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CAGE KETONES FROM DIMETHYL-1,4-BENZOQUINONES AND QUINONOID CARBANIONS ; A CHARGE-TRANSFER CONTROLLED SYNTHESIS

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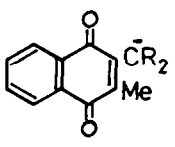
Abstract - 3-Methyl-1,4-naphthoquinon-2-ylmethyl anion (1a) adds 2,6-dimethyl-1,4-benzoquinone reversibly giving, in addition to products of types already known, a derivative (2) of the cage hydrocarbon decahydro-4,1,7-ethanylylidene-naphthalene which can be obtained as the major product. A similar reaction with 2,5-dimethyl-1,4-benzoquinone gives a similar cage compound (3) but derived from decahydro-8,2,5-ethanylylidenenaphthalene (14), a member of the twistane series. This reaction can be modified to yield the more complex cage compound (4) derived from the hydrocarbon tetradecahydro-5,8,9,10-[1,2,3,4]butatetraylanthracene.

Since the only anions that initiate cage formation in benzoquinones have themselves quinonoid structures it is suggested that charge-transfer complexation aligns the interacting rings and promotes reversibility in Michael reactions, thus allowing steric repulsions to control the regiospecificity.

INTRODUCTION

In the reactions between the naphthoquinonylmethyl anion (1a) and the isomeric dimethyl-1,4-benzoquinones[1] the nature of the base is critical. The earlier phases of the reaction are all reversible and under kinetic control; the later phases are promoted by stronger bases and longer reaction times and culminate in the cage structures (2), (3) and (4a). A part of this study has already been reported briefly.[2]

In the mildest conditions (dilute methanolic sodium acetate) the main product from anion (1a) and 2,6-dimethylquinone is the fluorene alcohol (5) which is clearly formed by Michael addition at an alkylated position of the benzoquinone followed by (or simultaneous with) an aldol condensation at the naphthoquinone carbonyl group. At the same time there is some attack at the non-alkylated position in the benzoquinone which must be supposed to lead to the alternative carbanion, although under the conditions used this was oxidised to the diquinone[1] (6).



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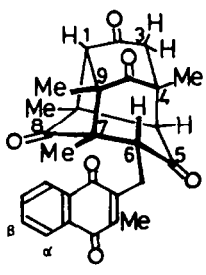
(1b) R=D



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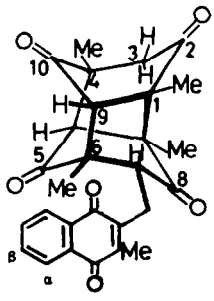

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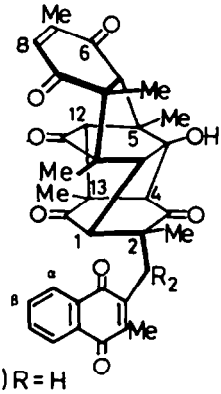

(4a) R=H
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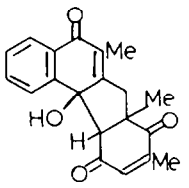

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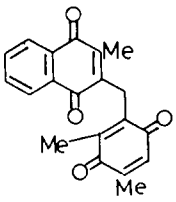

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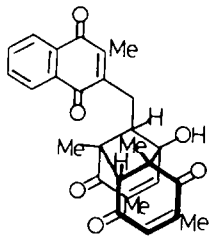

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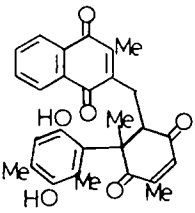


(8)

At higher basicities (concentrated sodium acetate or very dilute sodium hydroxide) more of the diquinone (6) is formed at the expense of the fluorene alcohol, a clear indication that the formation of the latter is reversible even though the two components must separate completely so as to recombine in the alternative manner. The increased presence of the carbanion also manifests itself in the addition of a second molecule of the benzoquinone; again a Michael addition followed by (perhaps simultaneous with) an aldol condensation produces the bridged quinone (7). In a secondary reaction the base unfastens the aldol link giving the quinol derivative (8) but, as reported already,[1] this is more cleanly obtained by the action of acids.

The bridged quinone (7) is still under kinetic control. In addition to the quinol derivative, further treatment with sodium hydroxide converts it into a compound for which we propose the cage tetraketone structure (2). This is the main product when the original carbanion (1a) reacts with the benzoquinone derivative in excess in the presence of methanolic sodium hydroxide, and appears to be the thermodynamically stable product.

The cage tetraketone (2) is yellow and clearly contains an unmodified methylnaphthoquinonylmethyl residue responsible for ir absorption at 1 667, 1 295 and 723 cm^{-1} and for ^1H nmr resonances at δ 2.12 (Me), 7.4 (α-ArH), and 8.0 (β-ArH). The loss of this residue also provides a major fragmentation in the mass spectrum. The remaining ir carbonyl bands are all above 1700 cm^{-1} and the remaining methyl proton resonances are all at fields higher than δ 1.4 (Table 1) There is no spectroscopic evidence for vinylic protons or for hydroxy groups. A cage structure appears to be inescapable, whether it has structure (2) or some other.

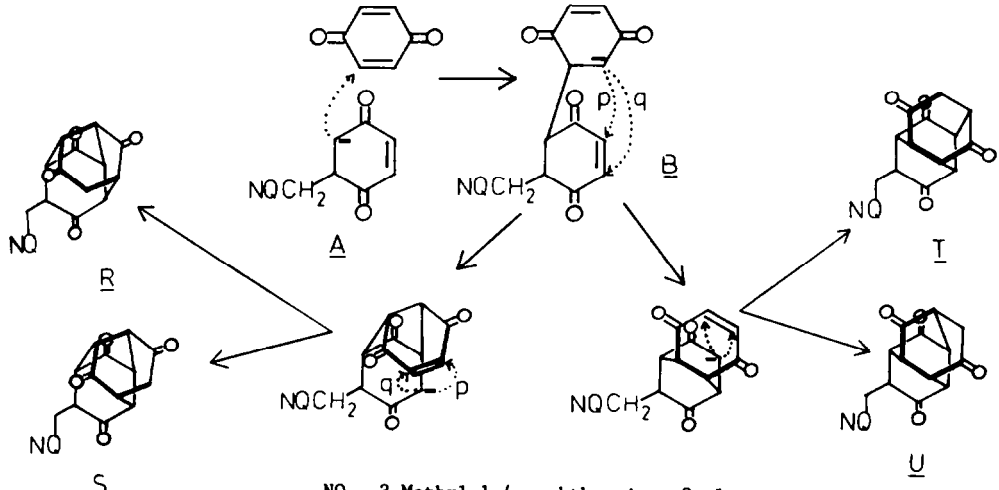
We conclude that the negative charge inserted by the naphthoquinonyl residue (1a) into one dimethylbenzoquinone residue is passed to and fro between this and a second dimethylbenzoquinone molecule until all their vinylic bonds have been eliminated. The negative charge may take several paths as shown in Scheme 1; we have assumed that no skeletal rearrangements have occurred since there is no reason to expect any, and those we have considered hypothetically seem unlikely because they lead to structures with more strain.

Scheme 1 is concerned solely with the ways in which the cage can be constructed and for the sake of clarity and generality the methyl substituents are not shown. Addition of the initial naphthoquinonyl carbanion ($NQCH_2^-$) to one quinone unit affords a carbanion A to which the second quinone residue becomes attached giving a new carbanion B and a choice of continuations. The charge may be returned to the first ring generating either a five-membered ring (p mode) or a six-membered ring (q mode). Finally, the charge is passed back again, and again there is a choice of five-membered ring (p mode) or six-membered ring (q mode). As there is no further opportunity for such interactions the system now accepts a proton from the solvent and the reaction is finished. All the steps

TABLE 1 Partial assignments for the ^{1}H nmr spectra of cage compounds[a]

Compound	Cage Me	Quinone Me	Cage CH	Cage or ring AB	Methylene link AB	Methylene link M	Vinyl Me	Vinyl CH	Quinone[b] β-H	Quinone[b] α-H
(2)	1.14	2.14	2.58	2.37[c]	2.62[d]	2.99[d]			7.67	8.06
	1.19		2.67	2.71[c]	2.83[d]				7.73	8.11
	1.23									
	1.35									
(3)	1.09	2.15	2.44	2.50[e]	2.70[e]	3.68[e]			7.69	8.05
	1.15		2.52	2.93[c]	2.75[e]				7.73	8.10
	1.18									
	1.27									
(4a)[f]	0.92	2.21	2.62	2.56[g]	2.45[h]		1.96[i]	6.41[i]	7.69	7.97
	1.28		3.21	2.70[g]	3.00[h]				(2H)	8.09
	1.40		3.23							
	1.55									
	1.62									
(4a)[j]	0.95	2.21	2.61	2.73[k]	2.47[l]		1.98[m]	6.43[m]	7.68	7.98
(acetate)	1.22		3.30	2.79[k]	3.06[l]				(2H)	8.06
	1.38		4.59							
	1.60									
	1.76									

[a] At 250.13 MHz in $CDCl_3$ with TMS as internal reference. Signals are singlets if no coupling is indicated. Analyses are first order only. δ Scale.
[b] Non-analysed multiplets. [c] Ring methylene; J_{AB} 19.2 Hz.
[d] J_{AB} 14; J_{AM} 6; J_{BM} 9 Hz. [e] J_{AB} 14; J_{AM} 5; J_{BM} 9 Hz; confirmed by double irradiation experiments. [f] OH band ca. δ 2.8 removed by D_2O.
[g] Vicinal protons, J_{AB} 1.6 Hz. [h] J 13.1 Hz. [i] J 1.4 Hz. [j] MeCO, δ 2.03.
[k] J 13 Hz. [l] J 13.1 Hz; absent from spectrum of (4b) acetate.
[m] J 1.4 Hz; confirmed by double irradiation.



NQ = 3-Methyl-1,4-naphthoquinon-2-yl

(other Me groups omitted for clarity)

Scheme 1

are Michael additions; there are no aldol reactions and the product does not contain an OH group.

Of the four arrangements that emerge in Scheme 1, only R includes two(fused) cyclopentanone rings, and only U contains none. The compound in mulls or in trichloromethane exhibits two carbonyl bands, one at 1 755 (which would normally be assigned to a cyclopentanone group) and one at 1 725 cm^{-1} (which would normally be assigned to a cyclohexanone carbonyl group). Intensity measurements[3] show that these absorptions are in the ratio 1:3 from which we conclude that there is only one five-membered ketone function and three ketone functions in larger rings. Hence the compound is derived from S or T.

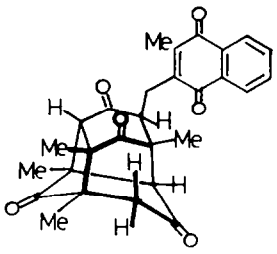
Since most i.r. atlases and reference books contain few examples of carbonyl groups in caged systems, which can vary greatly as regards stiffness and twisting, we thought it advisable to check the foregoing values and to this end culled about seventy examples from the literature (selected examples[4]). We found that (i) carbonyl groups in cage cyclohexane rings usually absorb in the range 1 720 ± 5 cm^{-1} no matter what ring fusions or bridges there are, though the full range is 1 690 - 1 725 cm^{-1}); (ii) carbonyl groups in seven-membered rings usually absorb in the range 1 710 ± 5 cm^{-1}; and (iii) carbonyl groups in cyclopentane rings absorb on average near 1 754 cm^{-1} but show considerable diversity, maxima falling in the range 1 720 - 1 780 cm^{-1} with band envelopes that are often wide and complex. We were, therefore, perturbed to find that our compound, when examined in KBr discs, showed three absorption bands, at 1 760, 1 738 and 1 723 cm^{-1}, of which the middle one might signal a second cyclopentanone carbonyl group resonating at the lower end of the range. However, we rejected this possibility because it contained none of the features that our survey had shown to be associated with low frequencies (e.g., conjugated double bonds or cyclopropane rings, or juxtaposed but not directly connected alkene links); moreover, models show that if two cyclopentanone residues are present they have to be fused and that further constraint within the rest of the cage framework produces considerable strain which would be expected to raise, not lower, the frequency.

The frameworks (S) and (T) are actually identical; it is only the location of the naphthoquinonyl residue that distinguishes them. This residue is attached to a methine group because the compound possesses an ABM spin system (Table 1) that can have no other origin. There is also an AB spin system (J 21 Hz) that has to be assigned to a ring methylene group and shows that the final protonation also occurred at a methine position. These facts allow the four methyl groups to be placed with certainty giving structures (2) and (9) for consideration.

The choice of structure (2) follows from a study of the ABM spin system. In related compounds[7] the M component resonates somewhere between δ 3.83 and 3.38 because the conformation adopted by the quinone ring brings this proton into the deshielding cone of one carbonyl group as depicted in diagram (10). In the present case the M proton resonates at δ 2.99 disclosing an upfield shift of about 0.7 p.p.m. that can only be provided by the shielding cone of a carbonyl group at an adjacent level. Structure (2) contains the necessary feature which, according to Pople-Jackman plots[8] or more recent calculations,[9] should give a shift of the right size (0.8 p.p.m.). Structure (9) places one ring methylene proton under the carbonyl group instead, but these protons signal no special effect, so this structure can be rejected.

When the naphthoquinonylmethyl anion (1a) reacts with 2,5-dimethyl-1,4-benzoquinone similar reactions take place. Equimolar reactants afford as the main products the methylenediquinone (11), the enedione (12), and the fluorene alcohol (13) and the yield of the last, which is very dependent upon the

concentration of the base, appears to be maximal at 40%. As the proportion of dimethylquinone is increased a cage tetraketone (3) appears and its yield rises as far as 25%. Further increases in the proportion of dimethylquinone or the concentration of base promote the formation of a kind of product not found in the 2,6-dimethylbenzoquinone series; a cage polyketone (4a) built up from the naphthoquinonyl carbanion and three dimethylbenzoquinone units. On the other hand we did not detect a bridged quinone like (7). The structures of the simpler products were determined without difficulty by the methods used in other cases and only the two cage products need discussion.



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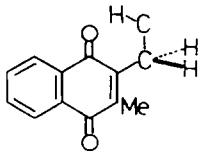

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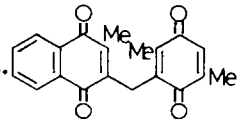

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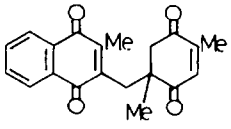

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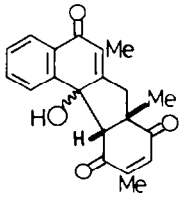
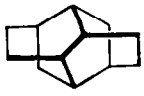


(13)



(14)

The cage tetraketone (3) was similar to its isomer (2); ir, nmr, and ms methods all evidenced the presence of a naphthoquinonyl residue linked to the rest of the molecule through a CH_2CH grouping; the molecule contained no hydroxy group; all the methyl nmr signals are singlets at higher fields and vinylic protons resonances are absent (Table 1). Most importantly, the ir spectrum contained no band attributable to a cyclopentanone residue; two bands, at 1 735 and 1 722 cm^{-1}, we attribute to cyclohexanone residues under various degrees of strain. Thus this cage is formed by the p,p sequence and contains the framework U (Scheme 1). In addition to the ABM spin system there is an AB spin system in the NMR spectrum, so the final proton must have been accepted at a methine site as before. This allows all the substituents to be inserted and structure (3) results unambiguously.

The parent cage hydrocarbon from which (3) is derived appears to be unknown either as such or as a derivative. It consists solely of twisted boat cyclohexane rings, diagram (14) depicting the symmetry and the chirality (the compounds discussed in this paper are, of course racemates). The hydrocarbon can be regarded as a member of the twistane series with five faces where the simplest has four and another recently described member has six.[10]

We now turn to a consideration of the cage polyketone formed from carbanion (1) and three molecules of 2,5-dimethyl-1,4-benzoquinone, for which some fifty arrangements can reasonably be envisaged at the outset. Although the compound crystallises without difficulty, the crystal proved unsuitable for X-ray studies so less direct methods were forced on us. The compound is yellow and the ir, nmr, and ms evidence establish the presence of a naphthaquinonylmethyl residue. Hence the cage part is formed solely from the benzoquinone residues.

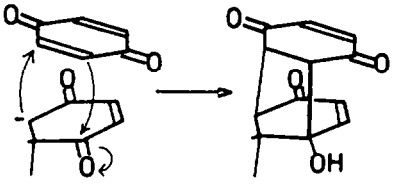
The compound is a tertiary alcohol ($\nu_{max.}$ 3 380 cm^{-1}) that is unaffected by acids (including methanolic hydrogen chloride and trifluoroacetic acid), by chromic acid in acetic acid, and by acetic anhydride with pyridine as catalyst. With acetic anhydride and sulphuric acid as catalyst, the compound forms an acetate ($\nu_{max.}$ 1 750 cm^{-1}) that retains all the quinonoid characteristics but lacks hydroxylic absorption. The ^{13}C nmr spectrum (Table 2) agrees that one tertiary alcohol function is present, that it is not part of a hemiacetal group, and that seven carbonyl groups remain intact.

TABLE 2 Partial assignment for the ^{13}C NMR spectrum[a] of alcohol (4)

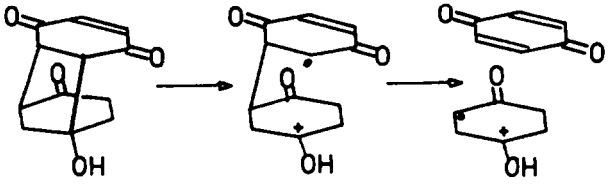
Me	$-CH_2-$	-C-	-CH-	-COH	=CH-	=C-	-C=O
14.26	32.71	48.49	49.08	84.29	125.77	131.68	184.23[b]
15.20		50.42[c]	55.84		127.11	131.68	184.37[b]
15.26		50.42[c]	63.10		133.40[d]	131.94	196.93
15.99		50.64	65.01		133.40[d]	143.37	199.64
20.27		54.64	68.78		128.37	144.38	210.79
20.37							210.99
22.07							211.93

[a] At 62.89 MHz in $CDCl_3$; TMS internal standard. [b] Quinone groups. [c,d] Single bands of higher intensity thought to correspond to two nuclei.

In the ^1H nmr spectrum of the acetate (Table 1) a vinylic group CH=CMe is disclosed by bands at δ 6.43 and 1.98 with a long-range coupling confirmed by double irradiation. One way to account for both this grouping and the tertiary alcohol function is to suppose that the third quinone bridged the carbanion thus:



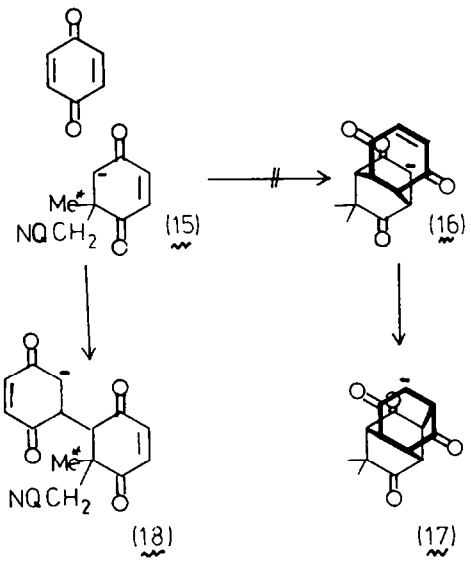
However, this cannot be the case. All authentic bridged compounds of this kind, e.g., (7), readily lose the bridging quinone. With sodium hydroxide in methanol immediate reverse aldol and Michael reactions disconnect the quinone which can be detected by t.l.c. or if necessary isolated on a larger scale,[1] but the present compound is stable and is the main product in the strongly alkaline conditions Again, such bridges are normally lost in a major mass spectral fragmentation[1] probably because a bond adjacent to hydroxy oxygen breaks readily and the radical centre produced then facilitates the breaking of another bond:



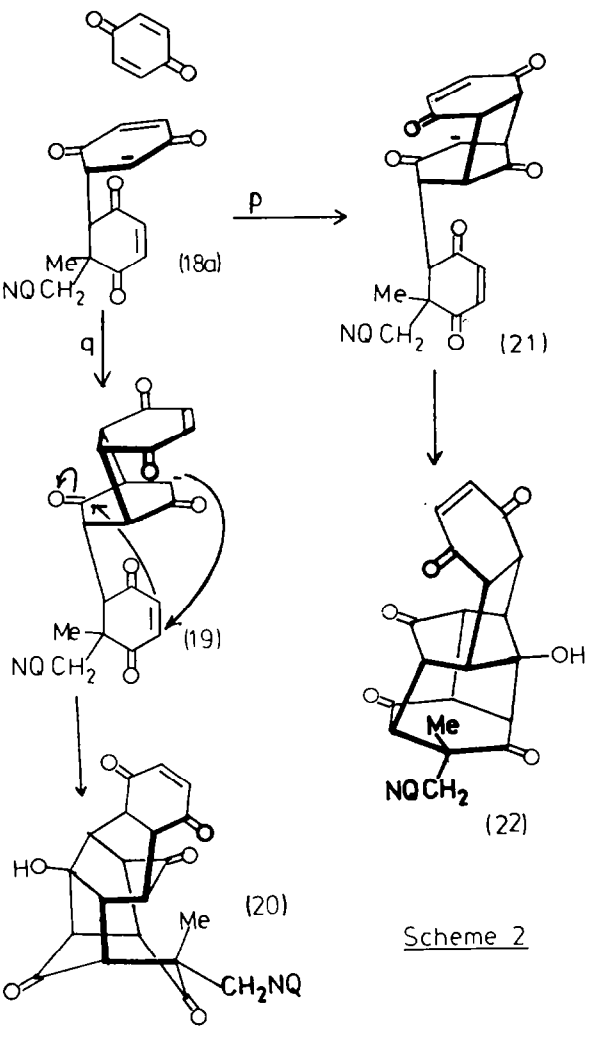
In the present case the corresponding ions are barely discernable thus confirming that the bridging quinone and the alcohol function are not closely associated.

Another important difference from the cage tetraketones is the absence of an ABM spin system; the AB part can still be seen (J = 13 Hz) and its origin has been firmly established by the use of deuteriated diazomethane to generate carbanion (1b) which then affords a product (4b) without these signals but with all others intact. A second AB spin system has a small coupling constant (J = 2.1 Hz) that defines it as a vicinal and not a ring-methylene coupling. There are no other cage couplings, so there can be no methylene or ethylidene groups in the molecule. Now when an anionic charge moves between quinone molecules, linking them together, its journey must be terminated by adding a proton and the resulting terminus must then constitute an hydroxy group, a ring methylene group, or a ring ethylidene group. If the medium is basic enough it is also possible for one charge-journey to end and for the base to remove a second proton thus starting a second, independent charge-journey. This happens in the synthesis of bridge triones discussed in other studies.[11] It is important that each independent charge-journey must have its own terminus, and that in the present compound there is only one such terminus, the hydroxy group. This proves that the entire molecule is constructed by the journey of a single charge originating from carbanion (1a).

We can now recognise that the naphthoquinonyl residue becomes attached at a site already bearing a methyl group (for convenience designated Me*) as in (15). The only other way to account for the absence of the M part of an ABM system would be to suppose that after reaction occurred to give such a system the M proton was removed and replaced by some other group. But this can only be done by starting a second charge-journey, which has already been ruled out. Hence, there is a methyl group (Me*) at the point where the naphthoquinonyl residue is attached. In agreement, a semiquantitative study of the relative yields of products show that the cage tetraketone (3) is not greatly affected by changes in catalyst or reactant concentrations, whereas the polyketone (4a) is formed at the expense of the fluorene alcohol (11) with the same type of attachment.



The next consideration is what happens when a second benzoquinone unit arrives to combine with the intermediate (15). As with the simpler cage tetraketones, Michael additions in modes p and q may be postulated and mode q leads to diagram (16). It is evident that, when the third (and last) benzoquinone unit arrives it can be accommodated only underneath the lower ring of (16) as a bridging aldol arrangement of the kind already proscribed. And if the charge in the lower ring is first passed to the upper ring giving (17) the third benzoquinone unit can be accommodated on top, but again only in the same unsatisfactory manner. These arguments apply equally when the p mode of addition is considered, and we are forced to conclude that neither mode is correct. Hence the second benzoquinone unit does not form a bridge across (15) at this stage but adds at one point only giving intermediate (18). To proceed we have to take cognizance of the fact that (18) is constructed from chiral elements the relative configurations of which will control the later possibilities. Scheme 2 shows the consequences for the particular arrangement



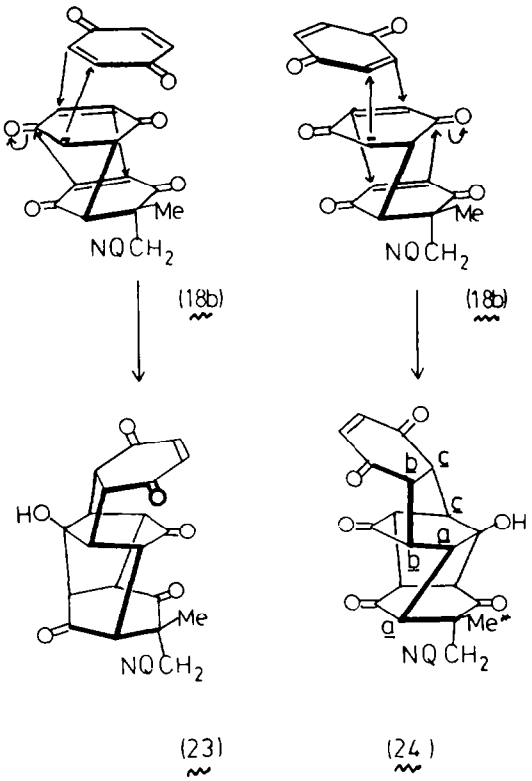
Scheme 2

in (18a). The third (and last) benzoquinone unit must form a bridge (but not an aldol) and can add in mode p or mode q, the latter giving intermediate (19) where the charge can continue its journey in various ways most of which can be dismissed at once because they lead to cyclobutanol derivatives that would not be stable in the alkaline conditions used. A more acceptable way is indicated in Scheme 2 by arrows and leads to framework (20) without small-ring strain, but with a cyclopentanone-type carbonyl group for which there is no evidence. The ir spectrum shows peaks for conjugated carbonyl groups ($\nu_{max.}$ 1 660 - 1 683 cm^{-1}) and cyclohexanone-type carbonyl groups ($\nu_{max.}$ 1 702 cm^{-1}) or strained cyclohexanone groups ($\nu_{max.}$ 1 720, 1 738 cm^{-1}) but none above 1 745 cm^{-1} demanding a smaller ring. Other reasons for excluding this framework appear later.

If intermediate (18a) (Scheme 2) adds the third benzoquinone unit in the p mode the product (21) must contain a cyclopentanone residue, but it happens that this carbonyl group can be the one that is destroyed in providing the terminal aldol function. Framework (22) results although it has to be eliminated eventually because the methyl substituents cannot be accommodated convincingly and because it fails to explain all the nmr findings.

Two more frameworks can be derived from the intermediate in its alternative configuration (18b) (Scheme 3). Addition in the p mode produces an arrangement (23) which, like (20) and (22), contains two fused cyclopentane rings which cannot be fitted into the rest of the framework without undue difficulty, whereas addition in the q mode leads neatly to framework (24). However, the most compelling reason for accepting framework (24) is that it provides sites with torsion angles for methine protons near to 60° demanded by a vicinal coupling of 1.6 Hz (Table 1); the other possess torsion angles no nearer than about 45°.

Methyl groups can now be added to framework (24) beginning with the lowest ring which has already been orientated. There are three sites (aa, bb, and cc) any one of which can provide the necessary torsion angle of 60°, the other two then bearing at least one methyl group. If we choose bb or cc we find that the methyl groups cannot be placed without incurring two 1,3-diaxial repulsions; if we choose aa then no major repulsions need result and structure (4a) is reached. Moreover, similar arguments force the rejection of all the alternative frameworks,



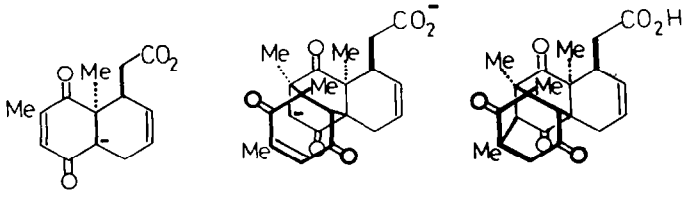
(23) (24)

Scheme 3

none of which can be mantled with substituents without substantial collisions. These are found mainly with the group Me* which has to lie on a folded seven-membered ring pointing inwards and jutting into any group or even hydrogen atom projecting from the opposite side. In the collision-free structure (4a) there is, of course, a seven-membered ring but it does not bear Me* and its opposing sites carry carbonyl groups that point away from (rather than towards) each other.

Now that structure (4) has been established a special feature of the ^{1}H nmr spectrum of the acetate can be understood. This is the marked downfield shift of 1.36 p.p.m. in the signal for one of the methine singlets (Table 1). No other signal is affected very much. A model of the acetate shows that the ester residue has to avoid the cage methyl groups nearest to it, and that when it does so the carbonyl oxygen atom points almost directly at the methine proton at position 4 and would certainly strongly deshield it. A similar situation has been reported for the acetate of granaticin.[13]

Since we first reported cage formation[2,12] two other examples have been reported.[14] Both products were assigned structures by X-ray methods and conform to the arguments advanced above. Thus, 2,6-dimethyl-1,4-benzoquinone adds in Diels-Alder fashion to sodium (E)-4,6-dienoate giving (if the solution is alkaline enough) the carbanion (25) which then adds another quinone molecule to form the intermediate (26) and thence the cage (27). Here the orientation of the bridge in intermediate (26) is that required to avoid collisions of methyl groups with others in 1,3-diaxial relations while the final ring closure can be completed by external addition of a proton to form a ring methylene group. The compound exhibits ir bands (in trichloromethane) at 1 765 (cyclopentanone) and 1 725 cm^{-1} (cyclohexanone and ester after esterification). With 2,5-dimethyl-1,4-benzoquinone a similar reaction gives a cage compound, but we cannot comment upon it because the nmr spectrum contains features that seem to be inconsistent with the structure allocated.

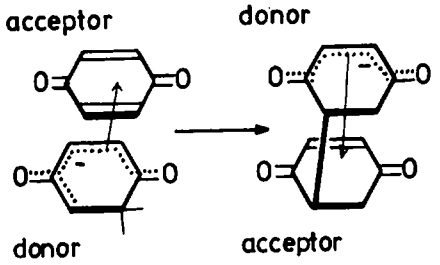


(25) (26) (27)

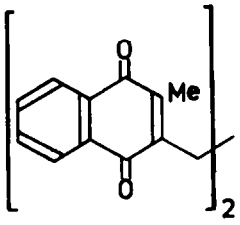
Theoretically, cage formation can be initiated by the Michael addition of any carbanion capable of reacting with a quinone, but in practice this is not

so. Very many quinone-anion reactions have been studied and we have repeated some (e.g., with malonate carbanions or cyanide ion) without detection cage formation.[15] What inter-ring additions are known are very limited.[16] We seem forced to conclude that cage formation (or even bridge formation) can only be initiated by an anion that either contains a quinone residue already or is an enedione derived from one. We, therefore, propose that the essential feature of these reactions is that they occur within charge-transfer complexes resembling quinhydrones.

When the naphthoquinonyl carbanion (donor) and the dimethylbenzoquinone (acceptor) first come together they are considered to do so in roughly parallel planes and with maximal overlap of the unsaturated centres involved in the charge-transfer stabilisation as in diagram (28). The point is that, when the Michael addition (or radical coupling) occurs, the charge-transfer stabilisation does not disappear; the two components retain approximately their geometrical relation but the benzoquinone residue becomes the donor and the naphthoquinone residue the acceptor as in diagram (29). The two components simply exchange their charge-transfer roles. Since the new carbanion is stabilised thereby it will be rather slow to accept a proton or to undergo other reactions and it can, therefore, have a lifetime long enough for another benzoquinone molecule to approach. This explains why the original carbanion has to be quinonoid for cage formation to be initiated.



(28) (29)



(30)

When the second benzoquinone residue takes up residence adjacent to the new anionic ring it takes over from the naphthoquinone residue the function of charge acceptor for which purpose maximal overlap is again required and the conditions for cage formation are now complete unless there are collisions amongst the methyl and other groups. If there are, the whole process can be repeated so as to add a third benzoquinone residue which, we believe, is what controls the sequence (18a)→(21)→(22). All the cage compounds have structures in agreement with the postulate of maximal overlap and so do all the bridged quinones such as (7) where their relative configurations have been fully established. It will be noted that this principle is required to assign a configuration to the enedione ring in the alcohol (4a) because we lack any convincing spectroscopic or other evidence on this score.

The charge-transfer phenomenon can also be supposed to make the Michael additions much more easily reversible than is usual when carbanions have to be extruded. In addition to exampled noted above, there is the base-catalysed collapse of the fluorene alcohol (13) which eventually supplies the ethylene diquinone[18] (30) as the chief product, evidently because the anion (1a) is formed reversibly until it is all removed as this dimer. This reversibility is important, because it allows some fairly small steric effects to dominate the orientations and secure selectivity. The existence of the steric effects, between methyl groups if no others, has long been clear from studies on quinhydrones.[17] Tetramethyl-1,4-benzoquinone is unable to form a quinhydrone at 20 °C though it can at lower temperatures. Accordingly, this quinone is not known to give cage or even bridge structures, and while trimethylbenzoquinone forms bridged systems by utilising its less substituted side, it is still unable to complete the formation of a cage system.

EXPERIMENTAL

Ir spectra were recorded on a Perkin-Elmer 125 spectrophotomer. Nmr spectra were recorded with a Perkin-Elmer R34 CW spectrometer (^{1}H; 220 MHz) or a Bruker WM250 spectrometer from FT spectra for both ^{1}H and ^{13}C nuclei. Mass spectra were obtained using AEI MS20 and VG Analytical 7070E machines.

Tetrahydrofuran was distilled from benzophenone-sodium immediately before use. Light petroleum refers to the fraction b.p. 40 - 60 °C and was distilled before use.

Cage Tetraketone (2) : 3,4,4a,6,7,8a-Hexahydro-4,7,8a,9-tetramethyl-6-(3-methyl-1,4-naphthoquinon-2-ylmethyl)-4,1,7-ethanylylidenenaphthalene-2(1H)-5,8,10-tetraone. - 3a,9a-Dihydro-9a-methyl-3H-benz[f]indazole-4,9-dione[18] (84 mg) in tetrahydrofuran (0.5 ml) was mixed with 2,6-dimethyl-1,4-benzoquinone (100 mg) in methanol (0.5 ml) and stirred at 0 °C during the gradual addition of 0.1M sodium hydroxide (0.2 ml). The mixture rapidly turned red and then very dark while nitrogen was evolved. After 20 minutes acidification with 2M hydrochloric acid gave a clear yellow solution that soon deposited yellow crystals along with a gum. The supernatant liquor was decanted and the residue washed with water and crystallised from ethanol to provide the tetraone as yellow prisms (53 mg; 30% based on indazole derivative), m.p. 230 - 233 °C, $\lambda_{max.}$ (EtOH) 246, 264 and 328 nm (log ε 4.32, 4.18 and 3.59), $\nu_{max.}$ (nujol) 1 755, 1 723, 1 660, 1 300 and 723 cm^{-1}, $\nu_{max.}$ (KBr) 1 760, 1 738, 1 723, 1 667, 1 295 and 728 cm^{-1} (Found: C, 73.1; H, 5.7%; M$^+$, 458. $C_{28}H_{26}O_6$ requires C, 73.4; H, 5.7%; M, 458).

Base Catalysed Isomerisation of Bridge Trione (7). - A solution of the bridge trione (7) (20 mg) in pyridine (1 ml) was diluted with methanol (2 ml) and then 0.1M sodium hydroxide was added. After 5 minutes the reaction was stopped by acidification with dilute hydrochloric acid, diluted with water, and extracted with ether. The extract furnished a solid that crystallised from methanol giving the cage tetraketone (2) (3 mg; 15%) identified spectroscopically. The mother liquors were concentrated and left to deposit the quinol (8) as yellow prisms (6 mg; 30%) also identified spectroscopically.

When the quinol (8) was further treated with alkali under the same conditions it darkened and decomposed giving intractable material not examined further. T.l.c. showed that the cage tetraketone (2) was not formed.

Fluorene Alcohol (13) ; 7a,11a-Dihydro-11b-hydroxy,6,7a,10,trimethyl-7H-benzo[a]fluorene-5-(11bH)-8,11-trione. - 3a,9a,-Dihydro-9a-methyl-3H-benz[f]-indazole-4,9-dione[18] (84 mg) in tetrahydrofuran (0.5 ml) and 2,5-dimethyl-1,4-benzoquinone (100 mg) in methanol (0.5 ml) were mixed and treated at 0 °C with 0.1M sodium hydroxide (0.2 ml). After 2 h the solution was acidified with dilute hydrochloric acid, diluted with water, and extracted with trichloromethane. The extract was dried ($MgSO_4$) and concentrated to a residue that crystallised from benzene to give the trione as tiny prisms (50 mg; 40% based on indazole derivative), m.p. 186 - 189 °C, $\lambda_{max.}$ (EtOH) 244 and 274 nm (log ε 4.15 and 3.79), $\nu_{max.}$ (nujol), 3 420, 1 670, 1 645 and 725 cm^{-1} (Found: M$^+$, 322.120 48. $C_{20}H_{18}O_4$ requires M, 322.120 50), δ (at 100 MHz) ($CDCl_3$), 1.36 (3H, s, 7a-Me), 1.65 (3H, 6-Me, long range coupling ca. 1 Hz with 7-CH_2), 2.44 and 3.79 (each 1H, d, J 18 Hz; 7-CH_2 with long range coupling ca. 1 Hz with 6-Me), 2.15 (3H, d, J 1.7 Hz; 9-Me), 6.68 (1H, m, vinylic H), 2.81 (1H, s, 11a-H), 7.29 (2H, m, 2-H and 3-H), 7.44 (1H, dd, 1-H), 7.83 (1H, dd, 4-H), and ca. 2.3 (OH, br, removed by D_2O).

This compound is sensitive to alkali. A sample (20 mg) in methanol (4 ml) at room temperature turned red and then deep purple when treated with 2M sodium hydroxide (1 drop) and after 20 min. t.l.c. and mass spectroscopy indicated the

presence of cage tetraketone (3), ethylenediquinone (30), methylenediquinone (11) and other compounds. After 1.5 h the solution was acidified and the products isolated by means of dichloromethane. Crystallisation from ethanol gave the ethylenediquinone[18] (30) as the major component (14 mg; 59%).

Cage Tetraketone (3); 3,4,4a,6,7,8a-Hexahydro-1,4,6,8a-tetramethyl-7-(3-methyl-1,4-naphthoquinon-2-ylmethyl)-4,1,6-ethanylylidenenaphthalene-2-(1H)-5,8,9-tetraone. - The mother liquors from the fluorene alcohol in the previous experiment were combined, the solvents removed *in vacuo*, and the residue chromatographed on silica from benzene-trichloromethane (9:1 v/v). The earliest eluates contained the desired material which crystallised from ethanol containing a little trichloromethane to yield the tetraone as hexagonal prisms (24 mg; 20%), m.p. 260 °C, $\lambda_{max.}$ (EtOH) 250, 258 sh, and 331 nm (log ε 4.46, 4.37 and 3.57), $\nu_{max.}$ (nujol), 1 728, 1 658, 1 295 and 732 cm^{-1}, $\nu_{max.}$ (KBr) 1 735, 1 722, 1 662, 1 290 and 722 cm^{-1} (Found: C, 73.1; H, 5.8; M^+ 458. $C_{28}H_{26}O_6$ requires C, 73.3; H, 5.7%; M, 458).

In solution (acetone best) this compound gives a deep blue colour with a drop of bench sodium hydroxide.

Cage Polyketone (4); 4a-Hydroxy-1,4,4a,5,5a,8a,9a,10a-octahydro-2,5,7,9a,10-13-hexamethyl-2-(3-methyl-1,4-naphthoquinone-2-ylmethyl)-1,4,5,10-buta[1,2,3,4]-tetraylanthracene-3(2H)- 6,9,11,14-pentaone. - 3a,9a-Dihydro-9a-methyl-3H-benzo[f]indazole-4,9-dione (0.84 g) in trichloromethane (10 ml) was mixed with 2,5-dimethyl-1,4-benzoquinone (2 g) in methanol (50 ml) at room temperature and treated with M-sodium hydroxide (0.13 ml). The mixture rapidly became red and then almost black and effervesced strongly. When the reaction subsided (about 15 min.) the mixture was acidified with dilute hydrochloric acid; it lightened in colour and when left for some hours deposited yellow crystals (1.1 g; 50%) of almost pure pentaone which, for analytical purposes, was recrystallised from ethanol-trichloromethane and then benzene and obtained as pale yellow needles, m.p. 315 - 317 °C (decomp.), $\lambda_{max.}$ (EtOH), 245, 261 and 330 nm (log ε 4.50, 4.25 and 3.59), $\nu_{max.}$ (nujol), 3 380, 1 730, 1 660, 1 297 and 720 cm^{-1}; $\nu_{max.}$ (KBr), 3 370, 1 738, 1 720, 1 702, 1 660, 1 294 and 710 cm^{-1} (Found: C, 72.4; H, 5.7% M^+, 594. $C_{36}H_{34}O_8$ requires C, 72.7; H, 5.8%; M, 594).

This compound is not very soluble in the usual solvents but dissolves a little in trichloromethane, benzene, or acetone. Ethanolic solutions are unaffected by bench sodium hydroxide and do not become coloured and give no sign (t.l.c.) of reaction, but pyridine solution becomes dark blue in contact with 10N-sodium hydroxide. The compound is relatively stable to acids, and is recovered from a solution in warm trifluoroacetic acid after several hours. It is recovered almost quantitatively from a solution in 80% acetic acid containing chromium trioxide.

The compound is unaffected by acetic anhydride containing sodium acetate but when it (0.15 g) is warmed to 50 °C for a few minutes with acetic anhydride (5 ml) containing a trace of sulphuric acid it is transformed into the acetate which separates from ethanol in pale yellow needles (0.12 g; 72%), m.p. 260 - 262 °C, $\lambda_{max.}$ (EtOH), 244, 260 and 328 nm (log ε 4.43, 4.16 and 3.51), $\nu_{max.}$ ($CHCl_3$), 1 753, 1 730, 1 717, 1 683, 1 295 and 728 cm^{-1} (Found: C, 71.6; H, 6.0%; M^+, 636. $C_{38}H_{36}O_9$ requires C, 71.7; H, 5.7%; M, 636).

Diazomethane-d_2 (ca. 0.70 g), prepared by Campbell's method,[19] was added to 2-methyl-1,4-naphthoquinone (0.70 g) in ether (50 ml) and supplied 3a,9a-dihydro-9a-methyl-3H-benzo[f]pyrazole-3,3-d_2-4,9-dione (0.48 g) in the same way as for the unlabelled compound.[18] Without further purification, this product (0.42 g) was dissolved in trichloromethane (5 ml),added to 2,5-dimethyl-1,4-benzoquinone (1.0 g) in methanol (25 ml), and treated with 1N-sodium hydroxide (0.065 ml). The reaction

was quenched with dilute hydrochloric acid after about 15 min., and the usual work-up and purification of the product from ethanol then gave 4a-hydroxy-1,4,4a-5,5a,8a,9a,10-octahydro-2,5,7,9a,10,13-hexamethyl-2-(3-methyl-1,4-naphthoquinon-2-ylmethyl-d_2)-1,4,5,10-buta[1,2,3,4]tetraylanthracene-3(2H)-6,9,11,14-pentaone (4b) as yellow crystals, m.p. 315° (Found: M, 596.23 405. $C_{36}H_{32}D_2O_8$ requires M, 596.23 792). The compound was further characterised as the acetate, m.p. 260° (Found: M, 638,26 066. $C_{38}H_{34}D_2O_9$ requires M, 638.24 705). The ^{1}H NMR spectrum of this acetate was identical with that of the unlabelled analogue except for the absence of methylenic bands (Table 1).

Minor Products from 2,5-Dimethyl-1,4-Benzoquinone. - The above reaction was conducted on a larger scale so as to secure the minor products. The tetrahydroindazole derivative [18] (1.06 g) in trichloromethane (10 ml) was mixed with 2,5-dimethyl-1,4-benzoquinone (2.0 g) in methanol (80 ml) and treated with sodium acetate trihydrate (1.4 g) in methanol (15 ml). After 30 min. crystalline material separated and was identified as cage tetraketone (3) (0.6 g). The solution was concentrated to 50 ml and kept for several hours to allow the separation of a yellow powder purified from benzene and identified as the cage polyketone (4) (0.88 g). The rest of the reaction mixture was acidified, diluted with water, and extracted with benzene. The product was examined by chromatography on silica from benzene-light petroleum (1:4 V/V) which eluted residual 2,5-dimethylbenzoquinone. Further elution with these solvents (1:1) then supplied 3-methyl-2-(3,6-dimethyl-1,4-benzoquinon-2-ylmethyl)-1,4-naphthoquinone (11) which crystallised from light petroleum as long yellow needles (0.14 g), m.p. 158 - 159 °C, $\lambda_{max.}$ 251, 260 and 332 nm (log ε 4.42, 4.41 and 3.50), $\nu_{max.}$ (nujol), 1 659, 1 645, 1 620, 1 591 and 729 cm^{-1}, δ (at 60 MHz) ($CDCl_3$), 2.30 and 2.18 (each 3H, s, quinone Me), 2.04 (3H, d, J 2 Hz; vinylic Me), 6.63 (1H, q, J 2 Hz; vinylic H), 3.80 (2H, br.s., CH_2), 7.77 (2H, m; aromatic β-H), and 8.11 (2H, m, aromatic α-H) (Found: C, 74.8; H, 5.0%. $C_{20}H_{16}O_4$ requires C, 75.0; H, 5.0%).

The next fraction was eluted by benzene-trichloromethane (4:1) and contained two components; one was hardly soluble in cold ethanol and supplied more (0.08 g) of the cage polyketone whereas the soluble component was found to be the enedione (12), 3-methyl-2-(1,4-dimethyl-2,5-dioxocyclohex-3-en-2-ylmethyl)-1,4-naphthoquinone, and separated from light petroleum as small yellow needles (0.18 g), m.p. 176 - 177 °C, $\lambda_{max.}$ 231, 256 and 301 nm (log ε 4.42, 3.98 and 3.27), $\nu_{max.}$ (nujol), 1 678, 1 660, 1 610, 1 596 and 718 cm^{-1}, δ (60 MHz) ($CDCl_3$), 1.32 (3H, s, angular Me), 2.18 (3H, br.s., quinone Me), 1.94 (3H, d, J 2 Hz, vinylic Me), 6.56 (1H, m, vinylic H), 2.87 and 3.13 (each 1H, d, J 13 Hz, CH_2), 2.71 and 2.86 (each 1H, J 15.5 Hz, CH_2), 7.72 (2H, m, aromatic β-H), and 8.03 (2H, m, aromatic α-H), (Found: C, 74.5; H, 5.5%. $C_{20}H_{18}O_4$ requires C, 74.5; H, 5.6%).

REFERENCES

1. F.M.Dean, G.H.Mitchell, R.Parvizi and C.Thebtaranonth, *J.Chem.Soc., Perkin Trans. 1*, 1976, 2067.
2. F.M.Dean, L.E.Houghton, R.Nayyir-Mashir and C.Thebtaranonth, *J.Chem.Soc., Chem.Commun.*, 1979, 98.
3. R.N.Jones, D.A.Ramsey, D.S.Kier and K.Dobriner, *J.Am.Chem.Soc.*, 1952, 74, 80: F.M.Dean and T.A.Geissman, *J.Org.Chem.*, 1958, 23, 596.
4. M.Nakazaki, K.Naemura and N.Arashiba, *J.Org.Chem.*, 1978, 43, 888; A.Nickon, H.R.Kwasnik, T.Mathew, T.D.Swartz, R.O.Williams and J.B.DiGiorgio, *J.Org. Chem.*, 1978, 43, 3904; J.I.Brauman and V.W.Laurie, *Tetrahedron*, 1968, 24, 2595; T.Sasaki, S.Eguchi, T.Kiriyama and O.Hiraoka, *Tetrahedron*, 1974, 30, 2707; W.G.Dauben and L.N.Reitman, *J.Org.Chem.*, 1975, 40, 835; S.Danishefsky, G.Koppel and R.Levine, *Tetrahedron Letts.*, 1968, 2257; A.J. Pearson, *Tetrahedron Letts.*, 1980, 21, 3929; E.H.Gold and D.Ginsberg, *J.Chem.Soc., (C)*, 1967, 15; R.C.Cookson and D.C.Warrell, *J.Chem.Soc., (C)*, 1967, 1391; R.Mitschka, J.M.Cook and U.Weiss, *J.Am.Chem.Soc.*, 1978, 100, 3973; K.B.Wiberg and A.deMeijere, *Tetrahedron Letts.*, 1969, 59;

A.S.Narula, *Tetrahedron Letts.*, 1979, 1921; M.Nakazaki, K.Naemura and Y.Kondo, *J.Org.Chem.*, 1979, 44, 16; T.Courtney, D.E.Johnston, M.A.McKerney and J.J.Rooney, *J.Chem.Soc., Perkin Trans. 1*, 1972, 2691; B.Föhlisch, E.Schupp, U.Dukek and I.Graessle, *Liebigs Ann.*, 1973, 1839; R.C.Cookson, E.Crundwell, R.R.Hill and J. Hudec, *J.Chem.Soc., (C)*, 1964, 3062; P.Yates, G.D.Abrams, and L.L.Williams, *Tetrahedron Letts.*, 1969, 4241; P.W.Hickmott and J.R. Hargreaves, *Tetrahedron*, 1967, 23, 3151; G.Mehta and D.Subrahmanyam, *J.Chem.Soc., Chem.Commun.*, 1985, 768; G.Mehta and M.S.Nair, *J.Chem.Soc., Chem.Commun.*, 1983, 439.

5. A.P.Marchand, R.Kaya and A.D.Baker, *Tetrahedron Letts.*, 1984, 25, 795; G.Klein and L.A.Paquette, *J.Org.Chem.*, 1978, 43, 1293; N.A.LeBel and R.N. Liesemer, *J.Am.Chem.Soc.*, 1965, 87, 4300; G.Jähre and R.Gleiter, *Angew. Chem.Suppl.*, 1983, 661; G.Mehta and M.S.Nair, *J.Chem.Soc., Chem.Commun.*, 1985, 629.
6. L.J.Bellamy, "Advances in Infrared Group Frequencies", Methuen, London, 1968.
7. F.M.Dean, L.E.Houghton and R.B.Morton, *J.Chem.Soc., (C)*, 1967, 1980.
8. L.M.Jackman and S.Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", Pergamon, Oxford, 1969.
9. J.W.ApSimon, P.V.Demarco, D.W.Mathieson, W.G.Craig, A.Karim, L.Saunders and W.B.Whalley, *Tetrahedron*, 1970, 26, 119.
10. K.Hirao and O.Yonemitsu, *J.Chem.Soc., Chem.Commun.*, 1980, 423.
11. F.M.Dean, K.B.Hindley and L.E.Houghton, *J.Chem.Soc., (C)*, 1971, 1171.
12. F.M.Dean, L.E.Houghton, R.Nayyir-Mashir, and C.Thebtaranonth, *J.Chem.Soc., Perkin Trans. 1*, 1980, 1994.
13. W.Keller-Schierlein, M.Brufani and S.Barcza, *Helv.Chim.Acta*, 1968, 51, 1257.
14. P.A.Grieco, P.Garner, K.Yoshida and J.C.Huffman, *Tetrahedron Letts.*, 1983, 24, 3807.
15. M.A.Aldersley, F.M.Dean and R.Nayyir-Mashir, *J.Chem.Soc., Perkin Trans. 1*, 1983, 1753.
16. C.H.Foster and D.H.Payne, *J.Am.Chem.Soc.*, 1978, 100, 2834; H.Igeta, T.Tsuchiya and C.Kaneko, *Tetrahedron Letts.*, 1971, 2883.
17. A.A.Bothner-By, *J.Am.Chem.Soc.*, 1951, 73, 4228; L.Michaelis and S.Granick, *J.Am.Chem.Soc.*, 1944, 66, 1023.
18. F.M.Dean, P.G.Jones, R.B.Morton and P.Sidisunthorn, *J.Chem.Soc.*, 1963, 1018.
19. J.R.Campbell, *Chem. and Ind.*, 1972, 540.