(100); 222(33); 207(56)	**6e**	282(3); 191(100); 147(72); 145(58)
8a	268(4); 181(100); 222(22); 207(51)	**8e**	282(2); 191(71); 147(59); 145(100)
9a	268(8); 181(100); 222(19); 207(46)	**9e**	282(2); 191(48); 147(100);145(73)

For competitive kinetic experiments 5 mmol of the vinyl ether **3** and 5 mmol of the alcohol **1** in 15 ml of hexane are used and the crude reaction product, after evaporation of the solvent, analyzed by integration of H-2 and H-4 signals in the ^1H NMR spectrum.

Epimerization experiments with 2,4,6-trimethylphenoxymagnesium bromide.

The proper 2,3-dihydro-2*H*-benzopyran (0.5 mmol) is added to a toluene solution (15 ml) containing 0.6 mmol of 2,4,6-trimethylphenoxymagnesium bromide. The reaction mixture is kept at 80°C for 3 h, then quenched with saturated aqueous ammonium chloride (10 ml) and extracted with diethyl ether (3 x 10 ml). The combined ethereal extracts are dried with anhydrous sodium sulphate, and after evaporation of the solvent the products are purified by preparative TLC using hexane/ethylacetate (99/1) as eluent.

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