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Regiospecific Fragmentation of Benzene Derivatives : Synthetic and Analytical Applications

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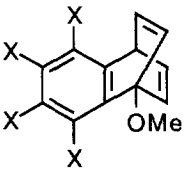
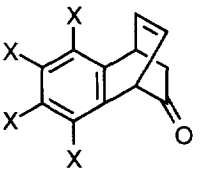
Abstract: *The cycloadducts formed from arenes and tetrachloro- and tetrafluorobenzyne have been shown to undergo specific addition-fragmentation reactions. These sequences are both simple syntheses of arenes with unusual substitution patterns and a convenient alternative to the other methods currently available for assaying the isotopic distribution in [^{14}C]-labelled benzene derivatives.*

Introduction

We have previously discussed[1] our need to prepare specifically radiolabelled derivatives of 1,4-dihydro-1-methoxy-1,4-ethenonaphthalene (**1**) (1-methoxybenzobarrelene) and its tetrachloro- (**2**) and tetrafluoro- (**3**) derivatives. It was anticipated[1a] that acid-catalysed rearrangement of these derivatives would distribute the radiolabel into various positions of the 3,4-dihydro-1,4-ethenonaphthalen-2(1*H*)-ones (**4-6**) (benzobarrelenones) produced. In order to be able to determine the amount of skeletal rearrangement we would need to be able to individually recover the carbon atoms of the non-benzo portion of the benzobarrelenones in a form suitable for radio-chemical assay. Moreover, we would also need to establish the specificity of the original labelling as a basis for comparison for subsequent results. The benzobarrelenes required for the study would be formed *via* cycloaddition of a tetrahalobenzyne[2] to a radiolabelled anisole. We would need to determine the specificity of the radiolabelling of either the cycloadduct or the original anisole. We were unimpressed by the heroic methods available[3] for the carbon-by-carbon degradation of anisole. It seemed clear that if a suitable solution could be found to the problem of specifically degrading benzobarrelene derivatives then that solution would simultaneously be a novel and specific degradation of the arene from which the benzobarrelene had been formed.

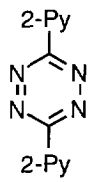


(**1**) X = H
(**2**) X = Cl
(**3**) X = F

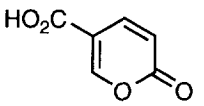


(**4**) X = H
(**5**) X = Cl
(**6**) X = F

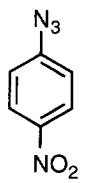
The etheno-bridges of benzobarrelenes are extruded above 200 °C, whereas the ethano-bridges of the corresponding dihydrobenzobarrelenes may be readily eliminated at lower temperatures.[2c,4] It seemed likely that if the fragment eliminated were itself aromatic then the fragmentation would be spontaneous at about room temperature.[5] Any reagent that would undergo cycloaddition with an acetylene to produce an aromatic compound would react with a benzobarrelene to remove a pair of carbon atoms selectively and unambiguously. Since the benzobarrelene would have been prepared[2,6] unambiguously from an arene the sequence would constitute a regiospecific fragmentation of the arene. The reagent would have to be not only reactive enough to undergo cycloaddition to an unactivated and relatively strain free olefin but also substituted so that the extruded aromatic fragment would be crystalline and different in its physical properties from the normally neutral and non-polar naphthalenes that would also be formed. Several 1,3-dienes might undergo the initial cycloaddition but 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**)[7] and coumalic acid (**8**)[8] appear to fulfil all of the criteria and were evaluated as reagents for this purpose. A range of 1,3-dipoles might also be considered and there is a brief report[9] that aryl azides will bring about the desired fragmentation in a similar system: 4-nitrophenylazide (**9**) should react relatively readily to give a crystalline triazole[10] with suitable physical properties so it was also evaluated as a fragmentation reagent.



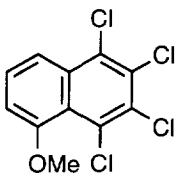
(**7**)



(**8**)



(**9**)



(**10**)

We were interested in two aspects of the cycloaddition-induced fragmentation. We needed to know firstly whether there were suitable reaction conditions and if so what they might be and secondly what sort of selectivity these reactions would exhibit under those conditions if the reaction were to be applied to unsymmetrical benzobarrelenes.

It seemed unlikely that benzobarrelenones would fragment under the influence of these reagents. We adopted two related strategies: in one approach the benzobarrelenones could be converted into benzobarrelenes so that cycloaddition-induced fragmentation reactions could be applied to the problem; in the other approach we sought to convert the oxoethano-bridge -a dihydroketene bridge - into a dihydro- derivative of a more stable olefin. Unpublished observations[11] in our laboratory had indicated that a tertiary hydroxyethano-bridge - a dihydroenol - might be an especially labile bridge. We have evaluated the Grignard reagent induced fragmentation as a method of degrading benzobarrelenones to molecules suitable for radiochemical assay.

We describe in this paper the development of fragmentation reagents for the specific degradation of benzobarrelenes and benzobarrelenones. The high yielding and specific nature of these processes allows them to be used as simple syntheses of their products. The combination of these methods with the well developed cycloaddition of tetrahalobenzynes to arenes provides a simple method for determining the distribution of an isotopic label within the arene. The applicability of and the limitations on this method are described.

Results and Discussion

The reaction with coumalic acid (**8**) was investigated first because it would form benzoic acid, which is a very convenient form in which to isolate a radioactive fragment. A series of small scale experiments was carried out using 1-methoxytetrachlorobenzobarrelene (**2**). The effects of varying the solvent, the reaction time and temperature, the relative amount of coumalic acid (**8**), and of adding catalysts to the reaction were investigated. The reaction products were separated into acidic and neutral fractions and the progress of the reaction was assessed by ^{1}H n.m.r. spectroscopy. The results are summarised in Table 1.

Table 1

The Effect of Solvent, Time, Temperature, and increasing Concentration of Coumalic Acid on the Reaction between 1-Methoxy-5,6,7,8-tetrachlorobenzobarrelene and Coumalic Acid

Equivalents of coumalic acid	Temperature (°C)	Time (h)	Solvent	% Reaction
2	195 ± 5	3.50	Acetic acid	95 [a]
2	195 ± 5	20.00	Acetic acid	> 97 [a]
2	195 ± 5	3.50	Di-n-butyl ether	84
2	195 ± 5	20.00	Di-n-butyl ether	> 98
2	195 ± 5	3.50	*p*-Xylene	88
2	195 ± 5	20.00	*p*-Xylene	> 98
2	195 ± 5	3.50	*N*-Me-pyrrolidone[c]	-
2	195 ± 5	20.00	*N*-Me-pyrrolidone[c]	48
1	205 ± 5	0	Acetic acid	0 [a]
1	205 ± 5	1.17	Acetic acid	44 [a]
1	205 ± 5	2.05	Acetic acid	68 [a]
1	205 ± 5	3.05	Acetic acid	70 [a]
1	205 ± 5	4.32	Acetic acid	77 [a]
1	205 ± 5	6.00	Acetic acid	79 [a]
1	160 ± 5	3.50	Acetic acid	27 [a]
1	180 ± 5	3.50	Acetic acid	33 [a]
1	205 ± 5	3.50	Acetic acid	71 [a,b]
1	220 ± 5	3.50	Acetic acid	82[a]
1	195 ± 5	20.00	*N*-Me-pyrrolidone[c]	26
2	195 ± 5	20.00	*N*-Me-pyrrolidone[c]	50
4	195 ± 5	20.00	*N*-Me-pyrrolidone[c]	75
8	195 ± 5	20.00	*N*-Me-pyrrolidone[c]	92

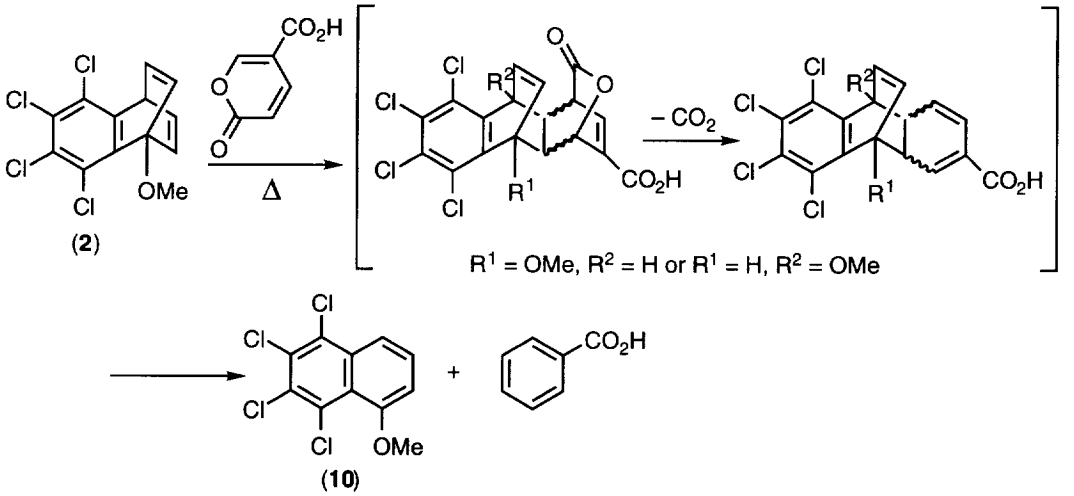
[a] 0.25 mmol of each reactant heated in acetic acid (1 mL) at the indicated temperature.

[b] value interpolated from time dependence study at this temperature.

[c] *N*-Me-pyrrolidone is *N*-methylpyrrolidone.

The reaction proceeded cleanly and rapidly at temperatures above about 200 °C in acetic acid, *p*-xylene, or di-*n*-butyl ether. *N*-Methylpyrrolidone was unsatisfactory. Although the characteristic "inverse electron-demand" of coumalic acid (**8**) cycloadditions[12] might be enhanced in acetic acid and diminished in *N*-methyl-pyrrolidone the marginal advantage of acetic acid over *p*-xylene and di-*n*-butylether suggests that the important feature of the solvent is that it should be inert under the reaction conditions. 1-Methoxybenzobarrelenes are known to be rearranged by strong acids[1b,9a,13] but proved to be stable to hot acetic acid in this case (but *vide infra*).

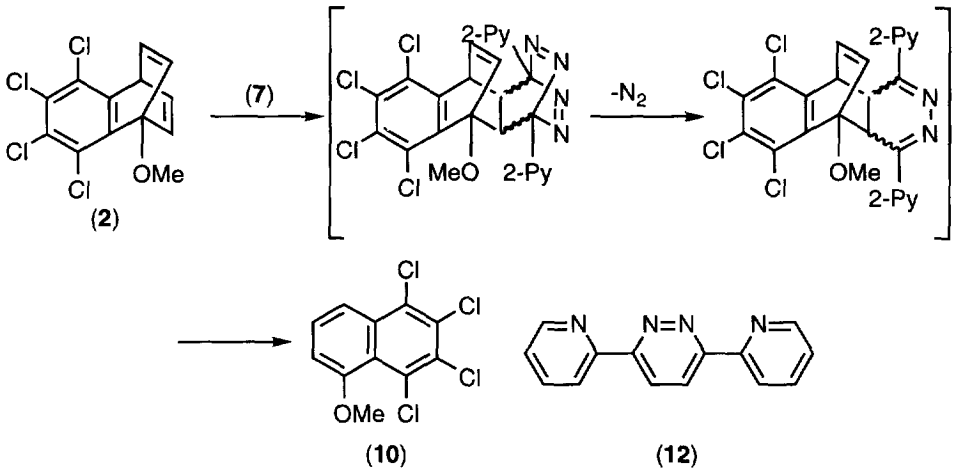
The ratio (**10**) : (**2**) from an equimolar reaction was linearly dependent on time and its logarithm showed an inverse linear dependence on temperature. The extent of reaction increased sharply as an excess of coumalic acid (**8**) was added. At no time were any intermediate products detected. These results are consistent[14] with a reaction that is first order in both 1-methoxytetrachlorobenzobarrelene (**2**) and coumalic acid (**8**)- second order overall - where the product of the first step decomposes rapidly and irrreversibly to the observed products (*Scheme 1*). Attempts to catalyse the cycloaddition with aluminium chloride or boron trifluoride etherate led to demethylation and other types of decomposition.



Scheme 1

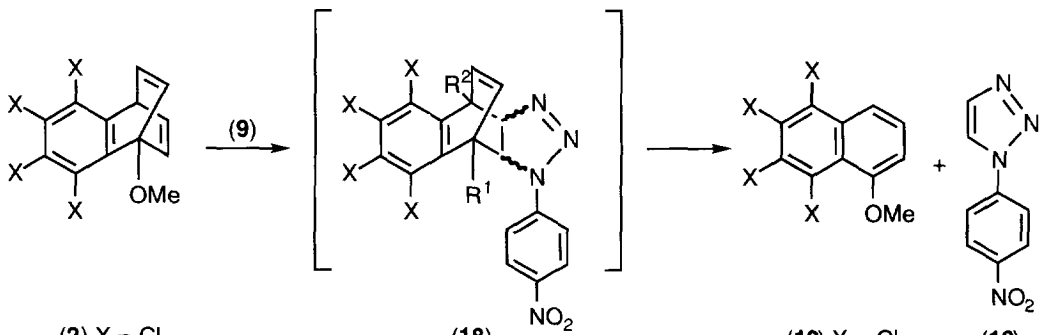
These experiments define conditions for the reaction. Thus when 1-methoxytetrafluorobenzobarrelene (**3**) was heated in *p*-xylene at 200 ± 5 °C for 4 h with 2 equivalents of coumalic acid (**8**) the reaction proceeded to completion to give 1,2,3,4-tetrafluoro-5-methoxynaphthalene (**11**) (94%) and benzoic acid (71%).

Although we had successfully defined the conditions for reactions with coumalic acid (**8**) they were more severe than we had wanted. The conditions for the other reactions were milder and more easily found. The reaction of equimolar amounts of 1-methoxytetrachloro-benzobarrelene (**2**) and 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) proceeded to completion in 2.5 h in boiling di-*n*-butylether to give 1,2,3,4-tetrachloro-5-methoxynaphthalene (**10**) (96%) and 3,6-di-(2'-pyridyl)pyridazine (**12**) (83%). The progress of this reaction is - as usual - easily followed by the disappearance of the bright red colour[15,16] of the tetrazine. No intermediates in or by-products of this reaction were observed (*Scheme 2*).



Scheme 2

The reaction of 1-methoxytetrachlorobenzobarrelene (**2**) with a slight excess of 4-nitrophenylazide (**9**) in boiling benzene for 24h gave the expected naphthalene (**10**) (84%) and 1-(4-nitrophenyl)-1,2,3-triazole (**13**) (69%). A similar reaction with 1-methoxytetrafluorobenzobarrelene (**3**) gave the expected naphthalene (**11**) (80%) and the triazole (**13**) (79%) (*Scheme 3*).



(**2**) X = Cl
(**3**) X = F

R^1 = OMe, R^2 = H or R^1 = H, R^2 = OMe

Scheme 3

Each of the three types of reaction described above provides a way in which an etheno-bridge may be removed from a benzobarrelene and each offers its own advantages. Degradation with coumalic acid (**8**) requires the most severe conditions and the most difficult experimental technique; however, separation of the products is particularly easy. Degradation with 4-nitrophenylazide (**9**) proceeds under mild conditions in high yield, but the reagent, although easily prepared, is light sensitive. The reaction should be carried out in the dark

and the products should be purified chromatographically. Degradation with 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) is experimentally very simple with a clear end-point. The product yields are marginally higher than with the other methods and chromatographic purification is little more difficult than a filtration. This reaction is considered to be the one of choice for degrading benzobarrelenes.

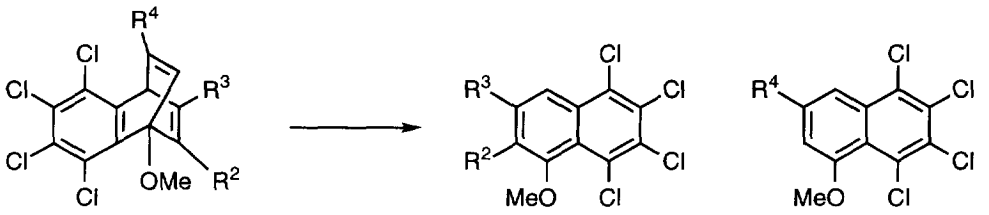
Benzobarrelenes with unsubstituted etheno-bridges constitute only a small proportion of the products obtained by cyclo-adding an aryne to an arene.[6] Generally the bridges will be substituted; very often the substitution will not be symmetrical. In such cases the usefulness of the fragmentation reagents just described will depend largely on the selectivity that they exhibit in the initial cycloaddition reaction. Depending on the application the preferred reaction may be one which exhibits complete specificity or a complete lack of specificity. In labelling experiments more information will be gained from random degradation provided that the products are different and separable.

The site selectivity was investigated by examining the reactivity of 2-methyl- (**14**), 3-methyl- (**15**), 2,3-dimethyl- (**16**), and 2,5-dimethyl- (**17**) derivatives of 1-methoxytetrachlorobenzobarrelene towards the fragmentation reagents (**7**), (**8**), and (**9**). Coumalic acid (**8**) (100% excess, 208 °C, 44.3h), 4-nitrophenylazide (**9**) (10% excess, boiling dioxan, 28h) and 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) (equimolar, boiling *p*-xylene, until complete) were in turn allowed to react separately with each of the methyl-substituted derivatives (**14**), (**15**), (**16**), and (**17**). The results are summarised in Table 2.

The reactions with 3,6-di-(2'-pyridyl)-s-tetrazine (**7**) and 4-nitrophenylazide (**9**) were clean and high yielding. No evidence was found for rearrangement or nitrogen loss from the triazolines (**18**), the presumed intermediates in the reactions with 4-nitrophenylazide (**9**). The reactions with coumalic acid (**8**) were generally unsatisfactory: extensive rearrangement was common even in *p*-xylene; in acetic acid the 2-methyl (**14**) and 2,5-dimethyl (**17**) analogues did not survive the reaction conditions even in the absence of coumalic acid. Reports of the acid-catalysed rearrangements of these derivatives (**14**) - (**17**) have either been published[13b,17] or are in preparation. All of the reagents exhibited regioselectivity. 4-Nitrophenylazide (**9**) was the least selective and 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) was the most selective reagent. There was a clear preference for initial cycloaddition at the unsubstituted etheno-bridge. When the cycloaddition had to take place on a substituted bridge, on (**17**), the reaction still proceeded without difficulty - with coumalic acid (**8**) rearrangement occurred instead - though there was a preference for reaction at the bridge methylated adjacent to the methoxy-group. This preference is quite consistent with the preferences exhibited by the two monomethyl analogues (**14**) and (**15**). If we designate the positions 2 and 6 as α and 3 and 5 as β the preferred order of attack is

i) unsubstituted > α-substituted >>β-substituted, and

ii) unsubstituted >α,β-disubstituted.



(**14**) R^2 = Me, R^3 = H, R^4 = H
(**15**) R^2 = H, R^3 = Me, R^4 = H
(**16**) R^2 = R^3 = Me, R^4 = H
(**17**) R^2 = Me, R^3 = H, R^4 = Me

(**46**) R^2 = Me, R^3 = H
(**47**) R^2 = H, R^3 = Me
(**48**) R^2 = R^3 = Me
(**46**) R^2 = Me, R^3 = H

(**10**) R^4 = H
(**10**) R^4 = H
(**10**) R^4 = H
(**47**) R^4 = Me

Table 2

Reactions of 1-methoxytetrachlorobenzobarrelenes (**14**) - (**17**) with 3,6-di-(2'-pyridyl)-s-tetrazine (**7**), coumalic acid (**8**), and 4-nitrophenylazide (**9**)[a]

Substrate	Reagent	Product 1[b]	product 2[b]	Yield 1 %	Yield 2 %
(14)	(7)	(46)	(10)	72 [c,f]	15 [c]
(14)	(8)	(46)	(10)	70 [e(i)]	trace
(14)	(9)	(46)	(10)	55	45
(15) [d]	(7)	(47)	(10)	91 [c,f]	-
(15) [d]	(8)	(47)	(10)	75 [e(ii)]	25
(15) [d]	(9)	(47)	(10)	25	10
(16)	(7)	(48)	(10)	96 [c,f]	-
(16)	(8)	(48)	(10)	25 [e(iii)]	-
(16)	(9)	(48)	(10)	80	20
(17)	(7)	(46)	(47) [c]	-	93 [c,f]
(17)	(8)	(46)	(47)	- [e(iv)]	-
(17)	(9)	(46)	(47)	20	80

[a] For the reaction conditions see the experimental section.

[b] Product ratios by ^{1}H nmr spectroscopy.

[c] Isolated yields of pure products.

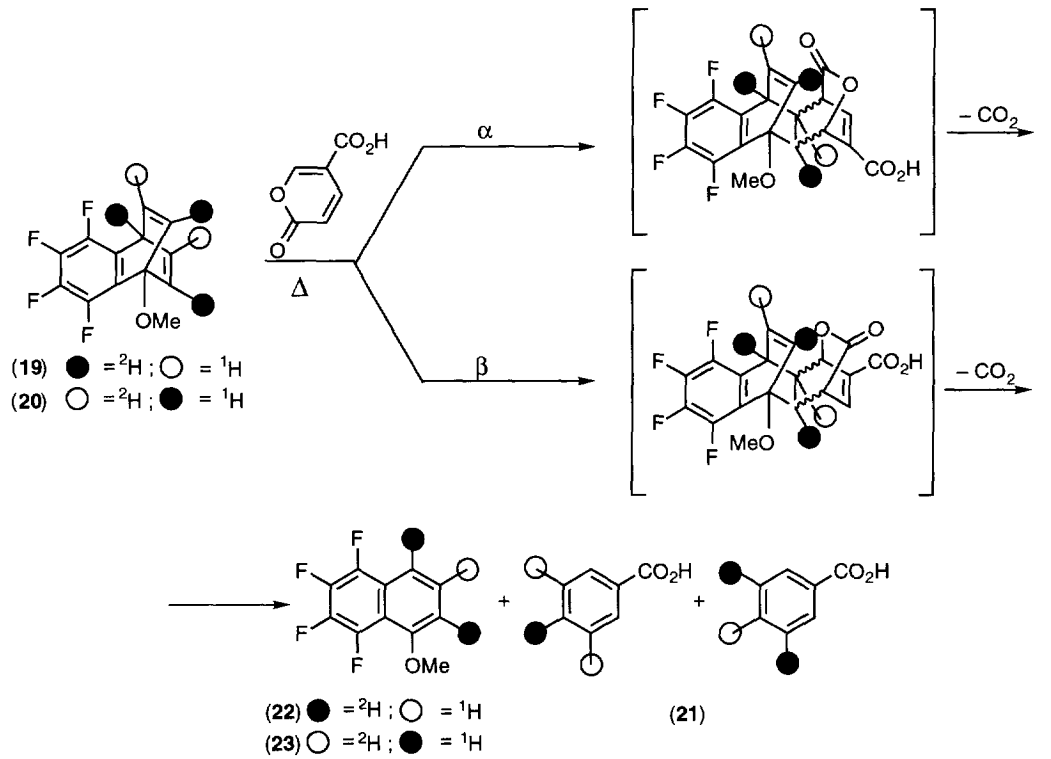
[d] Reference 2c.

[e] The mixture also contained products derived by acid catalysed rearrangement reactions: (i) *ca.* 30%; (ii) *ca.*trace; (iii) *ca.* 75%; (iv) *ca.* 100%.

[f] 4-Methyl-3,6-di-(2'pyridyl)pyridazine (*ca.* 85%) also isolated.

The discrimination in favour of reaction at the α-substituted instead of the β-substituted bridge of the dimethylated analogue (**17**) is interesting for the bridges would be equivalent were it not for the allylic methoxy-group. The methoxy-group clearly has a perturbing effect on the cycloaddition. If the perturbation were an

electronic effect it would be of the interaction between the ethenobridge and the diene. With an unsymmetrical diene such as coumalic acid (**8**) this would be reflected in the substitution pattern of the benzoic acid obtained. Coumalic acid (**8**) was reacted separately with 1-methoxy-2,4,6-[$^2H_3$]- (**19**) and 1-methoxy-3,5-[$^2H_2$] - (**20**) tetrafluorobenzobarrelene to give in each case a mixture of [^{2}H]-labelled benzoic acids (**21**) along with the corresponding naphthalene (**22**) and (**23**) (*Scheme 4*).



Scheme 4

It is clear from *Scheme 4* that if the 4-hydrogen of the benzoic acid produced were replaced in some derivative then the ratio between deuteriated and undeuteriated derivatives would be the ratio between the two regioisomeric pathways and hence a measure of the influence of the methoxy-group on the initial cycloaddition. The deuteriated benzoic acids (**21**) were each degraded to 2,4,6-tribromoaniline (**24**) and 4-bromoacetanilide (**25**) (*Scheme 5*). Both compounds are stable crystalline compounds showing good molecular ions during mass spectroscopy. The amount of residual [^{2}H] was determined by mass spectrometry. The results are collected in Table 3 and show that pathway (β) is consistently, but only marginally, preferred over pathway (α) (ca 55:45) suggesting that the methoxy-group on its own barely influences the interaction between the ethenobridge and the diene moiety of coumalic acid (**8**). As an additional point it is clear from the mass spectrometry of 1,2,3,4-tetrafluoro-5-methoxy-6,8-[^{2}H]naphthalene that the level of deuteriation is much too low. Since a similar phenomenon is not observed in the benzoic acid from this series or at all in the products of the other series protodedeuteriation cannot have occurred in the benzobarrelene (**19**) - protonation of which is

known[13b] to cause rearrangements that were not observed in this case - but must have resulted from exchange with the medium after the fragmentation. In keeping with this is the greater amount of exchange observed with the bromotrifluoro- analogue (**26**), which arises[2a] in the preparation of the tetrafluoro- derivatives and which is always visible during mass spectroscopy as a "ghost" molecular ion.

Table 3

[^{2}H]-Incorporation into 1-methoxytetrafluorobenzobarrelene (**3**) and the products of its degradation by coumalic acid (**8**)[a] determined by mass spectrometry

	Source of benzobarrelene labelling pattern						
	(**19**) (2,4,6-[$^2H_3$]				(**20**) 3,5-[$^2H_2$]		
Product	$^2[H]_0$	$^2[H]_1$	$^2[H]_2$	$^2[H]_3$	$^2[H]_0$	$^2[H]_1$	$^2[H]_2$
(**19**)	< 1	1	5	93			
(**20**)					4	22	74
Bromo-des fluoro (**19**)	1	1	6	92			
Bromo-des fluoro (**20**)					4	22	74
(**22**)	3	20	77	0			
(**23**)					13	87	0
Bromo-des fluoro (**22**)	2	28	70	0			
Bromo-des fluoro (**23**)					13	87	0
Benzoic acid (**21**)	5	95	0	0	13	87	0
(**24**)	60	40	0	0	53	47	0
(**25**)	54	46	0	0	15 [c]	87 [c]	0

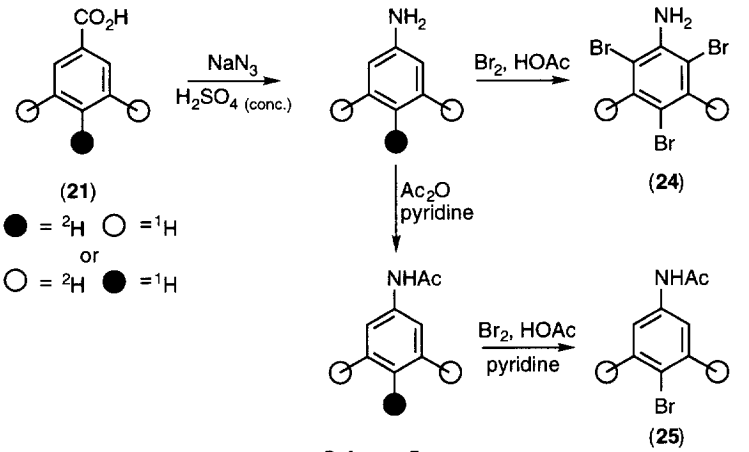
[a] The benzobarrelene and coumalic acid were reacted in *p*-xylene, for details see the experimental section.

[b] Reference 1(b).

[c] The values for acetanilide are given; 4-bromoacetanilide was not detected by mass spectrometry.

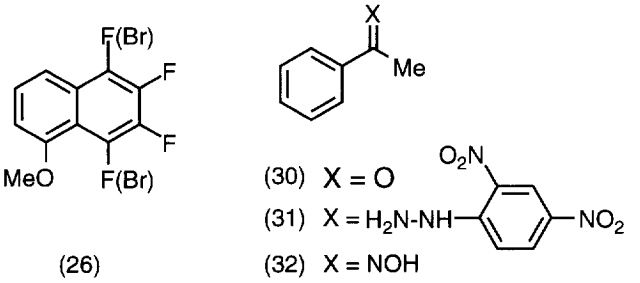
It seems likely that electronic effects on the cycloaddition would not account for the directing effect of the bridgehead methoxy group. A more likely explanation is that the cycloadditions are governed by steric effects - hence the order of selectivity 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) > 4-nitrophenyl-azide (**9**) - and that the steric clash between the 2-methyl-, the 1-methoxy-, and the buttressing peri-chlorine groups distorts the planarity of the double bond bearing a 2- (or α-) methyl group to an extent that the reactivity of the α-substituted ethenobridge is increased relative to the β-substituted bridge. Whatever the factors responsible 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) is a suitable reagent for the selective degradation of unsymmetrically substituted

benzobarrelenes whereas 4-nitrophenylazide (**9**) is not as selective and coumalic acid (**8**) is unsatisfactory because of the acid-catalysed rearrangements that it promotes.



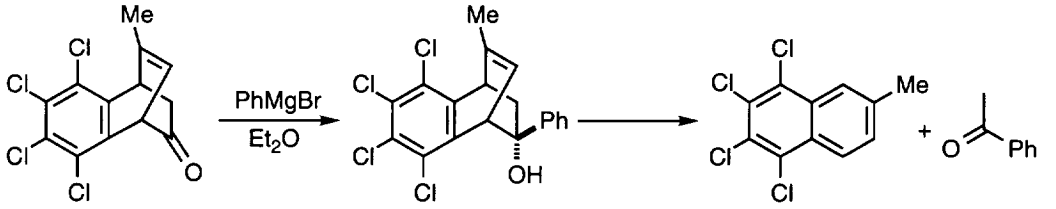
Scheme 5

Our work with benzobarrelenones was guided by our specific objectives: we wanted to develop a method of isolating at least one single carbon atom rather than just pairs of carbon atoms from a tetrachlorobenzyne-arene cycloadduct. This is a general requirement if the carbon atoms of an arene are to be completely resolved (*vide infra*); more specifically we required a method for excising *C*2 and *C*3 in separable form from tetrachloro-benzobarrelenone (**5**) and for separating *C*5 from *C*4 in tetrafluoro- (**6**), tetrachloro- (**5**), and the parent (**4**) benzobarrelenone.



When 5-methyltetrachlorobenzobarrelenone (**27**) was reacted with phenylmagnesium bromide in boiling tetrahydrofuran the only crystalline product isolated was 6-methyl-1,2,3,4-tetrachloronaphthalene (**28**). When a similar reaction was carried out in diethyl ether at room temperature the expected phenylcarbinol (**29**) (67%), m.p. 145°C dec., was obtained. Thin layer chromatographic analysis of the residue from the melting point determination showed that complete fragmentation to 6-methyl-1,2,3,4-tetrachloronaphthalene (**28**) and acetophenone (**30**) had occurred. In addition some 1-phenylethanol (20%) was detected as a product of the Grignard reaction which suggested the yield of the carbinol (**29**) had been reduced by fragmentation and

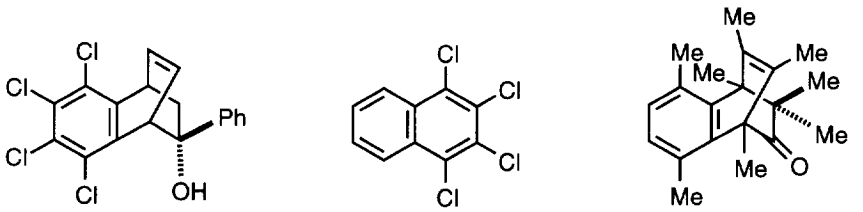
reduction steps at some stage of the reaction. A larger-scale pyrolysis yielded the naphthalene (**28**) (90%) and acetophenone (*Scheme 6*), which was isolated as its 2,4-dinitrophenylhydrazone (**31**) (66%).



(**27**) (**29**) (**28**) (**30**)

Scheme 6

The oxime (**32**) was also a suitable derivative for isolation of acetophenone on a small scale. A similar sequence with tetrachlorobenzobarrelenone (**5**) gave the expected carbinol (**33**) (100%) which was pyrolysed to give 1,2,3,4-tetrachloronaphthalene (**34**) (88%) and acetophenone (**30**) (isolated only as a solution). A solution of acetophenone (**30**) such as could be obtained by the above procedure was degraded to iodoform (57%) and benzoic acid (67%).

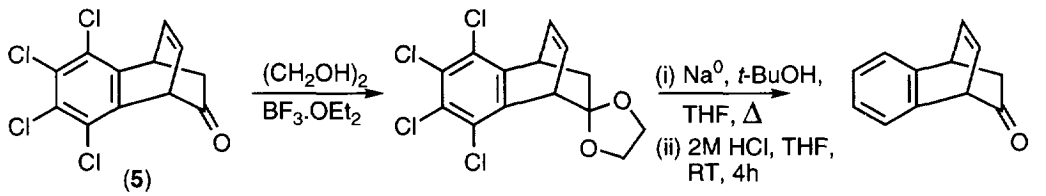


(**33**) (**34**) (**35**)

It is interesting that the tertiary carbinols such as (**29**) and (**33**) decompose so rapidly at their melting point, but the greater instability of the corresponding alkoxides is striking. The fragmentation can be viewed as a retro-Diels-Alder reaction in which the driving force would be stabilisation of the negative charge in the transition state relative to the ground state by delocalisation. If this view is correct our successful isolation of the phenylcarbinols could be attributed as much to the change of solvent[18] from tetrahydrofuran to diethylether as to the modest lowering of the reaction temperature. A similar fragmentation of an octamethylbenzobarrelenone (**35**) has been reported[19] with, for example, dimsyl sodium in dimethylsulfoxide, which is a solvent that would be expected to disrupt ion-pair stabilisation of the alkoxide form of the carbinol and so facilitate fragmentation. The promotion of electrocyclic reactions by delocalisation of alkoxides has become well established[18,20] in recent years and is held[20a] to be sensitive to the degree of association between the alkoxide and its counter ion. On the other hand benzobarrelenones have been cleaved[9a] to acids by sodium hydroxide in which case one of the bonds to the bridge is completely broken before the other. It is not clear whether the fragmentation of the phenylcarbinols (**29**) and (**33**) as their alkoxides is truly concerted although we favour the view that the increasing ease of extrusion along the series ethylene < 1-phenylethenol < 1-phenylethenolate reflects electronic effects in the approach to the transition state for concerted fragmentation.

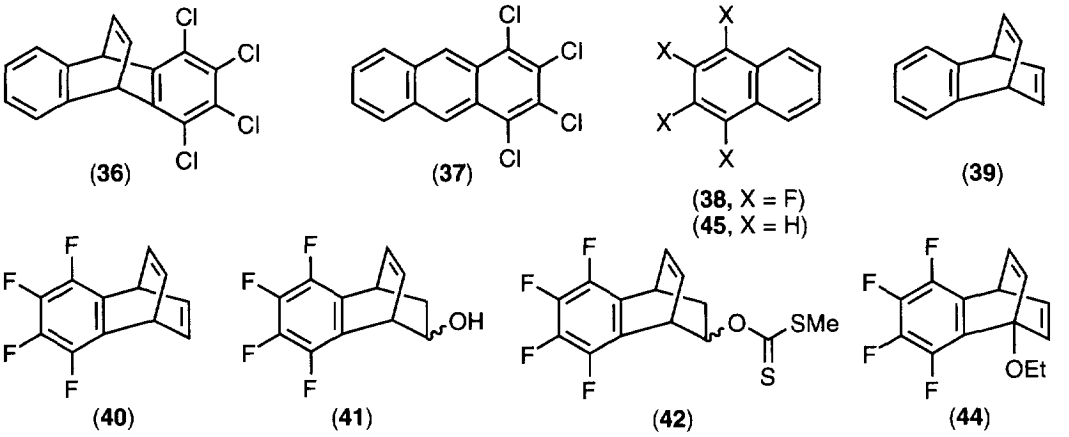
With this procedure we achieved our general objective - to isolate one of the carbon atoms of an arene ring free from the others - and one of our specific objectives - to isolate *C*2 of tetrachlorobenzobarrelenone.

We took this degradation further: 1,2,3,4-tetrachloronaphthalene (**34**) was reduced with hydrazine hydrate and palladised charcoal[21] to give naphthalene (70%). One reservation about this step is that the yield was not very reproducible. Dechlorination with sodium-t-butanol-tetrahydrofuran, which dechlorinates tetrachlorobenzobarrelenes so effectively,[22] led in this case to tetralin. Treatment of this naphthalene with tetrachlorobenzyne gave[2b] 1,2,3,4-tetrachloro-9,10-dihydro-9,10-ethenoanthracene (tetrachlorodibenzobarrelene) (**36**) (17%). The yield is based on naphthalene and is relatively low, but the progressive increase in weight as the degradation proceeds makes the process manageable. The reductive dechlorination was necessary as without it the cycloaddition of the aryne would not have occurred. The tetrachlorodibenzobarrelene (**36**) obtained in this way was reacted with 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) to give 1,2,3,4-tetrachloroanthracene (**37**) (90%) and 3,6-di-(2'-pyridyl)pyridazine (**12**) (72.5%). 4-Nitrophenylazide (**9**) was an unsuitable fragmentation reagent in this case: there is less driving force for aromatisation of the 9,10-dihydroanthracene than would be the case with a 1,4-dihydronaphthalene and the labile intermediate in azide induced fragmentations - a triazoline - could have decomposed by other routes, for example by loss of nitrogen.[23] Although applicable to the further degradation of both benzobarrelenone (**4**) and tetrachlorobenzobarrelenone (**5**) the procedure is not really suitable for the latter: the erratic dechlorination could seriously prejudice small scale work. However, tetrachlorobenzobarrelenone (**5**) can be converted into benzobarrelenone (**4**) itself in three almost quantitative steps:[24] ketalisation, reductive dechlorination with sodium-t-butanol-tetrahydrofuran and deprotection (*Scheme 7*).

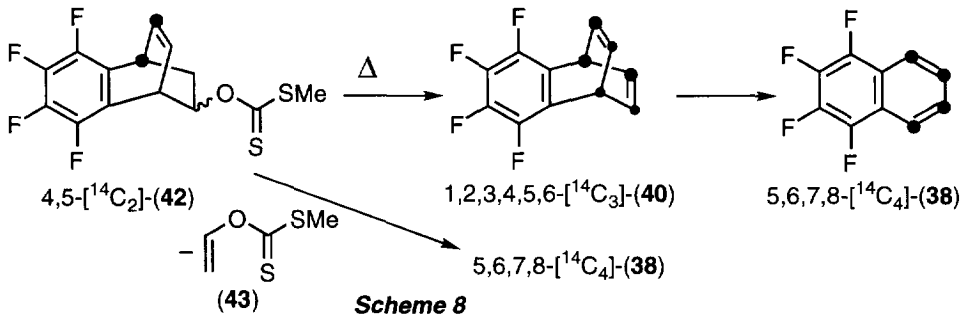


Scheme 7

Thus a modification of the procedure outlined in *Scheme 2* was found to be suitable for the separation of *C*4 and *C*5 of both benzobarrelenone (**4**) and tetrachlorobenzobarrelenone (**5**). A different method is required for tetrafluorobenzobarrelenone (**6**): tetrafluoronaphthalene (**38**) did not react with tetrachlorobenzyne and no reductive defluorination was available. However, at one time benzobarrelene (**39**) had to be made[2d] from the formerly slightly less inaccessible benzobarrelenone (**4**) and procedures had been developed for the conversion. Attempts to convert tetrafluorobenzobarrelenone (**6**) into tetrafluorobenzobarrelene (**40**) by Shapiro reaction of the tosylhydrazone were unsuccessful. The well established xanthate ester pyrolysis was better:[25] tetrafluorobenzobarrelenone (**6**) was reduced to the epimeric alcohols (**41**) which were trapped with carbon disulphide and methyl iodide to give xanthate esters (**42**). These esters were pyrolysed at 230 °C for 30 min to give an approximately 1:1 mixture of 1,2,3,4-tetrafluoronaphthalene (**38**) and tetrafluorobenzobarrelene (**40**), which could be separated by careful chromatography. The formation of a naphthalene in the pyrolysis is well precedented. It could arise from the xanthate esters (**42**) by loss of the enol xanthate (**43**) or it could arise by pyrolytic elimination of acetylene[2a,c] from tetrafluorobenzobarrelene (**40**) (*Scheme 8*).



Pyrolysis of an epimeric mixture of *S*-methyl-*O*-4,5-[$^{14}C_2$]tetrafluorobenzobarrelen-2-yl xanthates 4,5[^{14}C] (**42**) as above yielded 1,2,3,4-tetrafluoronaphthalene [^{14}C] (**38**) in which the level of radioactivity was intermediate between the level expected for formation by loss of the enol xanthate (**43**) and that for formation by loss of acetylene the equivalent of degradation of 1,2,3,4,5,6-[$^{14}C_6$] (**40**) by 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**)] (Table 4).



Scheme 8

Table 4
Degradation of *S*-methyl-*O*-2,3-dihydro-4,5-[$^{14}C_2$]tetrafluorobenzobarrelen-2-yl xanthates

Structure	Run 1. Specific Activity x 10^2/ (μCi/mmole)	Run 2. Specific Activity x 10^2/ (μCi/mmole)
4,5-[$^{14}C_2$] (**42**)	4.37	4.37
5,6,7,8-[$^{14}C_4$] (**38**) [a]	3.67	3.44
5,6,7,8-[^{14}C4] (**38**) [b]	2.70	2.80

[a] Obtained by pyrolysis of xanthate ester 4,5-[$^{14}C_2$] (**42**) using the method described in the experimental section.

[b] By degradation of tetrafluorobenzobarrelene 1,2,3,4,5,6-[$^{14}C_6$] (**40**) with 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) using the method described in the experimental section.

The results indicated 58% reaction by direct loss of enol xanthate (**42**) and 42% reaction by loss of acetylene from tetrafluorobenzobarrelene (**40**). In a similar experiment the rate of loss of enol xanthate : loss of acetylene was 38:62. The loss of so much acetylene is surprising as such low temperatures are not usually employed[2c,4] in benzobarrelene pyrolyses. The control data on the coumalic acid-induced fragmentation of 1-methoxytetrachlorobenzobarrelenes suggested no instability in the substrate at 200 °C. Neither the 3-methyl- nor 2,3-dimethyl-analogues [(**15**) and (**16**) respectively] gave any detectable naphthalenes after 3h at 200 °C in acetic acid. 1-Ethoxytetrafluorobenzobarrelene (**44**) is reported to give only 62% loss of acetylene after 12h at 250°C compared with 92% after 12h at 300°C for the 1-methoxy-analogue (**3**).[2c] It may be that the xanthate ester pyrolyses were carried out at the practical threshold of instability of tetrafluorobenzobarrelene (**40**). Alternatively, it may be that tetrafluorobenzobarrelene (**40**) is less stable in this reaction mixture than in an inert medium. When we applied similar xanthate ester pyrolyses to the tetrachloro-analogue and to the parent series[25] we were surprised to find that the relative amounts of the corresponding naphthalenes [(**34**) and (**45**) respectively] had increased to 9:1 and >9:1 in each case, as estimated by g.l.c.[26]

Reaction of tetrafluorobenzo-barrelene (**40**) obtained by this method with 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) gave 1,2,3,4-tetrafluoro-naphthalene (**38**) (34%) and 3,6-di-(2'-pyridyl)pyridazine (**12**) (29%) to complete the separation of *C*4 and *C*5 of tetrafluorobenzobarrelenone (**6**). All of the methods for separating *C*4 from *C*5 of the various benzobarrelenones suffer from the disadvantage that only half of the original *C*5 is separately recoverable because of symmetrisation of intermediates. Whether the phenyl carbinols (**29**) and (**33**) could be converted into the corresponding xanthate esters and hence into substituted benzobarrelenes that would be selectively fragmented with e.g. 3,6-di-(2'-pyridyl)-*s*-tetrazine (**7**) is an interesting point, but of no practical consequence to us: we have not developed other more specific routes. The applications of the work described above fall into two well defined categories. There are the analytical uses in which the reactions are employed to obtain information about the composition of arenes or of their cycloadducts. There are also synthetic uses although these will often be restricted by the availability of simpler or cheaper alternatives.

The obvious synthetic application of these reactions is in the preparation of naphthalenes. Extension of the method to the preparation of anthracenes is straightforward. One of the main advantages is the way in which a ring is added in one step with its substitution pattern or labelling already complete. Naphthalenes have been prepared from benzobarrelenes by pyrolysis,[2a,c] but in these reactions it is the more highly substituted etheno-bridge which is preferentially eliminated[2a] although the degree of selectivity is very low. The highly selective fragmentations described above allow confident predictions of the outcome of a synthesis. Among the restrictions must be noted that there are many functional groups that are not compatible with aryne reactions[6] and naphthalenes containing these groups may not be directly prepared in this way. Care must also be taken to select the aryne and arene substituents to maximise yield and minimise the formation of mixtures. Naphthalenes unsubstituted in one ring are easily available using this approach coupled to reductive dechlorination[2d,22,24] of tetrachlorobenzobarrelenes. These reactions represent an addition to the range[27] of aryne based polycyclic-arene syntheses. Although they are not practical general syntheses, there are naphthalenes that are much more difficult to synthesise by any other route. As an interesting corollary it may be observed that the benzobarrelenes act as easily unmaskable protected acetylenes and enols.

The main analytical use lies in the determination of the distribution of an isotopic label - an assay of activity. In the general case where the isotope is partially scrambled amongst all available positions, the amount of information available is not sufficient to determine the activity at each position: six independent measures of

activity would be needed to partition the total activity into the six ring positions of a benzene derivative that lacked all symmetry other than the molecular plane. Even in the case of an arene with C_{2v} symmetry the amount of information which can be obtained from the cycloaddition-induced fragmentation is insufficient because ring positions are always removed as adjacent pairs (Scheme 1). To determine the activity at each position the general principle is that the activity of at least one single position must be known as well as the pairwise estimates. The estimate of activity at a single position may come from the phenylcarbinol fragmentation or may arise in the special case where the activity of a pair of ring positions is zero. To which arenes and for what purpose may these reactions be applied? Arenes with C_{2v} symmetry and that form benzobarrelenenones are analysed particularly easily (e.g. anisole,[2c] dimethylaniline[28]). Even those arenes that form only benzobarrelenones[2c] (for practical purposes) may be analysed if the naphthalene formed in a phenylcarbinol fragmentation is further degraded (e.g. 4-methylanisole). As a corollary any arene that may be converted to such a benzobarrelenone forming arene may be assayed completely. The numerous methods available for introducing an oxygen-[29] or even a nitrogen-[29,30] function into an aromatic ring make this condition less restrictive than it might at first appear (e.g. nitrobenzene, bromobenzene, acetophenone etc.). Arenes lacking the symmetry axis but which form two separable benzobarrelenones may also be completely assayed (e.g. 2,4-dimethylanisole). Arenes that form only benzobarrelenes[6,31] may be completely assayed by the methods described above only in the special case that the activity of one of the fragments is zero. Even so it will not always be possible to determine with certainty the activities of each ring position. In spite of the restrictions outlined above the regiospecific fragmentation sequences provide a useful new chemical method for assaying arenes. The method will provide a check against scrambling[32] of a label in many benzobarrelene forming arenes and will separate *C*2, *C*4, and *C*5 of benzobarrelenones. This gives rise to particular satisfaction for it was for these purposes that the method was originally devised. Applications of the method to the assay of [^{14}C]anisole[33] and [^{14}C]-benzobarrelenones[33,34] will be reported separately.

We thank the S.R.C. for research studentships to N.J.H., J.H.H., and S.V.L. and The Imperial Smelting Corporation, Avonmouth, for supplies of bromopentafluorobenzene.

Experimental

General Procedures. - All reductive dechlorinations and reactions involving organometallic reagents were carried out in oven-dried glassware under an atmosphere of dry, oxygen-free nitrogen. All solvents were distilled and dried to the appropriate degree by conventional methods before use; the tetrahydrofuran used in reductive dechlorinations was stored over sodium wire. Light petroleum refers to the fraction boiling between 60-80 °C unless otherwise stated.

Analytical t.l.c. was carried out using 0.25 mm thick layers of silica-gel (GF254); preparative t.l.c. was carried out using 1.0 mm thick layers of silica-gel (PF254). Analytical g.l.c. was carried out using a Pye 104 series gas chromatograph fitted with a flame ionisation detector. Infra-red spectra were determined for potassium bromide discs, thin films, or solutions in chloroform, on a Perkin-Elmer 257 spectrophotometer. Ultraviolet spectra were determined on a Pye SP 8000 spectrophotometer. ^{1}H-n.m.r. spectra were determined for approximately 20% w/v solutions containing tetramethylsilane as internal standard at 90MHz on a Perkin-

Elmer R32 spectrometer. Mass spectra were determined on an A.E.I. MS12 mass spectrometer. Melting points were determined on a Kofler hot-stage apparatus, and are uncorrected.

Radioactivities were determined for dilute solutions of the sample (*ca.*1 mg) in DMF (0.2 mL) and scintillator (5 mL) using a Beckman Instruments CPM-100 liquid scintillation spectrometer. The scintillator was a solution of 2,5-diphenyloxazole (0.38%) and 1,4-bis-2-(4-methyl-5-phenyloxazolyl)benzene (0.02%) in toluene. The efficiency of the scintillator was determined using [^{14}C]hexadecane of known specific activity (obtained from the then Radiochemical Centre, Amersham) as standard.

The following compounds were prepared by published procedures: 5,6,7,8-tetrachloro-1,4-dihydro-1-methoxy-1,4-ethenonaphthalene (**2**) and its 2-methyl-, 3-methyl, 2,3-dimethyl and 2,9-dimethyl derivatives (**14**), (**15**), (**16**), and (**17**) respectively;[2c] 5,6,7,8-tetrafluoro-1,4-dihydro-1-methoxy-1,4--ethenonaphthalene (**3**)[2c] and its 2,4,10-[$^2H_3$]- and 3,9-[$^2H_2$]-derivatives (**19**)[1b] and (**20**)[1b] respectively; 5,6,7,8-tetrachloro-3,4-dihydro-1,4-ethenonaphthalen-2(1*H*)-one (**4**)[1b] and its 9-methyl derivative (**27**);[2c] 5,6,7,8-tetrafluoro-3,4-dihydro-1,4-ethenonaphthalen-2(1*H*)-one (**6**);[1b] 3,6-di-(2'-pyridyl)-1,2,4,5-tetrazine (**7**);[15]; coumalic acid (**8**);[35] and 4-nitrophenyl azide (**9**).[36]

General Procedure for the Reaction between 1,4-Dihydro-1,4-ethenonaphthalenes (benzobarrelenes) and Coumalic Acid (8)

The benzobarrelene, coumalic acid and the solvent in a 5 mL ampoule were degassed under nitrogen by three freeze-thaw cycles and then sealed at -78°C under nitrogen (0.2 mm Hg). The ampoules were heated in a thermostatted oven then cooled to room temperature and opened. (a) Analytical reactions (i) Volatile solvents were removed under reduced pressure and the residue was examined by ^{1}H-n.m.r. spectroscopy. (ii) Reactions in *N*-methylpyrrolidone were diluted with hydrochloric acid (2*N*) and extracted with ether (4 x 20 mL); the combined extracts were washed with hydrochloric acid (2*N*; 3 x 5 mL), dried ($MgSO_4$), and evaporated under reduced pressure to leave a residue that was examined by ^{1}H-n.m.r. spectroscopy. (b) Preparative reactions were diluted with ether (to 20 mL), extracted with aqueous sodium hydroxide (2*N*; 4 x 10 mL), dried ($MgSO_4$), and evaporated to give the corresponding naphthalene or naphthalenes. The combined aqueous extracts were acidified with conc. hydrochloric acid and extracted with ether (4x10 mL); the combined ethereal extracts were dried (Na_2SO_4) and evaporated under reduced pressure to give the corresponding benzoic acid or acids.

Reaction between 5,6,7,8-Tetrafluoro-1,4-dihydro-1-methoxy-1,4-ethenonaphthalene (1-Methoxytetrafluorobenzobarrelene) (3) and Coumalic Acid (8)

1-Methoxytetrafluorobenzobarrelene (**3**) (0.065 g, 0.25 mmole) and coumalic acid (**8**) (0.070 g, 0.50 mmole) were reacted in *p*-xylene (1 mL) at 200 ± 5 °C for 4 h using the general method (see above) to give (i) 1,2,3,4-tetrafluoro-5-methoxynaphthalene (**11**) (0.055 g, 94%), spectroscopically identical with our authentic sample[2c] and (ii) benzoic acid (0.022 g, 71%), spectroscopically identical with an authentic sample.

General Procedure for the Reaction between 1,4-Dihydro-1,4-ethenonaphthalenes (Benzobarrelenes) and 3,6-Di-(2'-pyridyl)-1,2,4,5-tetrazine (7)

A solution of the benzobarrelene and 3,6-di-(2'-pyridyl)-1,2,4,5-tetrazine (**7**) (1 equivalent) in a solvent was heated under reflux until the initial red colour was discharged. The solvent was evaporated under reduced pressure; the residue was examined by ^{1}H n.m.r. spectroscopy and then purified by chromatography (alumina; column or preparative t.l.c.) to give the corresponding naphthalene or naphthalenes followed by the corresponding pyridazine or pyridazines.

Reaction between 5,6,7,8-Tetrachloro-1,4-dihydro-1-methoxy-1,4-ethenonaphthalene (1-Methoxytetrachlorobenzobarrelene) (2) and 3,6-Di-(2'-pyridyl)-1,2,4,5-tetrazine (7)

1-Methoxytetrachlorobenzobarrelene (**2**) (0.080 g, 0.25 mmole) and 3,6-di-(2'-pyridyl)-1,2,4,5-tetrazine (**7**) (0.059 g, 0.25 mmole) were reacted in di-*n*-butyl ether (5 mL) for 2.5 h using the general method (see above) to give (i) 1,2,3,4-tetrachloro-5-methoxynaphthalene (**10**) (0.071 g, 96%), spectroscopically identical with our authentic sample[2c] and (ii) 3,6-di-(2'-pyridyl)pyridazine (**12**) (0.048 g, 83%), m.p. 180-181°C (from ethanol (lit.,[16] m.p. 179-180°C).

General Procedure for the Reaction between 1,4-Dihydro-1,4-ethenonaphthalenes (Benzobarrelenes) and 4-Nitrophenylazide (9)

A solution of the benzobarrelene and 4-nitrophenylazide (*ca.* 1.1 equivalents) in the solvent was heated under reflux until reaction was complete (t.l.c.). The solvent was evaporated under reduced pressure; the residue was examined by ^{1}H-n.m.r. spectroscopy and then purified by preparative t.l.c. (silica-gel) to give (i) the corresponding naphthalene or naphthalenes followed by (ii) the corresponding *vic*-triazole or -triazoles.

Reaction between 5,6,7,8-Tetrachloro- and 5,6,7,8-Tetrafluoro-1,4-dihydro-1-methoxy-1,4-ethenonaphthalene (1-Methoxytetrachloro- and 1-Methoxytetrafluoro-benzobarrelene) (2) and (3) and 4-Nitrophenylazide (9)

1-Methoxytetrachlorobenzobarrelene (**2**) (0.0322 g, 0.10 mmole) and 4-nitrophenylazide (**9**) (0.017 g, 0.104 mmole) were reacted in benzene for 24 h using the general method to give (i) 1,2,3,4-tetrachloro-5-methoxynaphthalene (**10**) (0.0237 g, 79%), spectroscopically identical with our authentic sample[2c] and 1-(4-nitrophenyl)-1,2,3-triazole (**13**) (0.0165 g, 84%), m.p. 208-210 °C (from ethanol) (lit.,[37] m.p. 206 °C), δ_H (90 MHz; $CDCl_3$) 7.92 (1 H, d, *J* 1.5 Hz), 7.98 (2 H, d, *J* 9 Hz), 8.11 (1 H, d, *J* 1.5 Hz), and 8.44 (2 H, d, *J* 9 Hz). A similar reaction using 1-methoxy-tetrafluorobenzobarrelene (**3**) (0.0256 g, 0.10 mmole) and 4-nitrophenylazide (**9**) (0.017 g, 0.104 mmole) gave (i) 1,2,3,4-tetrafluoro-5-methoxynaphthalene (**11**) (0.0198 g, 86%), spectroscopically identical with our authentic sample[2c] and (ii) 1-(4-nitrophenyl)-1,2,3-triazole (**13**) (0.0165 g, 84%), identical with material previously prepared.

2,4,6-Tribromoaniline (24) from Benzoic Acid by Schmidt Degradation and Bromination

A solution of benzoic acid (1.22 g, 10 mmole) in oleum (20% SO_3, 2 mL), sulphuric acid (98%, 3 mL) and chloroform (25 mL) at 40°C was treated with powdered sodium azide (0.75 g, 11.5 mmole). The mixture was heated under reflux for 2 h and then left at room temperature overnight. The mixture was poured into ice

(*ca.* 50 g), basified ($NaHCO_3$), and extracted with ether (3 x 10 mL). The combined extract was dried ($MgSO_4$) and carefully evaporated to leave a mobile brown oil. This product was dissolved in acetic acid (25 mL) and treated with bromine (1.6 mL, 4.8 g, 30 mmole). The solution was maintained at room temperature for 2 h, poured onto ice (*ca.* 100 g), neutralised ($NaHCO_3$), and filtered to give the product (2.89 g, 90%): one recrystallisation gave 2,4,6-tribromoaniline (**24**) (2.30 g 72%), m.p. 122°C (lit.,[38] m.p. 120 °C).

4-Bromoacetanilide (25) from Aniline by Acetylation and Bromination in Pyridine

Aniline (0.93 g, 10 mmole) was treated with a solution of acetic anhydride in pyridine (1*M*; 11 mL, 11 mmole) at room temperature for 20 h. Bromine (0.55 mL, 1.65 g, 10.3 mmole) was added dropwise to the swirled solution. The mixture was maintained at room temperature for 2h, quenched with ice (*ca.* 50 g), acidified (pH 4; conc. HCl) and filtered to give 4-bromoacetanilide (**25**) (1.95 g, 91%), m.p. 164-168°C (lit.,[38] m.p. 167°C).

5,6,7,8-Tetrachloro-1,4-dihydro-9-hydroxy-2-methyl-9-phenyl-1,4-ethanonaphthalene (2,3-dihydro-2-hydroxy-5-methyl-2-phenyltetrachlorobenzobarrelene) (29)

A slurry of 5-methyltetrachlorobenzobarrelenone (**27**)[20] (0.644 g, 2.0 mmole) in ether (20 mL) was added to a solution of phenylmagnesium bromide [from bromobenzene (3.14 g, 20 mmole) and magnesium turnings (0.50 g, 21 mmole) in ether (20 mL)]. The mixture was stirred at room temperature for 20h and then washed with hydrochloric acid (2*N*; 50 mL); the washings were extracted with ether (2 x 20 mL) and all of the ethereal phases were combined, dried, and evaporated under reduced pressure to give an oily residue that was purified by column chromatography (silica-gel) to give : (i) Biphenyl (0.152 g, 10% based on bromobenzene), spectroscopically identical to an authentic sample. (ii) 1,2,3,4-Tetrachloro-6-methylnaphthalene (**28**) (0.015 g, 3%), spectroscopically identical to an authentic sample.[29] (iii) 1-Phenylethanol, a clear oil (0.048 g, 20% based on 5-methyltetrachlorobenzobarrelenone), tentatively identified from its ^{1}H-n.m.r. spectrum. (iv) 5,6,7,8-Tetrachloro-1,4-dihydro-9-hydroxy-2-methyl-9-phenyl-1,4-ethanonaphthalene (2,3-dihydro-2-hydroxy-5-methyl-2-phenyltetrachlorobenzobarrelene) (**29**) (0.55 g, 67% m.p. *ca* 150°C dec. (from ethanol) (Found: C, 57.1; H, 3.6; $C_{19}H_{14}Cl_4O$ requires C, 57.0; H, 3.0%); ν_{max} (KBr) 3 540, 3 470 (broad), 3 050, 2 965, 2 945, 2 915, 1 445, 1 450, 1 380, 1 290, 1 270, 1 230, 1 165, 1 065, 1 045, 975, 760, 755, 730 and 695 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.75-2.15 (4 H, m); 2.27 (1 H, S, exchanged with ^2H_2O); 2.48 (1H, d, *J* 15 Hz); 4.42 (2 H, m); 6.25 (1H, broad d, *J* 6 Hz); 6.80 - 7.35 (5H, m).

Thermal Decomposition of 2,3-Dihydro-2-hydroxy-5-methyl-2-phenyltetrachlorobenzobarrelene (29)

A solution of 2,3-dihydro-2-hydroxy-5-methyl-2-phenyltetrachlorobenzobarrelene (**29**) (0.081 g, 0.22 mmole) in dimethylformamide (25 mL) was heated under reflux for 0.5h. The mixture was cooled, poured into brine (150 mL) and extracted with carbon tetrachloride (4 x 20 mL). The combined extract was dried and carefully concentrated under reduced pressure. The residue was purified by preparative t.l.c. (silica-gel) to give: 1,2,3,4-tetrachloro-6-methylnaphthalene (**28**) (0.051 g, 90%), m.p. 124.5°C. (lit.,[39] m.p. 125-127 °C); and acetophenone (0.016 g, 66%), spectroscopically identical to an authentic sample: a portion of this product was converted into its 2,4-dinitrophenylhydrazone (**31**) m.p. 229-235°C (lit.,[38] m.p. 237 °C).

5,6,7,8-Tetrachloro-1,4-dihydro-9-hydroxy-9-phenyl-1,4-ethanonaphthalene (2,3-dihydro-2-hydroxy-2-phenyltetrachlorobenzobarrelene) (33)

A stirred solution of phenylmagnesium bromide [from magnesium turnings (0.0122 g, 5 mg-atoms) and bromobenzene (just sufficient to react with the magnesium) in ether (*ca.* 50mL)] maintained at 10°C was treated with a solution of tetrachlorobenzobarrelenone[2c] (4) (0.120 g, 0.390 mmole) in ether (25 mL). The mixture was stirred at room temperature for 4h, poured into aqueous ammonium chloride (saturated; *ca.* 50 mL) and extracted with ether (3 x 25 mL). The combined extract was dried and evaporated under reduced pressure. The residue was purified by column chromatography (silica-gel) to give 5,6,7,8-tetrachloro-1,4-dihydro-9-hydroxy-9-phenyl-1,4-ethanonaphthalene (2,3-dihydro-2-hydroxy-2-phenyltetrachlorobenzobarrelene) (**33**) (0.152 g, 100%), m.p. 145°C dec. (from ethanol), (Found: C, 55.9; H, 3.0; $C_{18}H_{12}Cl_4O$ requires C, 55.9; H, 3.1%); ν_{max} (KBr) 3 550, 3 450 (broad), 3 080, 2 995, 2 975, 2 945, 1 450, 1 380, 1 345, 1 325, 1 315, 1 280, 1 265, 1 220, 1 195, 1 170, 1 090, 1 060, 1 020, 990, 785, 765, 735, 705, and 685 cm^{-1}; δ_H (90 MHz; $CDCl_3$) 1.91 (1 H, dd, *J* 3 and 16 Hz); 2.15 (1 H, broad s); 2.41 (1 H, dd, *J* 3.5 and 16 Hz); 4.45 - 4.75 (2 H, m); 6.6 - 7.2 (7H, m).

Thermal Decomposition of 2,3-Dihydro-2-hydroxy-2-phenyltetrachlorobenzobarrelene (33)

A solution of 2,3-dihydro-2-hydroxy-2-phenyltetrachlorobenzobarrelene (**33**) (0.34 g, 0.891 mmole) in dimethylformamide (25 mL) was heated under reflux for 0.5h. The cooled mixture was poured into water (50 mL) and extracted with carbon tetrachloride (5 x *ca.* 25mL). The combined extract was washed with water, dried, and carefully concentrated under reduced pressure to give a residue that was purified by preparative t.l.c. (silica-gel) to give (i) 1,2,3,4-tetrachloronaphthalene (0.208 g, 88% (m.p. 186 - 187°C lit.,[40] m.p. 198°C), spectroscopically identical to our authentic sample;[2b] and a solution containing acetophenone, identified by t.l.c. comparison with authentic material and by conversion into its oxime, m.p. 50-55°C (lit.,[41] 59-60°C).

Benzoic acid from Acetophenone

A stirred solution of acetophenone (0.16 g, 1.37 mmole) and potassium iodide (0.50 g, 3.0 mmole) in water (10 mL) and dioxan (acetaldehyde free; 10 mL) maintained at room temperature was treated with aqueous sodium hypochlorite (5%, *ca.* 3 mmole). Another portion of potassium iodide (0.30 g, 1.8 mmole) was added followed by another portion of sodium hypochlorite (*ca.* 1.8 mmole). The mixture was filtered to give iodoform, feathery yellow crystals, (0.304 g, 57%) m.p. 112-120°C (lit.,[28] m.p. 119°C). The filtrate was treated with sodium thiosulphate (*ca.* 3 g), acidified and extracted with ether (3 x 25 mL). The combined extract was dried and evaporated to give benzoic acid (0.166 g, 67%), m.p. 119-121°C (from hexane) (lit.,[38] m.p. 121°C).

1,2,3,4-Tetrachloro-9,10-dihydro-9,10-ethenoanthracene (36)

A solution of naphthalene (0.200 g, 1.6 mmole) in petroleum ether was added to a stirred solution of pentachlorophenyllithium [from *n*-butyllithium (*ca.* 2.0*M*; sufficient to completely react[22]) and hexachlorobenzene (0.600 g, 2.1 mmole) in ether] at -78°C. The mixture was allowed to warm to room temperature and left overnight. The mixture was washed with hydrochloric acid (2*N*, 2 x *ca.*20 mL), dried, and evaporated under reduced pressure. The dark oily residue was purified by preparative t.l.c. (silica-gel, light

petroleum) to give 1,2,3,4-tetrachloro-9,10-dihydro-9,10-ethenoanthracene (**36**), (0.090 g, 16.8%), m.p. 162-167°C (from ethanol) (lit.,[2b] m.p. 166°C.)

Reaction between 1,2,3,4-Tetrachloro-9,10-dihydro-9,10-ethenoanthracene (36) and 3,6-Di-(2-pyridyl)-1,2,4,5-tetrazine (7)

A solution of 1,2,3,4-tetrachloro-9,10-dihydro-9,10-ethenoanthracene (**36**) (0.200 g, 0.58 mmole) and 3,6-di-(2-pyridyl)-1,2,4,5-tetrazine (**7**) (0.150 g, 0.73 mmole) in di-*n*-butyl ether (25mL) was heated under reflux for 12h. The solvent was evaporated under reduced pressure. The oily residue was purified by preparative t.l.c. (silica-gel) to give (i) 1,2,3,4-tetrachloroanthracene (**37**) (0.166 g, 90%), m.p. 215-6°C (from benzene) (lit.,[42] m.p. 217-219°C); and (ii) after re-chromatography 3,6-di-(2-pyridyl)pyridazine (**12**) (0.100 g, 72.5%), m.p. 178-180°C (from ethanol) (lit.,[16] 179-180°C).

5,6,7,8-Tetrafluoro-1,4-dihydro-1,4-ethenonaphthalene (Tetrafluorobenzobarrelene) (40) from 5,6,7,8-Tetrafluoro-1,4-dihydro-1,4-ethenonaphthalen-2(1*H*)-one (Tetrafluorobenzobarrelenone) (6) by Xanthate Ester pyrolysis. - Lithium Aluminium Hydride Reduction

A solution of tetrafluorobenzobarrelenone (**6**) (0.290 g, 1.20 mmole) in ether (20 mL) was added at room temperature to a stirred slurry of lithium aluminium hydride (0.100 g, 2.63 mmole) in dry ether (20 mL). The mixture was stirred for 0.5h. Sulphuric acid (2*M*; 20 mL) was added and the mixture was extracted with chloroform (3 x 40 mL). The combined extract was dried and evaporated under reduced pressure to give an unpurified epimeric mixture of 2,3-dihydro-2-hydroxy-tetrafluorobenzobarrelenes (**41**), (0.270 g, 92% crude).

Xanthate Ester (42) Formation

A mixture of unpurified 2,3-dihydro-2-hydroxytetrafluorobenzobarrelenes (**41**) (0.270 g, ca 1.11 mmole), sodium hydride (0.100 g, 4.17 mmole), ethanol (95%; 3 drops), and benzene (40 mL) was stirred under nitrogen for 3h. Carbon disulphide (6 mL) was added and the mixture was stirred for 4.5h. Methyl iodide (6 g) was added and the solution was stirred for 12h. The mixture was washed with water (37 mL), dried, and evaporated under reduced pressure to give an unpurified epimeric mixture of *O*-2,3-dihydrotetrafluorobenzobarrelen-2-yl *S*-methyl xanthates (**42**), (0.330 g, 89% crude).

Tetrafluorobenzobarrelene (40). A mixture of unpurified *O*-2,3-dihydrotetrafluorobenzo-barrelen-2-yl *S*-methyl xanthates (**42**) (0.330 g, *ca.* 0.99 mmole) was heated under high vacuum (*ca.* 1mm Hg) at 230°C for 25min. in a pyrolysis tube to give an oil. The oil was purified by column chromatography [alumina; light petroleum (b.p. 40-60°C)] to give 1,2,3,4-tetrafluoronaphthalene (**38**), [0.080 g, *ca* 40%; 33.4% from (**6**)], m.p.106-109°C (lit.,[43] m.p. 110-111°C), followed by tetrafluorobenzobarrelene (**40**) [0.060 g, *ca.* 27%; 22% from (**6**)], m.p. 75-76°C (lit.,[44] m.p. 70-71°C).

Fragmentation of 5,6,7,8-Tetrafluoro-1,4-dihydro-1,4-ethenonaphthalene (Tetrafluorobenzobarrelene) (40) with 3,6-Di-(2'-pyridyl)-1,2,4,5-tetrazine (7)

Tetrafluorobenzobarrelene (**40**) (0.100 g, 0.442 mmole) and 3,6-di-(2'-pyridyl)-1,2,4,5-tetrazine (**7**) (*ca.* 0.130 g 0.55 mmole) were reacted in di-*n*-butyl ether (*ca.* 30 mL) for 6h using the general method (see above)

to give (i) 1,2,3,4-tetrafluoronaphthalene (**38**) (0.030 g, 34%), m.p. 105-107°C (lit.,[43] 110-111°C) and (ii) 3,6-di-(2-pyridyl)pyridazine (**12**) (0.030 g, 29%), m.p. 179-181°C (from ethanol) (lit.,[16] 179-180°C).

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