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The norcaradiene–cycloheptatriene equilibrium

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Contents

1. Introduction

Following Curtius'[1] first report of a diazocarbonyl compound in 1883 and subsequent work by Buchner focussing on the addition of diazo compounds to aromatic rings,[2,3] the norcaradiene–cyclo heptatriene (NCD–CHT) equilibrium has attracted significant attention;[4–6] the initial cyclopropanation product, the bicyclic norcaradiene tautomer, exists in equilibrium with the monocyclic cycloheptatriene tautomer in a thermally allowed disrotatory electrocyclic ring opening (Scheme 1).[6] This review summarises the substantial efforts made, particularly in the last 50 years, to understand this tautomerism and the factors which influence the relative population of both tautomers.

2. The norcaradiene–cycloheptatriene equilibrium

2.1. Early observation of the norcaradiene–cycloheptatriene equilibrium

Early work in the area of the equilibrium follows on from Curtius' initial work when, in 1885, Buchner carried out a study on the thermal decomposition of ethyl diazoacetate in benzene, which

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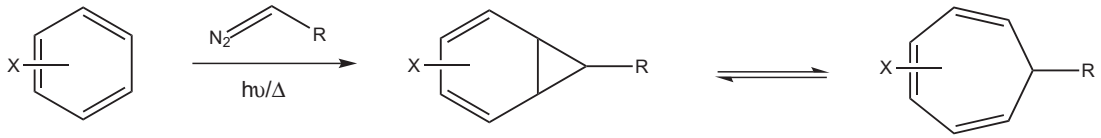
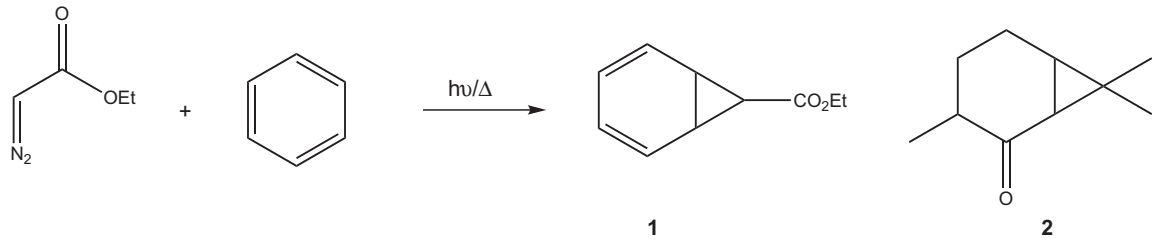


Scheme 1.

resulted in what Buchner initially postulated as the product, ethyl 7-norcaradienecarboxylate **1** (Scheme 2).[2,3,7] The product mixture also contained the esters of three isomeric cycloheptatrienecarboxylic acids. The bicyclic form was postulated as the sole product when ethyl diazoacetate was decomposed in benzene under photochemical conditions by Schenck.[8,9] The term 'norcaradiene' was given to the structure by Baeyer as a result of its similarity to the natural product, carone **2**.[4,10]

When Doering repeated Buchner's classical work, he confirmed that the product exists as a mixture of the isomeric trienones **5**–**7**, which come about following a series of sigmatropic shifts, thus confirming the existence of the cycloheptatriene **8**, which is in dynamic equilibrium with the norcaradiene **1**, as the kinetic product of the decomposition (Scheme 3).[16]

The parent compound cycloheptatriene **9** (Fig. 3) is readily available and has been prepared by several different routes.[12,17–20] The preparation of cycloheptatrienes and cycloheptatrienones was reviewed by Pietra.[21] A recent study by von Ragué Schlayer on cycloheptatriene **9** confirmed it as a neutral homoaromatic molecule.[22] Since Buchner's preliminary work, the norcaradiene–cycloheptatriene equilibrium has been the focus of intense research with several reviews written on the subject,[4–6,23–25] along with several theoretical studies.[26–28] While Buchner's aromatic addition reaction offers a useful route to the norcaradiene–cycloheptatriene systems, several of these equilibrating systems are prepared by alternative methodologies.



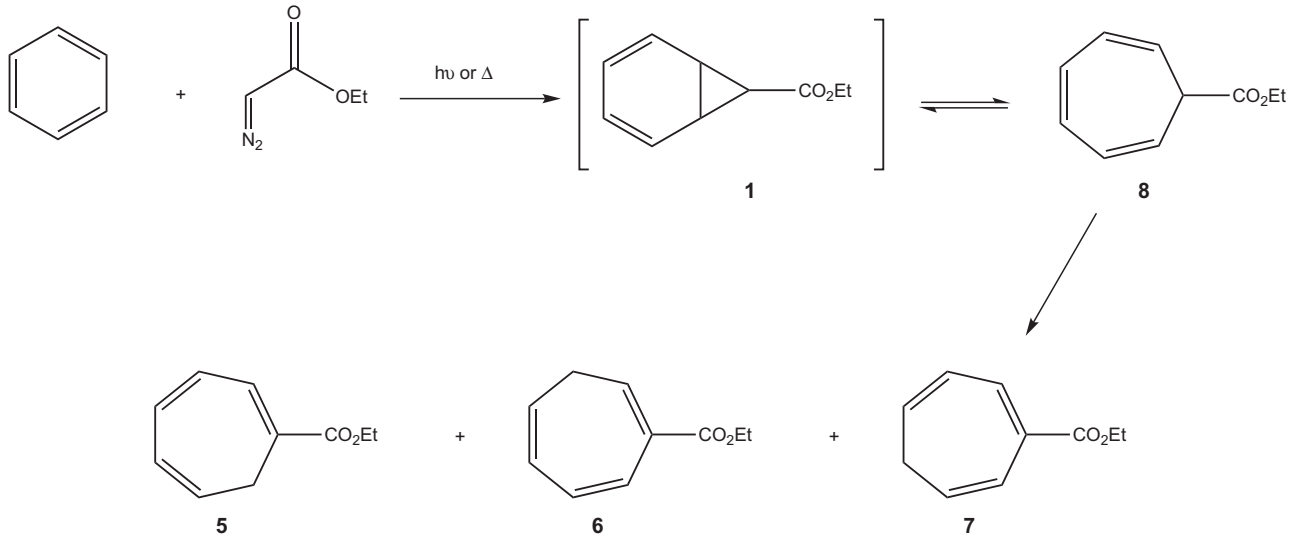
Scheme 2.

However, the exact nature of the product mixture ignited debate in the 1950s when work by Meerwein in 1957 described the product as mixture of the norcaradiene and cycloheptatriene, which he based on a series of hydrogenation experiments.[11] Doering reported that the cycloheptatriene tautomer was the sole tautomer present in his synthesis of tropolone **3**, but did not completely exclude the existence of the norcaradiene tautomer.[12,13] A review of Doering's work, particularly on the preparation of tropylium bromide **4**,[14] was recently summarised by Klärner and Jones (Fig. 1).[15]

Fig. 1.

In general, the equilibrium lies on the side of the cycloheptatriene (CHT) tautomer,[29] as a result of the strained cyclopropane ring present in the norcaradiene. Cycloheptatriene **9** is known to exist in the boat conformation with the planar structure estimated as ~6 kcal/mol higher in energy.[28] The molecule can undergo two dynamic processes, ring inversion and valence tautomerisation.[5]

In 1955, Corey described the first use of NMR spectroscopy to attempt resolution of the norcaradiene–cycloheptatriene equilibrium.[30] The NMR spectrum of the enol acetate **10** of the natural product, eucarvone **11**, indicated that it exists as the cycloheptatriene (Fig. 2).



Scheme 3.

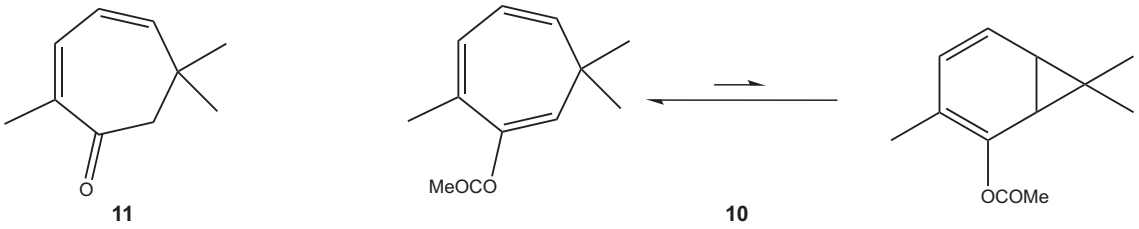


Fig. 2.

Following Corey's early work, further NMR studies by Anet,[31] Jensen and Smith[32] and Roberts[33] described efforts to detect the norcaradiene **9N** by variable-temperature NMR spectroscopy on the cycloheptatriene **9T**. Despite cooling the sample to −150 °C, distinctive NMR signals for the elusive norcaradiene were not observed. They found that cycloheptatriene **9T** is non-planar and undergoes interconversion between two boat conformations (Fig. 3).

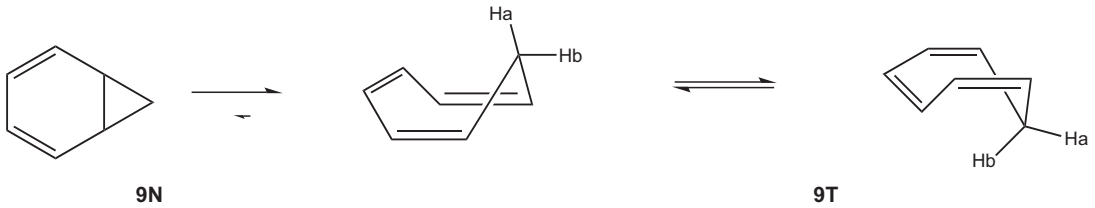


Fig. 3.

In 1975, Günther employed low-temperature ^{13}C NMR spectroscopy and found that the so-called 'Buchner's acid', i.e., the norcaradiene **12** (Fig. 4), exists as a component of a rapidly equilibrating mixture of the tautomers with only 3% norcaradiene tautomer observed.[34]

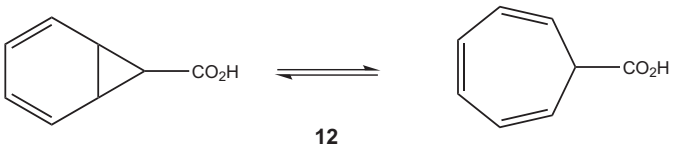


Fig. 4.

2.2. Direct observation of the norcaradiene

In 1981, Rubin described the first direct experimental observation of the unsubstituted norcaradiene **9N** as well as providing a description of the kinetics of its interconversion into the cycloheptatriene **9T**.[35] He followed this initial study with observation of the substituted norcaradienes, 2,4-di-*tert*-butyl norcaradiene **13** and 2,3,4,5-tetrachloronorcaradiene **14** (Fig. 5), in a similar fashion.[36]

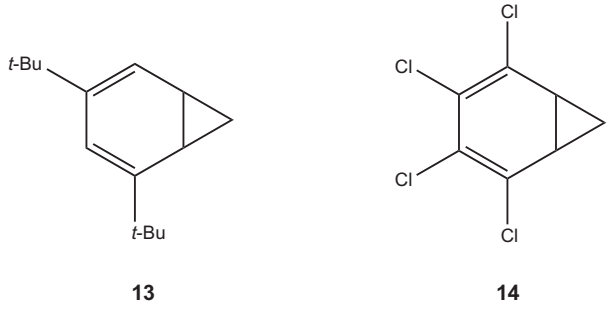


Fig. 5.

2.3. Substitution effects on the norcaradiene–cycloheptatriene equilibrium; towards the preparation of stable norcaradienes

Direct investigation of the norcaradiene–cycloheptatriene equilibrium is easiest with a system that contains a reasonable proportion of each of the tautomeric forms. The position of equilibrium can be dramatically altered with structural modification of the substrate. One of the earliest reports on the isolation of a molecule existing solely as the norcaradiene was by Ciganek in the 1960s with the preparation of the dicyano compound **15N**.[37–41] A sizeable body of work following Ciganek's initial finding focused on modification of the substrate with the goal of isolation of a stable norcaradiene. The structural modifications (Fig. 6) can be grouped as follows:

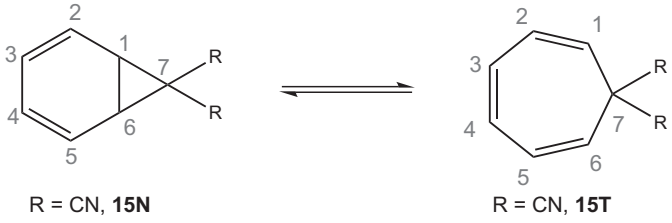


Fig. 6.

(a) placement of one (monosubstitution) or two (disubstitution) π-acceptor groups at the C(7) position (which includes Ciganek's work) as well as substitution on the cycloheptatriene ring, i.e., positions 1–6;
(b) extension of conjugation at appropriate positions in the norcaradiene form;
(c) shortening of the C(1)–C(6) bond by bridging these positions with a chain of carbon atoms or incorporation of the norcaradiene into a bridged system;

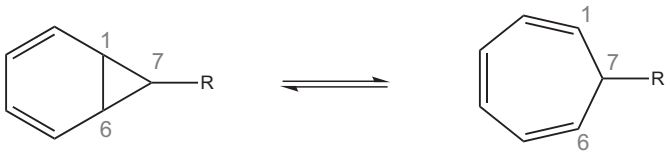
(d) steric destabilisation of the cycloheptatriene form **15T** by substitution with bulky groups at C(1) to C(6).

2.3.1. Introduction of substituents onto the NCD–CHT framework. As described above, the dicyano derivative **15** of cycloheptatriene **9T** provided one of the first examples of a stable norcaradiene. The following section describes various attempts to delineate the norcaradiene–cycloheptatriene equilibrium. Understanding of the equilibrating norcaradiene–cycloheptatriene system was enhanced with the advent of NMR spectroscopy and, thus, studies of the system occurred in earnest from the period of the 1950s–1980s. The numbering system used throughout this review in describing all NMR spectroscopic studies conducted is that used by Ciganek (Fig. 6). The indicative signals for the position of equilibrium of the system are the H-1 and H-6 protons as they exist in different hybridisation environments in the two tautomeric forms, i.e., sp^3 in the norcaradiene and sp^2 in the cycloheptatriene (Fig. 6), making NMR spectroscopy a useful method for analysis of these systems. The H-1 and H-6 protons can either appear as two individual signals or as a single signal.

As the interconversion of the norcaradiene and cycloheptatriene is essentially a pericyclic process, consideration of the orbitals involved is warranted at the outset.

2.3.1.1. Molecular orbital explanation of the stabilisation of norcaradienes. Hoffmann[29,42] and Günther[43] both rationalised the observations made by Ciganek in terms of the HOMO–LUMO interactions between the cyclopropane ring and the substituents. When there is a good π-acceptor or electron-withdrawing group at C(7), it possesses low-lying unoccupied molecular orbitals. They can efficiently overlap with the occupied HOMO Walsh orbital in the cyclopropane ring (Fig. 7). As a result, the two electrons in the Walsh orbital are delocalised over the vicinal π-system. This causes electron density to be drawn away from the cyclopropane into the π-system. The anti-bonding character of the C(1)–C(6) bond (the distal bond) is weakened and therefore becomes shorter. The vicinal bonds [C(1)–C(7) and C(6)–C(7)], as a result, are lengthened. This results in a stabilisation of the norcaradiene (depicted schematically in Fig. 7). Hoffmann and Günther's predictions have since been proven with the X-ray crystallographic data for a range of cyclopropanes discussed by Allen.[44–46] This illustrated the impact of the introduction of electron-withdrawing groups, which caused a shortening of the distal bond. Furthermore, Hoffmann predicted that structures substituted with π-donor substituents also interact via electron donation from the unoccupied 2p orbital of the substituent into the LUMO Walsh orbital of the cyclopropane ring (Fig. 7). This leads to an increase in anti-bonding character of the cyclopropane ring, thereby destabilising the norcaradiene, in contrast to the results obtained by von Ragué Schlayer, discussed shortly (see Table 1).[47]

Table 1
Substituent effects [at C(7)] on cyclopropanes,[47] with an estimation of the major tautomer in the norcaradiene–cycloheptatriene equilibrium



Substituent type	C_1C_7 (vicinal)	C_1C_6 (distal)	Major tautomer[a]
π-Acceptor	Longer	Shorter	NCD
π-Donor	Longer	Shorter	NCD
σ-Acceptor	Shorter	Longer	CHT
σ-Donor	Longer	Shorter	NCD

[a] Postulated as the major tautomer using von Ragué Schlayer's results for the vicinal and distal bond lengths. von Ragué Schlayer does not discuss this table of results in the context of norcaradienes and cycloheptatrienes.

However, a publication in 1977 by Staley and Cairncross described the stabilisation of a norcaradiene by the incorporation of π-electron donors, thus appearing to contradict Hoffmann and Günther's theory.[48] A significant study by Kollmar followed and showed that the cyclopropane ring is actually a weak π-electron acceptor, but a strong π-electron donor.[49] Thus, π-donor substituents contribute much less to stabilisation energies than π-acceptor substituents, explaining Staley and Cairncross' results. Kollmar also found that σ-electron-donating substituents are likely to stabilise the norcaradiene, while σ-electron-withdrawing substituents destabilise the norcaradiene, causing the cycloheptatriene to predominate. This explained the appreciable difference in the amounts of stabilised norcaradiene present in the dicyano compound **15N** in comparison with the compound substituted with two CF_3 groups described by Gale, which exists exclusively as the cycloheptatriene **16T** (Fig. 8).[50,51]

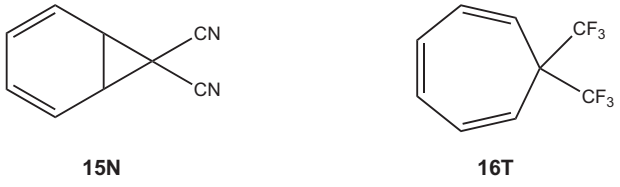


Fig. 8.

In 1984, von Ragué Schlayer described a key computational study on the stabilising effects of various substituents on cyclopropane rings.[47] This agreed with the results obtained by Kollmar.[49] The stabilising and destabilising effects of various substituents as described by von Ragué Schlayer, are summarised in Table 1.[47]

In summary, Hoffmann and Günther's theory considers π-interactions only, while Kollmar and von Ragué Schlayer have shown

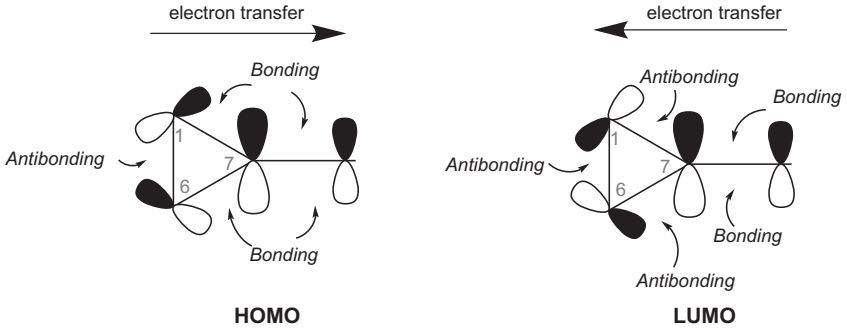


Fig. 7.

that σ-effects have a significant impact on the position of equilibrium. In general, σ-electron-donor substituents also have a stabilising effect along with π-electron-withdrawing groups. Liebman and Greenberg have also discussed the stabilisation of norcaradienes by π-acceptor substituents.[6]

2.3.1.2. Mono- and di-substitution at the C(7) position. Following Ciganek's preparation of **15**, the impact of a single cyano group at the C(7) position on the norcaradiene–cycloheptatriene equilibrium was then explored by Günther[34] and Bushweller[52] who explored the equilibrium of 7-cyanocycloheptatriene **17** using low-temperature ^{1}H NMR spectroscopy (Fig. 9). The norcaradiene tautomer was not observed. However, it is worthwhile noting that Adam and Balci later described the preparation of the norcaradiene-derived singlet-oxygen adducts of 7-cyanocycloheptatriene **17** indicating that the norcaradiene tautomer is present.[53]

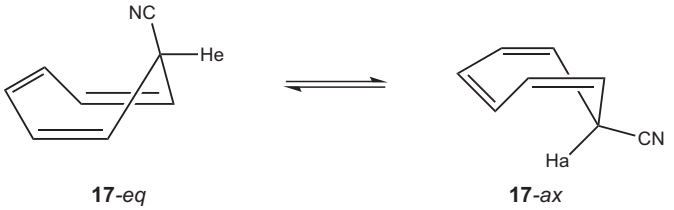


Fig. 9.

Substitution of the cyano group with carboxylic acid and aldehyde moieties also provided some interesting data on the nature of the norcaradiene–cycloheptatriene equilibrium. Cyclohepta-2,4,6-trienecarboxylic acid **12T** (Fig. 4) was discussed earlier with regard to Buchner's initial finding on the decomposition of ethyl diazoacetate in benzene.[2] In 1975, Günther calculated the concentration of norcaradiene present as being ~3%,[34] providing evidence that a carboxylic acid has a bigger stabilising effect than a cyano group, as it interacts more strongly with the Walsh orbital of the cyclopropane than the cyano group.

The aldehyde analogue, cycloheptatrienecarbaldehyde **18**, was subjected to variable-temperature NMR spectroscopic studies by Balci.[54] Lowering of the sample temperature allowed direct observation of these two dynamic processes (Fig. 10) and indicated that the norcaradiene tautomer was present in an amount of 7%.

Molecular orbital calculations predict the order of influence of the electron-withdrawing substituents described above on the amount of norcaradiene present in a system as increasing in the order CN<CO_2H<CHO;[42] this prediction is thus in agreement with the experimental results obtained by Günther and Balci.[34,54]

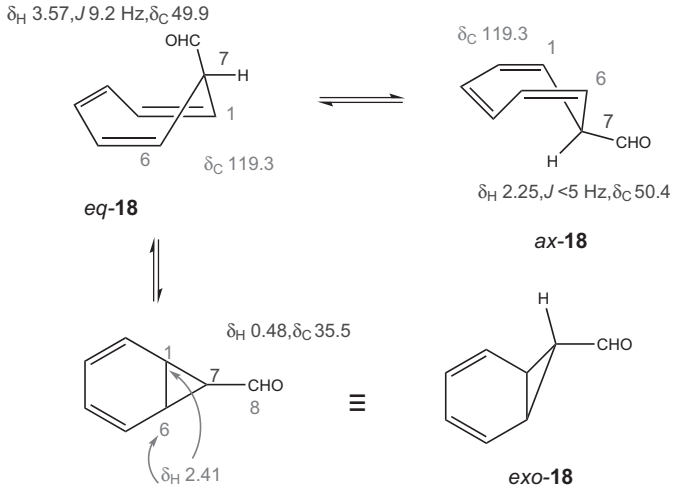


Fig. 10.

Alkyl substitution at C(7) was then considered by Günther with several C(7)-substituted cycloheptatrienes studied and he found that they existed with the substituent in a quasi-equatorial position (Fig. 11).[55] More importantly, they all exist entirely in the cycloheptatriene form. NMR spectroscopic studies of the *tert*-butyl derivative **19** were also discussed by Heyd.[56]

Hoffmann has pointed out that a carbonium ion is an excellent π-acceptor and thus should significantly stabilise the norcaradiene.[42] Indeed, Childs prepared the zwitterions **20** and **21** from 7-carbomethoxycycloheptatriene **22**.[57] The zwitterions were found to exist predominately as the norcaradiene (Scheme 4). In line with previous observations by Balci[54] on the orientation of cycloheptatrienecarbaldehyde **18**, the norcaradienes **20** and **21** were only observed in the *exo* conformation. The authors attributed this to the unfavourable secondary interactions in the *endo* isomer between the p orbital on C(7) and the diene molecular orbitals.

Childs also prepared the analogous amido compound **23** from the amide **24** (Scheme 5).[57] The system was found to shift towards the norcaradiene relative to the amide **24**; this was confirmed by the chemical shift of the H-1 and H-6 protons at δ_H 4.81 ppm, indicative of a system existing as an equilibrium of the two tautomeric forms **23T** and **23N**.[57]

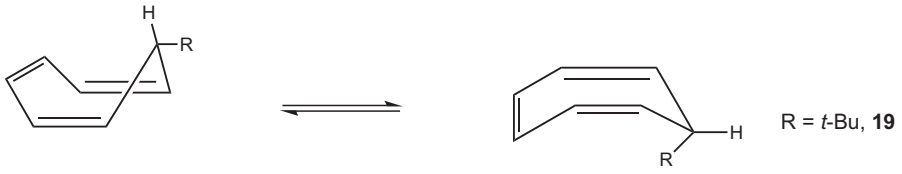
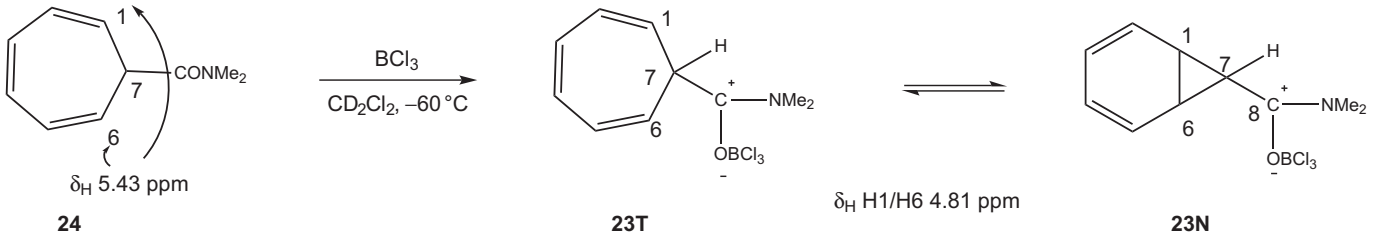


Fig. 11.

22 ($\delta_{H\text{-}1,6}$ 5.43 ppm)

X = Cl, **20**, $\delta_{H\text{-}1,6}$ 3.41 ppm
X = Br, **21**, $\delta_{H\text{-}1,6}$ 3.48 ppm

Scheme 4.



Scheme 5.

Daub et al. also explored the possibility of introducing a carbonium ion to stabilise the cyclopropane with a body of work, which began in 1972.[58–61] The dioxolonium salt **25** (Fig. 12) was found to exist as the norcaradiene **25N**,[58] which was confirmed by the ^{1}H NMR spectroscopic data (observed at −40 °C).

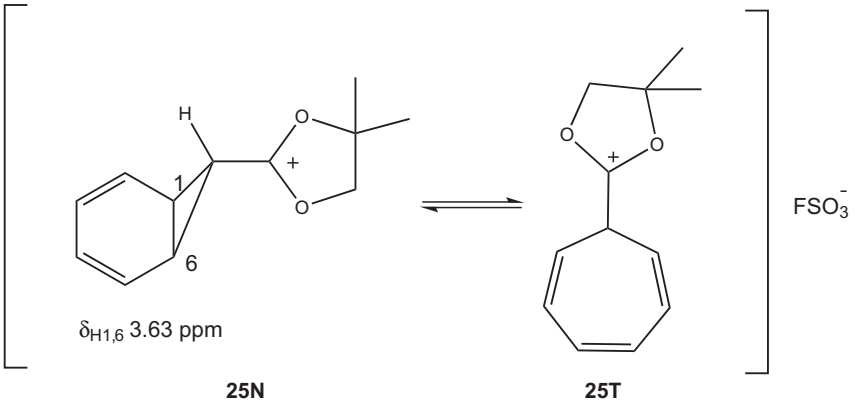


Fig. 12.

The analogous imidazolidine derivative **26** was, in contrast, found to exist predominately as the cycloheptatriene **26T** in the boat conformation (Fig. 13).[62]

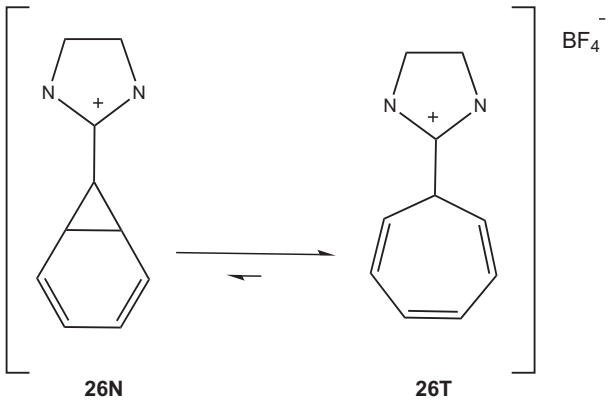


Fig. 13.

More recently, Gridnev has described the preparation of the C(7)-monosubstituted system, cycloheptatrienyl(dipropyl)borane **27** (Fig. 14).[63] The system **27** was found to exist as a mixture of the two tautomeric forms, confirmed by variable-temperature NMR spectroscopic studies. The cycloheptatrienylborane **27T** existed as the *exo* and *endo* forms, while the norcaradiene **27N** existed only as the *exo* form. The stability of the norcaradiene is thought to be due to favourable overlap with the unoccupied boron anti-bonding 2p orbital with the Walsh orbital of the cyclopropane ring of the norcaradiene.[63]

Furthermore, Gridnev found that the deuteropyridine complex **28T** existed as the cycloheptatriene, which appeared to be due to the overlap of the nitrogen lone pair with the empty boron 2p anti-bonding orbital, reducing overlap with the Walsh orbital of the cyclopropane, thereby destabilising the norcaradiene (Scheme 6).[63]

Interestingly, there is an isolated case of a single electron donor at the C(7) position stabilising the norcaradiene sufficiently to push the equilibrium to the bicyclic form (also described in Section 2.3.1.1). In 1977, Staley and Cairncross described the piperidine- and cyclohexyl-substituted systems **29** and **30**, which were found to exist as equilibrating mixtures of the norcaradiene and cycloheptatriene; this was confirmed by the ^{1}H NMR spectra of both **29** and **30**.[48] Thus, π-donors would appear to stabilise the norcaradiene relative to the cycloheptatriene. The analogous compound **31T** without the π-donors at C(7), described by Mukai,[64] is known to exist entirely as the cycloheptatriene (Fig. 15).

As described earlier, Ciganek's preparation of the dicyano derivative of cycloheptatriene **9T** provided one of the first observations of a stable norcaradiene. He prepared the norcaradienes **15N** and **32N** by the thermolysis of dicyanodiazomethane **33** in benzene and *p*-xylene (Scheme 7).[38] Fritchie described X-ray crystallographic studies on the norcaradiene **15N**;[65] the cyclopropane bond lengths were found to be 1.558, 1.553 and 1.500 Å. The bond angles were found to be 115 and 58° for NC–C–CN and C(1)–C(7)–C(6), respectively.

NMR spectroscopy confirming the bicyclic structure was carried out by Ciganek and also by Roberts.[38,66] The cyclopropyl protons were observed as a triplet at δ_H 3.47 ppm for **15N** and at δ_H 3.22 ppm for **32**; in contrast, the corresponding NMR signal for the mono-cyano compound **17** was reported at δ_H 5.33 ppm[52] Ciganek initially postulated that widening of the NC–C–CN angle as a result of dipole-dipole repulsions was the reason for the unusual stability of the norcaradiene **15N**, while the theoretical studies (discussed above) by Hoffmann, Günther, Kollmar and von Ragué Schlayer subsequently provided more insight into the stabilisation of the norcaradiene by π-acceptors. However, the angle between the substituents at the C(7) carbon is also known to be an important factor in the position of equilibrium (see Fig. 37, Scheme 26 and Scheme 27).

From Ciganek's initial findings, it appeared that simply the presence of two electron-withdrawing substituents at the C(7)

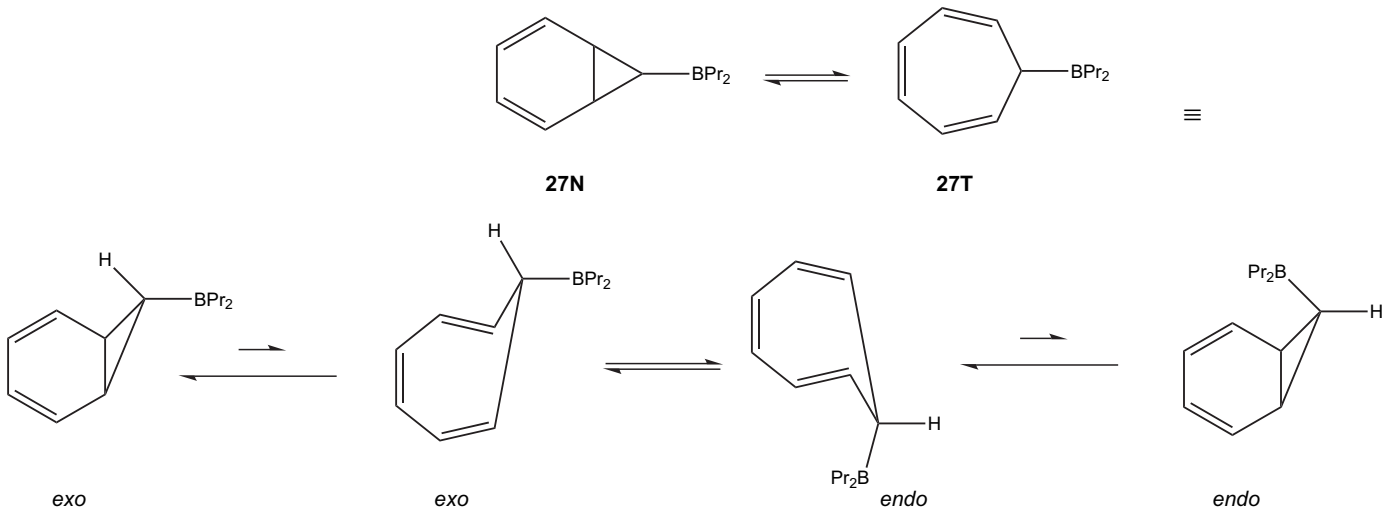
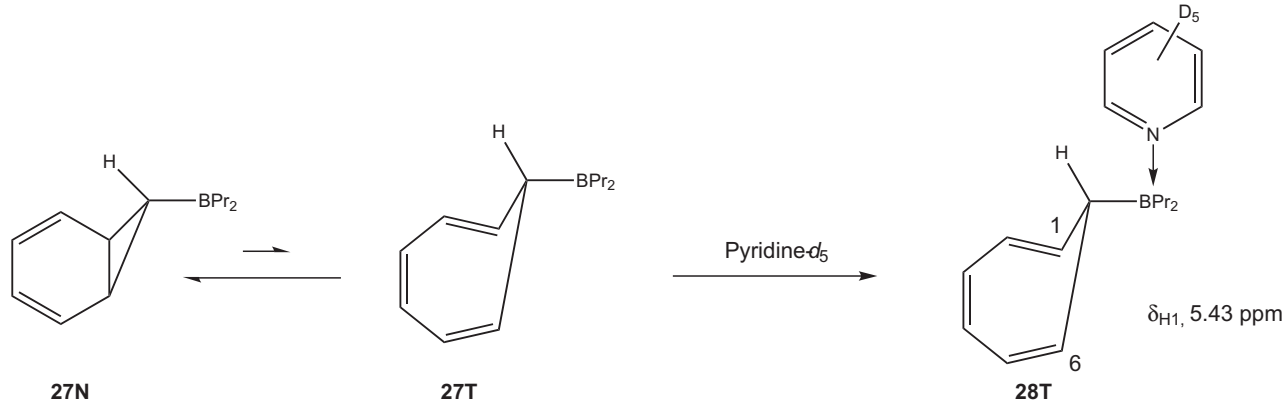


Fig. 14.



Scheme 6.

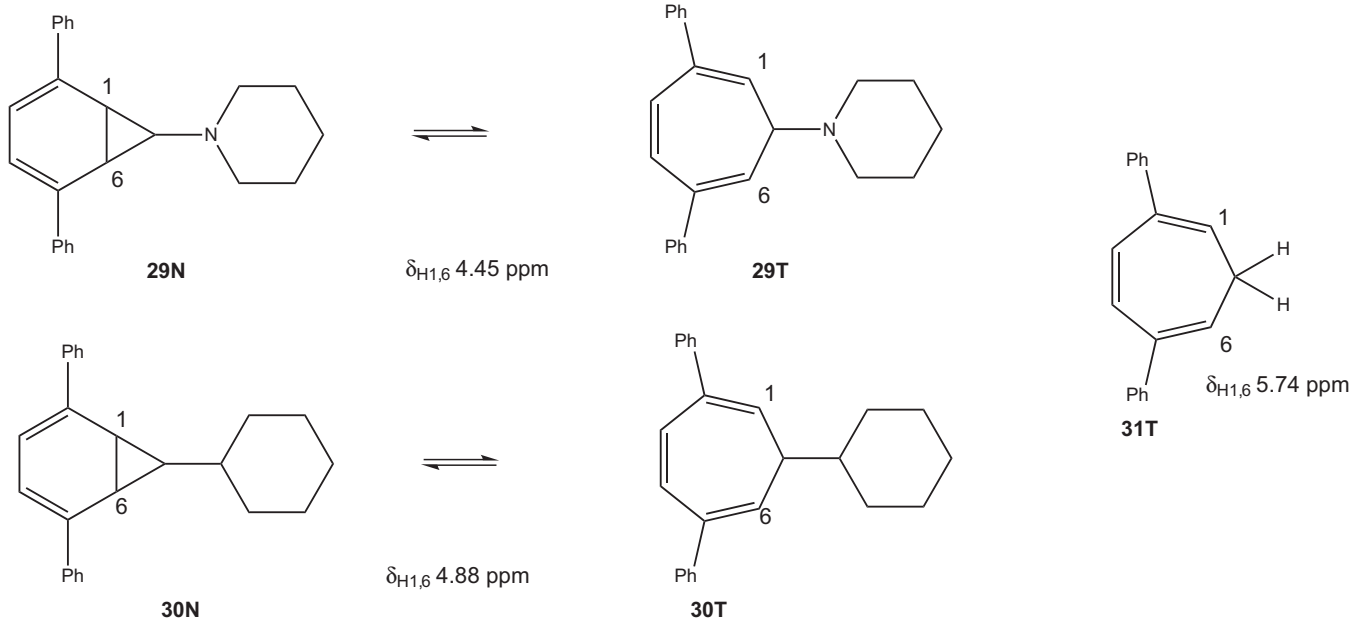
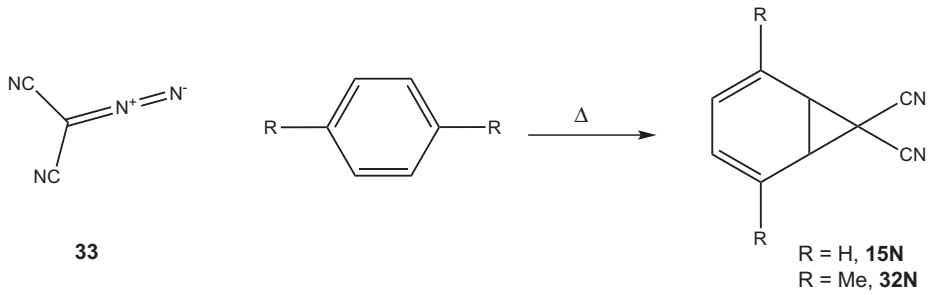


Fig. 15.



Scheme 7.

position of cycloheptatriene pushed the equilibrium towards the norcaradiene. However, the replacement of one of the cyano groups by a trifluoromethyl group by Ciganek provided **34**, which, in contrast to **15**, was rapidly equilibrating between the norcaradiene and cycloheptatriene, as confirmed using variable-temperature ^{1}H NMR spectroscopy (Fig. 16).[37] Indeed, the analogous systems, substituted with two perfluoro groups **16** and **35**,[67] prepared by Gale,[51] and confirmed using NMR spectroscopy by Roberts,[33] existed entirely as the cycloheptatriene.

tautomer **37** was confirmed by ^{1}H NMR spectroscopy; the C(1) and C(6) protons displayed ^{1}H NMR spectroscopic resonances as a doublet at δ_H 3.80 ppm and a quartet at δ_H 3.35 ppm, respectively.[38] The isomeric cycloheptatrienes **38** and **39** were isolated with a distinctive signal at δ_H 5.88 ppm assigned to the C(6) proton of **38**. Similar studies on benzonorcaradienes were described by Buchner and Vogel (see Fig. 26).[69,70]

Ciganek then explored the equilibria of disubstituted systems, along with Roberts.[71] The adducts **15**, **34** and **40**–**44** were each

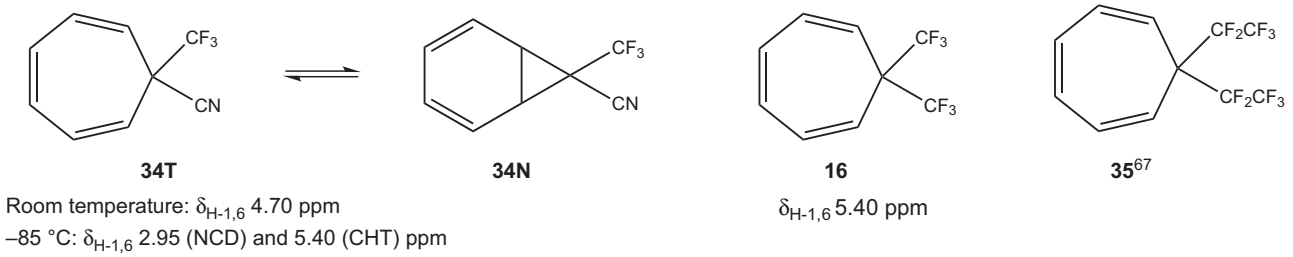
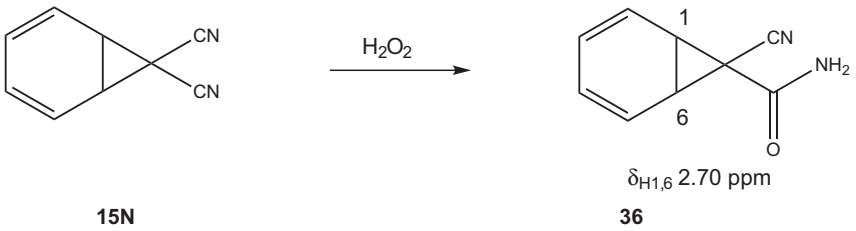


Fig. 16.

Interestingly, partial hydrolysis of the dicyano compound **15N** did not alter the position of equilibrium, as the amide **36** was also found to exist entirely as the norcaradiene (Scheme 8).[68]

prepared by the thermolytic and photolytic decomposition of the appropriate diazo compound in benzene (Scheme 9 and Table 2). The norcaradiene tautomer was dominant in the cyano-substituted



Scheme 8.

The decomposition of dicyanodiazomethane **33** in naphthalene was also explored by Ciganek and was found to result in three isomeric adducts, **37**, **38** and **39** (Fig. 17).[38] The norcaradiene

compounds (entries 1–4, Table 2) except the previously discussed compound **34**, which was obtained as a rapidly equilibrating mixture of the two tautomers (compare entry 2 and entries 1, 3–4).

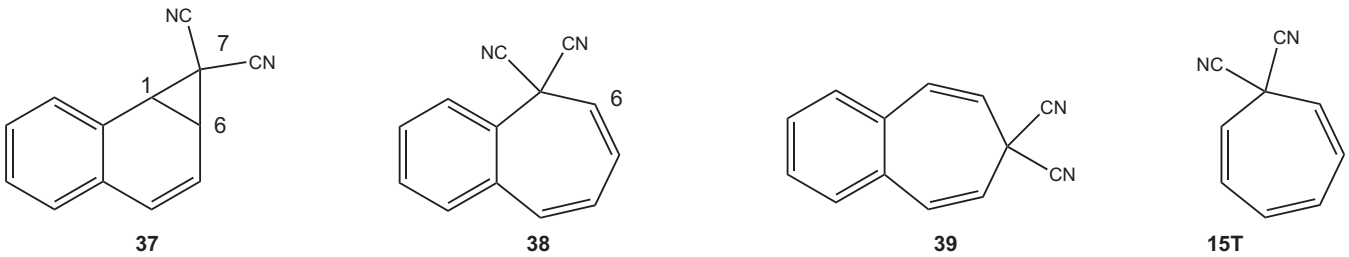
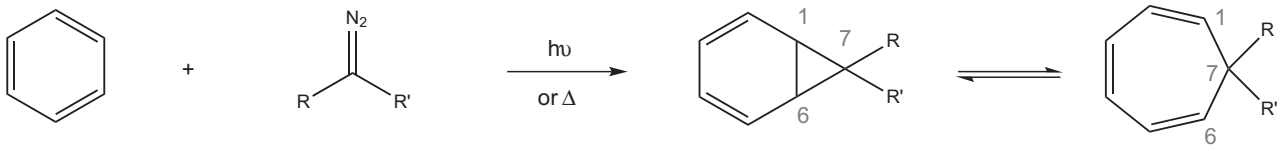
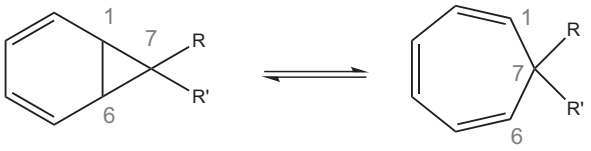


Fig. 17.



Scheme 9.

Table 2
Effect of different substituents at C(7) on the equilibrium of disubstituted [at C(7)] systems[41,71–74]

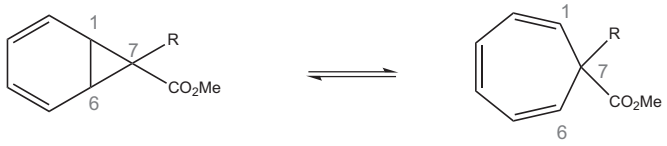


Entry	R	R′	Compound	$\delta_{H\text{-}1,6}$ (ppm)(32.5 °C)
1	CN	CN	**15**	3.47
2	CN	CF_3	**34**	4.70
3	CN	CO_2Me	**40**	3.25
4	CN	Ph	**41**	3.52
5	CO_2Me	Ph	**42**	4.38[71]
6	CO_2Me	*p*-MeO–C_6H_4	**43**	4.13[71]
7	CO_2Me	*p*-NO_2–C_6H_4	**44**	4.29[71]
8	CO_2Me	CO_2Me	**45**	5.04[74]

Overall, the ester-substituted compounds were found to exist as an equilibrating mixture of both tautomers (entries 5–8).

Other reports of systems substituted with a second substituent at the C(7) position, which led to an alteration in the norcaradiene–cycloheptatriene equilibrium, were then described. Substitution with an alkyl group at the C(7) position on ester-substituted systems was explored separately by Mukai[75] in 1974 and again in 1981 by Takahashi.[76] Mukai's study found that all compounds studied existed predominantly as the cycloheptatriene at room temperature; on cooling the sample, individual ^{1}H NMR signals for the tautomers were observed. Overall, as the steric demand of the alkyl group increased, the equilibrium shifted towards the cycloheptatriene (entries 1–3, Table 3).[75]

Table 3
Variable-temperature ^{1}H NMR spectroscopic studies on alkyl-substituted [at C(7)] methyl ester systems[75]



Entry	R	δ_H C(1),C(6) at room temperature	δ_H (NCD) at −100 °C	δ_H (CHT) at −100 °C
1	Me	4.03	2.49	5.26
2	Et	4.35	2.52	5.35
3	*i*-Pr	4.87	2.30	5.33

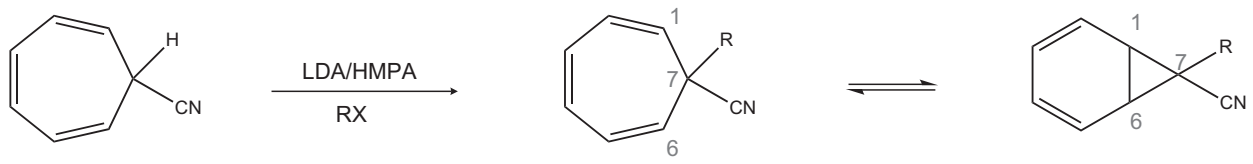
The impact of alkyl substitution on the 7-cyanocycloheptatrienes was further explored by Takahashi (Table 4).[76] A series of alkylated cyanocycloheptatrienes **46**–**50** were prepared with a similar trend to Mukai being observed, although the trend is not seen with the *tert*-butyl-substituted cycloheptatriene **46** (entries 1–3 and 5, Table 4). Variable-temperature ^{1}H NMR spectroscopic studies also allowed the direct observation of the norcaradiene (at δ_H 2.48 ppm) and the cycloheptatriene (at δ_H 5.28 ppm). Interestingly, the cyclopropene-substituted system (entry 4, Table 4) proved to exist almost entirely as the norcaradiene at room temperature. This provides a further illustration of the impact of a smaller external angle on the stability of the norcaradiene (discussed in Section 2.3.4.1).

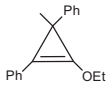
In 1972, Dürr described photochemical decomposition of the spiropyrazole **51**, which yielded the spiroheptatriene **52**, while decomposition of the dicyano derivative **53** gave the fulvenylnorcaradiene derivative **54** as the sole product (Scheme 10); the structure of the norcaradiene **54** was confirmed by the position of the cyclopropyl protons at δ_H 3.05 ppm. The corresponding cycloheptatriene was not observed, even on heating of the norcaradiene **54** at 110 °C.[77]

In 1988, L'Abbe and Dehaen described the decomposition of the triazole **55** in benzene to yield the cycloheptatriene **56** (Scheme 11).[78] In contrast, the *p*-nitrophenyl-substituted derivative **57** undergoes rearrangement to the analogous triazole **58**, which decomposes in the presence of benzene to the norcaradiene **59**. Again, structural confirmation of the norcaradiene was provided by the ^{1}H NMR spectra; in particular, the H-1 and H-6 protons appeared as one signal at δ_H 3.20 ppm.

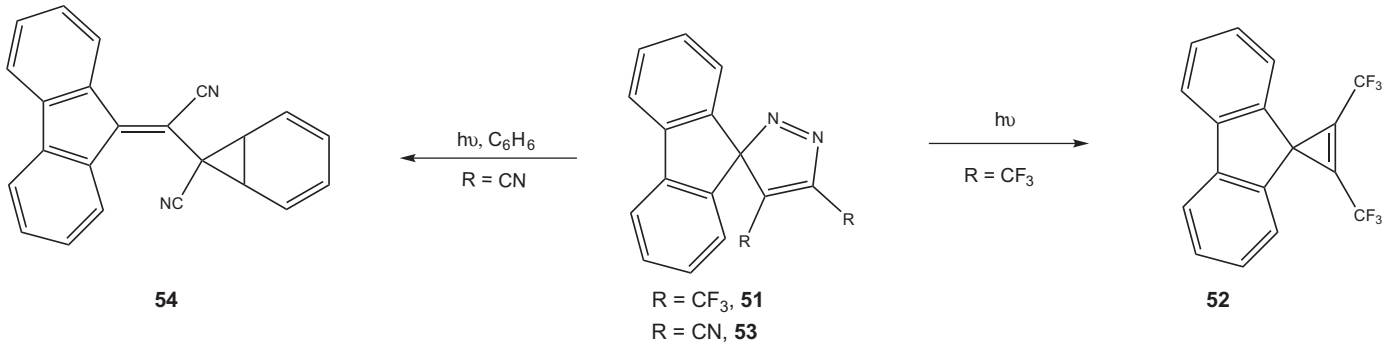
Thus, substitution at C(7) of the norcaradiene–cycloheptatriene equilibrating system can have a dramatic impact on the position of equilibrium with a vast array of substituents pushing the equilibrium towards the norcaradiene. In general, π-acceptor groups at C(7) (with one case of a π-donor substituent) favour the norcaradiene.

Table 4
Variable-temperature ^{1}H NMR spectroscopic studies on alkyl-substituted [at C(7)] cyano systems[76]

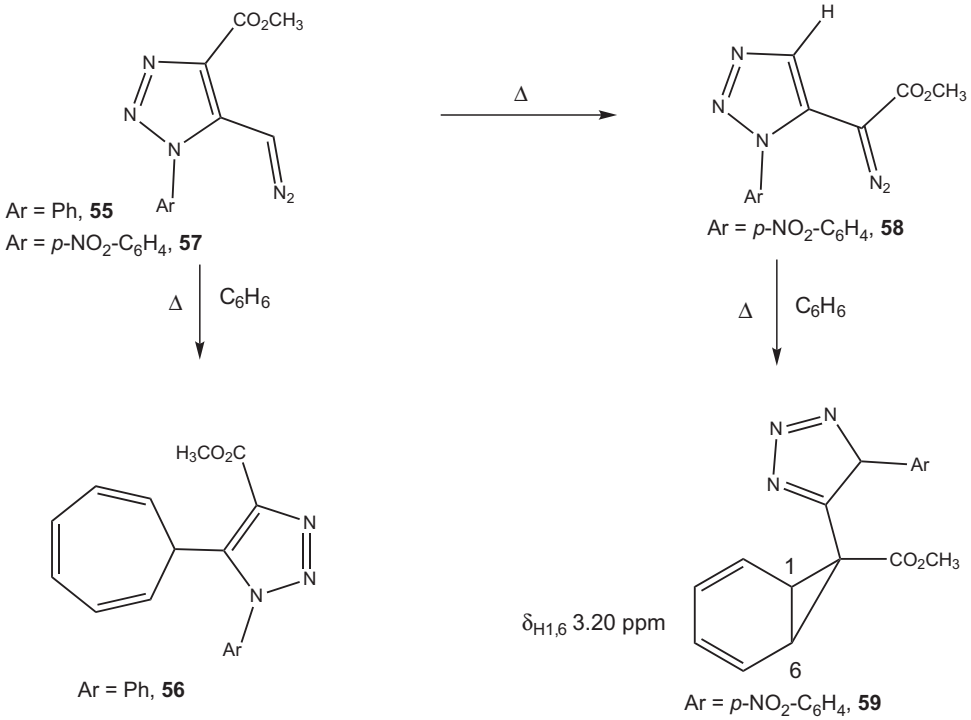


Entry	Product	R	$\delta_{H\text{-}1,6}$ 25 °C	$\delta_{H1,6}$ (NCD) −130 °C	$\delta_{H1,6}$ (CHT) −130 °C
1	47	Et	4.84	—[a]	—[a]
2	48	Bn	4.66	—[a]	—[a]
3	49	*i*-Pr	4.36	2.34	5.02
4	50		3.04	2.60 (−80 °C)	—
5	46	*t*-Bu	4.69	2.48	5.28

[a] Not reported.



Scheme 10.



Scheme 11.

The introduction of alkyl groups at C(7) on cyano- and ester-substituted systems can also have an impact on the position of equilibrium, with bulkier groups leading to less norcaradiene, cf. the results described by Mukai and Takahashi.[64,76]

2.3.1.3. Substitution on the cycloheptatriene ring. The impact that electron-withdrawing substituents have on the norcaradiene–cycloheptatriene equilibrium for C(7)-monosubstituted systems is well documented as occurring in the order CN<CO_2H<CHO.[54] Owing to the stability of the norcaradiene tautomer of the dicyano compound **15N**, it seems reasonable to presume that a system substituted with two carboxylic acid or ester groups would also stabilise the norcaradiene. However, the diester-substituted analogue **45**, was found by Görlitz and Günther to exist as a mixture of the two tautomeric forms, norcaradiene **45N** and cycloheptatriene **45T** (Table 2 and Fig. 18).[79]

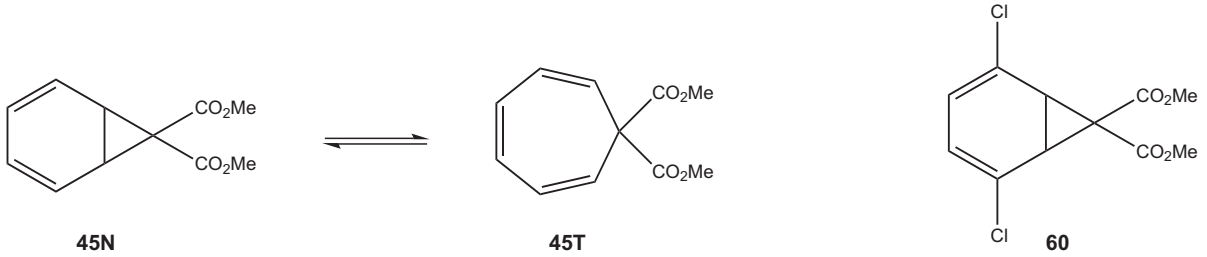
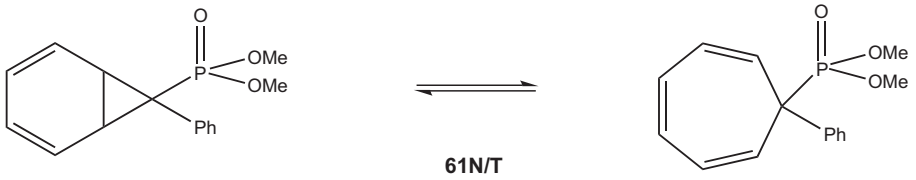


Fig. 18.

Interestingly, modification of the structure with two chlorine atoms at the 2- and 5-positions was described by Maas and Regitz and gave the dichloro compound **60**, which was found to exist entirely as the norcaradiene (Fig. 18).[80]

Regitz described phosphonate-substituted norcaradiene–cycloheptatriene derivatives (Scheme 12);[81] this product



Scheme 12.

61 was found to exist in solution as an equilibrating mixture of both tautomers **61N**/**T**, while it was found to exist as the norcaradiene **61N** in the solid state when the structure of **61** was determined crystallographically.[82,83] A rapidly equilibrating mixture was confirmed by the ^{13}C NMR spectrum, where the resonances of C(1) and C(6) appeared at δ_C 58.0 ppm, thus indicating norcaradiene to be the major tautomer.

Günther and Regitz also described the phosphonates **62** and **63** existing solely as the norcaradiene tautomer, analogous to their earlier study on the diester compound (Fig. 18).[84,85] Significantly, it was the introduction of the halogens, bromine and chlorine, at the C(2) and C(5) positions that shifted the system towards the norcaradiene, as the ester **64** and the phosphonate **61** existed as an equilibrating mixture of the two tautomers (Fig. 19).[81] Various other norcaradiene is stabilised by the incorporation of electron donors into the structure. A similar result was also observed by Matsumoto in 1995 (Scheme 15).[86,87]

Klärner found varying amounts of norcaradiene and cycloheptatrienes present in systems with ester and methyl substituents at the C(7) position; the equilibrium position was dependent on the other substituents around the ring.[73,88] In general, it was found that the addition of a methyl group at the 2-position forced the equilibrium towards the norcaradiene, a similar effect to that observed by Okamoto (discussed later) and by Maas and Regitz (Fig. 18).[80,83] In general, the order of stabilisation of the norcaradiene observed by Klärner was impacted by substituents in the order 2-Ph>2-Br ~ 2-Me>3-Me>*H*>1-Me (Table 5).[88]

Rearrangement of the tricyclic ketones **70**–**72** to the substituted equilibrating norcaradiene–cycloheptatriene systems **73N**/**T**–**75N**/**T** in the presence of sodium methoxide was described by Schmid et al.[89] The resultant rearranged products were found to exist as the norcaradiene **73N**–**75N** (Scheme 13).[89]

Smith described the preparation of C(7)-monosubstituted norcaradienes and cycloheptatrienes substituted with a triazole group,

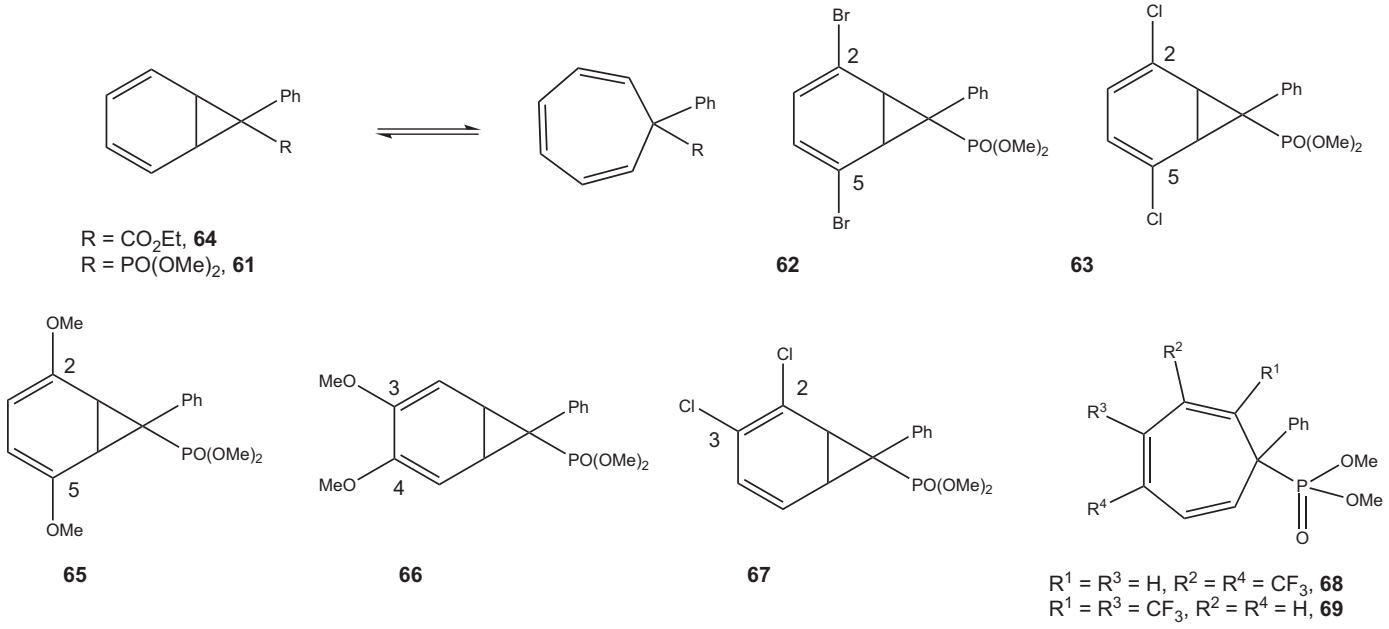
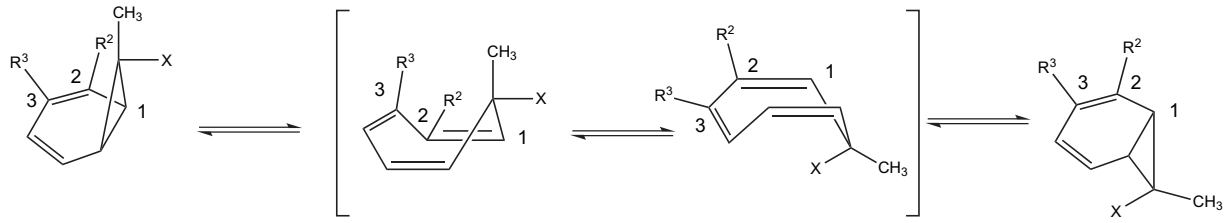


Fig. 19.

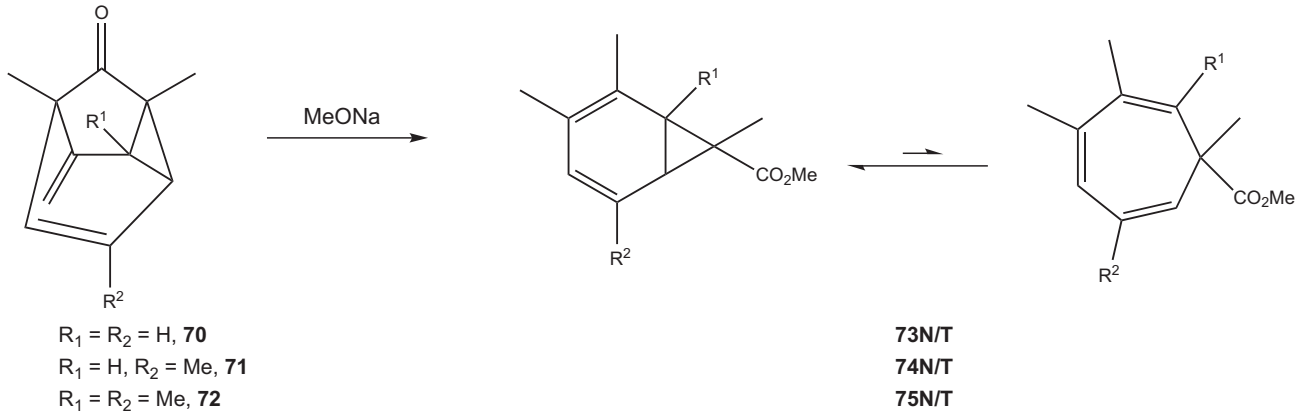
analogues **65**–**67** were prepared and found to exist, in each case, as the norcaradiene.[85] In contrast, the trifluoromethyl-substituted derivatives **68** and **69** were found to exist as the cycloheptatriene.[80] Structural modifications at the 2- and 5-positions appear to significantly stabilise the norcaradiene and are particularly noteworthy.

In particular, the incorporation of electron donors in the case of **65** and **66**, having methoxy groups at the 2,5- and 3,4-positions, is interesting as this is one of the few examples where the as shown in Table 6.[90,91] Thermolytic decomposition of 5-(diazomethyl)-1,4-diphenyl-1,2,3-triazole **76** (DPT–CHN_2) in the presence of alkylbenzenes, naphthalene and thiophene provided products with varying amounts of equilibrating norcaradiene and cycloheptatriene. Initial studies with benzene and toluene provided exclusively the cycloheptatriene adducts (entries 1 and 2, Table 6), while reaction with *o*- and *p*-xylene provided a significant shift towards the norcaradiene (entries 3 and 4, Table 6).[90,91] Decomposition

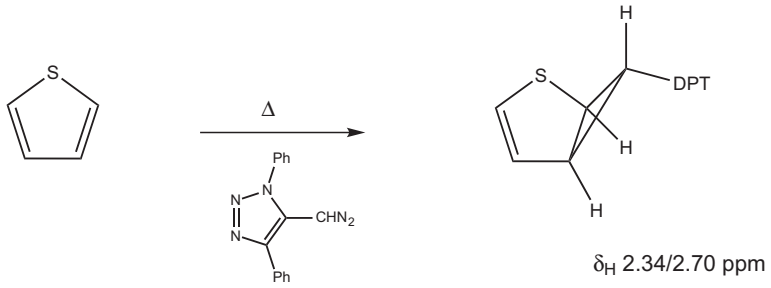
Table 5
Impact of substitution with alkyl groups on the cycloheptatriene ring



Entry	R^2	R^3	X	Ratio A:B:C
1	Ph	H	CN	24:61:15
2	Me	H	CN	4:16:80
3	H	H	CO_2H	46:0:54
4	H	H	CO_2Me	24:0:76
5	Br	H	CO_2Me	95:0:5
6	Me	H	CO_2Me	95:0:5
7	H	CH_3	CO_2Me	40:0:60



Scheme 13.

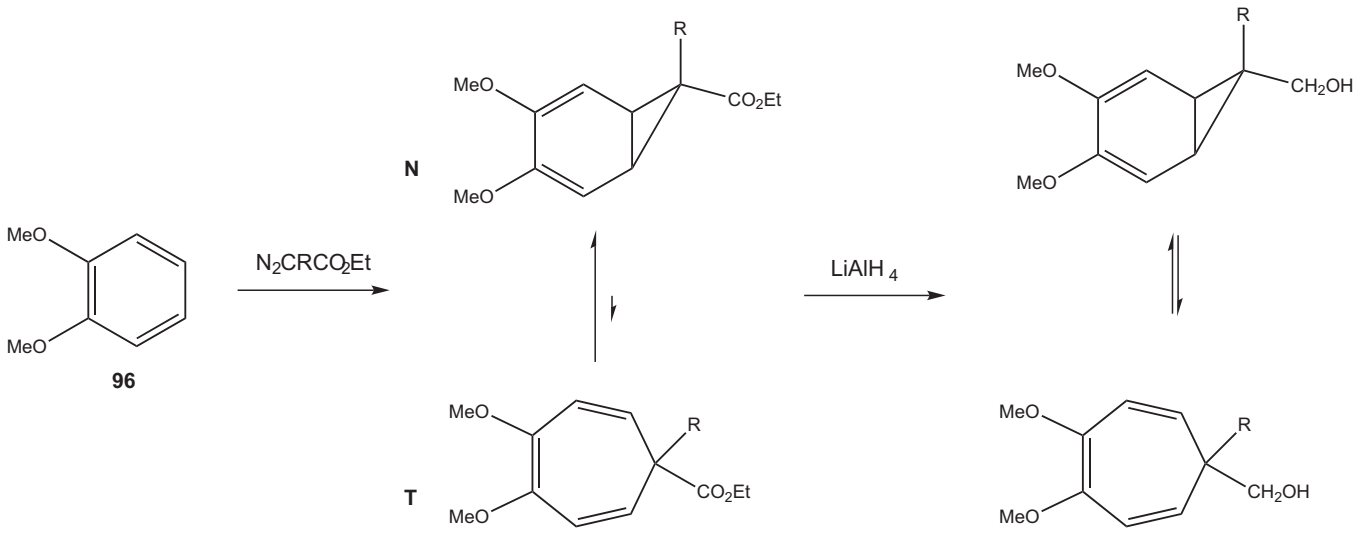


Scheme 14. (76=DPT–CHN_2).

of the triazole **76** in the presence of the more sterically demanding substrates, *p*-cymene, 4-*tert*-butyltoluene, mesitylene, durene and *p*-diisopropylbenzene, provided enough steric interactions to stabilise the norcaradiene (entries 5–12). The percentage norcaradiene present is strongly dependent on the position of the substituents, this being particularly evident in the decomposition of the triazole **76** with *p*-cymene and *tert*-butyltoluene, where two possible isomeric products result from aromatic addition of the carbene to different bonds (entries 5–8). Substitution at R^1 with bulky groups such as isopropyl and *tert*-butyl appears to result in large amounts of norcaradiene being present (entries 6, 8 and 9), again in line with previous studies by Klärner and Okamoto. Substitution with several smaller methyl groups at positions 1, 2, 4 and 5 (entry 12) caused the system to exist almost entirely as the norcaradiene.

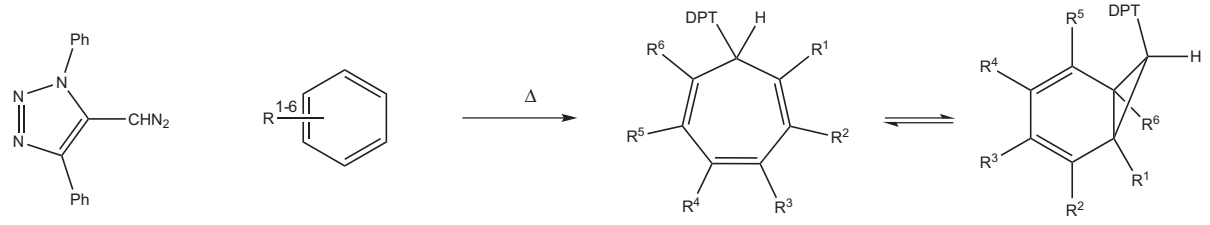
Smith also extended the scope of the transformation to include heterocycles. Preparation of the thiophene-derived adduct gave an exclusively norcaradiene-like product **77**, illustrated by a chemical shift of δ_H 2.34/2.70 ppm, indicative of the cyclopropyl protons (Scheme 14).

In keeping with previous work by Maas, Regitz and Klärner, Okamoto also described the introduction of *tert*-butyl groups at the 2- and 5-positions as favouring the presence of the norcaradiene.[92] The mono-substituted analogue, 2,5-di-*tert*-butyl-7-cyanocycloheptatriene **78**, was described; the incorporation of two *tert*-butyl groups at the 2- and 5-positions resulted in a system equilibrating between the norcaradiene and cycloheptatriene tautomers, as opposed to 7-cyanocycloheptatriene **17**, which exists essentially entirely as the cycloheptatriene, as previously described by



Scheme 15.

Table 6
Effect of substitution on the aromatic ring on the norcaradiene–cycloheptatriene equilibrium[90,91]



Entry	Substrate	Equilibrating product							
		R^1	R^2	R^3	R^4	R^5	R^6	$\delta_{H\text{-}1,6}$	% NCD
1	Benzene	H	H	H	H	H	H	5.32	~0
2	Toluene	Me	H	H	H	H	H	5.15	~0
3	*o*-Xylene	H	H	Me	Me	H	H	4.61	17.9
4	*p*-Xylene	Me	H	H	Me	H	H	4.90	7.5
5	*p*-Cymene	Me	H	H	*i*-Pr	H	H	4.63	17.1
6	*p*-Cymene	*i*-Pr	H	H	Me	H	H	3.54	56.0
7	4-*tert*-Butyltoluene	H	Me	H	H	*t*-Bu	H	5.10	—[a]
8	4-*tert*-Butyltoluene	*t*-Bu	H	H	Me	H	H	3.74	48.9
9	*p*-Diisopropylbenzene	*i*-Pr	H	H	*i*-Pr	H	H	3.34	63.2
10	Mesitylene	Me	H	Me	H	Me	H	3.71	20.0
11	Durene	Me	H	Me	Me	H	Me	—[b]	—
12	Durene	Me	Me	H	Me	Me	H	2.49	93.6

[a] Inseparable from the isomeric *tert*-butyl product (entry 8).
[b] Data not reported.

Bushweller (Fig. 9).[52] Distinct signals for all four tautomeric forms of **78** were observed by Okamoto employing variable-temperature NMR; the *endo* form was found to be more stable than the *exo* form of the norcaradiene (Fig. 20), which is in contrast to the acid- and aldehyde-substituted systems, **12** and **18** (Figs. 4 and 10) in which the substituent is oriented *exo*.

Substitution of the cyano group by an ethynyl or phenylethynyl group gave the compounds **79** and **80**, as reported by Okamoto in 1984, with the overall π-acceptor ability, and, therefore, the amount of norcaradiene increasing in the order: phenylethynyl>cyano> ethynyl (Fig. 21).[93]

Significantly, Okamoto described the introduction of *tert*-butyl groups around the cycloheptatriene ring, as well as at C(2) and C(5) and at C(7) (entries 1–5, Table 4).[92] This important study demonstrated the steric effect of certain substituents in driving the equilibrium to the norcaradiene side (Table 7). The position of the *tert*-butyl substituents on the ring was seen to have a dramatic impact on the position of equilibrium, often resulting in more norcaradiene being present, particularly in the case of the disubstituted compounds **81** and **82** (entries 4 and 5, Table 7). It is again clear that substitution at positions 2, 3 and 4 has a dramatic impact on the norcaradiene–cycloheptatriene equilibrium with the 2-*tert*-butyl

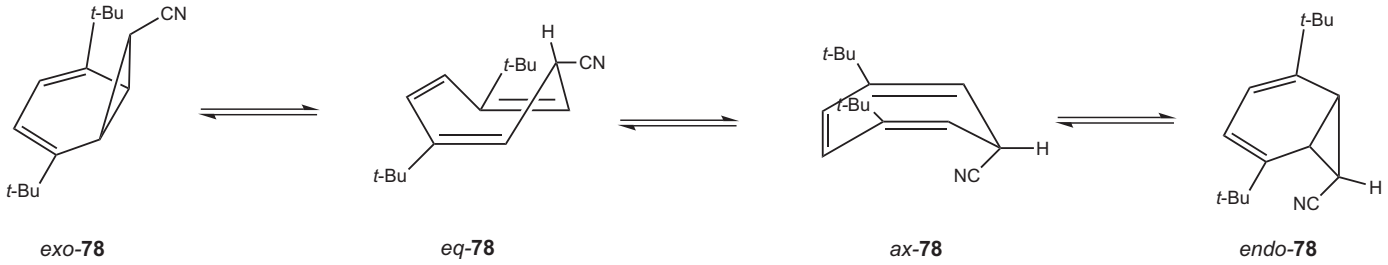


Fig. 20.

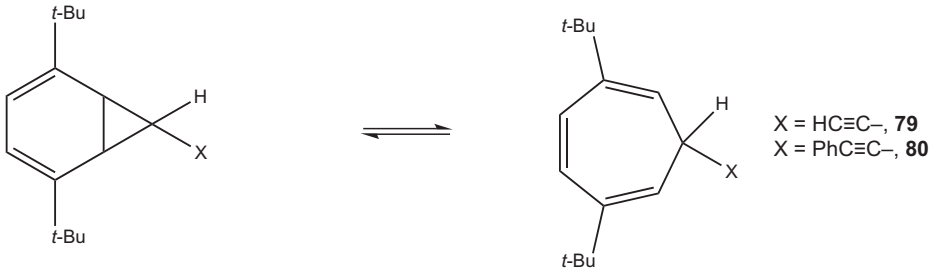
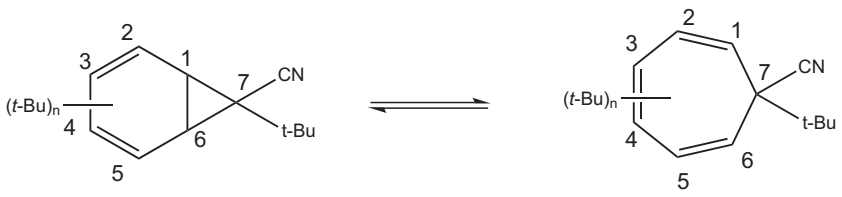


Fig. 21.

Table 7
Impact of introduction of *tert*-butyl substitution around cycloheptatriene ring



Entry	No (NCD/CHT)	*tert*-Butyl position	δ_H (25 °C) ppm		δ_H (−110 °C) ppm	
			H-1	H-6	H-1	H-6
1	**46N/T**	—	4.72	4.72	4.98	4.98
2	**83N/T**	2	2.72	2.59	2.46	2.32
3	**84N/T**	3	3.82–4.00	3.82–4.00	—	—
4	**81N/T**	2, 4	2.43	2.31	2.34	2.24
5	**82N/T**	2, 5	2.36	2.36	2.37	2.37

(**83**), 2,4-(**81**) and 2,5-di-*tert*-butyl-(**82**) substituted compounds existing almost entirely as the norcaradiene at room temperature, in line with studies by Klärner, Maas and Regitz, while the 3-*tert*-butyl compound (**84**) exists as an equilibrating mixture of tautomers (entries 2–5). Okamoto attributed the marked shift of the system to the norcaradiene side to the repulsive interactions between the *tert*-butyl group and the hydrogen atoms on adjacent carbon atoms, which leads to bending of the ring.

Interestingly, Okamoto found that the tetra-*tert*-butyl-substituted norcaradiene **85** was in equilibrium with the cycloheptatriene **85T**, albeit with the norcaradiene **85N** as the major tautomer, while the analogous system **86** was found to exist almost exclusively as the cycloheptatriene **86T** (Fig. 22).[94] The *tert*-butyl groups at the C(1) and C(6) positions of **86** presumably repel each other in the norcaradiene form **86N** thereby stabilising the monocyclic tautomer. In the case of **85**, the norcaradiene is more favourable, due to relief of repulsive interactions between the 1-, 3- and 5-*tert*-butyl groups and the H-2, H-4 and H-6 protons in the cycloheptatriene form, thereby stabilising the norcaradiene. There is also a significant relief of the repulsive strain between the axial 7-*tert*-butyl group and the π-electrons of the C(3)–C(4) double bond.

Okamoto then considered 7-phenyl-substituted cycloheptatrienes. Previous studies by Günther had shown that the parent compound, 7-phenyl-1,3,5-cycloheptatriene **87** (Fig. 23) exists in the cycloheptatriene form.[55,72] A study by Roberts in 1971 examined the equilibria of *para*-substituted 7-aryl-7-methoxycarbonylcycloheptatrienes.[71] However, Günther found that this system was unsuitable for examination of the equilibrium, as the aryl group is *endo* and cannot interact favourably with the cyclopropane ring, as it cannot assume a bisected conformation.[72]

Okamoto found that the substitution pattern on the aromatic ring can also have a dramatic impact on the norcaradiene–cycloheptatriene equilibrium of 7-aryl-di-*tert*-butylcycloheptatrienes.[95,96] As a result of their previous observations with the 2, 5-di-*tert*-butyl-substituted systems (Table 7), Okamoto et al. then demonstrated that the introduction of *tert*-butyl groups at the 2- and 5-positions of 7-arylcycloheptatrienes (Fig. 24) could stabilise the norcaradiene significantly.[95,96] It was found that, as predicted, electron donors, such as methoxy and methyl groups on the 7-aryl group stabilised the cycloheptatriene tautomer, while the more electron-withdrawing substituents stabilised the norcaradiene (Fig. 24).

In 1995, Matsumoto described an interesting example of the stable norcaradienes **88N**–**91N**, prepared from **96**, but instead of being stabilised by π-electron acceptors, the compounds appeared to be stabilised by the introduction of electron-donating methoxy groups at the 3- and 4-positions of the aromatic ring

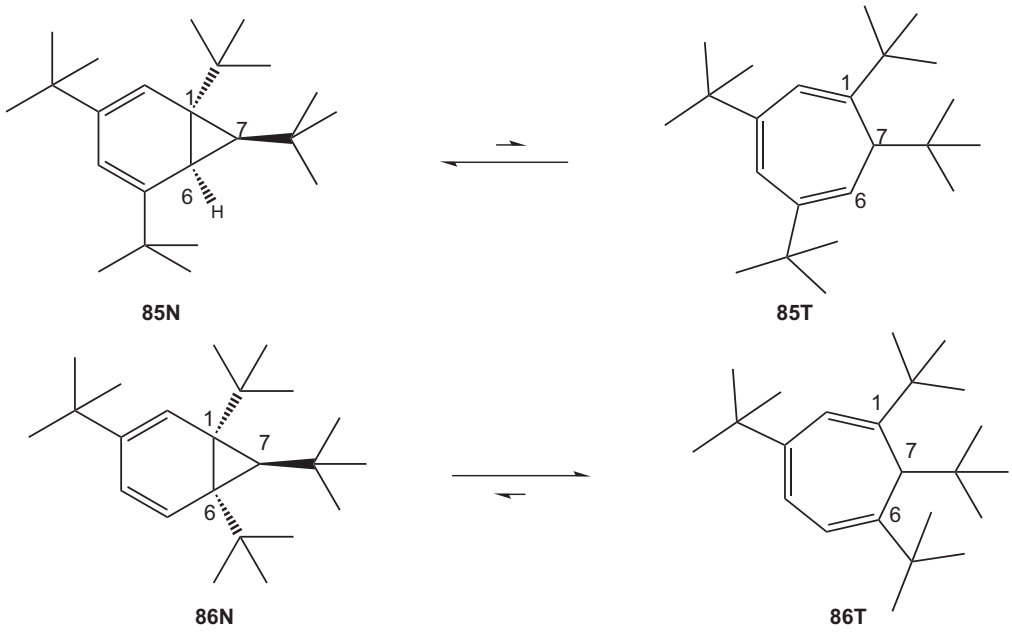


Fig. 22.

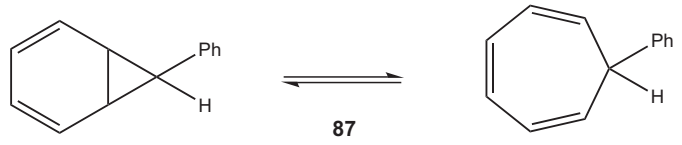


Fig. 23.

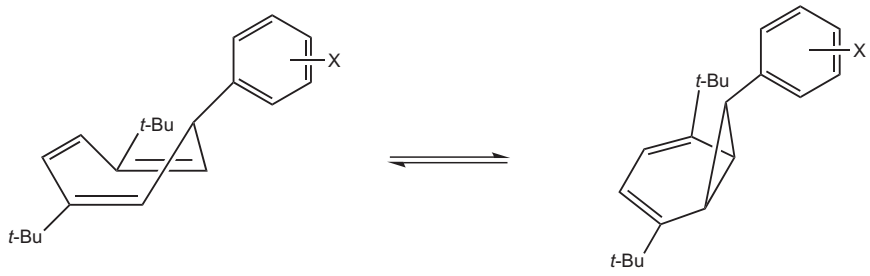
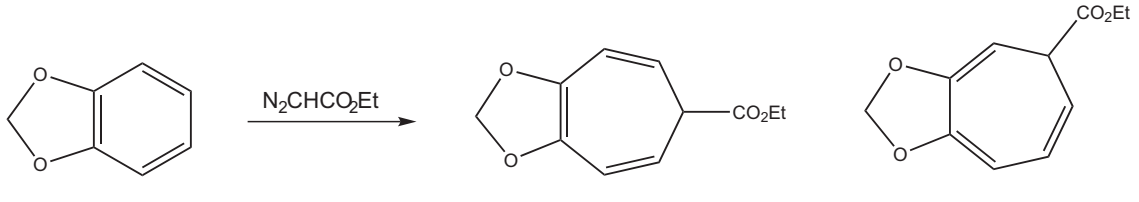


Fig. 24.

(Scheme 15).[86,87] Even when **88N** was heated to 80 °C, there was no trace of the cycloheptatriene **88T** observed. Matsumoto postulated that the introduction of the methoxy groups strengthens the C(1)–C(6) bond of the cyclopropane, thereby stabilising the norcaradiene tautomer (Scheme 15).

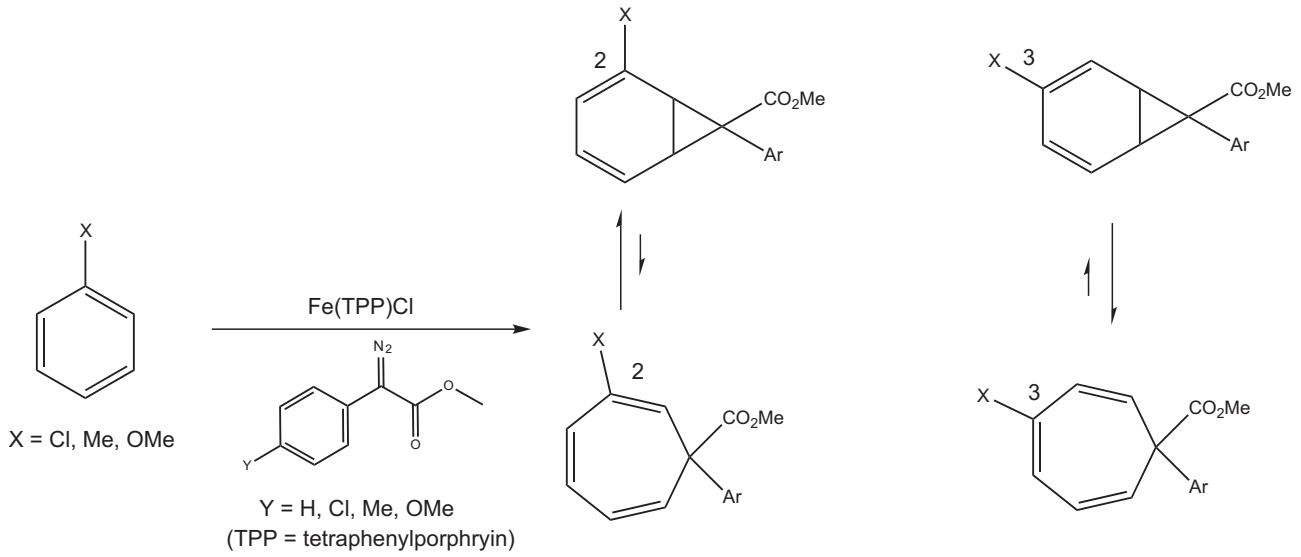
Significantly, reduction of the esters **88**–**91** to the primary alcohols **92**–**95** resulted in an equilibrating mixture of the two tautomers with differing ratios, dependent upon the substituent at C(7). Incorporation of a bulky 9-fluorenyl group (**95**) at the C(7) position results in a ratio of 82:18 NCD–CHT (Scheme 15). This change in equilibrium upon reduction of the ester to the alcohol illustrates that electron withdrawal by the ester on the system is a considerable factor, in addition to steric effects at C(7), contributing to the position of equilibrium(Scheme 15).[86,87]

Interestingly, Matsumoto also described the preparation of the methylenedioxy-bridged analogue of **98** from the reaction of benzo[*d*][1,3]dioxole **97** and ethyl diazoacetate; the two regioisomeric products found to exist were the cycloheptatrienes **98** and **99** with no trace of the norcaradienes being observed (Scheme 16).[86] This was thought to be due to a reduced interaction between the lone pairs on the oxygen and the π-system of the norcaradiene, thereby destabilising the norcaradiene.[86]



Scheme 16.

Recently, Woo described the addition of aryldiazoacetate-derived carbenes to arenes using an iron porphyrin catalyst (Scheme 17).[97] Equilibrating mixtures of norcaradienes and cycloheptatrienes resulted, the nature of which was dependent upon the position of

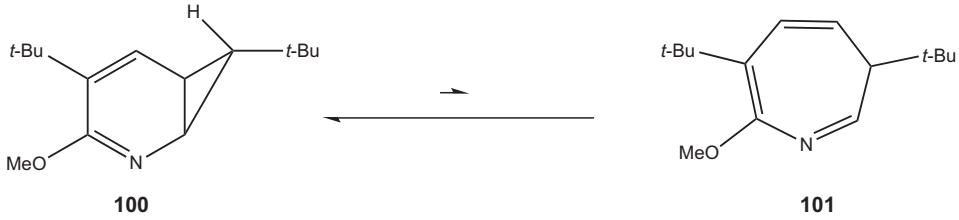


Scheme 17.

the substituents present on the aryldiazoacetate. As with previous reports (described above) by Günther and Regitz, substitution at C (2) of the norcaradiene–cycloheptatriene system shifted the equilibrium towards the norcaradiene, while substitution at C(3) saw the equilibrium favour the cycloheptatriene.

Interestingly, the incorporation of heteroatoms into the ring system can have a dramatic impact on the position of the equilibrium. Satake described the first preparation of 2-azanorcaradiene **100**, the valence isomer of the cycloheptatriene analogue, 3*H*-azepine **101**.[98] Even at room temperature, the azanorcaradiene did not revert to the azepine **101** (Fig. 25). However, the stabilisation of this norcaradiene-type molecule could also be due to the *tert*-butyl

2.3.2. Extension of conjugation in the norcaradiene–cycloheptatriene system. Incorporation of one or two double bonds into a condensed aromatic system also serves to shift the tautomeric equilibrium. Early studies by Buchner and Huisgen on the decomposition of ethyl diazoacetate in naphthalene found that the norcaradiene adduct **102N** was the product.[69,100] Isomerisation into the cycloheptatriene **102T** is unfavourable, as this involves dearomatisation of the benzene ring. Conversely, compounds **103** and **104** described by Wittig exist as the cycloheptatriene tautomers, as isomerisation to the norcaradiene here would involve unfavourable quinoid-ring formation (Fig. 26).[101] In 1964, Vogel described the variable-temperature NMR spectrum of the naphthalene adduct **105**, which indicated interconversion between the two antipodes (Fig. 26).[102] Vogel postulated that this interconversion of the antipodes **105N^1** and **105N^2** was a consequence of the norcaradiene–cycloheptatriene (**105T**) equilibrium. A similar study was described by Smith.[91]



100 **101**

Fig. 25.

and methoxy groups. Earlier studies on nitrogen heterocyclic systems were described by Binsch.[99]

Thus, the overall ability of substituents at C(7) to stabilise the norcaradiene is strongly dependent upon the electronic nature of these groups and, in general, two strong π-acceptors are required to stabilise the norcaradiene sufficiently to exist as the dominant tautomer. Balci described the overall ability of π-acceptors at C(7) to stabilise the norcaradiene as being in the order: $C(CN)_2$>C(Ph)(CO_2R)>C(Ph)$PO(OR)_2$>$C(CO_2R)_2$.[5] However, substituents on the cycloheptatriene, such as phenyl rings, halogens and even electron donors, such as methoxy and alkyl groups can also stabilise the norcaradiene, with the extent of stabilisation strongly influenced by the position of substitution.[80]

In 1965, Müller[103] described the preparation of the dibenzonorcaradiene **106** by the reaction of diazomethane with phenanthrene **107**. It was found to exist exclusively as the norcaradiene (Scheme 18). A benzonorcaradiene has been prepared by Spencer by the reduction of a naphthalic anhydride.[104] Interestingly, Popik has described the photolysis of dibenzonorcaradienes, which results in cleavage of the cyclopropane bonds and the formation of 1,3-diradicals.[105]

In 1967, Mukai prepared 2,5,7-triphenylnorcaradiene **108** (Scheme 19) by the reaction of phenylmagnesium bromide with the diphenyltropylium salt **109**,[64] in a method previously described by Dauben and extensively employed for the preparation of such systems.[106] 2,5,7-Triphenylnorcaradiene **108** is the first example of

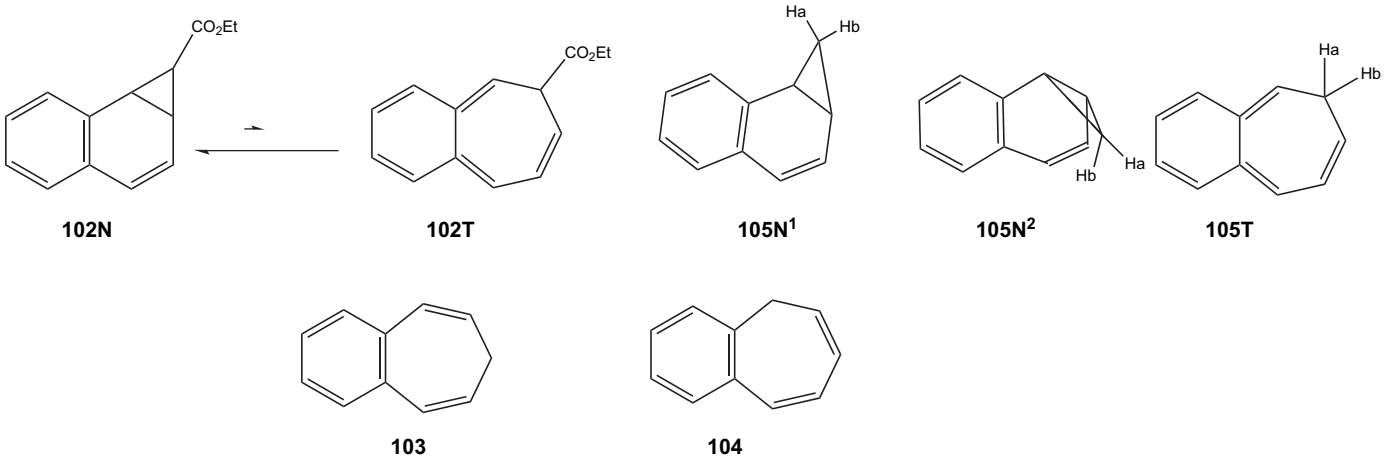
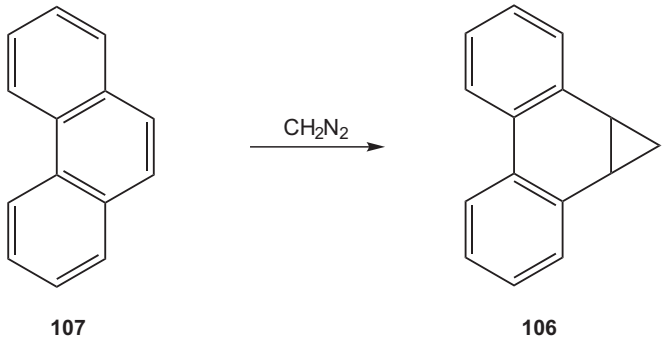


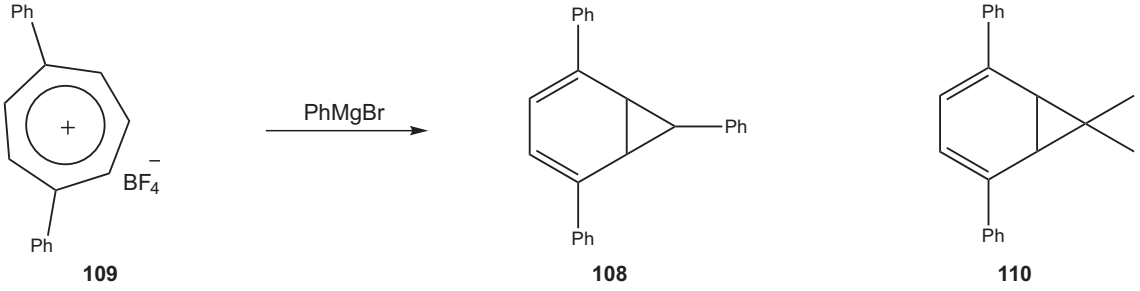
Fig. 26.



Scheme 18.

Thus, alteration of the conjugation of the norcaradiene–cycloheptatriene system can have a dramatic effect on the position of the equilibrium, this being particularly evident in Smith's and Klärner's results on the naphthalene (Fig. 26) and cyclobutene and cyclobutane derivatives (Fig. 27).

2.3.3. Forced shortening of the C(1)–C(6) bond in bridged systems and double norcaradienes. In 1963, Eschenmoser et al. described the preparation of the anhydride **115** during their synthesis of colchicine and found that it existed as the norcaradiene tautomer, one of the earliest observations of a stable norcaradiene.[111,112] In contrast, the dicarboxylic acid **116** existed as the cycloheptatriene form. In 1963 and 1966, Vogel and Radlick both described the preparation of a similar bridged system, namely the hydrocarbons **117** and **118**, and found that they existed entirely as the norcaradiene (Fig. 29).[113,114] These systems were forced into the norcaradiene tautomer by the introduction of the five-membered ring, which shortens the C(1)–C(6) bond, thereby stabilising the cyclopropane ring. However, when the five-membered ring was substituted for a six-membered-ring bridge,[70,115,116] i.e., **119**, the cycloheptatriene was preferred. Further lengthening of the chain in bridged steroid systems, described by Knox, also resulted in the dominance of the cycloheptatriene tautomer.[117,118] This again indicates the delicate balance, which exists in the stabilisation of the norcaradiene tautomer.



Scheme 19.

a system having a hydrogen atom at the C(7) position and existing exclusively as the norcaradiene. Thus, extension of conjugation into the phenyl groups stabilised the norcaradiene. Paquette prepared the analogous compound **110** in 1971 as the norcaradiene form.[107]

In 1982, Klärner explored the impact of annulated cyclobutene and cyclobutadiene rings on the norcaradiene–cycloheptatriene equilibrium.[108,109] The annulated derivatives **111** and **112** were prepared and **111** was found to exist solely as the norcaradiene, while **112** existed as the cycloheptatriene tautomer (Fig. 27). In contrast, the system **113** was found to exist as a mixture of the two tautomers. The annulated cyclobutadiene ring in **111** is destabilising the cycloheptatriene, while, in the cyclobutene system, the equilibrium is shifted in favour of the cycloheptatriene, as the cyclobutene ring contains an endocyclic double bond.

Further observations by Oda in 1987 reinforced Klärner's findings with the preparation of the analogous system **114**, which was found to predominate in the norcaradiene form.[110] Here, the antiaromaticity of cyclobutadiene destabilised the cycloheptatriene (Fig. 28).

An extensive body of work by Vogel followed,[119–121] with particular focus on extending the chain, with the preparation of a series of cyclodecapentaenes (a sub-group of annulenes), with the synthesis of the parent molecule, 1,6-methano[10]annulene **120**, described in 1964.[122] The initial product was the tricyclo [4.4.10]undeca-2,4,7,9-tetraene (the norcaradiene), which isomerised immediately to the cycloheptatriene (Fig. 30). Cremer also discussed this system in comparison to the simplest cycloheptatriene system **9**.[123]

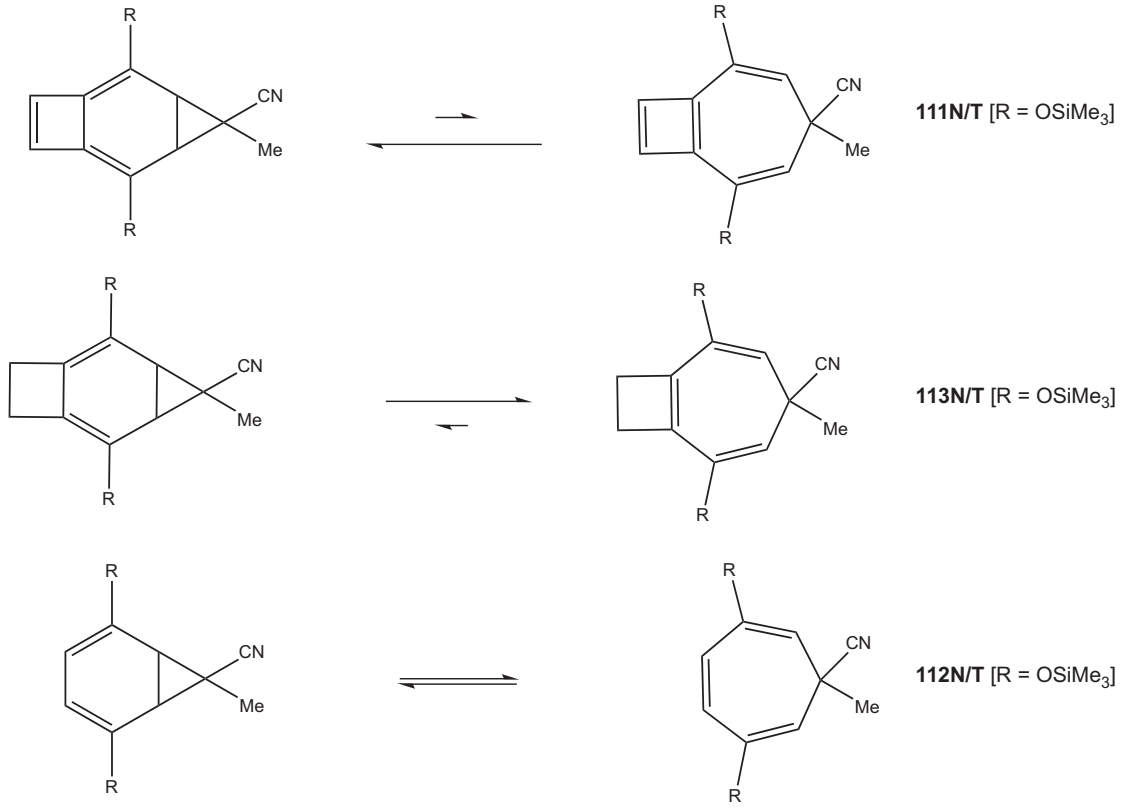
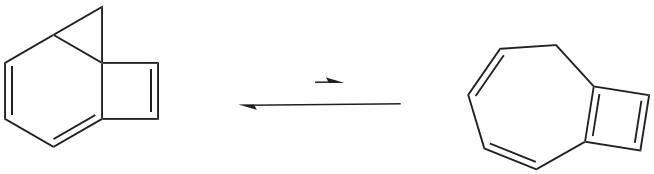
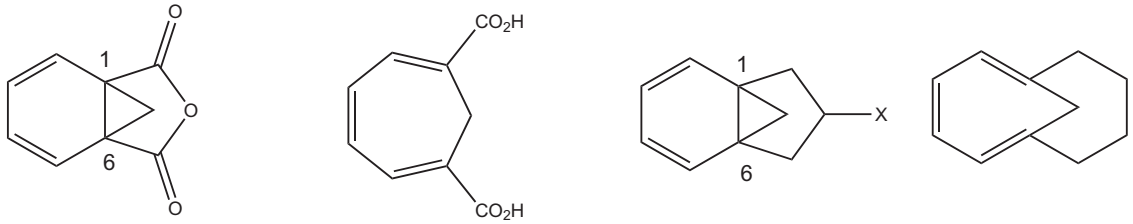


Fig. 27.



114N **114T**

Fig. 28.

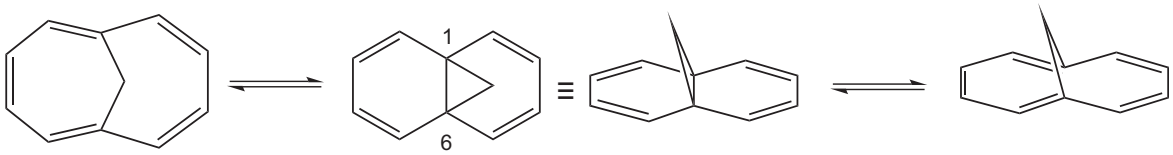


115 **116** X = H, **117** X = Cl, **118** **119**

Fig. 29.

Vogel followed this initial work with the preparation of the annulenes **121** and **122**, during the course of the synthetic sequence of which the norcaradienes **123** and **124** were prepared.[124,125] The norcaradiene **123** then underwent a spontaneous double norcaradiene–cycloheptatriene valence isomerisation to the isolated product **125**.[124] The norcaradiene **124** is an example of a stable norcaradiene prepared by the intramolecular aromatic addition of the carbene derived from the diazo ketone **126** to the aromatic moiety of the annulene framework (Scheme 20).[125] Vogel conducted a comprehensive review of the area in 1971,[119] with a review of current methods for the preparation of annulenes described by Oda in 2007.[126,127]

Monosubstitution of Vogel's annulene **119** with a cyano group led to two possible conformers, the *anti* and *syn* isomers of **127**. Interestingly, the *anti*-substituted isomer (*anti*-**127**) was found to exist as the cycloheptatriene, while introduction of the cyano group at the *syn* position, as in *syn*-**127**, gave essentially the norcaradiene.[70,115] This was revisited by Okamoto in a publication in 1983 in which he explained the differing positions of equilibria;[128] the cycloheptatriene of *syn*-**127** is much more unstable than the cycloheptatriene of *anti*-



120N/T

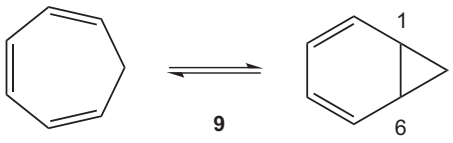


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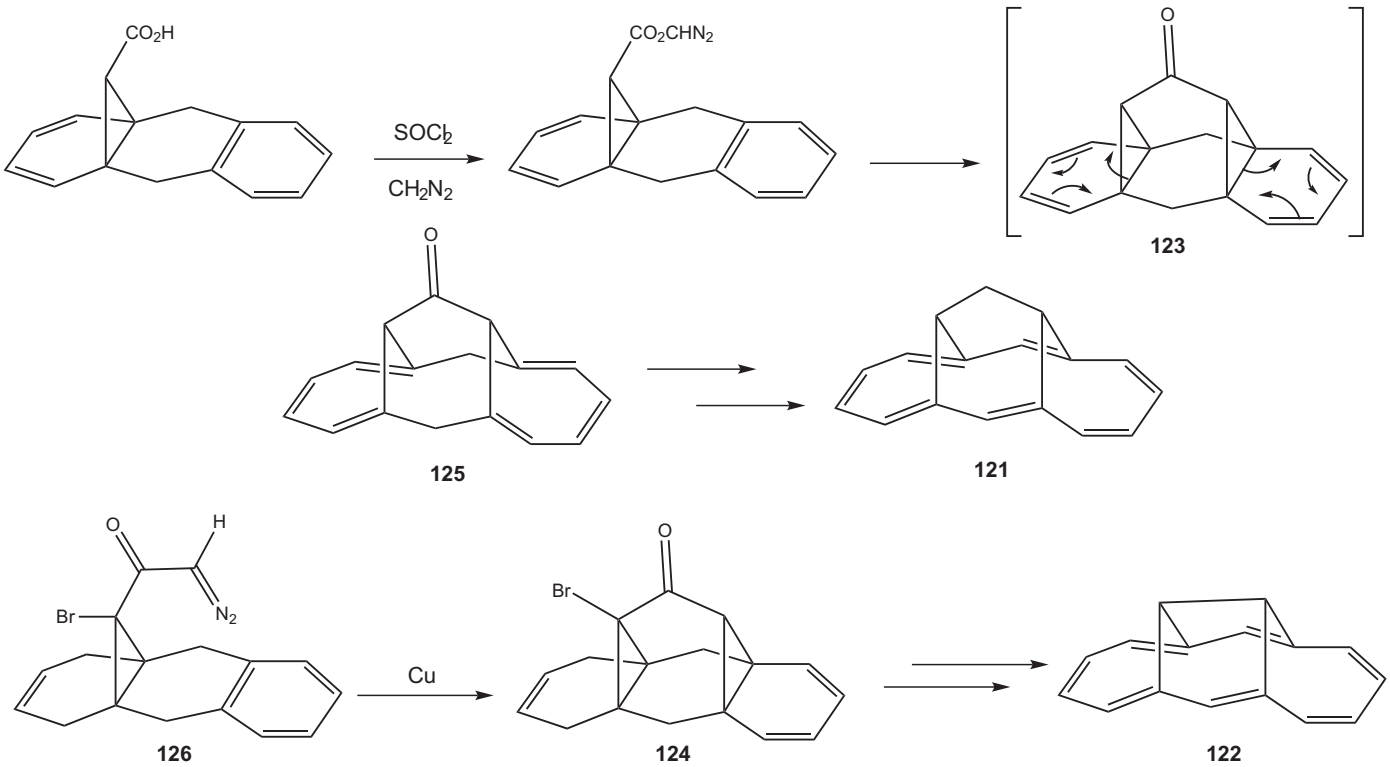
Fig. 30.



Scheme 20.

127, due to through-space repulsion between the cyano group and the π-electrons of the double bonds (Fig. 31).

The dicyano derivative of **120**, compound **128**, was predicted theoretically by Cremer[123] to exist as the norcaradiene and this was later confirmed experimentally by Vogel using ^{1}H and ^{13}C NMR spectroscopy and X-ray crystallography (Fig. 32).[129]

Hill described the preparation of **129**, a dibenzo derivative of **120**, which existed as the norcaradiene predominantly.[130]

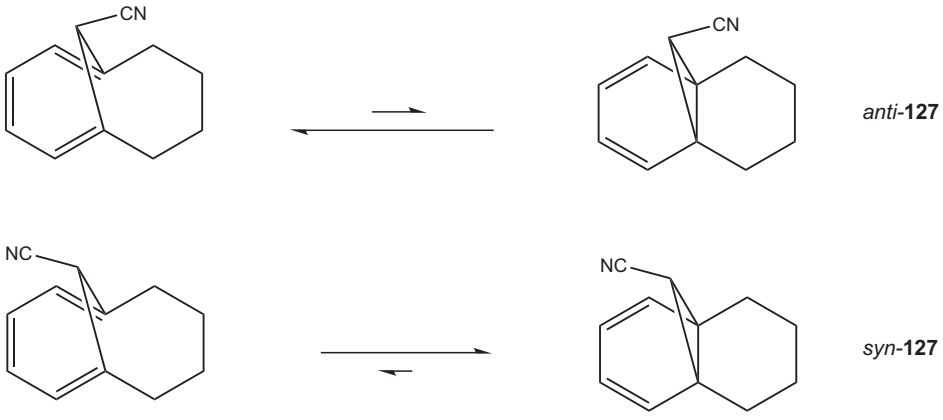
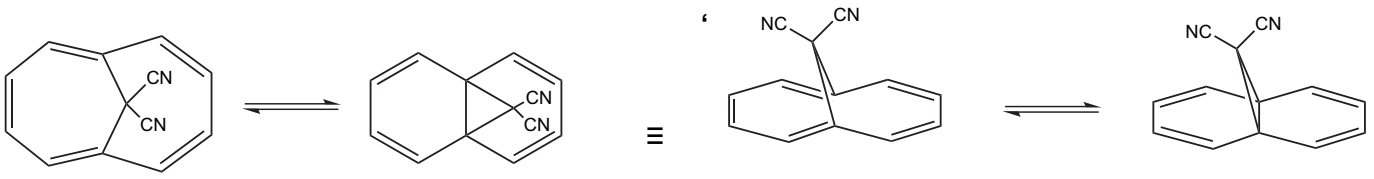


Fig. 31.

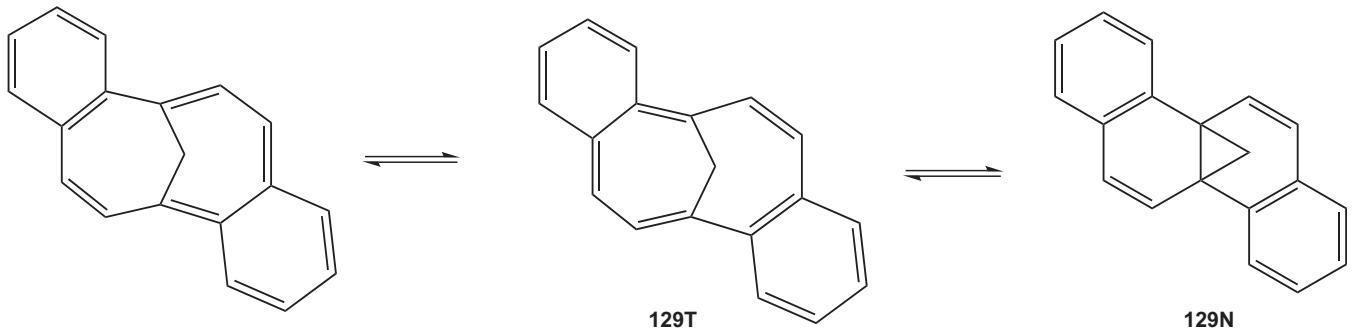


128N/T

Fig. 32.

Benzannelation is known to reduce the aromaticity of the parent ring and therefore tautomerisation of the cycloheptatriene **129T** to the norcaradiene **129N** is favourable, as the pentacyclic form retains more of the aromaticity of the system (Fig. 33).

In the 1990s, Mander et al. described the preparation of a stable norcaradiene in their synthesis of gibberellins, stabilised in a similar fashion to Eschenmoser's and Vogel's previous studies with the geometrical constraints imposed by the bridged system (Fig. 29 and



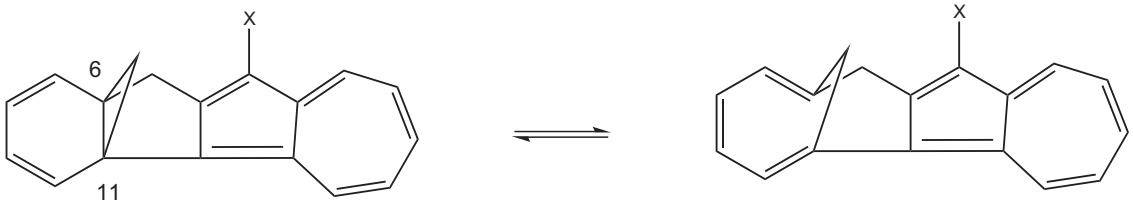
129T **129N**

Fig. 33.

More recently, Nitta has described further derivatives of Vogel's classic annulene, **120**.[131,132] The trifluoroacetyl-substituted triene **130** was found to exist solely as the norcaradiene; in contrast, the methyl ester-substituted triene **131** existed as a mixture of the two tautomers (Fig. 34), again confirmed by NMR spectroscopy. Thus, different substitution at remote positions of the bridged system can also have a dramatic impact on the position of equilibrium.

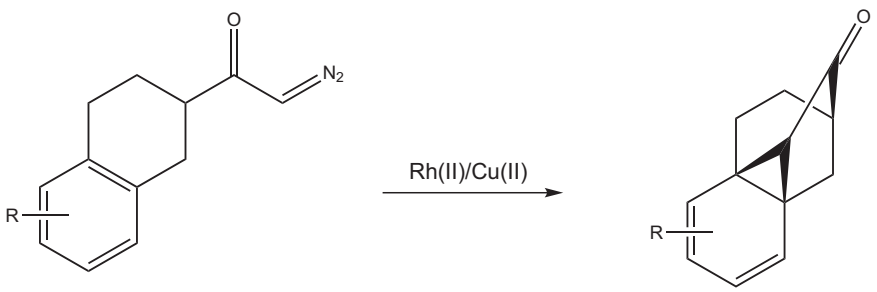
Scheme 20).[133,134] A variety of norcaradienes were prepared by the Rh(II) and Cu(II) transition-metal catalysed decomposition of the diazo ketones shown in Scheme 21.

One of the most recent examples of a norcaradiene–cycloheptatriene equilibrium was described by Oda in 2007 with the preparation of the cyclooctadecane derivative **132**, which, interestingly, was found to have both norcaradiene and cyclo-



X = $COCF_3$, **130N/T**
X = CO_2Me, **131N/T**

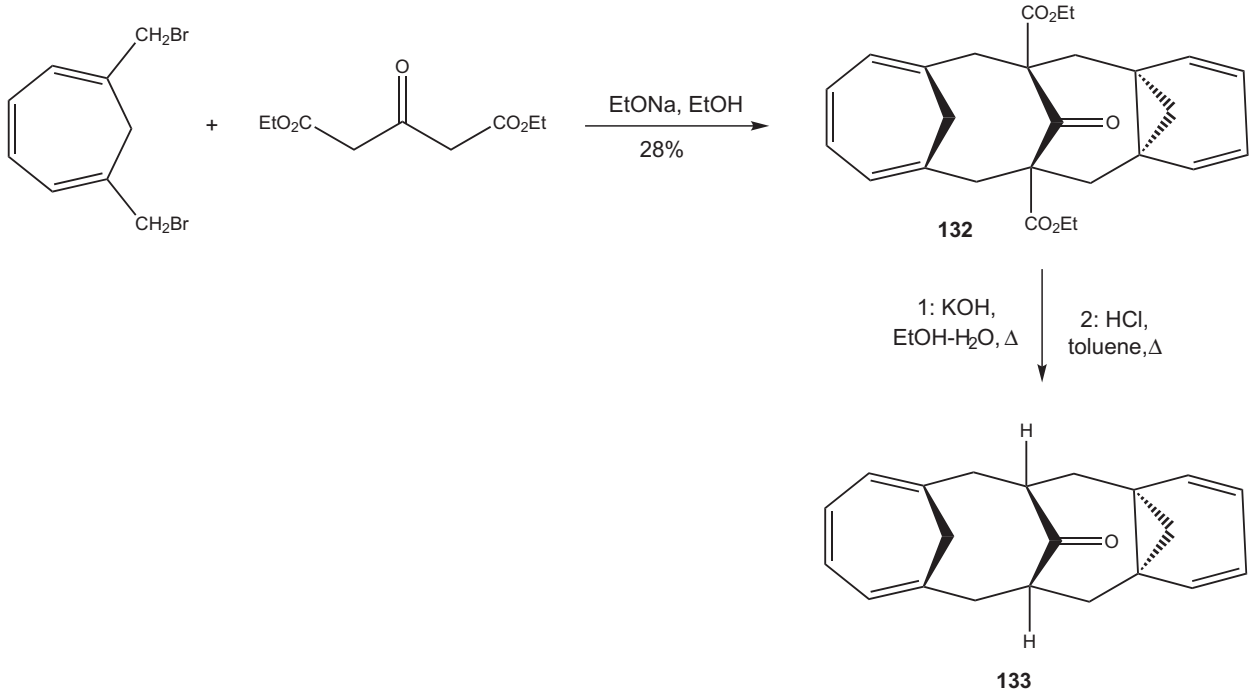
Fig. 34.



R = H, 5-OMe, 6- OMe, 7- OMe, 8-OMe, 6,7-di-OMe, 6,8-di-OMe

Scheme 21.

heptatriene moieties present (Scheme 22).[135] This was confirmed by NMR spectroscopy and also crystallographically. The decarboxylated compound **133** (Scheme 22) was also prepared and found to have a similar structure.



Scheme 22.

A norcaradiene stabilised as a result of incorporation into a polycyclic structure such as **134**, shown in Fig. 35, was described by Wenkert and Liu.[136] Interestingly, Stubbe has described the characterisation of a stable norcaradiene adduct **135** of a peptide, which resulted following the inactivation of the thymine hydroxylase enzyme.[137]

system has been shown to destabilise the cycloheptatriene, thereby shifting the system towards the norcaradiene. In 1966, Prinzbach prepared the norcaradiene **136** from the reaction of dimethyldibenzocalicene **137** with *N*,*N*-diethylbutadienylamine **138**,[138] to give **139**, followed by heating at 160–180 °C at 0.1 mmHg, which gave the norcaradiene **136** (Scheme 23).

More recently, an equilibrating norcaradiene–cycloheptatriene system was observed by Takeuchi in the preparation of the sterically crowded systems **140** and **141** (Fig. 36).[139] The system **141** was found to exist as an equimolar mixture of the tautomers, which

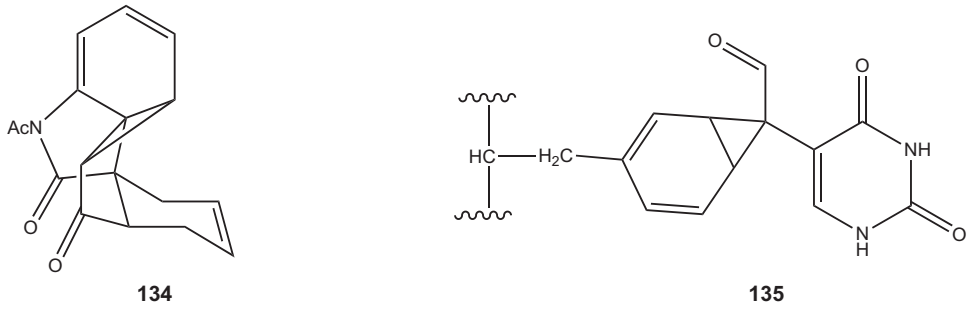


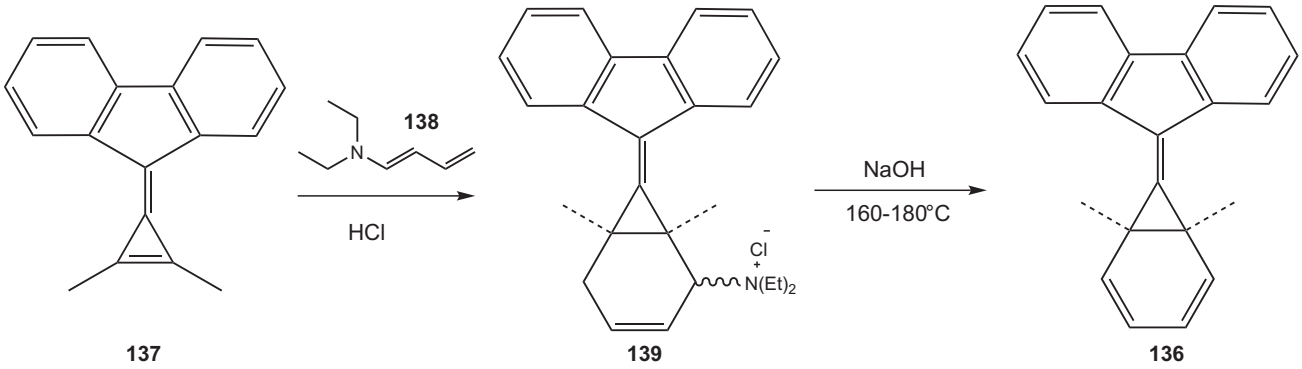
Fig. 35.

In general, the incorporation of an equilibrating norcaradiene–cycloheptatriene system into bridged or complex polycyclic systems, thereby shortening the C(1)–C(6) bond, can have a dramatic impact on the position of the norcaradiene–cycloheptatriene equilibrium. Vogel's early studies on the annulene derivatives have been continued with recent contributions on the study of the equilibrium in these compounds by Nitta and Oda (Fig. 34 and Scheme 22), as well as the use of bridged norcaradienes in the synthesis of natural products by Mander (Scheme 21).

2.3.4. Steric destabilisation of the cycloheptatriene. Incorporation of a series of bulky groups around the norcaradiene–cycloheptatriene

was confirmed by the variable-temperature ^{1}H and ^{13}C NMR spectra.

Hannemann followed Okamoto's work on C(7)-aryl-substituted systems with the 7,7-diaryl systems **142** and **143** (Scheme 24).[140] The *o*-tolyl-substituted system was found to exist almost entirely as the norcaradiene, confirmed by the ^{1}H and ^{13}C NMR spectra; in contrast, signals for **142** were observed at δ_H 4.54 ppm for the H-1 and H-6 protons and δ_C 96.2 ppm for the C(1) and C(6) carbons, indicating cycloheptatriene dominance. Hannemann postulated that this considerable stabilisation of the norcaradiene by the tolyl group is a result of increased steric interactions and that it represents an '*ortho*' effect. Thus, substitution of a small methyl group on



Scheme 23.

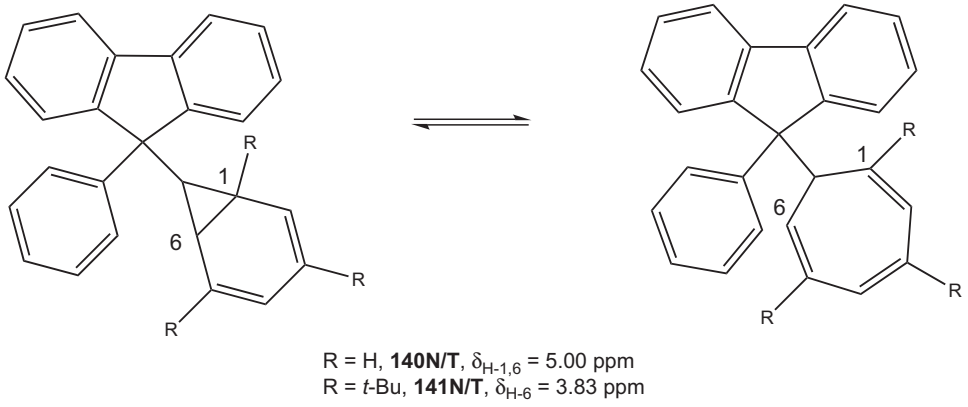
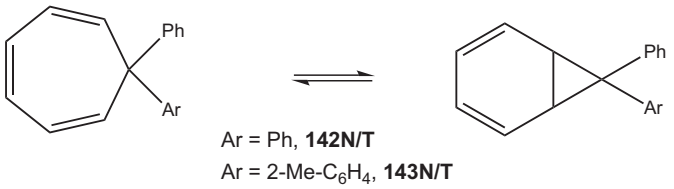


Fig. 36.



Scheme 24.

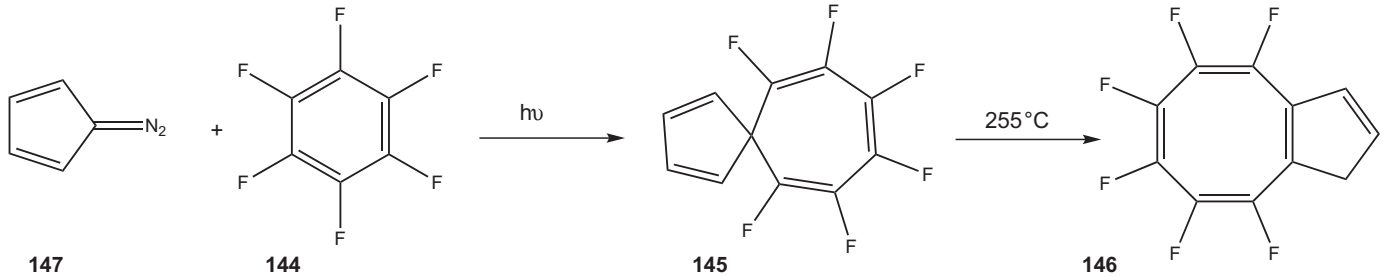
a C(7) substituent can have a dramatic impact on the position of equilibrium.[140]

2.3.4.1. Spironorcaradienes. The size of the angle at the C(7) position of the cycloheptatriene ring was found to have an influence on the equilibrium, as tautomerism of the norcaradiene to the cycloheptatriene is restricted, due to the small internal angle α. This causes a decrease in the anti-bonding character of the C(1)–C(6) bond and results in a shortening of the bond, subsequently resulting in increased stabilisation of the norcaradiene tautomer.

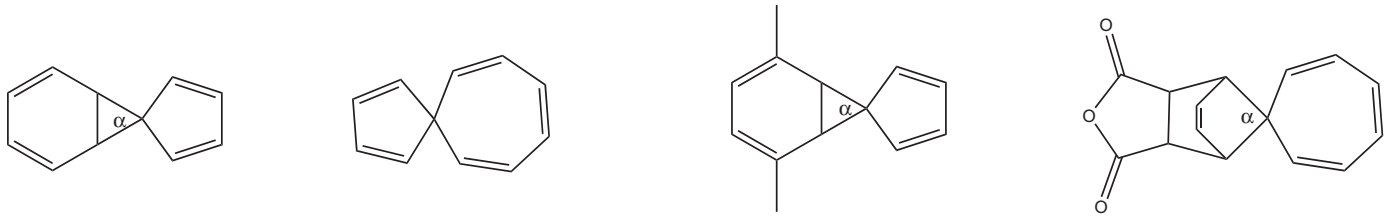
Early work by Jones and by Gale described the attempted preparation of adducts derived from hexafluorobenzene **144** and **147** (Scheme 25) in which this external angle is widened.[141,142] Unexpectedly, the cycloheptatriene **145** was recovered as the major tautomer.[141] Heating of the adduct **145** at 255 °C resulted in rearrangement to **146** (Scheme 25).

In 1969, two letters, from Schönleber and from Jones, described the synthesis of the spironorcaradienes **148** and **149** (Fig. 37),[143,144] in contrast to Jones' and Gale's previous attempts to prepare the perfluoro derivative (Scheme 25). Interestingly, despite the norcaradiene **148N** predominating, Schönleber described the thermal reaction of **148T** with maleic anhydride as giving the cycloheptatriene-derived adduct **150** (Fig. 37). In 1974, Moriarty and Churchill[145] also describe the preparation of the dimethyl analogue of **148**, the norcaradiene **151** (Fig. 37).

Jones described the synthesis of the spironorcaradiene **149**, prepared by photolysis of the diazo compound **152** in benzene



Scheme 25.



148N 148T 151 150

Fig. 37.

(Scheme 26). Heating of the norcaradiene **149** resulted in conversion into the isomer **153**.[144,146]

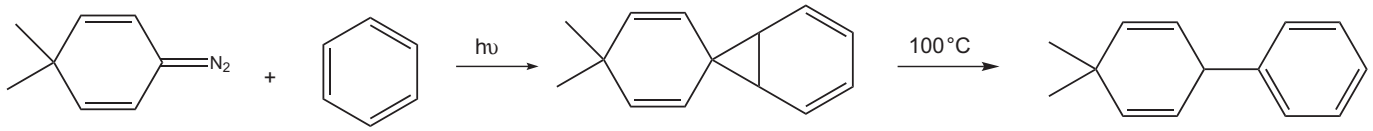
Jones and Jones have also described the preparation of various other spiro compounds with different observations in the position of equilibrium.[147–149] They both reported[147,149] the nonatriene derivatives, **154**,[149] **155** and **156**, which were found to exist predominantly as the cycloheptatriene, mainly due to the large external angle at the C(7) position of the cycloheptatriene ring.[147] Jones postulated that compression of the C(1)–C(2)–C(3) bond angle prevents isomerisation to the norcaradiene.[147] In cycloaddition with the dienophiles maleic anhydride **159** and dicyanoacetylene **160**, reaction via the cycloheptatriene tautomer resulted in the adducts, **157** and **158**, respectively (Scheme 27).[147]

In 1972, Tuchscherer described the preparation of the indene-derived system **161**, which exists as an equilibrating mixture of the norcaradiene **161N** and cycloheptatriene **161T** forms (Fig. 38).[150] Thus, conjugation has an impact here on the position of equilibrium substitution around the spiro substituent can also have a dramatic impact on the position of equilibrium.

Incorporation of a lactone group in a spiro compound can induce the norcaradiene as the predominant tautomer. Rapp and Daub described the norcaradiene **168N** (Fig. 40), which was stable as a result of the favourable conformation of the carbonyl group, which allows for increased overlap of the π-acceptor with the Walsh orbitals of the cyclopropane ring.[62,157]

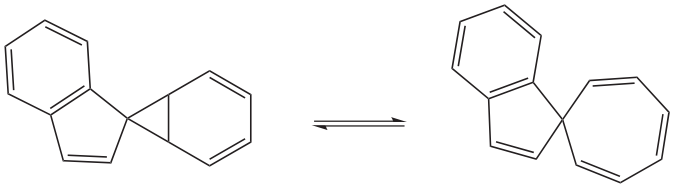
In 1990, Shechter described the thermolyis of 5-diazouracil **169** in benzene to yield a spironorcaradiene intermediate **170**, which rearranges to the product, 5-cycloheptatrienylidene-2,4-imidazolidinedione **171** (Scheme 28).[158]

More recently, Murata described (Scheme 29) the observation of a spironorcaradiene **172** (which existed in a keto-enol tautomeric equilibrium) as an intermediate in the photochemical decomposition of the bis-diazo compound **173**, along with the side product **174**.[159,160]



152 149 153

Scheme 26.



161N 161T

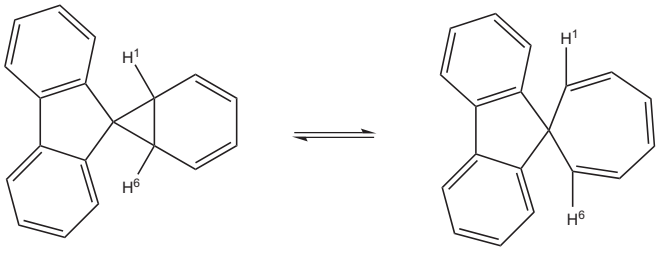
Fig. 38.

resulting in an equilibrating system, in contrast to previous work by Schönleber and by Jones (Fig. 37) and also by Jones (Scheme 26).

Dürr also described the preparation of many spironorcaradienes by photochemical decomposition of diazacyclopentadienes.[151–156] Preparation of the diazofluorene derivative **162** resulted in a stable compound, which was seen to exist as a rapidly equilibrating mixture of the two tautomers.[152] This was confirmed by a variable-temperature NMR spectroscopic study, where a doublet with δ_H 4.74 ppm began to broaden at −60 °C and, following coalescence, new signals appeared, attributable to the $H_{1,6}$ protons of the individual tautomers at δ_H 6.98 ppm (cycloheptatriene-**162T**) and δ_H 4.77 ppm (norcaradiene-**162N**) (Fig. 39).

A study by Dürr (Table 8, entries 1–5) illustrates the electronic dependence of the equilibrium, which lies towards the norcaradiene side in the most electron-poor system **163**, while favouring the cycloheptatriene in less-substituted systems **164**-**167**.[154] Thus,

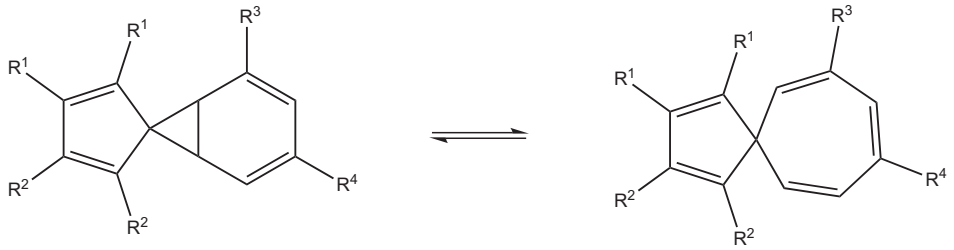
In conclusion, the magnitude of the angle at C(7) can have a dramatic impact on the position of the norcaradiene–cycloheptatriene equilibrium, favouring the norcaradiene with compression of the



162N 162T

Fig. 39.

Table 8
Impact by substitution of spiro group on position of norcaradiene–cycloheptatriene equilibrium



Entry	R_1	R_2	R_3	R_4	Product	Yield (%)	NCD (%)
1	Cl	Cl	CF_3	CF_3	**163N/T**	45	66
2	Cl	Cl	H	H	**164N/T**	30	19
3	Cl	Cl	CF_3	H	**165N/T**	40	28
4	Ph	*o*-Phenylene	H	H	**166N/T**	20–25	19
5	Ph	*o*-Phenylene	CF_3	H	**167N/T**	35	25

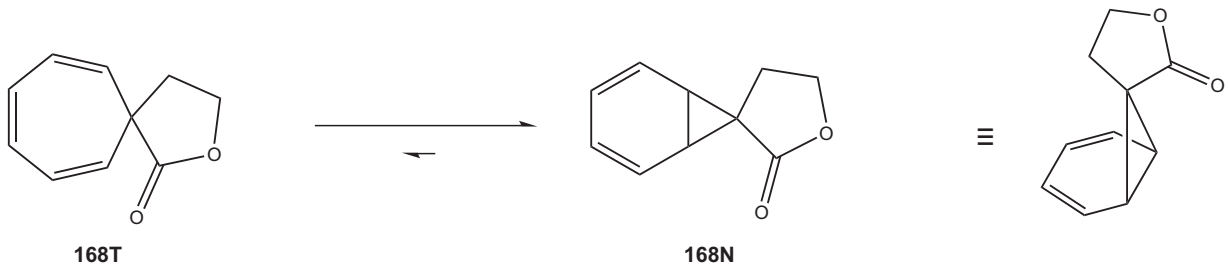
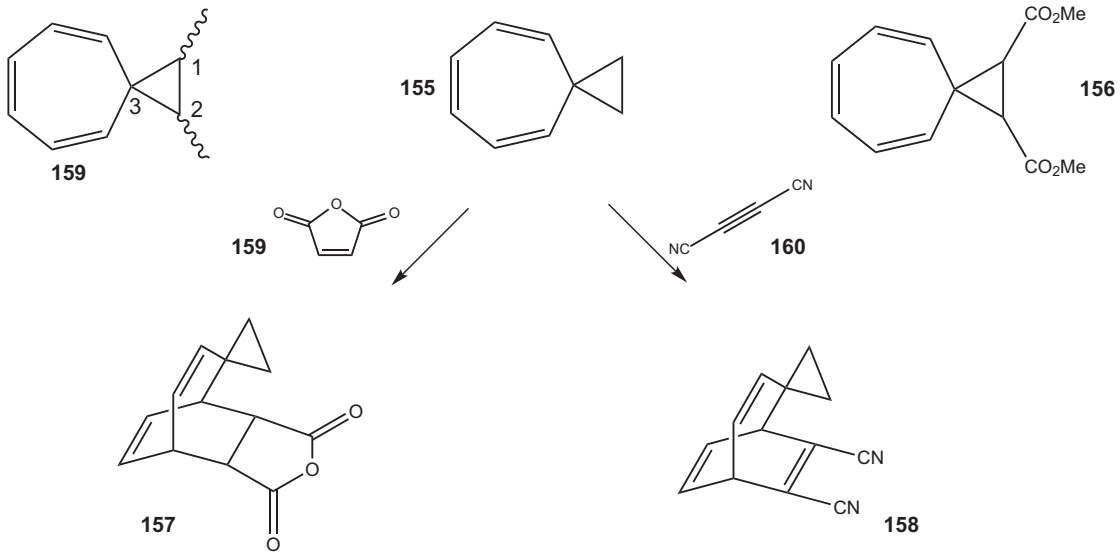


Fig. 40.



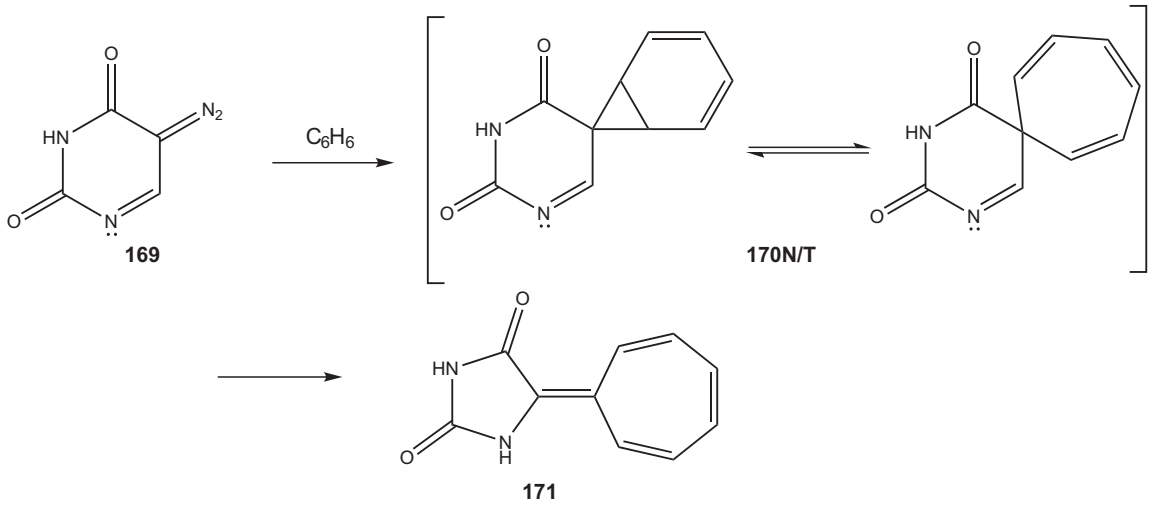
Scheme 27.

external angle, while the cycloheptatriene is favoured when the angle size is increased.

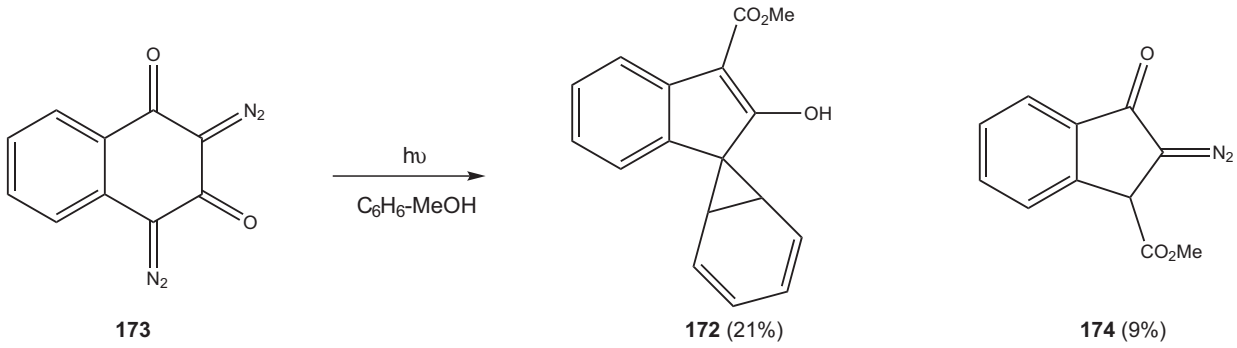
2.4. The norcaradiene–cycloheptatriene equilibrium in the products of the intramolecular aromatic addition; the impact of a fused cyclopentyl substituent

As illustrated in the earlier sections, the aromatic addition reaction is a useful synthetic methodology leading to NCD–CHT systems, but all examples of the addition of carbenes to arenes have been intermolecular. The intramolecular aromatic addition has also provided some substantial advances in the study of the norcaradiene–cycloheptatriene equilibrium, albeit not as extensive as the intermolecular aromatic addition.

The first example of a stable norcaradiene resulting from the intramolecular addition of a carbene to an aromatic ring was described by Kohmoto, in which he prepared a series of γ-lactone ring-fused norcaradienes.[161–163] Structural confirmation of the norcaradiene **175** (Fig. 41) by ^1H and ^{13}C NMR spectroscopy was described, with no observation of the valence tautomer.



Scheme 28.



Scheme 29.

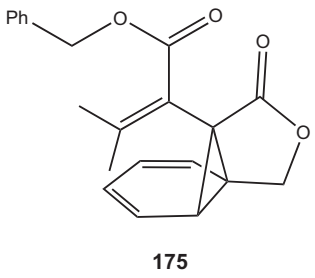
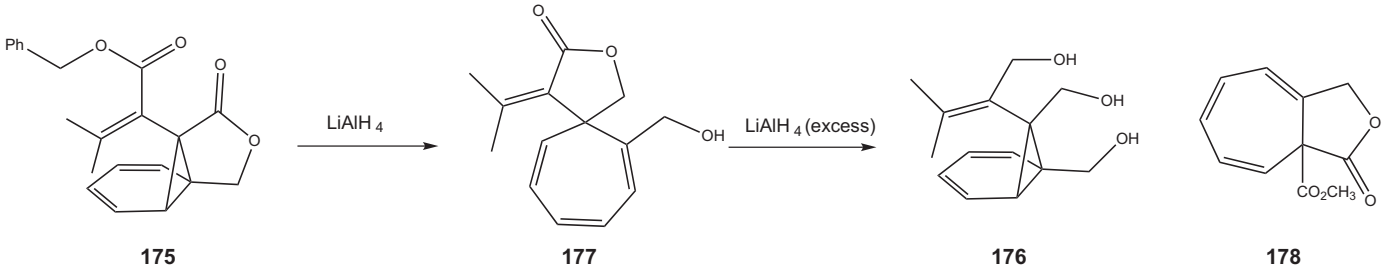


Fig. 41.

Stabilisation of the norcaradiene here was due to a combination of substitution at the C(7) position of the norcaradiene by the electron-withdrawing group and the γ-lactone linkage.

On reduction of the lactone **175** with an excess of lithium aluminium hydride, the triol **176** was formed, which also existed as the norcaradiene (Scheme 30).[162] Interestingly, reduction of **175** to the fully reduced triol norcaradiene product **176** proceeds through a partially reduced cycloheptatriene intermediate **177**. This result clearly highlights the fine balance that must be considered in order to predict the stability of norcaradienes. Kohmoto's work is in contrast to earlier work by Julia, who prepared an analogous compound **178** with an ester at the C(7) position, but did not observe any norcaradiene.[164] The lactone **175** compares with the spirolactone **168** described by Daub, which exists as the norcaradiene (Fig. 40).



Scheme 30.

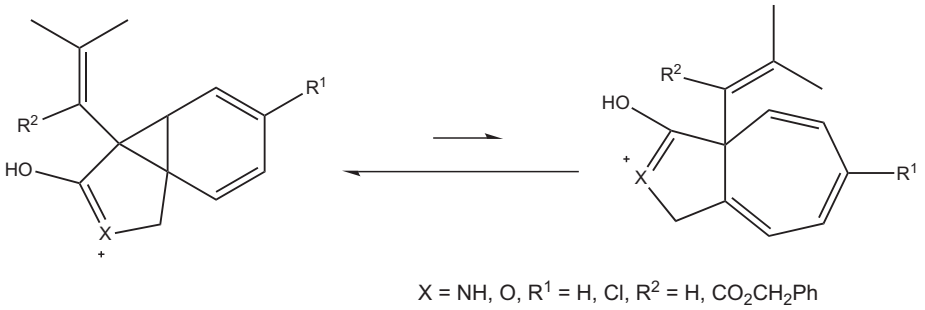
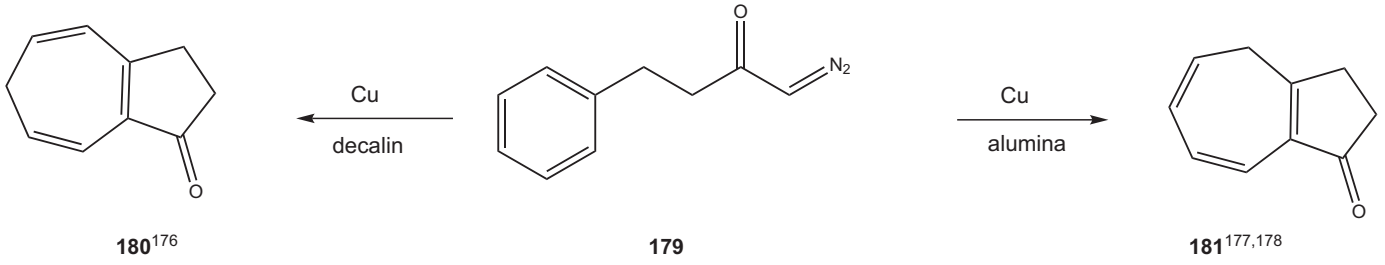


Fig. 42.

Kohmoto has recently described an alteration in the position of equilibrium of γ-lactone- and lactam-fused norcaradienes by protonation with trifluoroacetic acid (Fig. 42).[165] Protonation increased the electron-withdrawing nature of the C(7) substituents and stabilised the norcaradiene. This is reminiscent of earlier studies by Childs and Daub exploring the stabilisation of norcaradienes by placement of stabilised carbocations in the molecular structure (Section 2.3.1.2, Schemes 14 and 15, Figs. 12 and 13).

The intramolecular aromatic addition (or intramolecular Buchner reaction) has been described in the last 20–30 years, particularly as a result of its applicability to natural product synthesis described by McKervey and by Mander.[133,166–169] Several substrates have been subjected to intramolecular aromatic addition, such as α-diazo ketones,[167,170–172] diazo amides[173,174] and diazo esters,[175] which result in the tricyclic norcaradiene tautomer from the initial cyclopropanation of the carbene to the aromatic ring. The norcaradiene then rapidly equilibrates to the more thermodynamically stable bicyclic cycloheptatriene. Separate studies by Julia and by Scott on the decomposition of the diazo ketone **179** with copper had seen the isomeric trienones **180** and **181**, respectively, isolated (Scheme 31).[176–178]

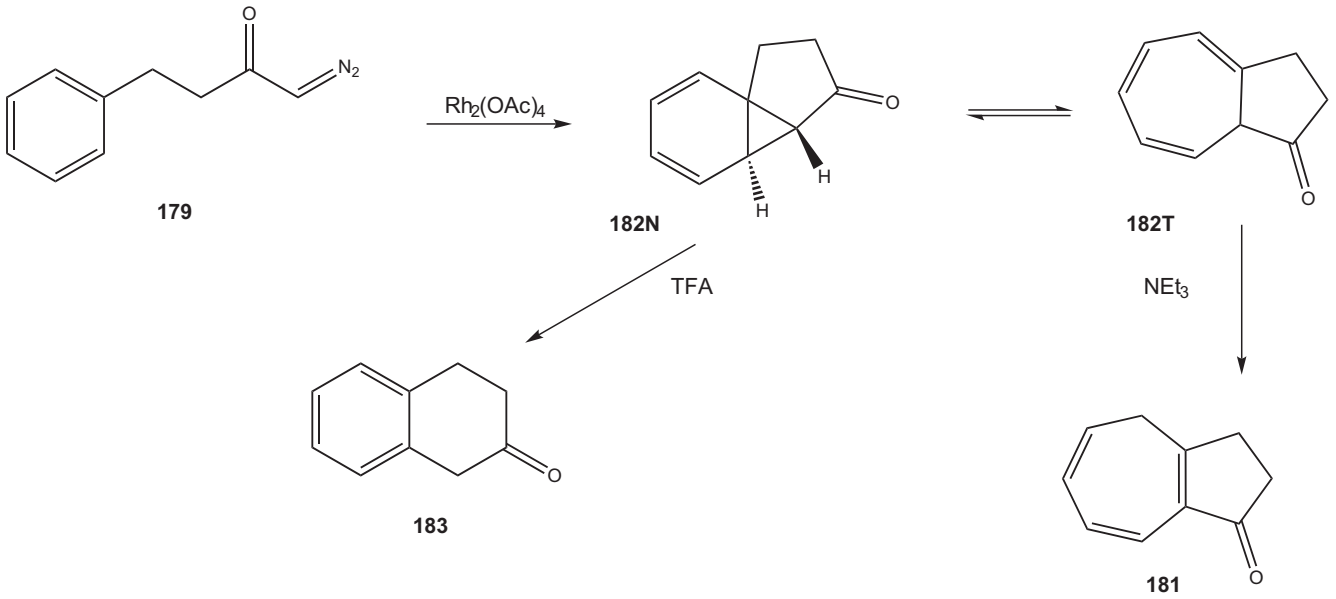


180[176] **179** **181**[177,178]

Scheme 31.

McKervey first postulated the existence of the norcaradiene–cycloheptatriene equilibrium in azulenones, the products of the intramolecular aromatic addition of aryl α-diazo ketones.[170,179] The cycloheptatriene **182T** was confirmed as the kinetic product of the reaction when carried out employing Rh(II) catalysis. McKervey confirmed the existence of the equilibrium in the azulenone **182** by the reactivity of the azulenone.[170] The system can undergo two distinct reaction pathways giving **181** or **183**, which indicates the two tautomeric forms are present (Scheme 32).

McKervey also found that the introduction of a methyl group onto the cyclopropyl ring of the azulenone **182**, i.e., azulenone **184**, prepared from **179**, significantly stabilised the norcaradiene with the signal for the H-8 proton observed at δ_H 4.28 ppm;[170]



179 **182N** **182T** **183** **181**

Scheme 32.

in contrast, the signal for the analogous azulenone **182** was seen at δ_H 5.06 ppm, indicating cycloheptatriene predominance (Fig. 43).

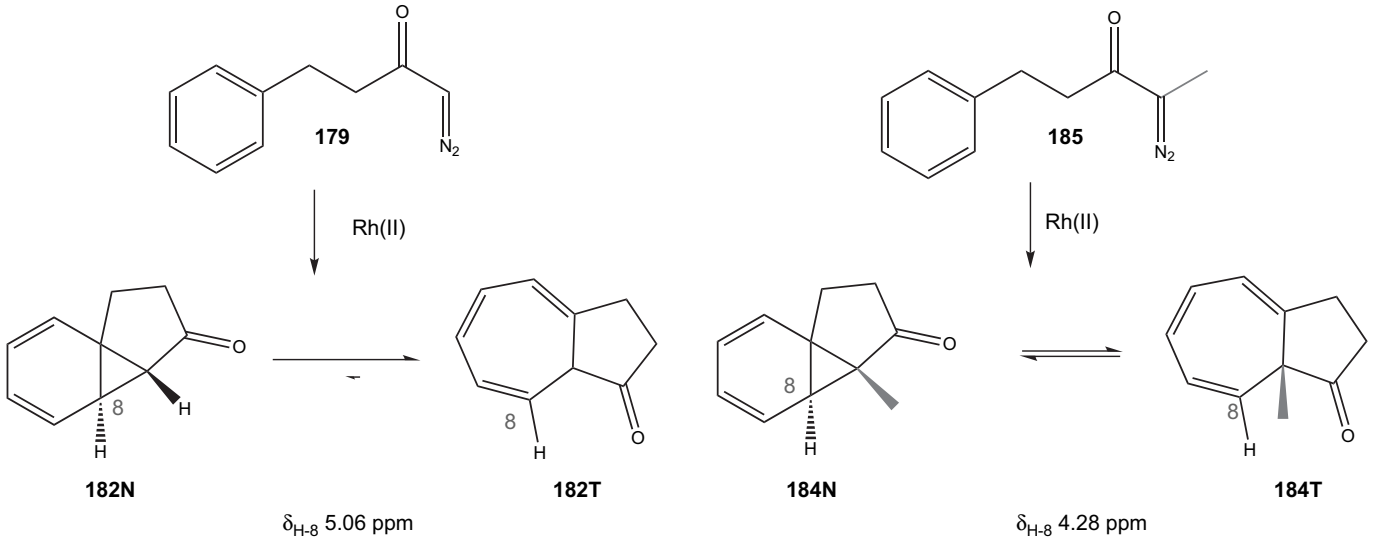


Fig 43.

In 1990, Saba described variable-temperature ^{1}H and ^{13}C NMR spectroscopic studies on an analogue of **182**, the azulenone, **186** (Fig. 44).[180] This displayed a signal for the H-8 proton at δ_H 3.86 ppm and for the C(8) carbon at δ_C 82.1 ppm, which represents a considerable stabilisation of the norcaradiene tautomer, by the introduction of the methyl group on the aromatic ring, relative to the azulenone **184**.[180]

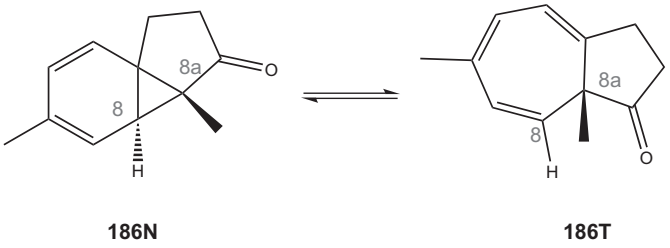


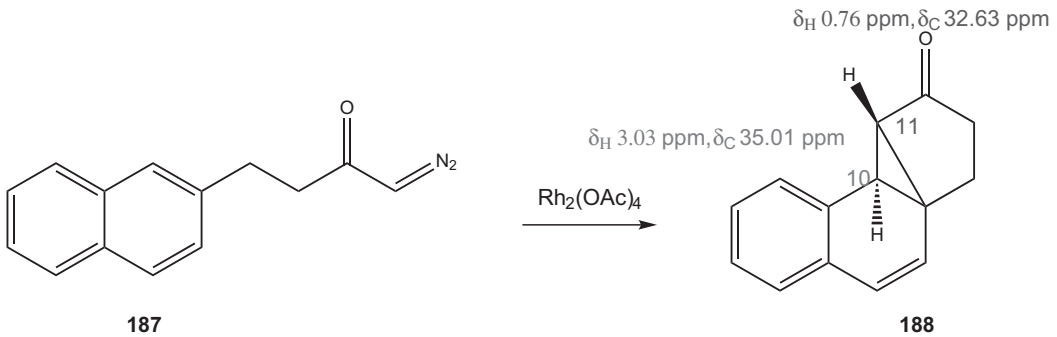
Fig. 44.

In 1995, Manitto described the first example of a stable norcaradiene derived from the Rh(II)-catalysed intramolecular aromatic addition of an α-diazo ketone **187** via the metal carbenoid with the preparation of the naphthyl norcaradiene, **188** (Scheme 33); ^{1}H and ^{13}C NMR spectroscopic data confirmed Manitto's assignment of the norcaradiene.[181] Incorporation of a naphthalene into the norcaradiene as a method of stabilisation of the structure is analogous to previous studies by Buchner, and by Vogel (Fig. 26) and also by Müller (Scheme 18).

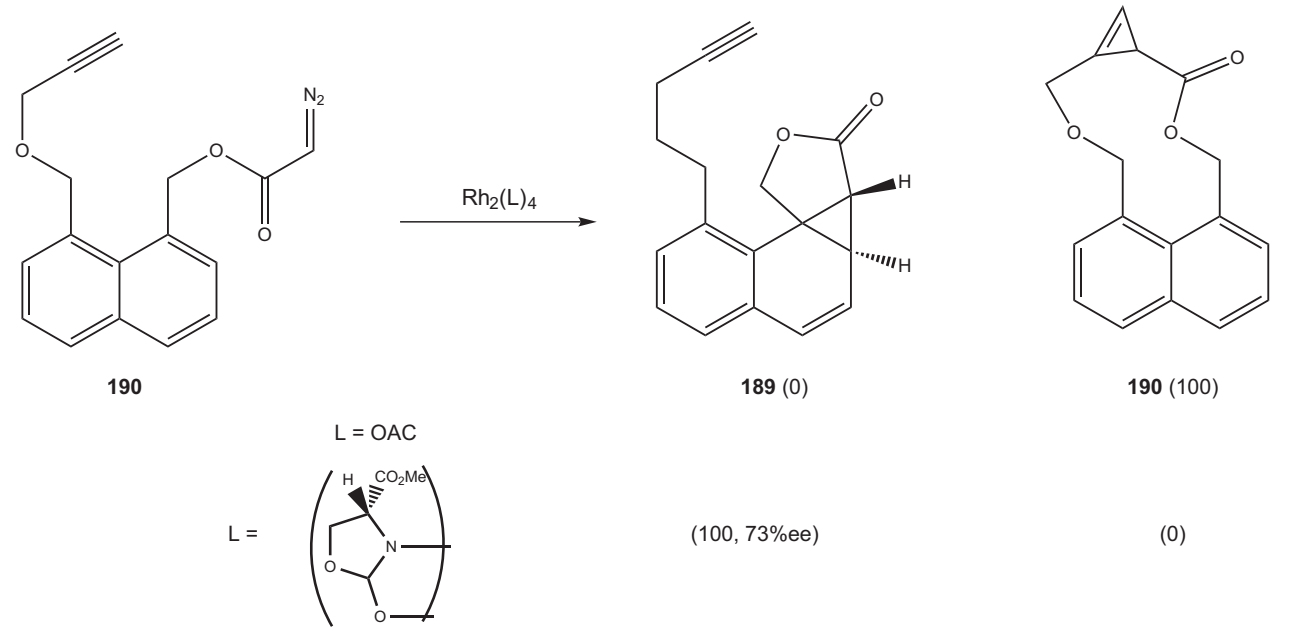
In 1999, Doyle described the preparation of the norcaradiene **189** (Scheme 34).[182] This was prepared by the Rh(II)-catalysed decomposition of the diazo ketone **190**, which gave a mixture of the aromatic addition product and the cyclopropenation product **191**, the ratios of which could be dramatically altered by the catalyst used (Scheme 34).

2.5. Study of the norcaradiene–cycloheptatriene equilibrium by chemical interception

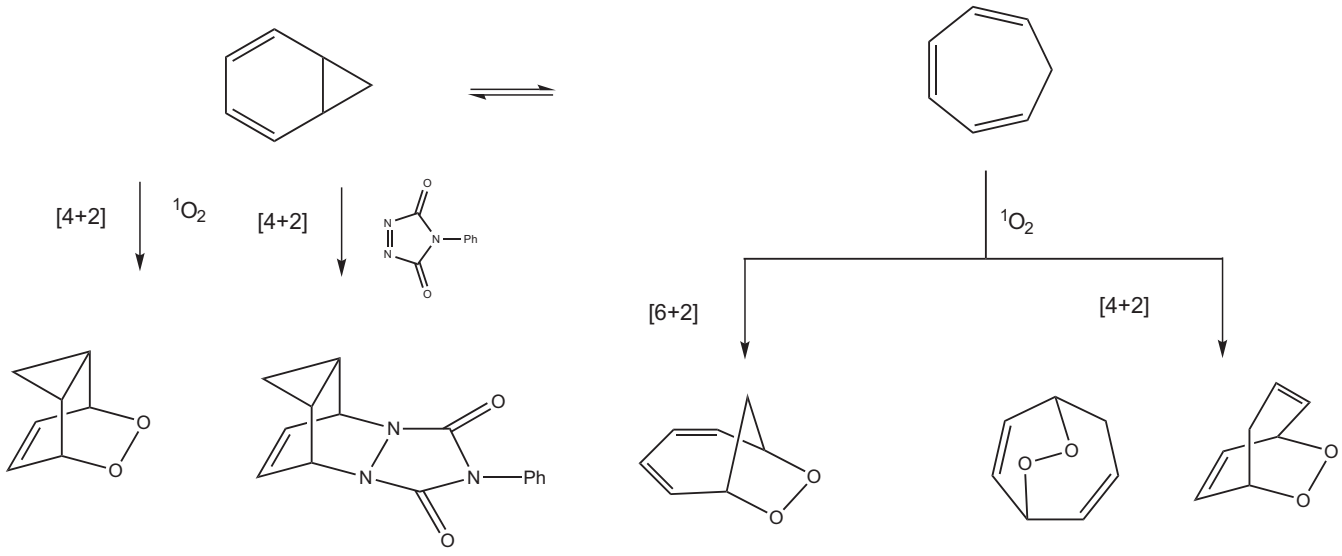
In general, analysis of the norcaradiene–cycloheptatriene equilibrium described in this review has been with the aid of NMR spectroscopy. However, a second method involving chemical interception and reactivity studies can be useful in determining the position of equilibrium of the system. In general, the norcaradiene and cycloheptatriene equilibrating system can undergo cycloadditions with dienophiles, such as singlet oxygen,[53,183–190] triazoline dienophiles,[53,188,189,191] and fluorinated dienophiles.[192,193] Reactivity studies, particularly under hydrogenation conditions, have been described by Adam and Balci.[186]



Scheme 33.



Scheme 34.



Scheme 35.

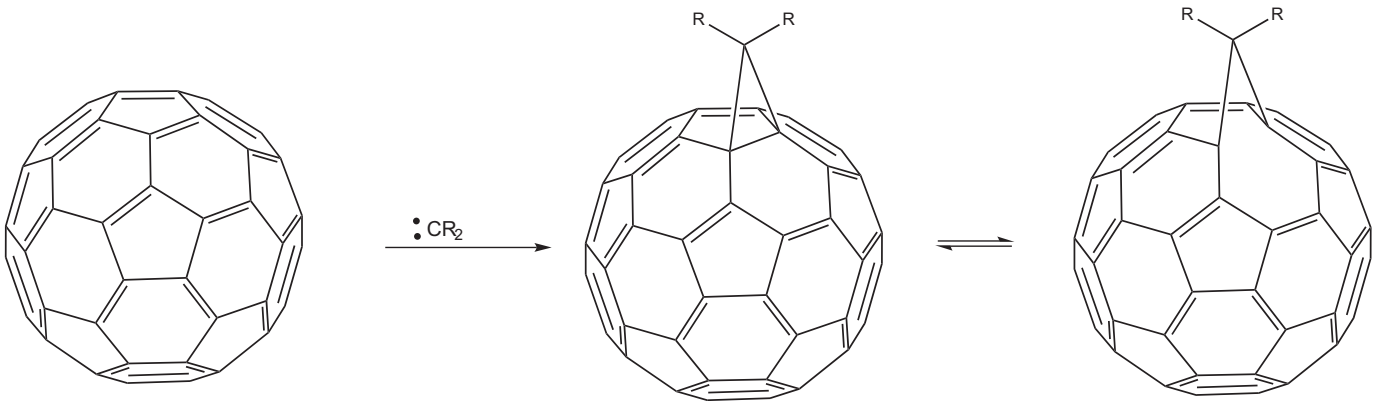
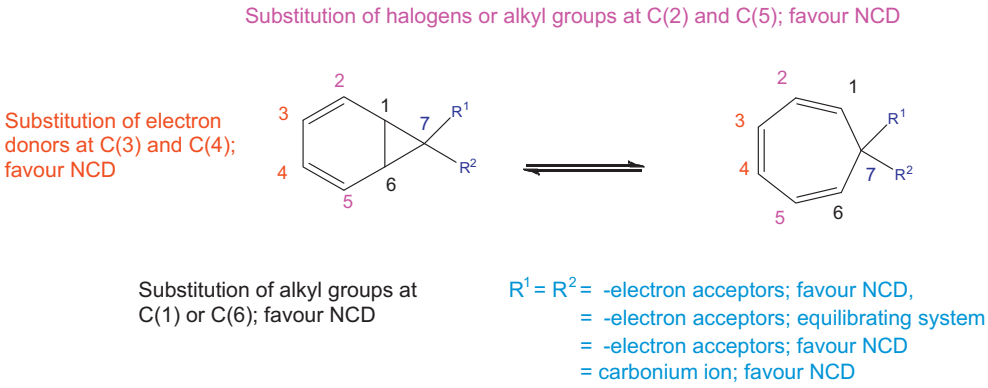


Fig. 45.



- Additional conjugation on either side of equilibrium can alter the position of equilibrium
- Incorporation of the C(1)-C(6) bond into a bridged system can alter the position of equilibrium

Fig. 46.

2.5.1. Trapping of the norcaradiene and cycloheptatriene in the Diels–Alder cycloaddition with singlet oxygen and triazoline diones. Early studies on the cycloaddition of cycloheptatriene **9T** with singlet oxygen were described by Schenk, by Takeshita and by Kitahara;[194–196] cycloaddition with the cycloheptatriene tautomer was only observed. However, cycloaddition with the minor norcaradiene tautomer was described extensively in the 1970s and 1980s by Adam and Balci.[53,183–190] Cycloaddition with singlet oxygen is a useful method for determining the equilibrium position, reacting with norcaradiene and cycloheptatriene tautomers indiscriminately.[53] In contrast cycloaddition with dienophiles, such as 4-phenyl-triazoline-2,5-dione (PTAD), maleic anhydride, maleimide or *N*-phenylmaleimide is generally via the norcaradiene tautomer, even in systems, which lie towards the cycloheptatriene (Scheme 35); however, there are some isolated reports of cycloadditions between PTAD and the cycloheptatriene tautomer.[188,197–201] Diels–Alder cycloadditions proceed favourably, generally in a [4+2] or [6+2] manner. However, Adam and Balci also described the cycloaddition of singlet oxygen to a cycloheptatriene in a [2+2] manner.[187]

Cycloadditions to the norcaradiene tautomers of azulenones, the products of the intramolecular aromatic addition reaction, have been well documented recently.[23,189,202–206] The influence of high pressures and temperatures on the outcome of cycloadditions with an equilibrating norcaradiene–cycloheptatriene system has been described by Jenner.[207,208]

2.6. The norcaradiene–cycloheptatriene equilibrium of fulleroids

Despite its apparent lack of functionality, the reactivity of buckminsterfullerene (C_{60}) has been intensively explored, with cycloadditions proving a key methodology for its funtionalisation.[209,210] Addition of dibromocarbene results in the formation of a cyclopropane (Fig. 45).[211] However, addition of a carbene unit employing the 1,3-dipolar cycloaddition of CR_2N_2, followed by loss of nitrogen results in two products, a cyclopropane along with a fulleroid.[212] A fulleroid results from the addition of the carbene across the 5,6-junction of C_{60} and is followed by a norcaradiene rearrangement, which results in an enlarged fullerene (or fulleroid).[209,213–216] Fullerenes and fulleroids are known to interconvert in a similar tautomerism to that for the norcaradiene–cycloheptatriene equilibrium.[213]

3. Conclusions

In summary (Fig. 46), in simple systems, the cycloheptatriene is generally favoured over the norcaradiene, due to relief of ring strain. However, through careful choice of substituents, the position of equilibrium can be significantly altered through the introduction of substituents with a clear impact of steric, electronic or conformational effects. Some of the general trends, which are seen include stabilisation of the norcaradiene through π-electron acceptors at C(7), the introduction of bulky alkyl substituents at C(1) and C(6) and extended conjugation in the norcaradiene tautomer. Diels–Alder-type cycloadditions can occur with either tautomer, providing an interesting mechanistic insight into this intriguing dynamic equilibrium.

Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2010.10.030.

References and notes

1. Curtius, T. *Ber.* **1883**, *16*, 2230–2231.
2. Buchner, E.; Curtius, T. *Ber.* **1885**, *18*, 2377–2379.
3. Buchner, E. *Ber.* **1896**, *29*, 106–109.
4. Maier, G. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 402–413.
5. Balci, M. *Turk. J. Chem.* **1992**, *16*, 42–90.
6. Liebman, J. F.; Greenberg, A. *Chem. Rev.* **1989**, *89*, 1225–1246.
7. Buchner, E.; Curtius, T. *Ber.* **1885**, *18*, 2371–2377.
8. Schenck, G. O.; Ziegler, H. *Naturwissenschaften* **1951**, *38*, 356.
9. Schenck, G. O.; Ziegler, H. *Justus Liebigs Ann. Chem.* **1953**, *584*, 221–238.
10. Baeyer, A.; Ipatiew, W. *Ber. Dtsch. Chem. Ges.* **1896**, *29*, 2796–2802.
11. Meerwein, H.; Disselnkotter, H.; Rappen, F.; Rintelen, H.; van de Vloed, H. *Justus Liebigs Ann. Chem.* **1957**, *604*, 151–167.
12. Doering, W. v; Knox, L. H. *J. Am. Chem. Soc.* **1950**, *72*, 2305–2306.
13. Doering, W.; Knox, L. H. *J. Am. Chem. Soc.* **1953**, *75*, 297–303.
14. Doering, W. v; Knox, L. H. *J. Am. Chem. Soc.* **1954**, *76*, 3203–3206.
15. Klärner, F.-G.; Jones, M., Jr.; Magid, R. M. *Acc. Chem. Res.* **2009**, *42*, 169–181.
16. Doering, W.; Laber, G.; Vonderwahl, R.; Chamberlain, N. F.; Williams, R. B. *J. Am. Chem. Soc.* **1956**, *78*, 5448.
17. Willstätter, R. *Justus Liebigs Ann. Chem.* **1901**, *317*, 204–265.
18. Kohler, E. P.; Tishler, M.; Potter, H.; Thompson, H. T. *J. Am. Chem. Soc.* **1939**, *61*, 1057–1061.
19. Müller, E.; Fricke, H.; Kessler, H. *Tetrahedron Lett.* **1963**, 1501–1503.
20. Winberg, H. E. *J. Org. Chem.* **1959**, *24*, 264–265.
21. Pietra, F. *Chem. Rev.* **1973**, *73*, 293–364.
22. Chen, Z.; Jiao, H.; Wu, J. I.; Herges, R.; Zhang, S. B.; Schleyer, P. v. R. *J. Phys. Chem. A* **2008**, *112*, 10586–10594.

23. Oda, M.; Kuroda, S. *Recent Res. Dev. Pure Appl. Chem.* **1998**, *2*, 145–155.
24. Le Noble, W. *Highlights of Organic Chemistry. An Advanced Textbook*. J. Studies in Organic Chemistry; Marcel Dekker: New York, NY, 1974; Vol. 3.
25. Okamura, W. H.; De Lera, A. R. *Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 5; 699–750.
26. Hayes, D. M.; Nelson, S. D.; Garland, W. A.; Kollman, P. A. *J. Am. Chem. Soc.* **1980**, *102*, 1255–1262.
27. Warner, P. M.; Lu, S. L. *J. Am. Chem. Soc.* **1980**, *102*, 331–337.
28. Schulman, J. M.; Disch, R. L.; Sabio, M. L. *J. Am. Chem. Soc.* **1982**, *104*, 3785–3788.
29. Hoffmann, R. *Tetrahedron Lett.* **1970**, 2907–2909.
30. Corey, E. J.; Burke, H. J.; Remers, W. A. *J. Am. Chem. Soc.* **1955**, *77*, 4941–4942.
31. Anet, F. A. L. *J. Am. Chem. Soc.* **1964**, *86*, 458–460.
32. Jensen, F. R.; Smith, L. A. *J. Am. Chem. Soc.* **1964**, *86*, 956–957.
33. Lambert, J. B.; Durham, L. J.; Lepoutere, P.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 3896–3899.
34. Wehner, R.; Günther, H. *J. Am. Chem. Soc.* **1975**, *97*, 923–924.
35. Rubin, M. B. *J. Am. Chem. Soc.* **1981**, *103*, 7791–7792.
36. Rubin, M. B. *Tetrahedron Lett.* **1984**, *25*, 4697–4700.
37. Ciganek, E. *J. Am. Chem. Soc.* **1965**, *87*, 1149–1150.
38. Ciganek, E. *J. Am. Chem. Soc.* **1965**, *87*, 652–653.
39. Ciganek, E. *J. Am. Chem. Soc.* **1967**, *89*, 1454–1458.
40. Reich, H. J.; Ciganek, E.; Roberts, J. D. *J. Am. Chem. Soc.* **1970**, *92*, 5166–5169.
41. Ciganek, E. *J. Am. Chem. Soc.* **1971**, *93*, 2207–2215.
42. Hoffmann, R.; Stohrer, W. D. *J. Am. Chem. Soc.* **1971**, *93*, 6941–6948.
43. Günther, H. *Tetrahedron Lett.* **1970**, 5173–5176.
44. Allen, F. H. *Acta Crystallogr., Sect. B* **1980**, *36*, 81–96.
45. Allen, F. H. *Acta Crystallogr., Sect. B* **1981**, *B37*, 890–900.
46. Allen, F. H. *Acta Crystallogr., Sect. B* **1981**, *B37*, 900–906.
47. Clark, T.; Spitznagel, G. W.; Klose, R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1984**, *106*, 4412–4419.
48. Staley, S. W.; Fox, M. A.; Cairncross, A. *J. Am. Chem. Soc.* **1977**, *99*, 4524–4526.
49. Durmaz, S.; Kollmar, H. *J. Am. Chem. Soc.* **1980**, *102*, 6942–6945.
50. Gale, D. M.; Middleton, W. J.; Krespan, C. G. *J. Am. Chem. Soc.* **1965**, *87*, 657–658.
51. Gale, D. M.; Middleton, W. J.; Krespan, C. G. *J. Am. Chem. Soc.* **1966**, *88*, 3617–3623.
52. Bushweller, C. H.; Sharpe, M.; Weininger, S. J. *Tetrahedron Lett.* **1970**, 453–456.
53. Adam, W.; Balci, M.; Pietrzak, B. *J. Am. Chem. Soc.* **1979**, *101*, 6285–6291.
54. Balci, M.; Fischer, H.; Günther, H. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 301–302.
55. Günther, H.; Görlitz, M.; Hinrichs, H. H. *Tetrahedron* **1968**, *24*, 5665–5676.
56. Heyd, W. E.; Cupas, C. A. *J. Am. Chem. Soc.* **1969**, *91*, 1559–1560.
57. Pikulik, I.; Childs, R. F. *Can. J. Chem.* **1975**, *53*, 1818–1828.
58. Daub, J.; Betz, W. *Tetrahedron Lett.* **1972**, 3451–3454.
59. Daub, J.; Luedemann, H. D.; Michna, M.; Strobl, R. M. *Chem. Ber.* **1985**, *118*, 620–633.
60. Betz, W.; Daub, J. *Chem. Ber.* **1974**, *107*, 2095–2114.
61. Stohrer, W. D.; Daub, J. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 86.
62. Bauer, W.; Daub, J.; Maas, G.; Michna, M.; Rapp, K. M.; Stezowski, J. J. *Chem. Ber.* **1982**, *115*, 99–118.
63. Gridnev, I. D.; Tok, O. L.; Gridneva, N. A.; Bubnov, Y. N.; Schreiner, P. R. *J. Am. Chem. Soc.* **1998**, *120*, 1034–1043.
64. Mukai, T.; Kubota, H.; Toda, T. *Tetrahedron Lett.* **1967**, 3581–3585.
65. Fritchie, C. J., Jr. *Acta Crystallogr.* **1966**, *20*, 27–36.
66. Ganter, C.; Roberts, J. D. *J. Am. Chem. Soc.* **1966**, *88*, 741–744.
67. The relevant ^{1}H NMR spectroscopic data for the cycloheptatriene was not reported by Gale but was described as being 'almost identical' with the ^{1}H NMR spectrum of the known cycloheptatriene described in the same report.
68. Ciganek, E. *J. Am. Chem. Soc.* **1967**, *89*, 1458–1468.
69. Buchner, E.; Hediger, S. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 3502–3509.
70. Vogel, E.; Maier, W.; Eimer, J. *Tetrahedron Lett.* **1966**, 655–660.
71. Hall, G. E.; Roberts, J. D. *J. Am. Chem. Soc.* **1971**, *93*, 2203–2207.
72. Günther, H.; Peters, W.; Wehner, R. *Chem. Ber.* **1973**, *106*, 3683–3694.
73. Klärner, F.-G.; Yaslak, S.; Wette, M. *Chem. Ber.* **1977**, *110*, 107–123.
74. Yang, M.; Webb, T. R.; Livant, P. *J. Org. Chem.* **2001**, *66*, 4945–4949.
75. Tsuruta, H.; Mori, S.; Mukai, T. *Chem. Lett.* **1974**, 1127–1130.
76. Takahashi, K.; Takase, K.; Toda, H. *Chem. Lett.* **1981**, 979–982.
77. Dürr, H.; Sergio, R.; Gombler, W. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 224–225.
78. L'Abbe, G.; Dehaen, W. *Tetrahedron* **1988**, *44*, 461–469.
79. Görlitz, M.; Günther, H. *Tetrahedron* **1969**, *25*, 4467–4480.
80. Maas, G.; Regitz, M. *Chem. Ber.* **1976**, *109*, 2039–2063.
81. Regitz, M.; Scherer, H.; Anschuetz, W. *Tetrahedron Lett.* **1970**, 753–756.
82. Maas, G.; Fischer, K.; Regitz, M. *Acta Crystallogr., Sect. B* **1974**, *30*, 1140–1145.
83. Maas, G.; Fischer, K.; Regitz, M. *Acta Crystallogr., Sect. B* **1974**, *B30*, 2853–2860.
84. Günther, H.; Tunggal, B. D.; Regitz, M.; Scherer, H.; Keller, T. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 563–564.
85. Scherer, H.; Hartmann, A.; Regitz, M.; Tunggal, B. D.; Günther, H. *Chem. Ber.* **1972**, *105*, 3357–3381.
86. Matsumoto, M.; Shiono, T.; Mutoh, H.; Amano, M.; Arimitsu, S. *J. Chem. Soc., Chem. Commun.* **1995**, 101–102.
87. Matsumoto, M.; Shiono, T.; Kasuga, N. C. *Tetrahedron Lett.* **1995**, *36*, 8817–8820.
88. Klärner, F.-G. *Tetrahedron Lett.* **1974**, 19–22.
89. Mukherjee-Müller, G.; Winkler, T.; Zsindely, J.; Schmid, H. *Helv. Chim. Acta* **1976**, *59*, 1763–1796.
90. Bedford, C. D.; Bruckmann, E. M.; Smith, P. A. S. *J. Org. Chem.* **1981**, *46*, 679–686.
91. Bedford, C. D.; Smith, P. A. S. *J. Org. Chem.* **1983**, *48*, 4002–4010.
92. Takeuchi, K.; Arima, M.; Okamoto, K. *Tetrahedron Lett.* **1981**, *22*, 3081–3084.
93. Takeuchi, K.; Senzaki, Y.; Okamoto, K. *J. Chem. Soc., Chem. Commun.* **1984**, 111–112.
94. Takeuchi, K.; Kitagawa, T.; Toyama, T.; Okamoto, K. *J. Chem. Soc., Chem. Commun.* **1982**, 313–314.
95. Takeuchi, K.; Fujimoto, H.; Okamoto, K. *Tetrahedron Lett.* **1981**, *22*, 4981–4984.
96. Takeuchi, K.; Fujimoto, H.; Kitagawa, T.; Fujii, H.; Okamoto, K. *J. Chem. Soc., Perkin Trans. 2* **1984**, 461–467.
97. Mbuvi, H. M.; Woo, L. K. *J. Porphyrins Phthalocyanines* **2009**, *13*, 136–152.
98. Satake, K.; Tawada, Y.; Okamoto, H. M. M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2015–2017.
99. Steigel, A.; Sauer, J.; Kleier, D. A.; Binsch, G. *J. Am. Chem. Soc.* **1972**, *94*, 2770–2779.
100. Huisgen, R.; Juppe, G. *Chem. Ber.* **1961**, *94*, 2332–2349.
101. Wittig, G.; Eggers, H.; Duffner, P. *Justus Liebigs Ann. Chem.* **1958**, *619*, 10–27.
102. Vogel, E.; Wendisch, D.; Roth, H. D. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 443.
103. Müller, E.; Kessler, H.; Suhr, H. *Tetrahedron Lett.* **1965**, 423–428.
104. Popovici-Muller, J. V.; Spencer, T. A. *Tetrahedron Lett.* **1997**, *38*, 8161–8164.
105. Bogdanova, A.; Popik, V. V. *Org. Lett.* **2001**, *3*, 1885–1888.
106. Dauben, H. J., Jr.; Honnen, L. R.; Harmon, K. M. *J. Org. Chem.* **1960**, *25*, 1442–1445.
107. Paquette, L. A.; Leichter, L. M. *J. Am. Chem. Soc.* **1971**, *93*, 5128–5136.
108. Klärner, F.-G.; Schmidt, E. K. G.; Rahman, M. A. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 138–139.
109. Klärner, F.-G.; Schmidt, E. K. G.; Rahman, M. A. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 139.
110. Kawase, T.; Iyoda, M.; Oda, M. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 559–561.
111. Schreiber, J.; Leimgruber, W.; Pesaro, M.; Schudel, P.; Threlfall, T.; Eschenmoser, A. *Helv. Chim. Acta* **1961**, *44*, 540–597.
112. Darms, R.; Threlfall, T.; Pesaro, M.; Eschenmoser, A. *Helv. Chim. Acta* **1963**, *46*, 2893–2905.
113. Vogel, E.; Wiedemann, W.; Kiefer, H.; Harrison, W. F. *Tetrahedron Lett.* **1963**, 673–678.
114. Radlick, P.; Rosen, W. *J. Am. Chem. Soc.* **1966**, *88*, 3461–3462.
115. Vogel, E.; Boell, W. A.; Biskup, M. *Tetrahedron Lett.* **1966**, 1569–1575.
116. Günther, H.; Hinrichs, H. H. *Tetrahedron Lett.* **1966**, 787–790.
117. Knox, L. H.; Velarde, E.; Cross, A. D. *J. Am. Chem. Soc.* **1963**, *85*, 2533–2535.
118. Knox, L. H.; Velarde, E.; Cross, A. D. *J. Am. Chem. Soc.* **1965**, *87*, 3727–3736.
119. Vogel, E. *Pure Appl. Chem.* **1971**, *28*, 355–377.
120. Günther, H.; Schmickler, H.; Bremser, W.; Straube, F. A.; Vogel, E. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 570–572.
121. Vogel, E.; Klug, W.; Breuer, A. *Org. Synth.* **1974**, *54*, 11–18.
122. Vogel, E.; Roth, H. D. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 228–229.
123. Cremer, D.; Dick, B. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 865–866.
124. Vogel, E.; Vogel, A.; Kuebbeler, H. K.; Sturm, W. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 514–516.
125. Vogel, E.; Reel, H. *J. Am. Chem. Soc.* **1972**, *94*, 4388–4389.
126. Kuroda, S.; Zuo, S.; Oda, M.; Fukuta, A.; Kajioka, T.; Saito, T.; Furuta, S.; Tsukumo, H.; Sano, K.; Miyatake, R.; Tomoda, S.; Hayakawa, C.; Nozawa, H. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 1659–1671.
127. Kuroda, S.; Kajioka, T.; Fukuta, A.; Thanh, N. C.; Zhang, Y.; Miyatake, R.; Mouri, M.; Zuo, S.; Oda, M. *Mini-Rev Org. Chem.* **2007**, *4*, 31–49.
128. Takeuchi, K.; Kitagawa, T.; Senzaki, Y.; Fujimoto, H.; Okamoto, K. *Chem. Lett.* **1983**, 69–72.
129. Vogel, E.; Scholl, T.; Lex, J.; Hohlneicher, G. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 869–870.
130. Hill, R. K.; Giberson, C. B.; Silverton, J. V. *J. Am. Chem. Soc.* **1988**, *110*, 497–500.
131. Nitta, M.; Takayasu, T. *Tetrahedron Lett.* **1997**, *38*, 7905–7908.
132. Nitta, M.; Takayasu, T. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1325–1334.
133. Morris, J. C.; Mander, L. N.; Hockless, D. C. R. *Synthesis* **1998**, 455–467.
134. Buttle, L. A.; Morris, J. C.; Mander, L. N. *ARKIVOC* **2003**, 118–134.
135. Kuroda, S.; Hirano, I.; Zhang, Y.; Thanh, N. C.; Oda, M. *Tetrahedron Lett.* **2007**, *48*, 5811–5815.
136. Wenkert, E.; Liu, S. *Synthesis* **1992**, 323–327.
137. Lai, M. t.; Wu, W.; Stubbe, J. *J. Am. Chem. Soc.* **1995**, *117*, 5023–5030.
138. Prinzbach, H.; Fischer, U.; Cruse, R. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 251–252.
139. Kitagawa, T.; Miyabo, A.; Fujii, H.; Okazaki, T.; Mori, T.; Matsudou, M.; Sugie, T.; Takeuchi, K. *J. Org. Chem.* **1997**, *62*, 888–892.
140. Hannemann, K. *Angew. Chem., Int. Ed. Engl.* **1988**, 284–285.
141. Jones, M., Jr. *J. Org. Chem.* **1968**, *33*, 2538–2539.
142. Gale, D. M. *J. Org. Chem.* **1968**, *33*, 2536–2538.
143. Schönleber, D. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 76.
144. Jones, M., Jr. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 76–77.
145. Moriarty, R. M.; Chen, K. N.; Churchill, M. R.; Chang, S. W. Y. *J. Am. Chem. Soc.* **1974**, *96*, 3661–3663.
146. Jones, M., Jr.; Harrison, A. M.; Rettig, K. R. *J. Am. Chem. Soc.* **1969**, *91*, 7462–7466.
147. Rostek, C. J., Jr.; Jones, W. M. *Tetrahedron Lett.* **1969**, 3957–3960.
148. Jones, W. M.; Ennis, C. L. *J. Am. Chem. Soc.* **1969**, *91*, 6391–6397.
149. Jones, M., Jr.; Petrillo, E. W., Jr. *Tetrahedron Lett.* **1969**, 3953–3956.
150. Rewicki, D.; Tuchscherer, C. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 44–45.
151. Dürr, H.; Scheppers, G. *Angew. Chem., Int. Ed. Engl.* **1968**, *7*, 371.
152. Dürr, H.; Kober, H. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 342.
153. Dürr, H.; Kober, H. *Tetrahedron Lett.* **1972**, 1255–1258.

154. Dürr, H.; Kober, H.; Fuchs, V.; Orth, P. *J. Chem. Soc., Chem. Commun.* **1972**, 973–974.
155. Dürr, H.; Kober, H. *Chem. Ber.* **1973**, *106*, 1565–1580.
156. Dürr, H.; Kober, H.; Halberstadt, I.; Neu, U.; Coburn, T. T.; Mitsuhashi, T.; Jones, W. M. *J. Am. Chem. Soc.* **1973**, *95*, 3818–3819.
157. Rapp, K. M.; Daub, J. *Tetrahedron Lett.* **1977**, 227–230.
158. Mathur, N. C.; Shechter, H. *J. Org. Chem.* **1990**, *55*, 3001–3002.
159. Murata, S.; Kobayashi, J.; Kongou, C.; Miyata, M.; Matsushita, T.; Tomioka, H. *J. Am. Chem. Soc.* **1998**, *120*, 9088–9089.
160. Murata, S.; Kobayashi, J.; Kongou, C.; Miyata, M.; Matsushita, T.; Tomioka, H. *J. Org. Chem.* **2000**, *65*, 6082–6092.
161. Kohmoto, S.; Kawatsuji, T.; Ogata, K.; Yamamoto, M.; Yamada, K. *J. Am. Chem. Soc.* **1991**, *113*, 5476–5478.
162. Kohmoto, S.; Funabashi, T.; Nakayama, N.; Nishio, T.; Iida, I.; Kishikawa, K.; Yamamoto, M.; Yamada, K. *J. Org. Chem.* **1993**, *58*, 4764–4766.
163. Kohmoto, S.; Koyano, I.; Funabashi, T.; Kishikawa, K.; Yamamoto, M.; Yamada, K. *Tetrahedron Lett.* **1995**, *36*, 553–554.
164. Ledon, H.; Cannic, G.; Linstrumelle, G.; Julia, S. *Tetrahedron Lett.* **1970**, 3971–3974.
165. Kohmoto, S.; Motomura, T.; Takahashi, M.; Kishikawa, K. *J. Mol. Struct.* **2010**, *964*, 47–51.
166. Kennedy, M.; McKervey, M. A. *J. Chem. Soc., Chem. Commun.* **1988**, 1028–1030.
167. Kennedy, M.; McKervey, M. A. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2565–2574.
168. Frey, B.; Mander, L. N.; Hockless, D. C. R. *J. Chem. Soc., Perkin Trans. 1* **1998**, 1555–1560.
169. Zhang, H.; Appels, D. C.; Hockless, D. C. R.; Mander, L. N. *Tetrahedron Lett.* **1998**, *39*, 6577–6580.
170. Kennedy, M.; McKervey, M. A.; Maguire, A. R.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1047–1054.
171. Duddeck, H.; Ferguson, G.; Kaitner, B.; Kennedy, M.; McKervey, M. A.; Maguire, A. R. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1055–1063.
172. Levin, S.; Nani, R. R.; Reisman, S. E. *Org. Lett.* **2010**, *12*, 780–783.
173. Doyle, M. P.; Shanklin, M. S.; Pho, H. Q. *Tetrahedron Lett.* **1988**, *29*, 2639–2642.
174. Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. *J. Am. Chem. Soc.* **1993**, *115*, 8669–8680.
175. Doyle, M. P.; Protopopova, M. N.; Peterson, C. S.; Vitale, J. P.; McKervey, M. A.; Garcia, C. F. *J. Am. Chem. Soc.* **1996**, *118*, 7865–7866.
176. Costantino, A.; Linstrumelle, G.; Julia, S. *Bull. Soc. Chim. Fr.* **1970**, 907–912.
177. Scott, L. T. *J. Chem. Soc., Chem. Commun.* **1973**, 882–883.
178. Scott, L. T.; Minton, M. A.; Kirms, M. A. *J. Am. Chem. Soc.* **1980**, *102*, 6311–6314.
179. McKervey, M. A.; Tuladhar, S. M.; Twohig, M. F. *J. Chem. Soc., Chem. Commun.* **1984**, 129–130.
180. Saba, A. *Tetrahedron Lett.* **1990**, *31*, 4657–4660.
181. Manitto, P.; Monti, D.; Speranza, G. *J. Org. Chem.* **1995**, *60*, 484–485.
182. Doyle, M. P.; Ene, D. G.; Forbes, D. C.; Pillow, T. H. *Chem. Commun.* **1999**, 1691–1692.
183. Adam, W.; Balci, M. *Angew. Chem.* **1978**, *90*, 1014–1015.
184. Adam, W.; Balci, M. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 954–955.
185. Adam, W.; Balci, M. *J. Am. Chem. Soc.* **1979**, *101*, 7537–7541.
186. Adam, W.; Balci, M. *J. Am. Chem. Soc.* **1979**, *101*, 7542–7547.
187. Adam, W.; Balci, M.; Cueto, O.; Pietrzak, B. *Tetrahedron Lett.* **1979**, 4137–4140.
188. Balci, M.; Atasoy, B. *Tetrahedron Lett.* **1984**, *25*, 4033–4036.
189. Celik, M.; Balci, M. *ARKIVOC* **2007**, 150–162.
190. Atasoy, B.; Balci, M. *Tetrahedron* **1986**, *42*, 1461–1468.
191. Altundas, A.; Akbulut, N.; Balci, M. *Helv. Chim. Acta* **1998**, *81*, 828–836.
192. Barlow, M. G.; Suliman, N. N. E.; Tipping, A. E. *J. Fluorine Chem.* **1995**, *70*, 109–120.
193. Petrov, V.; Marshall, W. *J. Fluorine Chem.* **2007**, *128*, 729–735.
194. Schenck, G. O. *Angew. Chem.* **1957**, *69*, 579.
195. Mori, A.; Takeshita, H. *Chem. Lett.* **1978**, 395–396.
196. Asao, T.; Yagihara, M.; Kitahara, Y. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2131–2135.
197. Saba, A.; De Lucchi, O. *Heterocycles* **1987**, *26*, 2339–2342.
198. Adam, W.; Rebollo, H.; Dürr, H.; Pauly, K. H.; Peters, K.; Peters, E. M.; Von Schnering, H. G. *Tetrahedron Lett.* **1982**, *23*, 923–926.
199. Adam, W.; Dürr, H.; Pauly, K. H.; Peters, E. M.; Peters, K.; Rebollo, H.; Von Schering, H. G. *J. Org. Chem.* **1984**, *49*, 1333–1338.
200. Sugimura, T.; Young Im, C.; Okuyama, T. *Tetrahedron Lett.* **2004**, *45*, 1519–1521.
201. Im, C. Y.; Okuyama, T.; Sugimura, T. *Chem. Lett.* **2007**, *36*, 314–315.
202. Maguire, A. R.; Buckley, N. R.; O'Leary, P.; Ferguson, G. *Chem. Commun.* **1996**, 2595–2596.
203. Maguire, A. R.; Buckley, N. R.; O'Leary, P.; Ferguson, G. *J. Chem. Soc., Perkin Trans. 1* **1998**, 4077–4092.
204. Maguire, A. R.; O'Leary, P.; Harrington, F.; Lawrence, S. E.; Blake, A. J. *J. Org. Chem.* **2001**, *66*, 7166–7177.
205. O'Leary, P.; Maguire, A. R. *ARKIVOC* **2009**, *xi*, 130–151.
206. Moody, C. J.; Miah, S.; Slawin, A. M. Z.; Mansfield, D. J.; Richards, I. C. *J. Chem. Soc., Perkin Trans. 1* **1998**, 4067–4076.
207. Papadopoulos, M.; Jenner, G. *Tetrahedron Lett.* **1985**, *26*, 3335–3338.
208. Jenner, G.; Papadopoulos, M. *J. Org. Chem.* **1986**, *51*, 585–589.
209. Diederich, F.; Thilgen, C. *Science* **1996**, *271*, 317–323.
210. Kroto, H. W.; Taylor, R.; Walton, D. R. M. *Pure Appl. Chem.* **1994**, *66*, 2091–2094.
211. Osterodt, J.; Vögtle, F. *J. Chem. Soc., Chem. Commun.* **1996**, 547–548.
212. Suzuki, T.; Li, Q.; Khemani, K. C.; Wudl, F.; Almarsson, O. *Science* **1991**, *254*, 1186–1188.
213. Warner, P. M. *J. Am. Chem. Soc.* **1994**, *116*, 11059–11066.
214. Kiely, A. F.; Haddon, R. C.; Meier, M. S.; Selegue, J. P.; Brock, C. P.; Patrick, B. O.; Wang, G.-W.; Chen, Y. *J. Am. Chem. Soc.* **1999**, *121*, 7971–7972.
215. Liu, J. F.; Kato, N.; Mori, A.; Takeshita, H.; Isobe, R. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1507–1509.
216. Duczek, W.; Radeck, W.; Niclas, H. J.; Ramm, M.; Coostisella, B. *Tetrahedron Lett.* **1997**, *38*, 6651–6654.

Biographical sketch

Anita R. Maguire was born in 1964 in Cork. She undertook undergraduate and postgraduate studies at University College Cork (B.Sc., 1985, Ph.D. 1989), focusing during her Ph.D. on asymmetric catalysis in reactions of α-diazo ketones. Following postdoctoral research in the Facultes Universitaires, Namur, Belgium and subsequently at the University of Exeter she returned to Cork in 1991. Her research interests include the development of new synthetic methodology, asymmetric synthesis, and the design and synthesis of bioactive compounds with pharmaceutical applications.

Orla A. McNamara obtained her undergraduate degree at University College Cork in 2004 and was awarded the Pfizer Pharmaceuticals Prize on the basis of her undergraduate achievements. She subsequently undertook a Ph.D. (2009), which involved the exploration of the synthetic and mechanistic aspects of the intramolecular aromatic additions of α-diazo ketones. She is currently working as a postdoctoral researcher in University College Cork, in a collaborative project with Eli Lilly.