RECENT PROGRESS IN THE ANNULENE FIELD

F. SONDHEIMER

Department of Chemistry, University College, London W.C. 1, UK

ABSTRACT

An account is given of recent progress made in the synthesis of annulene derivatives containing an odd number of carbon atoms in the ring. Three types of such 'odd' annulenes are discussed, namely macrocyclic conjugated ketones (annulenones), ions, and allenes. The synthesis of dehydroannulenones containing 13-, 15- and 17-membered rings has been achieved. As expected, the n.m.r. spectra of the dehydro[13]- and dehydro[17]annulenones revealed the existence of a paramagnetic ring current, showing them to be non-aromatic. Conversely, the n.m.r. spectrum of the dehydro[15]annulenone revealed the existence of a diamagnetic ring current, showing it to be aromatic. These ring current effects could be increased through protonation. One of the dehydro-[17]annulenones has been converted to a methoxydehydro[17]annulenyl anion, the first large-ring conjugated mono-anion to be prepared. The n.m.r. spectrum of this ion showed the existence of a strong diamagnetic ring current, as expected for an aromatic 18π-electron system. Attempts to convert some of the intermediates in these syntheses to allene-annulenes are described, but it has not yet been possible to prepare such compounds, presumably because of their instability.

As is now quite well known, the 'annulenes' is the name we gave several years ago to the completely conjugated monocyclic polyenes, and the 'dehydroannulenes' to the completely conjugated monocyclic polyenynes (that is to say, annulenes in which one or more of the double bonds have been replaced by acetylenes)[1]. These compounds are of considerable interest, since they should be aromatic if they contain a closed shell of $(4n + 2)$ out-of-plane π-electrons*, a reasonably planar carbon skeleton, and the ring size is below a certain limit[2].

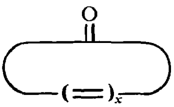
About twelve years ago at the Weizmann Institute of Science in Israel we developed a rather general method, which has enabled us to synthesize a whole range of annulenes and dehydroannulenes. In agreement with expectation, the [14]-, [18]-, and [22]-annulenes and/or dehydroannulenes all proved to be aromatic, as shown by the possession of a diamagnetic ring current in the nuclear magnetic resonance (n.m.r.) spectra. Conversely, the [12]-, [16]-, [20]-, and [24]-annulenes and/or dehydroannulenes all proved to be non-aromatic, as shown by the possession of a paramagnetic ring current in the n.m.r. spectra. I have lectured about most of this work on a number of occasions, and it has been adequately reviewed[3,4]. Therefore, I

---

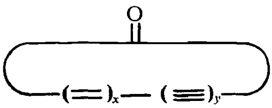
* This is the well known 'Hückel's rule', which has been adopted as the symbol for this symposium.

'ODD' ANNULENES

(1) KETONES



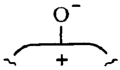
or



(1)
Annulenones

(2)
Dehydroannulenones

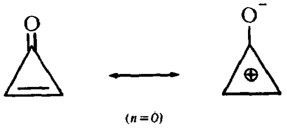
Polarization:



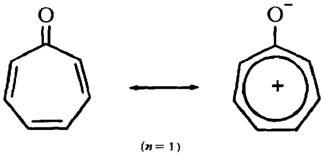
(3)

[4n + 3]Annulenone → (4n + 2)π-system

Examples:



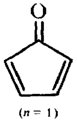
(4a) (4b)



(5a) (5b)

[4n + 1]Annulenone → (4n)π-system

Example:



(6)

will not deal with this aspect of annulene chemistry, involving rings made up of an *even* number of carbon atoms. Instead, I would like to give an account of recent progress made in the synthesis of annulenes containing an *odd* number of carbon atoms in the ring.

There are three different types of 'odd' annulenes which I would like to discuss. First, one may consider conjugated monocyclic ketones, formally derived from the annulenes by incorporating a carbonyl group into the ring. We may have the annulene derivatives themselves [type (**1**)], as well as the corresponding dehydroannulene derivatives [type (**2**)]. For convenience, we have named these groups of compounds 'annulenones' and 'dehydroannulenones', respectively. Since the direction of polarization of a carbonyl group is as shown in formula (**3**), an annulenone or dehydroannulenone containing a $(4n + 3)$-membered ring will represent a $(4n + 2)$ π-electron system and should therefore be aromatic. Well known examples are the aromatic cyclopropenone (**4**) ($n = 0$)[5] and tropone (**5**) ($n = 1$)[6], although the aromaticity of the last-mentioned substance has recently been questioned[7]. Conversely, such compounds containing a $(4n + 1)$-membered ring will represent a $4n$ π-electron system, and should therefore be non-aromatic. An example is cyclopentadienone (**6**) ($n = 1$)[8], which is very unstable and readily undergoes self-condensation. No annulenone, or simple derivative of an annulenone, containing a ring larger than the 7-membered one was known when we started our work in this field†. It appeared of interest to synthesize and study the properties of higher members, both in the theoretically aromatic $[4n + 3]$annulenone and the theoretically non-aromatic $[4n + 1]$annule-

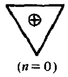
---

† Bridged [11]annulenones have now been prepared by Professor E. Vogel and his group[9].

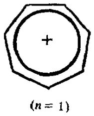
(2) IONS

$(4n + 3)$-Membered ring: Cation → $(4n + 2)\pi$-system

Examples:



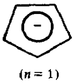
(7)



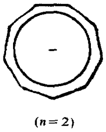
(8)

$(4n + 1)$-Membered ring: Anion → $(4n + 2)\pi$-system

Examples:



(9)



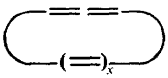
(10)

none series, in order to find out whether the same criteria for aromaticity apply as have been found for the hydrocarbons.

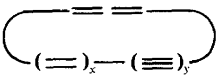
The second type of 'odd' annulenes I would like to discuss is monoionic species. If we have a $(4n + 3)$-membered ring, then the cation will be a $(4n + 2)$ π-electron system and should be aromatic. Well known examples are the cyclopropenium cation **(7)** $(n = 0)$[10] and the tropylium cation **(8)** $(n = 1)$[6]. Conversely, in a $(4n + 1)$-membered ring, the anion will be a $(4n + 2)$ π-electron system and should be aromatic. Examples are the cyclopentadienyl anion **(9)** $(n = 1)$[6] and the cyclononatetraenyl anion **(10)** $(n = 2)$[11]. In principle, it should be possible to synthesize and study a whole range of larger ring monoanions and cations, but the only such compound containing a ring larger than the 9-membered one to be prepared is the cation of a bridged 11-membered ring[12].

The third type of 'odd' annulenes I would like to mention is annulene derivatives containing an allene grouping. One may consider the allene-annulenes [type **(11)**] themselves, as well as the corresponding dehydro-annulene derivatives [type **(12)**]. The π-electron system in such compounds will possess a half-twist, since the substituents at each end of an allene grouping are perpendicular to each other, and this might have some interesting consequences. No examples of this type of compound are known (although there is some evidence for the existence of 1,2,4,5,7-cyclooctapentaene, a 'diallene-annulene', as a reactive intermediate[13]), and their synthesis is a challenge to the organic chemist.

(3) ALLENES

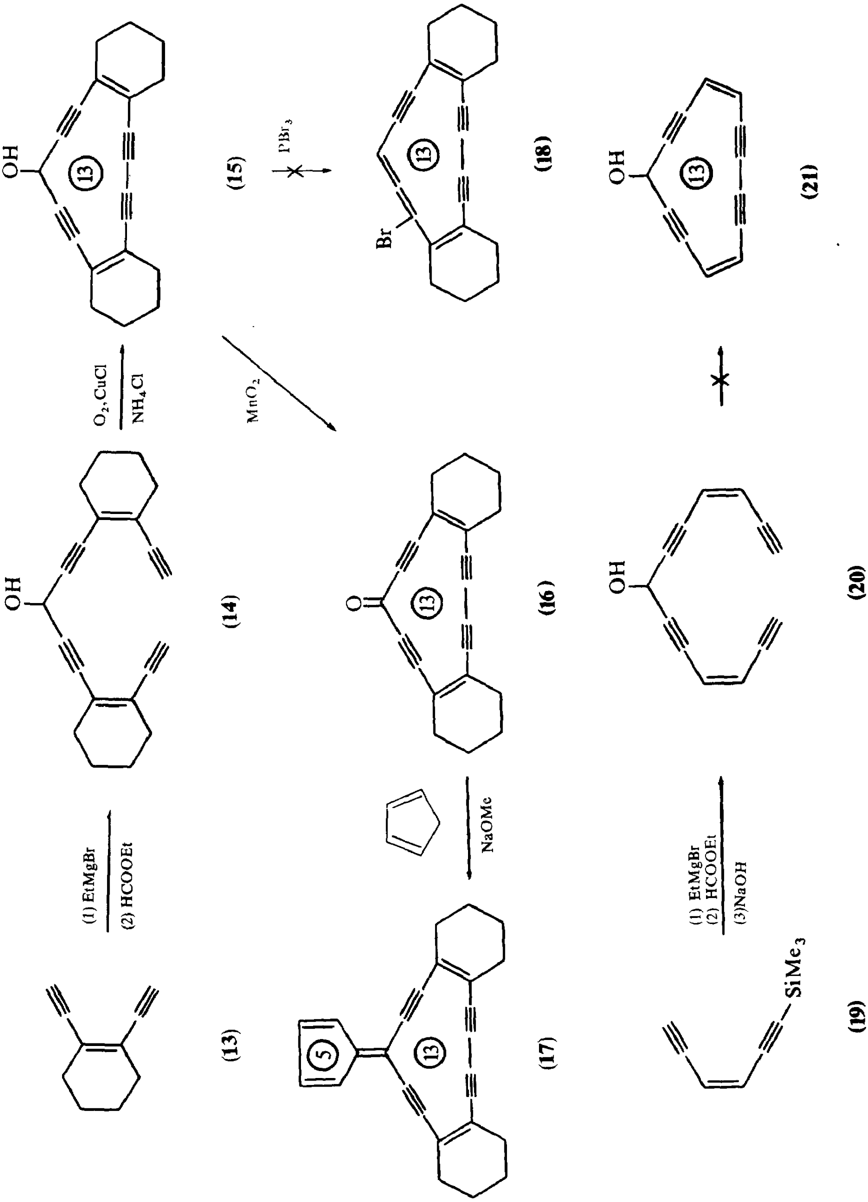


(11)



(12)

We have been studying the synthesis of all three types of 'odd' annulenes, and have succeeded in obtaining members belonging to the first two. In addition to these carbocyclic 'odd' annulenes, one may, of course, consider heterocyclic 'odd' annulenes. We have also been interested in the synthesis of such heterocyclic compounds, but lack of time prevents my discussion of this work.


(13)
(1) EtMgBr
(2) HCOOEt
OH
(14)
O$_2$,CuCl
NH$_4$Cl
OH
13
(15)
PBr$_3$
Br
13
(18)
MnO$_2$
O
13
(16)
NaOMe
5
13
(17)
SiMe$_3$
(19)
(1) EtMgBr
(2) HCOOEt
(3)NaOH
OH
(20)
OH
13
(21)

Our first experiments were carried out in the 13-membered ring series. After some early unsuccessful work utilizing 1,5-hexadiyne (for a brief review, see ref. 4), it was found that some success could be obtained when 1,2-diethynylcyclohexene (**13**) was employed as starting material. The cyclohexene ring in this substance ensures that the double bond possesses the required *cis* configuration, while its presence in the final conjugated systems should not seriously disturb the π-electron distributions.

The enediyne (**13**) was synthesized by two routes[14, 15], which I will not describe due to lack of time. Conversion to the mono-Grignard derivative by treatment with one equivalent of ethylmagnesium bromide and subsequent reaction with ethyl formate gave the secondary alcohol (**14**), which was coupled with oxygen, cuprous chloride, and ammonium chloride[14, 16]. The resulting unstable 13-membered ring alcohol (**15**), obtained in *ca.* 40 per cent yield, was then converted in over 90 per cent yield to the desired tetradehydro[13]annulenone (**16**) by oxidation with manganese dioxide[14, 16].

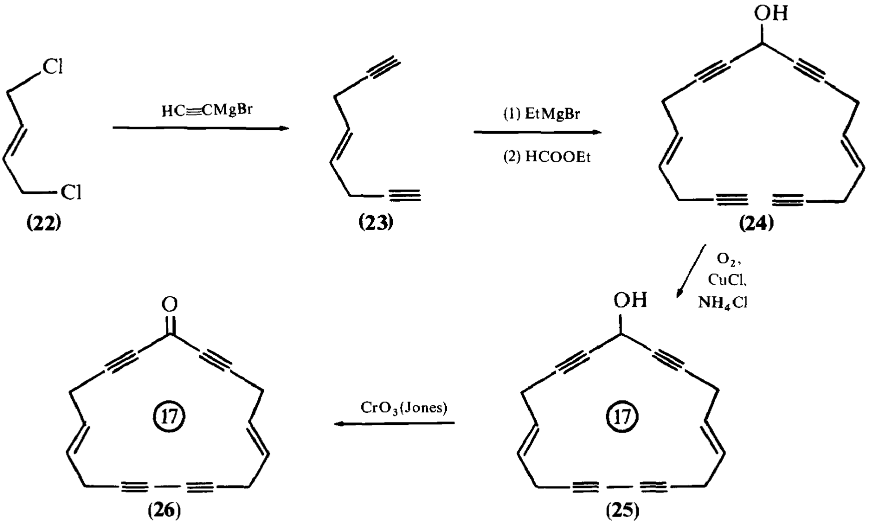
The ketone (**16**) was obtained as red prisms, which proved to be considerably more stable than the corresponding alcohol (**15**). The substance is a $[4n + 1]$annulenone derivative ($n = 3$). It should therefore be non-aromatic and sustain a paramagnetic ring current in an applied magnetic field[3, 4]. Unfortunately, no clear-cut evidence regarding this point could be obtained from the n.m.r. spectrum, since (**16**) contains no protons bound directly to the macrocyclic ring. This, of course, is a disadvantage of the cyclohexene ring fusion! However, the fact that the positions of the allylic methylene proton resonances in the n.m.r. spectrum of (**16**) were shifted upfield by about τ 0.3 compared with those in suitable model compounds was considered to be due, most likely, to a paramagnetic ring current[14, 16]. The significance of this shift has now been confirmed, as will be described in the sequel.

A number of reactions were carried out with the dehydro[13]annulenone (**16**). Probably the most interesting is the condensation with cyclopentadiene in the presence of sodium methoxide, which led to the relatively stable penta-tridecafulvalene (**17**) in 60 per cent yield[16, 17]. This is one of the first pentafulvalenes to be isolated which contains an unsubstituted cyclopentadiene ring.

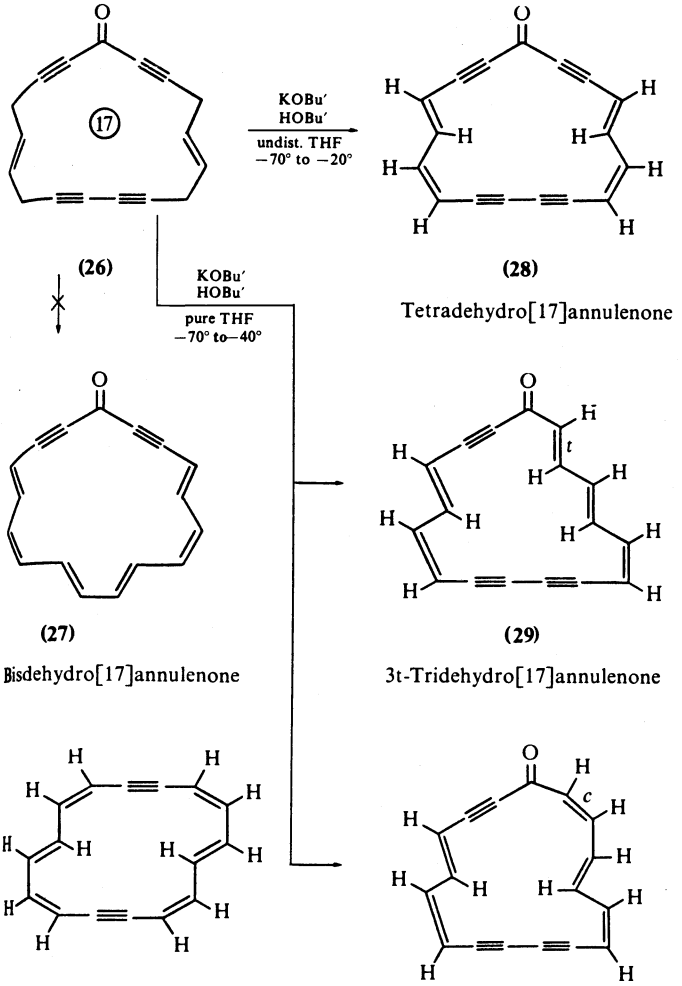
The 13-membered ring alcohol (**15**) was also a potential precursor of allene-annulene derivatives, the third type of 'odd' annulene which I discussed. It was hoped that reaction with phosphorus tribromide in tetrahydrofuran would lead to the completely 'conjugated' cyclic bromo-allene (**18**), since a closely related reaction to give an incompletely conjugated 13-membered ring cyclic bromo-allene had been carried out successfully by us[18]. Unfortunately, the product obtained under these conditions from (**15**) proved to be so extremely unstable that its structure could not be determined.

The fact that the tetradehydro[13]annulenone (**16**) contains no protons bound directly to the conjugated ring is obviously a disadvantage. In order to obtain the non-fused 2,6,8,12-tetradehydro[13]annulenone (in which the double bonds bear protons), it was necessary to use *cis*-3-hexene-1,5-diyne as starting material. A synthetic route to the last-mentioned substance was developed[19], and it was converted to the mono(trimethylsilyl) derivative (**19**) through successive reaction with ethylmagnesium bromide and chlorotrimethylsilane[20]. The Grignard derivative of (**19**) on treatment with ethyl formate and subsequent base hydrolysis gave *cis,cis*-3,10-tridecadiene-1,5,8,12-tetrayn-7-ol (**20**)[21]. There remained only the cyclization and oxidation of the hydroxyl group in order to achieve our objective. Unfortunately, all attempts to cyclize (**20**) to the 13-membered ring cyclic alcohol (**21**) were unsuccessful, only insoluble polymeric material being obtained[21]. Evidently, substance (**21**) is so unstable that it cannot be isolated, the greater stability of the closely related alcohol (**15**) presumably being due to the fusion of the two cyclohexenyl rings. The instability of the cyclic alcohol (**21**) is not unexpected, since a molecular model shows that such a 13-membered ring compound containing a 1,3-diyne grouping must be highly strained. For this reason we decided to work with larger ring compounds, in which the strain should be less, and our next experiments were designed to lead to 17-membered ring systems.

The starting material was *trans*-4-octene-1,7-diyne (**23**), which can be prepared readily by the condensation between *trans*-1,4-dichloro-2-butene (**22**) and an excess of ethynylmagnesium bromide[22]. Reaction of the mono-Grignard derivative of (**23**) with ethyl formate, as previously, led to the alcohol (**24**), which was coupled with oxygen, cuprous chloride, and ammonium chloride[23]. The resulting 17-membered ring alcohol (**25**), obtained in about 40 per cent yield, was then oxidized to the corresponding ketone (**26**), the best yield (> 90 per cent) in this case being achieved by use of chromium trioxide (Jones reagent)[23].



The cyclic ketone (**26**) contains 1,4-enyne groupings, and it was expected that rearrangement with potassium *t*-butoxide would lead to an isomeric bisdehydro[16]annulene [e.g. (**27**)], since closely related rearrangements have been carried out with cyclic 1,4-enyne hydrocarbons[24]. This expectation was not borne out in practice, since dehydrogenation as well as rearrangement was found to occur. In early experiments in which the ketone (**26**) was treated with potassium *t*-butoxide in *t*-butyl alcohol and undistilled tetrahydrofuran at −70° (followed by warming to −20°), the only conjugated product



(26)

(28)

Tetradehydro[17]annulenone

Yield: *ca*, 5%
i.r.: $\nu_{max.}$ 1 625 cm^{-1}
u.v.: main $\nu_{max.}$ 304 nm (ε 48 000)
n.m.r.: inner H, τ −0·31
outer H, τ 3·88 to 4·87

(27)

Bisdehydro[17]annulenone

(29)

3t-Tridehydro[17]annulenone

Yield: 25–30%
i.r.: $\nu_{max.}$ 1 625 cm^{-1}
u.v.: main $\lambda_{max.}$ 304 nm (ε 74 000)
n.m.r.: inner H, τ −0·50 to −0·10
outer H, τ 3·53 to 4·84

(31)

Bisdehydro[16]annulene
n.m.r.: inner H, τ 0·2
outer H, τ 3·92 to 4·73

(30)

2t-Tridehydro[17]annulenone

Yield: 15–20%
i.r.: $\nu_{max.}$ 1 609 cm^{-1}
u.v.: main $\lambda_{max.}$ 306 nm (ε 65 000)
n.m.r.: inner H, τ −0·10 to 0·42
outer H, τ 3·57 to 5·05

isolated (in about five per cent yield) was the symmetrical tetradehydro[17]-annulenone (**28**)[23]. This transformation involves the loss of four protons. When the reaction was carried out under similar conditions, but in freshly distilled tetrahydrofuran, two new conjugated ketones were isolated. Both of these proved to be tridehydro[17]annulenones, formed from (**26**) by loss of only two protons. One of the tridehydro[17]annulenones had the structure (**29**) containing three *trans* double bonds (three inner protons)[25], and the other had the structure (**30**) containing two *trans* double bonds (two inner protons)[26]. Under carefully controlled conditions, (**29**) and (**30**) could be obtained in yields of *ca.* 25–30 per cent and 15–20 per cent respectively[26].

The reason for the different result obtained in undistilled tetrahydrofuran is not known, but may be due to the presence of peroxides in this solvent.

The three dehydro[17]annulenones only differ in one of the multiple bonds adjacent to the carbonyl group, this being an acetylene in (**28**), a *trans* double bond in (**29**), and a *cis* double bond in (**30**). The structural assignments are based mainly on the mass spectra, and on the n.m.r. spectra, which will be mentioned later. All three substances were obtained as rather unstable dark red crystals, which are best stored in solution. The low infra-red carbonyl frequencies (1625, 1625, and 1609 cm^{-1}, respectively) are ascribed to the presence of the flanking multiple bonds, since acyclic models show similar carbonyl absorptions. The electronic spectra of the dehydro[17]annulenones all exhibited a main maximum at *ca.* 305 nm, the intensity of that of the tetradehydro compound (**28**), as expected, being lower than that of the tridehydro compounds (**29**) and (**30**).

The three dehydro[17]annulenones (**28**), (**29**) and (**30**) are the first monocyclic large-ring conjugated ketones to be prepared. Like the dehydro[13]-annulenone (**16**), they are $[4n + 1]$annulenone derivatives ($n = 4$). They should therefore be non-aromatic and sustain a paramagnetic ring current in an applied magnetic field. This proved to be the case, since in the n.m.r. spectra the inner proton resonances occurred at unusually low field [(**28**), τ −0.31; (**29**), −0.50–−0.10; (**30**), −0.10–0.42], and the outer proton resonances at considerably higher field [(**28**), τ 3.88–4.87; (**29**), 3.53–4.84; (**30**), 3.57–5.05][23,25,26]. These positions are close to those of the similarly placed protons in the n.m.r. spectrum of the bisdehydro[16]annulene (**31**), a related 16 π-electron hydrocarbon model [inner protons, τ 0.2; outer protons, 3.92–4.73][27].

Of the three dehydro[17]annulenones, the tri-*trans*-tridehydro compound (**29**) was obtained most readily, and was generally used for further studies. Inspection of a molecular model (*Figure 1*) indicates that it may possess a

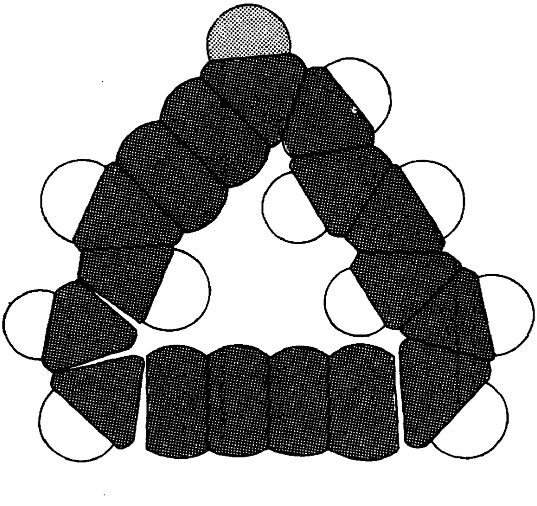
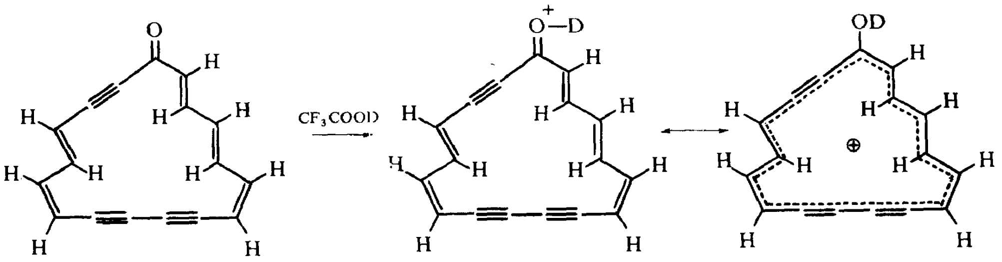


Figure 1. Molecular model of the tri-*trans*-tridehydro[17]annulenone (**29**).



(29) **(32a)** **(32b)**

3t-Tridehydro[17]annulenone
n.m.r.: inner H, τ -0.50 to -0.10
outer H, τ 3.53 to 4.84

Deep purple solution
n.m.r.: inner H, τ -2.31 to -1.78 (Δ *ca.* τ -1.7)
outer H, τ 3.65 to 4.94 (Δ *ca.* τ $+ 0.1$)

relatively strain-free planar structure, and this appears to be true also for its transformation products, to be described later.

It was shown in the case of the tri-*trans*-tridehydro[17]annulenone (**29**) that, as expected, the paramagnetic ring current is increased by protonation. Thus, the n.m.r. spectrum of the deep purple solution of the deuteronated

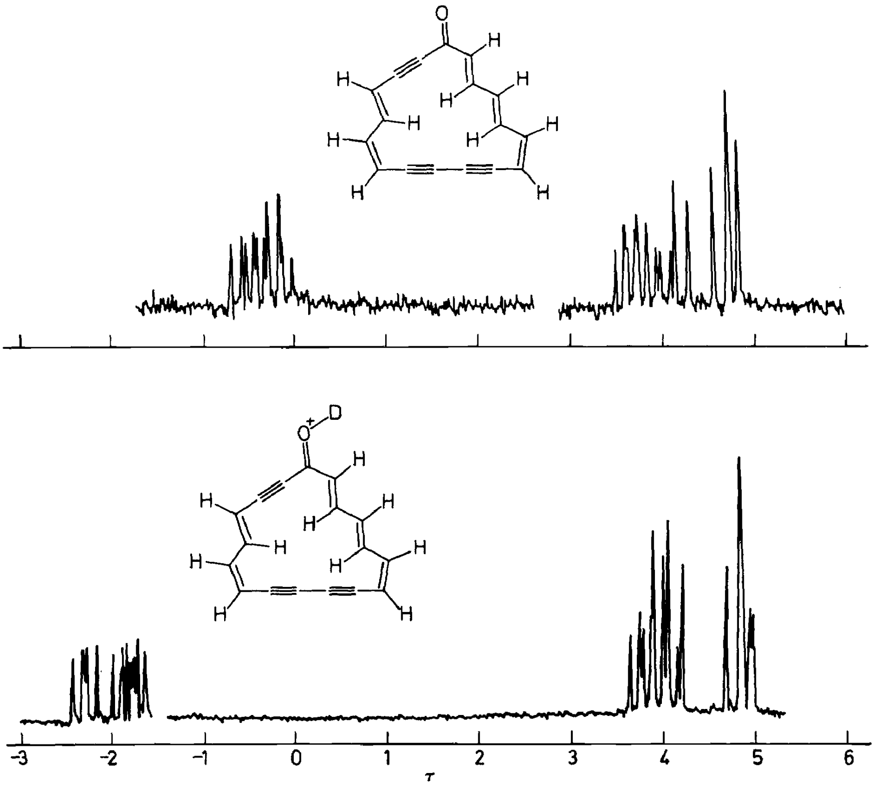
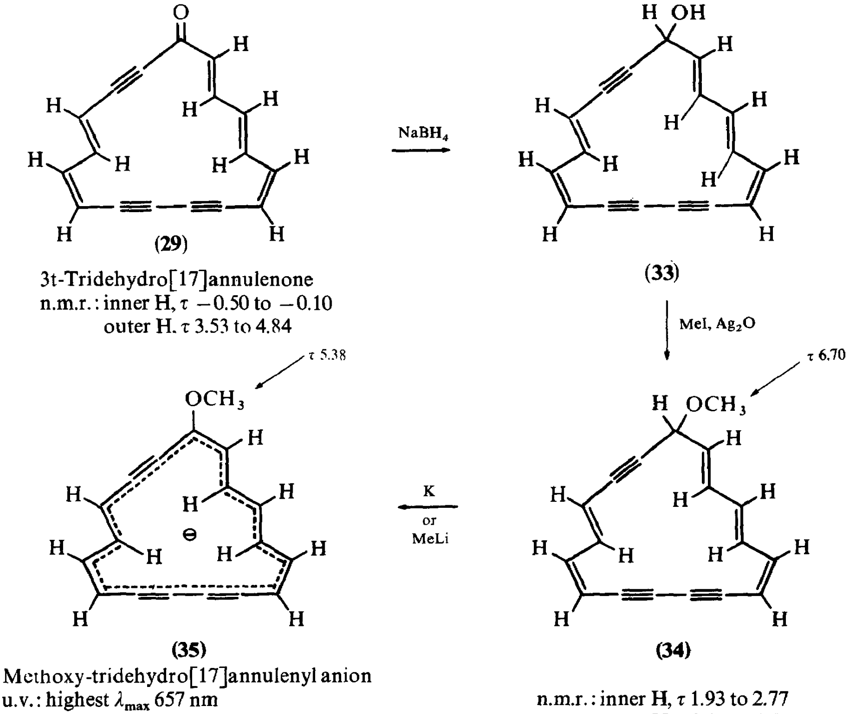


Figure 2. The n.m.r. spectra of the tri-*trans*-tridehydro[17]annulenone (**29**), measured at 100 MHz in deuteriochloroform (upper curve) and in deuteriotrifluoroacetic acid (lower curve).

species (**32**), obtained by treatment of (**29**) with deuteriotrifluoroacetic acid, showed bands at τ $-2.31--1.78$ due to the inner protons, and at τ 3.65–4.94 due to the protons[28]. The inner proton resonances have therefore been shifted downfield by *ca.* τ 1.7, and the outer proton ones have been shifted upfield by *ca.* τ 0.1. The change in the n.m.r. spectrum of (**29**) effected by treatment with deuteriotrifluoroacetic acid is shown in *Figure 2*. The fact that the shift of the inner proton resonances is much more marked than that of the outer protons is presumably due, in part, to the positive charge. The deshielding of all the protons caused by the positive charge reinforces the downfield shift of the inner protons, but counteracts the upfield shift of the outer protons, caused by the increased paramagnetic ring current.

The catalytic partial hydrogenation of the tridehydro[17]annulenones (**29**) and (**30**) was investigated. Although evidence was obtained that the di-*trans* isomer (**30**) gives rise to bisdehydro- and monodehydro[17]annulenones, there was no indication that [17]annulenone itself was formed[26]. It is quite possible that [17]annulenone is a very unstable substance, undergoing self-condensation in the same way as the lower homologue cyclopentadienone (**6**)[8]. The presence of the acetylenic bonds in the dehydro[17]annulenones would be expected to stabilize these substances, and they may well owe their existence to the presence of these acetylenic bonds.

The dehydro[17]annulenones are potential precursors of aromatic 17-membered ring anions, members of the second type of 'odd' annulenes



(**29**)

3t-Tridehydro[17]annulenone
n.m.r.: inner H, τ -0.50 to -0.10
outer H, τ 3.53 to 4.84

(**33**)

(**35**)

Methoxy-tridehydro[17]annulenyl anion
u.v.: highest λ_{max} 657 nm
n.m.r.: inner H, τ 18.54 to 19.09
outer H, τ -0.47 to 2.16

(**34**)

n.m.r.: inner H, τ 1.93 to 2.77
outer H, τ 3.15 to 4.67

I discussed, and such a transformation could be realized in practice. The tri-*trans*-tridehydro[17]annulenone (**29**) on reduction with sodium borohydride gave the very unstable alcohol (**33**), which was converted to the corresponding methyl ether (**34**) by shaking with methyl iodide and silver oxide in ether[25]. In the n.m.r. spectrum of (**34**), the inner proton resonances (τ 1.93–2.77) still appeared at lower field than the outer proton ones (τ 3.15–4.67), although the difference was not as great as in the dehydroannulenone (**29**). We believe this effect to be due, most probably, to the fact that the carbon–oxygen bond in (**34**) is still polarized to some extent, giving rise to a small paramagnetic ring current. This explanation is supported by the n.m.r. spectra of related 'homo-annulenes', to be discussed later.

Treatment of the methyl ether (**34**) in tetrahydrofuran with potassium at *ca.* −80° led to the potassium salt of the methoxy-tridehydro[17]annulenyl anion (**35**)[25], the allylic-propargylic proton rather than the methoxyl group in (**34**) being removed. After some experimentation, it was found that the anion (**35**) (as the lithium salt) was generated most simply by the reaction of (**34**) with a saturated solution of methyl-lithium in tetrahydrofuran at *ca.* −80°, methane being evolved[25]. The potassium or lithium salt of (**35**) formed a dark blue solution, the electronic spectrum of which showed the highest wavelength maximum at 657 nm.

The methoxy-tridehydro[17]annulenyl anion (**35**) is an 18π-electron system, and should therefore be aromatic. This could be confirmed dramatically by the n.m.r. spectrum (determined in tetrahydrofuran-d_8 at −35°; see *Figure 3*)[25], in which the inner proton resonances now appeared at very high

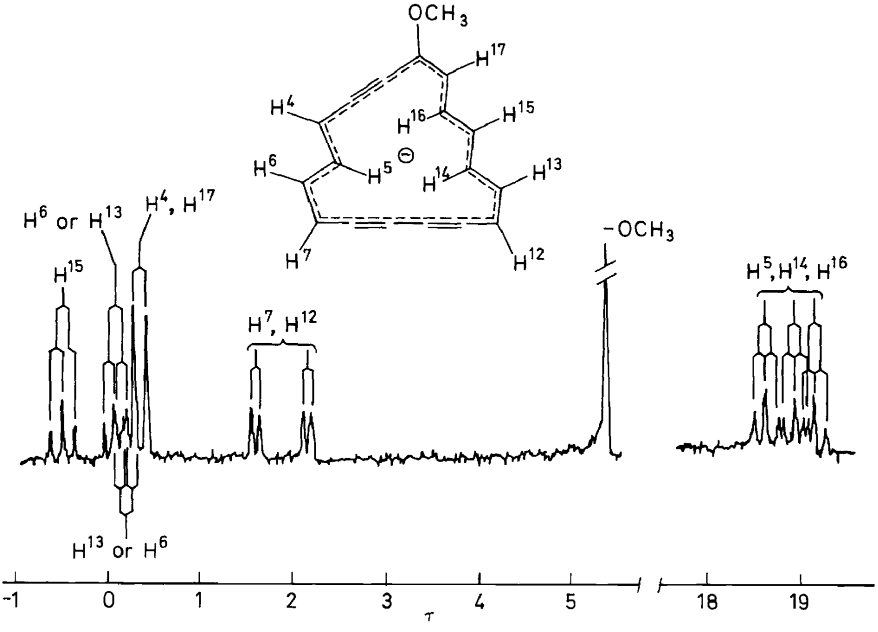
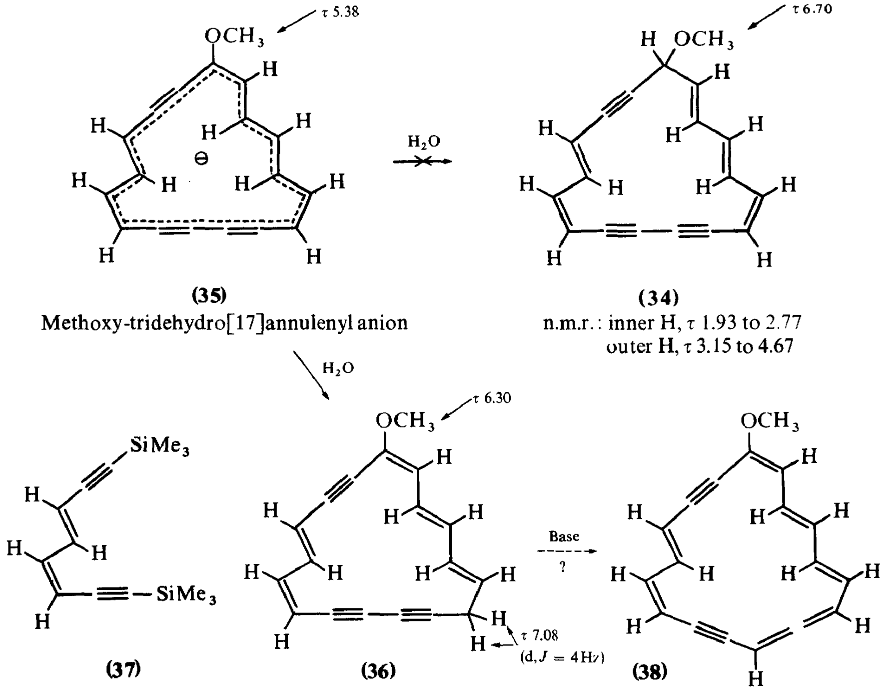


Figure 3. The n.m.r. spectrum at −35° of the methoxy-tridehydro[17]annulenyl anion (**35**), measured at 100 MHz in tetrahydrofuran-d_8.

field (τ 18.54–19.09) and the outer proton ones at low field (τ −0.47–2.16). This is clear indication of a diamagnetic ring current, a reversal of the paramagnetic ring current in the 16π-electron precursor (**29**). The very high field position of the inner proton bands is particularly noteworthy, the value of τ *ca.* 19 being the highest yet recorded for a proton bound to carbon. The relatively low field position (τ 5.38) of the methoxyl proton band in the n.m.r. spectrum (cf. anisole, τ 6.22) is also indicative of a marked diamagnetic ring current. It is of interest that H^7 and H^{12} resonate at unusually higher field than the other outer protons (see *Figure 3*), a phenomenon which suggests that the charge densities at C-7 and C-12 are greater than at the other carbon atoms.

Quenching of the anion (**35**) with water did not regenerate (**34**), but led to the isomeric ether (**36**)[25]. The presence of an enol ether grouping in the



(35)
Methoxy-tridehydro[17]annulenyl anion

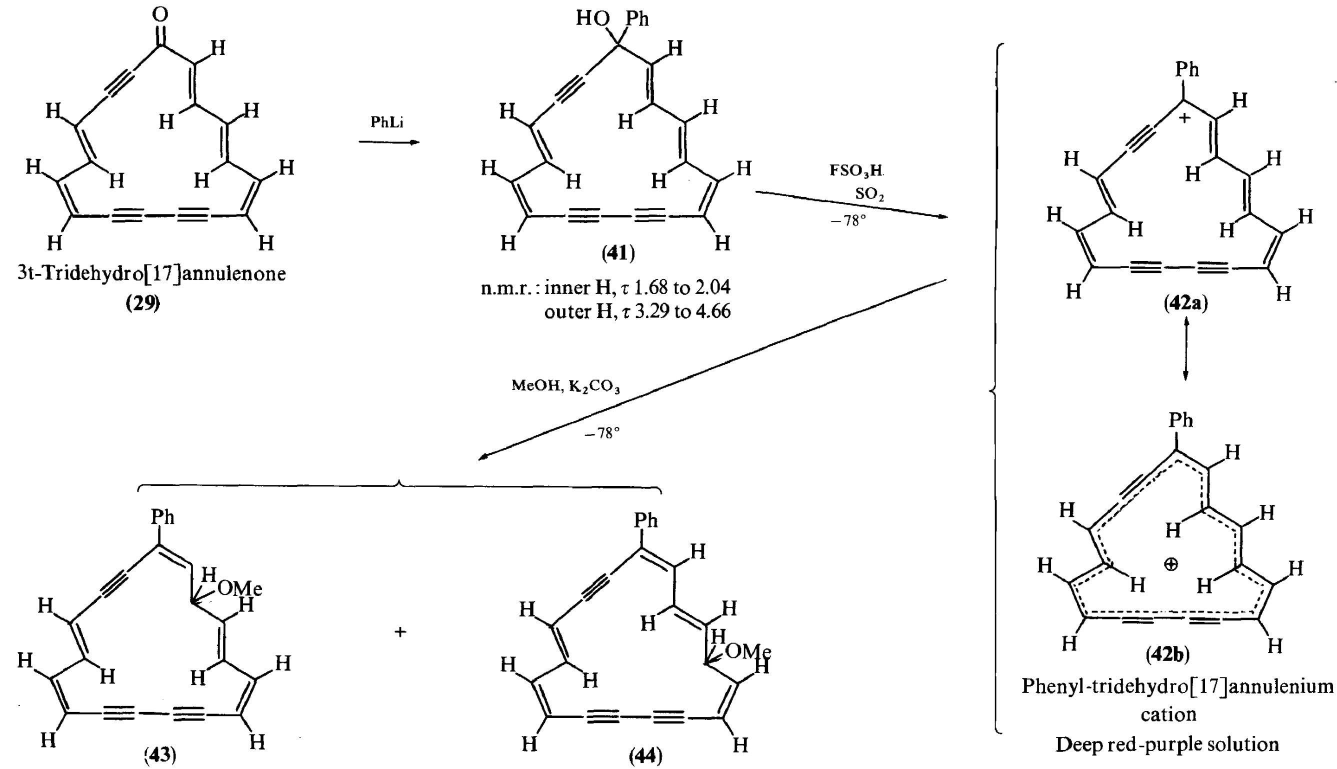
(34)
n.m.r.: inner H, τ 1.93 to 2.77
outer H, τ 3.15 to 4.67

(37) **(36)** **(38)**

n.m.r.: olef. H, τ 2·85 to 4·46 n.m.r.: olef. H, τ 2.84 to 4.50

$$\underset{\mathbf{39}}{R{-}C{\equiv}C{-}CH_2{-}CH{=}CH{-}R'} \xrightarrow{\text{Base}} \underset{\mathbf{40}}{R{-}CH{=}C{=}CH{-}CH{=}CH{-}R'} \rightarrow \text{etc.}$$

product (**36**) was confirmed by the fact that the methoxy proton band in the n.m.r. spectrum (τ 6.30) had been shifted downfield by τ 0.40 as compared with the ether (**34**) (τ 6.70). The n.m.r. spectrum of (**36**) also showed a doublet (J = 4 Hz) at τ 7·08 due to the methylene protons, and bands at τ 2.84–4.50 due to all the olefinic protons. The positions of the olefinic proton resonances in the n.m.r. spectrum of (**36**) are very similar to those of the acyclic model (**37**) (τ 2.85–4.46), to be described later, and indicates that the paramagnetic



3t-Tridehydro[17]annulenone
(29)

(41)
n.m.r.: inner H, τ 1.68 to 2.04
outer H, τ 3.29 to 4.66

(42a)

(42b)
Phenyl-tridehydro[17]annulenium cation
Deep red-purple solution

(43)

(44)

n.m.r.: inner H, τ 1.01 and 1.54 (1 part), 1.31 and 1.69 (2 parts)
outer H, τ 3.3 to 4.9
methyl H, τ 6.55 (1 part), 6.53 (2 parts)

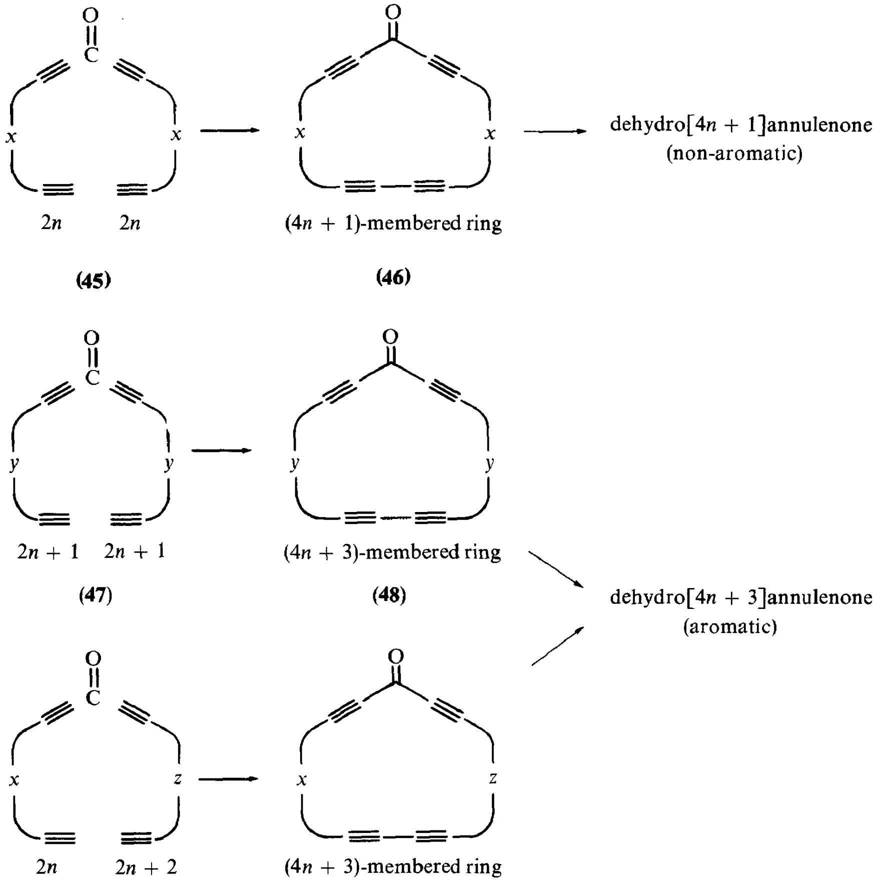
ring current observed in the isomer (**34**) is not present in (**36**). This observation provides support for the explanation given for the ring current in (**34**), since the carbon atom separating the conjugated system carries an oxygen substituent in (**34**), but not in (**36**).

The ether (**36**) is a monocyclic compound containing a 1,4-enyne grouping, in addition to conjugated double and triple bonds. It is known that linear 1,4-enynes [type (**39**)] are rearranged readily with base to conjugated allenes [type (**40**)][29], which may then rearrange further. The possibility existed, therefore, that rearrangement of (**36**) with base would lead to the methoxy-allene-dehydroannulene (**38**). In practice, treatment of either the ether (**34**) or (**36**) with base (aqueous sodium hydroxide or 1,5-diazabicyclo[4,3,0]non-5-ene) gave a complex mixture of at least three violet compounds, which proved to be extremely unstable, and no structural information could be obtained by spectral means[26]. This approach to cyclic 'conjugated' allenes was therefore not pursued further.

Experiments have also been carried out designed to transform the tri-*trans*-tridehydro[17]annulenone (**29**) to a cation, such as the phenyl-tridehydro[17]annulenium cation (**42**). This is a 16π-electron system, like (**29**) itself, and should be non-aromatic. The objective was reached simply by the reaction of (**29**) with phenyl-lithium to give the tertiary alcohol (**41**), followed by treatment with fluorosulphonic acid in sulphur dioxide at −78°[28]. The resulting deep red-purple solution presumably contained the cation (**42**), although it has not yet been obtained in sufficient concentration so that the n.m.r. spectrum could be determined. The structural assignment is based mainly on the result of quenching with a suspension of potassium carbonate in methyl alcohol at −78°. This led to a *ca.* 2:1 mixture of the methyl ethers (**43**) and (**44**), as evidenced by the n.m.r. spectrum and catalytic hydrogenation to the corresponding saturated ethers[28]. It can be seen from the n.m.r. data given for substances (**41**), (**43**), and (**44**) that the inner proton resonances in each one again appear at lower field than the outer proton ones, indicative of a paramagnetic ring current. The carbon atom separating the conjugated systems in (**41**), (**43**) and (**44**) carries an oxygen substituent, as in (**34**) (which also shows this effect), but unlike (**36**) (which does not). This gives further support for our explanation that the ring current is due to polarization of the carbon–oxygen bond.

The 13- and 17-membered ring dehydroannulenones prepared by us are all ($4n + 1$)-membered, and are therefore non-aromatic. The fact that they are ($4n + 1$)-membered follows from the synthetic route, involving the joining by one carbon atom of two identical terminal diacetylenes, each containing an even number ($2n$) of carbon atoms [see formulae (**45**) and (**46**)]. Obviously, it was of interest also to synthesize ($4n + 3$)-membered ring dehydroannulenones, which should be aromatic. One way to achieve this objective is to commence with two identical terminal diacetylenes, each containing an odd number ($2n + 1$) of carbon atoms [see formulae (**47**) and (**48**)]. Another way is to commence with two non-identical 'even' diacetylenes, differing by two carbon atoms [see formulae (**49**) and (**50**)]. Both of these approaches have been investigated, and the second one has led to success.

The ($4n + 3$)-membered dehydroannulenone we aimed for was a dehydro-[15]annulenone ($n = 3$). To this end, we synthesized 4,11-cyclopentadeca-

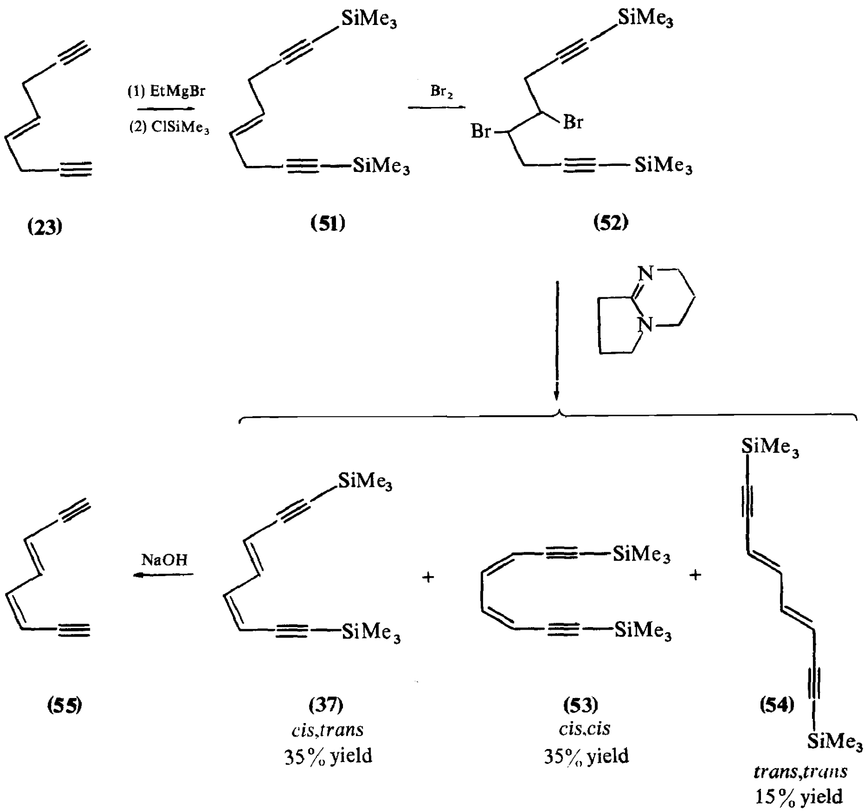


(45) **(46)** **(47)** **(48)** **(49)** **(50)**

diene-2,6,8,14-tetrayn-1-one (an incompletely conjugated 15-membered ring ketone containing 1,4-enyne groupings)[21], starting from *cis*-3-hexene-1,5-diyne and *trans*-4-octene-1,7-diyne **(23)**. Unfortunately, all attempts to transform this cyclic ketone with base to a dehydro[15]annulenone failed[21], despite the fact that the conversion of the closely related 17-membered ring ketone **(26)** to dehydro[17]annulenones had succeeded.

It was therefore decided to build up a dehydro[15]annulenone from completely conjugated C_6 and C_8 terminal diacetylenes, so that no rearrangement to a conjugated system as a final step was necessary. The use of completely conjugated terminal diacetylenes had, of course, already been employed successfully for the synthesis of the dehydro[13]annulenone **(16)**.

The completely conjugated C_8 terminal diacetylene which we required as one of the components was the unknown *cis,trans*-3,5-octadiene-1,7-diyne **(55)**. Several routes to this substance were investigated, but only the best one is described. Reaction of *trans*-4-octene-1,7-diyne **(23)** with an

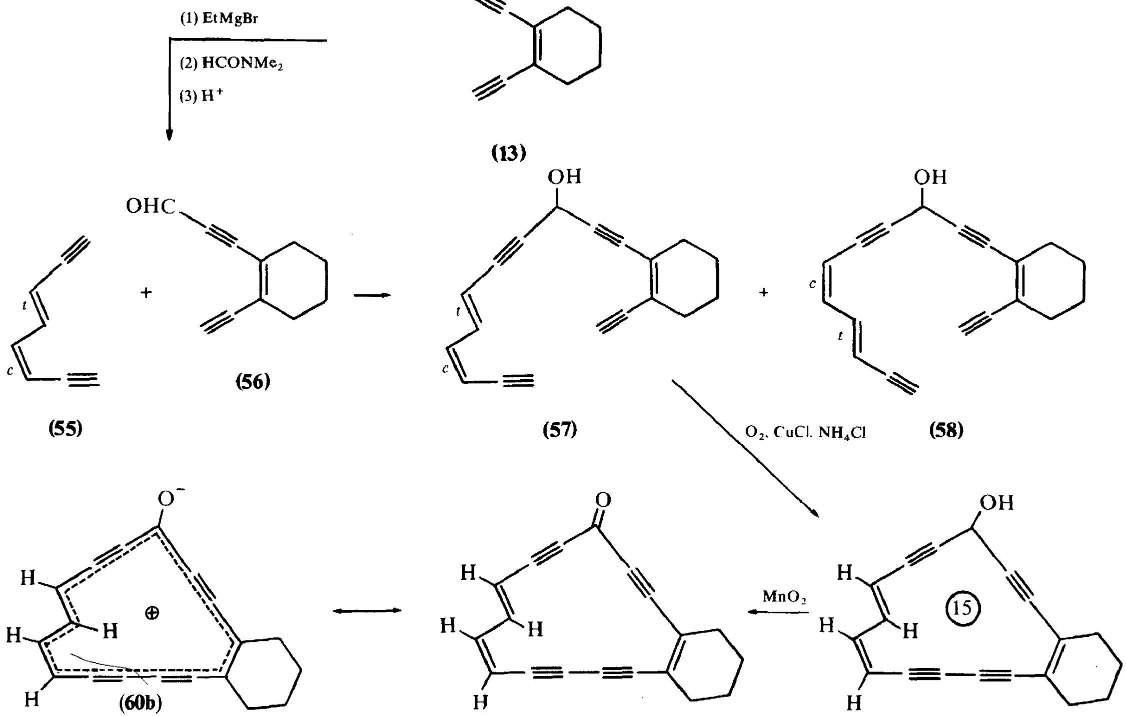


(23) (51) (52)

(55) (37) *cis,trans* 35% yield (53) *cis,cis* 35% yield (54) *trans,trans* 15% yield

excess of ethylmagnesium bromide and then with chlorotrimethylsilane gave the bis(trimethylsilyl) derivative (**51**), which on bromination was converted to the dibromide (**52**) in about 50 per cent overall yield[13]. Dehydrobromination of (**52**) with 1,5-diazabicyclo[4,3,0]non-5-ene, followed by separation of the product by a combination of chromatography and fractional distillation, led to 35 per cent of the *cis,trans* dienediyne (**37**), 35 per cent of the *cis,cis* isomer (**53**), and 15 per cent of the *trans,trans* isomer (**54**)[13]. Further amounts of the *cis,trans* compound (**37**) could be obtained by photoisomerization of either (**53**) or (**54**), each of which gave an equilibrium mixture of the three isomers, containing *ca.* 45 per cent of (**37**)[30]. Removal of the protecting groups from (**37**) with aqueous sodium hydroxide, or preferably by the silver nitrate–potassium cyanide method[31], then yielded the free *cis,trans* dienediyne (**55**) as a rather unstable liquid[13, 32]. It is of interest that similar removal of the protecting groups from the *cis,cis* isomer (**53**) led to the very unstable free *cis,cis* dienediyne, which at room temperature was rapidly converted to the dimer of benzocyclobutadiene (presumably via 1,2,4,5,7-cyclooctapentaene, a 'diallene-annulene')[13].

The completely conjugated C_6 terminal diacetylene available to us as the other component was the previously mentioned *cis*-3-hexene-1,5-diyne, or the corresponding cyclohexene-fused derivative (**13**), and we chose the last-



(13) (55) (56) (57) (58) (59) (60a) (60b)

Tetramethylene-tetradehydro[15]annulenone
i.r.: $\nu_{max.}$ 1 613 cm^{-1}
u.v.: main $\lambda_{max.}$ 306 nm (ε 41 000)
n.m.r.: inner H, τ 4.99
outer H, τ 2.35 to 3.72

mentioned substance for practical reasons. Reaction of the mono-Grignard derivative of (**13**) with dimethylformamide and subsequent treatment with dilute sulphuric acid[33] yielded the aldehyde (**56**), which was condensed with the mono-Grignard derivative of the C_8 component (**55**)[32]. The product consisted of a *ca.* 1:1 mixture of the stereoisomeric alcohols (**57**) and (**58**) (as shown by the n.m.r. spectrum), but no attempt at separation was made since inspection of molecular models indicated that only (**57**) could form the corresponding cyclic monomer.

Oxidative coupling of the mixture of (**57**) and (**58**) with oxygen, cuprous chloride, and ammonium chloride led to the 15-membered ring alcohol (**59**) as sole monomeric product, in addition to insoluble polymeric material[32]. The alcohol (**59**) was exceedingly unstable, and was oxidized directly with manganese dioxide. This procedure gave rise to the desired tetramethylene-tetradehydro[15]annulenone (**60**) in about ten per cent yield [based on (**57**) and (**58**)] as orange-yellow needles[32].

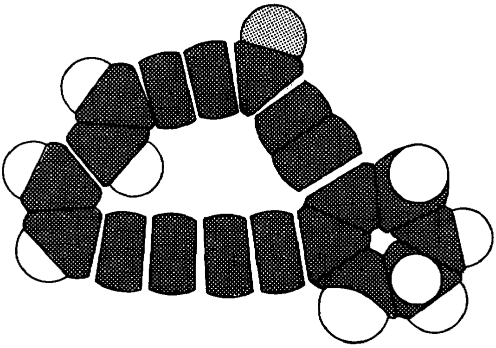
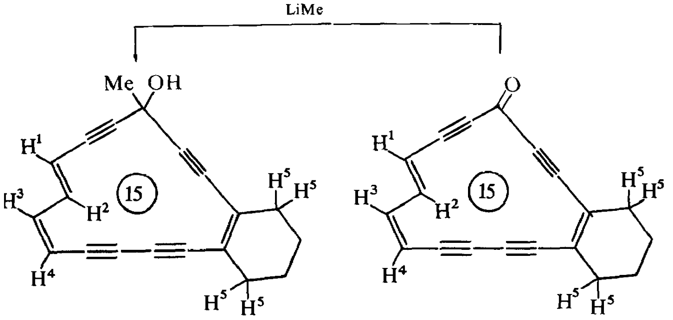


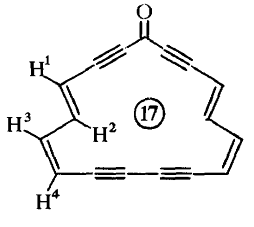
Figure 4. Molecular model of the tetramethylene-tetradehydro[15]annulenone (**60**).

Inspection of a molecular model (*Figure 4*) indicates that the dehydro[15]-annulenone (**60**) may be a relatively strain-free planar molecule. The substance proved to be considerably more stable than its precursors; for instance the crystals suffered only about ten per cent decomposition after 20 hours in light and air. The low infra-red carbonyl frequency (1 613 cm^{-1}) of (**60**) is again ascribed to the presence of the flanking acetylenic bonds, since acyclic α,α′-diacetylenic ketones show similar carbonyl absorptions. In the electronic spectrum of (**60**), the main maximum occurred at 306 nm, which is compatible with the assigned structure.

The ketone (**60**) is a $(4n + 3)$-membered dehydroannulenone. It should therefore be aromatic, and sustain a diamagnetic ring current in an applied magnetic field. This was borne out in practice, since in the n.m.r. spectrum the inner proton resonance (τ 4.99) occurred at considerably higher field than those of the outer protons (τ 2.35–3.72)[32]. This, of course, is a reversal of the behaviour of the dehydro[17]annulenones (**28**), (**29**) and (**30**) in the n.m.r. spectrum, and indicates that there is appreciable contribution by the delocalized structure (**60b**).



(61) **(60)**

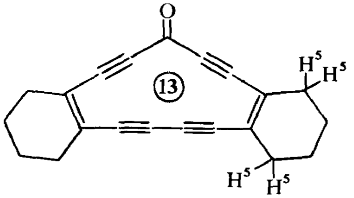


(28)

(61)
H^1, τ 4.23 (d)
H^2, 3.03 (dd)
H^3, 3.17 (dd)
H^4, 4.43 (d)
H^5, 7.50–7.85 (m)

(60)
H^1, τ 3.55 (d) Δ −0.68
H^2, 4.99 (dd) +1.96
H^3, 2.35 (dd) −0.82
H^4, 3.72 (d) −0.71
H^5, 7.15–7.50 (m) −0.35

(28)
H^1, τ 4.87 (d) Δ +0.64
H^2, −0.31 (dd) −3.34
H^3, 3.88 (dd) +0.71
H^4, 4.95 (d) +0.52

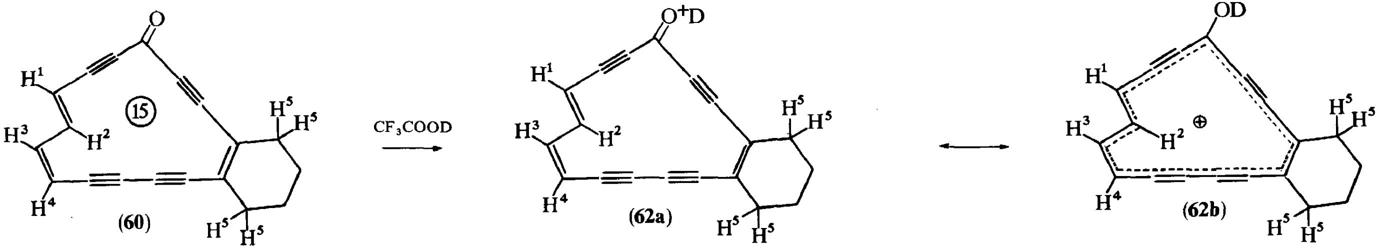


(16)

H^5, τ 7.85–8.20 (m) Δ + 0.35

A suitable cyclic model lacking a ring current was obtained by treatment of the dehydro[15]annulenone (**60**) with methyl-lithium[32]. The n.m.r. spectrum of the resulting tertiary alcohol (**61**) is indicated under the formula. The lack of a ring current is shown by the observation that the inner H^2 and outer H^3 proton resonances (τ 3.03, 3.17) are very close; the fact that the outer H^1 and H^4 protons resonate at rather higher field (τ 4.23, 4.43) is usual for protons adjacent to an acetylene[3]. It is of interest that the oxygenated ($4n + 3$)-membered 'homo-annulene' (**61**) does not possess a ring current, unlike the related ($4n + 1$)-membered ring compounds (**34**), (**41**), (**43**) and (**44**), in which a small paramagnetic ring current was observed.

We now have examples of the yne-(*trans*)ene-(*cis*)ene-yne chromophore incorporated into the incompletely conjugated system (**61**), into the theoretically aromatic dehydro[15]annulenone (**60**), and into the theoretically non-aromatic dehydro[17]annulenone (**28**). The olefinic proton resonances in the n.m.r. spectra of these three substances are given under the formulae, as well as the shifts in these resonances on passing from (**61**) to (**60**) and to (**28**). It can be seen that in the dehydro[15]annulenone (**60**) the inner H^2 proton band has shifted *upfield* by τ 1.96 compared with that of the model (**61**), while the outer H^1, H^3, and H^4 proton bands have each shifted *downfield* by about τ 0.7. Conversely, in the dehydro[17]annulenone (**28**) the inner



(60)

(62a)

(62b)

Tetramethylene-tetradehydro[15]annulenone

n.m.r.: H^1, τ 3.55 (d)
H^2, 4.99 (dd)
H^3, 2.35 (dd)
H^4, 3.72 (d)
H^5, 7.15–7.50 (m)

Deep orange-brown solution

n.m.r.:		Δ
H^1, τ	3.12 (d)	-0.43
H^2,	6.51 (dd)	$+1.52$
H^3,	1.93 (dd)	-0.42
H^4,	3.26 (d)	-0.46
H^5,	6.95–7.30 (m)	-0.20

H^2 proton band has shifted *downfield* by τ 3.34 compared with that of the model (**61**), while the outer H^1, H^3 and H^4 proton bands have each shifted *upfield* by about τ 0.6. The same type of effect can be seen in the allylic proton (H^5) bands in the n.m.r. spectra of the cyclohexene-fused compounds, also given under the formulae. Thus, in the theoretically aromatic dehydro-[15]annulenone (**60**) this band has been shifted *downfield* by τ 0.35 compared with that of the model (**61**), while in the theoretically non-aromatic dehydro-[13]annulenone (**16**) it has been shifted *upfield* by τ 0.35. These shifts provide strong support that the $(4n + 3)$-membered dehydroannulenone (**60**) possesses a diamagnetic ring current, and the $(4n + 1)$-membered dehydroannulenones (**28**) and (**16**) a paramagnetic ring current. These results parallel those found by us for the annulenes and dehydroannulenes, in which the $(4n + 2)$-membered compounds show a diamagnetic ring current, and the $4n$-membered ones a paramagnetic ring current[3].

Our conclusion that the dehydro[15]annulenone (**60**) is aromatic is in contrast to the apparent lack of aromaticity of the lower $[4n + 3]$annulenones tropone[7] and 4,9-methano[11]annulenone[9]. Further studies are clearly necessary in order to resolve this apparent discrepancy. In this connection it is of interest that in both the dehydroannulene and the dehydroannulenone

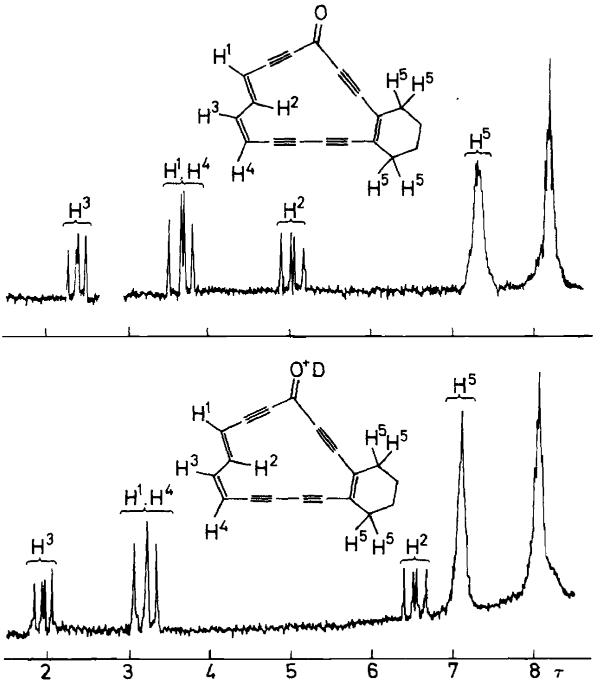


Figure 5. The n.m.r. spectra of the tetramethylene-tetradehydro[15]annulenone (**60**), measured at 100 MHz in deuteriochloroform (upper curve) and in deuteriotrifluoroacetic acid (lower curve).

series, it is not possible to distinguish between aromatic and non-aromatic compounds by the first-order coupling constants of the olefinic proton resonances in the n.m.r. spectra. Thus, in the n.m.r. spectra of (**61**), (**60**) and (**28**), in each case H^1 was a doublet ($J = 16$ Hz), H^2 a double doublet ($J = 16, 12$ Hz), H^3 a double doublet ($J = 12, 10$ Hz), and H^4 a doublet ($J = 10$ Hz).

The diamagnetic ring current in the dehydro[15]annulenone (**60**) was increased by protonation, in the same way as already found for the paramagnetic ring current in the dehydro[17]annulenone (**29**). Treatment of (**60**) with deuteriotrifluoroacetic acid led to a deep orange-brown solution of the deuteronated species (**62**). The n.m.r. spectrum of (**62**), as well as that of the precursor (**60**), is given in *Figure 5*, and the positions of the individual bands are indicated under the formulae (the coupling constants again are unaffected)[32]. It can be seen that deuteronation has shifted the inner H^2 proton band upfield by τ 1.52, the outer H^1, H^3 and H^4 proton bands downfield by about τ 0.4, and the allylic H^5 proton band downfield by τ 0.2. Passing from the model (**61**) to the dehydro[15]annulenone (**60**) and then to the deuteronated species (**62**) therefore causes a progressive shift to higher field of the inner H^2 proton resonance, and a progressive shift to lower field of the outer H^1, H^3, H^4 and H^5 proton resonances.

This brings me to the end of my lecture. To summarize, we have synthesized several large-ring conjugated ketones, both aromatic and non-aromatic; we have also prepared an aromatic large-ring conjugated anion and a (presumably) non-aromatic cation, and have shown that the same type of criteria for aromaticity apply to these substances as have been found for the annulenes and dehydroannulenes. Of course, a number of problems remain. For instance, it should be possible to convert the dehydro[15]annulenone (**60**) to an aromatic large-ring conjugated cation and to a non-aromatic anion (examples of which are still unknown), and work towards this end is in progress. Moreover, the synthesis of a completely 'conjugated' large-ring allene still remains to be accomplished.

Finally I would like to express my gratitude to my co-workers, namely Drs G. W. Brown, G. P. Cotterell, J. Griffiths, R. M. McQuilkin, G. V. Meehan, G. H. Mitchell and G. M. Pilling. The work I have described has involved considerable experimental difficulties, and the successful syntheses have been due mainly to the skill and enterprise of these dedicated scientists. I also wish to thank Drs P. J. Garratt and H. M. R. Hoffmann for stimulating discussions.

REFERENCES

[1] F. Sondheimer and R. Wolovsky, *J. Am. Chem. Soc.* **84**, 260 (1962).

[2] H. C. Longuet-Higgins and L. Salem, *Proc. Roy. Soc. A*, **251**, 172 (1959);
H. C. Longuet-Higgins and L. Salem, *Proc. Roy. Soc. A*, **257**, 445 (1960);
C. A. Coulson and W. T. Dixon, *Tetrahedron*, **17**, 215 (1962);
M. J. S. Dewar and G. J. Gleicher, *J. Am. Chem. Soc.* **87**, 685 (1965).

[3] F. Sondheimer, *Pure Appl. Chem.* **7**, 363 (1963);
F. Sondheimer, *Proc. Roy. Soc. A*, **297**, 173 (1967);
F. Sondheimer, I. C. Calder, J. A. Elix, Y. Gaoni, P. J. Garratt, K. Grohmann, G. di Maio, J. Mayer, M. V. Sargent and R. Wolovsky. *Spec. Publ. No. 21*, p 75. The Chemical Society, London (1967).

[4] F. Sondheimer, *Proceedings of the Robert A. Welch Foundation Conferences on Chemical Research.* XII. Organic Synthesis, p 125. Houston, Texas (1968).

[5] See R. Breslow, G. Ryan and J. T. Groves, *J. Am. Chem. Soc.* **92**, 988 (1970).

[6] See A. Streitwieser, *Molecular Orbital Theory for Organic Chemists*, Chapter 10. Wiley: New York (1961).

[7] D. J. Bertelli and T. G. Andrews, *J. Am. Chem. Soc.* **91**, 5280 (1969);
D. J. Bertelli, T. G. Andrews and P. O. Crews, *J. Am. Chem. Soc.* **91**, 5286 (1969).

[8] For a review, see M. A. Ogliaruso, M. G. Romanelli and E. I. Becker, *Chem. Revs.* **65**, 261 (1965)

[9] E. Vogel, *Proceedings of the Robert A. Welch Foundation Conferences on Chemical Research.* XII. Organic Synthesis, p 215. Houston, Texas (1968);
W. Grimme, J. Reisdorff, W. Jünemann and E. Vogel, *J. Am. Chem. Soc.* **92**, 6335 (1970).

[10] R. Breslow, J. T. Groves and G. Ryan, *J. Am. Chem. Soc.* **89**, 5048 (1967);
D. G. Farnum, G. Mehta and R. S. Silberman, *J. Am. Chem. Soc.* **89**, 5048 (1967);
R. Breslow and J. T. Groves, *J. Am. Chem. Soc.* **92**, 984 (1970).

[11] T. J. Katz and P. J. Garratt, *J. Am. Chem. Soc.* **86**, 5194 (1964);
E. A. LaLancette and R. E. Benson, *J. Am. Chem. Soc.* **87**, 1941 (1965).

[12] W. Grimme, H. Hoffmann and E. Vogel, *Angew. Chem.* **77**, 348 (1965);
E. Vogel, R. Feldmann and H. Düwel, *Tetrahedron Letters*, 1941 (1970).

[13] G. H. Mitchell and F. Sondheimer, *J. Am. Chem. Soc.* **91**, 7520 (1969).

[14] G. M. Pilling and F. Sondheimer, *J. Am. Chem. Soc.* **90**, 5610 (1968).

[15] G. M. Pilling and F. Sondheimer, *J. Am. Chem. Soc.* **93**, 1970 (1971).

[16] G. M. Pilling and F. Sondheimer, *J. Am. Chem. Soc.* **93**, 1977 (1971).

[17] G. M. Pilling and F. Sondheimer, *J. Am. Chem. Soc.* **90**, 5611 (1968).

[18] C. C. Leznoff and F. Sondheimer, *J. Am. Chem. Soc.* **90**, 731 (1968).

[19] W. H. Okamura and F. Sondheimer, *J. Am. Chem. Soc.* **89**, 5991 (1967).

[20] R. M. McQuilkin, P. J. Garratt and F. Sondheimer, *J. Am. Chem. Soc.* **92**, 6682 (1970).

[21] R. M. McQuilkin, unpublished experiments.

[22] Y. Gaoni, C. C. Leznoff and F. Sondheimer, *J. Am. Chem. Soc.* **90**, 4940 (1968).

[23] G. W. Brown and F. Sondheimer, *J. Am. Chem. Soc.* **91**, 760 (1969).

[24] I. C. Calder, Y. Gaoni and F. Sondheimer, *J. Am. Chem. Soc.* **90**, 4946 (1968).

[25] J. Griffiths and F. Sondheimer, *J. Am. Chem. Soc.* **91**, 7518 (1969).

[26] J. Griffiths and G. V. Meehan, Unpublished experiments.

[27] I. C. Calder, Y. Gaoni, P. J. Garratt and F. Sondheimer, *J. Am. Chem. Soc.* **90**, 4954 (1968).

[28] G. V. Meehan, Unpublished experiments

[29] See W. Oroshnik, A. D. Mebane and G. Karmas, *J. Am. Chem. Soc.* **75**, 1050 (1953);
M. Bertrand, *C.R. Acad. Sci., Paris*, **247**, 824 (1958);
A. Cozzone, J. Grimaldi and M. Bertrand, *Bull. Soc. Chim. (France)*, 1656 (1966).

[30] G. H. Mitchell, Unpublished experiments.

[31] J. F. Arens and H. M. Schmidt, *Rec. Trav. Chim. Pays-Bas*, **86**, 1138 (1967).

[32] G. P. Cotterrell, G. H. Mitchell, F. Sondheimer and G. M. Pilling, *J. Am. Chem. Soc.* **93**, 259 (1971).

[33] See E. R. H. Jones, L. Skattebøl and M. C. Whiting, *J. Chem. Soc.* 1054 (1958).