The synthesis of carbocyclic aromatic systems

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Reviewing the literature published between 1 January 1992 and 31 December 1995

1 Introduction

This article is concerned solely with the *de novo* synthesis of carbocyclic aromatic rings and systems: modification of pre-existing rings by, for example, functional group interconversion or electrophilic substitution processes is beyond its scope. Furthermore, only the synthesis of non-charged systems is covered; aromatic species such as cyclopentadienyl anions, cycloheptatrienyl cations and their related analogues and homologues are intentionally omitted. Whilst they remain of interest from the point of view of defining the concept of aromaticity, and as test cases of bonding theory, the synthetic utility of, for example, higher annulenes is somewhat limited. For this reason, and because of space limitations, they are not discussed here.

A number of reactions and processes which it might be thought would naturally fall within the area under discussion have been well reviewed in the literature very recently. These include the synthesis of aromatic systems from non-aromatic precursors, which is reviewed in *Annual Reports on the Progress of Chemistry*,[1–6] and the conversion of enediynes to aromatics *via* Bergman cyclisation and related processes, which has been reviewed both elsewhere and in great detail in earlier editions of this journal.[7,8] Similarly the benzannulation reaction of Fischer carbene complexes with alkynes to produce phenols has been excellently covered elsewhere.[9]

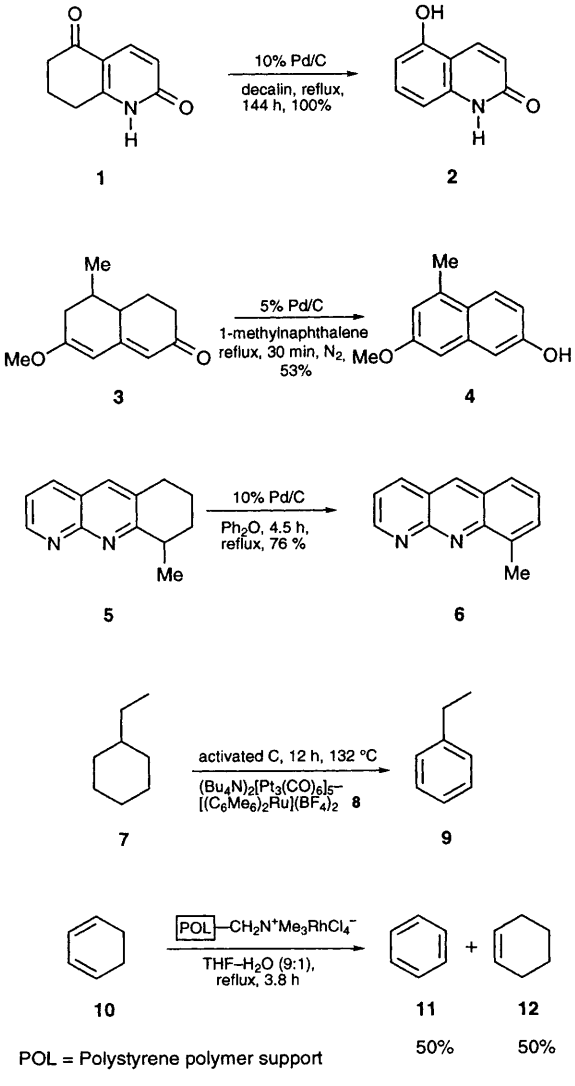
The volume of literature covering this topic, if one considers 'synthesis' of aromatic systems in its most general sense, is so vast that it would be most surprising if the synthetic methods discussed herein were not thought by some readers to reflect the subjective bias of the author. That may well be true, however, as wide a range of readily accessible literature sources as possible has been covered, focusing on the most synthetically useful, novel and interesting reactions, whilst trying to provide some level of historical context to the most recent applications of the more well established reagents and reactions. The wide range of reactions that might potentially be covered in this article have meant that it can in no way pretend to be comprehensive, and space limitations have meant that it has not been possible to give full reaction schemes for every cited reference. Readers should consult the references where closely related reactions or further uses of a particular reagent are indicated.

2 Aromatisation reactions

The last chemical transformation involved in many synthetic sequences leading to an aromatic final product is very frequently an aromatisation. This may involve such processes as dehydrogenation, dehydration, reduction, oxidation (other than dehydrogenation), dehalogenation and dehydrohalogenation. Where this occurs as a separate, well-defined step, and can therefore sensibly be considered a 'reaction' in its own right, it is discussed in this section. It will readily be apparent to the reader that it is not possible, in many cases, to divorce the aromatisation step from the preceding annulation steps of a reaction or sequence, and these cases are discussed later, under the general headings describing the ring-forming reactions. In these later sections, an attempt will be made to define at what point, and using which reagents, aromatisation is effected.

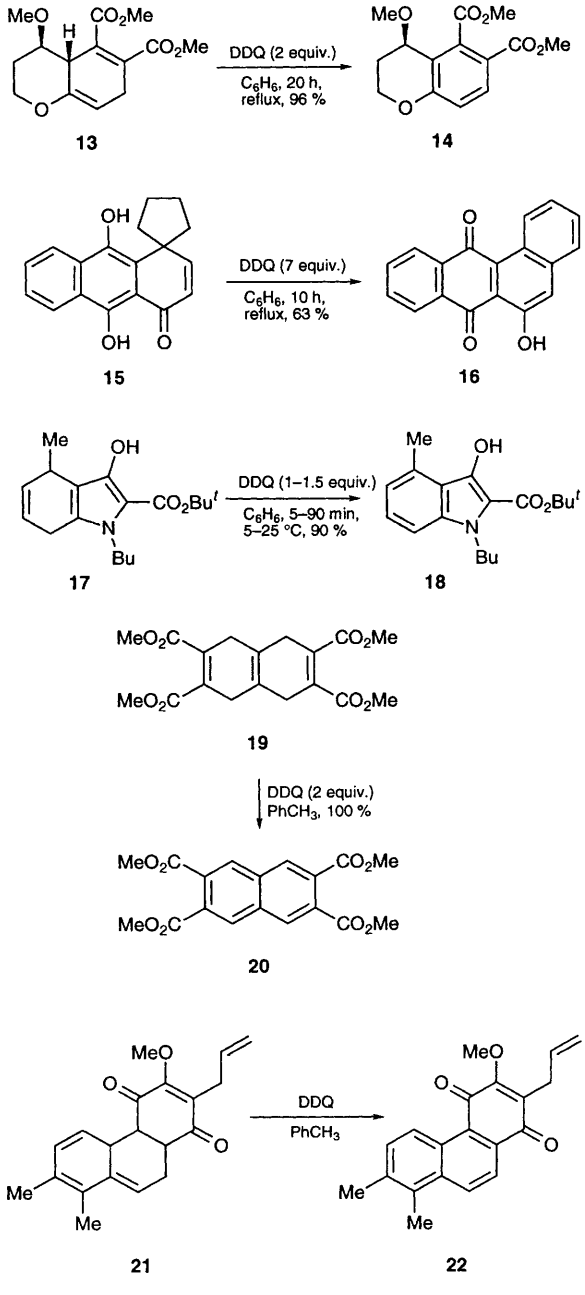
2.1 Dehydrogenation reactions using noble metal catalysts

The 'traditional' hydrogenation catalysts have a long history of use as dehydrogenation catalysts for the aromatisation of, especially, six-membered alicyclic rings.[10] Recent examples from the literature serve to show the continued utility of these substances, and to illustrate the directions in which the field is developing. 5-Hydroxyquinolone **2** was prepared in quantitative yield by heating the ketone **1** with 10% palladium-on-charcoal at reflux in decalin for 144 hours.[11] In related reactions the ketone **3** was converted in 53% yield to the naphthol **4**, and the benzo[*b*][1,8]naphthyridine **6** prepared in 76% yield.[12,13] More recent developments in catalysts are exemplified by the composite platinum–ruthenium catalyst **8** which has been described for the liquid-phase dehydrogenation of alkanes,[14] and the polystyrene-supported rhodium(III) chloride–quaternary ammonium ion pair, which efficiently catalysed the disproportionation of cyclohexadiene **10** to benzene **11** and cyclohexene **12**.[15] The use of platinum for a closely related transformation has recently been exemplified.[16]

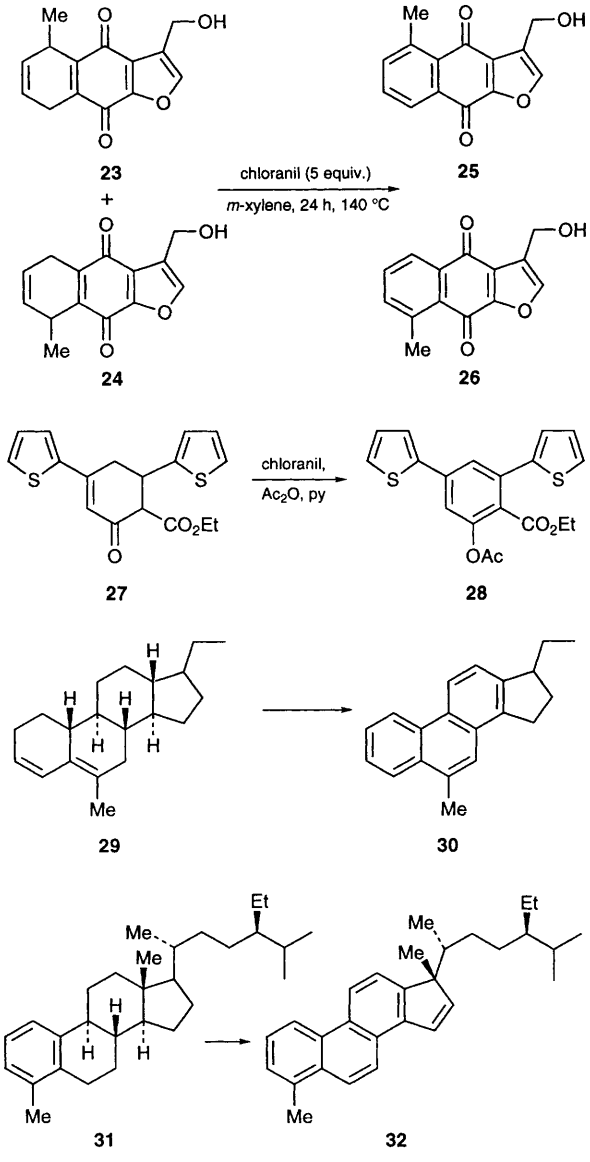


2.2 Aromatisations using quinones

By far the most frequently used quinone in aromatisation reactions is DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone). Suitable solvents are aromatic hydrocarbons at ambient to reflux temperatures, solvent and conditions being largely dictated by substrate solubility and susceptibility to oxidation. The following examples illustrate the range of substrates accepted by this reagent and the compatible functional groups.[17–21] In the conversion of **13** to **14**, it is interesting to note that aromatisation is not accompanied by elimination of methanol. The oxidation of **15** to **16** is accompanied by a dienone–phenol rearrangement. Many further examples of the use of DDQ (illustrated by the conversions of **17** to **18**, **19** to **20**, **21** to **22**) have been described.[22–32]



Other quinones have been used less frequently. The isomeric quinones **23** and **24** were converted to maturone **25** and isomaturone **26** by chloranil (2,3,5,6-tetrachloro-1,4-benzoquinone),[33] cyclohexenone **27** to 1,2,3,5-tetrasubstituted arene **28**,[34] **29** to steroid hydrocarbon **30** by a combination of chloranil and phenanthrenequinone,[35] and **31** to **32** by chloranil.[36]

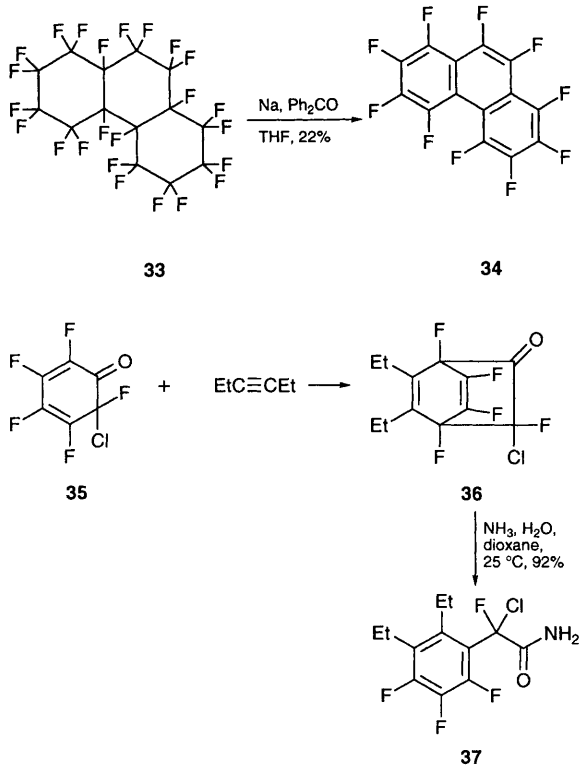


23 25 24 26 27 28 29 30 31 32

2.3 Dehalogenation and dehydrohalogenation

These methods are discussed together due to their close mechanistic relationship and similarity in terms of reagents employed, reaction conditions and suitable substrates.

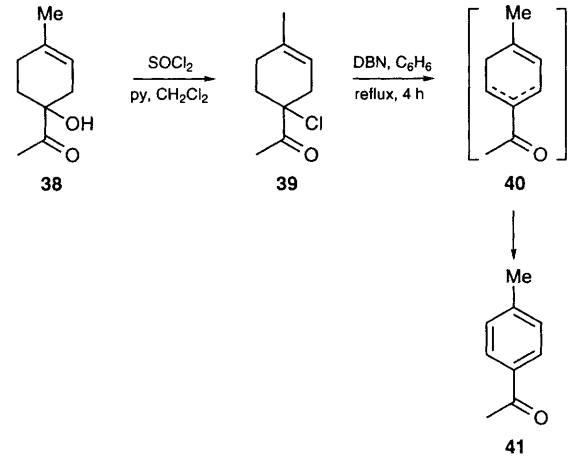
The reductive defluorination of saturated perfluorocarbons to highly fluorinated aromatic compounds has recently been described.[37] The perfluorophenanthrene **34** was prepared in 22% yield from the perfluoroalkane **33** using sodium–benzophenone. The authors also described the electrochemical reduction of this and closely related



33 34 35 36 37

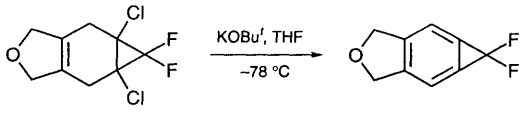
systems. A closely related reduction of perfluoromethylcyclohexane has recently been described.[38] Reaction of **36** with ammonia was accompanied by ring-opening and elimination of hydrogen fluoride, to give the amide **37** in 92% yield.[39]

Conversion of alcohol **38** to 4-methylacetophenone **41** was achieved in 73% yield: presumably the initial dehydrochlorination is followed by an aerial oxidation of the cyclohexadiene (**Scheme 1**).[40] Dehydrochlorination of the cyclohexene **42** gave the benzocyclopropane **43** in 43% yield.[41,42]



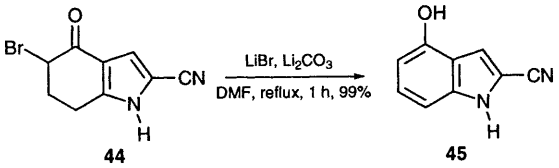
38 39 40 41

Scheme 1

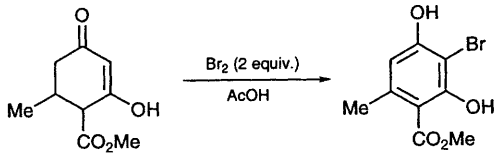


42 43

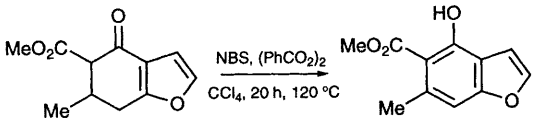
A common strategy employs a bromination–dehydrobromination sequence for the aromatisation of cyclohexanones and cyclohexenones in particular. Dehydrobromination of **44** with lithium bromide and lithium carbonate, in DMF at reflux, gave the sensitive 4-hydroxyindole **45** in excellent yield.[43] Similarly **46** gave **47** in 49% yield[44] and **48** gave **49** in 68% yield.[45] Further closely related reactions have been published.[46–49] A number of examples of closely related iodination–dehydroidination sequences leading to **51**, **53**, **55**, **57** and **59** have also been described.[50,51]



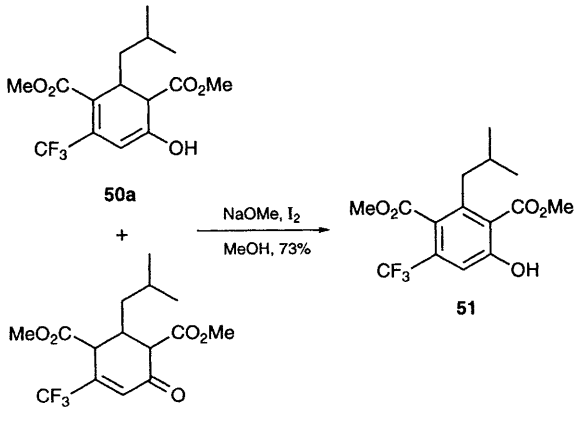
44 **45**



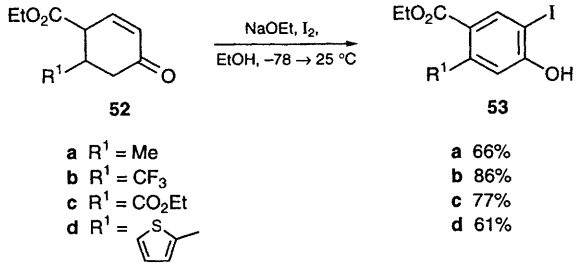
46 **47**



48 **49**

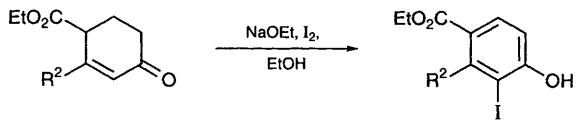


50a + **50b** **51**



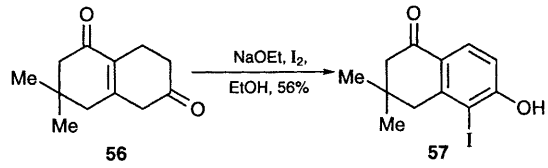
52 **53**

a R^1 = Me **a** 66%
b R^1 = CF_3 **b** 86%
c R^1 = CO_2Et **c** 77%
d R^1 = S **d** 61%

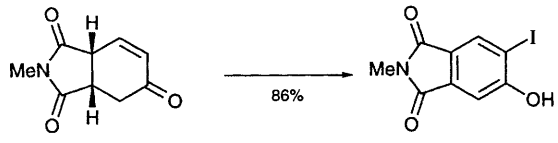


54 **55**

a R^2 = Me **a** 78%
b R^2 = CF_3 **b** 65%
c R^2 = Ph **c** 64%



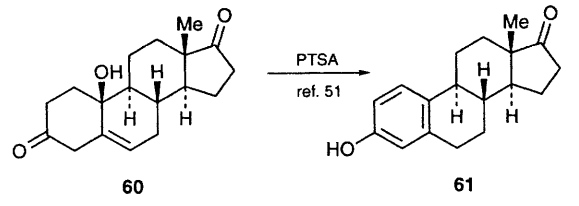
56 **57**



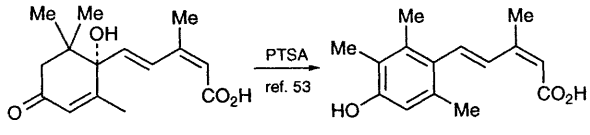
58 **59**

2.4 Other methods

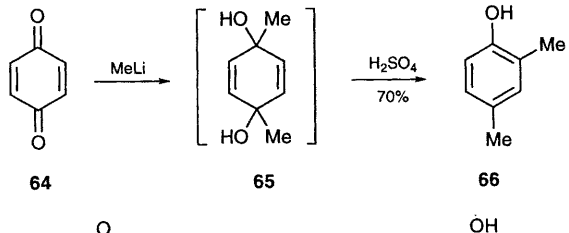
Acid-catalysed dehydration, with or without concomitant skeletal rearrangement, has been used in a number of cases to effect aromatisation as in the conversion of **60** to **61**, **62** to **63**, **64** to **66**, **67** to **68** and **69** to **70**.[52–60] The closely related loss of an alcohol is exemplified by the reduction–elimination of **71** to tetrahydroquinoline **72**[61] and the loss of methanol from **73** and **75** to give **74** and **76**.[62]



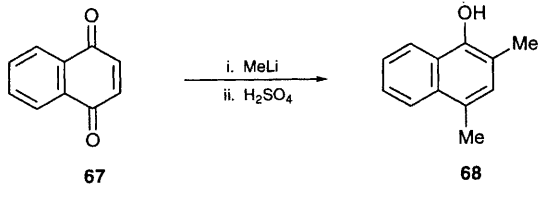
60 **61**



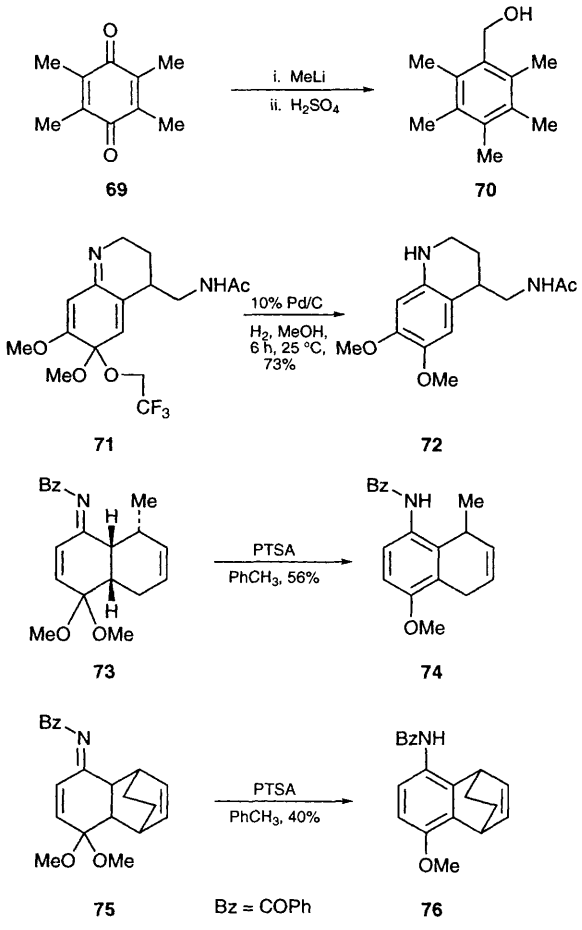
62 **63**



64 **65** **66**

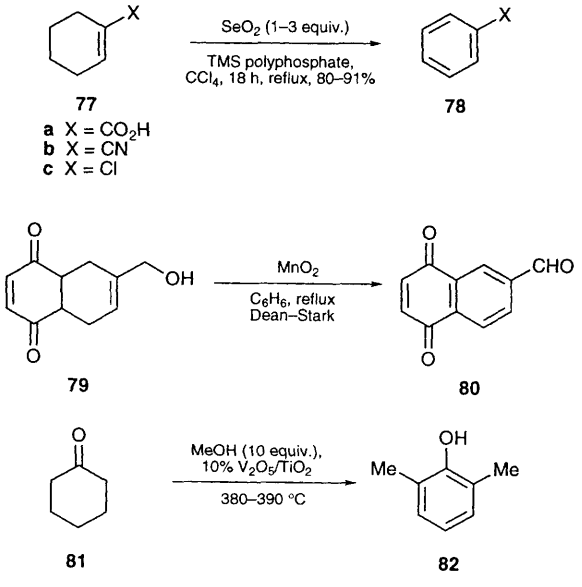


67 **68**



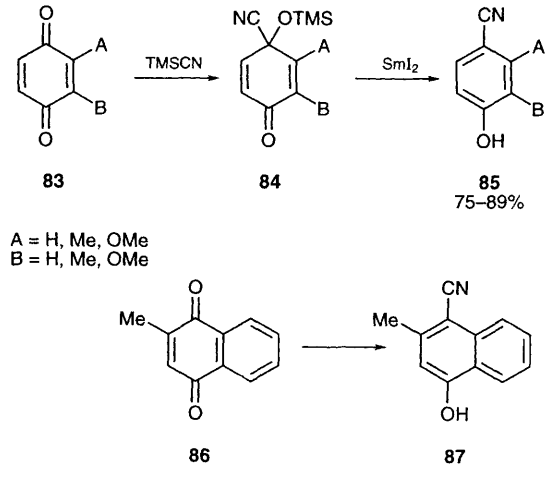
Related transformations, resulting in dihydrobenzofurans and tetrahydrofurans have recently appeared in the literature.[63]

Selenium dioxide and manganese dioxide have been used for the aromatisation of cyclohexenes **77** and **79** respectively.[64–66] Vanadium pentoxide on titanium dioxide in the presence of methanol effected alkylative aromatisation of cyclohexanone **81** to 2,6-dimethylphenol **82** in 100% conversion.[67]



Other oxidising agents which have found application are Jones' reagent,[68] potassium oxide–chromium trioxide on carbon/alumina,[69] the $[PV_2Mo_{10}O_{40}]^{5-}$ heteropolyanion[70] and molecular oxygen.[71] It will be appreciated that the actual oxidant in the so-called 'spontaneous' aromatisations occurring following an annulation reaction is, for the most part, atmospheric oxygen, which probably makes it the most widely, but unwittingly, 'used' aromatisation reagent of all.

One reductive aromatisation, of potential utility for the construction of highly functionalised benzonitriles has recently been described by Danishefsky.[72] A quinone **83** is converted to a protected monocyanohydrin **84**, which is then reduced with samarium(II) iodide to yield a hydroxybenzonitrile **85** (**Scheme 2**); for unsymmetrical substrates excellent regioselectivity (10:1 to 20:1) was obtained. Fused quinones such as **86** also gave the desired nitriles in good yield, as did phenanthrenequinone.



Scheme 2

3 Cycloadditions

This constitutes perhaps one of the most active fields during the period under review. As will become apparent a large number of aromatic systems, both mono- and poly-cyclic, from simply to highly functionalised, may be prepared by this method. In many cases an aromatisation step follows the construction of the carbon skeleton: this may be, for example, a DDQ oxidation, or elimination of a small molecule such as ethene, carbon dioxide, sulfur dioxide, nitrogen or water. The organisation of this section reflects a need at least to attempt some systematisation of the subject matter. 'Simple' cycloaddition reactions are discussed first, the name having been chosen to differentiate them from the transition metal-templated reactions which follow. These two broad areas are further separated into inter- and intramolecular reactions, and within each of these

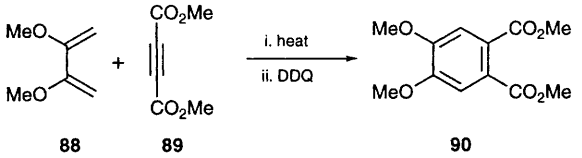
subsections the reactions are arranged according to the complexity of aromatic ring system constructed (mono-, bi-, tri-cyclic and higher order). The subject matter in the sub-sections is arranged approximately in order of increasing degree of substitution.

3.1 Simple cycloadditions

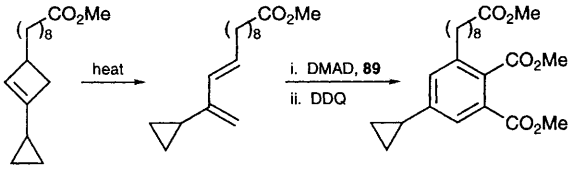
3.1.1 Intermolecular reactions

3.1.1.1 Monocyclic systems

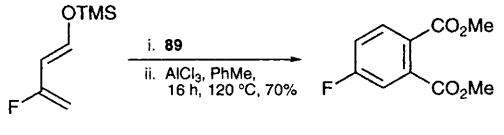
The simple [4+2] cycloaddition of a diene to an alkene or alkyne leads to a cyclohexene or cyclohexadiene. Clearly some aromatisation or dehydrogenation must occur if an aromatic system is to result. As will be seen from the following examples, this may be effected by the addition of an agent such as DDQ subsequent to the construction of the carbon skeleton (see Section 2.2), or may occur by elimination of a small molecule subsequent to the cycloaddition process. The diene **88** underwent smooth reaction with dimethyl acetylenedicarboxylate **89** (DMAD), to give a cyclohexadiene which was aromatised, without isolation, by treatment with DDQ,[73] to give the tetrasubstituted arene **90**. Similarly the cyclobutene **91** underwent thermal cycloreversion to diene **92**, which then underwent cycloaddition with DMAD followed by DDQ oxidation to give **93**;[74] a similar transformation has recently been reported.[75] Cycloaddition of fluorodiene **94** with DMAD, followed by loss of the elements of trimethylsilanol, gave fluoro diester **95** in 70% yield.[76] A number of related reactions have been described.[77–79] The Alder–Rickert reaction involves a [4+2] cycloaddition followed by a loss of an alkene, to give an aromatic system directly, even in the presence of groups which might eliminate under normal Diels–Alder conditions. Recent examples which illustate the utility of this process for the construction of highly functionalised aromatics include an intermediate **97** in an unambiguous synthesis of hericenone A,[80] daunomycinone,[81] and the chlorophenols **100** and **102**.[82] A recent example was employed in a synthesis of anacardic acids **103–105**;[83] further examples of the use of this reaction may also be found.[84]



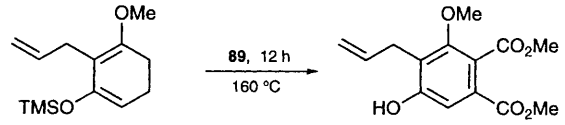
88 89 90



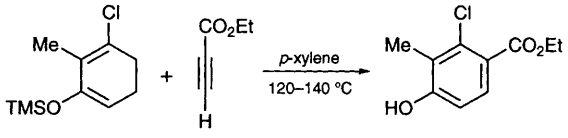
91 92 93



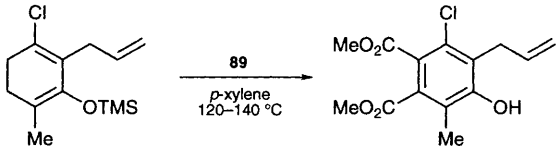
94 95



96 97



98 99 100

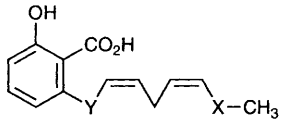


101 102

103 104

a $R^1 = (CH_2)_{10}CH_3$
b $R^1 = (CH_2)_{16}CH_3$
c $R^1 = (CH_2)_6$—⟨⟩—$(CH_2)_6CH_3$

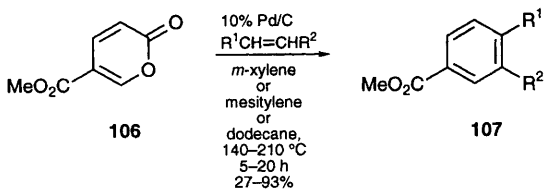
a Y = $(CH_2)_7$, Z = $(CH_2)_3$
b Y = $(CH_2)_7$, Z = $(CH_2)_5$



105

a X = $(CH_2)_2$, Y = $(CH_2)_7$
b X = $(CH_2)_4$, Y = $(CH_2)_7$

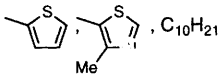
Other small molecules may also be lost to give aromatic products, one of the commonest being carbon dioxide. The cycloaddition of a 2-pyrone with an alkyne followed by loss of carbon dioxide gives an aromatic species directly. The reaction is generally less successful with alkenes, because the intermediate cyclohexadiene may itself react further with the alkene. A recent modification, which involves performing the cycloaddition in the presence of a dehydrogenation catalyst to aromatise the intermediate cyclohexadiene as soon as it is formed, overcomes this difficulty.[85] By this route good yields of phenyl and biphenyl derivatives are



i, R^1 = 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-$Bu^tOC_6H_4$, 4-$C_{10}H_{21}C_6H_4$, 4-ClC_6H_4, 4-$MeO_2CC_6H_4$, 4-$NO_2C_6H_4$, 2-ClC_6H_4, 2,4-$Cl_2C_6H_3$
R^2 = H

ii, $R^1 = R^2$ = Ph

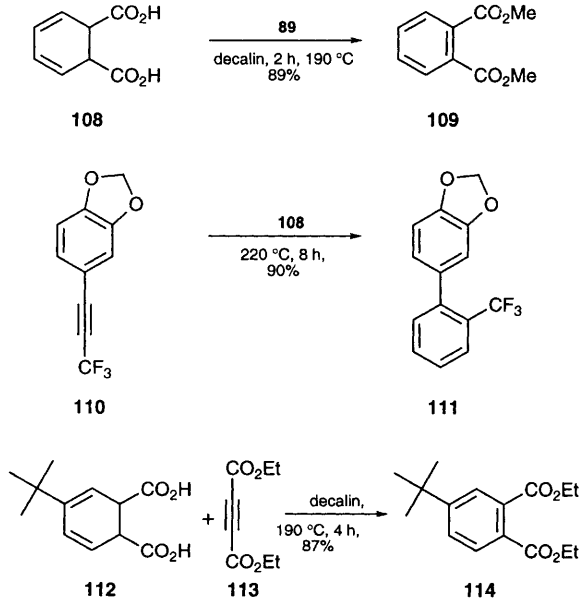
iii, R^1, R^2 = 

iv, R^1 = 4-py, 2-py, R^2 = H 

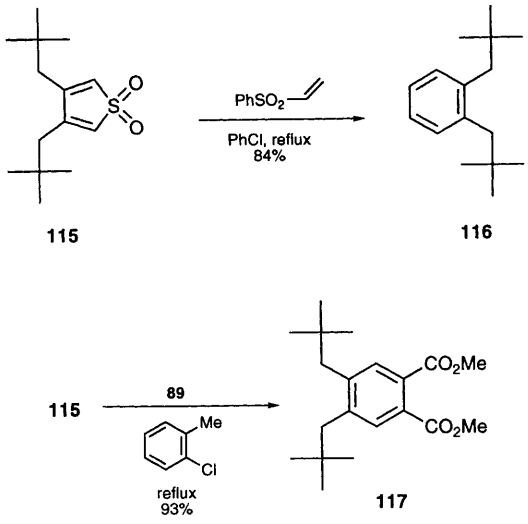
v, R^1, R^2 = $(CH_2)_6$

Scheme 3

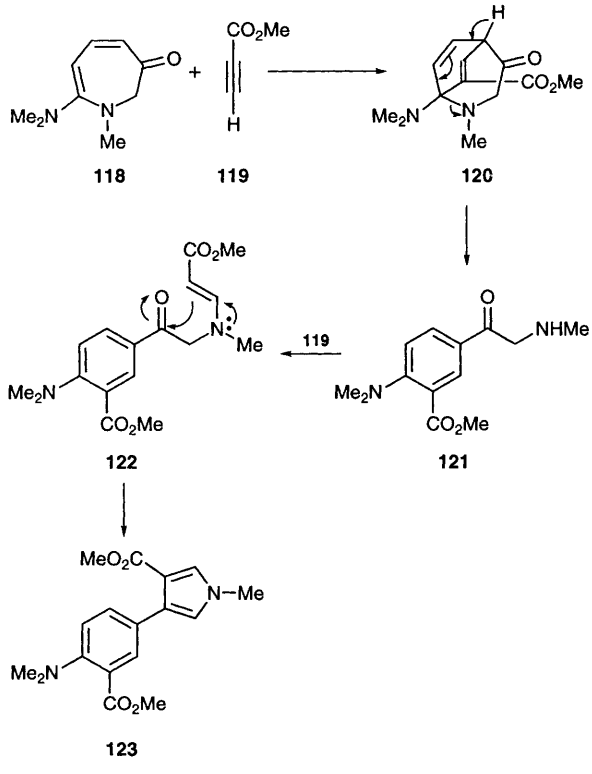
obtained from readily available alkenes (**Scheme 3**). The Diels–Alder reactions of 2-pyrones have been reviewed.[86] Dihydrophthalate esters, or dihydrophthalic acids, prepared by the electrochemical reduction of phthalates or phthalic acids, react with alkynes such as DMAD to yield a range of 1,2-disubstituted arenes and biaryl systems, with the elimination of dimethyl fumarate or fumaric acid (**Scheme 4**).[87] Loss of sulfur dioxide has been used as a means of aromatising [4+2] cycloadducts, for example in the conversion of **115** to **116** and **117**;[88] a recent report describes the cycloadditions of thienopyrrole dioxides.[89] The conversion of **115** to **116** also involves loss of one mole of benzenesulfinic acid.



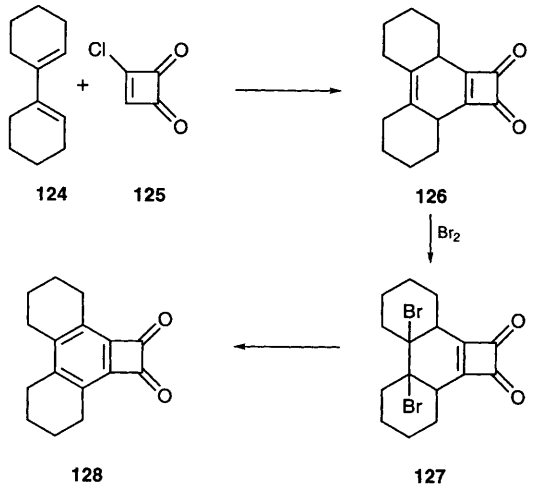
Scheme 4



Aromatic systems have also been formed by loss of dimethylamine from [4+2] adducts,[90] in related reactions by loss of pyrrolidine and morpholine,[91–93] and by addition of allyl silanes to benzyl cations.[94] A more complex loss still is involved in the conversion of **118** to **123**. This proceeds as shown in **Scheme 5**, *via* [4+2] cycloaddition, fragmentation, Michael addition and ring closure.[95] Aromatisation of the initially formed cycloadduct **126** from diene **124** and 3-chlorocyclobutane-1,2-dione **125** was achieved by a bromination–dehydrobromination sequence (**Scheme 6**);[96] the same group has reported further applications of this strategy.[97] Alkynes such as phenylethyne **130** and trimethylsilylethyne **132** react

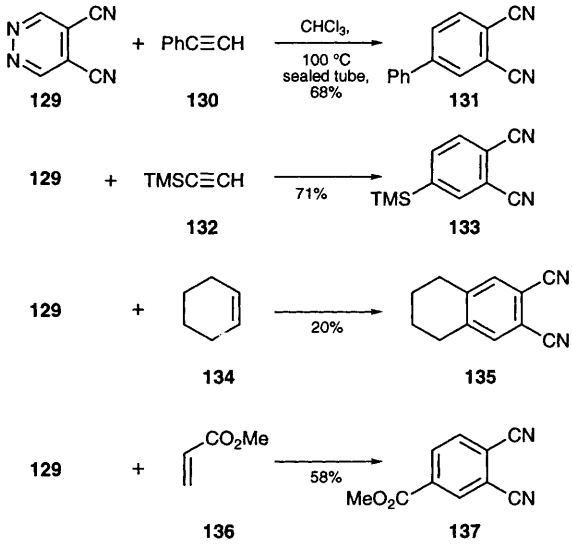


Scheme 5



Scheme 6

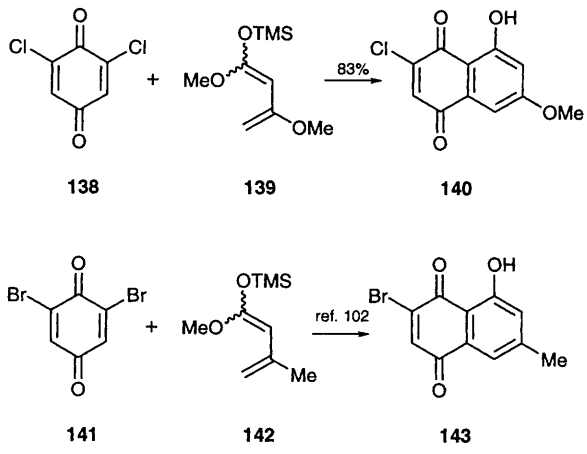
with 4,5-dicyanopyridazine **129** at 110 °C, in chloroform in a sealed tube, to give arenes **131** and **133** after loss of nitrogen. Alkenes such as **134** and **136** partially or completely aromatise after cycloaddition to give tetralin **135** and ester **137** (**Scheme 7**).[98] Related cycloadditions of ynamines and pyridopyridazines have been reported.[99,100] Thermal cyclisations of enynones have been used in the synthesis of, for example, juncusol.[101]



Scheme 7

3.1.1.2 Bicyclic systems

Because of their wide occurrence in natural products, much interest and synthetic effort has been focused on developing synthetic routes to naphthoquinones and related molecules: many of these routes have involved cycloadditions. Reaction of 2,6-dichloro-1,4-benzoquinone **138** with Danishefsky diene **139**, followed by mild acid

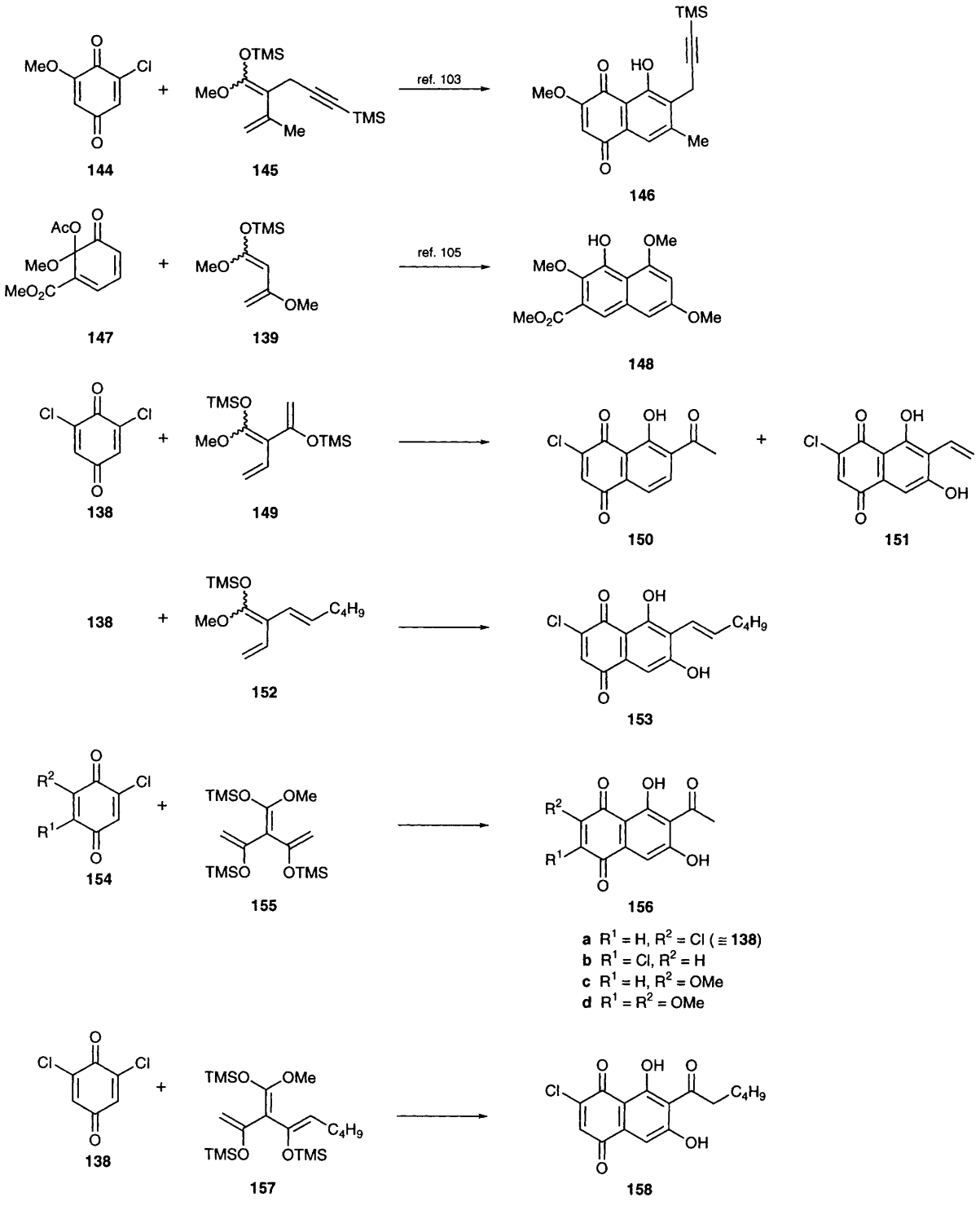


hydrolysis gave the 2-chloro-6-methoxy-8-hydroxynaphthoquinone **140** in 83% yield.[102] The bromoquinone **143** was prepared similarly. This general approach is highly flexible, and capable of being adapted to produce a number of more highly substituted naphthoquinones (**Scheme 8**).[103–109]

The Alder–Rickert reaction and variants thereof have also found utility in this area.[110–112] Pyrrolo-fused 2-pyrones {1,6-dihydropyrano[4,3-*b*]pyrrol-6-ones} such as **159** undergo cycloadditions with, for example, DMAD to give, after loss of carbon dioxide, substituted indoles exemplified by **160**.[113] Another route to indoles involved the cycloaddition of *N*-phenylmaleimide **162** to the osmium-complexed vinylpyrrole **161**, followed by decomplexation and DDQ oxidation.[114] A completely substituted quinoline **165** has been prepared by the cycloaddition of DMAD and thiophene **164**.[115] The aromatisation step involved here is extrusion of the ring sulfur atom from **166** with loss of the methylthio group. The Diels–Alder adducts of quinone imine ketal **167** with dienes **168** and **171** gave naphthalenes **170** and **173** in 91 and 36% yields.[62] 2,3-Disubstituted naphthalenes are also available from the cycloaddition of 2,3-naphthoquinodimethanes and acrylates or maleates (**Scheme 9**).[116] The cycloaddition of DMAD-type dienophiles with isobenzofurans (and heteroaromatic analogues thereof), followed by acid-catalysed rearrangement is typified by the conversion of **179** to **180**.[117] Many further examples of this sequence have been reported in the review period.[118–121]

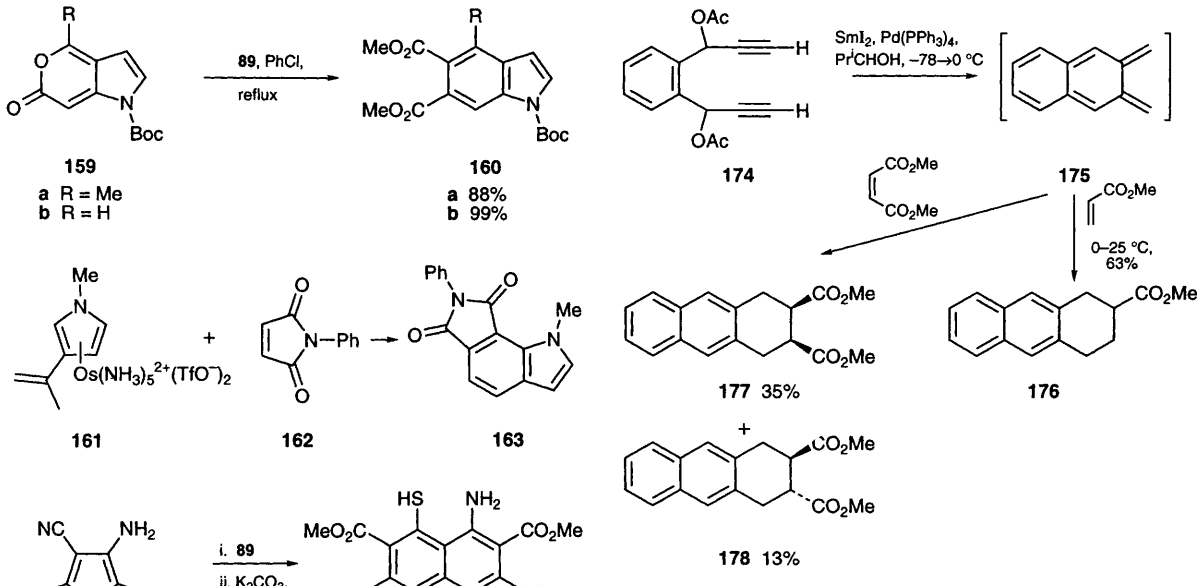
3.1.1.3 Tricyclic systems

Extending their work on the cycloadditions of 2,3-naphthoquinodimethanes to reactions with fumarates, followed by a DDQ aromatisation, Inanaga and co-workers have recently described a synthesis of 2,3-disubstituted anthracenes **181** (**Scheme 10**).[116] Polyhydroxylated anthraquinones occur widely in natural products, and many groups have devised synthetic strategies towards these targets based upon cycloadditions.[122–126] As part of their route to the pigments G-ZN and G-ZA Kelly and co-workers further elaborated the 3-chloro-5-hydroxy-7-methoxyjuglone **140** to the anthra-

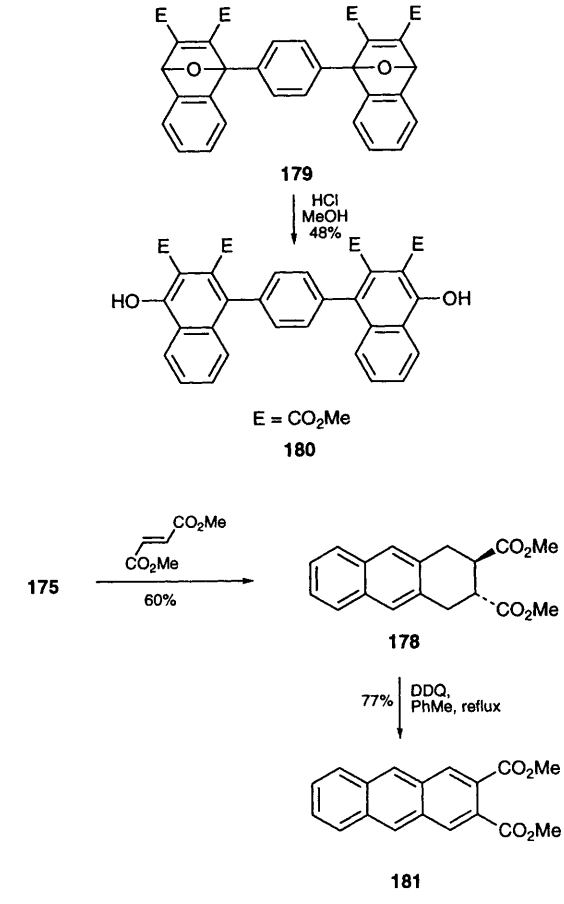


Scheme 8

quinone **183**.[102] The diene **182** can be prepared in a single step from commercially available ethyl α-ethylacetoacetate by deprotonation with LDA followed by quenching with chlorotrimethylsilane. Brassard and Couturier have described the construction of a number of closely related systems,[105] haematommone **188**, norsolorinic acid **189**, solorinic acid **191** and averythrin **190** amongst others (**Scheme 11**). Related routes to pachybasic acid, rhein, aloe-emodin, parietinic acid, emodic acid, fallacinol and citreorosein have also been reported.[127] Lehn has used a double quinone–diene cyclisation to produce building blocks for self assembled supramolecular rigid rods.[128] The reaction of 4,5-dicyanopyridazine **129** with alkenes and alkynes (Section 3.1.1.1) has been extended.

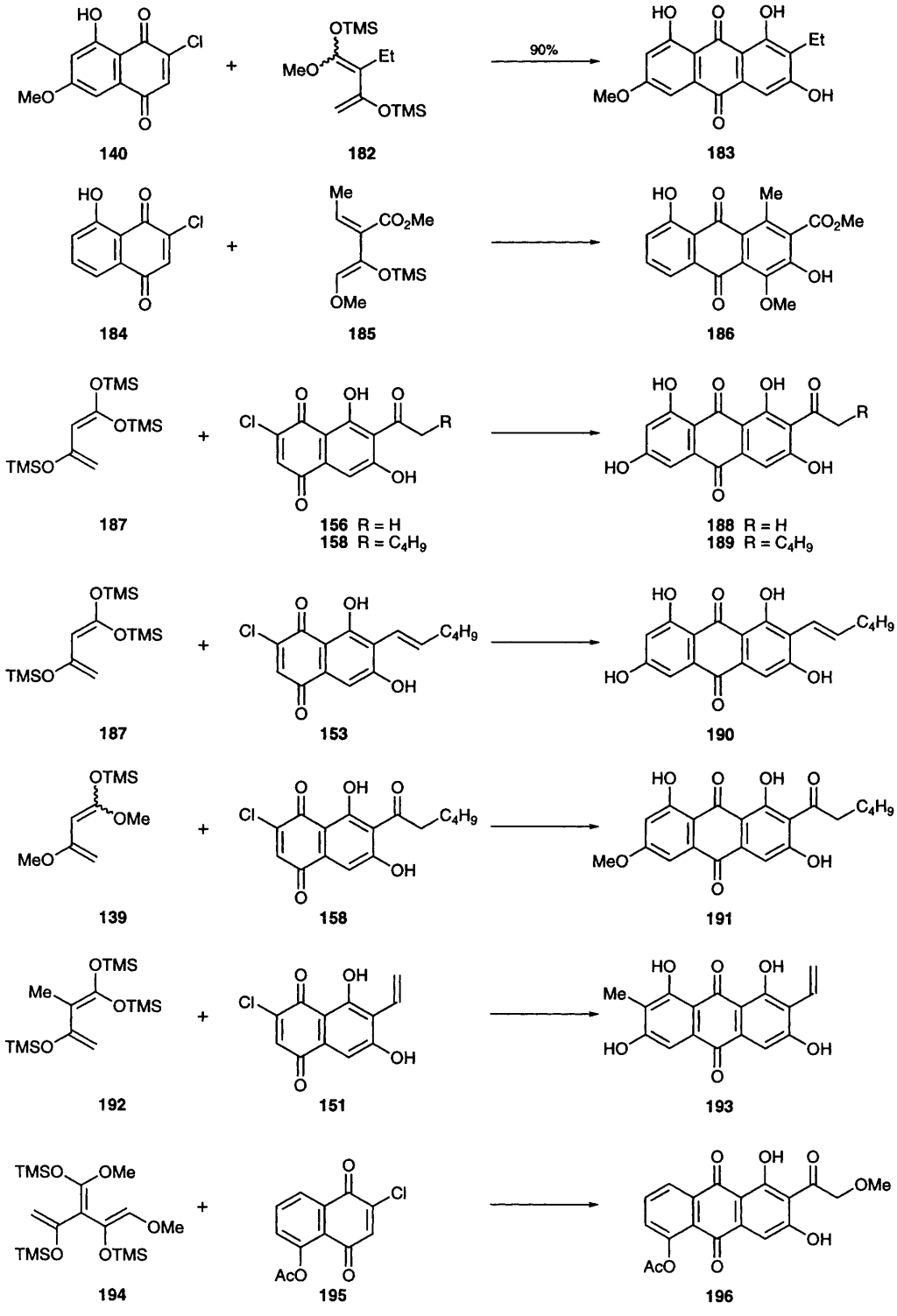


Scheme 9



Scheme 10

Reaction with indoles **197a** and **197b** gave carbazoles **198a** and **198b** in 59 and 53% yield respectively.[98] A related reaction involves the addition of DMAD to quinoxalino-2,3-quinodimethane.[129] Ultrasound was used to promote the cycloaddition of *o*-quinone **200** with diene **199** in a

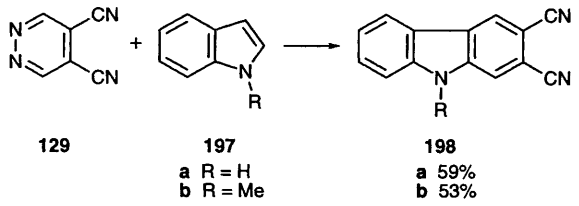


Scheme 11

recent synthesis of (±)-tanshindiol A.[130] Reactions of the related tryptamine-4,5-dione have also been reported.[131] Aminocarbazoles have been synthesised by the addition of DMAD to 2,4-dihydropyrrolo[3,4-*b*]indoles **203**.[132] Vogel has described the use of his 'naked sugar' technology in a recent synthesis of a tetrahydronaphthacene.[133]

3.1.1.4 Higher-order polycyclic systems

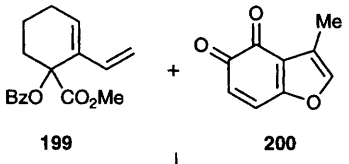
Building upon the use of halojuglones to prepare anthraquinones (Section 3.1.1.3), a recent report has detailed the cycloaddition of unsymmetrical quinones such as **205** with furanoquinodimethanes **206** to give anthraquinones **207** and **208**.[134] An



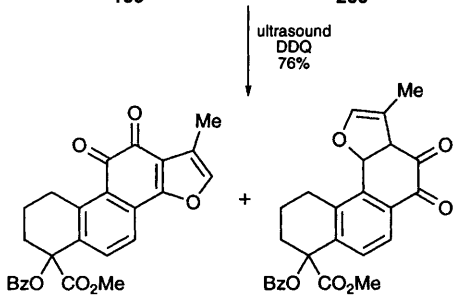
129 197 198

a R = H
b R = Me

a 59%
b 53%

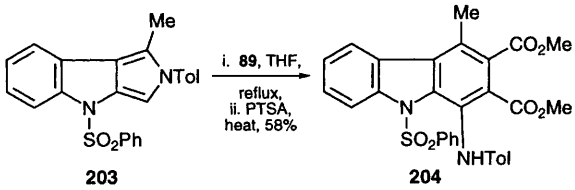


199 200

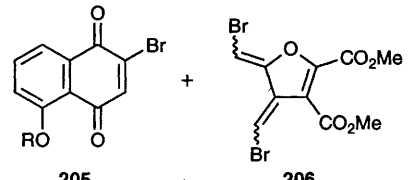


201 202

201 : 202 = 2.5 : 1

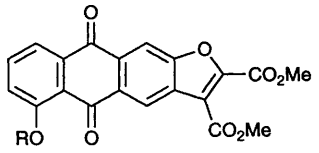


203 204

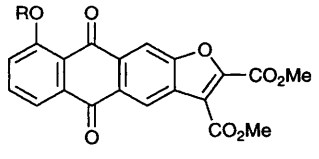


205 206

a R = H
b R = Ac



207



208

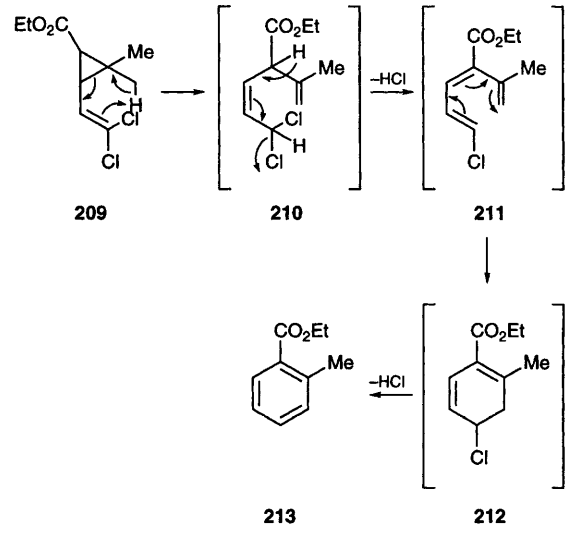
a 72% 207 : 208 = 4 : 1
b 72% 207 : 208 = 3 : 1

approach to unsymmetrically substituted triphenylenes has been described.[135]

3.1.2 Intramolecular cycloadditions

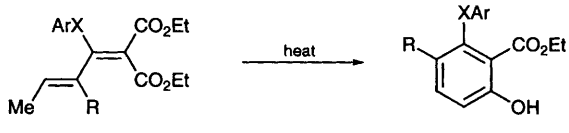
3.1.2.1 Monocyclic systems

Cyclisation of cyclopropane **209** to toluate **213** is thought to proceed *via* an ene–Cope–dehydrochlorination sequence (**Scheme 12**).[136] Thermolysis of diesters **214** gave the substituted salicylates **215**, probably *via* the enol.[137] Coupling of the aminosilane **216** with alcohol **217**, followed by intramolecular Diels–Alder reaction, gave the tetrasubstituted arene **219** (accompanied by a larger quantity of unaromatised cyclohexadiene).[138] Cyclisation of the furan derivatives **220** and **222**, followed by (or perhaps following?) a base-catalysed rearrangement, gave the phenols **221** and **223** in good yields.[139,140] Later work by the same group showed that alkyne to allene isomerisation preceded



209 210 211 213 212

Scheme 12

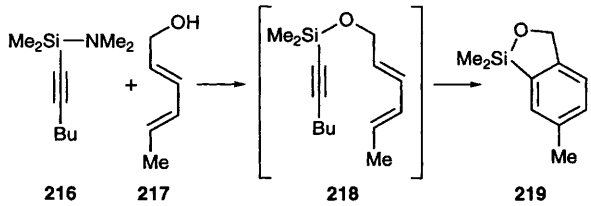


214

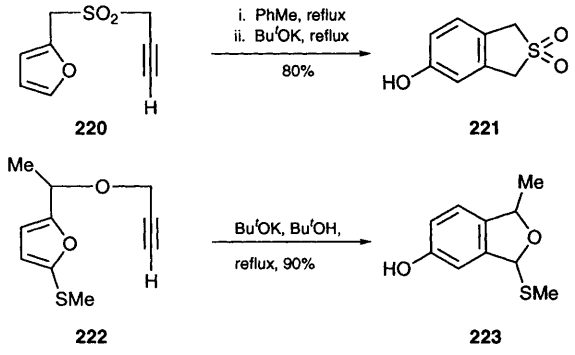
a Ar = Ph, X = O, R = H
b Ar = Ph, X = O, R = Me
c Ar = 4-MeOC$_6$H$_4$, X = O, R = H
d Ar = Ph, X = S, R = H
e Ar = 4-ClC$_6$H$_4$, X = S, R = H

215

a 75%
b 29%
c 56%
d 43%
e 61%

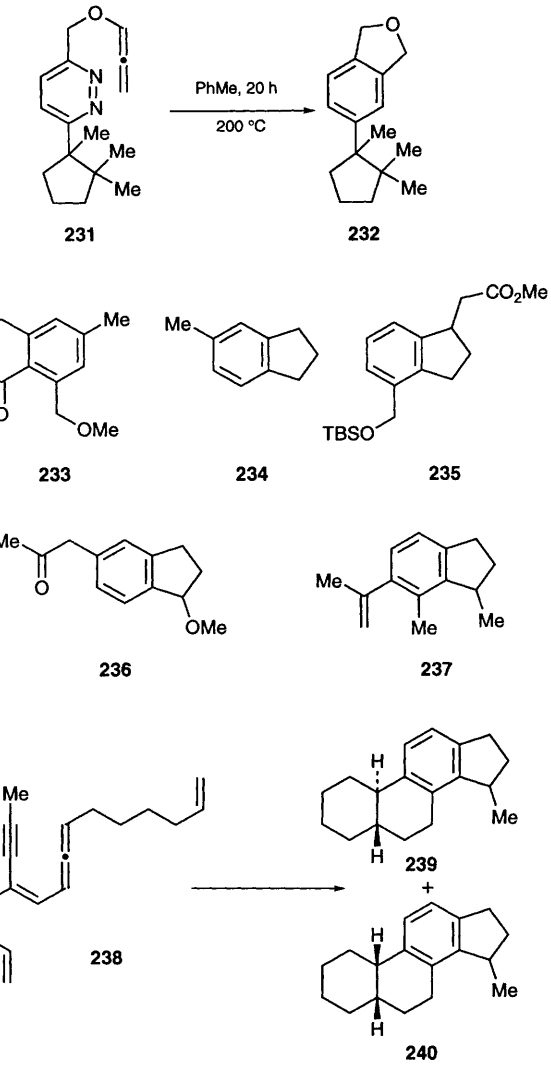


216 217 218 219



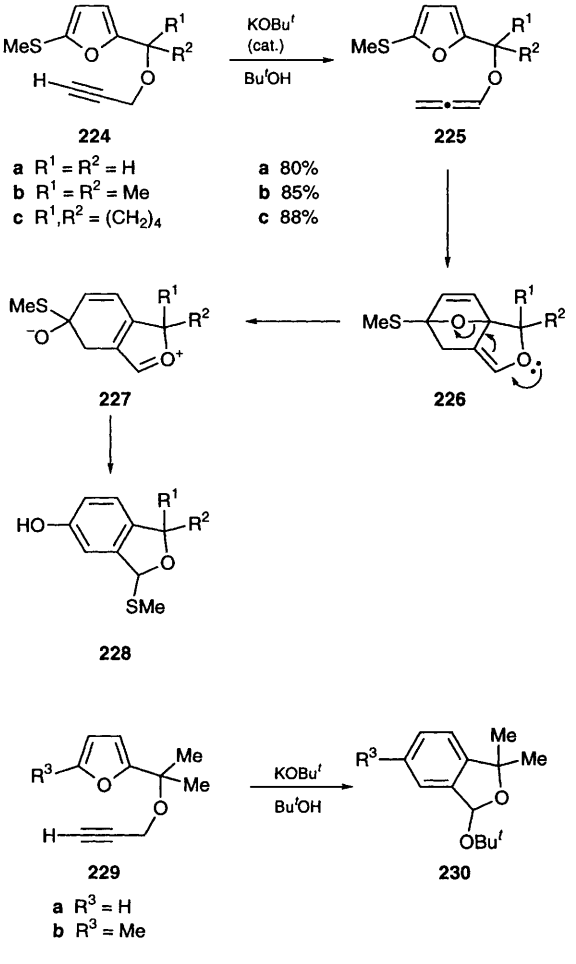
220 221 222 223

cycloaddition, and that the final products were formed *via* zwitterionic intermediates (**Scheme 13**).[141] The related reaction of thiophenes, followed by oxidation and extrusion of sulfur dioxide, has been reported.[142] Isomerisation of allene **231** to an alkyne, followed by cyclisation and loss of nitrogen gave dihydrobenzofuran **232**.[143] A number of synthetic strategies have been devised, mechanistically based upon the enediyne antibiotics, whose synthesis and chemistry are reviewed in earlier editions of this journal.[8,144] These are typified by the preparations of tetralone **233**,[145] indanes **234**,[145] **235**,[146] **236**[147] and **237**[148] and steroid skeletons **239**



231 232 233 234 235 236 237 238 239 240

and **240** from **238**.[149] Further related cyclisations have been reported,[150–153] and a number of higher-order polycyclic aromatic systems prepared.[154–157] Cyclisation of ester **241**, followed by loss of the elements of isobutyric acid gave tetralone **242** in 24% yield.[158] The triene **243**, after *in situ* oxidation of the initially formed cycloadduct, gave the indane **244**.[159] Because of its occurrence in a range of

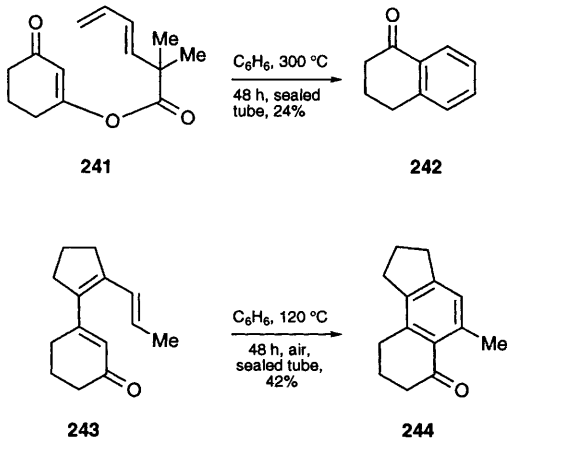


224 225 226 227 228 229 230

a $R^1 = R^2 = H$
b $R^1 = R^2 = Me$
c $R^1,R^2 = (CH_2)_4$

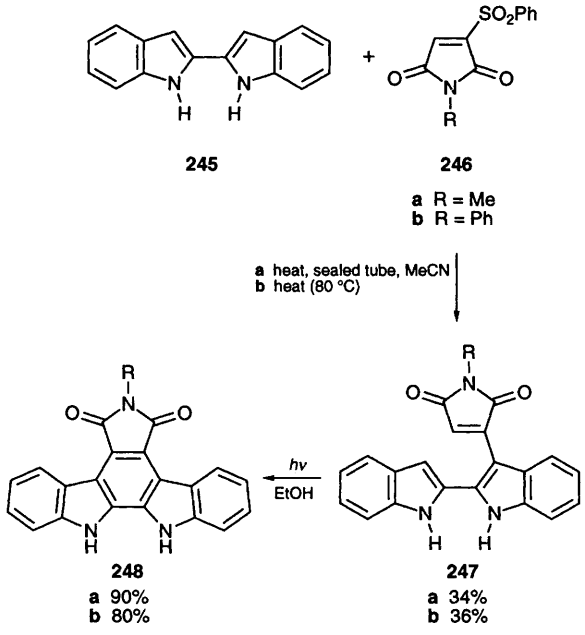
a $R^3 = H$
b $R^3 = Me$

Scheme 13



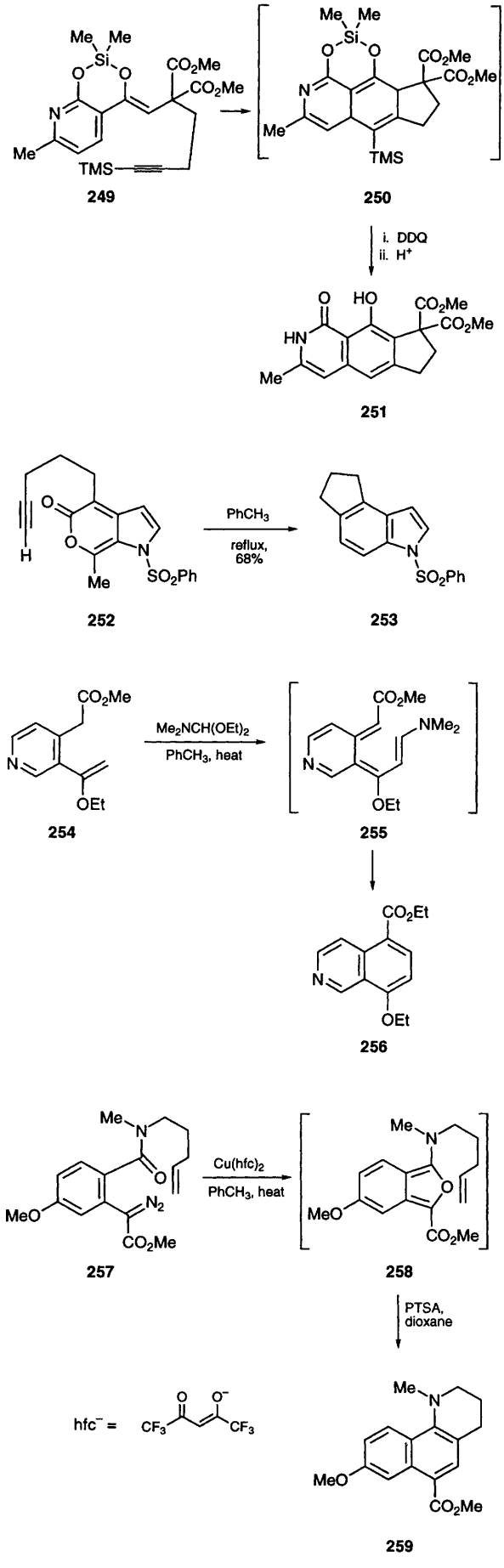
241 242 243 244

natural products, there is continued interest in novel syntheses of the indolo[2,3-*a*]carbazole skeleton. A recent approach involves Michael addition of the bisindolyl **245** to maleimide **246**, elimination of benzenesulfinic acid, followed by photocyclisation with *in situ* oxidation to give **248**.[160] Closure of the central carbocyclic ring is a commonly employed strategy in this area.[161–166]



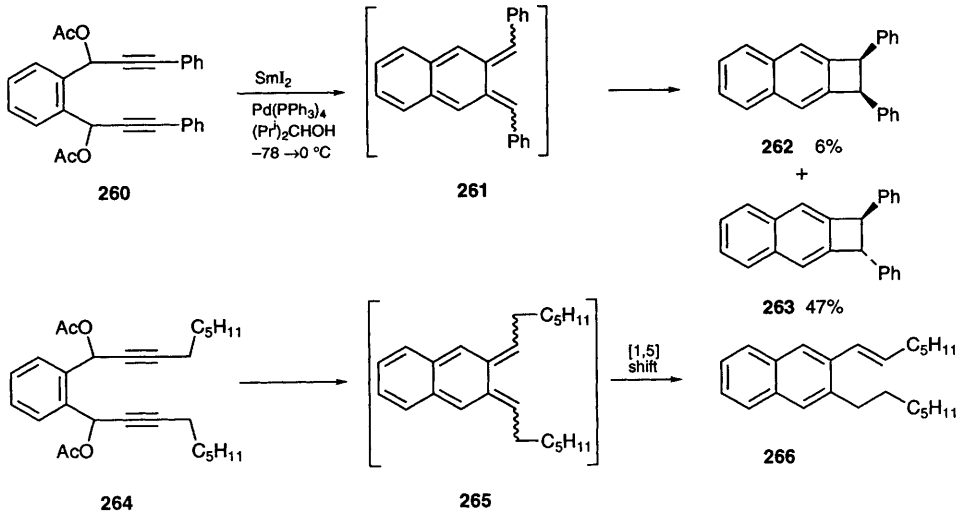
3.1.2.2 Bicyclic systems

Cyclisation of the silylene-protected 2-pyridone **249** followed by DDQ oxidation gave, after hydrolysis, the hydroxyisoquinolone **251**, which was used in a synthesis of the DEF ring fragment of fredericamycin A.[167] As discussed in Sections 3.1.1.1 and 3.1.1.2, 2-pyrones will react with alkynes to give, after loss of carbon dioxide, benzenoid aromatics. In an intramolecular variant of this Moody and co-workers have prepared the substituted indole **253** from 1,5-dihydropyrano[3,4-*b*]pyrrol-5-one **252**.[168] Conversion of ester **254** to enamine **255** by reaction with *N*,*N*-dimethylformamide diethyl acetal was followed by intramolecular cyclisation and elimination of dimethylamine, to give isoquinoline **256**.[169] Conversion of amide **257** to tetrahydrobenzoquinoline **259** was effected *via in situ* formation of the isobenzofuran **258** and dehydration.[170] Intramolecular [2+2] cycloaddition and [1,5] sigmatropic hydrogen shifts in appropriately functionalised 2,3-naphthoquinodimethanes gave various 2,3-disubstituted naphthalenes (**Scheme 14**).[116] Tri-, tetra- and penta-substituted naphthalenes have been prepared by microwave irradiation of 4-aryl-4-alkylhex-5-en-2-ones.[171]



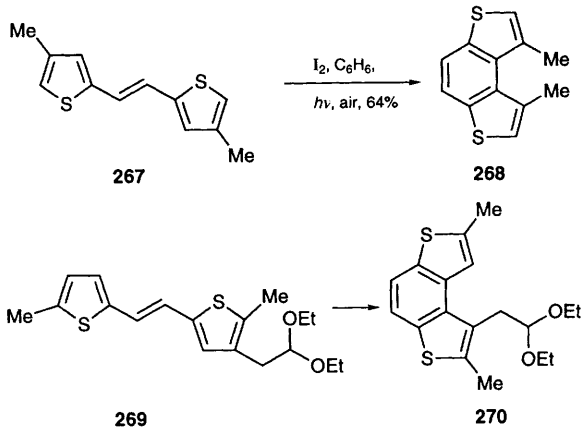
3.1.2.3 Tricyclic systems

In an extension of their intramolecular pyrone cycloaddition strategy, Moody and co-workers have



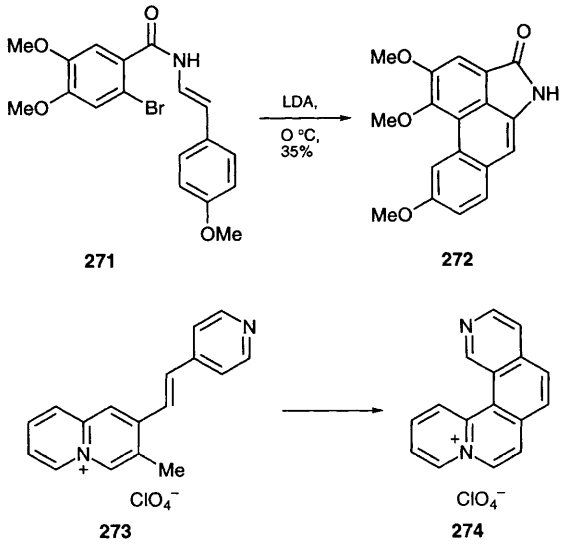
Scheme 14

recently reported a carbazole synthesis.[172] Further intramolecular Diels–Alder approaches to carbazoles have also been described.[173,174] Isomerisation of alkene **267** was followed by photocyclisation and aerial oxidation to give tricyclic **268**.[175] Similarly **269** was converted to **270**.[176] Stilbene–phenanthrene cyclisation remains a frequently adopted approach to this ring system.[177,178] Intramolecular cyclisation of benzynes to, for example, aristolactam **272** has been recently described.[179] Substituted anthracenes and phenanthrenes have been prepared in reactions proceeding from didehydro[10]annulenes *via* diradical intermediates.[180]



3.1.2.4 Higher order polycyclic systems

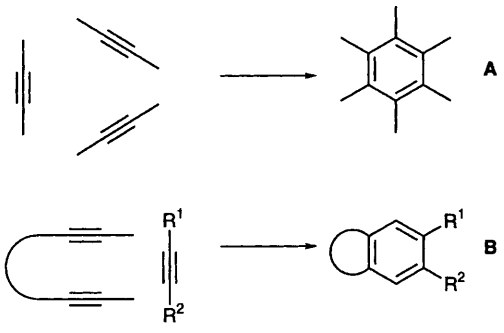
In a sequence entirely analogous to that discussed for **268** and **270** in 3.1.2.3, the quinolizinium salt **273** was cyclised to the 6-methylisoquinolino[7,8-*a*]quinolizinium salt **274** in excellent yield.[181] A halogen radical-initiated diyne cyclisation resulting in a range of polycyclic aromatic hydrocarbons has been reported.[182] A simple route from stilbenoids to extended aromatic hydrocarbons *via* cycloaddition–cyclodehydrogenation has been described.[183] Cyclo-

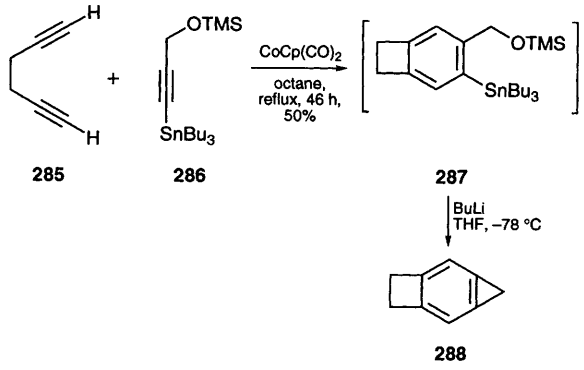


addition-based strategies for the preparation of higher-order polycyclic aromatic hydrocarbons and helicenes have been employed.[184,185]

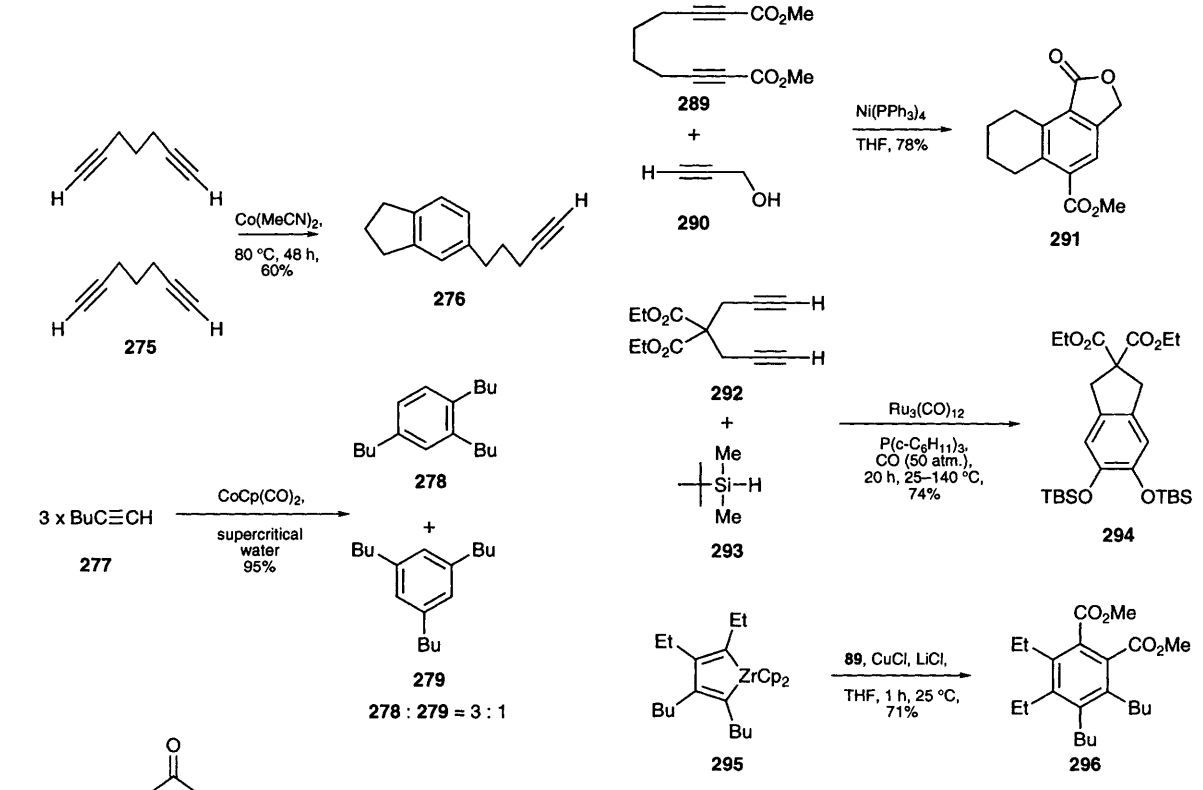
3.2 Transition metal-templated cycloadditions

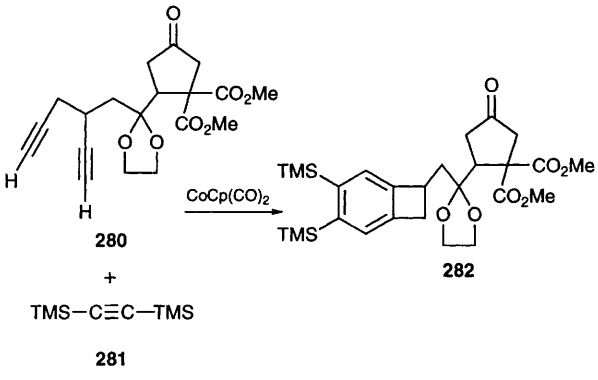
A number of transition metals have been used to catalyse the conversion of three moles of alkyne into an arene. This may involve cyclisation of three molecules of a mono-alkyne, path **A**, or a diyne plus mono-alkyne cyclisation path **B** (**Scheme 15**).[186] There is a particularly large body of literature describing the use of cobalt carbonyl complexes for these cyclisations, the wide scope of which is only hinted at by the examples shown.[187–194] Other metals which have been used include rhodium,[195] nickel[196] and zirconium.[197,198] In the reaction of diyne **292** with *tert*-butyldimethylsilane **293**, two moles of carbon monoxide were incorporated to produce the catechol derivative **294**.[199] In a related reaction, allenylcyclopropanols were rearranged to 2,3-disubstituted hydroquinones, with the incorporation of

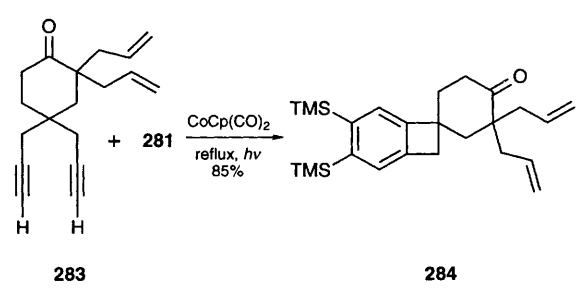




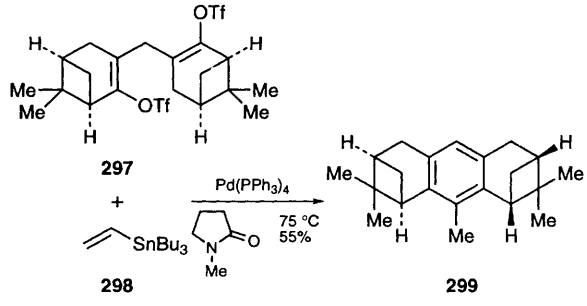
Scheme 15

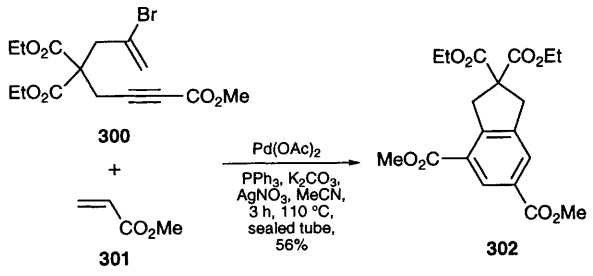




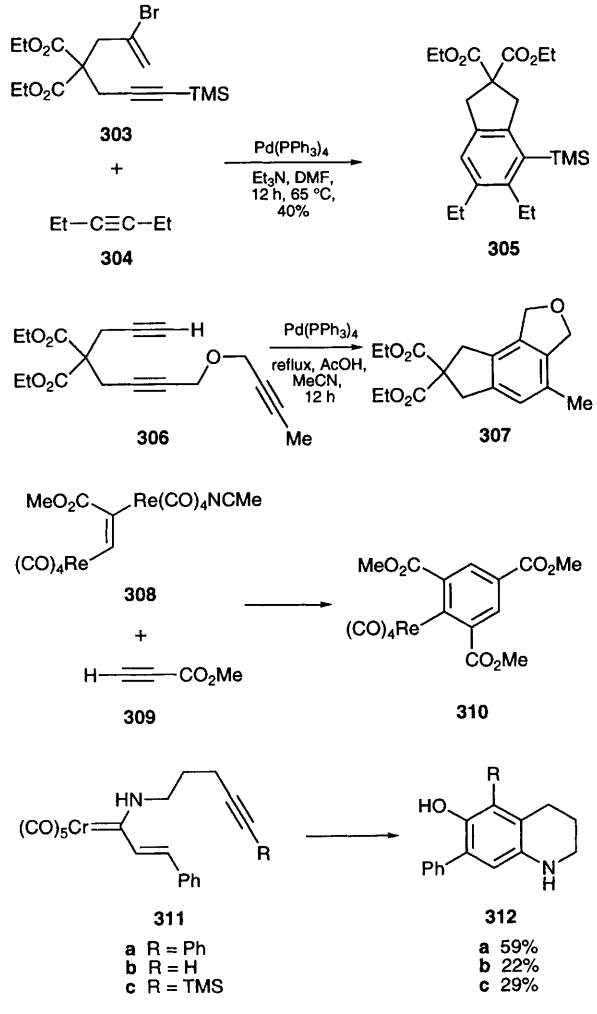


one mole of carbon monoxide.[200] The tetraalkylphthalate **296** was produced in 71% yield by copper(I)-catalysed cycloaddition of alkynes to zirconacyclopentadiene **295**.[198] Tandem Stille coupling–intramolecular Heck vinylation of bis(trifluoromethanesulfonate) **297** with vinylstannane **298**, under palladium(0) catalysis, gave a 55% yield of pentasubstituted arene **299**.[201] Other palladium(0)-mediated cyclisations converted bromoalkenes **300**



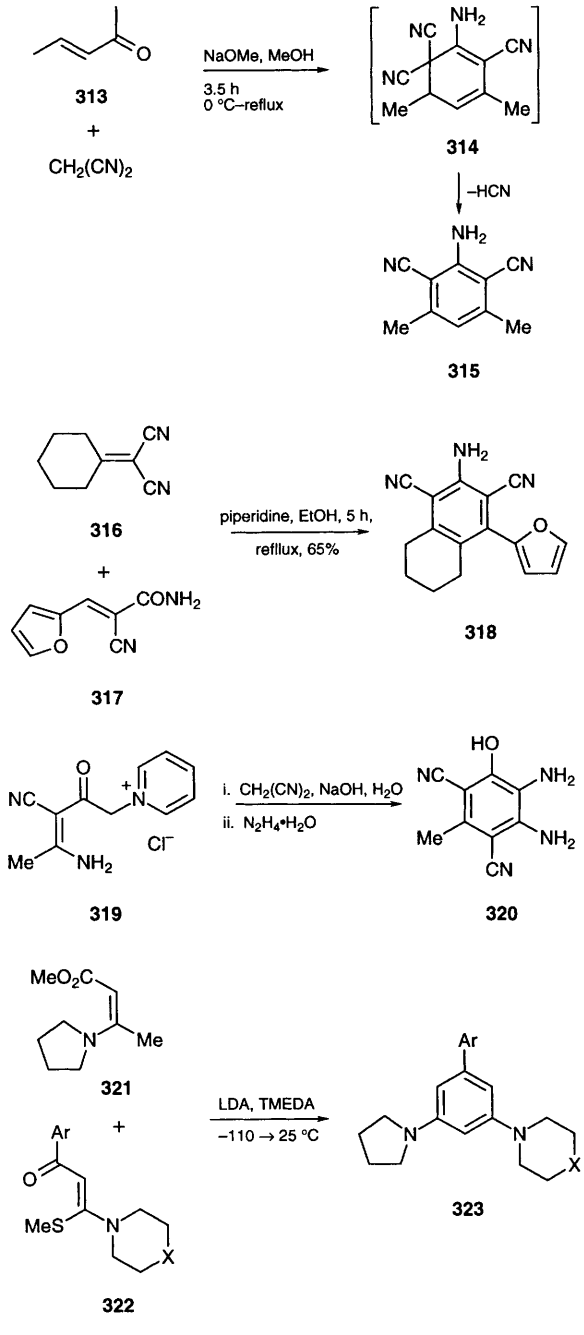


and **303** to indanes **302** and **305**[202,203] and triyne **306** to **307**.[202] Negishi has recently reported the intramolecular Heck reaction of bromoarylallenes, giving substituted naphthalenes.[204] The dirhenium carbonyl complex **308** coupled with two moles of methyl propiolate to give the rhenium aryl complex **310**.[205] The aminocarbene complexes **311** underwent cyclisation to the tetrahydroquinolines **312** upon heating.[206] Allenes have been coupled with DMAD-type alkynes using palladium or platinum catalysts to give, after DDQ oxidation, 2,3,6,7-tetrasubstituted naphthalenes.[207] For further examples readers should refer to the excellent review of this area, to be found in *Comprehensive Organometallic Chemistry II*.[186] The Dotz benzannnulation reactions of Fischer carbene complexes have been reviewed;[9] some very recent examples of this approach have appeared in the literature subsequent to this review.[208–211]

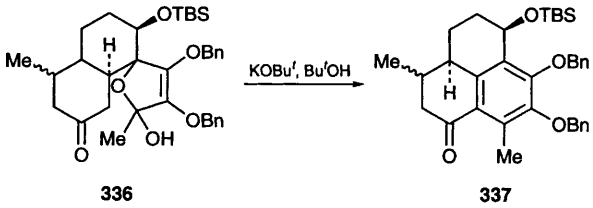


4 Base-catalysed condensations

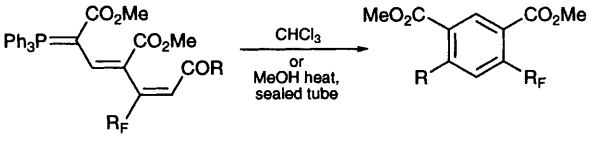
Malononitrile condensed with enone **313** with sodium methoxide in methanol to give aminodinitrile **315**;[212] in a related reaction, cycloalkylidene malononitriles such as **316** condensed with arylmethylenecyanoacetamides such as **317**, to produce cycloalkano-fused arenes **318**.[213] The pyridinium salt **319** condensed with malononitrile to give, after treatment with hydrazine, phenylenediamine **320**.[214] 3,5-Bis(cycloalkylamino)biphenyls **323** were generated by the reaction of the anion of enamino ester **321** with α-oxoketene-*N*,*S*-acetals **322**.[215] The anion



of methyl propiolate **325** condensed with cyclohexenone **324** to give the dihydronaphthalene derivative **326**.[216] Dihydroxyisoquinolone **328** was prepared in 76% yield by the Dieckmann cyclisation of keto ester **327**.[217] Related base-catalysed condensations converted pyrimidinedione **329** to thioethers **331** and **333**,[218] and pyrimidinecarboxylate **334** to diester **335**.[219] Hydroxyquinazolines were prepared in a similar manner.[220] Ring closure of hemiacetal **336** to tetralone **337** was effected by treatment with potassium *tert*-butoxide in *tert*-butyl alcohol, with the loss of two moles of water.[221] Heating the phosphoranes **338** in chloroform or methanol led to the formation of substituted isophthalates **339**.[222] A general process for the preparation of 3-alkyl and 2,3-dialkyl-1-naphthols **341** by the base-catalysed cyclisation of alkynyl aceto- and propio-phenones **340** has been reported.[223] Lithiation of 1,2-dimethylindole-3-carbaldehyde furnishes an indole-2,3-dienolate, which has been trapped with a variety of

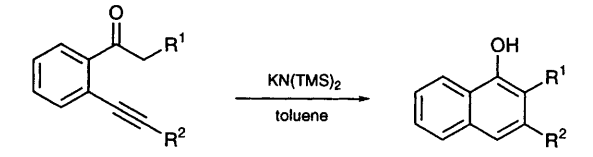


336 **337**



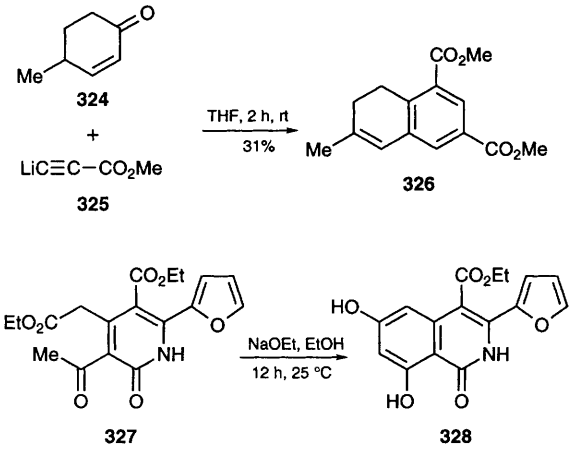
338 **339**

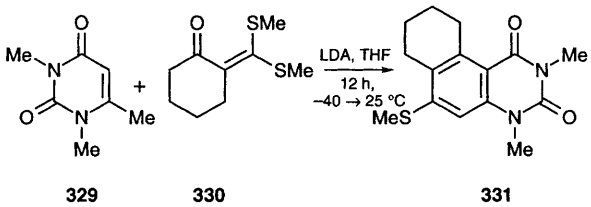
a R = Me, $R_F = CF_3$
b R = Me, $R_F = C_3F_7$
c R = Ph, $R_F = CF_3$
d R = Ph, $R_F = C_3F_7$

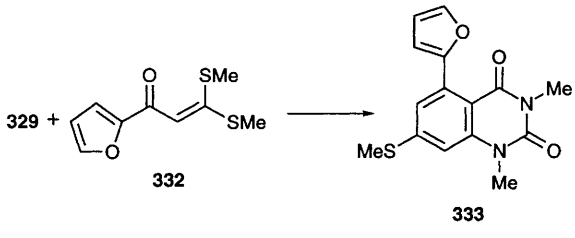


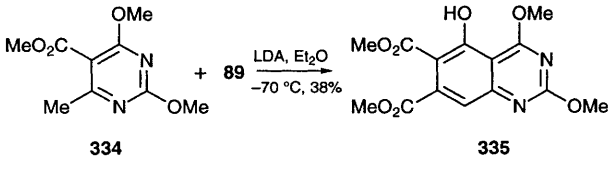
340 **341**

a R^1 = H, R^2 = Me	**a** 74%
b R^1 = H, R^2 = c-C_6H_{11}	**b** 92%
c R^1 = H, R^2 = Bu^t	**c** 75%
d R^1 = H, R^2 = Bn	**d** 95%
e R^1 = H, R^2 = Ph	**e** 0%
f R^1 = Me, R^2 = C_6H_{13}	**f** 70%



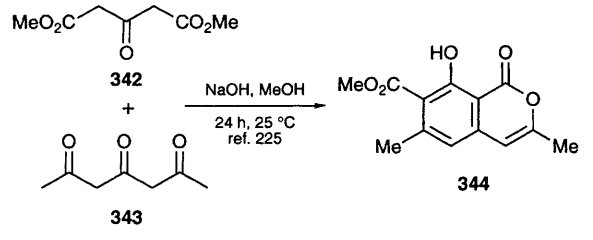


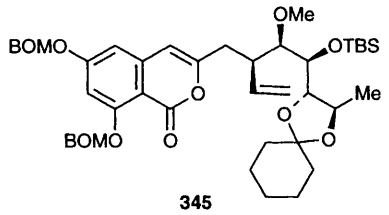




alkynes and alkenes to give carbazoles and dihydrocarbazoles, through an anionic [4+2] cycloaddition or a tandem Michael–aldol process depending on your point of view.[224]

Base-catalysed condensations of polyketides have found wide application for the construction of complex natural product aglycones, for example in fredericamycin A,[225] olivin[226] and in the conversion of **347** to **349**.[227] A related condensation was employed in the synthesis of urdamycinone B.[228] Intramolecular base-catalysed condensation, followed by reduction and dehydration, gave the ellipticine analogue **351**.[229] Addition of anion **352** to enone **353**, followed by loss of methanol and benzenesulfenic acid, gave the methoxsalen precursor **354** in 77% yield.[230] The same group reported a very similar route to benzo[*f*]indenone **356**.[231] Reaction of anions **357** with furanone **358**, followed by dehydration and dehydrogenation gave the aryl-substituted naphthofuranones **359**.[232]





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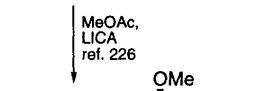
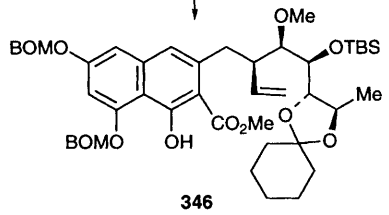
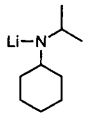
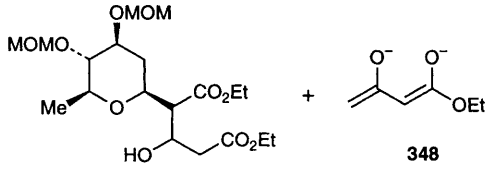




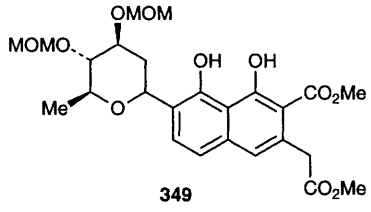
346

BOM = $PhCH_2OCH_2$

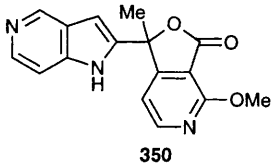
LICA = 



347 348

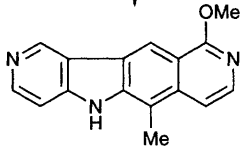


349

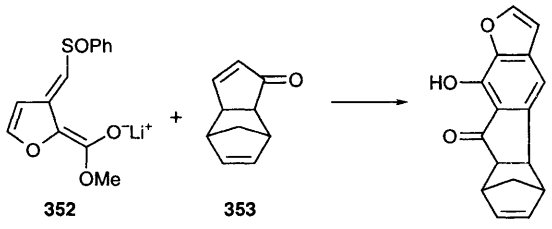


350

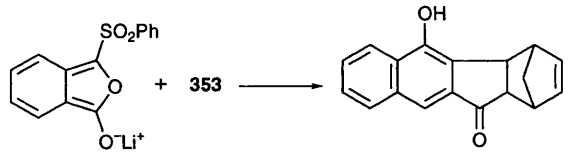
i. NaOH, MeOH, H_2O, 0–20 °C
ii. $NaBH_4$, diglyme, 130 °C



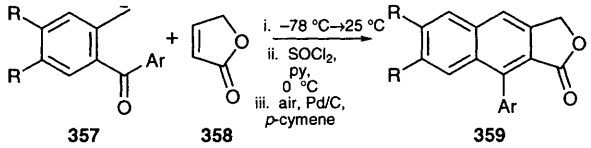
351



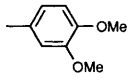
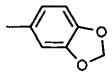
352 353 354



355 356



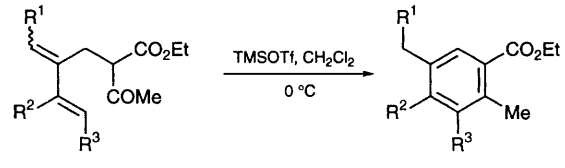
357 358 359

a R = H, Ar = Ph
b R = OMe, Ar = 
c R = OMe, Ar = 

a 31%
b 46%
c 26%

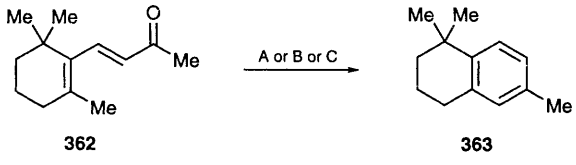
5 Acid-catalysed condensations

Treatment of the diene esters **360** with trimethylsilyl trifluoromethanesulfonate led to the formation of benzoates **361**.[233] Cyclisation of β-ionone **362** to tetralin **363** has been effected by a number of reagents, for example iodine[234] and bromoform.[235] The yields are comparable to those obtained with toluene-*p*-sulfonic acid reported much earlier.[236] As might be expected, Friedel–Crafts-based cyclisations have been widely employed for the construction of aromatic systems of various degrees of complexity. For example the dihydrobenzopyran **365** was obtained in 78% yield upon treatment of the acid **364** with oxalyl chloride,[237] and the indenes **367** and **369** from fulvenes **366** and **368**.[238] Friedel–Crafts



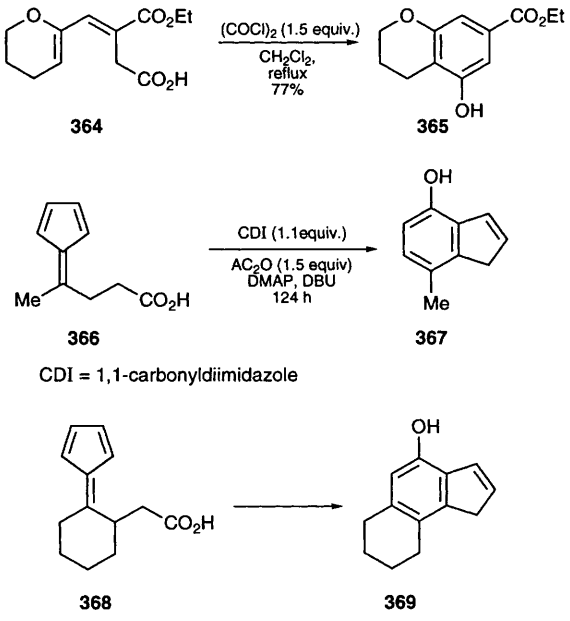
360 361

a R^1 = Ph, R^2 = R^3 = H — a 50%
b R^1 = Ph, R^2, R^3 = $(CH_2)_4$ — b 70%
c R^1 = $(CH_2)_6Me$, R^2 = R^3 = H — c 0%
d R^1 = $(CH_2)_6Me$, R^2 = Me, R^3 = H — d 53%
e R^1 = H, R^2 = Me, R^3 = H — e 29%



362 363

A. I_2, 30 min, 110 °C, 80–95%
B. $CHBr_3$, icosane, Ar, 27 h, 20 °C, ultrasound, 79%
C. PTSA (cat), C_6H_6, N_2, reflux, 8 h, 95 %



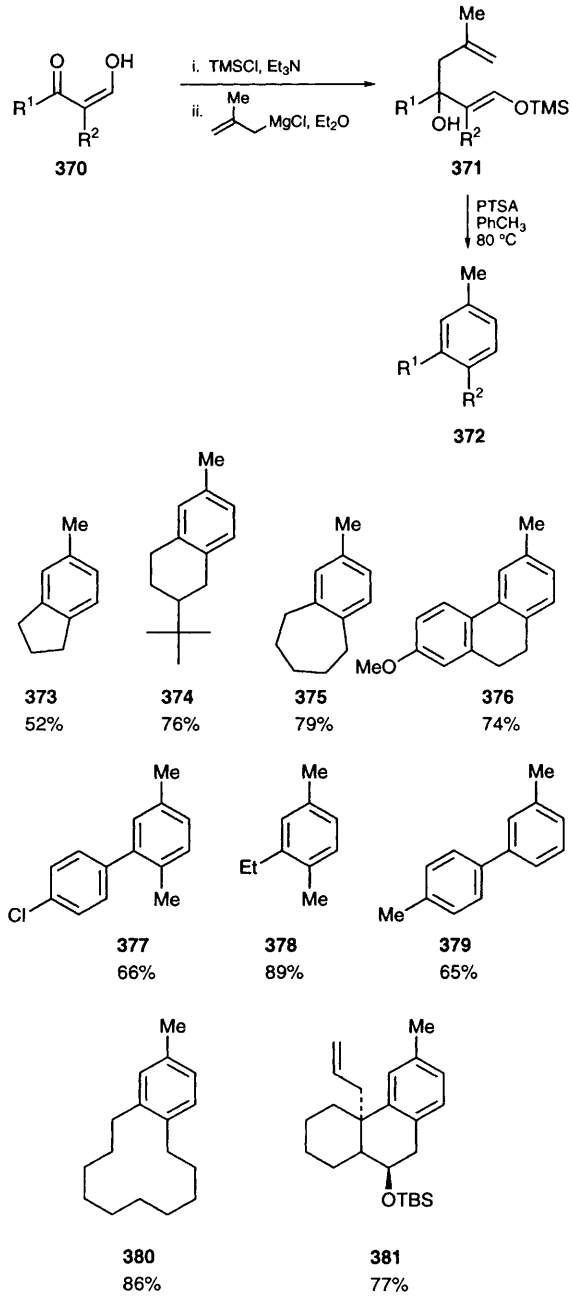
364 365 366 367

CDI = 1,1-carbonyldiimidazole

368 369

reactions have been used to prepare anthrols, anthraquinones, indoles and anthracenes.[239–242] Appropriately substituted dinitriles have been cyclised to cyanonaphthylamines with sulfuric acid.[243] A practical and efficient method for the benzannulation of ketones has been described, involving the addition of a Grignard reagent to a ketone, followed by acid-catalysed cyclisation (**Scheme 16**).[244] The range of products accessible by this route is indicated by **373** to **381**. The use of other Grignard reagents and cyclisation conditions is also discussed.

Cyclisation of the acids **382** to the juglone precursors **383** was achieved in good yields. The juglones were used to prepare a range of naturally occurring anthraquinone-2-carboxylic acids (Section 3.1.1.3).[127] Reaction of keto diester **384** with diacetal **385** in the presence of titanium(IV) chloride gave the 2-hydroxyisophthalate **386** in 58% yield.[245] In a related condensation, tricarbonyl compounds reacted with enaminoamines.[246] Treatment of the anion of 3,5-dimethylisoxazole **388** with α-oxoketene dithioacetals **387**, followed by treatment with boron trifluoride, gave the benzoisoxazoles **389** in yields from 54 to 81%.[247] A wide range of substituents R^1 was tolerated; 20 examples were quoted. The reaction failed for $R^1 = R^2 = Me$; $R^1 = Ph$, $R^2 = Me$ and $R^1 - R^2 = -(CH_2)_3-$. Four related demethylthio compounds **391** were also prepared by reaction of β-methylthioenones **390** with anion **388** (**Scheme 17**). Treatment of ketone **392** with toluene-*p*-sulfonic acid in refluxing toluene gave the indole **393** in 48% yield, together with 15% of the isomer **394**.[248,249] In a similar manner indoles **396** and **398** were formed from their respective precursors;[250] further indole syntheses closing the carbocyclic ring have been described.[251] Treatment of cyclopropanecarbonyl chlorides **399** with arenes **400** and aluminium chloride gave aryl-substituted naphthols **401** in yields from 23 to 81% (**Scheme 18**).[252] In related reactions aryl-substituted naphthols **404** and



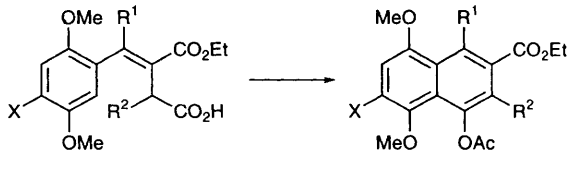
370 371 372

373 52% 374 76% 375 79% 376 74%

377 66% 378 89% 379 65%

380 86% 381 77%

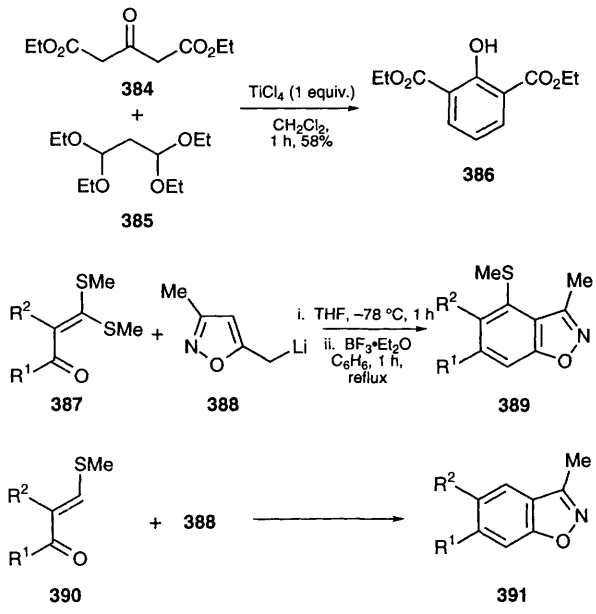
Scheme 16



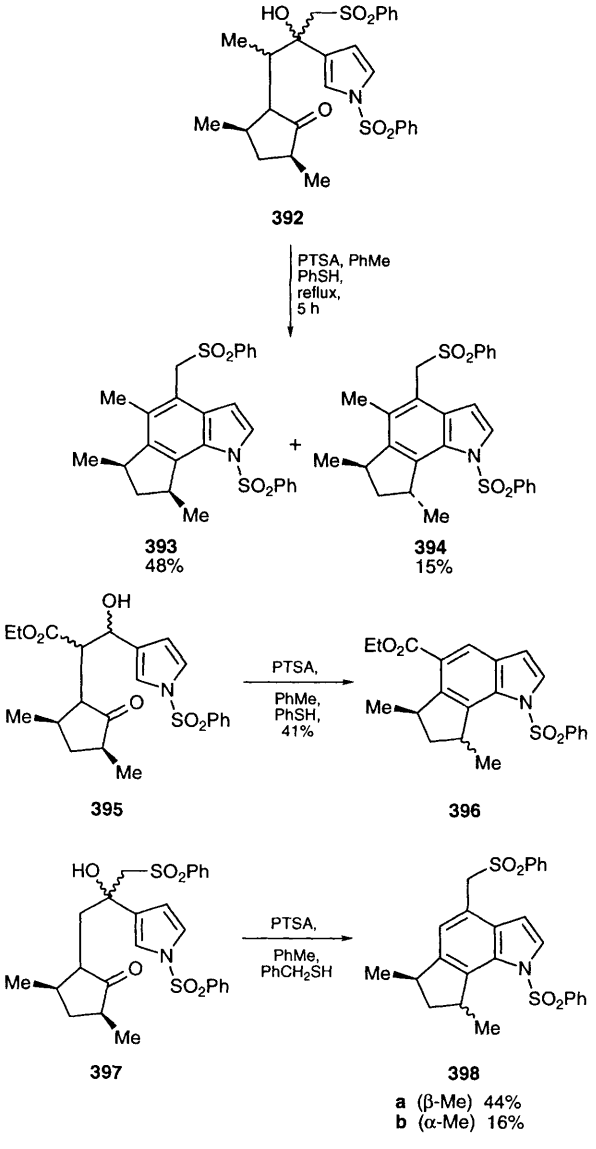
382 383

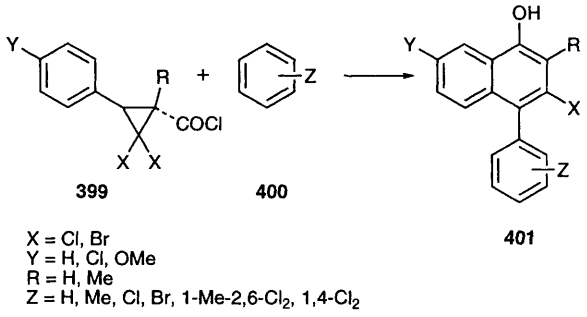
a X = R^1 = R^2 = H
b X = Cl, R^1 = R^2 = H
c X = R^1 = H, R^2 = Me
d X = Cl, R^1 = H, R^2 = Me
e X = H, R^1 = Me, R^2 = H
f X = Cl, R^1 = Me, R^2 = H

a–e 65–70%
f 5%

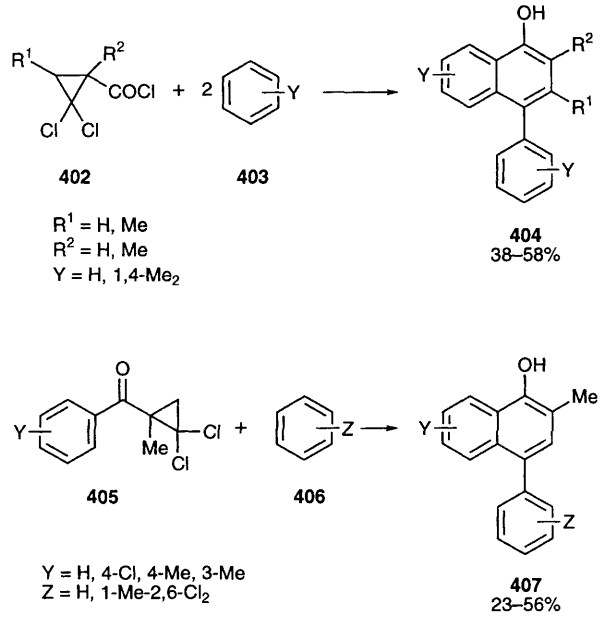


Scheme 17



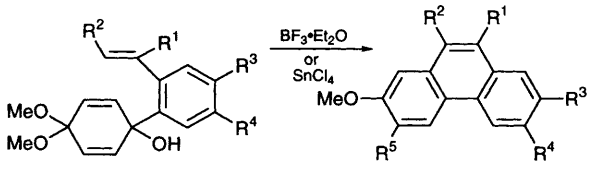


Scheme 18



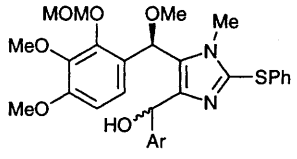
Scheme 19

407 were also prepared (**Scheme 19**). In the first case intramolecular Friedel–Crafts reaction is followed by intermolecular; in the second case one intermolecular Friedel–Crafts reaction is followed by a second, then by an intramolecular Friedel–Crafts cyclisation. The final case supports the proposed mechanism, starting from independently prepared ketones **405** which would be intermediates in the conversion of **402** to **404**. Acid-catalysed cyclisation of quinol ketals **408** gave the phenanthrenes **409** in good yields.[253] Treatment of the imidazole **410** with acetic anhydride, followed by polyphosphoric acid gave the naphthoimidazole **411** in almost quantitative yield:[254] further examples of this approach have been reported.[255,256] Treatment of enol ether **412** with hydrogen chloride in acetic acid–acetic anhydride gave 1-fluoroellipticine **413** in 54% yield.[257] Enamino ketones **414** gave 5-hydroxyquinolones **415** upon treatment with concentrated hydrochloric acid.[258] Acid treatment of the nitrile **416** gave a mixture of 5-hydroxy- and 5-dimethylamino-quinolones **417a** and **417b**. Mild acid treatment of **414a** gave the dimeric tetracycle **418**.

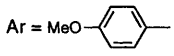


408 409

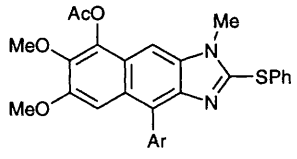
a R^1–R^5 = H — a 64%
b R^1 = Me, R^2–R^5 = H — b 72%
c R^2 = Me, R^1 = R^3 = R^4 = R^5 = H — c 60%
d R^1,R^2 = —$(CH_2)_3$—, R^3–R^5 = H — d 58%
e R^1 = Me, R^2–R^4 = H, R^5 = OMe — e 40%
f R^1 = R^2 = H, R^3 = OMe, R^4 = R^5 = H — f 55%
g R^1 = Me, R^3 = OMe, R^2 = R^4 = R^5 = H — g 42%
h R^1 = Me, R^3,R^4 = —OCH_2O—, R^2 = R^5 = H — h 52%



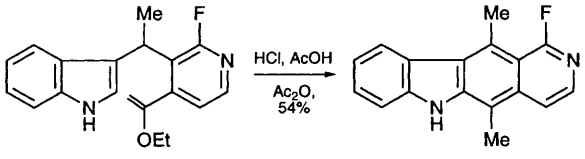
410



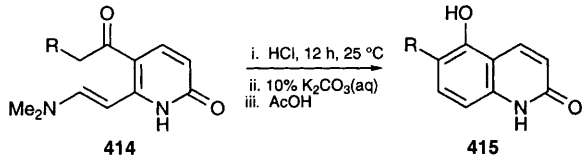
Ar = MeO



411

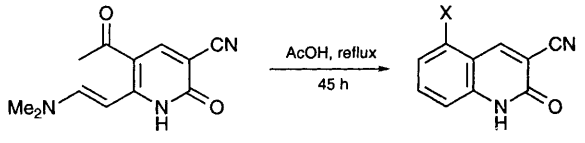


412 413



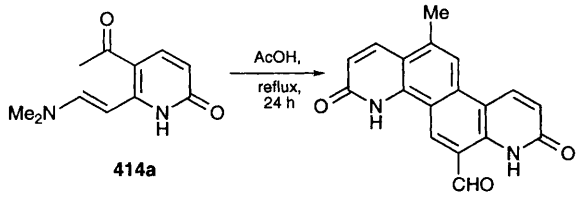
414 415

a R = H — a 90%
b R = Me — b 77%



416 417

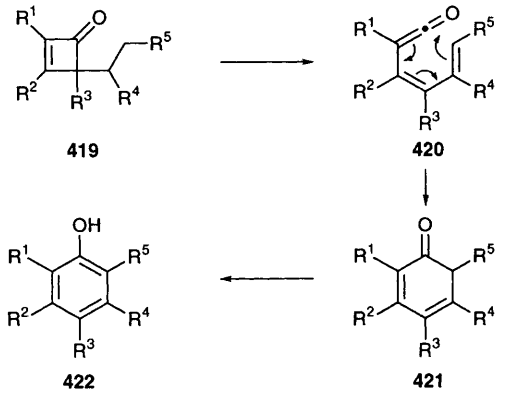
a X = OH, 13%
b X = NMe_2, 34%



414a 418

6 Rearrangements

Two groups, those of Liebeskind and Moore, have developed general routes to highly functionalised arenes based upon the rearrangement of cyclobutenones substituted with unsaturated groups (**Scheme 20**). Flexible routes to the cyclisation precursors have been developed by both groups, allowing variation of the substituents R^1–R^5; space allows only an indication of the full scope of these processes.

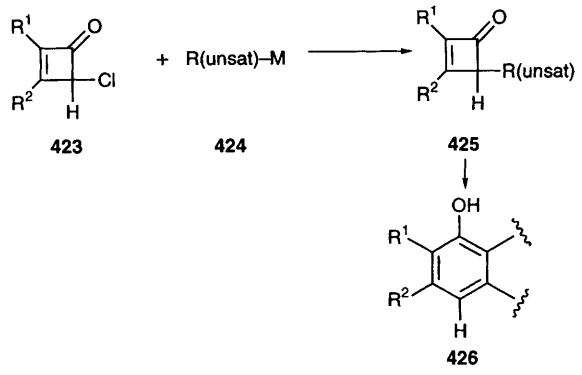


419 420 421 422

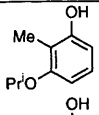
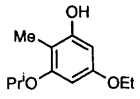
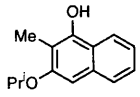
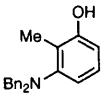
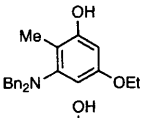
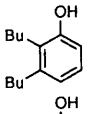
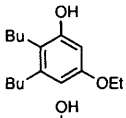
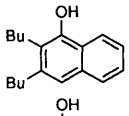
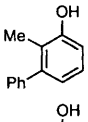
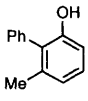
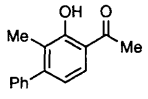
Scheme 20

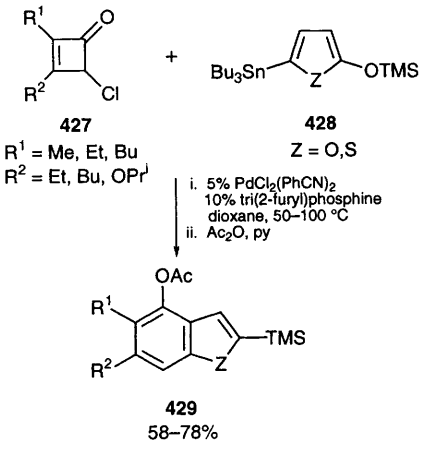
Coupling of the chlorocyclobutenones **423** with stannanes **424** under palladium catalysis gave unsaturated cyclobutenones **425** which rearranged to the phenols **426** (**Scheme 21**).[259] Methods for coupling chlorocyclobutenones with vinylzirconium reagents and subsequent rearrangement of the resulting products were also described. The method has also been applied to the benzannulation of aromatic heterocycles (**Scheme 22**),[260] and has been used as an approach to the otherwise relatively inaccessible benzocyclobutenedione monoacetals **435** and **438** (**Scheme 23**).[261] Examination of the general scheme (**Scheme 20**) shows that hydroquinones **422** (R^3 = OH) and resorcinols **422** (R^2 or R^4 = OR) are readily accessible. By making use of the conjugate addition of unsaturated organometallics **440** to cyclobutenediones **439**, trapping of the enolate so formed, and thermolysis, monoprotected catechols **442** may be prepared (**Scheme 24**).[262] The scope of this reaction variant is illustrated in **Schemes 25** to **27**. By using metallated benzo- or naphthoquinones, highly substituted naphtho- and anthraquinones have been prepared.[263] Recent extensions to the work have been a general route to highly oxygenated, angularly fused polycyclic aromatic hydrocarbons **452**,[264] and acyl-substituted aromatics **453** and **454**.[265]

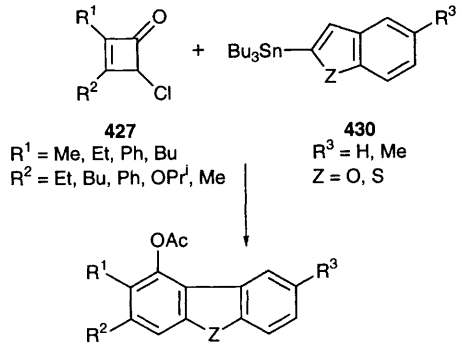
Moore has described a method, based upon the same general principle described above (**Scheme 20**) which allows the preparation of chlorophenols **456** and chloronaphthols **458** (**Scheme 28**).[266] Prior displacement of the halogen substituted with alcohols and thiols gave, after rearrangement, the

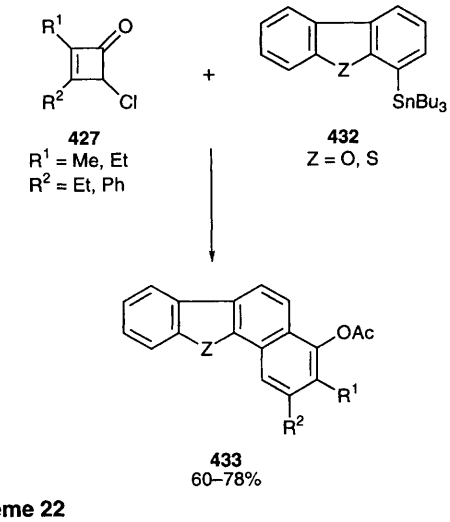


Scheme 21

	R^1	R^2	424	426	Yield (%)
a	Me	OPr^i	$SnBu_3$		67
b	Me	OPr^i	OEt, $SnBu_3$		55
c	Me	OPr^i	$PhSnMe_3$		53
d	Me	NBn_2	$SnBu_3$		62
e	Me	NBn_2	OEt, $SnBu_3$		74
f	Bu	Bu	$SnBu_3$		74
g	Bu	Bu	OEt, $SnBu_3$		54
h	Bu	Bu	$PhSnMe_3$		77
i	Me	Ph	$SnBu_3$		75
j	Ph	Me	$SnBu_3$		75
K	Me	Ph	EtO, COMe, $SnBu_3$		50

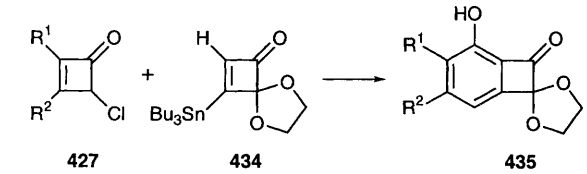






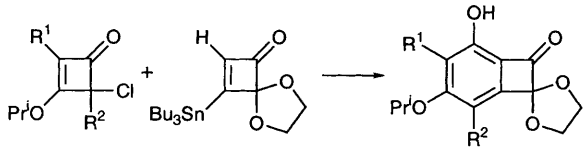
Scheme 22

naphthols **460** and **462**.[266] Rearrangement of alkynyl-substituted chlorocyclobutenones necessarily goes through a diradical of structure **465** (**Scheme 29**).[266] The fate of this depends upon the nature of the substituents R^1 and R^2. Thus, the dipentynylcyclobutenone **466** gave **469** and **470** upon thermolysis, resulting from the two alternative modes of cyclisation of the rearranged radical **468** (**Scheme 29**). The homologous compound **471** gave four products, again resulting from single hydrogen transfer–ring closure (**474** and **475**) or double hydrogen transfer (**472** and **473**). The isomeric cyclobutenone **476** gave the expected spiro compound **477** and alkene **478**, none of the isomeric chromanol, and the radical fragmentation product **479**. Thermolysis of diynes **480** gave only the cyclised products **481**, resulting from ring closure of the rearranged prop-2-ynyl



427 434 435 (56–99%)

R^1 = Me, Et, Bu, Bu^s,Bu^t, Ph
R^2 = Me, Et, Bu, Ph, OPr^i



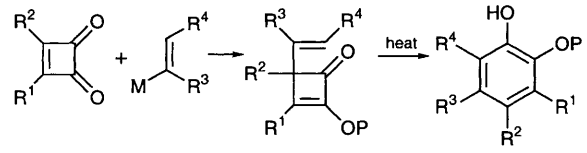
436 437 438

a $R^1 = R^2$ = Bu
b R^1 = Ph, R^2 = Me

a 79%
b R^1 = Me, R^2 = Ph } 57%
c R^1 = Ph, R^2 = Me

438b : 438c = 2 : 1

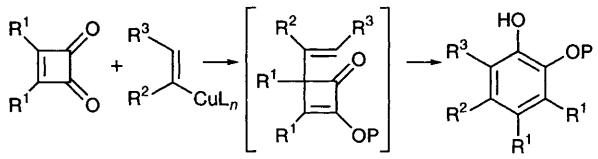
Scheme 23



439 440 441 442

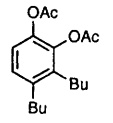
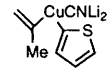
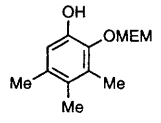
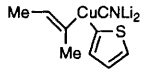
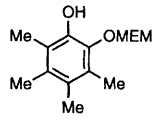
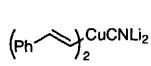
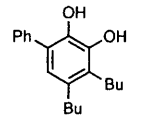
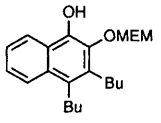
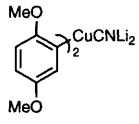
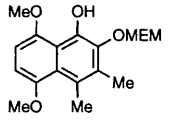
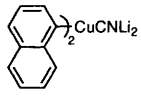
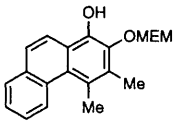
Scheme 24

radicals.[267] A recent application of this approach to pyranoquinone synthesis has been reported.[268] The hydroxycyclobutanone **482** rearranged in 46% yield to hydroquinone **483**.[269] The alkynylmethylenecyclobutene **484** rearranged, on heating in methanol, to the phenol **485** in 42% yield. The diradical **486** is thought to undergo [1,5] hydrogen atom migration to give a quinomethane which was trapped with solvent. Evidence for the intermediacy of diradical **486** came from the isolation, in 65% yield, of phenol **487**, when the reaction was performed in cyclohexa-1,4-diene, arising from hydrogen atom abstraction from the solvent (**Scheme 30**).[270] Rearrangement of allene-substituted alkylidene cyclobutenes **488** gives benzocyclobutenes **489**, *via* orthoquinodimethanes (**Scheme 31**).[271] The geometrical isomers of starting materials **488** were cyclised independently, hence the ranges of yields quoted. The benzocyclobutene **489d** was accompanied by 5% of phenol **490**, which was thought to be derived from an orthoquinodimethane by a [1,5] hydrogen shift. The furanohydroquinone **492** was obtained in good yield upon thermolysis of cyclobutenone **491** in toluene.[272] An application of this methodology to isochromanquinone synthesis has been described (**Scheme 32**).[273] The yields of hydroquinones were not quoted; those shown in **Scheme 32** are minima, in that they represent the isolated yield of quinone, after deprotection and oxidation. Recently, Moore has described a



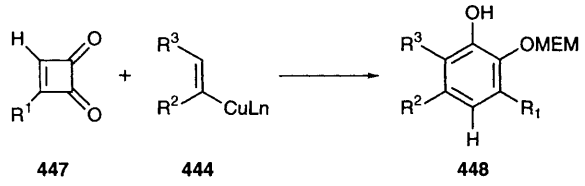
443 444 445 446

Scheme 25

	R^1	444	P	446	Yield (%)
a	Bu	$CuMeCNLi_2$	Ac		95
b	Me		MEM		95
c	Me		MEM		64
d	Bu		Ac		83
e	Bu	$Ph_2CuCNLi_2$	MEM		83
f	Me		MEM		82
g	Me		MEM		64

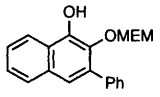
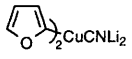
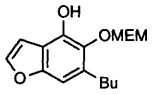
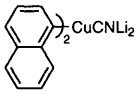
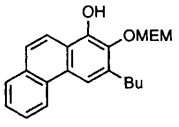
strategy for the synthesis of naphthols complementary to that of Liebeskind,[259] which depends upon the reductive dehydroxylation of 4-hydroxycyclobutenones, rather than a palladium cross-coupling, for the construction of the cyclisation precursors (**Scheme 33**).[274] An extension of this approach involves treating the cyclobutenones **502** with alkyllithium reagents **503**, to give the allenes **504**, which thermolyse to give the acylnaphthalenes **505** in high yield (**Scheme 34**).[275] The synthetic uses of cyclobutenones have been reviewed.[276,277]

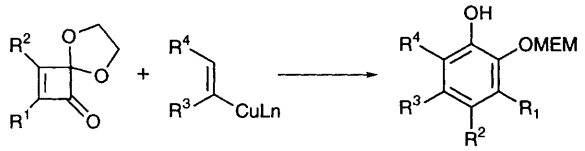
In addition to the general methods described above, a number of reactions of more restricted utility have been reported. Thermal rearrangement of spirothioether **506** gave tetrahydrobenzothiepine **507** in 82% yield.[278] Treatment of the thiazolidines **508** and **510** with *N*-bromosuccinimide in chloroform gave the 2,3-dihydrobenzothiazines **509** and **511** in excellent yields:[279] the authors also described the formation of phenothiazines. Under very similar



447 444 448

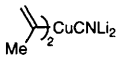
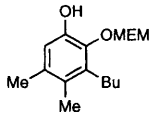
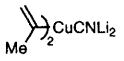
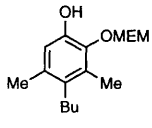
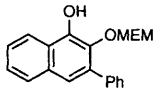
Scheme 26

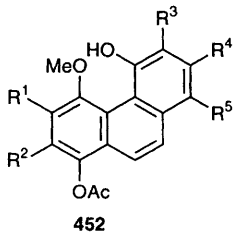
	R^1	444	448	Yield (%)
a	Ph	$Ph_2CuCNLi_2$		69
b	Bu			82
c	Bu			77



449 450 451

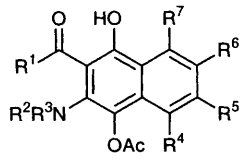
Scheme 27

	R^1	R^2	450	451	Yield (%)
a	Bu	Me			86
b	Me	Bu			94
c	Ph	H	$Ph_2CuCNLi_2$		69



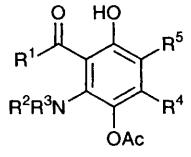
452

R^1 = Me, Ph; R^2 = Me, OPr^i; R^3 = Me, Et, Ph; R^4 = Et, OPr^i; R^5 = H, OAc; 17–96%



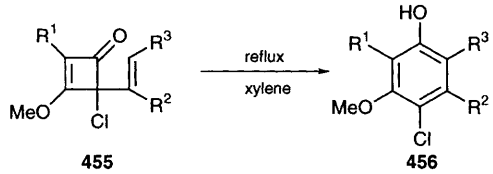
453

R^1 = Ph; R^2,R^3 = $(CH_2)_5$; R^4 = H, OMe; R^5 = H, OMe, NMe_2; R^4,R^5 = benzo; R^6 = H, OMe; R^7 = H, OMe; R^6,R^7 = benzo; 0–91%



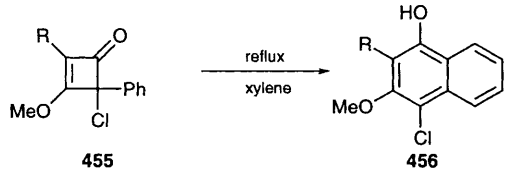
454

R^1 = Me, Ph; R^2= H, Bn; R^3 = Bu^t, Bn; R^2,R^3 = $(CH_2)_5$; R^4 = H, R^5 = Me; R^4,R^5 = CH=CHO, SCH=CH, OCH_2CH_2, $O(CH_2)_3$; 82–100%



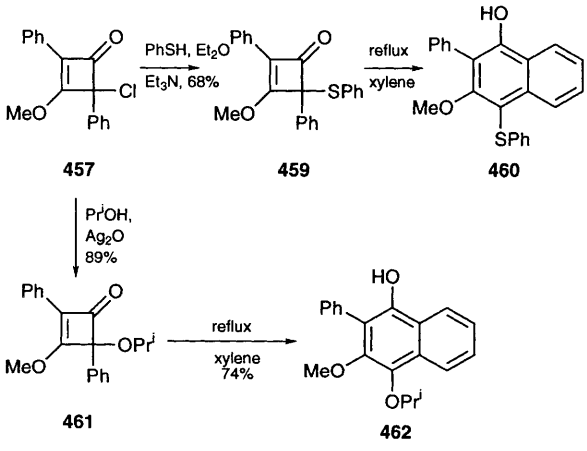
455 456

a R^1 = Ph, R^2 = R^3 = H	a 80%
b R^1 = Ph, R^2 = Me, R^3 = H	b 65%
c R^1 = Bu, R^2 = Me, R^3 = H	c 87%
d R^1 = Bu, R^2 = R^3 = Me	d 59%
e R^1 = BuC≡C, R^2 = R^3 = H	e 48%
f R^1 = PhC≡C, R^2 = R^3 = H	f 45%



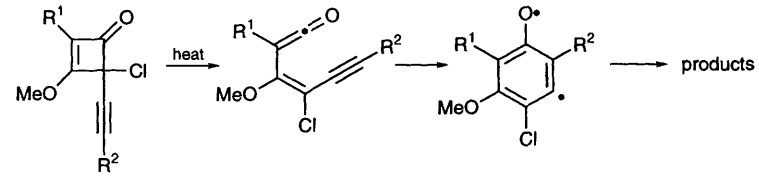
455 456

a R = Bu	a 62%
b R = Me	b 34%
c R = Bu^s	c 80%
d R = PhC≡C	d 76%
e R = BuC≡C	e 78%

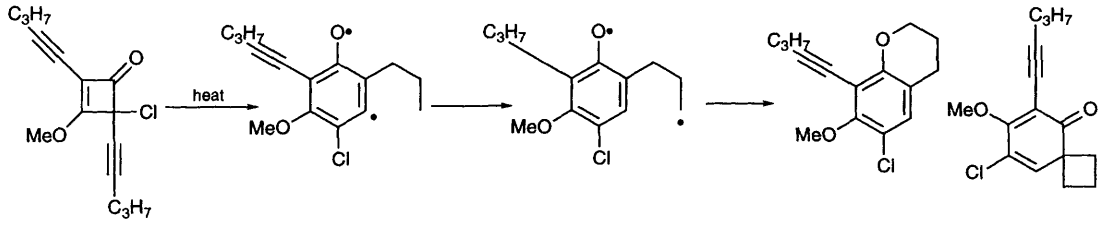


457 459 460 461 462

Scheme 28

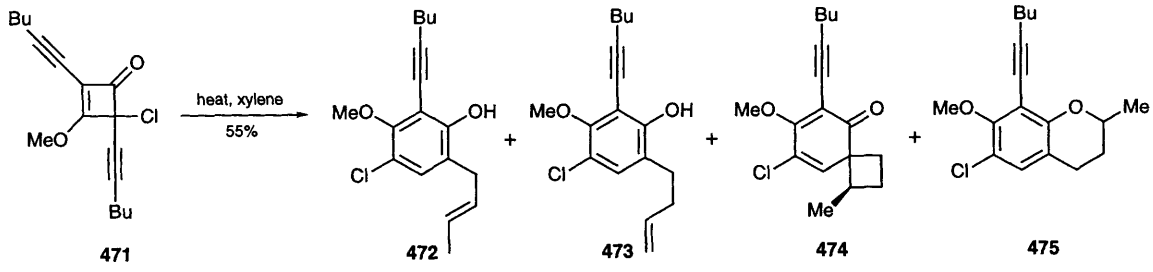


463 464 465



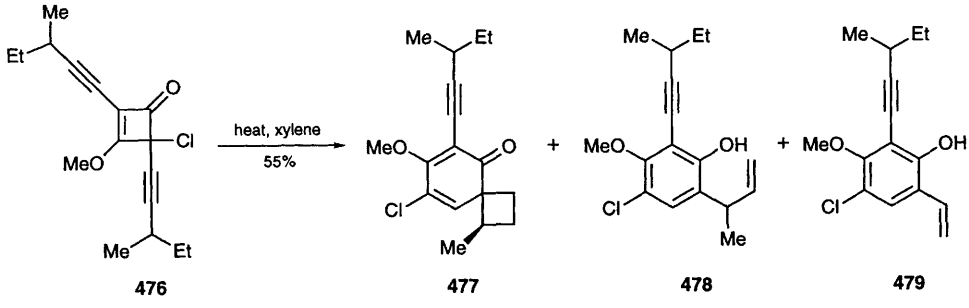
466 467 468 469 470

469 : 470 = 2 : 1



471 472 473 474 475

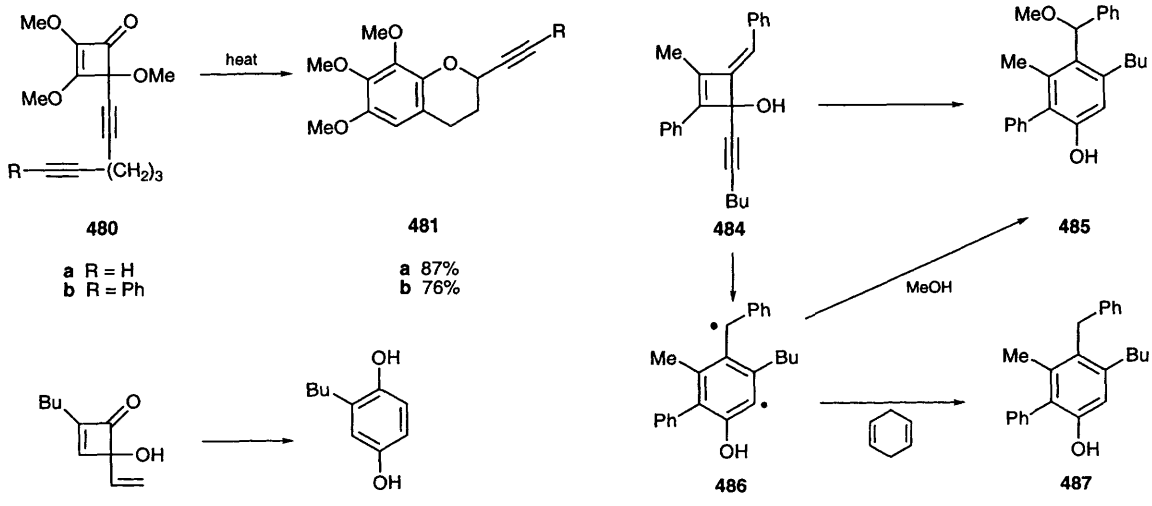
471 : 472 : 473 : 474 = 1 : 1 : 1.3 : 2.5



476 477 478 479

477 : 478 : 479 = 2 : 1 : 1

Scheme 29

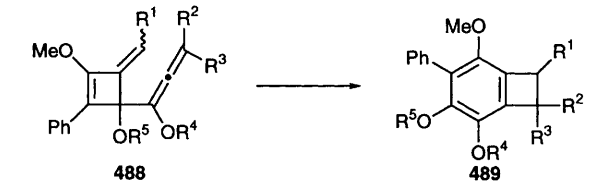


480 481 482 483 484 485 486 487

a R = H
b R = Ph

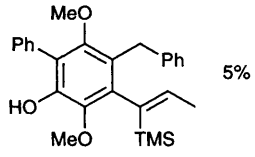
a 87%
b 76%

Scheme 30



488 489

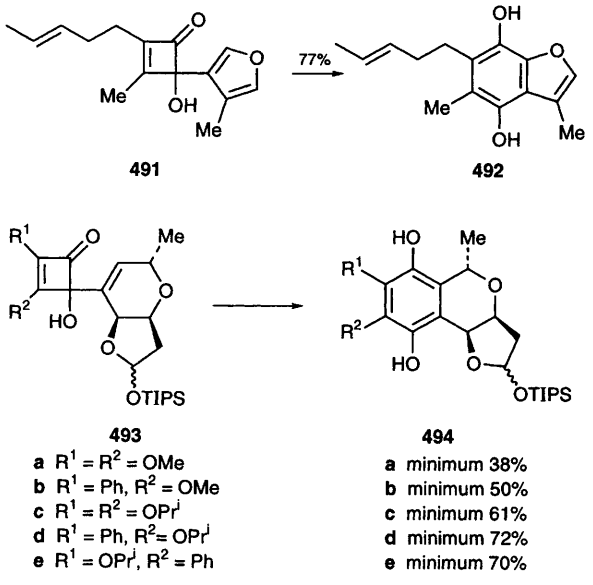
a R^1 = Ph, R^2 = R^3 = H, R^4 = Me, R^5 = TMS — **a** 49–82%
b R^1 = Ph, R^2 = R^3 = TMS, R^4 = Bu^t, R^5 = H — **b** 49–64%
c R^1 = C_5H_{11}, R^2 = R^3 = TMS, R^4 = Bu^t, R^5 = H — **c** 35%
d R^1 = Ph, R^2 = TMS, R^3 = C_3H_7, R^4 = Me, R^5 = H — **d** 30%



5%

490

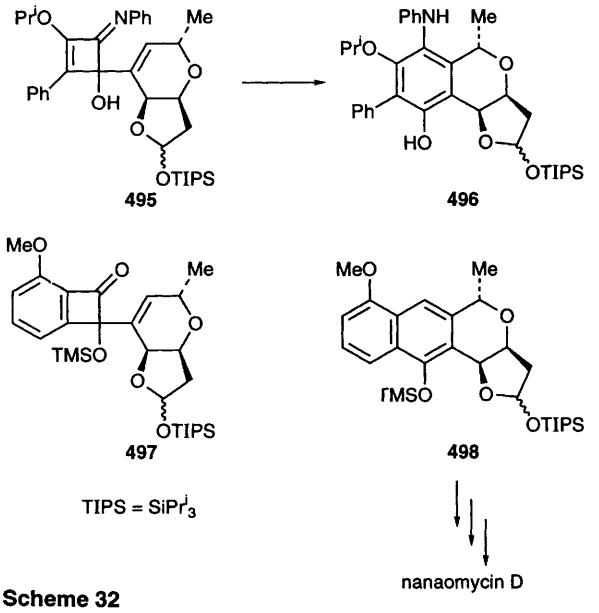
Scheme 31



491 492

493 494

a R^1 = R^2 = OMe — **a** minimum 38%
b R^1 = Ph, R^2 = OMe — **b** minimum 50%
c R^1 = R^2 = OPr^i — **c** minimum 61%
d R^1 = Ph, R^2 = OPr^i — **d** minimum 72%
e R^1 = OPr^i, R^2 = Ph — **e** minimum 70%



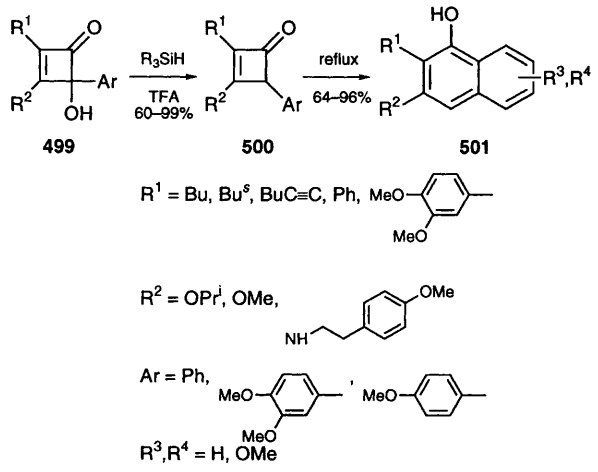
495 496

497 498

TIPS = $SiPr^i_3$

nanaomycin D

Scheme 32



499 500 501

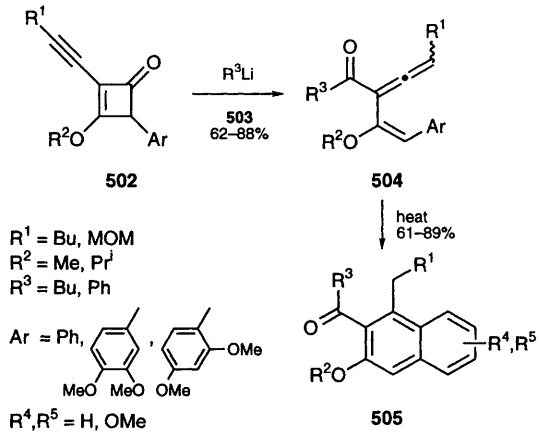
R^1 = Bu, Bu^s, BuC≡C, Ph, MeO-C6H3(OMe)-

R^2 = OPr^i, OMe,

Ar = Ph,

R^3,R^4 = H, OMe

Scheme 33



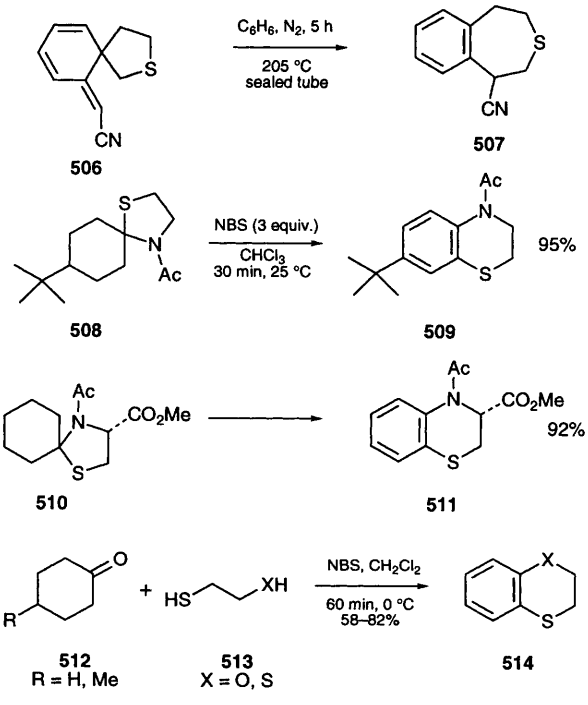
502 504 505

R^1 = Bu, MOM
R^2 = Me, Pr^i
R^3 = Bu, Ph

Ar = Ph,

R^4,R^5 = H, OMe

Scheme 34



506 507

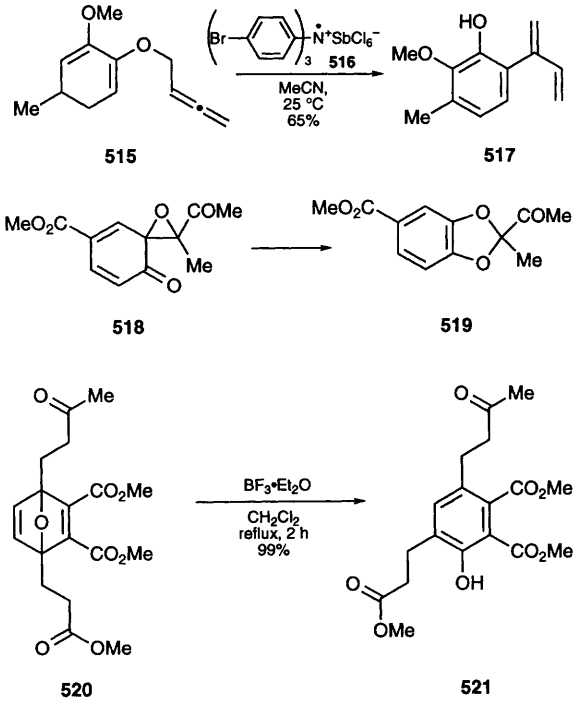
508 509

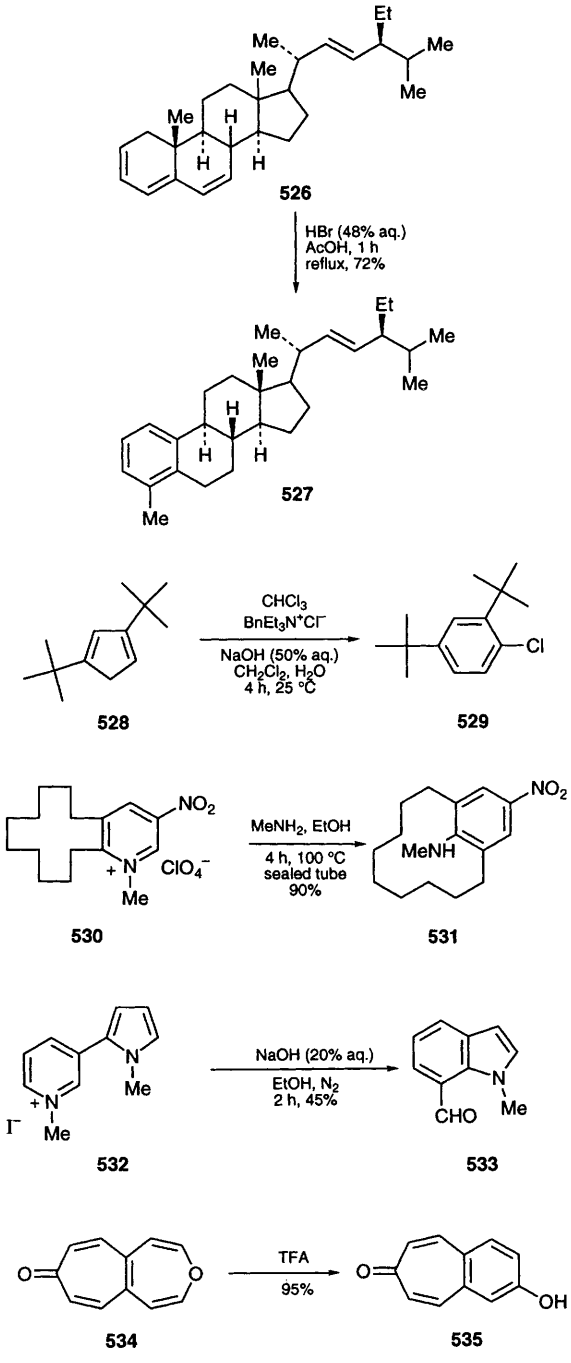
510 511

512 513 514

R = H, Me
X = O, S

conditions cyclohexanones **512** were converted to 2,3-dihydro-1,4-benzodithiines and 1,4-benzoxathiines **514**.[280] The conversion of allenyl enol ether **515** to catechol **517** was initiated by treatment with cation radical **516**;[281] protected catechol **519** was formed upon rearrangement of epoxide **518**.[282] Treatment of Diels–Alder adduct **520** with a catalytic quantity of boron trifluoride in dichloromethane at reflux gave a 99% yield of phthalate **521**.[283] The benzyne-derived cycloadduct **522** gave the naphthol **523** upon treatment with methanolic hydrogen chloride.[284] Acid-catalysed rearrangement of methano[10]annulene derivative **524** gave the naphthocyclopropanecarboxylate **525**.[285] Related acid-catalysed rearrangements forming substituted monocyclic arenes have been reported.[286,287] Acid-catalysed rearrangement of tetraene **526**, using hydrobromic acid in acetic acid, gave the monoaromatic steroid **527** in 72% yield.[36] Reaction of dihalocarbenes with alkylated cyclopentadienes gave halodialkylbenzenes, for example in the conversion of **528** to **529**.[288] Basic or nucleophilic rearrangement of pyridinium salts has been used to prepare substituted nitroanilines (**530** to **531**)[289] and indoles (**532** to **533**).[290] Treatment of the oxaheptalenone **534** with trifluoroacetic acid gave the benzotropone **535** in 95% yield.[291] Aryl-substituted naphthalenes have been prepared by the photolysis of 5,5-diaryl-4,5-dihydrofurans,[292] and tri-substituted naphthalenes by pyrolysis of arylmethylidene Meldrum's acid.[293]





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