https://doi.org/10.1070/RCR4971

Cycloaddition reactions of *o*-quinone methides with polarized olefins

Vitaly A. Osyanin, Anton V. Lukashenko, Dmitry V. Osipov

Samara State Technical University,
ul. Molodogvardeiskaya 244, 443100 Samara, Russian Federation

The review summarizes and systematizes the [4 + 2]-cycloaddition reactions of *o*-quinone methides with electron-rich and electron-deficient olefins. The electron-rich substrates include vinyl ethers, vinyl sulfides, enamines, enamides, enols, furans, benzofurans and indoles, while the electron-deficient substrates are esters of unsaturated carboxylic acids, vinyl azides and quinones. Reactions with push-pull and captodative olefins are also considered. The mechanisms of some reactions are presented. A separate part of the review addresses reactions of *p*-quinone methides containing an *o*-hydroxyphenyl substituent at the exocyclic carbon atom, which can isomerize to *o*-quinone methides. Much attention is paid to oligomerization of *o*-quinone methides, which proceeds in the absence of active dienophiles or nucleophiles.
The bibliography includes 217 references.

Contents

1. Introduction 324
2. Cycloaddition of *o*-quinone methides with electron-rich olefins 326
   2.1. Reactions of *o*-quinone methides with compounds containing alkoxyvinyl moiety 326
   2.2. Cycloaddition of vinyl sulfides to *o*-quinone methides 331
   2.3. Reactions of *o*-quinone methides with furans and benzofurans 332
   2.4. Cycloaddition of enols to *o*-quinone methides 337
   2.5. Reactions of *o*-quinone methides with *o*-alkenylnaphthols and -phenols 339
   2.6. Reactions of *o*-quinone methides with enamines and enamides 340
   2.7. Diels – Alder reactions of *o*-quinone methides with indoles 342
3. Cycloaddition of *o*-quinone methides to olefins with electron-withdrawing groups 345
   3.1. Reactions of *o*-quinone methides with electrophilic olefins 345
   3.2. Oligomerization of *o*-quinone methides 348
4. Reactions of *o*-quinone methides with push-pull olefins 353
   4.1. Acyclic push-pull olefins 353
   4.2. Cyclic push-pull olefins 360
   4.3. Push-pull buta-1,3-dienes 362
5. Reactions of *o*-quinone methides with captodative olefins 364
6. [4 + 2]-Annulation reactions involving *o*-hydroxyphenyl-substituted *p*-quinone methides 365
7. Conclusion 369
8. List of abbreviations and designations 369

V.A.Osyanin. Doctor of Chemical Sciences, Professor at the Department of Organic Chemistry, SSTU. E-mail: vosyanin@mail.ru
Current research interests: chemistry of heterocyclic compounds, chemical transformations of highly reactive intermediates (quinone methides, aza-quinone methides, synthetic equivalents of carbenes, *etc*.), development of new cascade and multicomponent reactions.
A.V.Lukashenko. Candidate of Chemical Sciences, Assistant at the same Department. E-mail: orghimek@gmail.com
Current research interests: chemistry of heterocyclic compounds, transformations of *o*-quinone methides, development of new approaches to 4*H*-chromenes.
D.V.Osipov. Candidate of Chemical Sciences, Associate Professor at the same Department. E-mail: osipovdv25@mail.ru
Current research interests: dearomatization of highly polarized heterocycles, design of new cascade and multicomponent reactions, synthesis of natural compounds, development of new approaches to furans and pyrans.

Translation: Z.P.Svitanko

1. Introduction

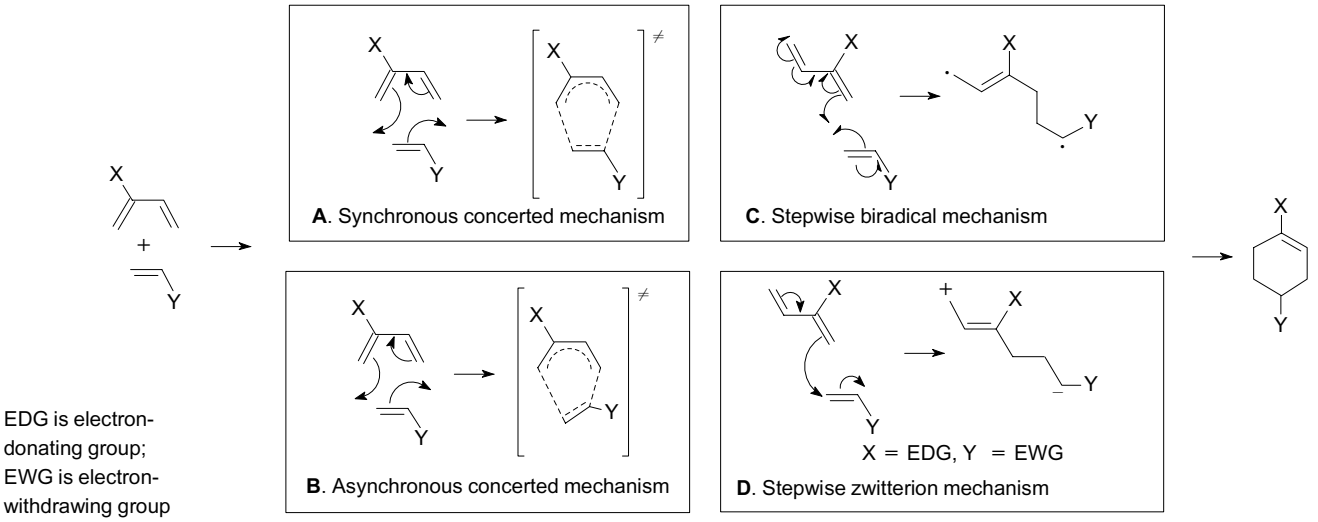
Currently, *o*-quinone methides (*o*-QMs) are strongly recognized as effective tools for the synthesis of oxygen-containing heterocycles and functionally substituted phenols.[1 – 4] The cycloaddition reactions of various dienophiles with *o*-QMs are often used to construct chroman and chromene systems. An advantage of this approach is the possibility of using various *o*-QM precursors. This makes it possible, first, to vary the conditions of synthesis over a broad range and, second, to obtain chromans and chromenes with a diversified set of substituents, which are valuable for the subsequent transformations and for medicinal chemistry. In addition, wide occurrence of chroman systems among natural and biologically active products[5 – 7] makes development of new methods for their synthesis a relevant task.

A key approach to the preparation of carbo- and heterocyclic compounds is the Diels – Alder reaction,

Received 15 June 2020

© 2021 Uspekhi Khimii, ZIOC RAS, Russian Academy of Sciences and IOP Publishing Limited

Scheme 1



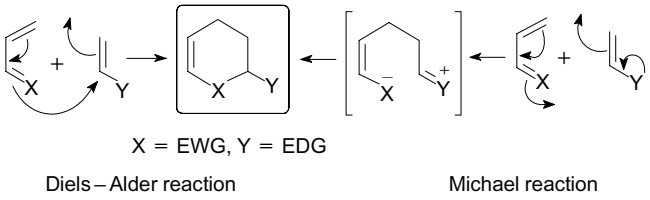
which has a number of advantages such as 100% atomic economy, high regio- and stereoselectivity, broad range of applicable dienes and dienophiles and the possibility of generating structures of various complexity due to the existence of numerous intramolecular and intermolecular reactions of this type.

The cycloaddition reactions can be classified into concerted (synchronous and asynchronous) and non-concerted, or stepwise, reactions, which give zwitterion or biradical intermediates. A traditional example is the reaction of buta-1,3-diene with ethylene, which follows synchronous concerted mechanism **A**. The asynchronous concerted mechanism **B** is implemented when two new σ-bonds are not formed simultaneously, which is the case when electron-donating or -withdrawing substituents are present in the diene or dienophile. Stepwise biradical mechanism **C** should also be mentioned. Zwitterion intermediates are formed only in the extreme case of asynchronous reaction, caused by a high degree of polarization of reactants (stepwise zwitterion mechanism **D**) (Scheme 1).

Unlike the synchronous mechanism, which can be proposed for a narrow range of reactants, the polar asynchronous mechanism is encountered much more often. Zwitterion intermediates are formed in reactions of highly polar compounds; they can be stabilized either due to electronic effects of substituents or by aromatization. In some cases, intermediates of this type can be experimentally isolated or detected by NMR or IR spectroscopy.

If an electron-withdrawing group is a part of the diene system, the reaction can follow either asynchronous concerted mechanism or stepwise mechanism, which comprises the Michael reaction to give a zwitterion intermediate, which then undergoes 6-*exo*-*trig*-cyclization. The higher the degree of polarization of reactants, the higher the probability of the latter mechanism (Scheme 2).

Scheme 2

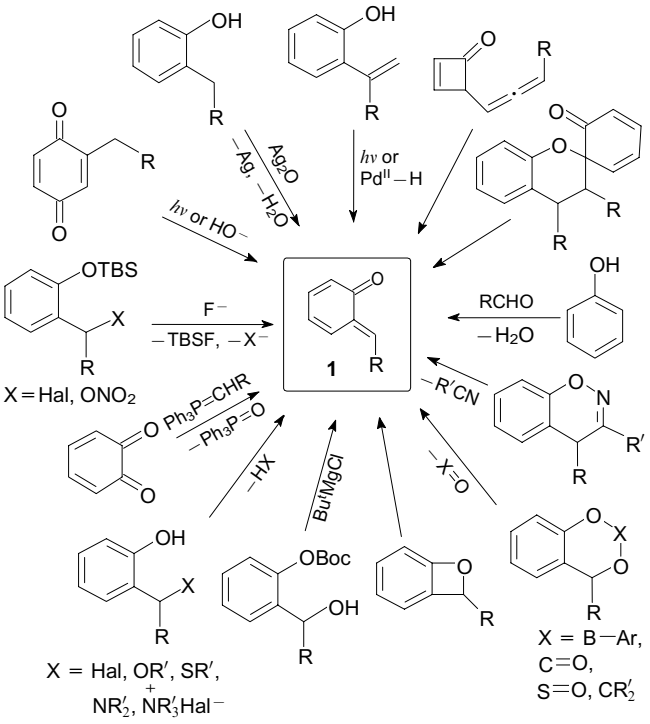


According to published data,[8] the formation of chromans from various precursors such as Mannich bases, salicyl alcohols, *o*-chloromethylphenols, *o*-alkylphenols and so on proceeds as an asynchronous concerted [4 + 2]-cycloaddition involving *o*-QMs generated *in situ*. The formation of *o*-QMs in these reactions is indirectly evidenced by quite a few factors, in particular, structures of *o*-QM dimers and trimers, their intra- and intermolecular cycloaddition products and trapping of *o*-QMs by various nucleophiles. Nevertheless, some reactions might involve potential *o*-QM precursors, without the formation of *o*-QMs. For example, the reaction of *o*-QMs with salicyl alcohols in an acid medium may give *o*-hydroxybenzyl carbocations, which are converted to formal [4 + 2]-cycloaddition products upon subsequent transformations.[9]

o-Quinone methides **1** can be generated as intermediates under various conditions (heating, irradiation or treatment with acids, bases or enzymes) from various precursors such as *o*-alkylphenols, Mannich bases, *o*-hydroxystyrenes, *o*- and *p*-benzoquinones, *etc.* (Scheme 3).[1, 4] The instability and high reactivity of *o*-QMs are important factors that hamper their handling.

The inverse electron demand Diels – Alder reactions of *o*-QMs are usually carried out for electron-rich olefins. From the standpoint of frontier orbital theory, this type of reactions corresponds to interaction between the lowest unoccupied molecular orbital (LUMO) of *o*-quinone methide and the highest occupied molecular orbital (HOMO) of the dienophile. To attain a reasonable yield of the product, it is necessary to use a large excess of the 2π-electron reagent. The Diels – Alder reactions between *o*-QMs and olefins containing weakly electron-donating or electron-withdrawing substituents proceed with difficulty. In the absence of olefins and nucleophiles, *o*-QMs undergo oligomerization, in which they act as both dienes and dienophiles, to give spirocyclic oxygen-containing systems. The cycloaddition to *o*-QMs is driven by restoration of the aromaticity of the six-membered carbocycle. The diastereoselectivity of the Diels – Alder reaction of *o*-QMs substituted at the methylene group is determined by *o*-QM geometry, dienophile and diene orientation in the transition

Scheme 3

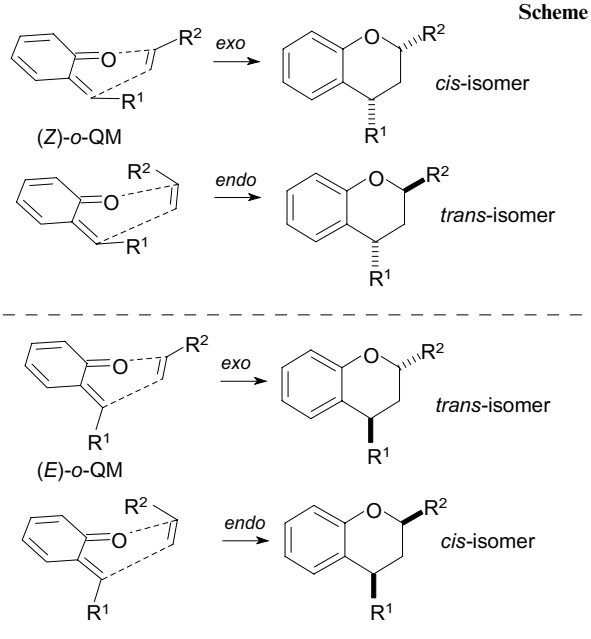


R^1, R^2 = Alk; TBS is *tert*-butyldimethylsilyl, Boc is *tert*-butoxycarbonyl

state (*exo*- or *endo*-approach) and the stability of the corresponding diastereomers (Scheme 4).

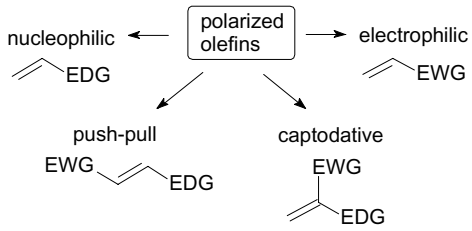
Since the 1960s, the chemistry of *o*-QMs has continuously attracted the attention of researchers, as indicated by a number of reviews, including those published over the past ten years. These reviews address various aspects of *o*-QM chemistry, most often, *o*-QM generation [10, 11] and possible practical applications,[12] in particular, for bioorthogonal ligation [13] and for the synthesis of natural compounds.[2, 14, 15] In addition, a lot of attention was devoted to chemical transformations of *o*-QMs in reactions with nucleophiles and dienophiles [4, 16] and the use of *o*-QMs in the synthesis of oxygen-containing heterocycles, first of all, chromans and chromenes [17] and phenol derivatives. The use of *o*-QMs in organocatalyzed asymmetric reactions [18, 19] and cascade reactions [1] has been described. However, none of the mentioned publications consider in detail the reactions of *o*-QMs with polarized olefins, while parts of the reviews devoted to Diels – Alder reactions of *o*-QMs consider almost exclusively non-polar dienophiles and vinyl ethers, including cyclic ones.[2–4, 8, 15, 16, 20, 21] Therefore, the present review does not pay much attention to these reactions, but gives only the most illustrative examples. Meanwhile, reactions of *o*-QMs with other types of electron-rich dienophiles (vinyl sulfides, indoles, benzofurans, *etc.*) have not been systematically addressed before. Finally, reactions with electron-deficient, push-pull and captodative olefins have not been described previously, and this review addresses these reactions as fully as possible. Owing to the foregoing, this review is expected to occupy a rightful position among survey papers on this subject.

Scheme 4



The reactions of *o*-QMs are mainly arranged in terms of the type of olefin acting as the 2π-component. Highly polar olefins can be classified into nucleophilic (electron-rich), electrophilic (electron-deficient), push-pull (with electron-donating and -withdrawing groups at different ends of the double bond) and captodative olefins (with electron-donating and -withdrawing groups at the same carbon atom) (Scheme 5).

Scheme 5



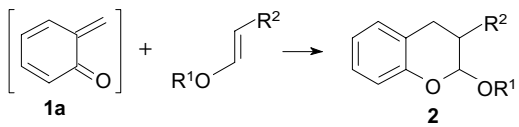
2. Cycloaddition of *o*-quinone methides with electron-rich olefins

2.1. Reactions of *o*-quinone methides with compounds containing alkoxyvinyl moiety

Vinyl ethers actively participate in inverse electron demand [4 + 2]-cycloaddition reactions owing to the electron-donating effect of the oxygen atom. When allowed to react with *o*-QMs, they can potentially act as synthetic equivalents of alkynes if an alcohol molecule is eliminated from the initially formed cycloadduct. However, stable cyclic acetals **2** are usually formed as the final products in these reactions (Scheme 6).

The simplest *o*-QM **1a**, generated by treatment of 2-hydroxybenzyl acetate (**3a**) with a minor excess of isopropylmagnesium chloride, reacts with ethyl and n-butyl vinyl ethers to give chromans **4a**,**b**.[22] The reactions of **3a** with 2,3-dihydrofuran and 3,4-dihydro-2*H*-pyran resulted in the isolation of *cis*-adducts **5a**,**b**, while ethers with

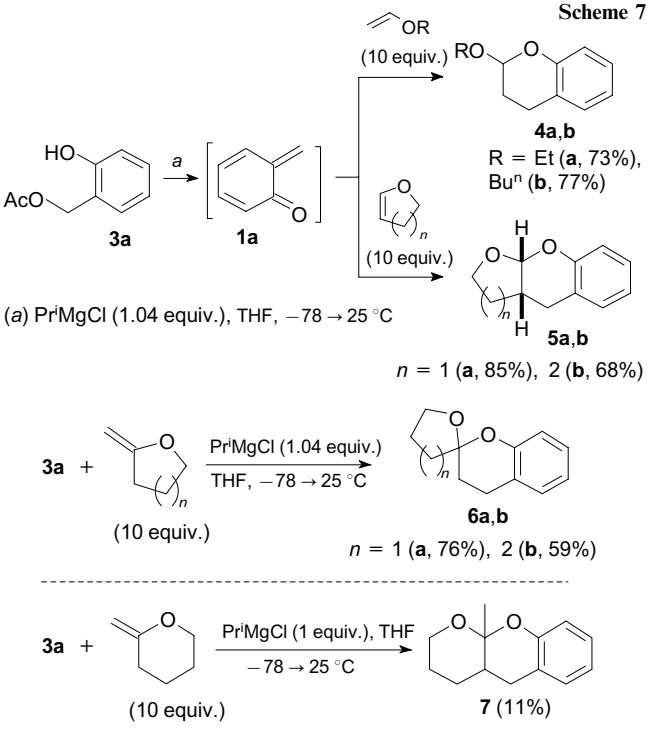
Scheme 6



R^1, R^2 = Alk, Ar

exocyclic double bond provide a pathway to spirochromans **6a**,**b**. It is noteworthy that in the case of 2-methylenetetrahydropyran in the presence of an equimolar amount of the Grignard reagent, 10a-methyl-3,4,4a,10a-tetrahydro-2*H*,5*H*-pyrano[2,3-*b*]chromene (**7**) was isolated as the major product as a result of isomerization of 2-methylenetetrahydropyran to 2-methyldihydropyran. The reactions depicted in Scheme 7 can be carried out at reduced temperature, although dienophiles of this type usually undergo cycloaddition reactions under more drastic conditions.

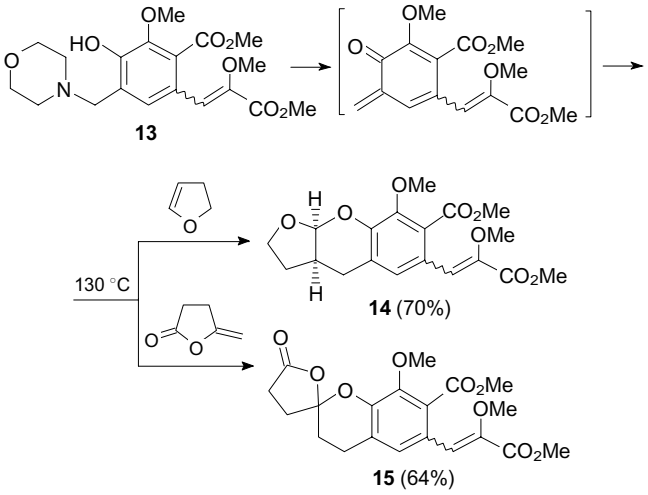
Scheme 7



Heating of 3,4-dihydropyran with salicyl alcohols **8a**,**b** in acid medium mainly gives cycloadducts **5b** and **9** rather than tetrahydropyranyl derivatives, which attests to the generation of *o*-QM under the reaction conditions. At room temperature (rt), *o*-QM is not apparently formed, and acetal **10** is isolated in 75% yield. In the case of n-butyl vinyl ether, which is less stable in acid medium than dihydropyran, the reaction in refluxing toluene results in the formation of only compound **11**, acetal of salicyl alcohol and acetaldehyde (the latter is formed upon acid hydrolysis of n-butyl vinyl ether by water released upon dehydration of salicyl alcohol). Only in the absence of an acid catalyst, 2-butoxychroman (**4b**) is obtained in the reaction in a low yield, while acetal **12** is the major product (Scheme 8).[23]

Heating of Mannich base **13** with an excess of dihydrofuran or with γ-methylene-γ-butyrolactone at 130 °C affords acetal **14** or spiroketal **15**, respectively. In the latter case, the use of a quaternized *o*-QM precursor does not give the cycloadduct (Scheme 9).[24]

Scheme 9

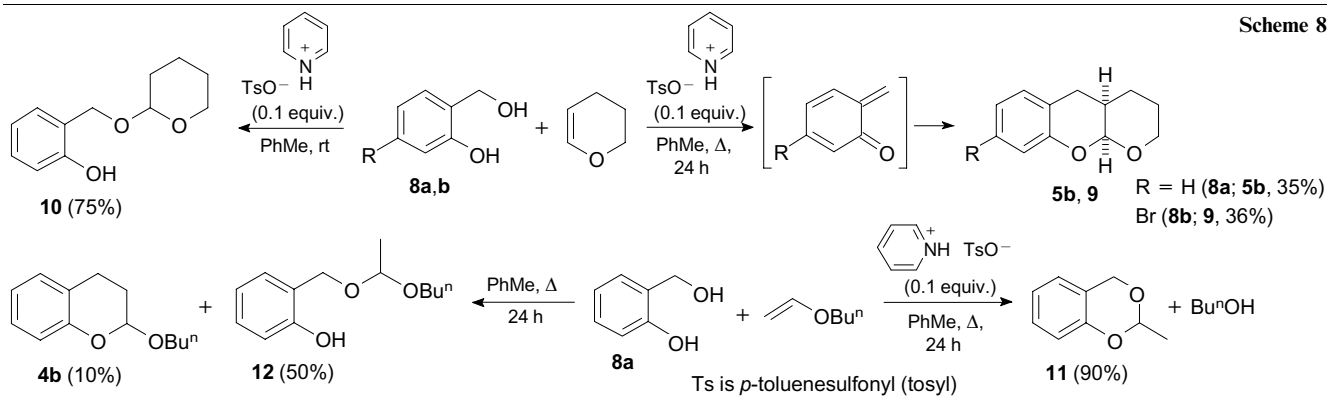


The use of β-aryl-substituted vinyl methyl ethers as dienophiles in the [4 + 2]-cycloaddition with *o*-QMs is a synthetic route to acetals **16**, which can serve as precursors of a number of natural isoflavonoids, *e.g.*, equol (**17a**) and vestitol (**17b**) (Scheme 10; yields of products **17a**,**b** over three steps).[25]

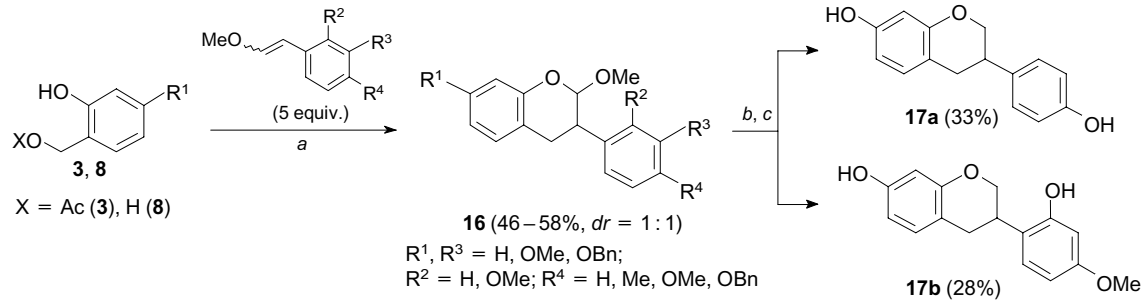
When Boc-protected salicyl alcohol **18** is used as the *o*-QM precursor, reactions with dihydroisobenzofuran **19** or dihydrobenzofuran **20** give spirocyclic adducts **21** and **22**, respectively. The yield of cycloadduct **22** is much lower due to isomerization of compound **20** to 2-methylbenzofuran (**23**), which does not react with *o*-QM under these conditions. The cause is that the loss of aromaticity of the furan ring is energetically unfavourable. Higher diastereoselectivity of the reaction of 4-methylene-1,3-dioxolanes **24** with *o*-QM, which gives products **25**, is attributable to the presence of a bulky aromatic substituent R^2. However, in the case of 2-methylenetetrahydrofurans **26**, the diastereoselectivity of formation of compounds **27** decreases (Scheme 11).[26]

2,3-Naphthoquinone 3-methide generated upon photodegradation of 3-hydroxymethyl-2-naphthol reacts with

Scheme 8

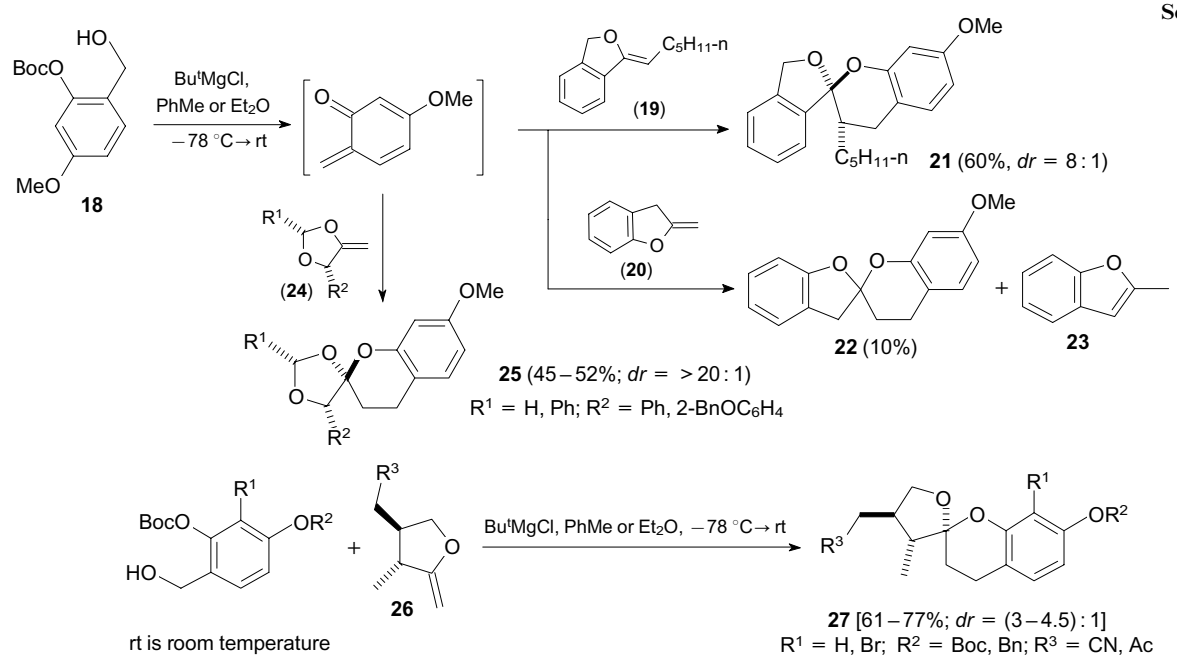


Scheme 10



(*a*) PhH, 80 °C or PhMe, 115 °C (in a sealed tube); (*b*) Et_3SiH, $BF_3 \cdot OEt_2$, CH_2Cl_2, 0 °C, 30 min; (*c*) H_2 (10% Pd/C), EtOAc, 24 h; *dr* is diastereomeric ratio

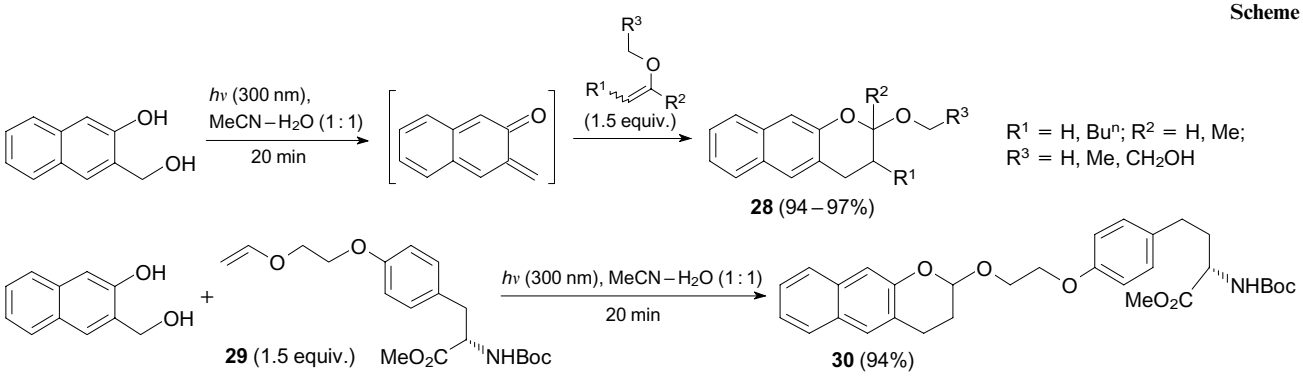
Scheme 11



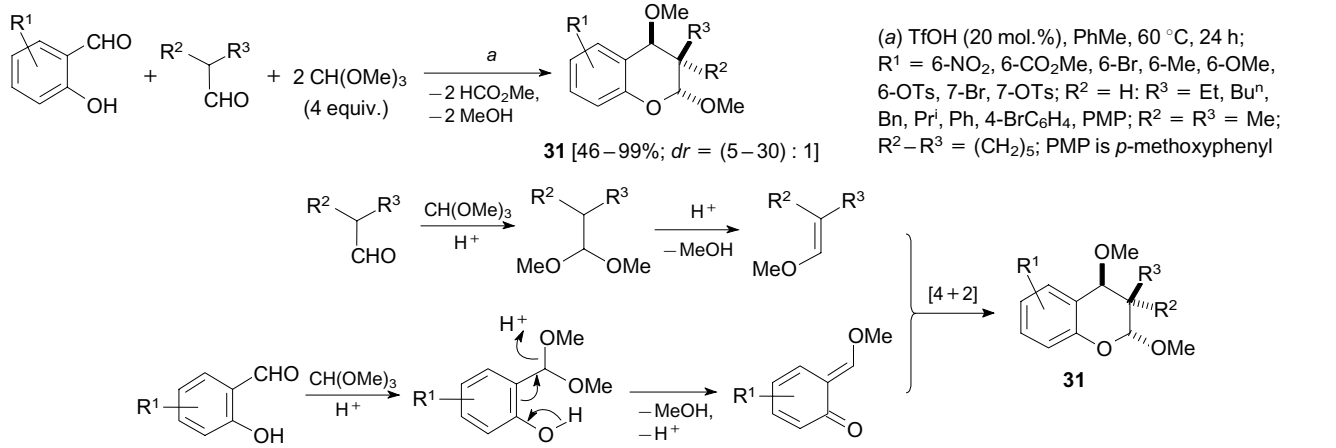
vinyl ether to give photostable chromans **28**.[27] In relation to tyrosine derivative **29** (Scheme 12), it was shown that using this method, *o*-QM can be reacted with amino acid derivatives containing an alkoxyvinyl moiety to prepare, for example, acetal **30**. However, vinyl phenyl ether does not react with *o*-QM, neither do other vinyl ethers under thermal activation conditions.

A one-pot method was proposed for the synthesis of 3-alkyl- and 3-arylchromans **31** from aliphatic aldehydes and salicylaldehydes in the presence of TfOH [Tf is trifluoromethanesulfonyl (triflyl)] and an excess of trimethyl orthoformate. The reaction has high regio- and diastereoselectivity. When α,α-disubstituted aldehydes are used, 3,3-disubstituted chromans are formed. This reaction can be carried out for salicylaldehydes containing both electron-donating and -withdrawing substituents. The mechanism of this transformation includes the following main steps. First, aliphatic aldehyde and salicylaldehyde are converted to

Scheme 12



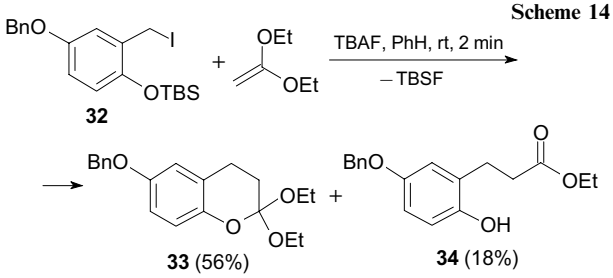
Scheme 13



dimethyl acetals under the action of orthoester. The subsequent elimination of methanol leads to vinyl ether and *o*-QM, respectively; this is followed by cycloaddition to give chromans **31** (Scheme 13).[28] For the synthesis of polysubstituted isoflavanes by this reaction, arylacetaldehydes were replaced by their dimethyl acetals.[29]

Ketene acetals can also be regarded as electron-rich dienophiles. The reaction of 1,1-diethoxyethylene with *o*-QM precursor **32** in the presence of tetra-n-butylammonium fluoride resulted in the isolation of 6-benzyloxy-2,2-diethoxychroman (**33**) as a mixture with ester **34** (Scheme 14).[30] Ester **34** is probably formed from chroman **33** upon nucleophilic ring opening, induced by the iodide ion, which is released upon generation of *o*-QM from precursor **32**.

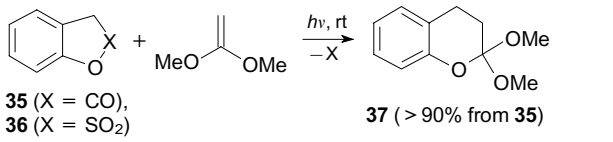
Scheme 14



TBS is *tert*-butyldimethylsilyl; TBAF is tetra-n-butylammonium fluoride

When no strong nucleophiles are present in the reaction mixture, the reaction follows a more unambiguous pathway. For example, trapping of unsubstituted *o*-QM, generated upon photodecarbonylation of benzofuran-2(3*H*)-one (**35**) or upon elimination of SO_2 from benzosultone (**36**), with 1,1-dimethoxyethylene results in the formation of 2,2-dimethoxychroman (**37**) in a high yield (Scheme 15).[31]

Scheme 15



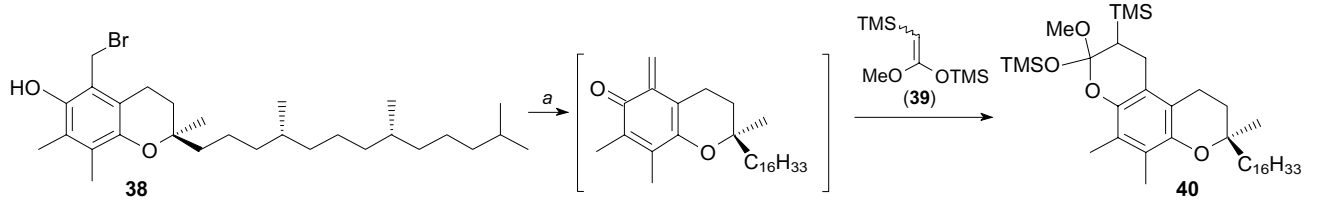
The reaction of tocopherol derivative (vitamin E) **38** with *O*-methyl-*C*,*O*-bis(trimethylsilyl)ketene acetal (**39**) affords 1,2,3,8,9,10-hexahydropyrano[3,2-*f*]chromene **40** *via* the step of generation of *o*-QM (Scheme 16).[32]

Ketene silyl acetals **41** can also act as dienophiles in reactions with stable *o*-QMs.[33] Desilylation of compound **41** gives rise to ketene enolate, which, being an electron-rich olefin, adds to *o*-QM in a stepwise manner to afford 3,4-dihydrocoumarin **42**, predominantly as a single enantiomer. The coordination of the positively charged quinidine moiety of catalyst **I** and the naphtholate anion ensure the stereocontrol of the reaction (Scheme 17).

The oxidative generation of *o*-QM from α-tocopherol (**43**) in the presence of 2,3-dehydro-*N*-methylmorpholine, which can be considered as both a vinyl ether and enamine, furnishes a mixture of regioisomeric pyrano[3′,2′:5,6]chromeno[1,4]oxazines **44a**,**b** (Scheme 18).[34] Although quantum chemical calculations predict a higher thermodynamic stability for product **44b**, the kinetically controlled product **44a** is formed predominantly. According to experimental data, the activation free energy of formation of chroman **44a** is lower than that for isomer **44b** by 32.4 kJ mol^{-1}.

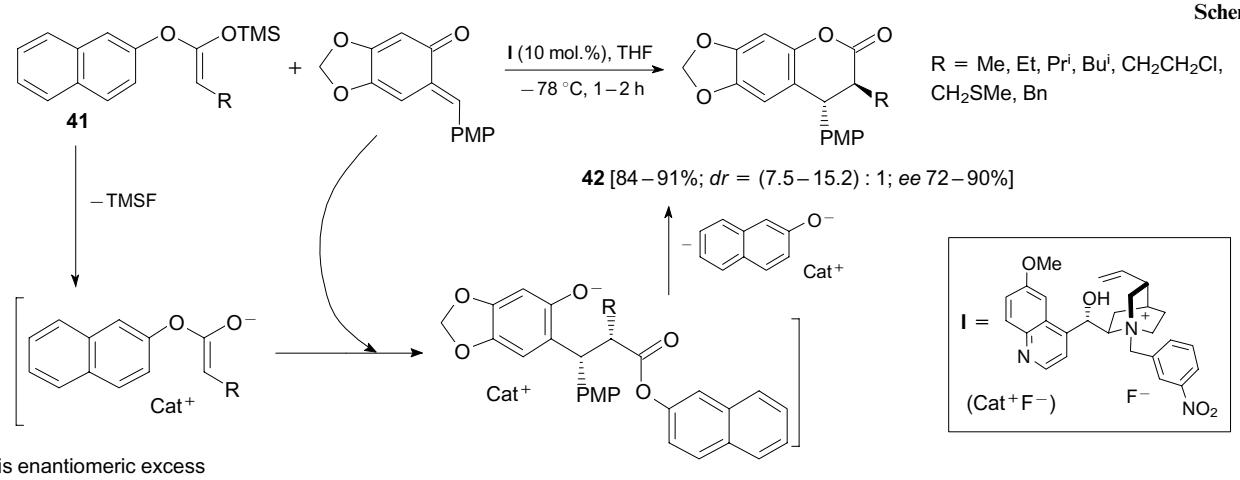
2*H*-Chromenes **45** dimerize in the presence of $FeCl_3$ to give chromeno[2,3-*b*]chromenes **46** and chromeno[4,3-*b*]chromenes **47** as a result of two competing reactions.[35] A part of chromene **45** undergoes the electrocyclic opening to afford *o*-QM **48**, while the other part isomerizes to 4*H*-chromene **49** upon hydride shift. When alkyl or electron-withdrawing groups R^1 and R^2 are present in the

Scheme 16



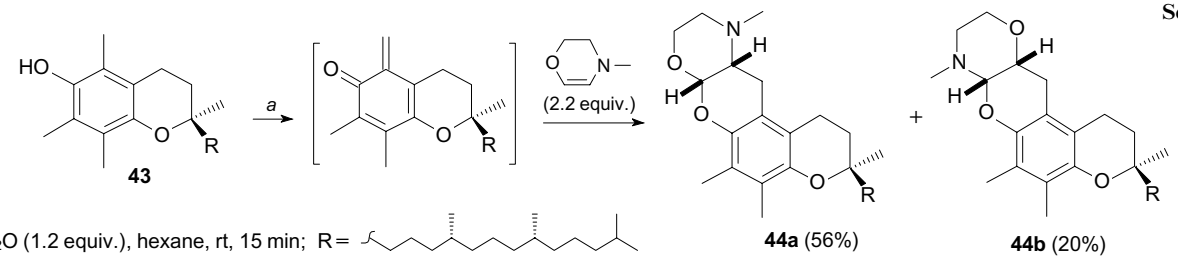
(*a*) $ZnCl_2$, MeCN, 70 °C, 1 h; TMS is trimethylsilyl

Scheme 17



ee is enantiomeric excess

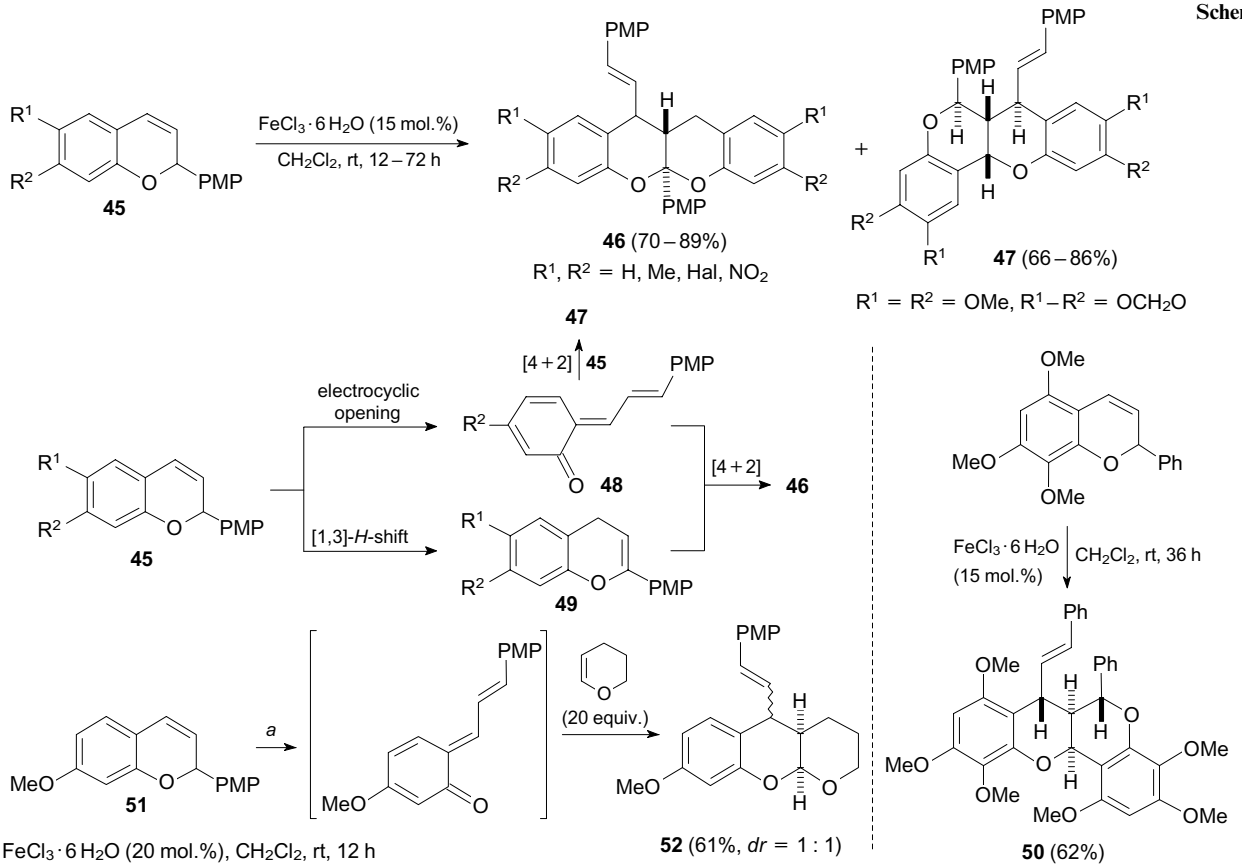
Scheme 18



(*a*) Ag_2O (1.2 equiv.), hexane, rt, 15 min; R =

starting 2*H*-chromene **45** molecule, cycloaddition of intermediates **48** and **49** leads to chromeno[2,3-*b*]chromenes **46**. In the case of electron-donating groups R^1 and R^2, the [4 + 2]-cycloaddition of *o*-QM **48** to the starting 2*H*-chromene **45** takes place to form dimers **47**; this was used for the synthesis of dependensin (**50**).[36] Apparently, the generation

Scheme 19



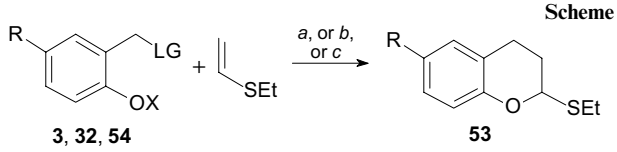
(*a*) $FeCl_3 \cdot 6H_2O$ (20 mol.%), CH_2Cl_2, rt, 12 h

of more stable *o*-QM **48** with electron-donating groups is faster than the hydride shift in 2*H*-chromenes; this is responsible for the regioselectivity of this type. The treatment of 2*H*-chromene **51** with an excess of dihydropyran in the presence of $FeCl_3$ furnishes Diels – Alder adduct **52** as a mixture of diastereomers (Scheme 19).

2.2. Cycloaddition of vinyl sulfides to *o*-quinone methides

Vinyl sulfides, being electron-rich dienophiles, thio analogues of vinyl ethers, readily undergo [4 + 2]-cycloaddition reactions with *o*-QMs. The reaction of vinyl ethyl sulfide with hydroxybenzyl acetate (**3a**) in the presence of isopropylmagnesium chloride furnishes 2-(ethylthio)chroman (**53a**, R = H).[22] In the case of reactive *o*-QM precursors, iodides **32**, the reaction with vinyl ethyl sulfide induced by fluoride ions is completed in only 2 min at room temperature.[30] Apart from iodides, benzyl nitrates **54** (Scheme 20),[37] *o*-cresols and 2-methyl-1-naphthols are used as *o*-QM precursors.[38]

Scheme 20



3, **32**, **54** **53**

3: X = H, LG = OAc;
32: X = TBS, LG = I;
54: X = TBS, LG = ONO_2

(*a*) Pr^iMgCl, dienophile (10 equiv.), THF, −78 → 25 °C (from **3**), R = H (59%); (*b*) TBAF, PhH, rt, 2 min (from **32**), R = BnO (83%); (*c*) TBAF, PhH, rt, 2 min (from **54**), R = H (17%), OBn (74%); LG is leaving group

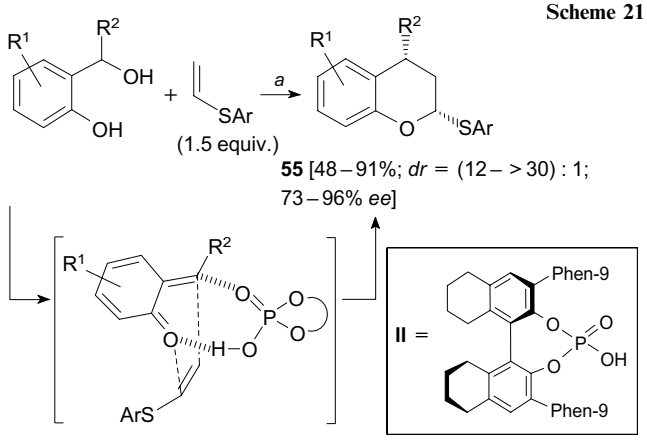
The [4 + 2]-cycloaddition of *o*-QMs to aryl sulfides catalyzed by chiral phosphoric acids yields chromans **55**. The hydrogen bonding between chiral catalyst **II** and *o*-QM provides for the stereocontrol of the reaction. The predominant formation of 2,4-*cis*-disubstituted chroman is attributable to the *endo*-addition of vinyl sulfide to *o*-QM. It is noteworthy that arylthiochromans **55** thus formed are convenient precursors of various 4-aryl-substituted chromans **56** and benzopyrans **57** owing to the lability of the arylsulfonyl group, which can be easily formed from the arylthiol group on treatment with *m*-chloroperbenzoic acid (*m*-CPBA) (Scheme 21).[39]

Recently, cycloaddition of salicyl alcohol **58** to vinyl phenyl sulfide giving adduct **59** was used as the key step of the total synthesis of the flavonoid caesalpinnone A, catalyzed by racemic BINOL-phosphoric acid (BPA) (BINOL is 1,1′-bi-2-naphthol) (Scheme 22).[40] Attempts to perform an asymmetric version of this reaction did not provide, however, the desired outcome: the maximum enantiomeric excess of the product was 38%.

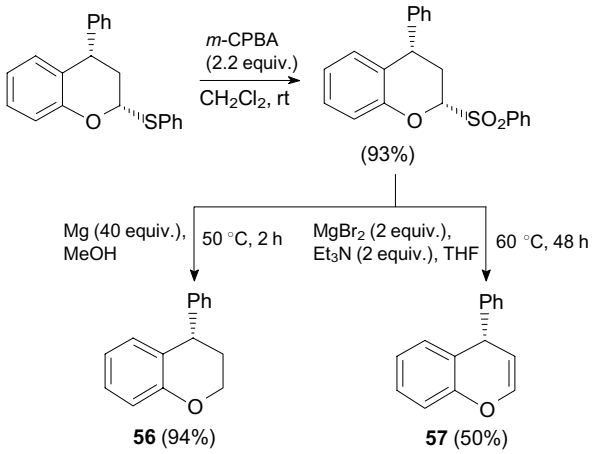
The reaction of salicyl alcohol **60** with an excess of vinyl ethyl sulfide proceeded *via* the generation of two different *o*-QMs and gave a mixture of isomeric chromans **61a**,**b** in 4 : 1 ratio in a total yield of 42% (Scheme 23).[41] The predominant formation of thiochroman **61a** can be attributed to the higher stability of the corresponding *o*-QM, caused by the presence of an intramolecular hydrogen bond.

The bioorthogonal ligation of biomolecules in living systems by click reactions involving *o*-QMs and vinyl

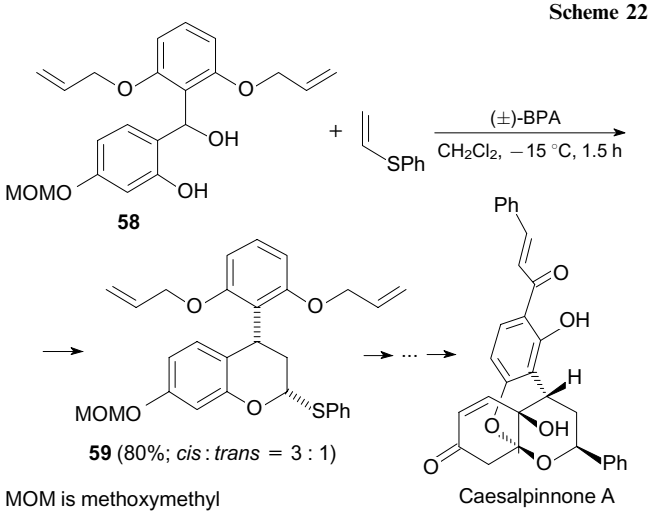
Scheme 21



(*a*) **II** (10 mol.%), CH_2Cl_2, −20 °C, 4 days;
R^1 = H, 6-Me, 7-Me, 6-OMe, 6-Cl, 6-Br;
R^2 = Ph, 4-FC_6H_4, 4-ClC_6H_4, PMP, 4-$MeSC_6H_4$, 4-PhC_6H_4, 4-$CH_2{=}CHC_6H_4$, 2-$MeOC_6H_4$, 2-Th, 3-Th, $PhC{\equiv}C$;
Ar = Ph, 2-Tol, 1-Naph, 2-Naph; Th is thienyl, Tol is tolyl, Naph is naphthyl, Phen is phenanthryl



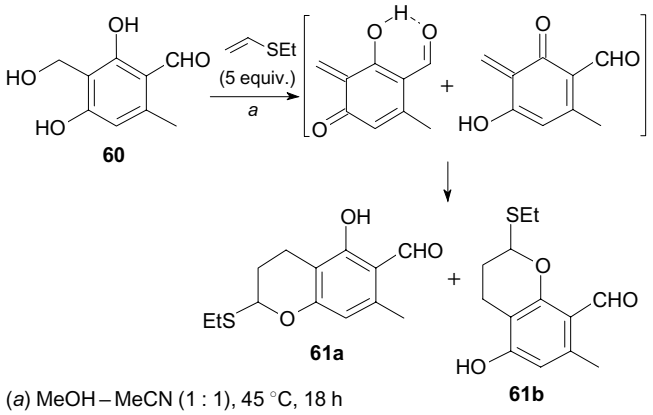
Scheme 22



MOM is methoxymethyl

sulfides is of considerable interest for medicinal studies.[42 – 45] First, the model reaction of quinoline derivative **62** and vinyl sulfide **63** gave adduct **64** in a high yield. Then *o*-QM precursor **65** containing a fluorescein moiety was

Scheme 23



(*a*) MeOH – MeCN (1 : 1), 45 °C, 18 h

successfully used for *in vitro* ligation of polypeptides and the cytostatic agent paclitaxel (Scheme 24).[46]

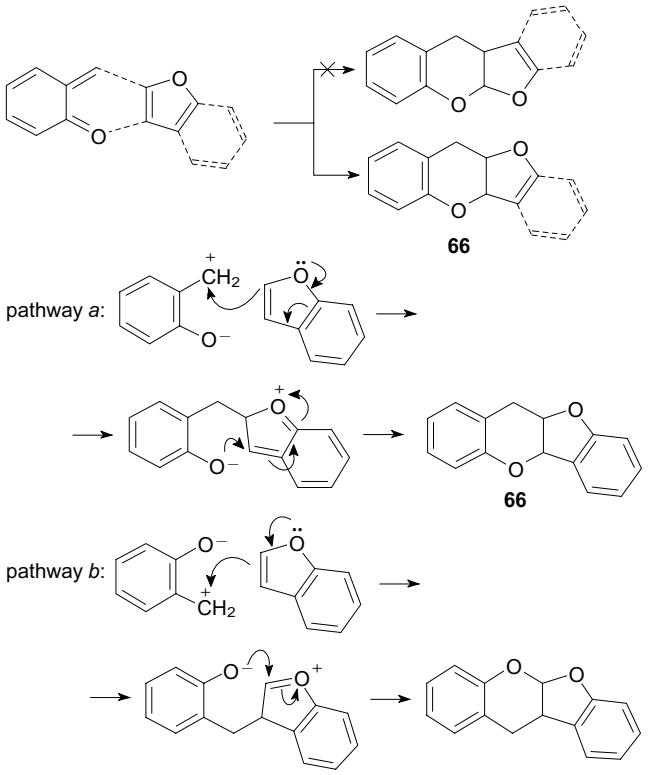
2.3. Reactions of *o*-quinone methides with furans and benzofurans

Furan derivatives act rather rarely as dienophiles in the direct electron demand Diels – Alder reaction, as a rule, in the presence of a strong electron-withdrawing group in the β-position to the oxygen atom. Few examples of inverse electron demand cycloaddition involving unsubstituted (benzo)furans are also known.[47, 48]

Restoration of aromaticity of the six-membered ring during the cycloaddition of furans to *o*-QMs is more favourable than retention of the aromatic system of the furan moiety; this was used to prepare biologically active dihydro-9*H*-furo[3,2-*b*]chromenes **66**. Almost in all cases, the regioselectivity was opposite to the regioselectivity of cycloaddition involving vinyl ethers. Similarly to other examples of electrophilic substitution in the benzofuran series, this reaction can proceed as an initial electrophilic attack by *o*-QM on the α-carbon atom of the furan ring to give zwitterion intermediate (pathway *a*). There are also a few examples of the preparation of benzofuro[2,3-*b*]chromenes according to pathway *b* (Scheme 25).

On treatment of Boc-substituted 2,4-dihydroxybenzaldehyde with methylmagnesium chloride, *o*-QM is generated under very mild conditions; *o*-QM is trapped by furan, which serves as both the 2π-component and the solvent. The reaction proceeds diastereoselectively to give 3a,9a-dihydro-9*H*-furo[3,2-*b*]chromene **67** (Scheme 26).[49]

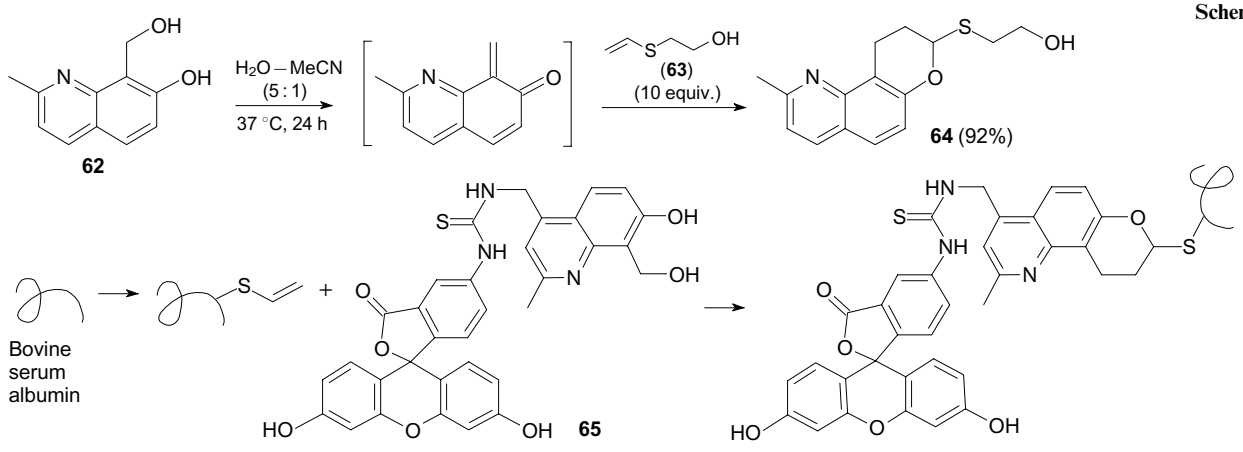
Scheme 25



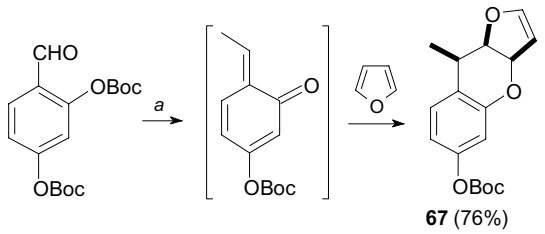
2,5-Dimethylfuran obtained from plant biomass is a readily available raw material for the synthesis of various products. It reacts with *o*-QM generated from salicyl alcohol **68a** to give a mixture of compounds **69a** – **71a** in a ratio depending on the reaction time and the nature of the acid catalyst (Table 1, Scheme 27). When molecular sieves, which bind water, are added to the reaction mixture, the reaction affords chromanofuran **69a**, while without molecular sieves, acid hydrolysis of compound **69a** takes place, resulting in the formation of 3-hydroxychroman **70a**.[50]

A variety of chromanofurans **69** and 3-hydroxychromans **70** containing both electron-donating and -withdrawing substituents in the benzene ring were synthesized. In the case of electron-donating groups, which stabilize *o*-QM, the yields of products increase. The key steps of the mechanism of formation of 3-hydroxychromans **70** include *endo*-cycloaddition, furan ring opening as a result of hydrolysis, retro-Michael reaction and intramolecular conjugate addition.

Scheme 24



Scheme 26



(*a*) MeMgCl (1.1 equiv., 2.45 M solution in THF), −78 °C→ rt

The presence of a hydrogen bond between the carbonyl oxygen atom and the phenolic hydroxyl proton leads to the predominant formation of one diastereomer. For most aryl-substituted hydroxychromans **70**, the diastereomeric ratio exceeds 20 : 1. Only for R^1 = PMP, 2-Naph, 2-Th and Me, the diastereoselectivity decreases: *dr* is 2 : 1, 14 : 1, 5 : 1 and 2 : 1, respectively. For all chromanofurans **69**, the diastereomeric ratio exceeds 20 : 1. Products **71** result from the conjugate addition of 2,5-dimethylfuran to the corresponding *o*-QMs (Scheme 28).

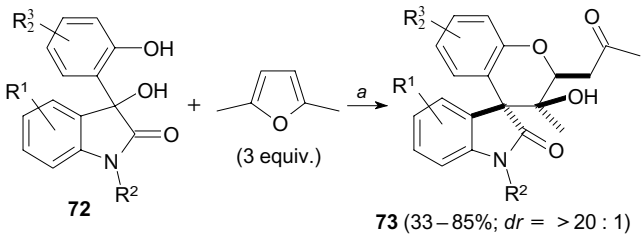
Oxindole salicyl alcohol derivatives **72a**,**b** can also act as *o*-QM precursors in the reaction with 2,5-dimethylfuran catalyzed by *p*-toluenesulfonic acid monohydrate (PTSA) (Scheme 29). The lowest yields of spiro[chroman-4,3′-oxindoles] **73** were obtained when the substituent R^1 was located in position 4 of the oxindole moiety, which could be due to steric factors.[51]

Table 1. Products of reaction of salicyl alcohol **68a** with 2,5-dimethylfuran (see Scheme 27).[50]

Catalyst (Cat)	Time	Yield (%)		
		69a	**70a**	**71a**
$MeSO_3H$	< 10 s	15	73	Traces
AcOH	24 h	0	0	0
$InBr_3$	3 h	26	Traces	52
1,1′-Binaphthyl-2,2′-diyl hydrogen phosphate	24 h	Traces	82	Traces
1,1′-Binaphthyl-2,2′-diyl hydrogen phosphate, MS 4 Å	12 h	81	10	Traces
(−)-Camphor-10-sulfonic acid	5 h	Traces	91	Traces

Note. MS are molecular sieves.

Scheme 29

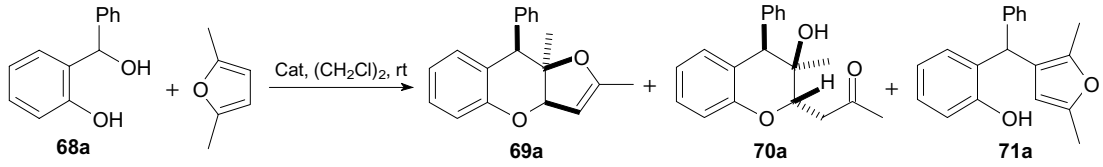


R^1 = H, Hal, Me; R^2 = Me, Et, Bn, cyclo-C_3H_5, cyclo-$C_3H_5CH_2$; All, $HC{\equiv}CCH_2$; R^3_2 = OCH_2O, benzo;
(*a*) PTSA (10 – 20 mol.%), $(CH_2Cl)_2$, rt; All is allyl

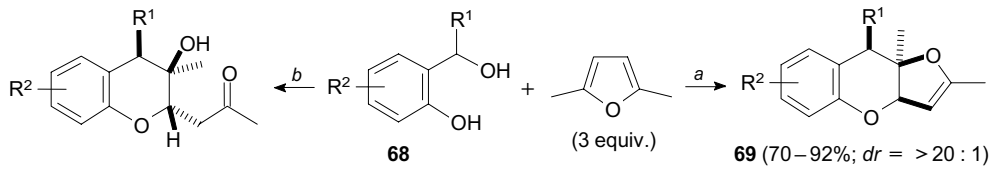
Cycloadducts that are initially formed from *o*-QMs and 2-(diarylmethyl)furans **74** in the presence of acid are further rearranged to 2-arylidene derivatives **75**. In the case of 5-methylfuran-2(3*H*)-one (**76**), which exists in equilibrium with its tautomer, 5-methylfuran-2-ol, the regioselectivity of the formation of product **77** is the same as for vinyl ethers. When an unsubstituted α-carbon atom is present in the furan ring, conjugate addition products **78a**,**b** are formed (Scheme 30).[51]

It is noteworthy that the reaction of salicyl alcohols with 2-substituted furans catalyzed by TfOH [52] or $CuBr_2$ [53] also proceeds initially as the Friedel – Crafts alkylation to give 2-(2-hydroxybenzyl)furans **79**, which are rearranged under the reaction conditions to benzofurans **80** (Scheme 31).

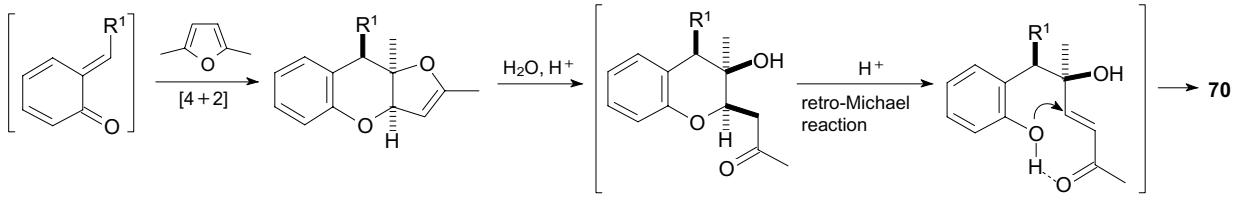
Scheme 27



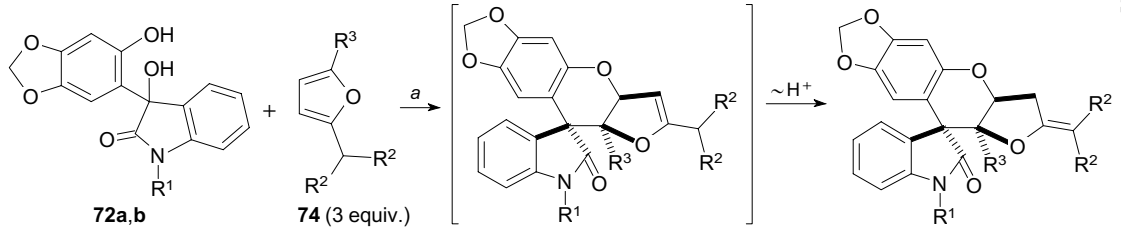
Scheme 28



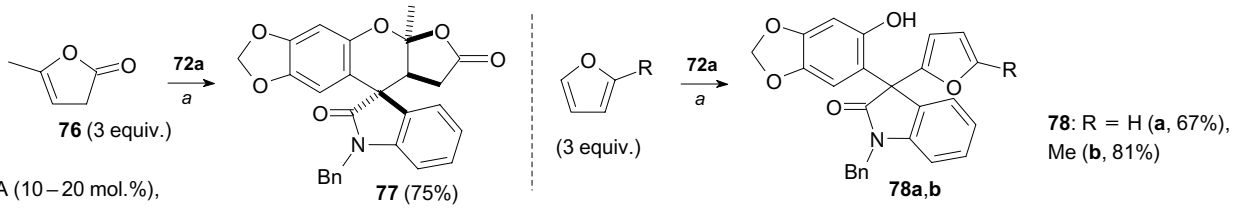
(*a*) 1,1′-binaphthyl-2,2′-diyl hydrogen phosphate (10 mol.%), $(CH_2Cl)_2$, MS 4 Å, rt, 12 h; (*b*) (−)-camphor-10-sulfonic acid (5 mol.%), $(CH_2Cl)_2$, rt, 5 h



Scheme 30

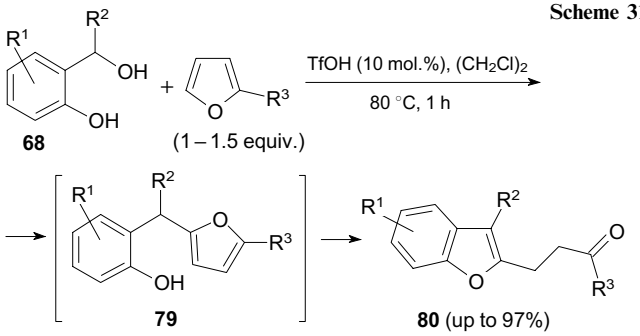


R^1 = Bn (**a**), Me (**b**); R^2 = Ph, PMP, 4-FC_6H_4; R^3 = Me, Et



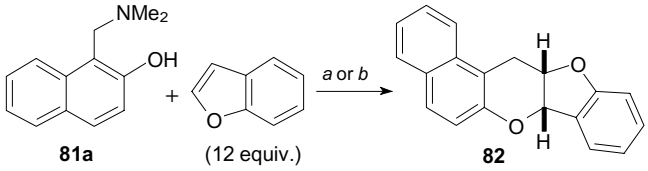
(*a*) PTSA (10 – 20 mol.%), $(CH_2Cl)_2$, rt (*dr* = > 20 : 1)

Scheme 31



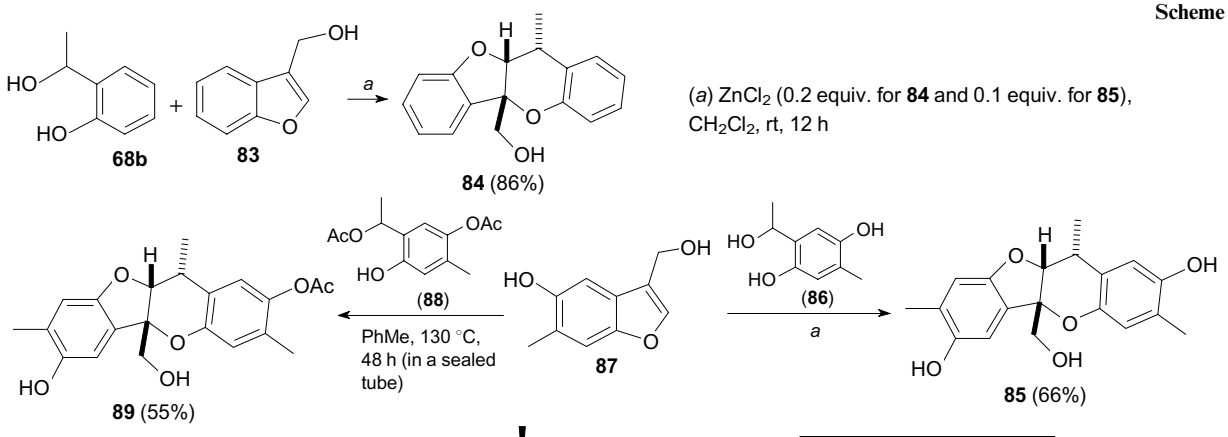
R^1 = H, Me, Cl, Br, OMe, NO_2; R^2 = H, Ar, Me, Pr^i, Bu^t, Bn, Cy; R^3 = Me, Et, Bu^t, 4-ClC_6H_4

Scheme 32

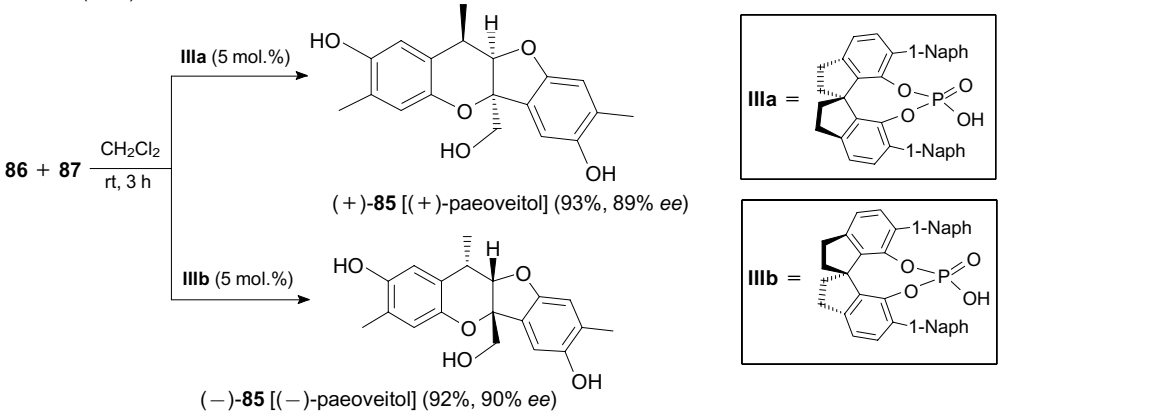


(*a*) in a sealed tube without a solvent, 135 °C, 4.5 h (15% yield);
(*b*) without a solvent, N_2, 170 °C, 3 h (97%)

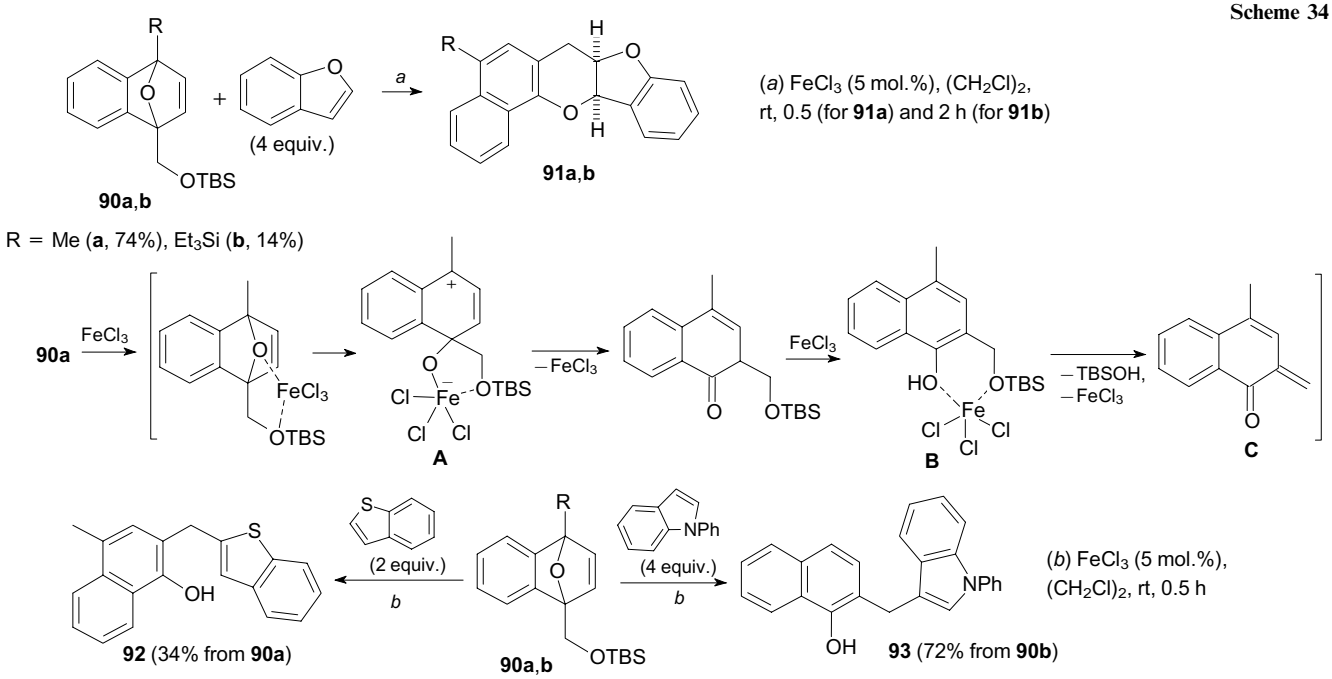
Scheme 33



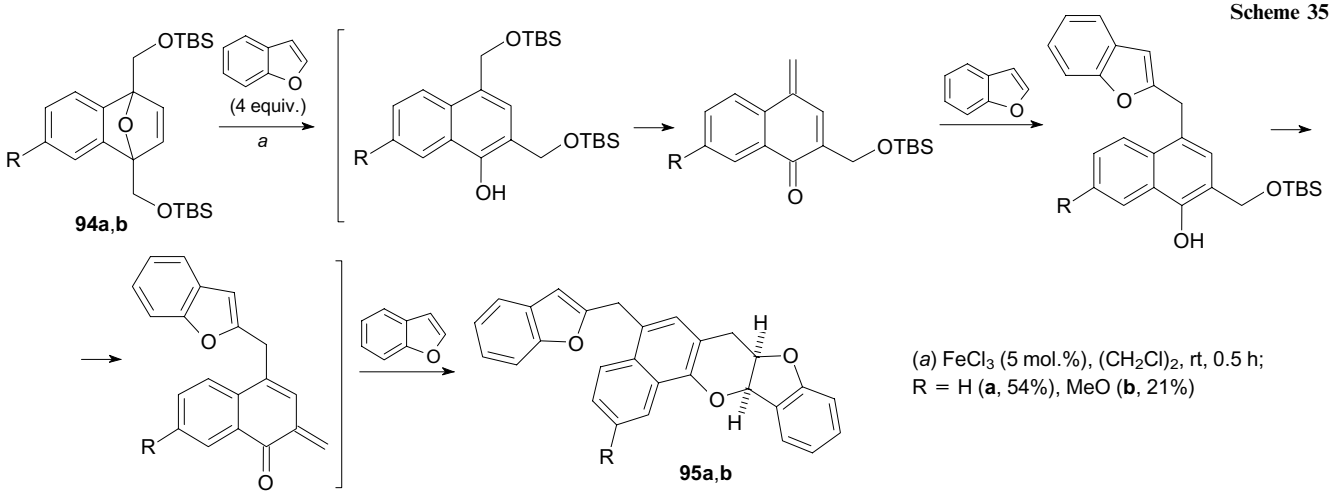
(*a*) $ZnCl_2$ (0.2 equiv. for **84** and 0.1 equiv. for **85**), CH_2Cl_2, rt, 12 h



Scheme 34



Scheme 35

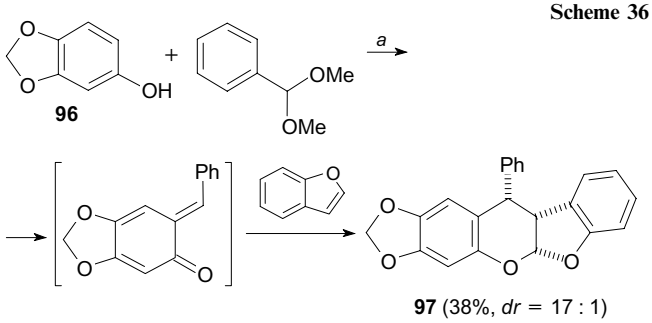


The reaction of 2-naphthol Mannich base **81a** with an excess of benzofuran leads to dearomatization of the five-membered heterocycle and gives 7a,12a-dihydro-13*H*-benzo[*f*]benzofuro[3,2-*b*]chromene (**82**) (Scheme 32).[54]

The reaction of 3-(hydroxymethyl)benzofuran **83** with salicyl alcohol **68b** catalyzed by $ZnCl_2$ resulted in the isolation of furanochroman **84**. This approach was implemented to synthesize the norditerpene (±)-paeoveitol (**85**) in gramme amounts, with hydroquinone-based *o*-QM precursor **86** and benzofuran **87** being used as substrates.[55] Another catalyst used for the synthesis of racemic paeoveitol is $Sc(OTf)_3$ (92% yield).[56] Thermolysis of *o*-QM precursor **88** in the presence of benzofuran **87** without a catalyst furnishes *O*-acyl derivative of paeoveitol **89** as the only diastereomer.[57] Catalysis by chiral phosphoric acids **IIIa**,**b** allowed for the enantioselective synthesis of paeoveitol (Scheme 33).[58]

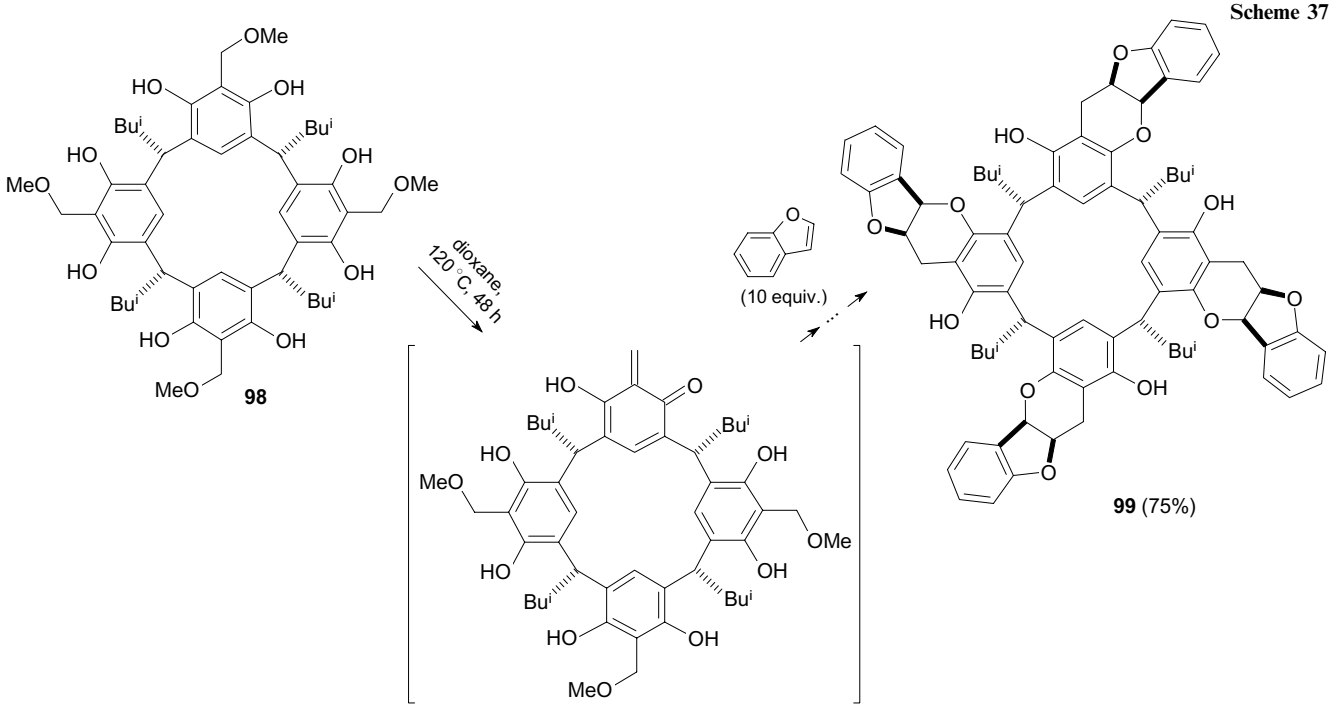
The $FeCl_3$-catalyzed cycloaddition of benzofuran to *o*-QM generated from 1,4-epoxy-1,4-dihydronaphthalenes **90a**,**b** produces benzo[*h*]benzofuro[3,2-*b*]chromenes

Scheme 36

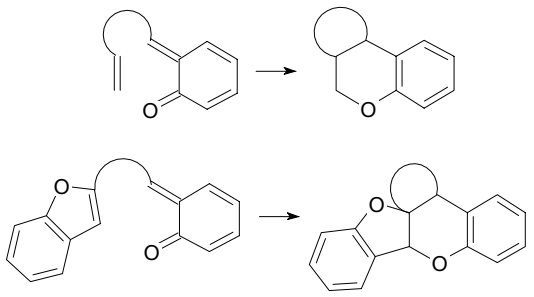


91a,**b**.[59] When trifluoroacetic anhydride (1 equiv.) is used instead of $FeCl_3$, the yield of adduct **91a** decreases from 74% to 62%. The mechanism of generation of 1,2-naphthoquinone 2-methide under the action of $FeCl_3$ is apparently initiated by cleavage of the 1,4-epoxide moiety in substrate **90a** *via* a five-membered transition state to give

Scheme 37



Scheme 38



carbocationic intermediate **A**. The subsequent shift of the silyloxymethyl group to position 2 and aromatization give intermediate **B**, which generates *o*-QM **C** upon elimination of silanol. The conjugate addition products **92** and **93** are formed under analogous conditions from benzothiophene and *N*-phenylindole. In addition, these compounds can be considered as the products of Friedel – Crafts alkylation; in the case of *N*-phenylindole, desilylation induced by chloride ions generated from $FeCl_3$ also takes place (Scheme 34).

1,4-Disilyloxymethylated 1,4-epoxy-1,4-dihydronaphthalene derivatives **94a**,**b** react with benzofuran to give pentacyclic compounds **95a**,**b** *via* the successive generation of both *para*- and *ortho*-substituted naphthoquinone methides (Scheme 35).[59]

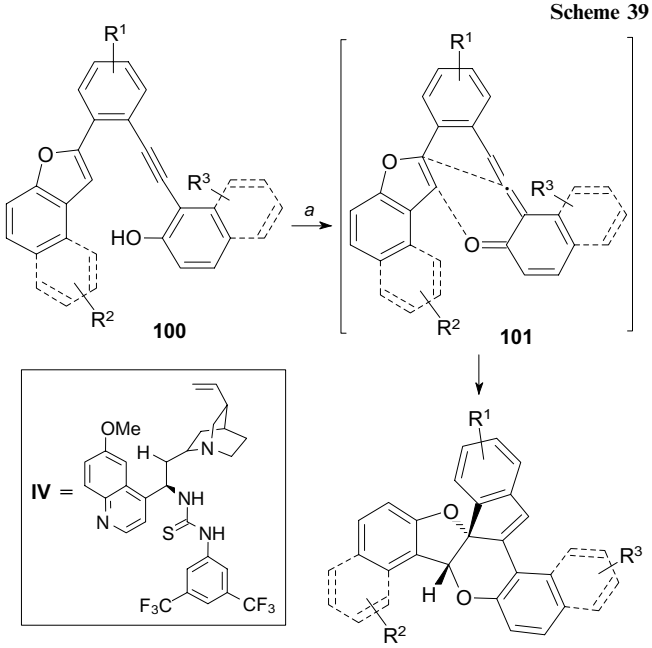
o-Quinone methide, formed upon condensation of sesamol (**96**) and benzaldehyde dimethyl acetal, reacts with benzofuran to give chromenofuran **97** (Scheme 36). The untypical structure of the three-component condensation product suggests a stepwise mechanism of cycloaddition.[60]

Heating of resorcinol-based calix[4]arene **98** with an excess of benzofuran induces four successive generations of *o*-QMs and gives cycloadduct **99** as a single diastereomer, the crude yield of which is 75% and the yield after recrystallization is 62% (Scheme 37).[61]

The intramolecular cycloaddition involving *o*-QM is an efficient approach to the synthesis of polycyclic compounds, including natural products. The presence of benzofuran and *o*-QM moieties in the same molecule allows for the synthesis of, for example, tri- and pentacyclic molecules (Scheme 38).

Treatment of ethynylnaphthols **100** with triethylamine results in the generation of arylidene *o*-quinone methides **101**,[62] which are converted to fused chromans **102** with high enantiomeric excess with good diastereoselectivity under asymmetric catalysis with cinchonine-based thiourea (**IV**)

Scheme 39

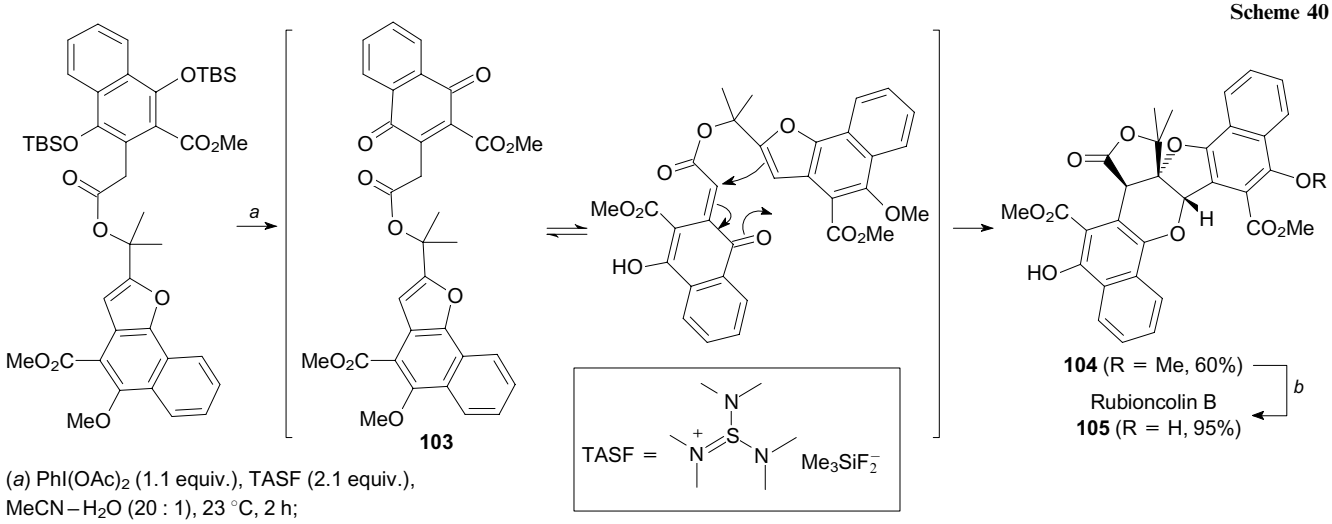


R^1 = H, OMe, Me, OMOM, O(CH$_2$)$_2$O;
R^2, R^3 = H, Br, Ac

102 (63 – 98%;
dr = > 20 : 1; *ee* > 99%)

(*a*) **IV** (10 mol.%), $CHCl_3$, 25 – 40 °C, 36 – 48 h

Scheme 40



(*a*) $PhI(OAc)_2$ (1.1 equiv.), TASF (2.1 equiv.), $MeCN-H_2O$ (20 : 1), 23 °C, 2 h;
(*b*) BBr_3 (1.1 equiv.), CH_2Cl_2, −78 °C, 15 min

(Scheme 39).[63] The same transformations were successfully accomplished in the asymmetric version using cinchonine or cinchonidine as a catalyst.[64]

The cascade transformation including *o*-QM generation *via* tautomerization of 1,4-naphthoquinone **103** and intramolecular cycloaddition to the double bond of the furan moiety resulted in the synthesis of compound **104**, a precursor of rubioncolin B (**105**) (Scheme 40).[65]

2.4. Cycloaddition of enols to *o*-quinone methides

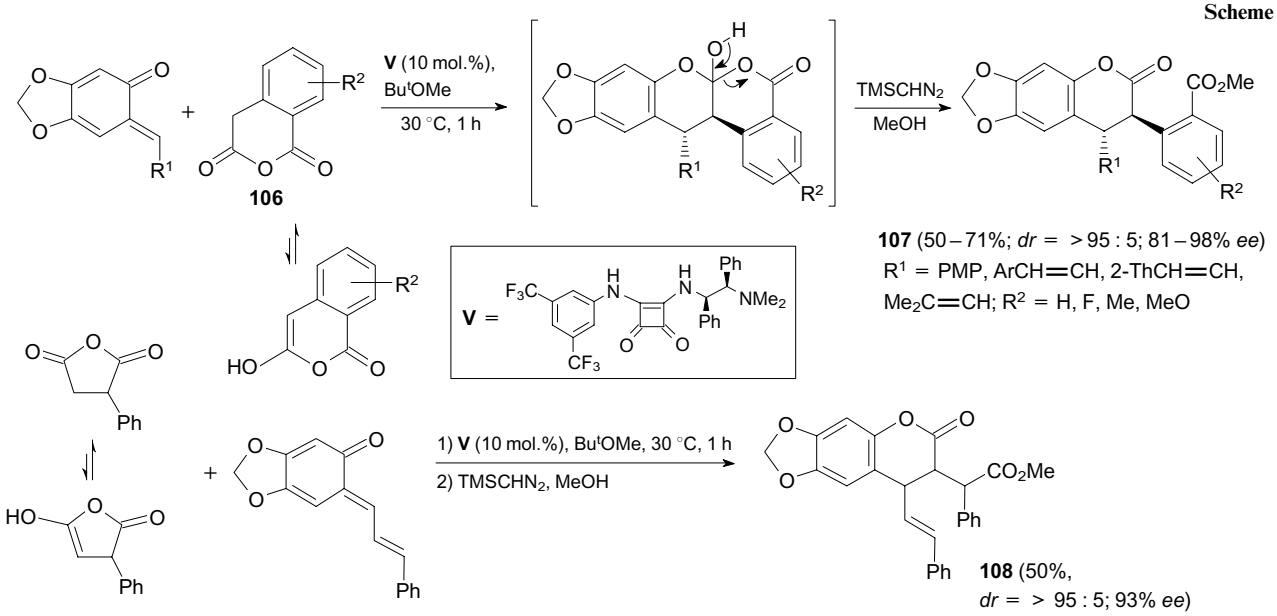
In the presence of chiral catalyst **V**, the enol form of homophthalic anhydride **106** adds to stable *o*-QMs; the subsequent methylation with trimethylsilyl diazomethane gives dihydrocoumarin derivatives **107** with high enantio- and diastereoselectivity. The range of stable *o*-QMs is limited to compounds containing electron-donating groups in the quinoid moiety and additional conjugated groups at the exocyclic carbon atom. The initially formed cycloadducts are unstable, and ring opening yields dihydrocoumarins. Phenylsuccinic anhydride is also introduced in this reaction, which gives product **108** (Scheme 41).[66]

In a basic medium, *o*-QM **109a** generated from 3-hydroxymethyl-2-naphthol is stabilized by cycloaddition to the initial 3-hydroxymethyl-2-naphthol followed by elimination of water to give 14*H*-dibenzo[*a*,*i*]xanthene **110** (Scheme 42).[67]

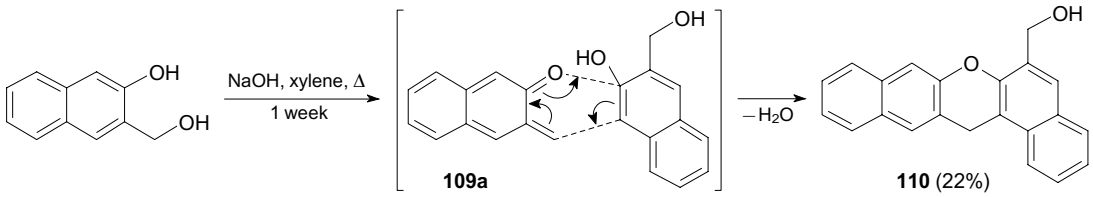
In the presence of Brønsted acids, *o*-QMs undergo [4 + 2]-cycloaddition reaction with the enol forms of azlactones **111**. The cycloadducts thus formed are usually unstable and are converted to 2*H*-chromen-2-ones (3,4-dihydrocoumarins) *via* opening of the five-membered ring (Scheme 43).

The reaction of azlactones **111** with *o*-hydroxystyrenes catalyzed simultaneously by chiral phosphoric acid **IIIc** and guanidine **VI** results in the synthesis of acetylaminodihydrocoumarins **112**.[68] Guanidine promotes enolization of azlactone, while the acid is necessary for the transformation of styrene into *o*-QM. The enantioselectivity of the cycloaddition is provided by both catalysts. 2-(1-Tosylalkyl)phenols and naphthols **113** react with azlactones under mild conditions and under basic catalysis by squaramide (**VII**) to be converted to chiral dihydrocoumarins **114**.[69] Azlactones

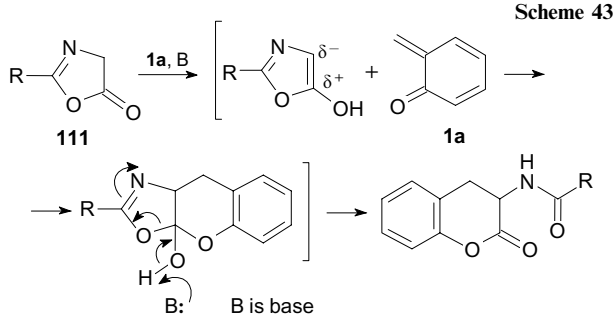
Scheme 41



Scheme 42



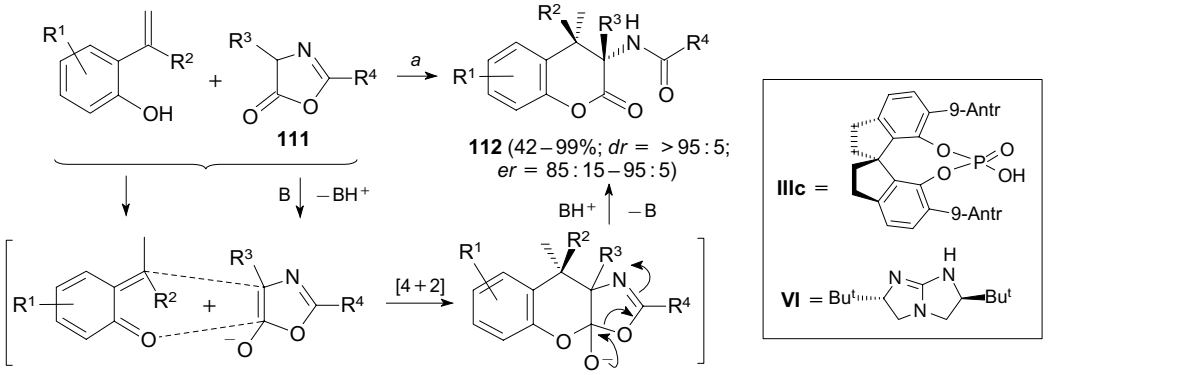
Scheme 43



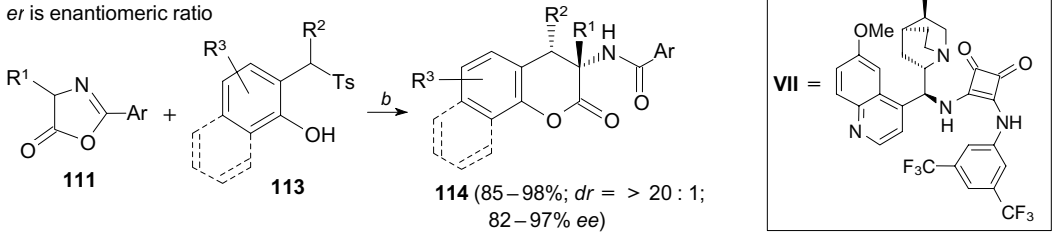
react with stable *o*-QMs **115** to give 7,8-dihydro-6*H*-[1,3]dioxolo[4,5-*g*]chromen-6-ones **116**. The reaction proceeds in the presence of a catalytic system containing imidazole needed for enolization of azlactone, scandium triflate and chiral *N*,*N*-dioxide **L**[1] as a ligand; this ensures high enantio- and diastereoselectivity (up to 96% *ee* at *dr* = > 19 : 1). When the reaction was monitored by IR spectroscopy, no potential conjugate addition product was detected, which confirms the concerted mechanism of the reaction (Scheme 44).[70]

The reaction of stable *o*-QM **115a** with enolates generated from ketoketenes on treatment with *N*-heterocyclic carbenes has been reported (Scheme 45).[71] Carbenes are generated immediately prior to use by treatment of appropriate tetrafluoroborates with caesium carbonate. The addition of carbene to ketene affords enolate **A**, which undergoes [4 + 2]-cycloaddition followed by fragmentation to afford dihydrocoumarin **117**, while catalyst **VIII** is regenerated.

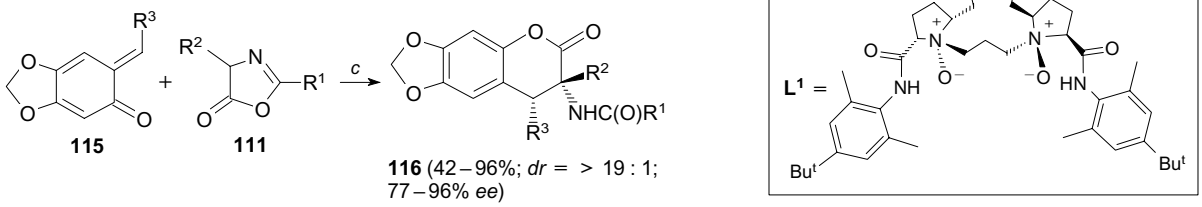
Scheme 44



(*a*) **IIIc** (10 mol.%), **VI** (20 mol.%), PhMe, $MgSO_4$, 30 °C, 16 h;
R^1 = H, Hal, OMe, OEt; R^2 = Me, Et; R^3, R^4 = Ar;
er is enantiomeric ratio

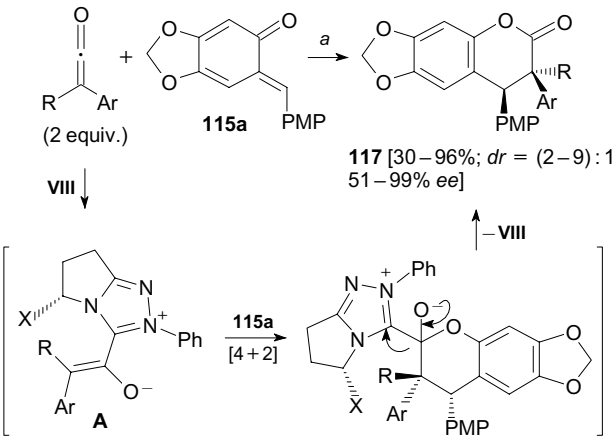


(*b*) **VII** (10 mol.%), Na_2CO_3 (1.2 equiv.), $CHCl_3$, 30 °C, 36 – 120 h;
R^1 = Bn, Et, Cy; R^2 = Ar, Et; R^3 = H, OMe, OCH_2O



(*c*) $Sc(OTf)_3$ – **L**[1] (1.05 : 1) (10 mol.%), imidazole (0.15 equiv.), THF, 35 °C, 72 h;
R^1 = Ar, Bn; R^2 = H, Me, Bn, 4-Hal$C_6H_4CH_2$; R^3 = PMP, 4-EtOC_6H_4;
Cy is cyclohexyl, Antr is anthryl

Scheme 45

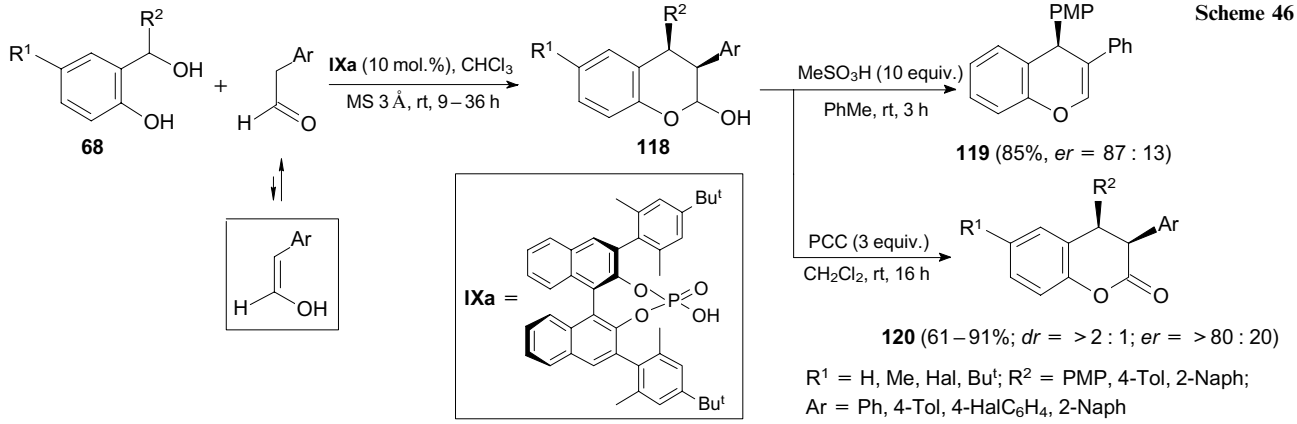


2-Chromanols **118**, prepared from salicyl alcohols **68** and enol forms of arylacetaldehydes, were converted without isolation to 4*H*-chromene **119** by treatment with $MeSO_3H$ or to 2-oxochromans **120** by oxidation with pyridinium chlorochromate (PCC) (Scheme 46).[72]

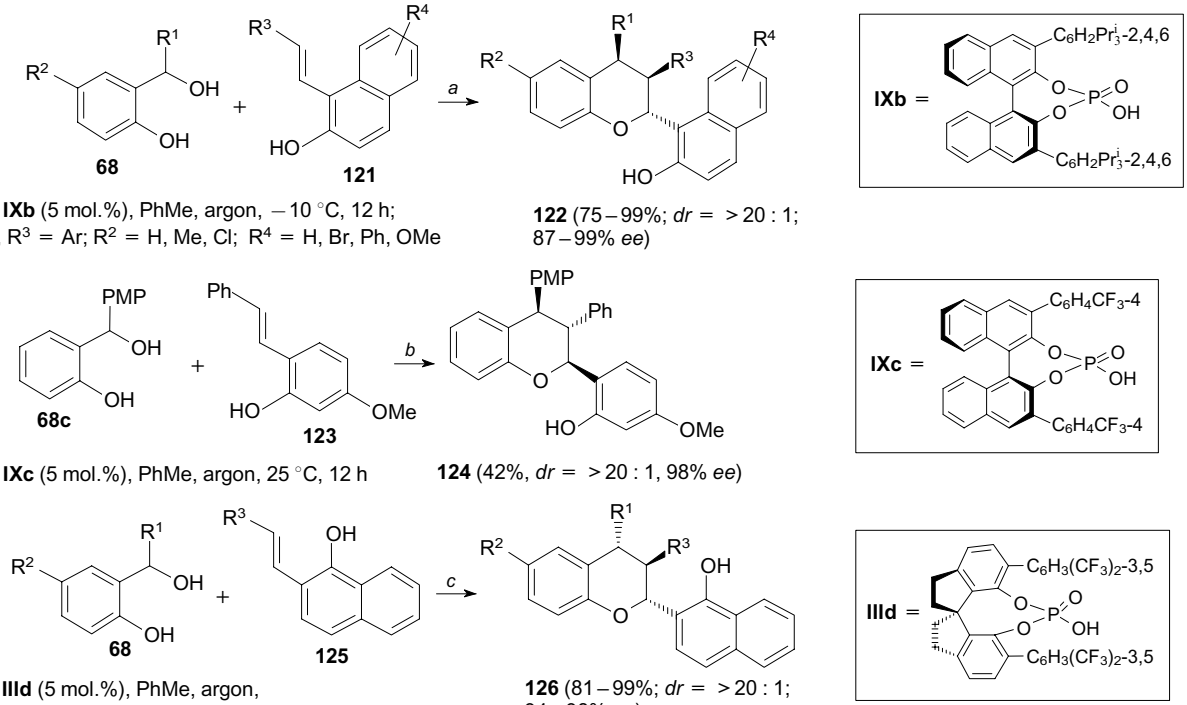
2.5. Reactions of *o*-quinone methides with *o*-alkenylnaphthols and -phenols

In the presence of chiral phosphoric acid **IXb**, biomimetic asymmetric [4 + 2]-cycloaddition of 1-alkenyl-2-naphthols **121** to *o*-QM precursors **68** affords 2,3,4-trisubstituted chromans **122** in high yields (up to 99%) and with high enantio- and diastereoselectivity (up to 98% *ee*; up to > 20 : 1 *dr*). Similarly, phenol **123** is converted to product **124** using acid **IXc** as the catalyst, while 2-alkenyl-1-naphthols **125** are converted to compounds **126** in the presence of catalyst **IIId**. It is noteworthy that in the case of 1-alkenyl-2-naphthols **121**, *trans-cis*-trisubstituted chromans **122** are formed selectively, while for 2-alkenyl-1-naphthols **125** and phenol **123**, *trans-trans*-diastereoselectivity is observed (Scheme 47).[73] The reaction between 1-[(2-aryl)vinyl]-2-naphthols and *o*-QM precursors **68** catalyzed by other chiral phosphoric acids is also highly enantioselective.[74]

Scheme 46



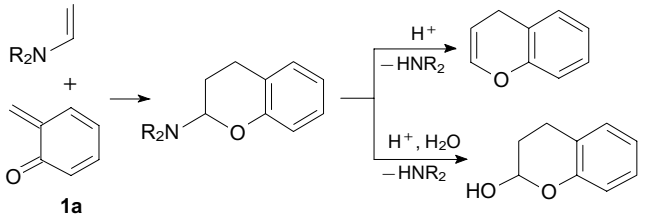
Scheme 47



2.6. Reactions of *o*-quinone methides with enamines and enamides

Enamines belong to the class of electron-rich dienophiles widely used in the Diels – Alder reactions. The initially formed cycloadducts may eliminate an amine molecule upon protonation; the ease of elimination is caused by the favourable formation of conjugated structures. For example, the reaction of enamines with *o*-QMs gives first 2-aminochromans, which can also be considered as semicyclic *N*,*O*-acetals or heterocyclic hemiaminals; subsequently, they are converted to 4*H*-chromenes *via* deamination or to 2-chromanols *via* acid hydrolysis (Scheme 48). In many cases, there is no need to use presynthesized enamines; they are generated from aldehydes or ketones *in situ*.

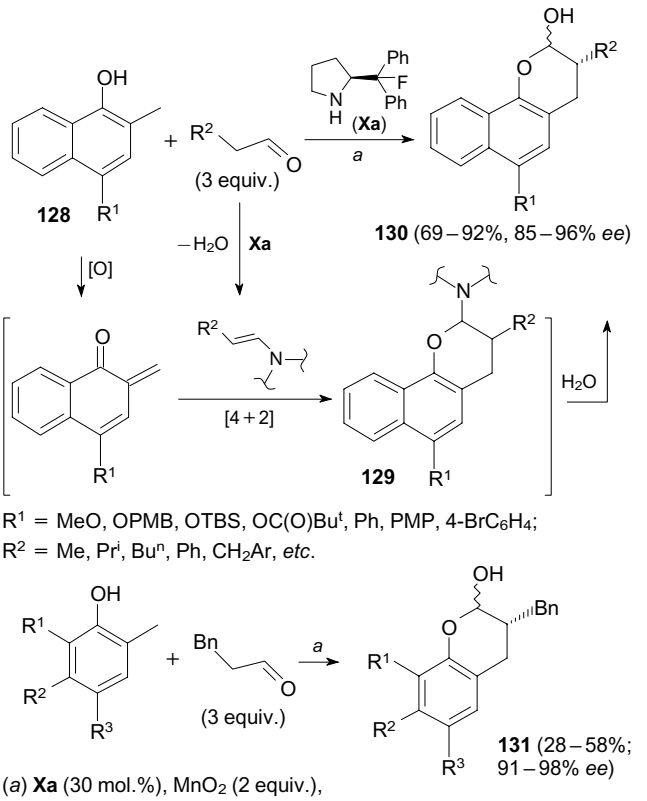
Scheme 48



A series of 3,3-dimethyl-2-morpholinochromans **127** were prepared from isobutyric aldehyde and salicylaldehydes under microwave irradiation (MW). First, salicylaldehyde reacts with 2 equiv. of morpholine (MorH) to give aminal, which eliminates an amine molecule, thus generating *o*-QM. Meanwhile, 2-methylpropanal and morpholine react to form the corresponding enamine. The subsequent Diels – Alder reaction of the enamine with *o*-QM affords chromans **127**, which undergo acid hydrolysis in the presence of HCl, AcOH or *p*-toluenesulfonic acid to be converted to chroman-2-ols.[75] The formation of *trans*-isomers can be attributed to the more advantageous *endo*-orientation of reactants due to the secondary orbital interaction between the electron-deficient π-system of *o*-QM and the lone pair of nitrogen, while the regioselectivity is due to the interaction between the partial charges on the reaction centres (Scheme 49).

The Diels – Alder reaction involving enamines, generated from aldehydes in the presence of pyrrolidine-based catalyst **Xa**, and 1,2-naphthoquinone-2-methides, which are formed upon oxidation of 2-methyl-1-naphthols **128** with manganese dioxide, provides the route to 2-aminochromans **129**. The latter are converted to 3,4-dihydro-2*H*-benzo[*h*]-chromen-2-ols **130** under the reaction conditions. The reaction with *o*-benzoquinone methide precursors proceeds in a similar way, but products **131** are formed in lower yields, especially in the presence of weak electron-donating groups (Scheme 50).[76]

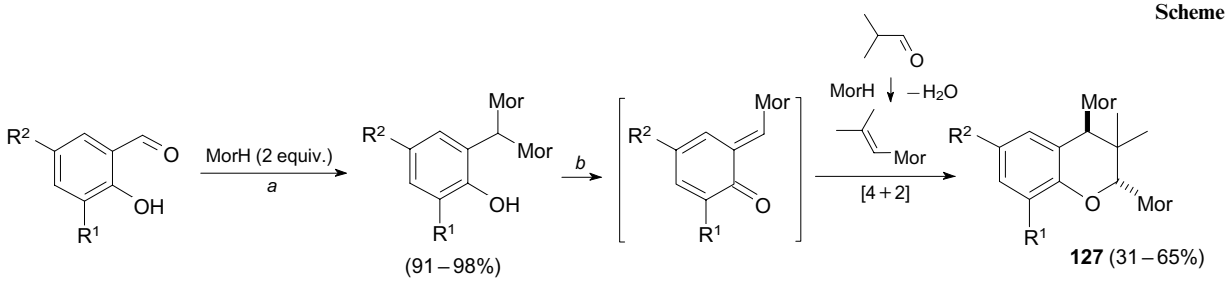
Scheme 50



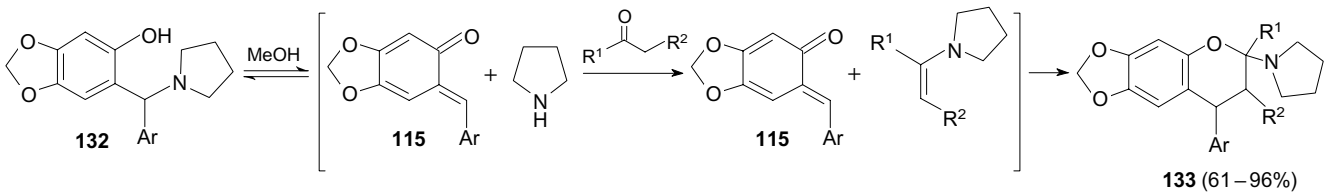
Mannich bases **132**, prepared from sesamol, pyrrolidine and aromatic aldehydes, react with ketones (acetone, butanone, cyclopentanone, cyclohexanone), ethyl acetoacetate and propanal to give 2-pyrrolidinylchromans **133** as a mixture of diastereomers. It is noteworthy that the Mannich bases containing morpholine or piperidine residues as the amine moiety do not react with aldehydes and ketones. In a methanol solution, and equilibrium is established between the Mannich base and *o*-QMs **115**. The released pyrrolidine reacts with the added carbonyl compound to give enamine, which undergoes [4 + 2]-cycloaddition with *o*-QM (Scheme 51).[77]

The presynthesized enamines, especially those based on cyclic carbonyl compounds, are also widely used to prepare chromans.[49, 78 – 85] In the search for new glucocorticoid receptor antagonists structurally similar to lead compound

Scheme 49

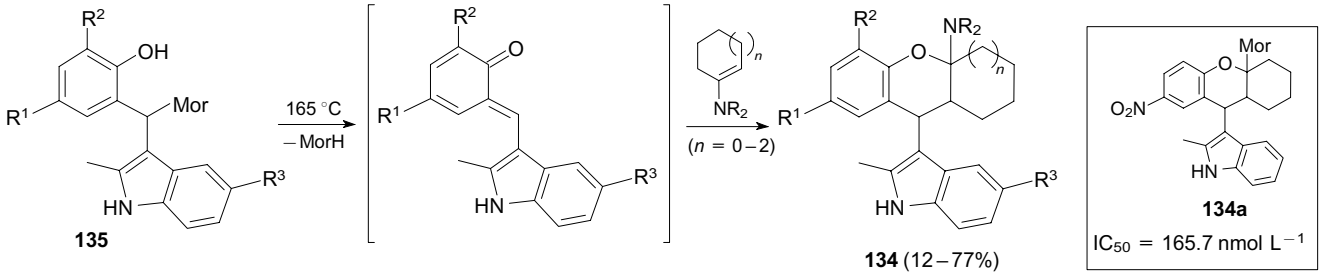


Scheme 51



R^1 = H, Me; R^2 = H, Me, CO_2Et; $R^1–R^2$ = $(CH_2)_3$, $(CH_2)_4$

Scheme 52



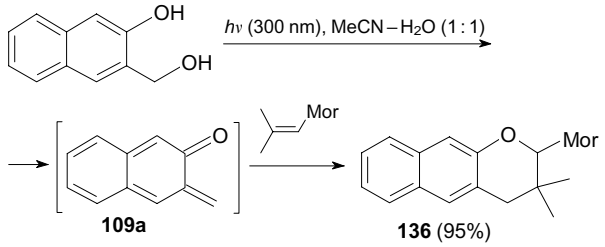
R^1 = H, Cl, Br, O_2N, CF_3O, MeO; R^2 = H, F, Br, All; R^3 = H, MeO; NR_2 = Mor, , , NPr^n_2

134a, the reaction between phenolic Mannich bases **135** and enamines was used to prepare a series of fused chromans (Scheme 52).[86–88]

The photochemical generation of 2,3-naphthoquinone 3-methide **109a** in the presence of *N*-(isobutenyl)morpholine results in the formation of 4-(3,3-dimethyl-3,4-dihydro-2*H*-benzo[*g*]chromen-2-yl)morpholine (**136**) in a high yield (Scheme 53).[27]

The reaction of 1,1-bis(morpholino)ethylene (**137**) with Mannich bases derived from phenol and 2-naphthol as

Scheme 53

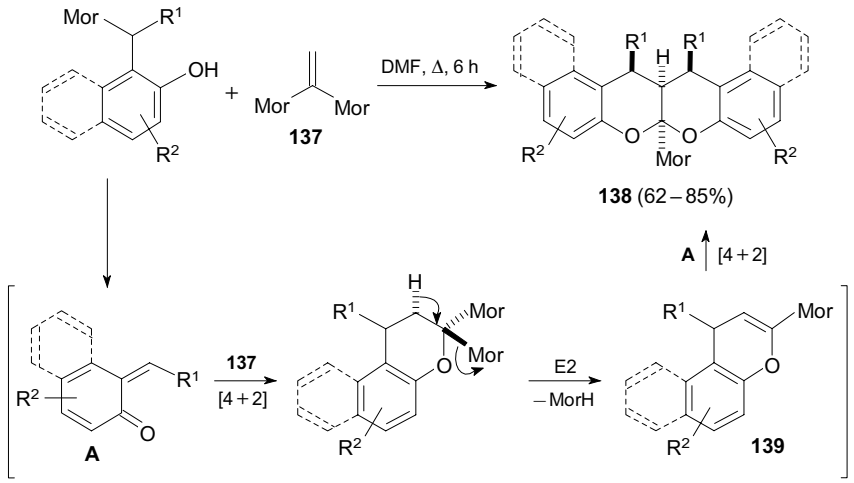


o-QM precursors conducted by refluxing in DMF furnishes a series of chromeno[2,3-*b*]chromenes **138**. The reaction mechanism includes the hetero-Diels–Alder reaction of ketene aminal with *o*-QM **A**, elimination of the morpholine molecule and [4 + 2]-cycloaddition of the intermediately formed chromene **139** to *o*-QM (Scheme 54).[89]

2-Methyleneindolines **140a–c** represent a special type of enamines. When reacting with 2-chloromethyl-4-nitrophenol, they give formal [4 + 2]-cycloaddition products — spiro[chroman-2,2′-indolines] **141a–c** (Scheme 55). Compounds of this type are of interest as chemosensors for cyanide ions[90] and ultrafast molecular photoswitches.[91]

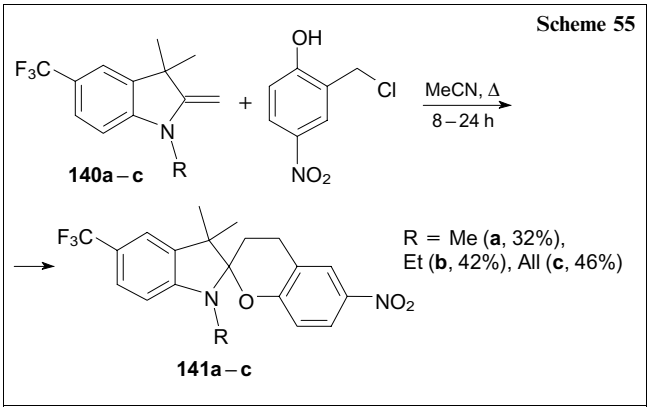
N-Vinylimidazole is used rather rarely as a dienophile. One example of its reaction with 1,2-naphthoquinone 1-methide generated from Mannich base **81a** has been reported. To attain a reasonable yield of benzochroman **142**, long-term heating of reactants at high temperature in the presence of hydroquinone is required in order to suppress radical oxidation and oligomerization reactions (Scheme 56).[92]

Scheme 54

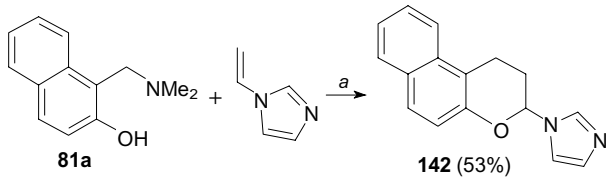


R^1 = H, Ph, 2-Th; R^2 = H, Bu^t, 1-Ad;
Ad is adamantyl;
Mor is morpholino

Scheme 55



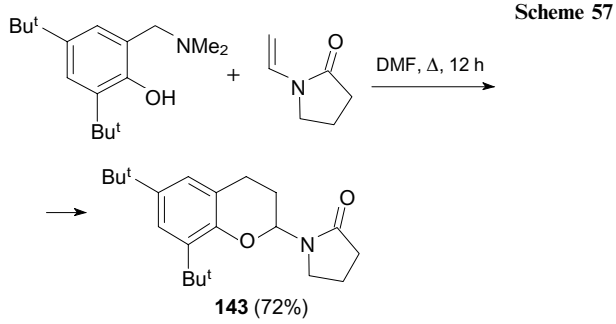
Scheme 56



(*a*) Ph_2O, hydroquinone, N_2, 200 °C, 20 h

N-Vinyl-2-pyrrolidone, which can be regarded as a cyclic enamide, often serves for trapping of *o*-QMs to prove that they are involved in particular reactions. For example, chroman **143** was isolated upon the reaction of 2,4-di-*tert*-butylphenol Mannich base with *N*-vinylpyrrolidone (Scheme 57).[93]

Scheme 57

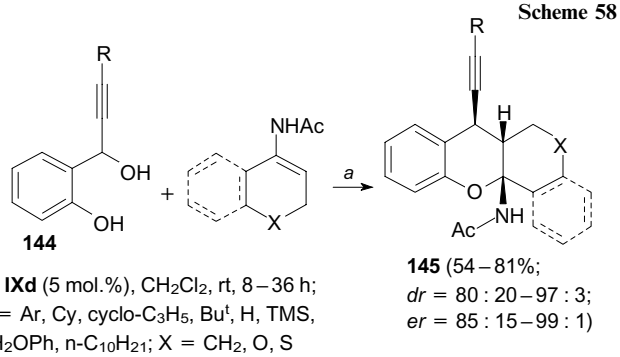


o-(α-Benzotriazolylalkyl)phenols,[94] 4*H*-1,2-benzoxazines,[95,96] Koshland's reagent [97] and *o*-alkylphenols [38] are also used as *o*-QM precursors, while *N*-vinylacetamide can be employed as enamine instead of *N*-vinylpyrrolidone.[98]

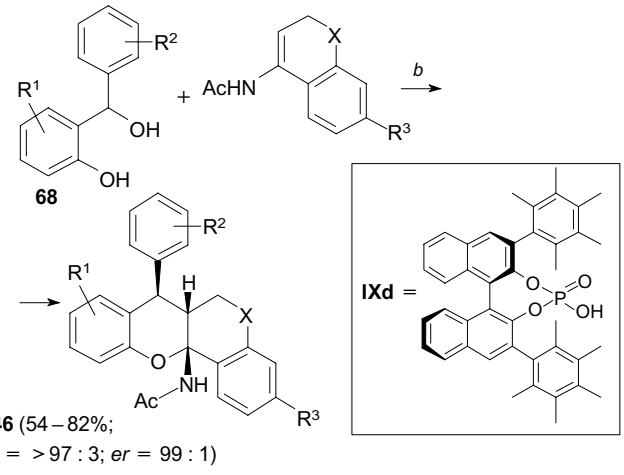
The reaction of 1-(*o*-hydroxyphenyl)propargyl alcohols **144** with enamides catalyzed by chiral phosphoric acids was used to synthesize a series of annulated chromans **145**. The reaction proceeds under mild conditions at room temperature with a relatively low amount of catalyst **IXd** being sufficient to attain a high enantioselectivity.[99] Aryl-substituted salicyl alcohols **68** can also be used in this reaction instead of propargyl derivatives, while BINOL derivatives serve as catalysts (Scheme 58).[100] The reaction gives products **146**.

2-Vinylindoles can also be classified as vinylogues of enamines, because the nitrogen atom in these compounds is in conjugation with double bonds. It was found that when salicyl alcohols react with 3-methyl-2-vinylindoles **147**, cycloaddition products **148** are formed with high diastereoselectivity,[101] and only *N*-unsubstituted indoles react with

Scheme 58



(*a*) **IXd** (5 mol.%), CH_2Cl_2, rt, 8 – 36 h;
R = Ar, Cy, cyclo-C_3H_5, Bu^t, H, TMS, CH_2OPh, n-$C_{10}H_{21}$; X = CH_2, O, S



(*b*) **IXd** (5 mol.%), MS 4 Å, CH_2Cl_2, rt, 12 – 84 h;
R^1, R^2, R^3 = H, Alk, OAlk, Hal; X = CH_2, O, S

o-QM precursors to give the corresponding cycloadducts. It is also noteworthy that the double bond configuration has no effect on the course of the reaction. It was shown that the reaction with either the pure *Z*-isomer or a mixture of *E*- and *Z*-isomers of olefin **147a** gives one and the same result. The isomerization of the starting olefin under the reaction conditions is indicated by the fact that a minor amount of the *E*-isomer was detected in the reaction mixture when the pure *Z*-isomer was used for the reaction. The presence of a substituent in position 3 of indole is also a key point for successful cycloaddition. Indeed, in the case of salicyl alcohol **68a** and 3-unsubstituted 2-styrylindole (**149**), only the conjugated addition product **150** is isolated (Scheme 59).

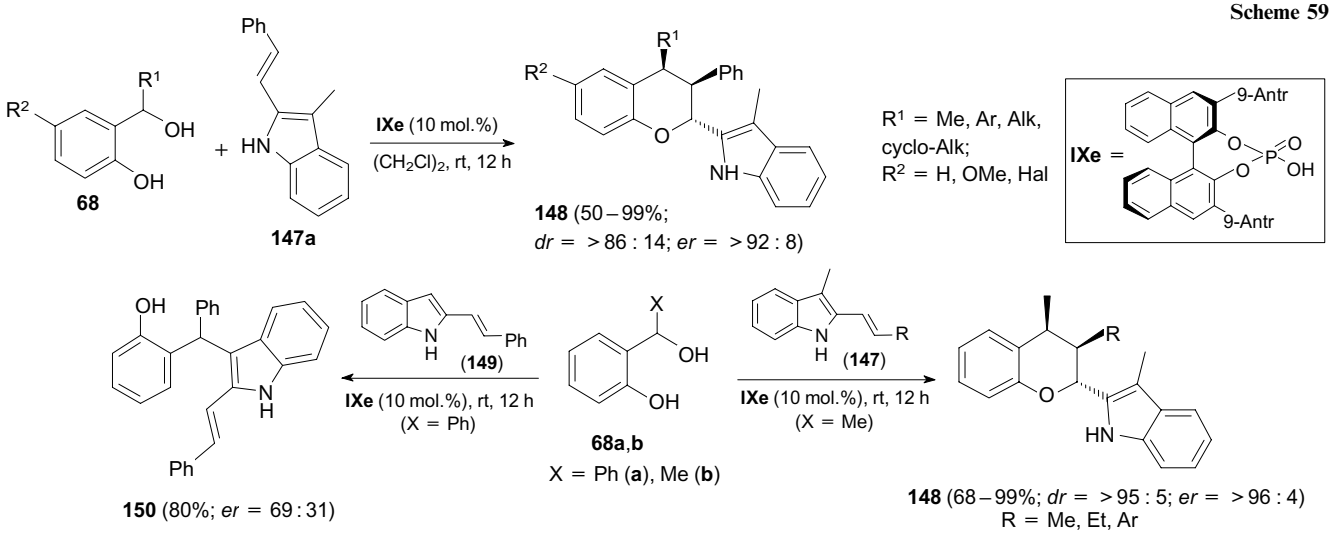
Instead of *o*-hydroxybenzyl alcohols, stable *o*-QMs based on sesamol were also used in the reaction with 3-methyl-2-vinylindoles.[102]

Recently, a method has been developed (Scheme 60) for the synthesis of 3-tosylaminomethyl-4*H*-chromene **151** from *N*-allenamides and *o*-hydroxybenzyl alcohols **68** using Ag^I as the catalyst. The presence of silver salts promotes the generation of *o*-QMs and activates the allene towards the subsequent cycloaddition. The initially formed cycloadduct is then isomerized to 4*H*-chromene.[103]

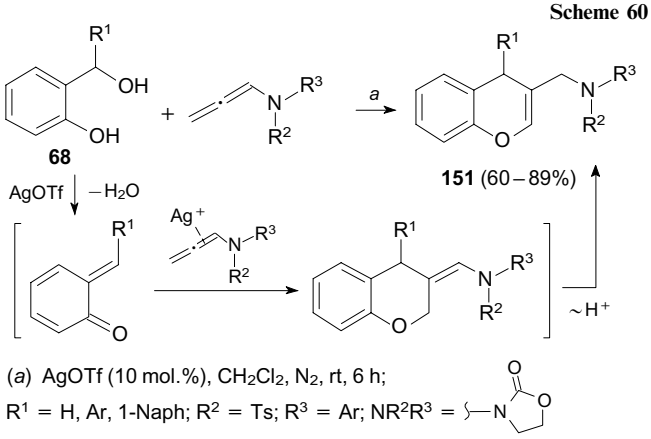
2.7. Diels – Alder reactions of *o*-quinone methides with indoles

In most cases, the reactions of indoles with *o*-QM precursors give *C*- and *N*-(*o*-hydroxybenzyl)indoles.[104,105] Nevertheless, [4 + 2]-cycloaddition products **152a**,**b** were isolated upon reactions of skatole (3-methylindole) and 2,3-dimethylindole with 2-chloromethylphenols in aqueous dioxane

Scheme 59



Scheme 60



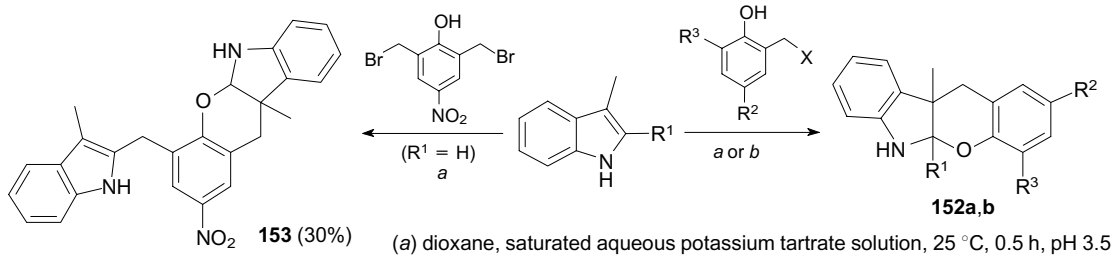
at pH ~3.5. The synthesis of 5a,6,10b,11-tetrahydrochromeno[2,3-*b*]indole **152b** was accomplished using the corresponding salicyl alcohol under anhydrous conditions in the presence of boron trifluoride etherate. In the case of 2,6-bis(bromomethyl)-4-nitrophenol and skatole (1 : 2 ratio), cycloaddition is accompanied by benzylation of skatole into position 2 to give product **153**.[106] In the case of 2-(bromomethyl)-4-nitrophenol (Koshland's reagent), the yield of tetrahydrochromeno[2,3-*b*]indole **152a** in aqueous acetone is 70%.[107] *N*-Methyl-2,3-disubstituted indoles react with Koshland's reagent in the presence of potassium carbonate to give Diels – Alder adducts **154a** – **e**, which are of interest as photochromic indicators for cyanide ions (Scheme 61).[108, 109]

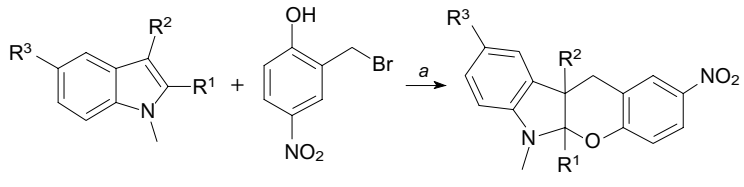
The reaction of 1,3-disubstituted indoles with alkyl-*p*-benzoquinones in the presence of a base furnishes polycyclic indolines **155**. It is believed that on treatment with triethylamine, quinone is isomerized to *o*-QM **156**, which acts as a heterodiene in the reaction with indoles (Scheme 62).[110]

Ketal **157** was employed to prepare compound **158**, an analogue of the natural alkaloid nomofungin. Thermolysis of the ketal results in the generation of *o*-QM upon elimination of an acetone molecule. The subsequent intramolecular [4 + 2]-cycloaddition promotes dearomatization of the indole ring to give *N*,*O*-acetal **158** (Scheme 63).[111]

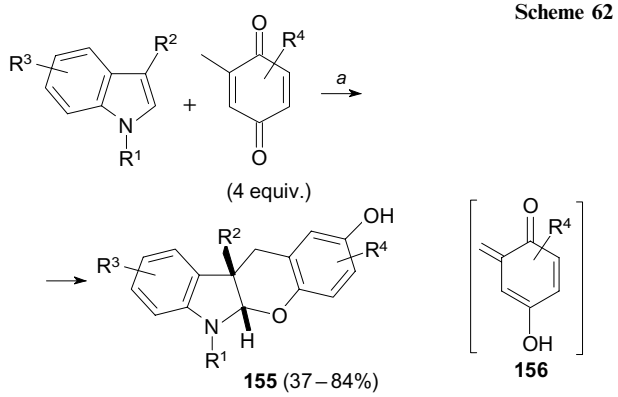
The intramolecular organocatalytic dearomatization of the indole ring also takes place when a catalytic amount of

Scheme 61



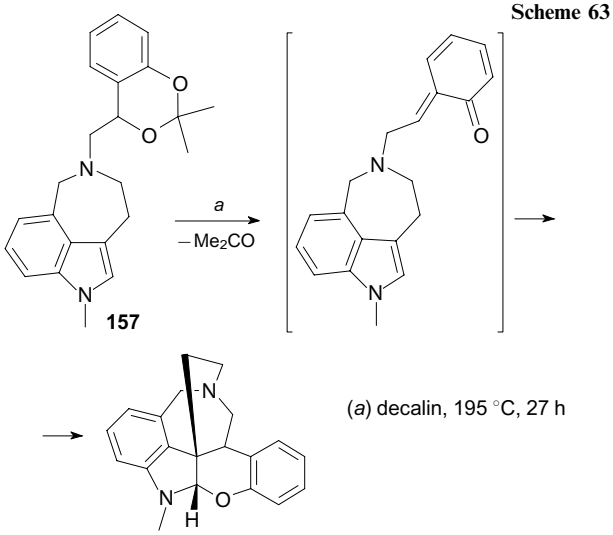


Scheme 62



(*a*) Et_3N (20 mol.%), EtOH, 70 °C, 12 – 48 h;
R^1 = Me, Bn, All; R^2 = Me, Bn, $(CH_2)_2OTBS$;
R^3 = H, Cl, Br, OMe; R^4 = Me, Pr^i, OMe, Cl

Scheme 63



(*a*) decalin, 195 °C, 27 h

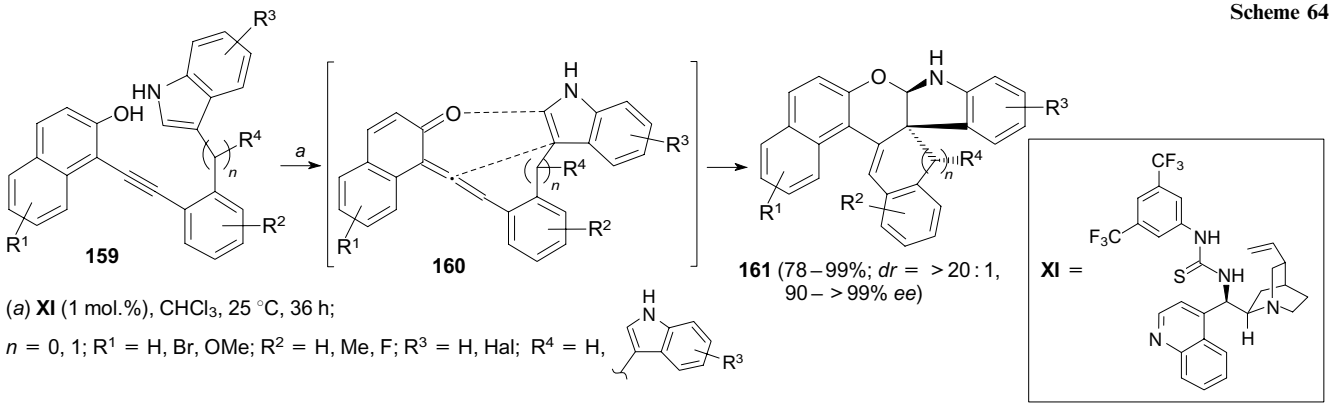
an optically active base is added to 2-(phenylethynyl)naphthols **159**. In the presence of catalyst **XI**, the reaction has high diastereo- and enantioselectivity. The key step of the reaction mechanism is the prototropic rearrangement of 2-(phenylethynyl)naphthol to vinylidene type *o*-QMs **160** (Scheme 64). Some of the obtained products **161** exhibit anticancer activities.[112]

The oxidation of 1,3-dimethyl-2-naphthol under the action of cumene hydroperoxide in the presence of an excess of *N*-methylindole and catalytic amounts of quinuclidinium salt **162** leads to polycyclic *N*,*O*-acetal **163**, in which the dihydropyran ring is opened during purification on silica gel to give formal electrophilic substitution product **164** (Scheme 65).[38] Evidently, the reaction proceeds *via* the generation of 1,2-naphthoquinone 1-methide **165**. When Ag_2O is used as the oxidant, the yield of indole **164** is only 29%. The generation of *o*-QM **166** is energetically less favourable due to the loss of aromaticity of both benzene rings.

1*H*-Isochromene **167** existing in equilibrium with *o*-QM **168** reacts with 1,2,3,4-tetrahydrocarbazole to give polycyclic indoline **169** in a low yield (Scheme 66).[113]

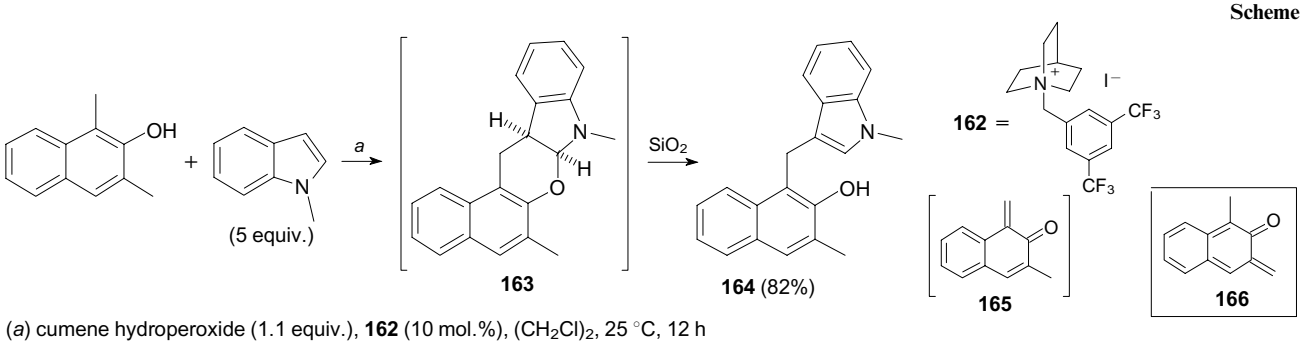
Thus, consideration of rather scanty data on the reactions of indoles with *o*-QMs provides the conclusion that cycloadducts can be isolated only for 3-substituted indoles. In other cases, the products of Friedel – Crafts hydroxybenzylation of indoles are formed most often.

Scheme 64



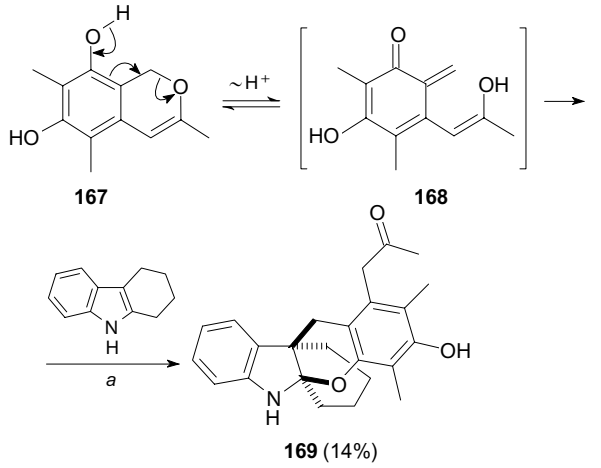
(*a*) **XI** (1 mol.%), $CHCl_3$, 25 °C, 36 h;
n = 0, 1; R^1 = H, Br, OMe; R^2 = H, Me, F; R^3 = H, Hal; R^4 = H,

Scheme 65



(*a*) cumene hydroperoxide (1.1 equiv.), **162** (10 mol.%), $(CH_2Cl)_2$, 25 °C, 12 h

Scheme 66



(*a*) $BF_3 \cdot Et_2O$ (10 mol.%), MeCN, rt, 30 min

3. Cycloaddition of *o*-quinone methides to olefins with electron-withdrawing groups

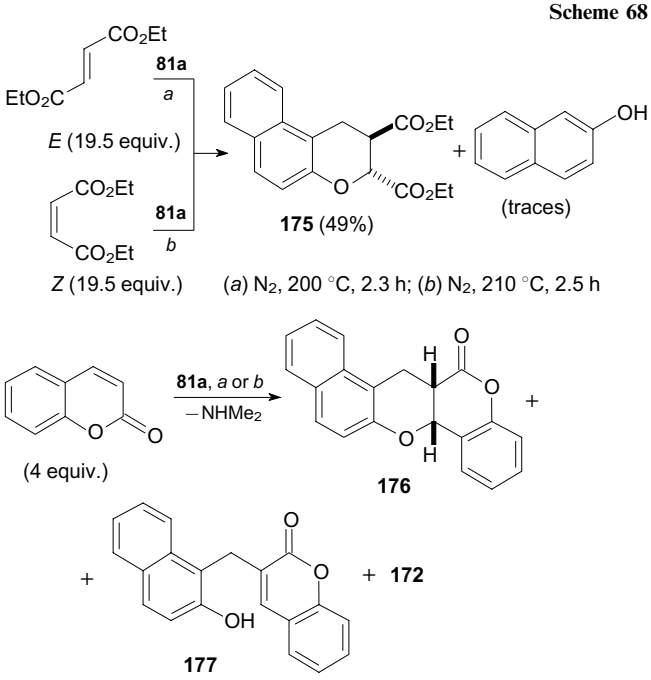
3.1. Reactions of *o*-quinone methides with electrophilic olefins

The inertness of *o*-QMs towards dienophiles with electron-withdrawing substituents can be attributed to the fact that *o*-QMs themselves are electron-deficient heterodienes due to the presence of the carbonyl oxygen atom. Nevertheless, there are examples of this type of transformations, first of all, involving unsaturated carbonyl compounds. According to quantum chemical calculations, these reactions proceed as concerted inverse electron demand [4 + 2]-cycloaddition because of a relatively low LUMO energy of *o*-QMs; therefore, the interaction between the LUMO of *o*-QMs and the HOMO of dienophiles proves to be more favourable.[114]

The formation of 2-benzo[*f*]chromenecarboxylic acid esters **170** from Mannich base **81a** and various unsaturated esters is one of the first examples of such reactions.[54] In the case of ethyl crotonate, bis(2-hydroxy-1-naphthyl)methane **171** and dihydro-1,2-naphthoquinone 1-methide spirodimer **172** are also detected in the reaction mixture. In the reaction of ethyl cinnamate, benzochroman derivative **173** is formed as the major product; however, apart from 2-naphthol, ester **174** is also detected in a small amount. This product may result from dihydropyran ring opening of compound **173** induced by dimethylamine released upon thermolysis of Mannich base **81a** (Scheme 67).

It is worth noting that for both diethyl fumarate and diethyl maleate, the *trans*-isomer of diethyl dihydro-1*H*-benzo[*f*]chromene-2,3-dicarboxylate (**175**) is formed as the major product. Apparently, the released dimethylamine induces isomerization of the *cis*-isomer to more stable *trans*-diester *via* conjugate addition of amine to diethyl maleate followed by its elimination. The reaction with coumarin gives rise to the cycloadduct in a low yield; the proportion of the product **177** resulting from dihydropyran ring opening of 6a,14a-dihydro-6*H*,7*H*-benzo[*f*]chromeno[4,3-*b*]chromen-6-one **176** increases with temperature rise. Apparently, this process is also catalyzed by the released dimethylamine (Scheme 68).[54]

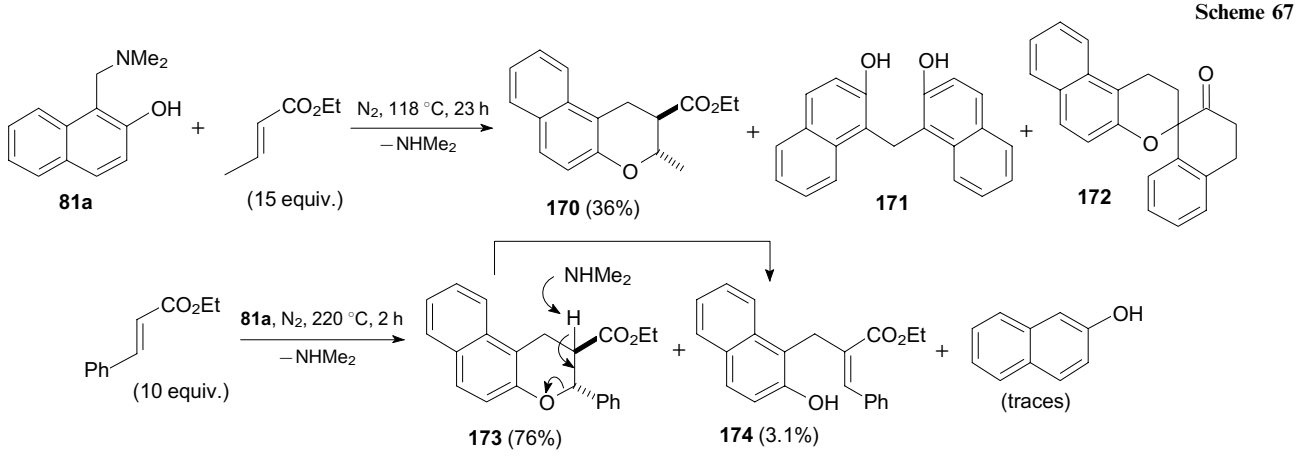
Scheme 68



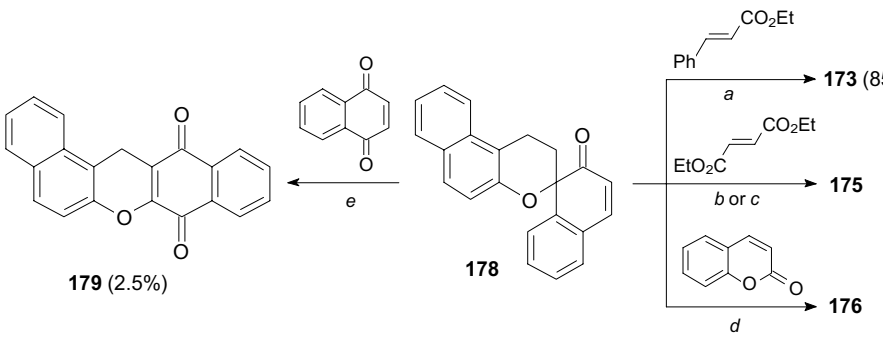
(*a*) tetralin, 140 °C, 20 h [8.8% (**176**), 2.7% (**177**)];
(*b*) tetralin, 208 °C, 1.3 h [3% (**176**), 22% (**177**)]

In all reactions depicted in Schemes 67 and 68, 1,2-naphthoquinone 1-methide spirodimer **178** is formed as one of the products. It was found that at high temperature, it can serve as an efficient precursor of 1,2-naphthoquinone 1-methide. An advantage of using spirodimer **178** over the use of other *o*-QM precursors is the absence of any low-

Scheme 67

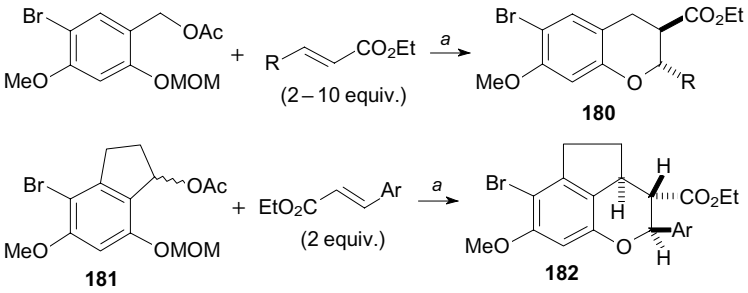


Scheme 69



(*a*) ethyl cinnamate (excess), N_2, 220 °C, 3 h; (*b*) diethyl fumarate (excess), N_2, 210 °C, 2 h (28%); (*c*) in a sealed tube, 205 °C, 12 h (56%); (*d*) mesitylene, N_2, 165 °C, 2 h (8% yield), 30 h (91%); (*e*) mesitylene, N_2, 165 °C, 1.5 h

Scheme 70



R = Ph (33%, *dr* = > 99 : 1), PMP (76%, *dr* = > 99 : 1), Ph (33%, *dr* = 10 : 1)

Ar = 4-BnOC$_6$H$_4$ (69%), 2,5-(MeO)$_2$C$_6$H$_3$ (38%), 4,5-(MeO)$_2$C$_6$H$_3$ (45%), 3,4-(OCH$_2$O)C$_6$H$_3$ (64%), 3,4,5-(MeO)$_3$C$_6$H$_2$ (43%), 2,3,4-(MeO)$_3$C$_6$H$_2$ (22%), 2-MeO-4-BrC$_6$H$_3$ (13%)

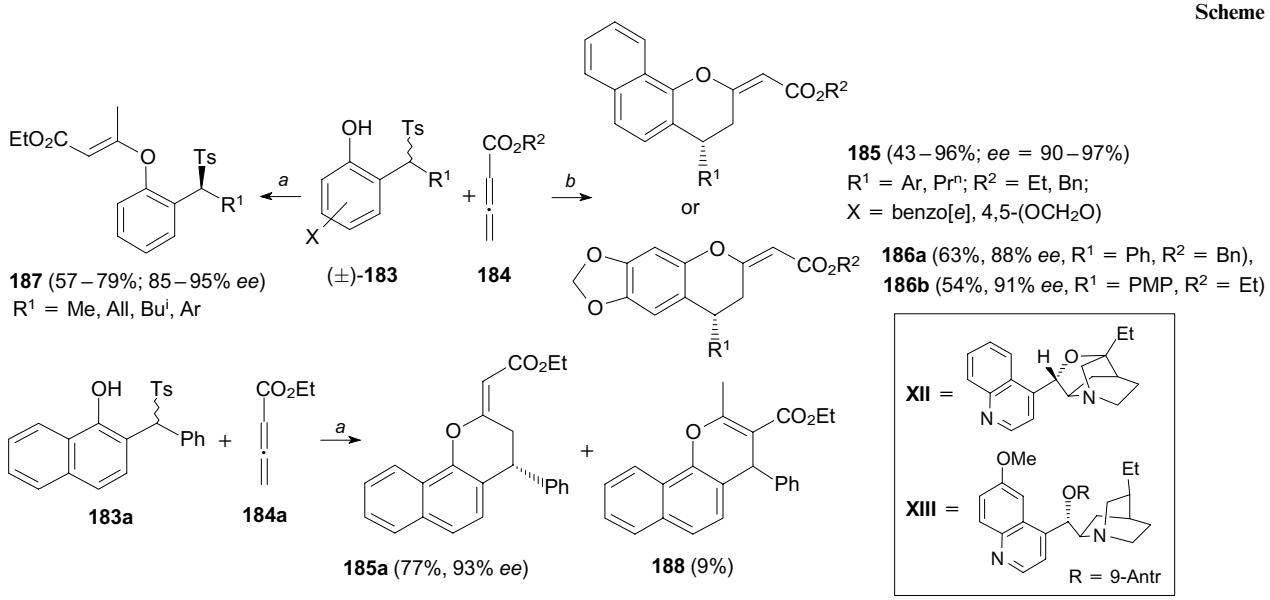
$PtCl_4$ (10 mol.%), CH_2Cl_2, rt, 4 – 18 h

molecular-mass products (dimethylamine, water, *etc.*). For example, on long-term heating of this compound with coumarin, the yield of cycloadduct **176** markedly increases to reach 91%, while the product of dihydropyran ring opening **177** is not detected. However, the reaction with 1,4-naphthoquinone leads to the oxidized Diels – Alder heteroadduct **179** in a very low yield (Scheme 69). It is noteworthy that diethyl maleate does not react with the spirodimer, as it is cannot be isomerized under the indicated conditions in the absence of dimethylamine.

Since the Diels – Alder reaction is reversible, the efficiency of using spirodimer **178** is determined by the fact that naphthoquinone methide is more easily generated from **178** than from benzochroman cycloadducts. Usually, it is energetically more favourable, since the generation of 2 equiv. of 1,2-naphthoquinone methide from the spirodimer requires that aromaticity be lost for only one benzene ring, whereas the generation of 2 equiv. of 1,2-naphthoquinone methide from 2 equiv. of chroman leads to the loss of aromaticity for two rings.[54]

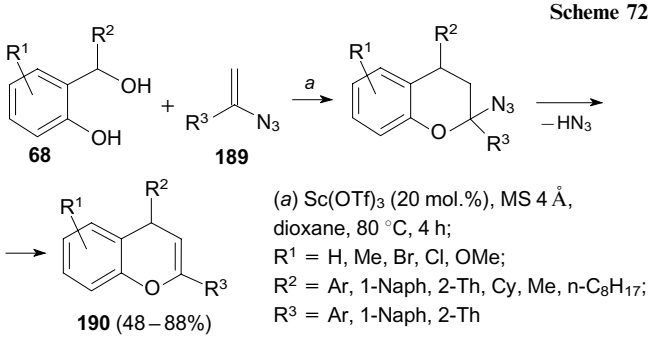
The formation of chroman-3-carboxylic acid esters **180** from esters of unsaturated carboxylic acids was reported to proceed *via* the Pt^{IV}-catalyzed generation of *o*-QM.[115] When a methoxy group is present in the *para*-position of the benzene ring, the product yield considerably increases. Note that under these conditions, the *o*-QM formed proves

Scheme 71



(*a*) **XII** (20 mol.%), Et_3N (1 equiv.), $CHCl_3$, −20 °C, 5 days, 0 °C, 1 day; (*b*) **XIII** (20 mol.%), K_2CO_3 (2 equiv.), PhCl, rt, 24 h

Scheme 72



to be inert towards electron-rich dienophiles such as 3,4-dihydropyran, vinyl acetate and vinyl ethyl ether. In the reaction of *o*-QM, generated from acetate **181**, with cinnamic acid esters, the highest yield of cycloadduct **182** is attained for the unsaturated ester containing a benzyloxy group in the *para*-position. Esters containing electron-withdrawing groups (NO_2, Cl) in the benzene ring do not react at all.[116] In addition, for stabilization of the generated *o*-QM, the starting acetate **181** should contain a bromine atom in the *para*-position relative to phenolic hydroxyl protected by the methoxymethyl group (Scheme 70).

The reaction of 2-sulfonylalkyl 1-naphthol and 1,3-benzodioxole derivatives **183** with allenes **184** results in the synthesis of a series of chromans **185** and **186a**,**b**.[117] When phenolic derivatives are used as potential *o*-QM precursors, the generation of *o*-QM occurs less efficiently, and enantiomerically enriched vinyl phenyl ethers **187**, resulting from the nucleophilic addition to the terminal C=C bond, are formed as the major products. It is noteworthy that the Diels – Alder reaction with *o*-QMs catalyzed by complexes **XII** and **XIII** involves regioselectively the less electron-deficient terminal double bond of the allene system, which is not directly conjugated with the ester group. Meanwhile, the addition of triethylamine to the reaction mixture of compounds **183a** and **184a** results in the formation of both possible regioisomers (**185a** and **188**) (Scheme 71).

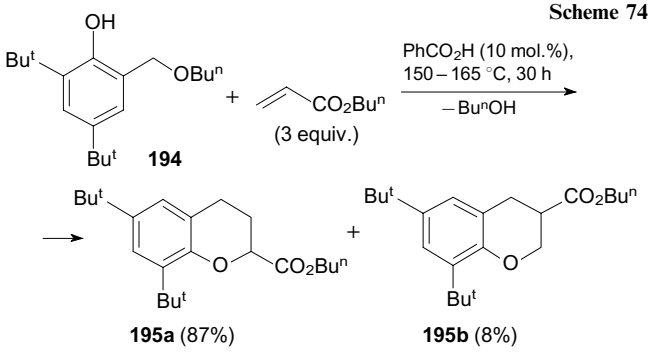
α-Aryl vinyl azides **189** can also act as dienophiles in the reaction with salicyl alcohols.[118] The subsequent elimination of HN_3 from the initially formed cycloadducts gives 4-substituted 4*H*-chromenes **190**, which allows α-aryl vinyl azides to be considered as synthetic equivalents of alkynes (Scheme 72).

The reaction of paraformaldehyde with 2-fluorohydroquinone in the presence of catalytic amounts of di-n-butylamine in refluxing acetic acid results in the generation of all three possible *o*-QMs, which are converted, in the presence of methyl methacrylate, into a mixture of chroman isomers **191a** – **c**. However, only the first product was preparatively isolated in a moderate yield.[119] The cycloaddition of *o*-QM to electron-deficient dienophile, methyl methacrylate, to give chroman **192** is one of the steps of synthesis of trolox (**193**), a water-soluble analogue of vitamin E (Scheme 73).[120] When the reaction is carried out without di-n-butylamine in the presence of water (180 °C, 3 h) and an excess of methyl methacrylate, the yield of product **192** is 69%, but the use of an autoclave is necessary.[121]

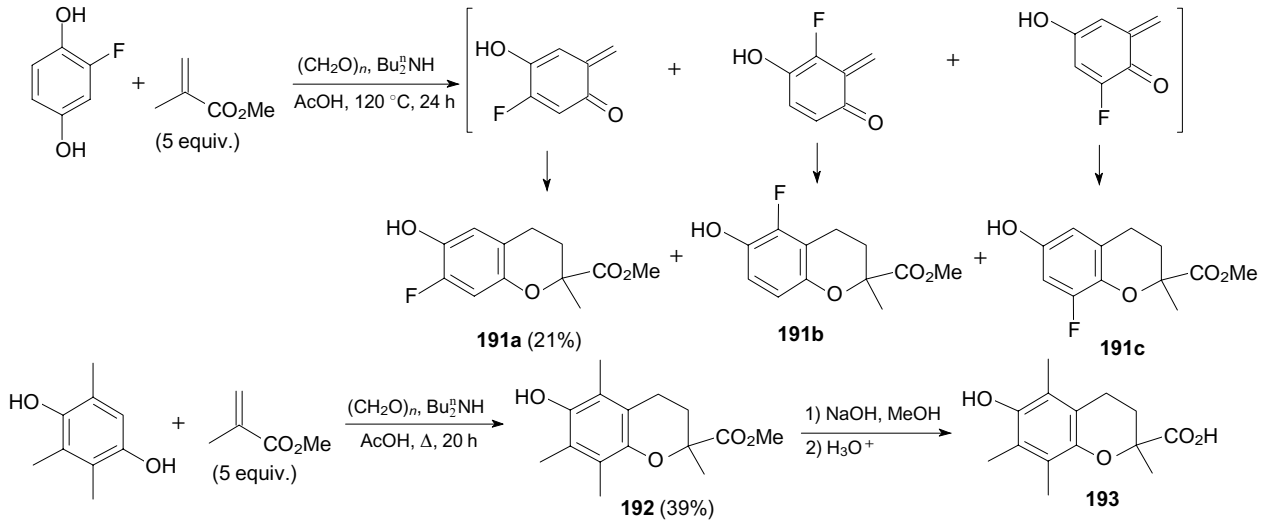
Heating of 2-(n-butoxymethyl)phenol **194** with an excess of n-butyl acrylate affords 2-chromancarboxylic acid derivative **195a** as the major reaction product (Scheme 74).[122] According to quantum chemical calculations, electron-withdrawing substituents in the dienophile decrease the difference between the activation energies for the formation of 2- and 3-substituted chromans in the reaction with *o*-QM, while the electron-donating substituents increase this difference.[123] This may account for the fact that this reaction is not regiospecific (product **195b** is present).

Thermolysis of benzosultones **196**, which are readily obtained from 2-hydroxytoluene-α-sulfonic acids and $POCl_3$, results in extrusion of SO_2 and generation of *o*-QMs, which react with *N*-substituted maleimides to

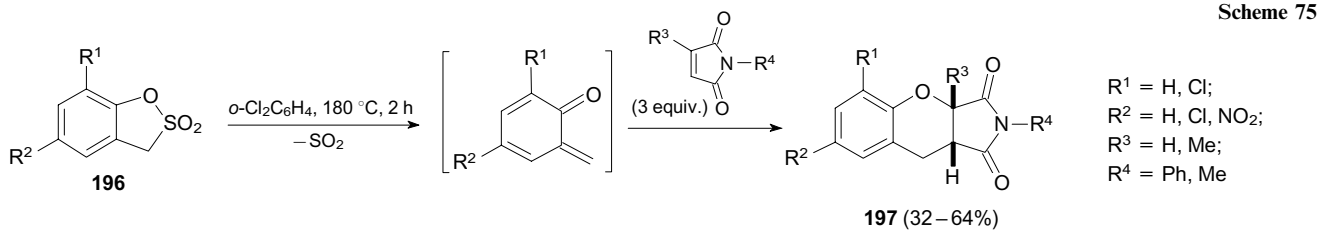
Scheme 74



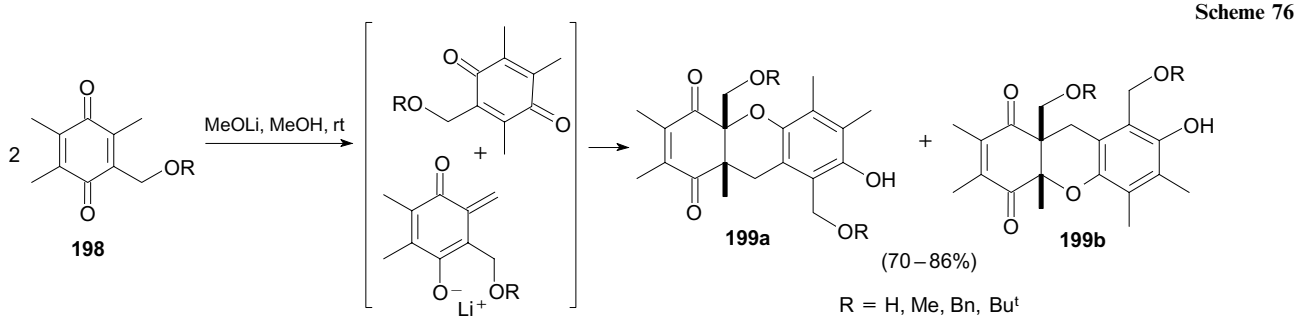
Scheme 73



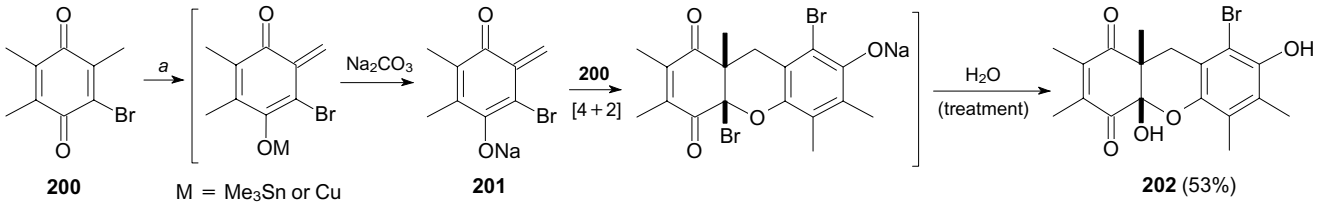
Scheme 75



Scheme 76



Scheme 77



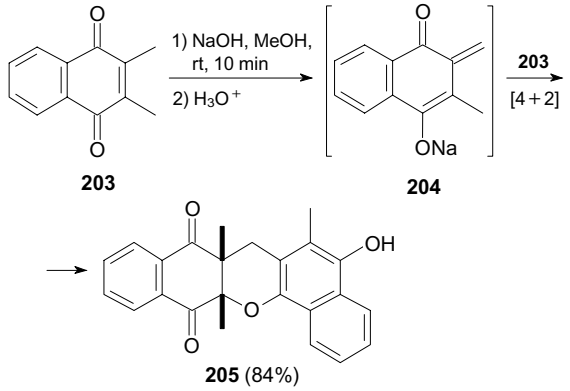
(*a*) $(Me_3Sn)_2$, CuI (0.5 equiv.), (±)-BINAP, DMF, rt, 7 h; BINAP is 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene

give 9,9a-dihydrochromeno[2,3-*c*]pyrrole-1,3(2*H*,3a*H*)-diones **197** in moderate yields (Scheme 75). When an equimolar mixture of the reactants is taken, *o*-QM dimers and trimers are also detected among the reaction products. However, in the presence of 3 equiv. of maleimide, their formation is suppressed. The reaction of benzosultones with 2-methyl-*N*-phenylmaleimide can potentially give two isomeric cycloadducts; however, analysis of the crude reaction mixture shows the presence of only chromans containing a methyl group in the α-position relative to the dihydropyran oxygen atom. It is noteworthy that thermolysis of benzosultones in the presence of dimethyl maleate, dimethyl fumarate or 2,3-dimethyl-*N*-phenylmaleimide yields only traces of the expected chromans. The reaction with electron-rich 2-phenoxyethyl vinyl ether produces only products of *o*-QM di- and trimerization.[124]

Treatment of 2-hydroxymethyl- and 2-alkoxymethyl-3,5,6-trimethyl-1,4-benzoquinones **198** with lithium methoxide leads to the selective formation of the enolate stabilized by chelation with the neighbouring oxygen atom. The subsequent cycloaddition of the enolate to the starting quinone yields Diels – Alder adducts **199a**,**b** as a mixture of regioisomers in a ratio varying over a broad range: from 32 : 1 (for R = H) to 1 : 1 (for R = Bu^t) (Scheme 76).[125]

The cycloaddition of 2-bromo-3,5,6-trimethyl-1,4-benzoquinone (**200**) to *o*-QM sodium derivative **201**, generated from the starting *p*-benzoquinone on treatment with $(Me_3Sn)_2$ and CuI, is the key step of dimerization to semiketal **202** (Scheme 77).[126]

Scheme 78

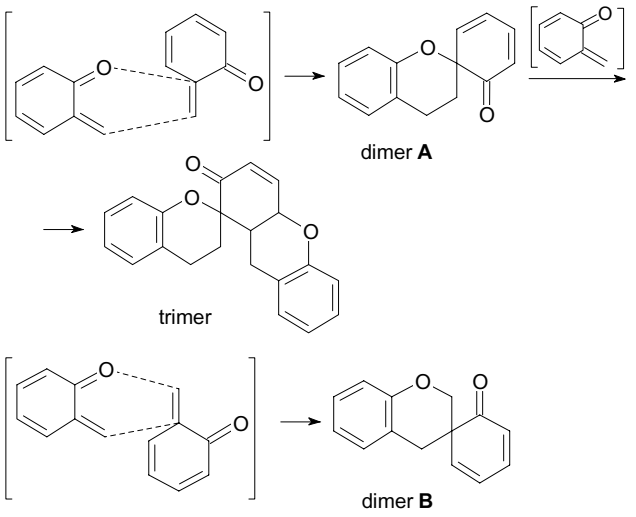


On treatment with a solution of NaOH in methanol, 2,3-dimethyl-1,4-naphthoquinone (**203**) is converted to intermediate tautomeric *o*-QM **204** (as sodium phenoxide) and then dimerizes to 7a,13a-dihydro-7*H*-dibenzo[*b*,*h*]xanthene-8,13-dione **205** (Scheme 78).[127] Duroquinone dimerizes in a similar way;[128] however, 2,3-diethyl-1,4-naphthoquinone does not form dimers of this type.

3.2. Oligomerization of *o*-quinone methides

One way of stabilization of *o*-QMs in the absence of active nucleophiles and dienophiles is self-condensation *via* the Diels – Alder mechanism to give two types of dimers — **A** and **B** (Scheme 79). The 1-oxabutadiene moiety of one

Scheme 79



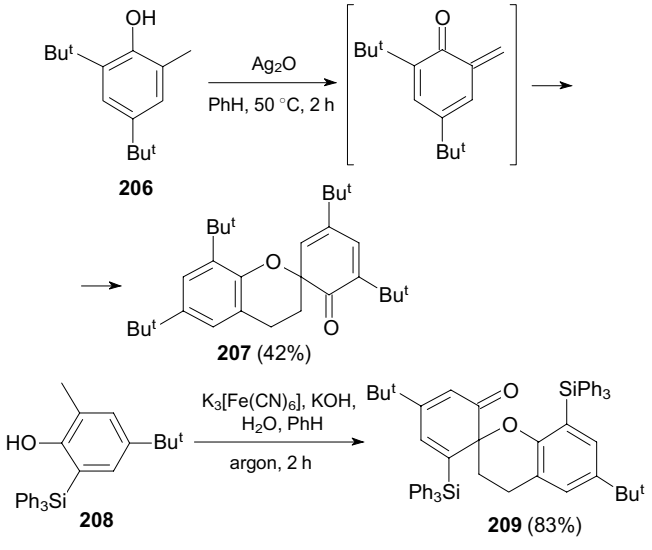
o-QM molecule reacts with the electron-deficient exocyclic C═C bond of the other molecule. Type **A** dimers are mainly formed from *o*-QMs containing no substituents at the exocyclic carbon atom. In the case of reactive *o*-QMs, further oligomerization may take place to form a complex mixture of products.

On treatment of sterically hindered 2,4-di(*tert*-butyl)-6-methylphenol (**206**) with freshly prepared Ag_2O, spirocyclic dimer **207** is isolated.[129] The absence of the trimerization product in the reaction mixture can be attributed to the presence of bulky *tert*-butyl groups in dimer **207**. The replacement of the *tert*-butyl group by the triphenylsilyl substituent (compound **208**) also results in the selective formation of dimer **209** (Scheme 80).[130] In addition, several dimers and trimers were synthesized on alkaline treatment of 2-chloromethylphenols.[131]

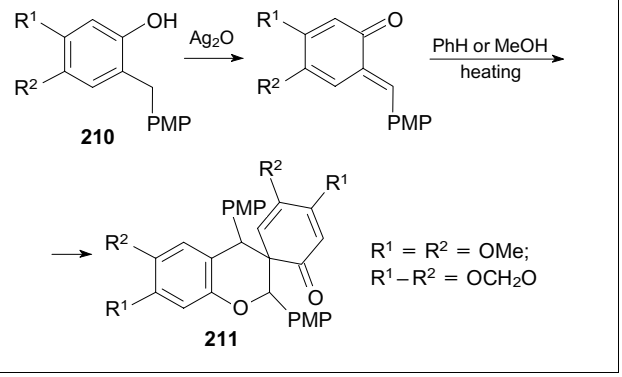
The stable *o*-QMs obtained by the oxidation of phenols **210** can be isolated in the crystalline state. However, they are often unstable in solution and, even on heating in methanol or benzene, they form dimers of a second type — compounds **211** (Scheme 81).[132]

The oxidative generation of *o*-QMs **212** from vitamin E (**43**) on treatment with Ag_2O proceeds to completion in less

Scheme 80

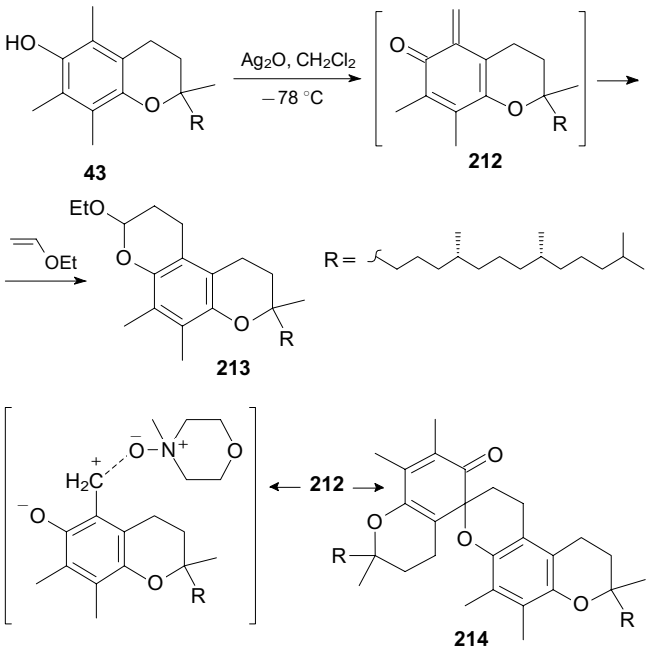


Scheme 81



than 10 s at −78 °C; by adding highly polar *N*-methylmorpholine *N*-oxide, *o*-QMs **212** can be stabilized for up to several minutes at low temperature in the form of a complex. The substrate conversion to *o*-QMs **212** was determined by the addition of an excess of vinyl ethyl ether, which reacted with *o*-QMs **212** to give chroman **213**. The *o*-QM dimer, spiro chroman **214**, was isolated when the reaction was carried out in the absence of vinyl ethyl ether (Scheme 82). The kinetic parameters of the oxidation of vitamin E (**43**) to *o*-QMs **212** were measured from the ratio of products **213** and **214**.[133]

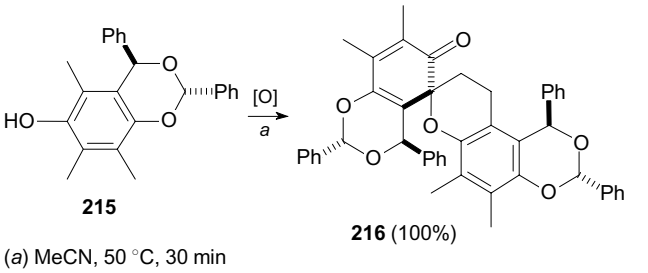
Scheme 82



The oxidative generation of *o*-QMs is often performed by chloranil, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, pyridinium chlorochromate or *N*-methylmorpholine *N*-oxide. In the absence of nucleophiles, *trans*-5,7,8-trimethyl-2,4-diphenyl-4*H*-1,3-benzodioxin-6-ol (**215**) was converted to compound **216** as a result of *o*-QM dimerization in a quantitative yield (Scheme 83).[134]

By merely refluxing a solution of Mannich base **81a** in *o*-xylene in an inert atmosphere, spirocyclic dimer **178** of unsubstituted 1,2-naphthoquinone 1-methide is obtained (Scheme 84).[135]

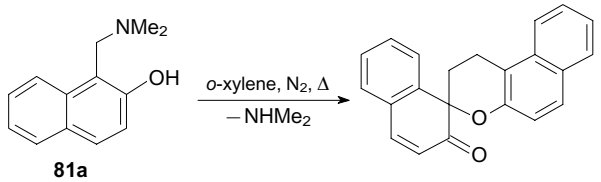
Scheme 83



215 **216** (100%)

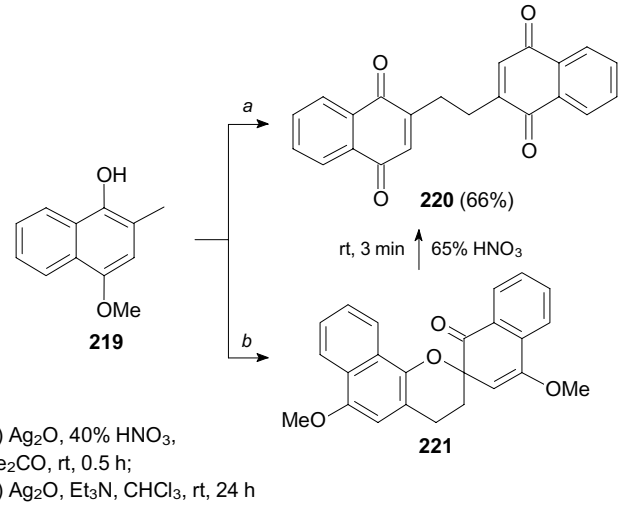
(*a*) MeCN, 50 °C, 30 min

Scheme 84



81a **178** (52%)

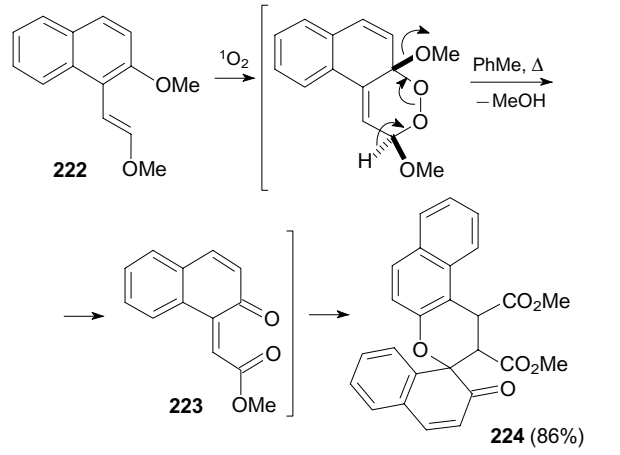
Scheme 86



219

(*a*) Ag_2O, 40% HNO_3, Me_2CO, rt, 0.5 h;
(*b*) Ag_2O, Et_3N, $CHCl_3$, rt, 24 h

Scheme 87



Photolysis of quinone **217** in 30% aqueous acetonitrile yields dimer **218** as a mixture of diastereomers (Scheme 85).[136]

On treatment of an acetone solution of 4-methoxy-2-methyl-1-naphthol (**219**) with a mixture of Ag_2O and 40% nitric acid, the intermediately formed *o*-QM dimer cannot be isolated as it is oxidized to bis(1,4-naphthoquinone) **220**.[137] If oxidation is carried out by treatment with Ag_2O in the presence of triethylamine in chloroform, dimer **221** can be isolated and then converted to quinone **220** by treatment with 65% nitric acid (Scheme 86).

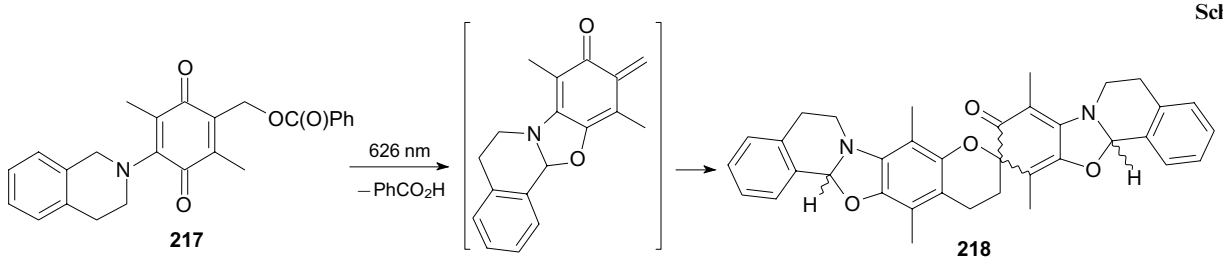
The [4 + 2]-cycloaddition of singlet oxygen to vinyl ether **222** results in a peroxide, stable in refluxing hexane, but being converted to *o*-QM **223** *via* elimination of methanol on refluxing in toluene. This gives dimer **224** (Scheme 87).[138]

Nitrosoquinone methides generated by treating 2-naphthol-1-carbaldehyde oximes **225a – c** with lead(IV) tetraacetate can react along two routes. Apart from dimers **226a – c**, these reactions give electrocyclization products — naphthoxazines **227**.[139] In the case of oximes containing an electron-withdrawing group in position 6, the yield of spirodimers **226** is higher, while naphthoxazines **227** are not detected at all (Scheme 88).

o-Quinone methide **228**, generated from benzylidenetriphenylphosphorane and 9,10-phenanthrenequinone by the Wittig reaction, is rapidly converted to dimer **229** on heating.[140] It should be noted that phenanthrene *o*-QMs **230 – 233**, containing bulky or electron-withdrawing groups at the exocyclic carbon atom, are not dimerized (Scheme 89), which is attributable to their higher stability due to a more extended conjugation chain and steric factors.

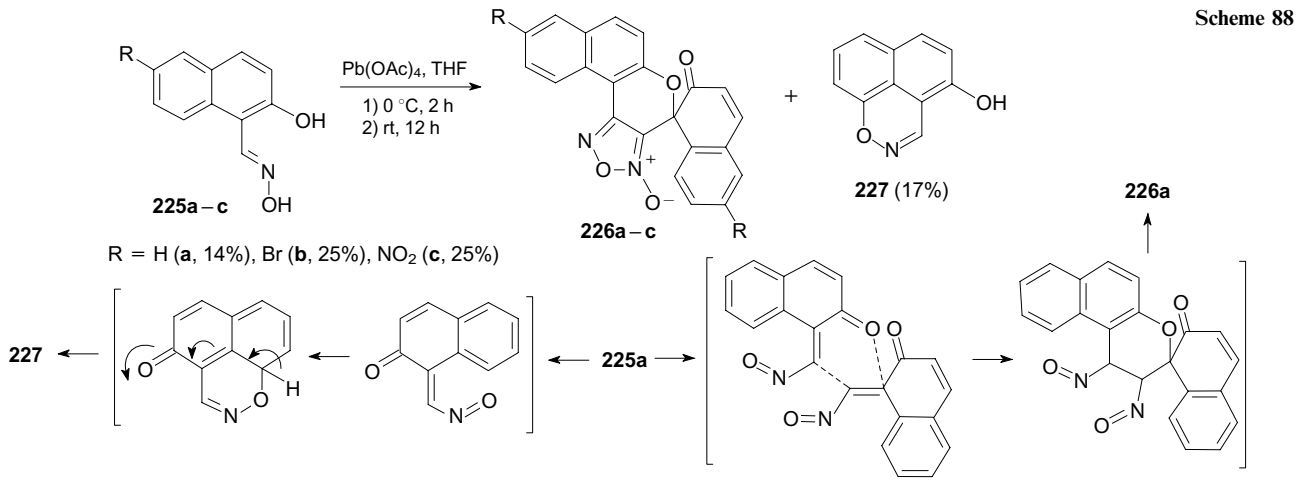
Dimerization of 1,2-naphthoquinone 1-methide generated from acetal **234** on treatment with a base gives spirocycle **235**, resulting from [4 + 2]-cycloaddition with the aromatic ring of naphthalene, in addition to traditional dimer **178** (Scheme 90).[141] Table 2 summarizes data on the effect of the natures of the solvent and the base on the yields of dimers **178** and **235**. At elevated temperatures, dimers **235** can also be obtained by the rearrangement of classical dimer **178**, which is markedly less stable in acetic acid than in mesitylene.[142] Complete conversion of spirochroman **178** to dimer **235** occurs in 12 and 6 h on refluxing in decalin and n-dodecane, respectively.

Scheme 85

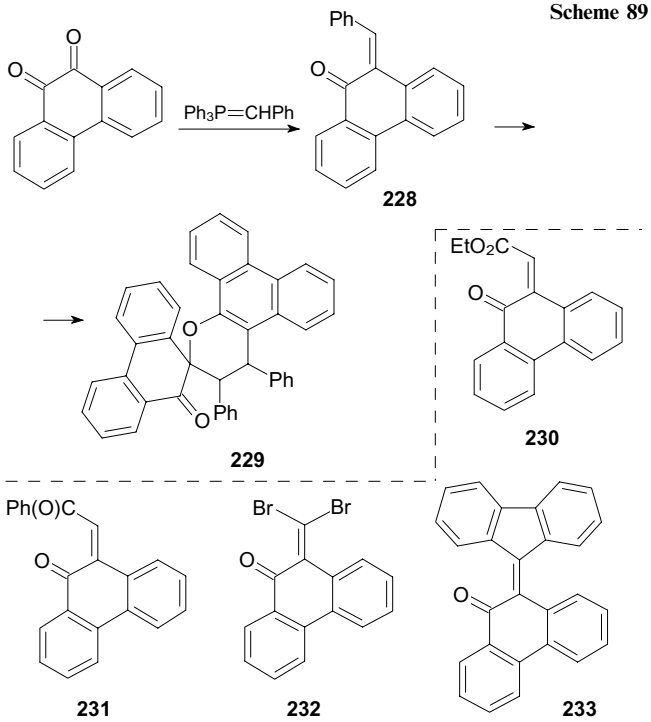


217 **218**

Scheme 88



Scheme 89



Scheme 90

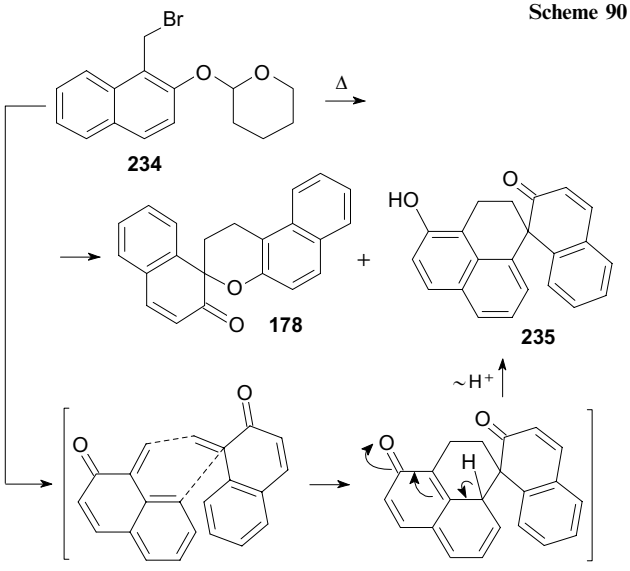
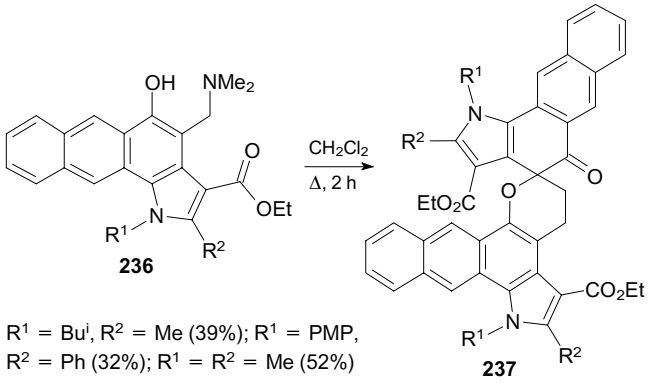


Table 2. Effect of the nature of solvent and base on the yields of dimers **178** and **235** (see Scheme 90).[141]

Base	Solvent	Yield of **178** (%)	Yield of **235** (%)
K_2CO_3	Me_2CO	20	16
K_2CO_3	MeCN	32	24
Na_2CO_3	MeCN	13	8
MeONa	MeCN	38	25
Et_3N	MeCN	32	21

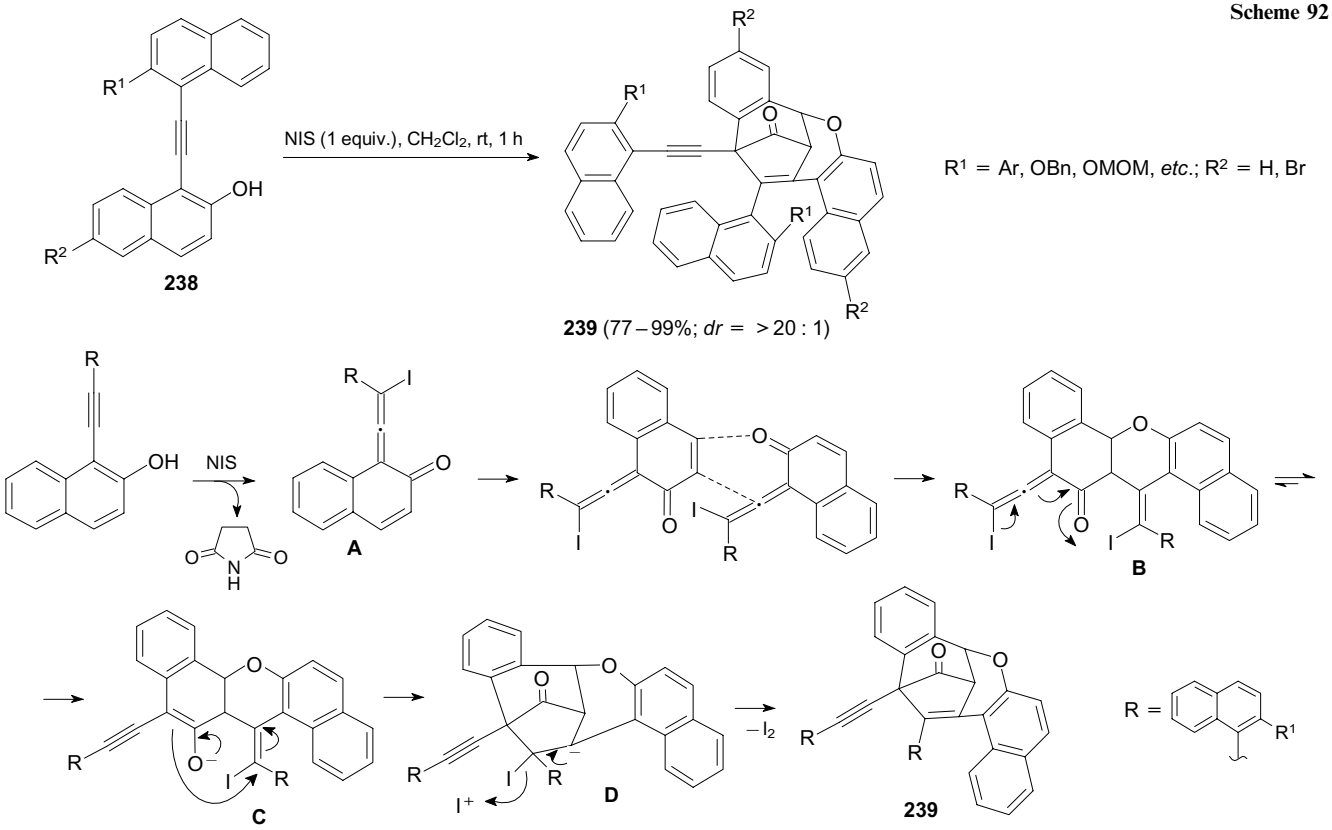
In the case of additional resonance stabilization of *o*-QMs, they are generated under considerably milder conditions. For example, 1*H*-naphtho[2,3-*g*]indoles **236** are converted to spirocyclic dimers **237** in moderate yields by refluxing in dichloromethane (Scheme 91).[143]

Scheme 91

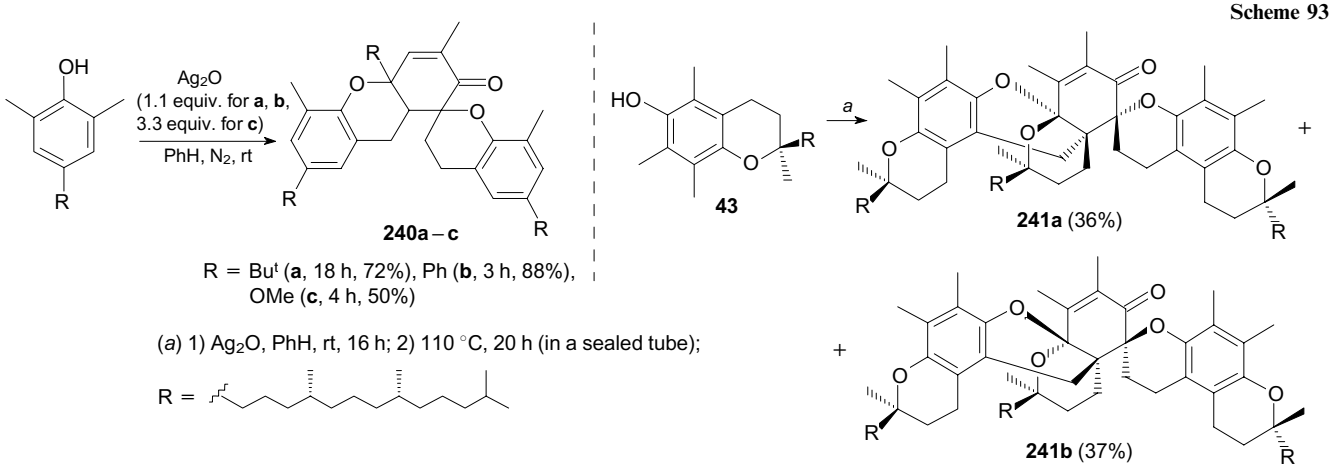


An unusual dimerization takes place when 2-alkynylnaphthols **238** are treated with *N*-iodosuccinimide (NIS). The reaction proceeds under mild conditions to give bridging polycyclic products **239**, containing a bicyclo[3.2.1]-octane moiety, in high yields and with good diastereoselectivity. The steric effect of substituents plays a crucial role in this transformation. Unlike usual dimerization, in this case, the endocyclic double bond acts as the dienophile moiety in the cycloaddition. The electrophilic iodination results in the conversion of 2-alkynylnaphthol to vinylidene type 1,2-naphthoquinone 1-methide **A**, which undergoes homodimerization to give chroman **B** followed by its spontaneous transformation to enolate **C** with the

Scheme 92



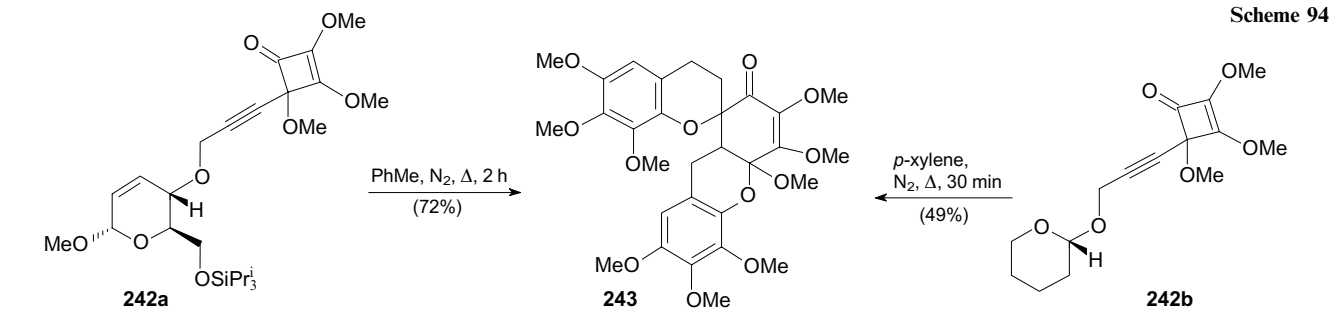
Scheme 93



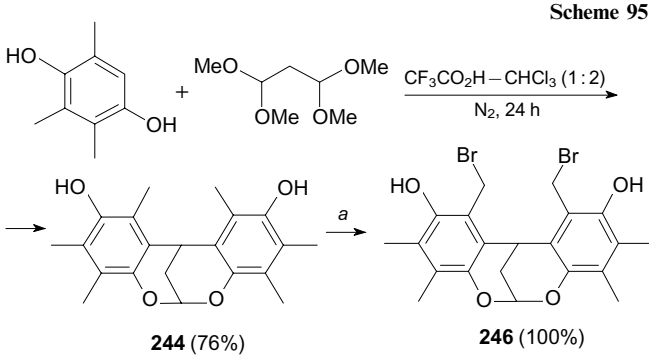
release of electrophilic iodine (I^+). The subsequent intramolecular displacement of the iodine atom by the addition – elimination mechanism promotes the formation of final product **239** and release of molecular iodine (Scheme 92).[144]

Trimers **240a – c** were prepared by the oxidation of *p*-substituted 2,6-dimethylphenols with Ag_2O in anhydrous benzene.[145] Similarly, diastereomers **241a**,**b** were obtained

Scheme 94

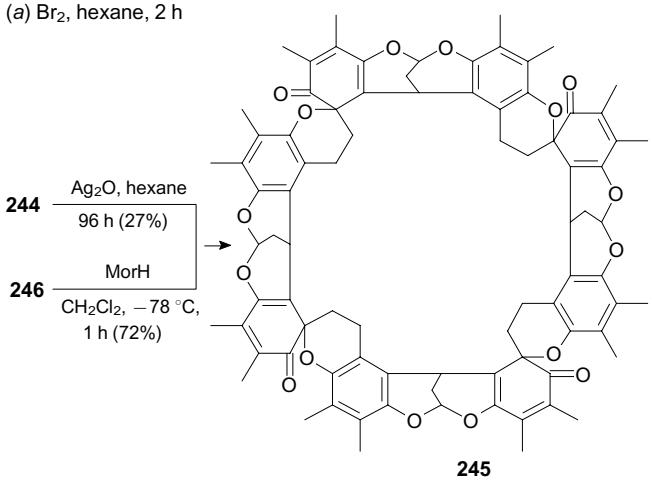


Scheme 95



244 (76%) **246** (100%)

(*a*) Br_2, hexane, 2 h



245

in 1 : 1 ratio in a total yield of 73% from natural (+)-α-tocopherol (Scheme 93).[146]

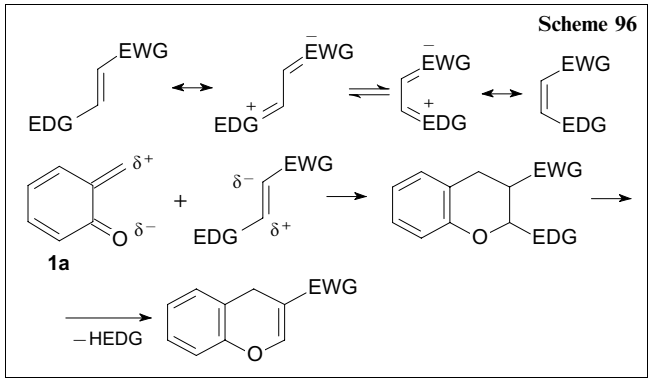
Squaric acid derivatives **242a**,**b** in refluxing toluene can be used to synthesize trimer **243**, an analogue of the triterpenoid (±)-schefflone [147] (Scheme 94).[148]

Calixarene-like structures can be prepared by oligomerization of *o*-QMs.[149] For example, the condensation of malonic aldehyde tetramethyl acetal with trimethylhydroquinone affords bis-phenol **244**, which is oxidized with Ag_2O to give cyclic tetramer **245** in a low yield. The yield of tetramer **245** increases in the case of brominated *o*-QM precursor **246**; small amounts of higher oligomers are also detected in the reaction mixture (Scheme 95). More examples of oligomerization of *o*-QMs can be found in a recent review.[1]

4. Reactions of *o*-quinone methides with push-pull olefins

The interest in push-pull olefins containing electron-withdrawing and electron-donating groups at different ends of the C=C bond is due to their unusual physicochemical properties. The push-pull effect in these systems is based on the donor-acceptor interaction between substituents existing in direct conjugation and, as a consequence, involves a substantial transfer of electron density. High degree of polarization makes compounds of this type sensitive to both electrophilic and nucleophilic attacks; therefore, they are valuable building blocks and are widely used in synthetic organic chemistry.[150–152] In this case, the electron-donating substituent is most often represented by a thiol or amino group (more rarely, a hydroxy or alkoxy group), which can be easily eliminated under the reaction conditions

Scheme 96

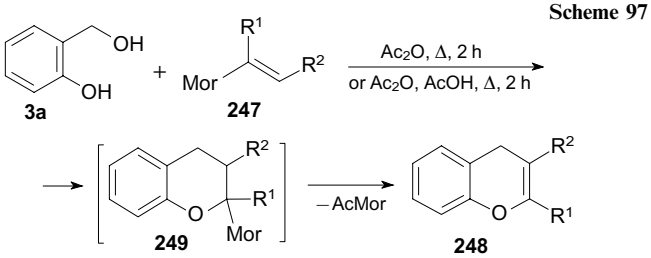


to give electron-deficient 4*H*-chromenes containing an electron-withdrawing substituent in the β-position relative to the pyran oxygen atom (Scheme 96).

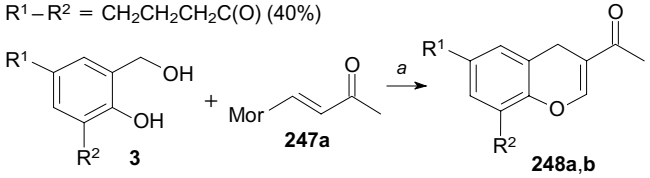
4.1. Acyclic push-pull olefins

The reaction of enamines **247** with salicyl alcohols in the presence of acetic anhydride is one of the first examples of synthesis of 4*H*-chromenes **248** containing an electron-withdrawing group in position 3 from push-pull olefins **247** (Scheme 97). The yield of 4*H*-chromenes substantially depends on the nature of the electron-withdrawing group in the enamine and varies from 12% (for $R^2 = CO_2Et$) to 89% (for R^2 = Bz).[153] Apparently, the reaction involves the formation of intermediate **249**.

Scheme 97



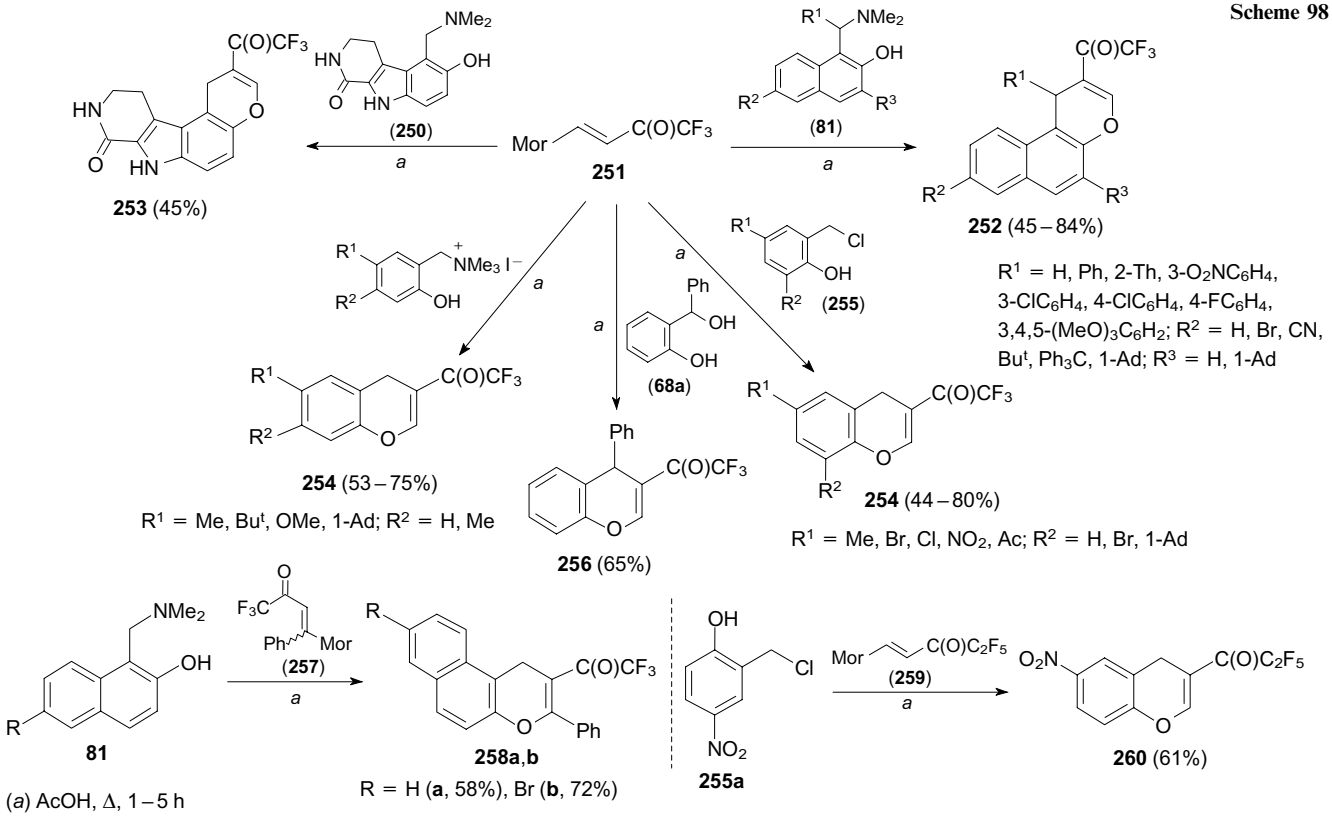
R^1 = H: R^2 = CO_2Et (12%), NO_2 (62%), CHO (40%), Ac (88%), Bz (89%); R^1 = Me: R^2 = Ac (40%), Bz (38%); R^1-R^2 = $CH_2CH_2CH_2C(O)$ (40%)



(*a*) Ac_2O, Δ; R^1 = OMe, R^2 = H (**a**, 87%); R^1 = H, R^2 = OMe (**b**, 78%)

2-Naphthol Mannich bases **81** containing both electron-donating and electron-withdrawing substituents in the naphthalene and aryl moieties or carboline derivative **250** react with 1,1,1-trifluoro-4-morpholinobut-3-en-2-one (**251**) in refluxing acetic acid to give 1*H*-benzo[*f*]chromenes **252** or 2-trifluoroacetyl-7,9,10,11-tetrahydropyrano[3,2-*e*]pyrido[3,4-*b*]indol-8(1*H*)-one (**253**).[154] Conduction of the reaction in an acid medium facilitates both the generation of *o*-QM from Mannich base and elimination of morpholine from the initially formed cycloadduct. Trifluoroacetylchromenes **254** were obtained from enaminone **251** and phenol Mannich base methiodides used as *o*-QM precursors. Although *o*-chloromethylphenols **255** possess a large synthetic potential, they are rarely used as *o*-QM precursors due to low stability and tendency to oligomerization. Mean-

Scheme 98



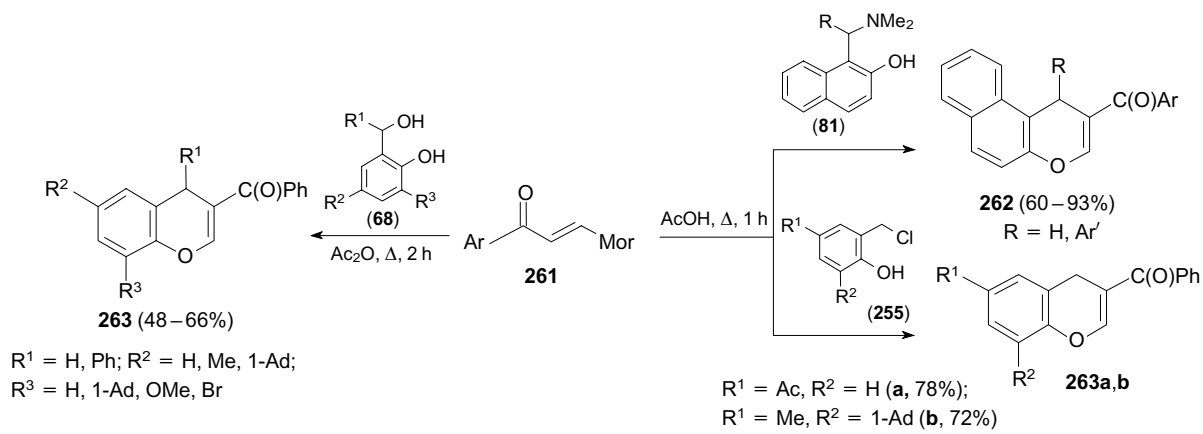
while, the stability of these precursors considerably increases when their molecules contain bulky or electron-withdrawing substituents, which was utilized in the preparation of 3-trifluoroacetylchromenes **254**.[155] The thermal generation of *o*-QMs from *o*-hydroxybenzyl alcohols gives only water, apart from *o*-QMs, which is a benefit from the standpoint of green chemistry. For example, the reaction of 2-[hydroxy(phenyl)methyl]phenol **68a** with enaminone **251** resulted in the isolation of 3,4-disubstituted 4*H*-chromene **256** in 65% yield. The reaction of Mannich bases with 1,1,1-trifluoro-4-morpholino-4-phenylbut-3-en-2-one (**257**) yields α-phenyl-substituted 1*H*-benzo[*f*]chromenes **258a**,**b**,[156] while the reaction of 2-chloromethyl-4-nitrophenol (**255a**) and enamino ketone **259** results in the synthesis of perfluoropropanoyl-4*H*-chromene **260** (Scheme 98).[157]

Naphthol Mannich bases and 1-aryl-3-morpholinoprop-2-en-1-ones **261** were used to synthesize a series of 1*H*-benzo[*f*]chromen-2-yl aryl ketones **262**. When salicyl alcohols **68** serve as *o*-QM precursors, the reaction is carried out in refluxing acetic anhydride. Under the action of the anhydride, alcohols are first converted to acetates, which are more reactive *o*-QM precursors, and morpholine is eliminated as the *N*-acyl derivative.[154] 3-Benzoyl-4*H*-chromenes **263a**,**b** are formed in good yields from *o*-chloromethylphenols **255** by refluxing the reactants in acetic acid (Scheme 99).[155]

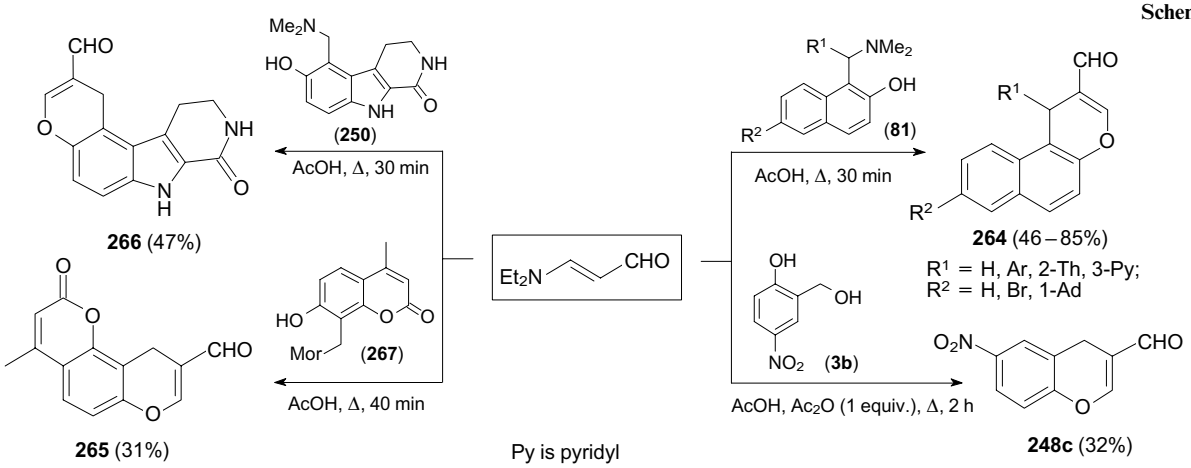
Chromenocarbaldehydes **264** – **266** are formed in moderate to high yields when 2-naphthol Mannich bases **81**, 7-hydroxycoumarin **267** and 6-hydroxy-2,3,4,9-tetrahydro-γ-carbolin-1-one **250** are refluxed in acetic acid with 3-(*N*,*N*-diethylamino)acrolein. The same synthesis of 6-nitro-4*H*-chromene-3-carbaldehyde (**248c**) from nitrosalicyl alcohol (**3b**) requires the addition of 1 equiv. of acetic anhydride (Scheme 100).[158, 159]

The reaction of cross-conjugated push-pull enamino ketones **268** with Mannich bases derived from 2-naphthol

Scheme 99

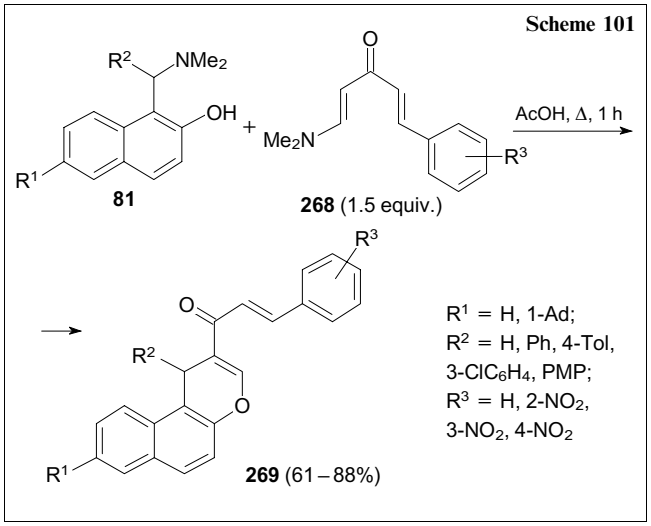


Scheme 100



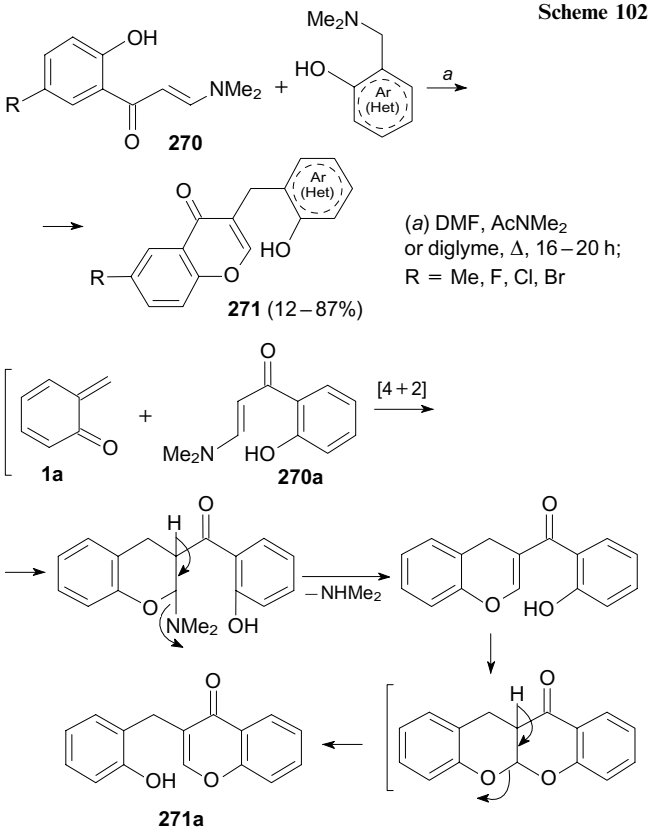
provided the synthesis of 1*H*-benzo[*f*]chromenes **269**, including both 1-unsubstituted and 1-aryl-substituted derivatives (Scheme 101). The cascade process includes the hetero-Diels – Alder reaction of 1,2-naphthoquinone 1-methide with enaminone **268** and the subsequent elimination of dimethylamine. The cycloaddition is regioselective, being directed to the highly polarized C=C bond. The presence of electron-donating or -withdrawing groups in aryl substituents does not substantially affect the yield of products.[160]

Scheme 101



A number of aromatic and heterocyclic analogues of homoisoflavonoids **271** were prepared from 3-(*N,N*-dimethylamino)-1-(2-hydroxyphenyl)prop-2-en-1-ones **270** and phenol Mannich bases in refluxing DMF, diglyme or dimethylacetamide (Scheme 102). The yields of products considerably vary depending on the nature of the substrate. Phenol, 2-naphthol, 5-hydroxyindole, 5-hydroxybenzofuran and 7-hydroxycoumarin derivatives and some other compounds are used as *o*-QM precursors. The mechanism of this cascade reaction apparently includes the oxa-Diels – Alder reaction involving the generated *o*-QM and enamino ketone, elimination of dimethylamine and oxa-Michael reaction. Dihydrochromeno[2,3-*b*]chromen-11-one thus formed is unstable and is stabilized *via* opening of the dihydropyran ring to give 3-(2-hydroxybenzyl)chromone **271a** (see Scheme 102; shown for *o*-QM **1a** and substrate **270a**).[161]

Scheme 102

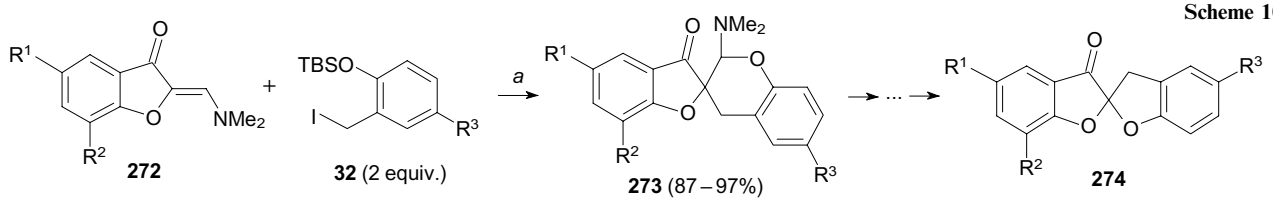


Under mild conditions, enamino ketones **272** readily add to *o*-QMs generated from silyl derivatives under the action of fluoride ions. During purification on acidic silica gel, *N,O*-acetals **273** thus formed are converted to spiro[5,5]ketals **274** *via* hydrolysis, decarbonylation and cyclo etherification. However, when silica gel is treated with triethylamine, they can be isolated in a pure state in high yields (Scheme 103).[162]

Refluxing equimolar amounts of Mannich base **81a** and β-aminoacrylonitriles **275** in DMF gives rise to mixtures of benzochroman-2-carbonitriles **276a – e** and 2-[(2-hydroxynaphthalen-1-yl)methyl]-2,3-dihydro-1*H*-benzo[*f*]chromene-2-carbonitriles **277a – d** (Scheme 104, Table 3).[163]

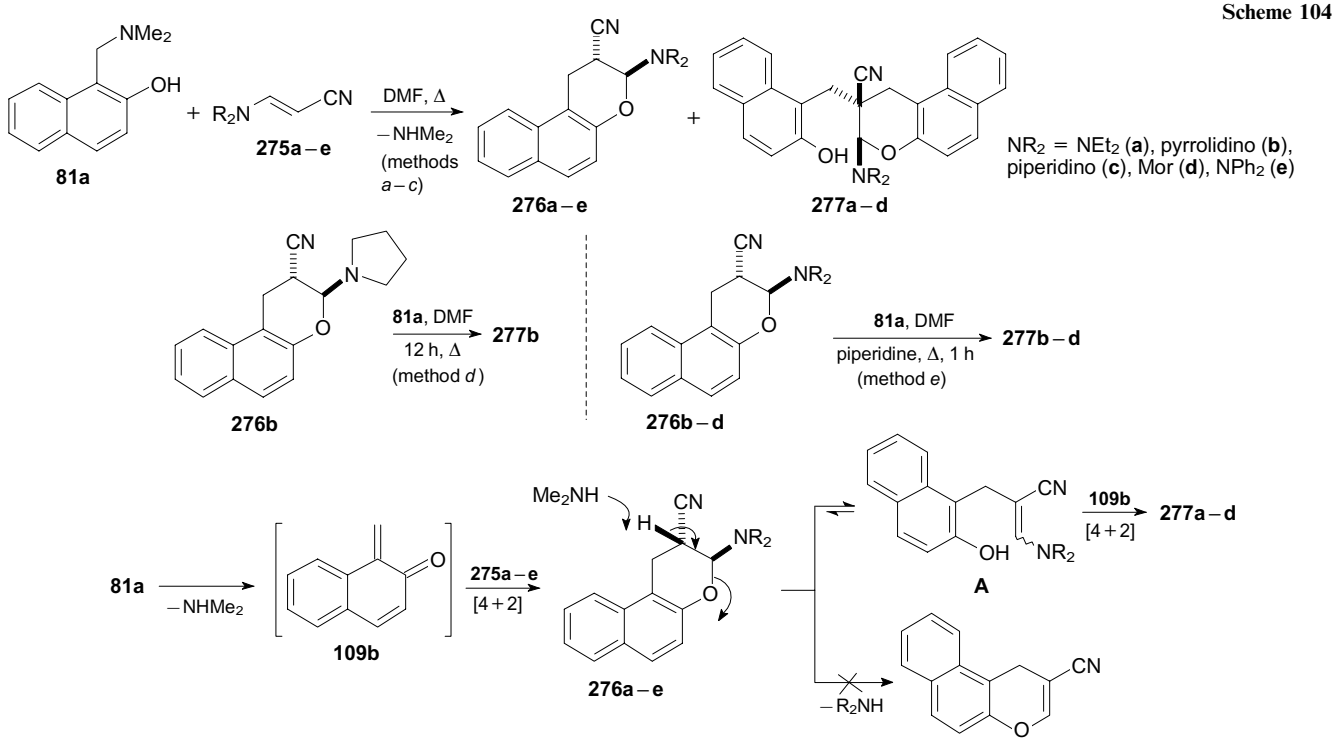
Even when 2 equiv. of Mannich base **81a** are used in the reaction with enaminonitriles **275** (method *b*) and the time of reaction is increased to 12 h, compounds **276** are not

Scheme 103



(*a*) TBAF (2.8 equiv.), CH_2Cl_2, rt, 1 h; R^1 = H, Br, OMe; R^2 = H, OMe; R^3 = H, Me, Br, CO_2Et

Scheme 104



completely converted to benzochromans **277**. Meanwhile, benzochroman-2-carbonitriles **276** are selectively formed upon slow addition of an equimolar amount of Mannich base **81a** to a solution of nitrile **275** in DMF heated almost to boiling (method *c*). Refluxing Mannich base **81a** with equimolar amounts of 3-amino-2,3-dihydro-1*H*-benzo[*f*]-chromene-2-carbonitriles **276b – d** in DMF in the presence of 1 equiv. of piperidine as a base also furnishes benzochromans **277b – d** in good yields (method *e*). In the absence of piperidine, the yield of product **277b** is only 23% (method *d*).

The key step is the Diels – Alder reaction of 1,2-naphthoquinone 1-methide **109b**, generated *in situ*, with push-pull enamino nitrile **275** (Scheme 104). It is noteworthy that enamino nitriles of this type very rarely act as dienophiles. The formation of benzochromans **277** can be explained by dimethylamine- or piperidine-induced opening of the dihydropyran ring in the initially formed cycloadducts and addition of one more 1,2-naphthoquinone 1-methide molecule **109b** to push-pull olefin **A**.

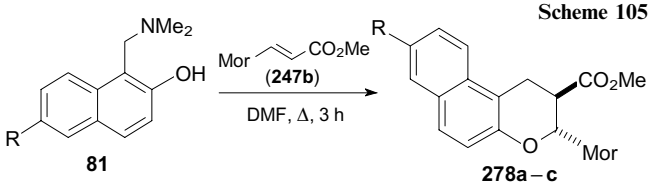
It should be noted that the reaction of naphthol Mannich bases with methyl 3-morpholinoacrylate in refluxing DMF yields only cycloadducts **278a – c**. Even the use of 2 equiv. of the 1,2-naphthoquinone 1-methide precursor does not lead to products with two naphthalene moieties (Scheme 105).[163]

Table 3. Products of reactions of Mannich base **81a** with β-aminoacrylonitriles **275** (see Scheme 104).[163]

Method	Compound (yields of **276** + **277**, %)				
	a	**b**	**c**	**d**	**e**
a	41 + 18	43 + 17	46 + 15	52 + 16	78 + 0
b	24 + 54	29 + 51	30 + 48	–	–
c	72 + 0	80 + 0	83 + 0	84 + 0	–
d	–	0 + 23	–	–	–
e	–	0 + 81	0 + 77	0 + 74	–

Note. The following conditions were used: method (*a*) **275** (1.5 mmol), **81a** (1.5 mmol), DMF, Δ, 1 h; method (*b*) **275** (1.5 mmol), **81a** (3.0 mmol), DMF, Δ, 1 h; method (*c*) **275** (1.5 mmol), **81a** (1.5 mmol), DMF, 150 °C; addition of **81a** to **275** for 30 min; method (*d*) **276** (1.0 mmol), **81a** (1.0 mmol), DMF, Δ, 12 h; method (*e*) **276** (1.0 mmol), **81a** (1.0 mmol), piperidine (1.0 mmol), DMF, Δ, 1 h. The dash means that the reaction was not carried out.

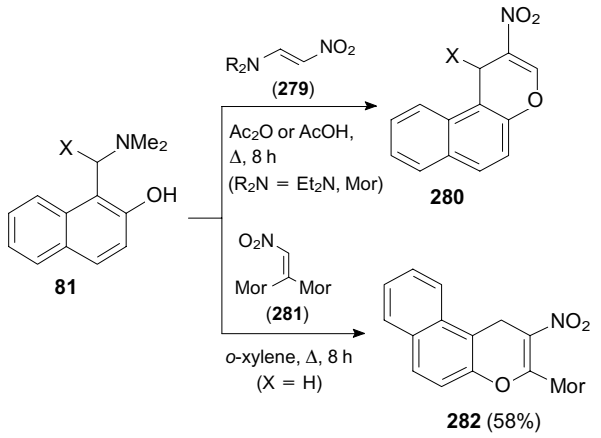
Scheme 105



R = H (**a**, 73%), Br (**b**, 77%), 1-Ad (**c**, 81%)

Push-pull β-nitroenamines and their functional derivatives are widely used in the synthesis of various heterocycles. For example, naphthol Mannich bases **81** react with (2-nitrovinyl)amines **279** to give a series of 2-nitro-1*H*-benzo[*f*]chromenes **280** in 32 – 85% yields.[164] The reaction of 1-[2-(dimethylamino)methyl]-2-naphthol (**81a**) with *N*,*N*-ketene acetal **281** can be effected only by long-term refluxing in *o*-xylene; this gives *N*-(2-nitro-1*H*-benzo[*f*]chromenyl)morpholine (**282**) as a result of [4 + 2]-cycloaddition and elimination of one morpholine molecule (Scheme 106). This example is a rare case of elimination of amine from cycloadduct in a neutral medium.[156]

Scheme 106

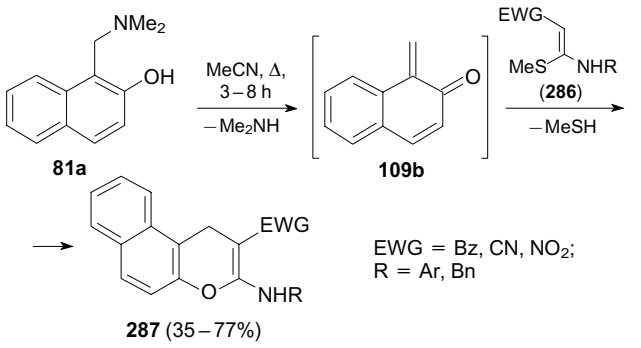


280: X = H (60%), Ph (75%), 2-Th (85%), 3-$O_2NC_6H_4$ (32%), 4-ClC_6H_4 (61%), PMP (80%), 3,4-$(MeO)_2C_6H_3$ (60%), 3,4,5-$(MeO)_3C_6H_2$ (45%), 1,3-benzodioxol-5-yl (46%)

Note that 2-(nitromethylene)pyrrolidine or -imidazolidine **283** reacts with *o*-QM precursors without forming spirocyclic chromans or products of five-membered ring opening **284**; instead, 1-[2-nitro-2-(pyrrolidin-2-ylidene)ethyl]- or 1-[2-(imidazolidin-2-ylidene)-2-nitroethyl]-2-naphthols **28** are formed as a result of dihydropyran ring opening (Scheme 107).[165]

Ketene *N*,*S*-acetals **286** react with Mannich base **81a** to give 3-amino-1*H*-benzo[*f*]chromenes **287** containing an electron-withdrawing group in the β-position relative to the oxygen atom (Scheme 108). The reaction is accompanied by the elimination of methanethiol from the initially formed cycloadduct, while elimination of primary amine does not occur in refluxing acetonitrile. This can be attributed to either stabilization of chromenes **287** by an intramolecular NH···O hydrogen bond or lower energy of the

Scheme 108

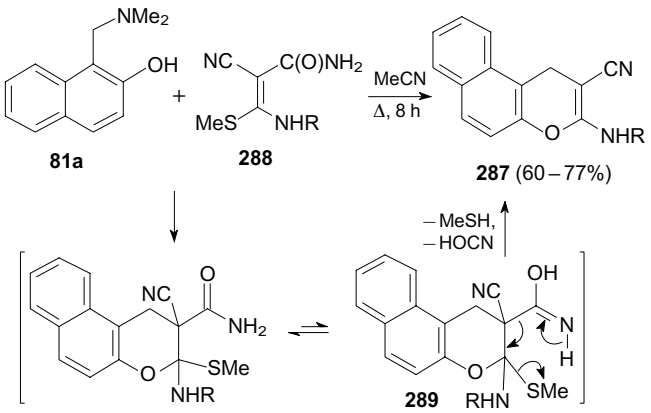


C – S bond in comparison with the C – N bond. Quantum chemical calculations were carried out to check whether the Diels – Alder reaction is synchronous; it was shown to be the asynchronous concerted [4 + 2]-cycloaddition.[166]

When α-cyanoketene *N*,*S*-acetals are used as dienophiles, the yields of nitriles **287** (EWG = CN) are only 35 – 38%. However, in the case of ketene *N*,*S*-acetals **288** containing an amide moiety, the yield of products **287** can be increased to 60 – 77%. The formation of benzochromenes **287** can be explained by deamidation of Diels – Alder adducts *via* transformation of intermediate **289** into a six-membered transition state, which is accompanied by elimination of a methanethiol molecule and cyanic acid (Scheme 109).[166]

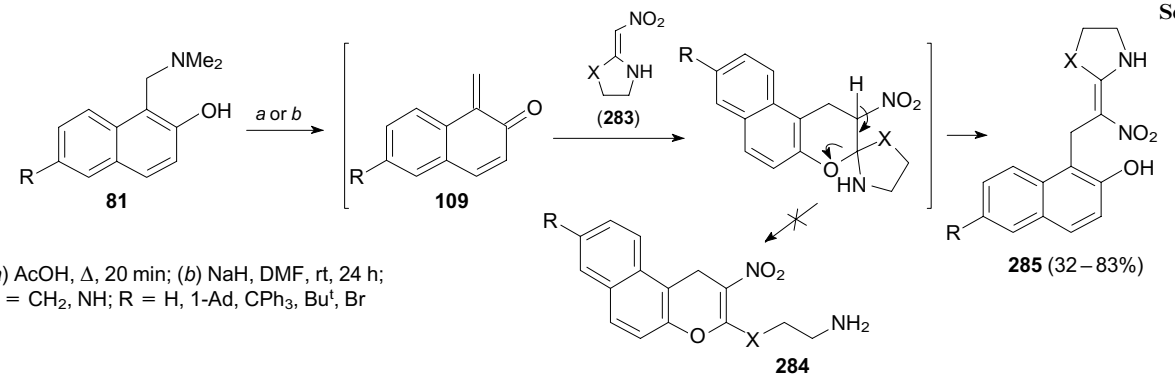
The multicomponent reaction of *N*-methyl-1-(methylthio)-2-nitroethenamine (**286a**), aromatic aldehydes and

Scheme 109



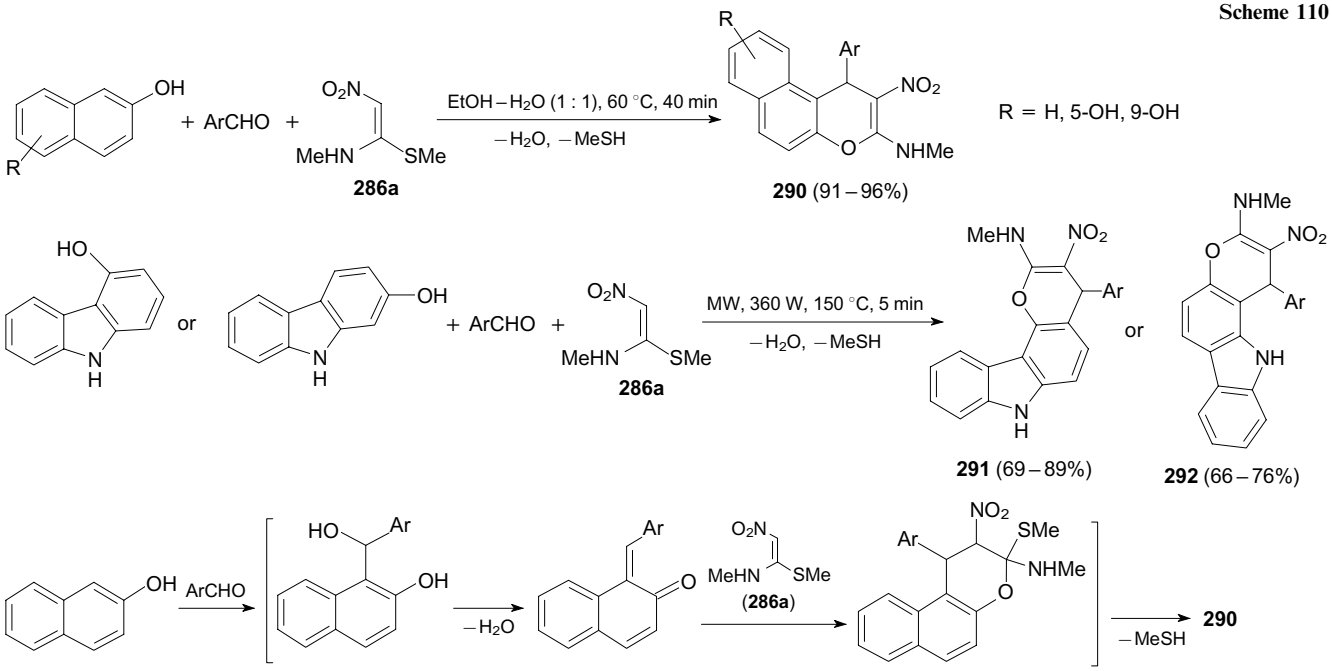
R = 4-Tol, PMP, 4-ClC_6H_4, 4-BrC_6H_4, 1-Naph

Scheme 107

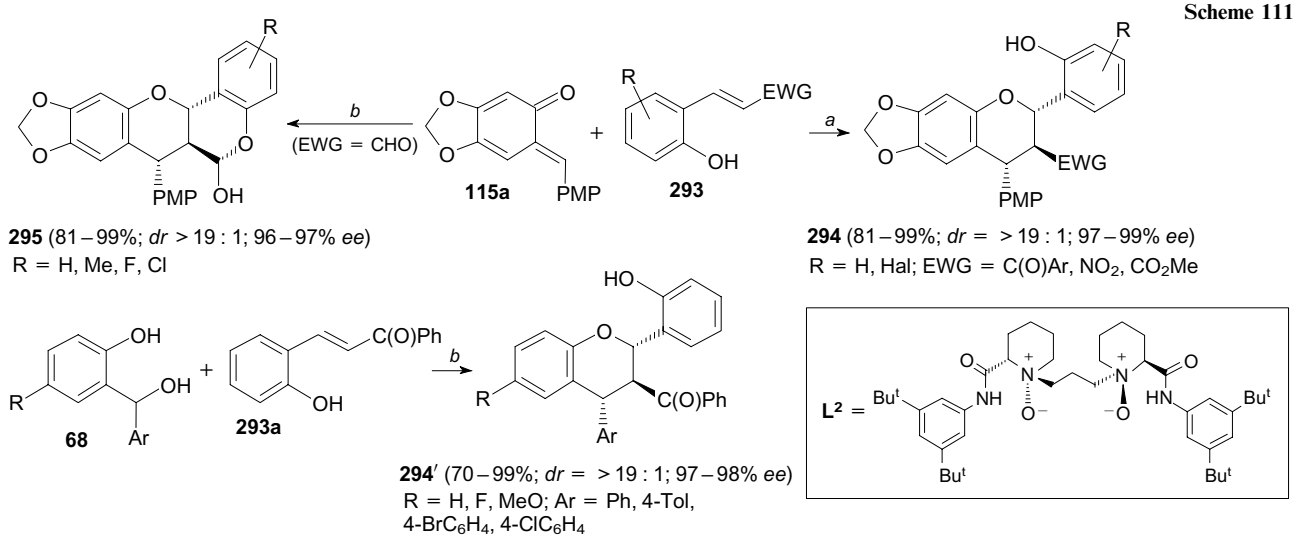


(*a*) AcOH, Δ, 20 min; (*b*) NaH, DMF, rt, 24 h; X = CH_2, NH; R = H, 1-Ad, CPh_3, Bu^t, Br

Scheme 110



Scheme 111



(*a*) $Sc(OTf)_3$ – **L²** (1 : 1) (0.01 – 0.1 mol.%), CH_2Cl_2, 5 °C, 36 h;
(*b*) $Sc(OTf)_3$ – **L²** (1 : 1) (1 mol.%), CH_2Cl_2, 35 °C, 24 h

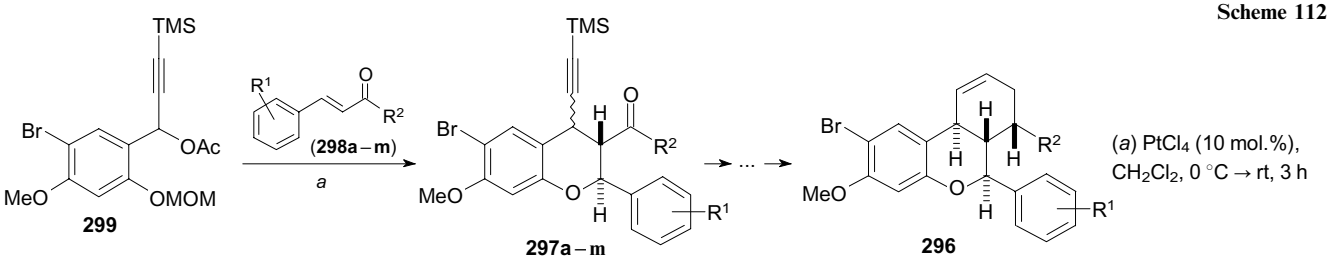
2-naphthols in aqueous ethanol produces 1-aryl-2-nitro-1*H*-benzo[*f*]chromene-3-amines **290** in high yields.[167] Instead of naphthols, 2- and 4-hydroxycarbazoles are used in microwave-assisted reactions without a solvent.[168] The reactions proceed without a catalyst and products **290** – **292** usually do not require column chromatography for purification. Apparently, the reaction starts with hydroxybenzylation of electron-rich aromatic compounds induced by aldehydes and accompanied by water elimination, which results in the generation of *o*-QMs. The cycloaddition of *o*-QMs to push-pull nitroenamines and elimination of methanethiol afford substituted chromenes (Scheme 110).

o-Hydroxystyrenes **293**, containing an electron-withdrawing group in the β-position, can also act as dienophiles. The reactions with stable *o*-QM **115a** or 2-hydroxybenzyl alcohols **68** yield *trans*,*trans*-2,3,4-trisubstituted chromans **294** or **294′** with high enantioselectivity in the presence of a scandium triflate complex with ligand $\mathbf{L}^2$. When *o*-hydroxycinnamaldehydes are used as 2π-components in the Diels – Alder reaction, the intramolecular interaction between the aldehyde and phenolic hydroxyl group takes place to afford pyrano[4,3-*b*]chromans **295** (Scheme 111).[169]

A key step of the synthesis of tetrahydro-6*H*-benzo[*c*]chromenes **296**, structural analogues of palodesangrens, is the formation of 3-aroylchromans **297a** – **m** from chalcones **298a** – **m** and *o*-QM generated from **299** (Scheme 112).[170]

In the case of unsubstituted chalcone **298a** (R^1 = H, R^2 = Ph), the corresponding chroman **297a** is formed in only trace amounts. However, when methoxy groups are present in both aromatic moieties of chalcone, chromans **297** can be prepared as *trans*,*trans*-isomers in moderate to high yields. It should be noted that in the case of R^1 = 3-OMe, the push-pull nature of the multiple bond diminishes, which leads to decreasing yield of the cyclo-

Scheme 112



Scheme 113

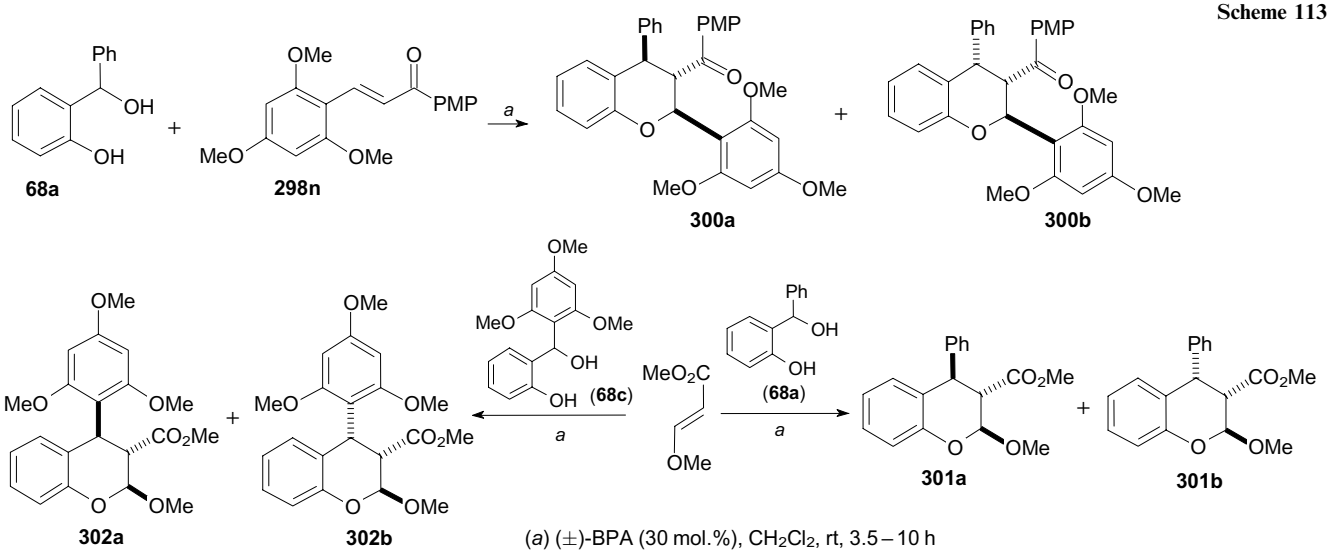


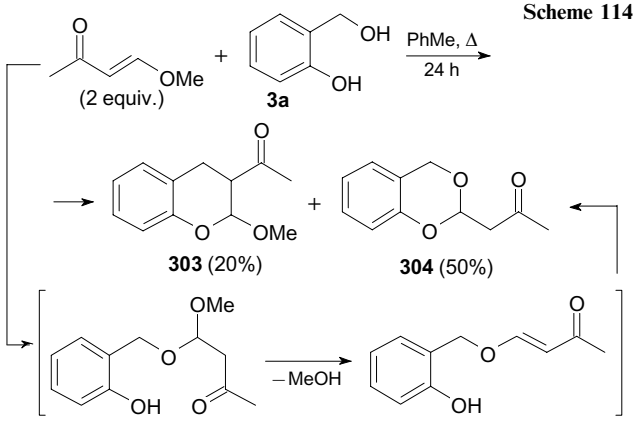
Table 4. Effect of the nature of substituents on the yield of products **297** and diastereoselectivity (*dr* = 2,4-*cis* : 2,4-*trans*) in the reaction of chalcones **298** with *o*-QM precursor **299** (see Scheme 112).[170]

Compounds **297**, **298**	R^1	R^2	Yields (%)	*dr*
a	H	Ph	Traces	
b	4-MeO	PMP	85	8 : 1
c	3,4-$(MeO)_2$	PMP	56	8 : 1
d	3,4,5-$(MeO)_3$	PMP	41	7 : 1
e	4-MeO	3-$MeOC_6H_4$	60	> 99 : 1
f	3,4-$(MeO)_2$	3-$MeOC_6H_4$	68	> 99 : 1
g	3,4,5-$(MeO)_3$	3-$MeOC_6H_4$	44	6 : 1
h	4-MeO	3,4-$(MeO)_2C_6H_3$	98	8 : 1
i	3,4-$(MeO)_2$	3,4-$(MeO)_2C_6H_3$	70	9 : 1
j	3,4,5-$(MeO)_3$	3,4-$(MeO)_2C_6H_3$	38	5 : 1
k	4-MeO	3,4,5-$(MeO)_3C_6H_2$	53	> 99 : 1
l	3,4-$(MeO)_2$	3,4,5-$(MeO)_3C_6H_2$	42	> 99 : 1
m	3,4,5-$(MeO)_3$	3,4,5-$(MeO)_3C_6H_2$	41	5 : 1

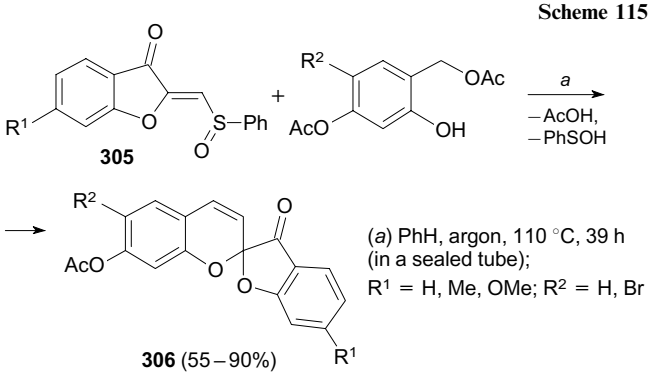
addition product (56% for **297c** and 85% for **297b**, see Table 4). Chalcones containing methoxy groups in both *meta*-positions are even less reactive (< 12% yield; not indicated in Table 4).

In the presence of BINOL-phosphoric acid, chalcone **298n** reacts with substituted salicyl alcohol **68a** to give diastereomeric chromans **300a**,**b** in 1 : 2 ratio (90% total yield). The reaction of β-methoxyacrylate with arylsalicyl alcohols **68a**,**c** in the presence of BPA produces diastereomeric mixtures of chromans **301a**,**b** (2 : 1, 68%) and **302a**,**b** (8 : 1, 73%) (Scheme 113).[171]

Scheme 114



Scheme 115



2-Methoxychroman **303** and acetal **304** were prepared from 4-methoxy-3-buten-2-one in refluxing toluene in a low yield (Scheme 114).[23] The formation of acetal **304** can be attributed to the oxa-Michael reaction followed by elimination of methanol and one more oxa-Michael reaction involving the phenolic hydroxyl group.

Benzofuran-3(2*H*)-one-based vinyl sulfoxides **305** react with *o*-QM precursors with high regioselectivity to give functionalized spiroketals **306**, a structural moiety of which is present in some natural compounds. The reaction is accompanied by elimination of benzenesulfonic acid from the initially formed cycloadduct (Scheme 115).[172]

4.2. Cyclic push-pull olefins

Enamino ketone based on dimedone — 3-dimethylamino-5,5-dimethyl-2-cyclohexen-1-one (**307b**) stable on storage — often serves as a versatile trap for various *o*-QMs. The use of Mannich bases, their methiodides and salicyl alcohols as *o*-QM precursors gives rise to a series of 8,9,10,12-tetrahydro-11*H*-benzo[*a*]xanthen-11-ones **308** and 2,3,4,9-tetrahydro-1*H*-xanthen-1-ones **309**.[173] These transformations were also accomplished using enaminone **307a** based on cyclohexane-1,3-dione. A β-carboline Mannich base, compound **250**, was also used as a *o*-QM precursor and was converted to pentacyclic compound **310**. The aminomethyl espintanol derivative **311** reacts with enamino ketone **307b** in refluxing DMF to give 2,3,4,9-tetrahydro-1*H*-xanthen-1-one **312**.[147] The reaction of morpholine Mannich base **313** with enaminone **307b** involves the generation of more stable *o*-QM **314**, which is stabilized by the intramolecular hydrogen bond between the hydroxyl proton and carbonyl oxygen atom. The formation of regioisomeric xanthene was not detected, compound **315** being the only isolated product (Scheme 116).[173]

Symmetrical cycloadducts **316** – **318** were prepared from enaminones **307a**,**b** and Mannich bases derived from hydroquinone, phloroglucinol and catechol, respectively (Scheme 117).[173 – 175]

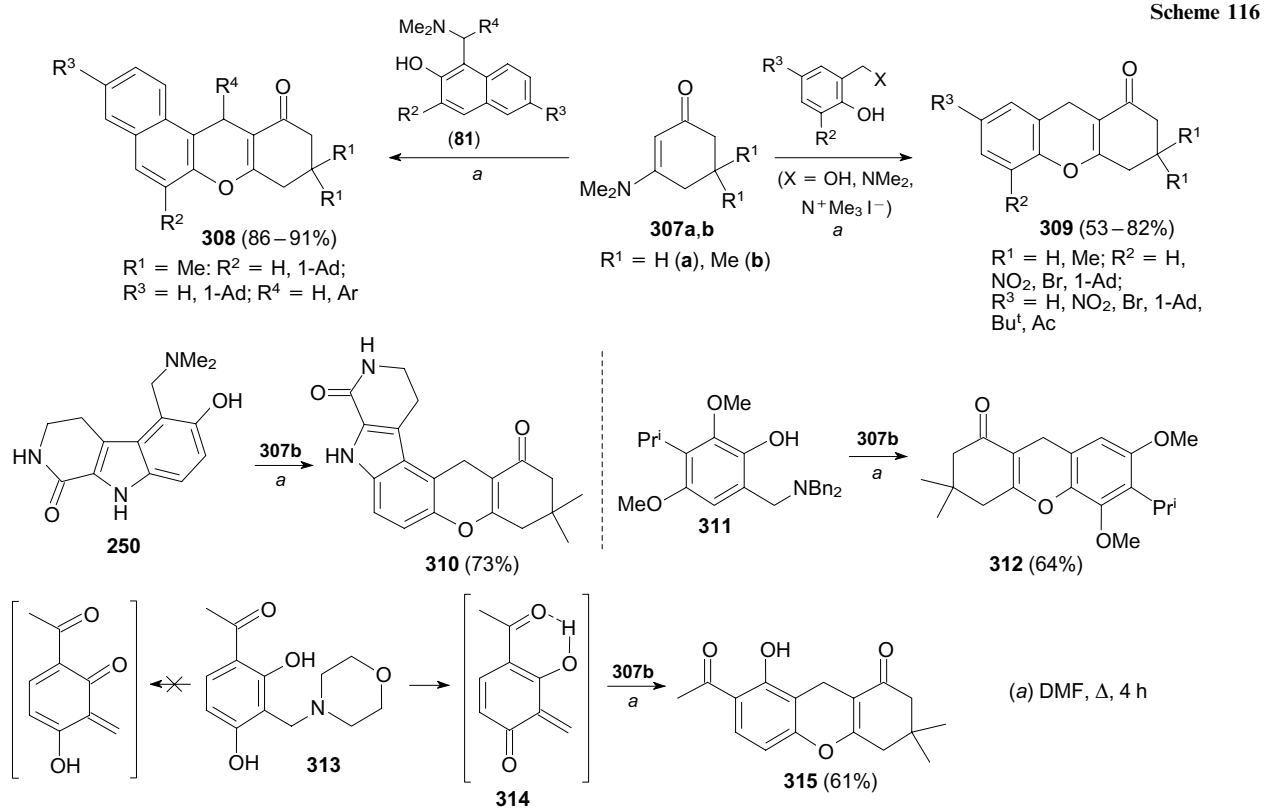
Osyanin *et al.*[176] reported the use of 8-hydroxyquinoline derivative **319** as a *o*-QM precursor for the cycloaddition reaction with enamino ketones based on cyclohexane-1,3-diones, which gives heterocycles **320a**,**b**. Mannich bases **321** obtained from 7-hydroxyisoflavones are converted to 4*H*,11*H*-pyrano[2,3-*a*]xanthene-4,11-diones **322** (Scheme 118).[177]

On exposure to light, *p*-benzoquinone **323** is converted to oxazolidine **324** as a result of electron transfer in the excited state from the pyrrolidine nitrogen atom to the C=O bond and the subsequent migration of hydrogen from the methylene group to the oxygen atom. The elimination of a benzoic acid molecule from oxazolidine **324** results in the generation of *o*-QM **325**, which reacts with enaminone **307b** to give cycloadduct **326**.[178, 179] It is worth noting that the presence of electron-donating groups markedly decreases the reactivity of *o*-QM, which no longer reacts with vinyl ethyl ether, ketene silyl acetal and other electron-rich dienophiles. In the absence of enaminone, *o*-QM **325** reacts with the starting quinone **323**, which can be considered as both a push-pull olefin and a captodative olefin, giving rise to product **327** (Scheme 119).

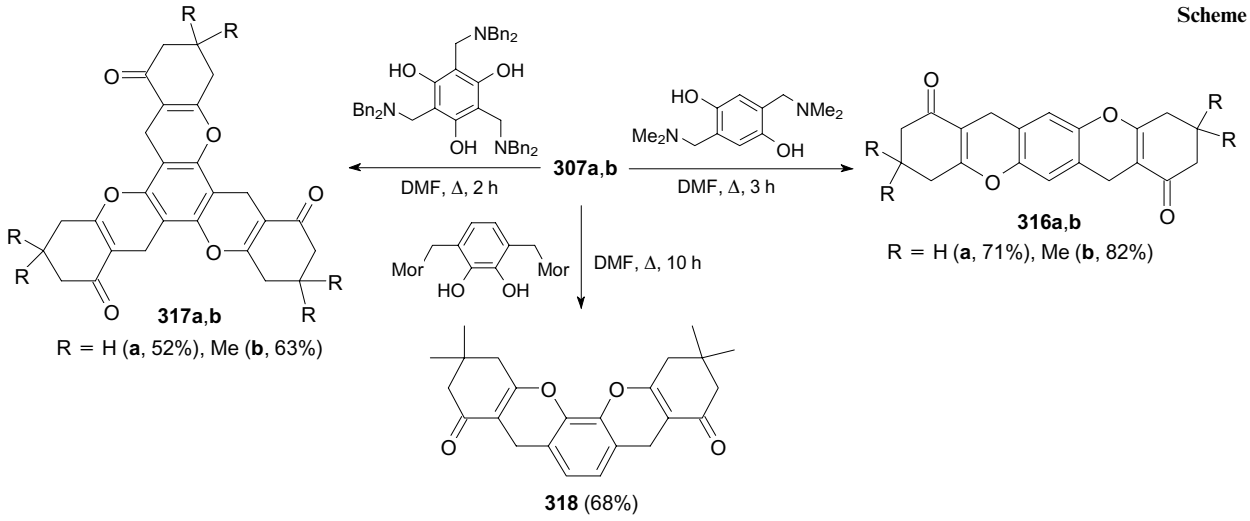
Cyclic enaminone **328** reacts with hydroxyphenylpropargyl alcohols to afford diastereomerically and enantiomerically enriched (1-oxoxanthen-4-yl)acetamides **329** (Scheme 120).[99] A transformation of this type was also performed for 1-(*o*-hydroxyphenyl)anisyl alcohol.[100]

Owing to the highly polar C=C bond, 6-chlorouracil and 6-amino-1,3-dimethyluracil can also be regarded as push-pull olefins. They react with various *o*-benzoquinone methide precursors (salicyl alcohols, phenol Mannich bases

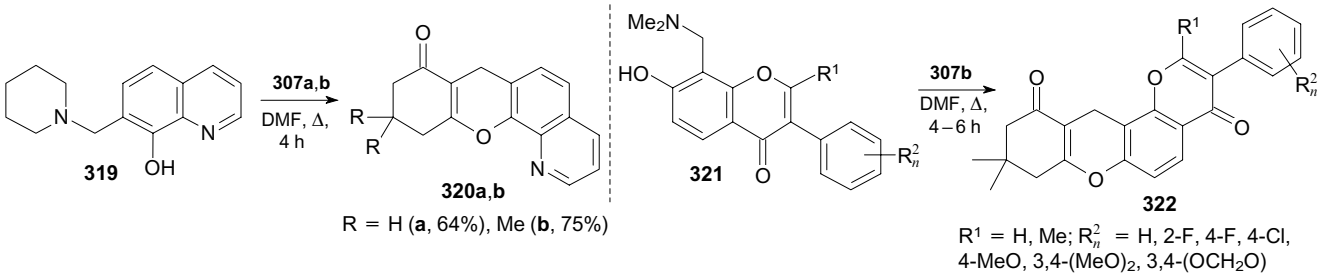
Scheme 116



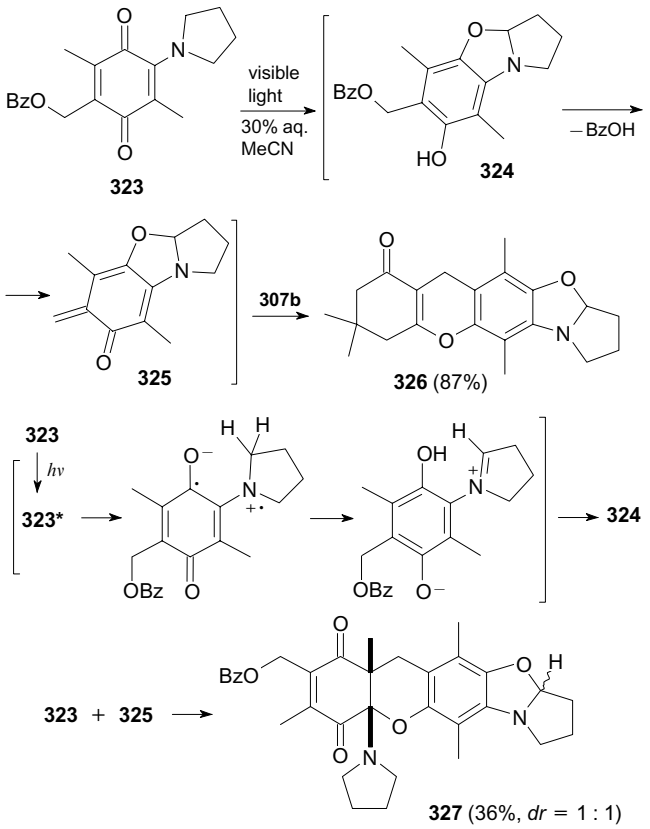
Scheme 117



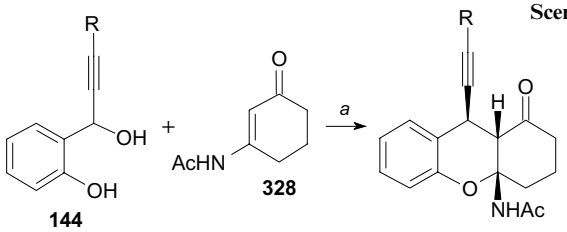
Scheme 118



Scheme 119



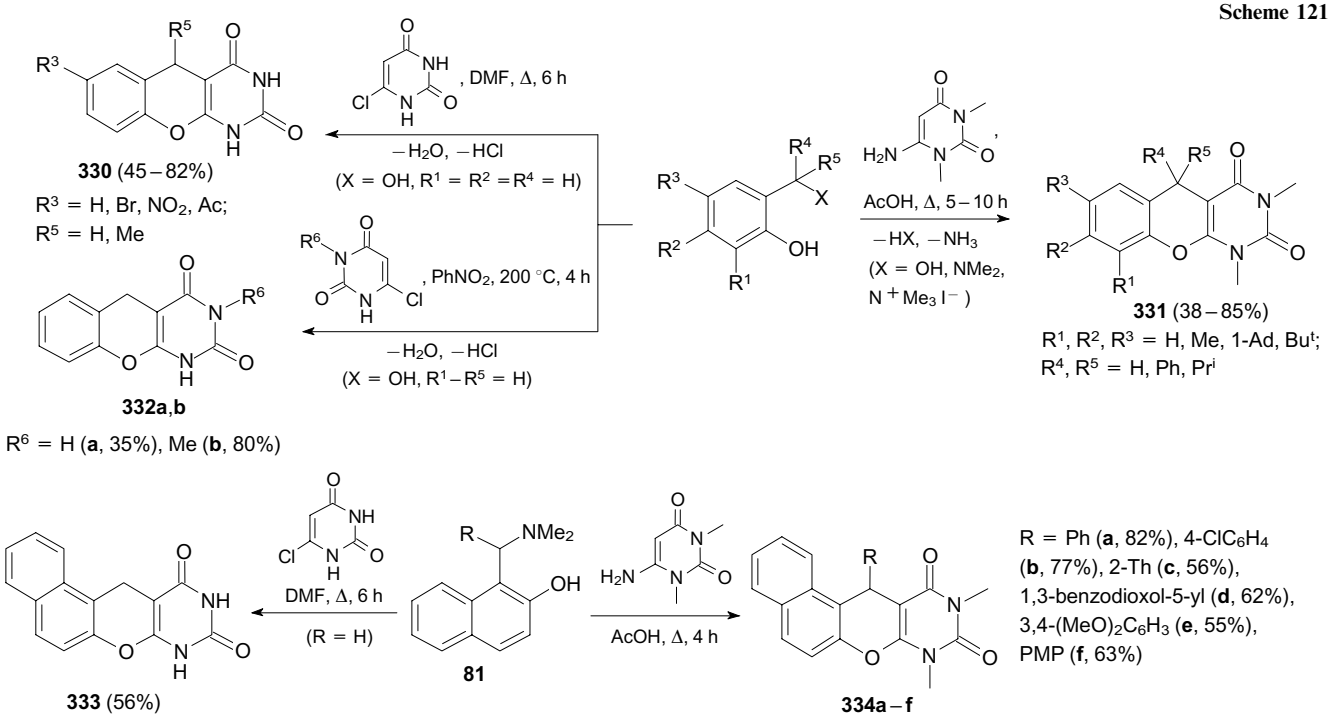
Sceme 120



and their methiodides) containing electron-donating and -withdrawing groups and sterically bulky groups in refluxing DMF or acetic acid to yield 2*H*-chromeno[2,3-*d*]pyrimidinediones **330** – **332** as a result of [4 + 2]-cycloaddition and elimination.[180 – 182] This method makes it possible to synthesize derivatives unsubstituted in position 5. In the presence of an excess of salicyl alcohol (3 equiv.), the reaction with 6-chlorouracils is also carried out in nitrobenzene at 200 °C.[183] Naphthalene Mannich bases were converted to 8,12-dihydro-9*H*-benzo[5,6]chromeno[2,3-*d*]-pyrimidine-9,11(10*H*)-diones **333**, **334** (Scheme 121).[181]

Refluxing spirodimer **178**, a precursor of 1,2-naphthoquinone 1-methide **109b**, with thiazine derivatives (in 2 : 1 ratio) in mesitylene results in the formation of tetracyclic heteroaromatic chromans **335a**,**b** and **336**. In the case of 1,3-dimethyluracil, partial opening of the dihydropyran ring in adduct **337** takes place, and substituted pyrimidinedione **338** is also isolated as a reaction product. Meanwhile, only

Scheme 121



two regioisomeric chromans **339** and **340**, differing in the coupling of heterocyclic moieties, are formed in 5.3 : 1 ratio upon the reaction with 1,3,6-trimethyluracil (Scheme 122).[135]

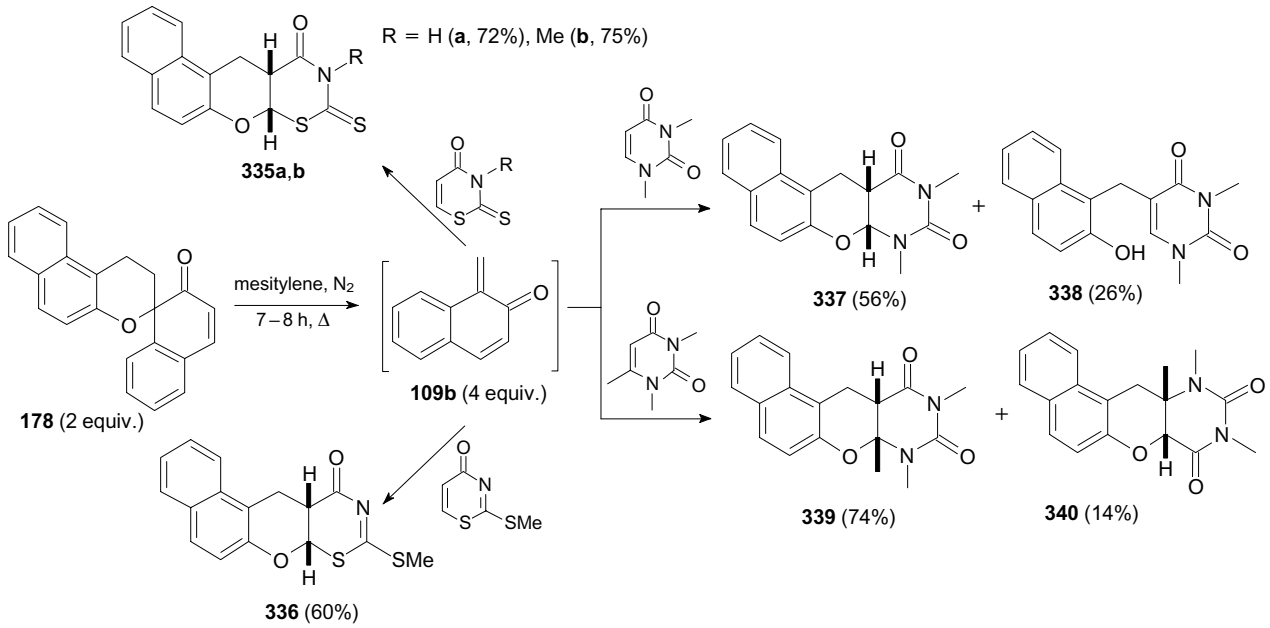
Stereoselective cycloaddition of *o*-QMs, generated *in situ* from salicyl alcohols **68**, to azlactone enol forms in the presence of chiral phosphoric acid **IXe** as the catalyst affords dihydrocoumarins **341** with a high degree of optical purity (Scheme 123).[184] The push-pull nature of the double bond in the azlactone enol form is due to the presence of an electron-withdrawing (ester or trifluoroacetyl) group.

3-Methylbutanal dimethyl acetal (**342**), acylphloroglucinol **343** and syncarpic acid (**344**) in refluxing isopropyl alcohol were used for the acid-catalyzed one-step synthesis of rhodomyrtosone B (**345**), a potential antibiotic active against gram-positive bacteria. Model experiments demonstrated that *o*-QM is generated from the dimethyl acetal and acylphloroglucinol, while syncarpic acid is converted to enol ester. The subsequent cycloaddition and elimination of isopropyl alcohol and water furnish rhodomyrtosone B (**345**) (Scheme 124).[185]

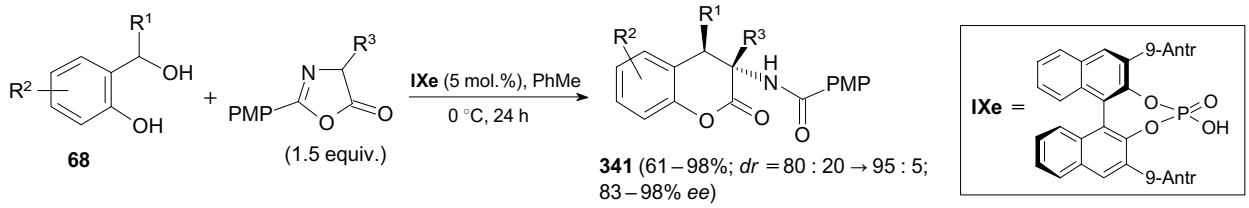
4.3. Push-pull buta-1,3-dienes

Owing to certain similarity of the chemical reactivity and electronic structures of ketones (or aldehydes) and compounds containing the $C(CN)_2$ moiety instead of the carbonyl oxygen atom, Knoevenagel adducts prepared from malononitrile and 3-(*N*,*N*-diethylamino)acrolein or 3-mor-

Scheme 122

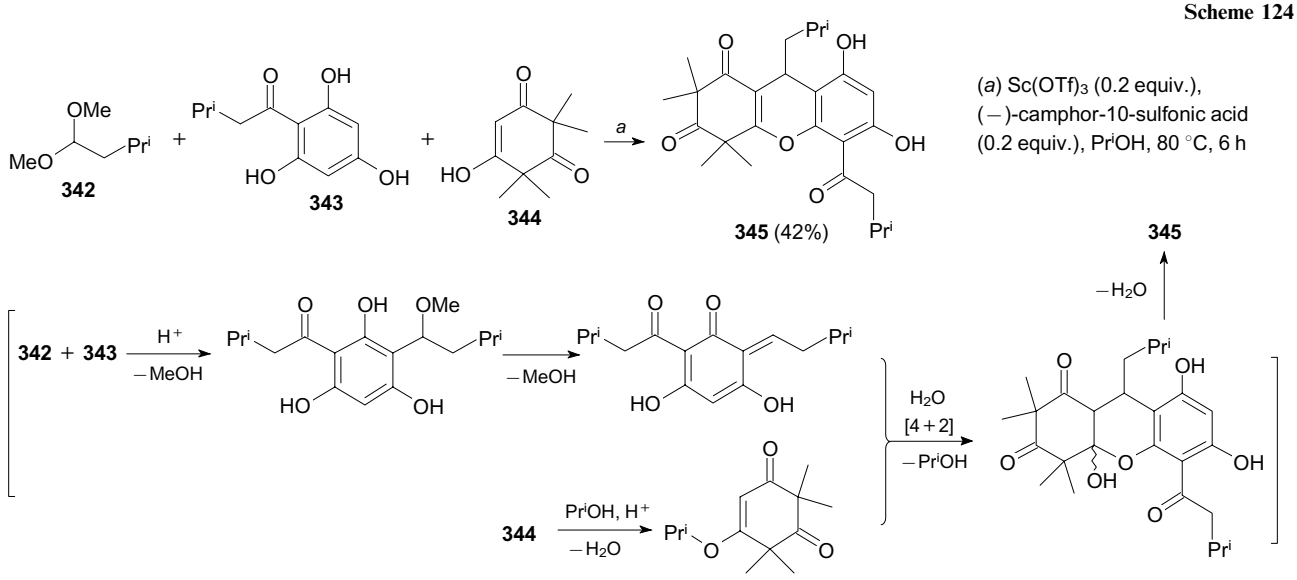


Scheme 123



R^1 = Ar, All, Cy, vinyl, alkynyl; R^2 = H, Me, Cl, NO_2, Br, OCH_2O; R^3 = CO_2Et, $C(O)CF_3$

Scheme 124

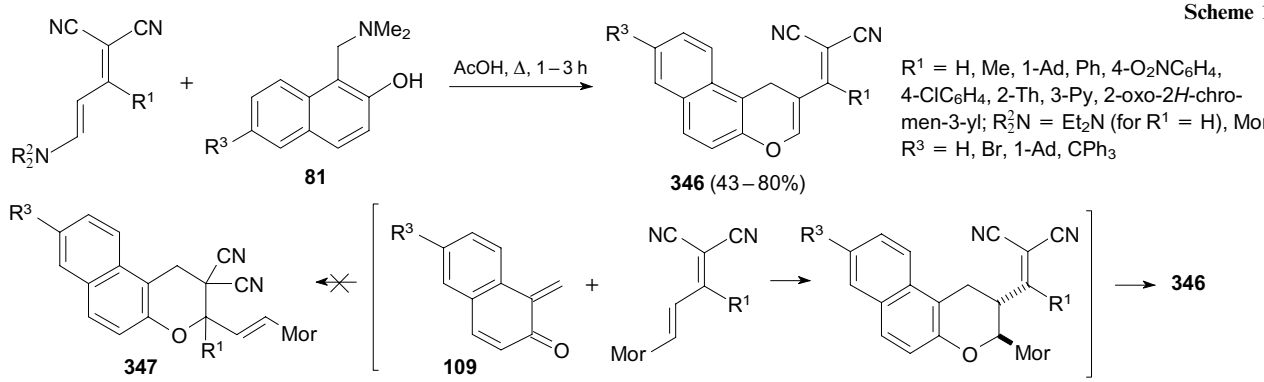


pholinoacrolein react with *o*-QM precursors similarly to β-enaminones. The reactions of naphthalene Mannich bases **81** with 2-(3-R_2N-allylidene)malononitriles yield a series of 1*H*-benzo[*f*]chromenes **346** (Scheme 125). Despite the possibility of competing addition of 1,2-naphthoquinone 1-methide **109** to the C=C(CN)$_2$ double bond, no formation of product **347** is observed. This fact is attributable to the electron-rich character of the double bond directly bound to the morpholine ring, which accounts for the regioselectivity of inverse electron demand [4 + 2]-cycloaddition.[156]

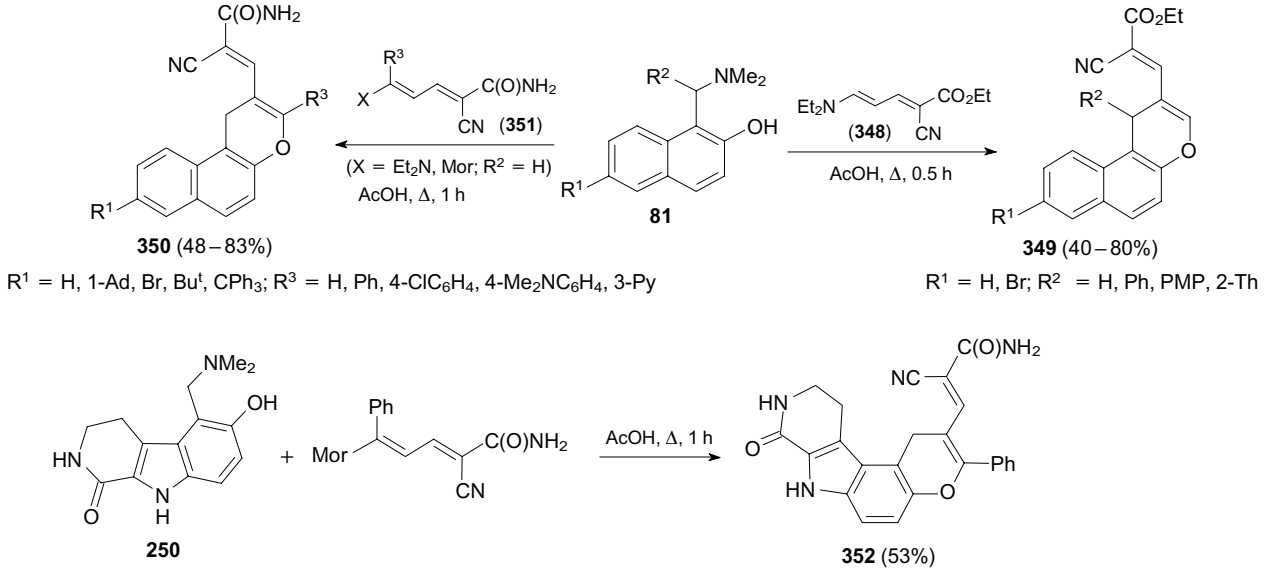
Ethyl 2-cyano-5-diethylaminopenta-2,4-dienoate (**348**) was allowed to react with 2-naphthol Mannich bases **81** in refluxing acetic acid, which resulted in the synthesis of 1*H*-benzo[*f*]chromene-2-cyanoacrylic acid esters **349**. A series of 3-(1*H*-benzo[*f*]chromen-2-yl)-2-cyanoacrylamides **350** were synthesized under analogous conditions from push-pull 5-aryl-5-dialkylamino-2-cyanopenta-2,4-dienamides **351** and naphthalene type *o*-QM precursors. The use of Mannich bases **250** provides the synthesis of 7,9,10,11-tetrahydropyrano[3,2-*e*]pyrido[3,4-*b*]indol-8(1*H*)-one **352** (Scheme 126).[156]

The reaction of 2-[hydroxy(aryl)methyl]phenols **68** with β-(indol-3-yl)acrylates in which the exocyclic double bond has a push-pull nature, catalyzed by copper(II) salts, affords hybrid heterocycles **353** containing chroman and indole pharmacophore rings. The degree of diastereoselectivity of the reaction varies over a broad range depending on the nature of substituents (Scheme 127).[186] This reaction is directed towards the double bond located near the ester group because dearomatization of the pyrrole moiety is unfavourable.

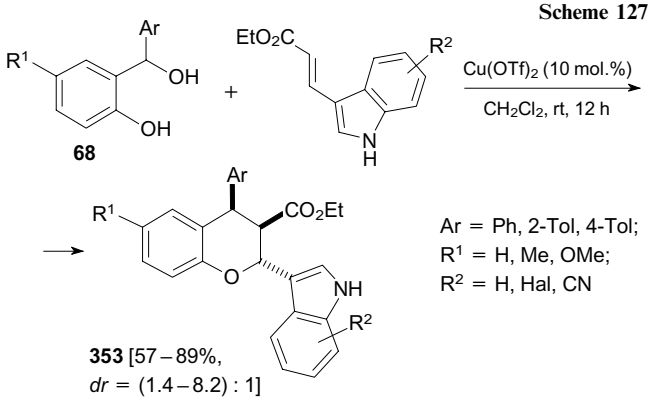
Scheme 125



Scheme 126



Scheme 127

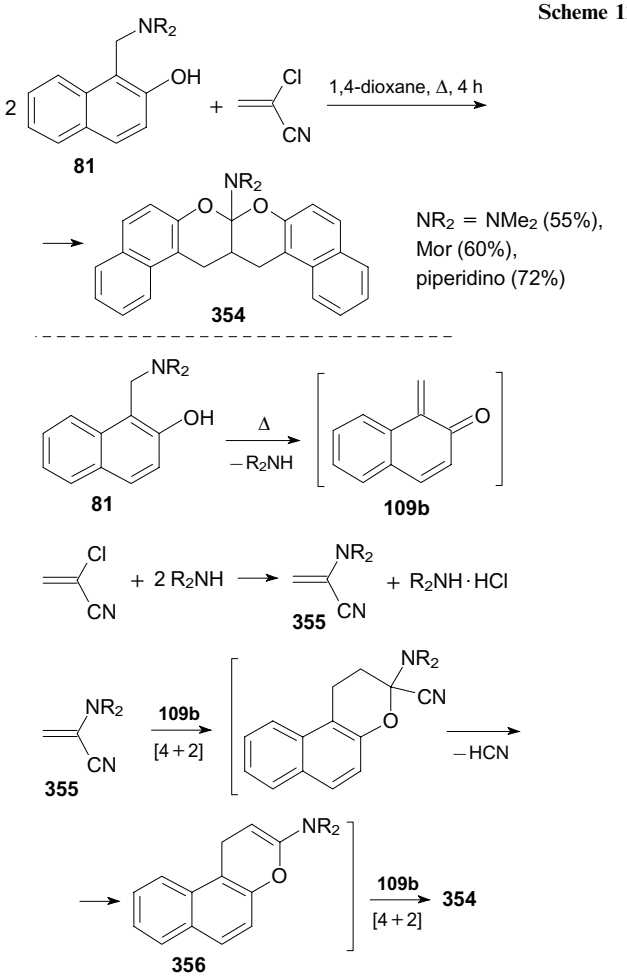


5. Reactions of *o*-quinone methides with captodative olefins

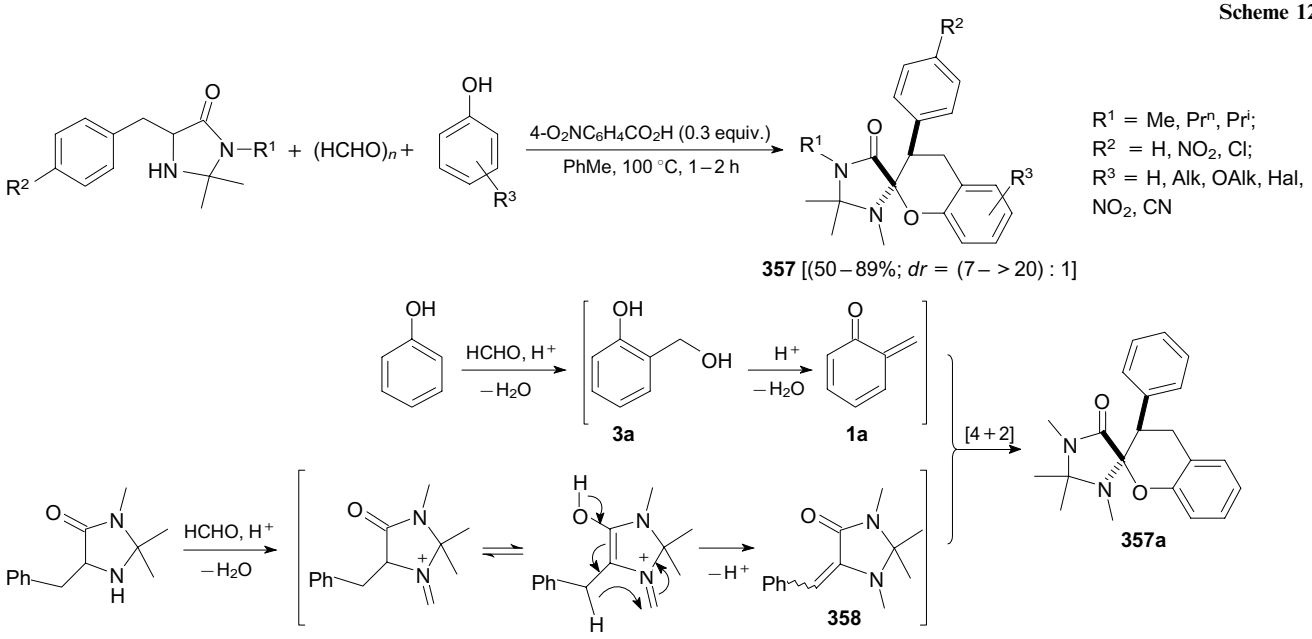
In captodative olefins, electron-donating and -withdrawing groups are located at the same carbon atom.[187, 188] The *o*-QM reactions with captodative olefins reported in the literature include only a few examples. Thus it was shown that thermolysis of 2-naphthol Mannich bases **81** in refluxing dioxane in the presence of α-chloroacrylonitrile results in the formation of 7a,15a-dihydro-7a-15*H*,16*H*-naphtho[2,1-*b*]naphtho[1′,2′:5,6]pyrano[3,2-*e*]pyrans **354**. Initially, the chlorine atom in α-chloroacrylonitrile is displaced on treatment with secondary amine, generated upon decomposition of the Mannich base. α-Cyanoenamines **355** thus formed can be considered as captodative olefins. Then they undergo the [4 + 2]-cycloaddition reaction with *o*-QM; however, the primary cycloadducts prove to be unstable and give off HCN to be converted to 2-aminonaphthopyrans **356**. In turn, the latter react with a second *o*-QM molecule **109b** to give symmetrical benzoannulated pyrano[3,2-*e*]pyrans **354** (Scheme 128).[189]

The three-component reaction of phenols, 5-benzylimidazolidin-4-ones and paraformaldehyde (1 : 3 : 1.2 ratio) affords spirocyclic chroman type *N*,*O*-acetals **357** with high diastereoselectivity. The mechanism of the cascade reaction includes, on the one hand, hydroxymethylation of phenol, which generates *o*-QM in an acid medium, and, on the other hand, the formation of the iminium cation from formaldehyde and 5-benzylimidazolidin-4-one. The subsequent hydride transfer and deprotonation yield 5-benzylideneimidazolidin-4-one **358**, predominantly as the *E*-isomer. This compound can be considered as a captoda-

Scheme 128



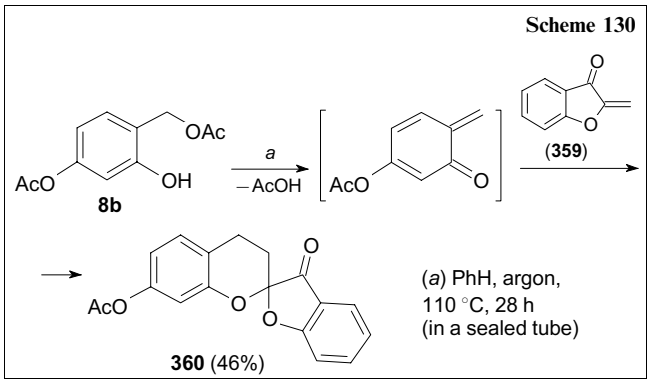
Scheme 129



tive olefin due to the presence of carbonyl and amino groups at the same double bond carbon atom (Scheme 129).[190]

2-Methylenebenzofuran-3(2*H*)-one (**359**), in which the exocyclic double bond is captodative because of the carbonyl group and the endocyclic oxygen atom, reacts with *o*-QM precursor **8b** to give spiroketal **360** in a moderate yield (Scheme 130).[172]

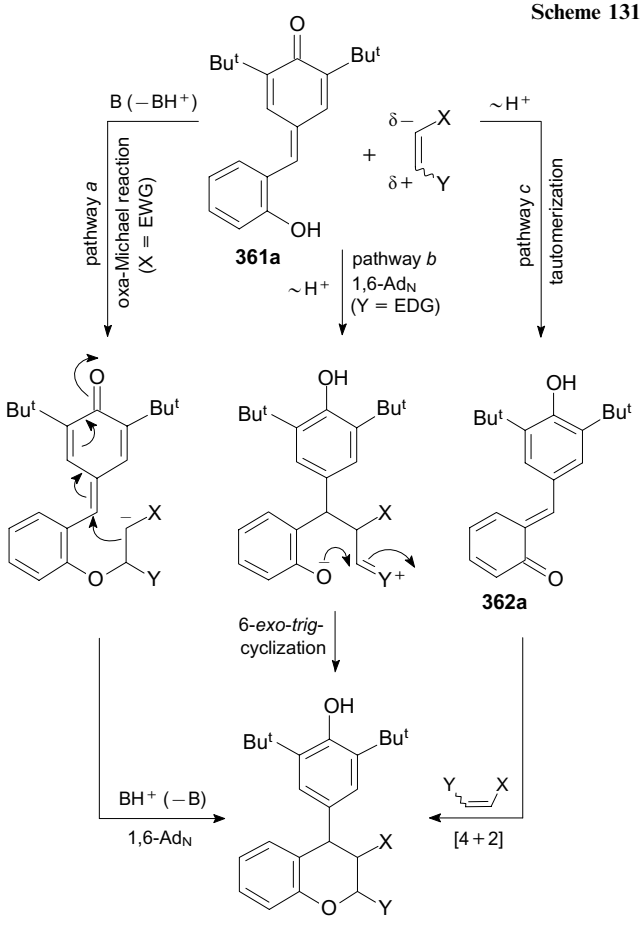
Scheme 130



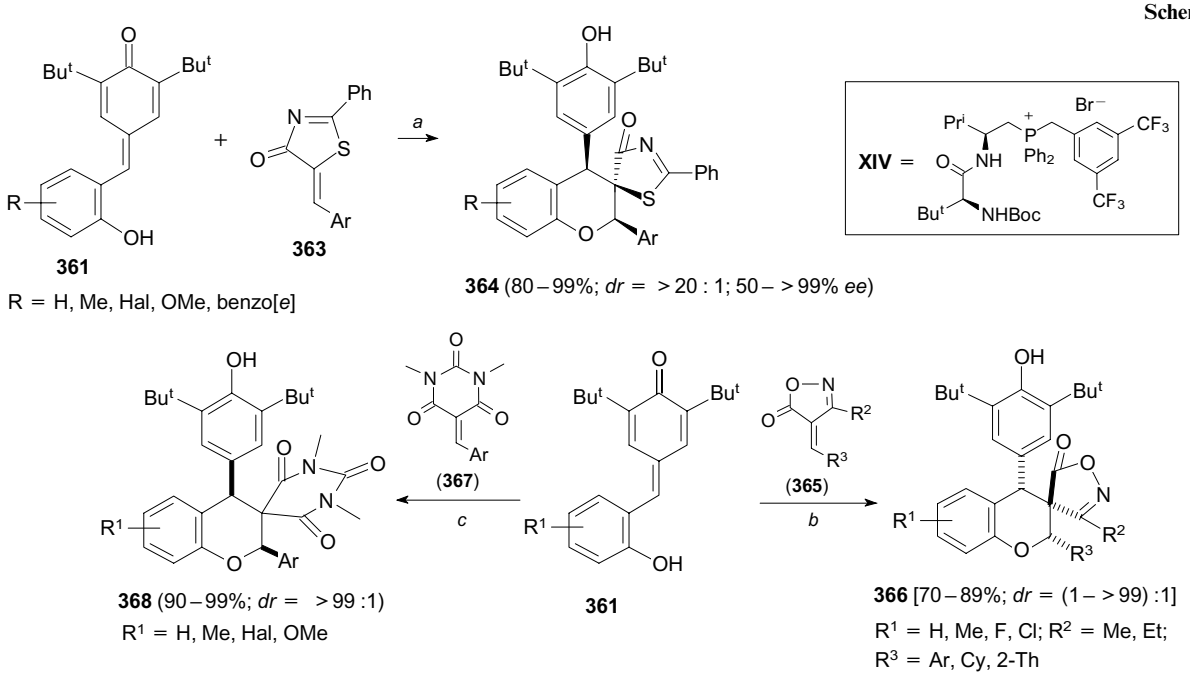
6. [4 + 2]-Annulation reactions involving *o*-hydroxyphenyl-substituted *p*-quinone methides

Stable *o*-hydroxyphenyl-substituted *p*-QMs **361** have attracted considerable researchers' attention in recent years, as they can potentially act as four-atom building blocks in various types of [4 + *n*]-annulation reactions. First of all, this refers to [4 + 2]-cyclization reactions, which lead to diverse functionally substituted chromans, 4*H*-chromenes, dihydrocoumarins, *etc*.[17, 172, 191 – 195] Both electron-deficient and electron-rich olefins can be introduced in these reactions as C_2-synthons. Several possible mechanisms have been proposed for the six-membered heterocycle formation (Scheme 131). In the case of electron-deficient olefins, especially in the presence of a base, a cascade reaction may take place, including the oxa-Michael reaction and nucleophilic 1,6-addition (pathway *a*). For electron-rich olefins, the initial conjugate 1,6-addition followed by 6-*exo*-*trig*-cyclization may take place (pathway *b*). The reactions can be catalyzed by Lewis and Brønsted acids *via* coordination to the carbonyl oxygen atom of *p*-QMs, which enhances polarization of the quinoid system and increases the electrophilicity of the exocyclic carbon atom. Finally, isomerization of *p*-QMs **361** to *o*-isomers **362** followed by the Diels – Alder reaction is possible (pathway *c*). Quantum

Scheme 131



Scheme 132



(*a*) **XIV** (5 mol.%), $K_3PO_4 \cdot 7H_2O$ (4 equiv.), petroleum ether, rt, 12 h; (*b*) Et_3N (20 mol.%), EtOH, 50 °C, 48 – 72 h;
(*c*) Et_3N (20 mol.%), MeCN, rt, 6 – 8 h

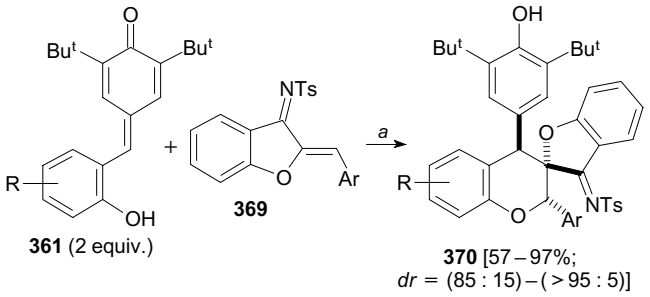
chemical calculations show that the energy of isomerization is only 6.7 kcal mol^{-1}; therefore, the tautomerization can take place at room temperature.[196 – 198] In addition, it was shown for several examples that in the absence of a hydroxyl group in the substrate or in the case of *O*-protected compounds, reactions with olefins do not proceed, nor the 1,6-addition to the *p*-QM moiety. These facts attest to the participation of *o*-QMs in the heterocyclization. In any case, no matter by what mechanism these transformations occur, they can formally be considered as [4 + 2]-cycloaddition reactions of polarized olefins with *o*-QMs.

It should also be noted that the use of chiral bases and acids in reactions with *o*-hydroxyphenyl-substituted *p*-QMs opens up wide opportunities for the preparation of optically active chroman derivatives. In addition, *tert*-butyl groups needed for stabilization of *p*-QM can be easily removed in acid medium.[196, 199, 200]

It was shown that enantioselective [4 + 2]-annulation of 5-alkenylthiazolones **363** with 2-hydroxyaryl-substituted *p*-QMs in the presence of chiral dipeptide-based phosphonium salt **XIV** affords spirocycles **364**, containing chroman and thiazolone moieties, in high yields. The reaction has high diastereoselectivity and, in most cases, also good enantioselectivity with a low required amount of the catalyst and proceeds under mild conditions.[201] In the presence of triethylamine as a base, arylideneisoxazolones **365** are converted to spiroisoxazolonochromans **366**.[202] Arylidenebarbiturates **367** are converted to spirobarbituratochromans **368** in high yields and with high diastereoselectivity (Scheme 132).[203]

The base-catalyzed [4 + 2]-annulation reaction between benzofuran derivatives **369** containing an azadiene moiety and sterically crowded *p*-QMs **361** gives spirobenzofurans **370** with high diastereoselectivity.[204] This reaction can be conducted only in the presence of Cs_2CO_3, whereas Na_2CO_3, K_2CO_3 or organic bases are inefficient (Scheme 133).

Scheme 133



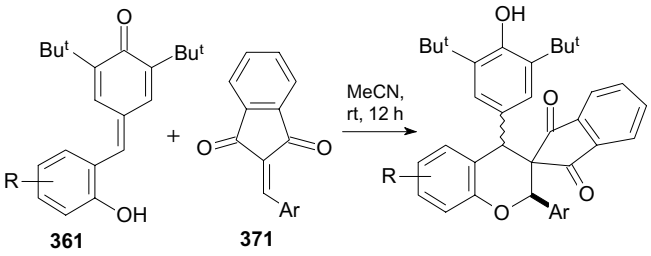
(*a*) Cs_2CO_3 (1 equiv.), PhBr, – 10 °C, 9 h;
R = H, F, Cl, Br, OMe; Ar = Ph, 3-Tol, 4-Tol, 3-BrC_6H_4

2-Arylideneindane-1,3-diones **371** react with stable *p*-QM **361** at room temperature without any catalyst to give products **372** containing simultaneously two pharmacophores — chroman and spiroindane-1,3-dione moieties.[205] Spiro-substituted chromans are formed as mixtures of diastereomers, which can be preparatively separated. It should be noted that the presence of the *tert*-butyldimethylsilyl group on the oxygen atom completely suppresses the reaction, which indirectly attests to isomerization of *p*-QM into *o*-QM and the subsequent [4 + 2]-cycloaddition. The formation of diastereomers is due to the *endo*- or *exo*-approach of the reagents (Scheme 134).

In the presence of chiral thiourea **XV**, *N*-protected oxindoles **373** are converted to spiro-substituted chromans **374**, containing an oxindole pharmacophore moiety, in high yields (up to 98%) and with high diastereo- and enantioselectivity (up to 99% *ee*) (Scheme 135).[206]

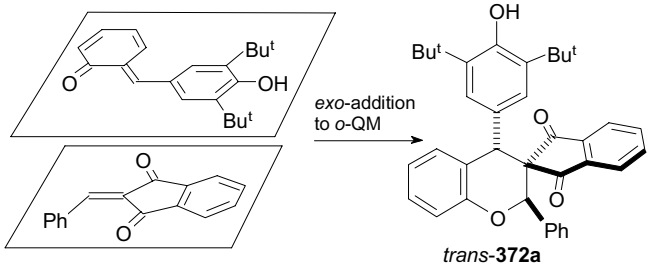
Racemic 3-nitrochromans **375a**,**b** were synthesized in 50 – 95% yields and with low (60 : 40) to good (90 : 10) diastereoselectivity from nitroolefins (mainly from β-nitrostyrenes) in the presence of DMAP (Scheme 136).[199] In

Scheme 134

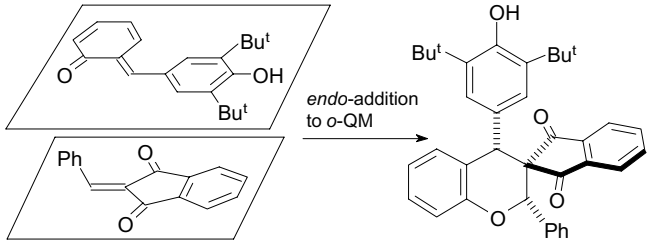


R = H, Me, Cl, Br, OMe

372 [*trans* 48 – 95%, *cis* up to 42%; *dr* (*trans* : *cis*) = (1.1 – 3.8) :1]



trans-**372a**



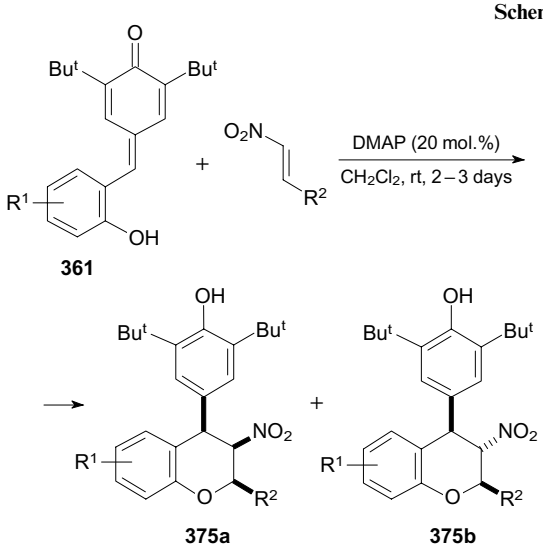
cis-**372a**

order to attain reasonable yields of products, it is necessary to keep the reaction mixture for 2 – 3 days. The reaction can also be carried out in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), triethylamine and diisopropylethylamine.

In the reaction of *o*-hydroxyphenyl-substituted *p*-QMs with 2,4-dienals **376**, only the more electron-rich γ,δ-double bond of the aldehyde is involved in the formation of the dihydropyran ring of product **377** (Scheme 137). The reaction is catalyzed by a chiral pyrrolidine derivative in the presence of triethylamine. It is assumed that the reaction starts with the formation of the iminium salt from the aldehyde and the catalyst.[207]

Azlactone enol forms containing both nucleophilic [C(4) atom] and electrophilic [C(5) atom] centres can participate in the Diels – Alder reaction as electron-rich dienophiles. A series of dihydrocoumarins **378** with > 20 : 1 diastereomeric

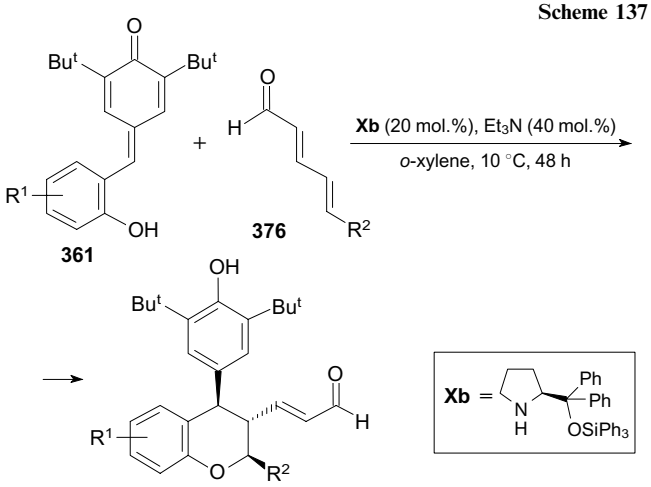
Scheme 136



R^1 = H, Me, Hal, OMe; R^2 = Ar, 2-Th, Bu^i

ratio and a yield of up to 98% were prepared from *p*-QMs **361** and azlactones (Scheme 138). An enantiomeric excess of > 98% can be attained using BINOL-based chiral phosphoric acid **IXb**. The initially formed cycloadduct proves to be unstable and undergoes oxazoline ring opening. The

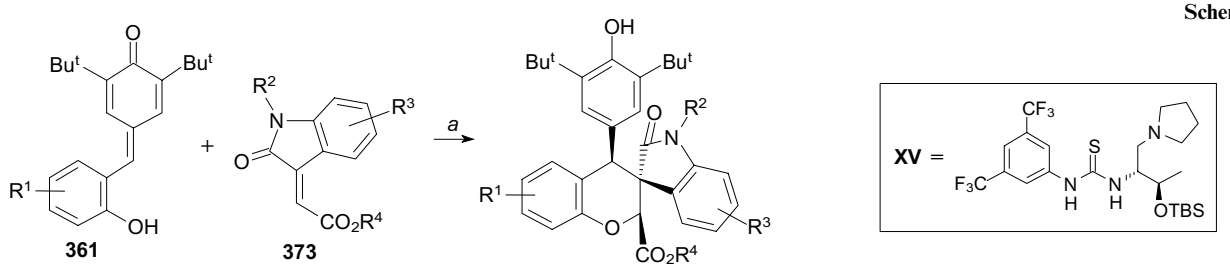
Scheme 137



377 [36 – 84%; *dr* = (3 – 12) : 1; 76 – 99% *ee*]

R^1 = H, Me, Br, Cl, OMe; R^2 = Me, Et, n-C$_5$H$_{11}$, Ph(CH$_2$)$_2$, Cy, 2-O$_2$NC$_6$H$_4$

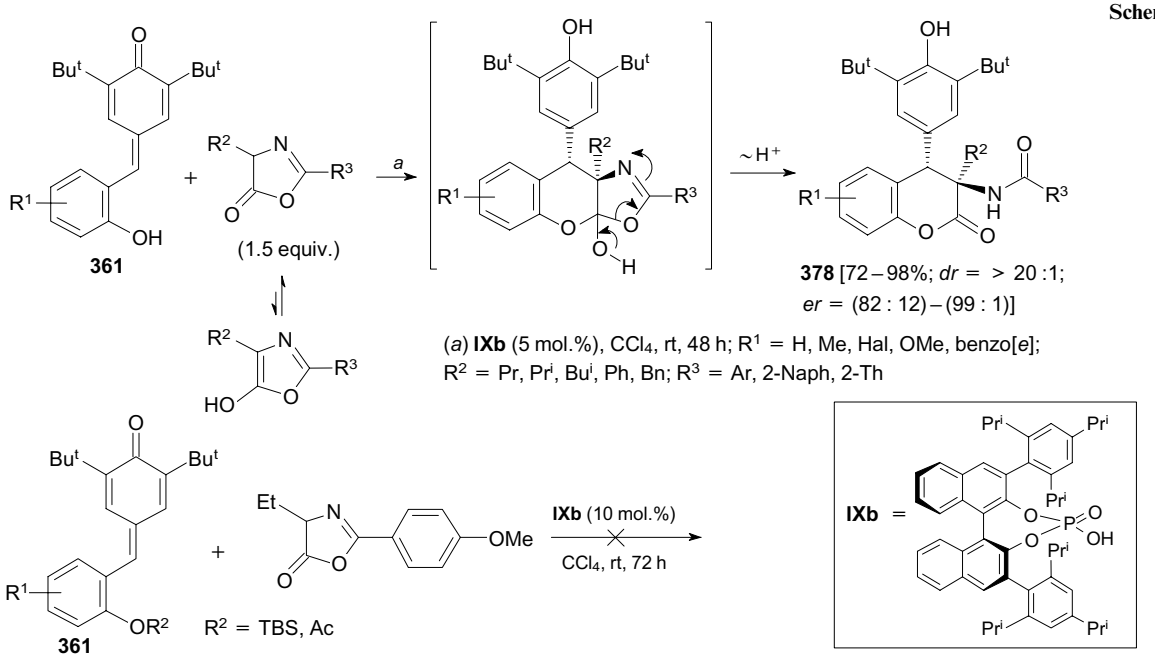
Scheme 135



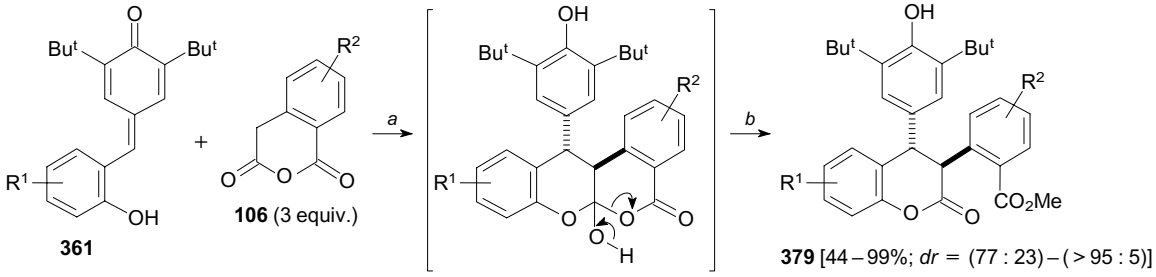
374 [43 – 98%; *dr* = (10 – 20) : 1, 95 – 99% *ee*]

(*a*) **XV** (5 mol.%), PhMe, rt, 12 – 72 h; R^1 = H, Me, Br, Cl, OMe; R^2 = Boc, CO$_2$Bn, CO$_2$Me, CO$_2$Ph; R^3 = H, NO$_2$, OMe, Hal, OCF$_3$; R^4 = Me, Et, Bn

Scheme 138



Scheme 139



(*a*) *m*-xylene, 30 °C, 16 h; (*b*) $TMSCHN_2$, MeOH, 30 min; R^1 = H, Me, Hal, OMe, Bu^t; R^2 = H, F, Me

presence of a free hydroxyl group in *p*-QMs **361** is critical for the reaction to proceed. In the case of the protected group, the reaction does not occur, which also attests to the participation of *o*-QMs in the cycloaddition. Chiral phosphoric acid not only accelerates the *in situ* generation of *o*-QMs and enolization of azlactone, but also activates such intermediates *via* the formation of hydrogen bonds. The reaction between the enol form of azlactone and *o*-QM occurs mainly as the *endo*-addition.[200]

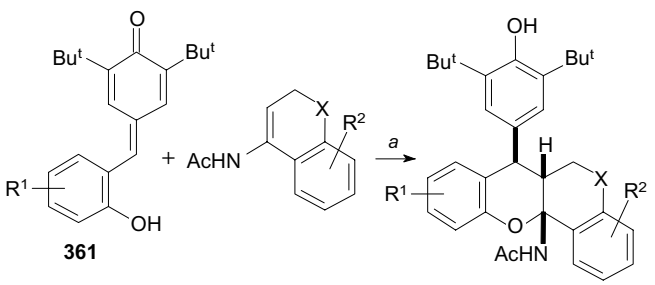
The asymmetric synthesis of dihydrocoumarins was also performed in perfluorobenzene at room temperature.[196] In addition, this transformation was also carried out with high diastereoselectivity in the presence of diphenyl phosphoric acid $(PhO)_2P(O)OH$ in acetonitrile.[208]

The reaction of *p*-QMs **361** with homophthalic anhydrides **106** without a catalyst also yields dihydrocoumarins **379** with good diastereoselectivity. The products are isolated as methyl esters after treatment with trimethylsilyl diazomethane. Apparently, the key reaction intermediates are *o*-QMs and the enol form of homophthalic anhydride. Substituted dihydrocoumarins **379** are mainly formed as more stable *trans*-isomers in which the steric repulsion between the aryl groups is lower (Scheme 139).[209]

The reactions of *p*-QMs **361** with cyclic enamides in the presence of *p*-toluenesulfonic acid give polycyclic chromans **380** in up to 99% yields under mild conditions.[210] The methyl group present in the enamide in the β-position to the acetylamino group suppresses the reaction almost completely, and the target chroman is detected in trace amounts (Scheme 140). The reaction conducted in CH_2Cl_2 at room temperature in the presence of chiral phosphoric acids based on 1,1′-bi-2-naphthol proceeds asymmetrically and gives products in high yields and with high enantio- and diastereoselectivity.[197]

There are several reported examples of reactions between *p*-QMs and 1-styryl-2-naphthols, which can be

Scheme 140



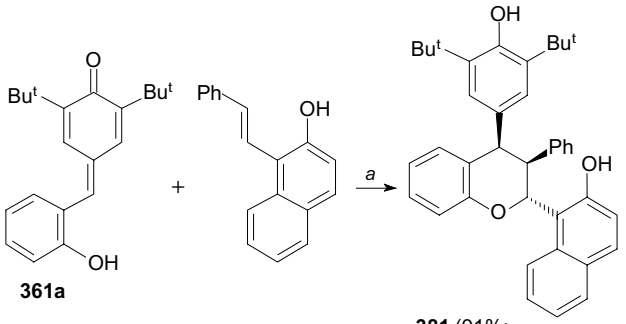
(*a*) PTSA (10 mol.%), CH_2Cl_2, rt; R^1 = H, Me, Hal, OMe, Bu^t; R^2 = H, Me, OMe, OBn, Et, F, Cl; X = O, CH_2, $(CH_2)_2$, S, none

considered as electron-rich dienophiles because of the presence of the electron-donating hydroxyl group in conjugation.[73, 74] 2-(2-Hydroxy-1-naphthyl)chroman **381** was prepared in this way (Scheme 141).

The asymmetric [4 + 2]-cycloaddition involving 3-alkyl-2-styrylindoles, which act as electron-rich dienophiles, catalyzed by chiral phosphoric acids **IXe**,**f** gives products **382** in high yields (up to 98%) with high stereoselectivity (up to > 95 : 5 *dr*, up to 96% *ee*) (Scheme 142). Note that *N*-substituted indoles do not react under these conditions.[211]

Owing to the electron-donating nitrogen atom and a conjugated electron-withdrawing group in the vinyl moiety, the exocyclic double bond in 3-vinylindoles **383** has a push-pull nature. In the presence of $Cu(OTf)_2$, these compounds are converted to 2-(indol-3-yl)chromans **384** formed as racemic mixtures of diastereomers (Scheme 143). The yields of chromans and diastereoselectivity of the reaction vary over a broad range depending on the nature of substituents.[186]

Scheme 141

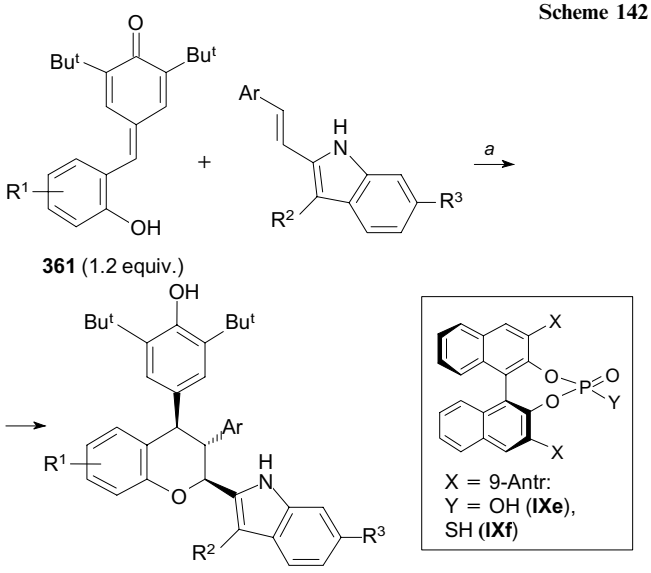


361a

(*a*) **IXb** (5 mol.%), PhMe, −10 °C, 12 h

381 (91%; *dr* = > 20 : 1, 95% *ee*)

Scheme 142

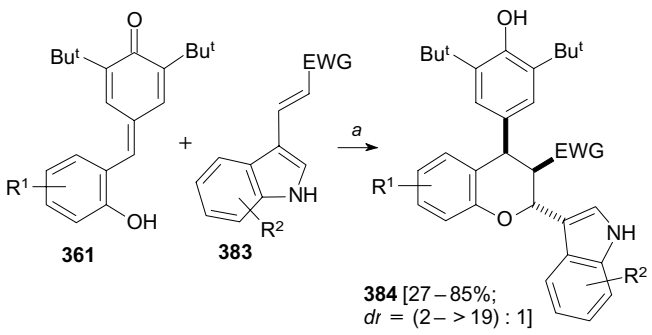


361 (1.2 equiv.)

382 [63 – 98%; *dr* = (78 : 22) – (> 95 : 5); 90 – 96% *ee*]

(*a*) **IXe**,**f** (10 mol.%), MS 5 Å, *o*-xylene, −20 °C, 12 h;
R^1 = H, Me, Br, OMe; R^2 = Me, Et, Bn; R^3 = H, Cl

Scheme 143



361 **383**

384 [27 – 85%; *dr* = (2 – > 19) : 1]

(*a*) $Cu(OTf)_2$ (10 mol.%), CH_2Cl_2, rt, 12 h; R^1 = H, Me, Hal, OMe; R^2 = H, Me, Et, CN, OMe; EWG = CO_2Et, NO_2, Ac

7. Conclusion

Currently, the chemistry of *o*-QMs is a vigorously developing and important area of organic synthesis. The Diels – Alder reactions of *o*-QMs with various dienophiles serve as an efficient tool for the preparation of various fused carbo- and heterocyclic pyran systems. The driving force for most of cycloaddition reactions is aromatization of the quinone methide moiety, which crucially distinguishes *o*-QMs from most other α,β-unsaturated carbonyl compounds.[212] An important benefit is the ability to use various *o*-QM precursors in the synthesis of various chromans and chromenes, including natural products, often with high diastereoselectivity. Meanwhile, enantioselective reactions can be accomplished only in the case of relatively high stability of *o*-QMs, caused by the presence of sterically bulky and electron-donating substituents or by elongation of the chain of conjugation. Enantioselective versions of reactions of unstabilized *o*-QMs have scarcely been developed to date, which emphasizes the necessity of devising new methods for the generation of *o*-QMs and designing new catalytic systems to extend the range of chromans and chromenes prepared on optically pure state.

The vast majority of the described reactions include *o*-benzo- and *o*-naphthoquinone methides. However, heterocyclic *o*-QMs are still poorly studied, although the use of such compounds would provide an access to diverse heteroannulated 4*H*-pyrans. In addition, attention is attracted by the fact that the reactivity of *o*-QMs with electron-withdrawing substituents is much less studied than that of *o*-QMs containing electron-donating groups.

It is also noteworthy that reactions of *o*-QMs with electron-rich olefins are rather widely represented in the literature. However, reactions of *o*-QMs with electron-deficient and push-pull dienophiles are much fewer in number, and data on these reactions are fragmentary. Reactions of *o*-QMs with captodative olefins are even more rarely encountered. However, exensive studies on the use of *o*-QMs as intermediates in organic synthesis are currently underway, as indicated by a large number of publications on this topic that appeared in recent years.†

This review was prepared with the financial support of the Russian Foundation for Basic Research (Project No. 19-13-50441).

8. List of abbreviations and designations

Ad — adamantyl,
All — allyl,
Antr — anthryl,
B — base,

† When the review was prepared for the publication, several new relevant papers appeared, see, for example, Refs 213 – 217.

BINAP — 2,2′-bis(diphenylphosphino)-1,1′-binaphthalene,
BINOL — 1,1′-bi-2-naphthol,
Boc — *tert*-butoxycarbonyl,
BPA — BINOL-phosphoric acid,
m-CPBA — *m*-chloroperbenzoic acid,
Cy — cyclohexyl,
de — diastereomeric excess,
DBU — 1,8-diazabicyclo[5.4.0]undec-7-ene,
DMAP — 4-dimethylaminopyridine,
dr — diastereomeric ratio,
EDG — electron-donating group,
ee — enantiomeric excess,
er — enantiomeric ratio,
EWG — electron-withdrawing group,
FVT — flash vacuum thermolysis,
HOMO — highest occupied molecular orbital
LG — leaving group,
LUMO — lowest unoccupied molecular orbital,
MOM — methoxymethyl,
Mor — morpholino,
MS — molecular sieves,
MW — microwave irradiation,
Naph — naphthyl,
NIS — *N*-iodosuccinimide,
PCC —pyridinium chlorochromate,
Phen — phenanthryl,
PMB — *p*-methoxybenzyl,
PMP — *p*-methoxyphenyl,
PTSA —*p*-toluenesulfonic acid monohydrate,
Py — pyridyl,
QM — quinone methide,
rt — room temperature,
TBAF —tetra-n-butylammonium fluoride,
TBS — *tert*-butyldimethylsilyl,
Tf — trifluoromethanesulfonyl (triflyl),
Th — thienyl,
TMS — trimethylsilyl,
Tol — tolyl,
Ts — *p*-toluenesulfonyl (tosyl).

References

1. D.V.Osipov, V.A.Osyanin, Yu.N.Klimochkin. *Russ. Chem. Rev.*, **86**, 625 (2017)
2. B.Yang, S.Gao. *Chem. Soc. Rev.*, **47**, 7926 (2018)
3. J.J.Bruins, B.Albada, F.van Delft. *Chem. – Eur. J.*, **24**, 4749 (2018)
4. R.W.Van De Water, T.R.R.Pettus. *Tetrahedron*, **58**, 5367 (2002)
5. J.E.Aho, P.M.Pihko, T.K.Rissa. *Chem. Rev.*, **105**, 4406 (2005)
6. R.Pratap, V.J.Ram. *Chem. Rev.*, **114**, 10476 (2014)
7. M.Costa, T.A.Dias, A.Brito, F.Proenca. *Eur. J. Med. Chem.*, **123**, 487 (2016)
8. *Quinone Methides*. (Ed. S.E.Rokita). (Hoboken, NJ: Wiley, 2009)
9. T.Aoyama, T.Yamamoto, S.Miyota, M.Hayakawa, T.Takido, M.Kodomari. *Synlett*, **25**, 1571 (2014)
10. N.Basarić, K.Mlinarić-Majerski, M.Kralj. *Curr. Org. Chem.*, **18**, 3 (2014)
11. M.M.Toteva, J.P.Richard. *Adv. Phys. Org. Chem.*, **45**, 39 (2011)
12. J.L.Bolton. *Curr. Org. Chem.*, **18**, 61 (2014)
13. Q.Li, T.Dong, X.Liu, X.Zhang, X.Yang, X.Lei. *Curr. Org. Chem.*, **18**, 86 (2014)
14. N.J.Willis, C.D.Bray. *Chem. – Eur. J.*, **18**, 9160 (2012)
15. C.D.-T.Nielsen, H.Abas, A.C.Spivey. *Synthesis*, **50**, 4008 (2018)
16. W.-J.Bai, J.G.David, Z.-G.Feng, M.G.Weaver, K.-L.Wu, T.R.R.Pettus. *Acc. Chem. Res.*, **47**, 3655 (2014)
17. S.B.Ferreira, F.de Carvahlo da Silva, A.C.Pinto, D.T.G.Gonzaga, V.F.Ferreira. *J. Heterocycl. Chem.*, **46**, 1080 (2009)
18. L.Caruana, M.Fochi, L.Bernardi. *Molecules*, **20**, 11733 (2015)
19. Z.Wang, J.Sun. *Synthesis*, **47**, 3629 (2015)
20. M.S.Singh, A.Nagaraju, N.Anand, S.Chowdhury. *RSC Adv.*, **4**, 55924 (2014)
21. P.Barta, F.Fülöp, I.Szatmari. *Beilstein J. Org. Chem.*, **14**, 560 (2018)
22. C.D.Bray. *Org. Biomol. Chem.*, **6**, 2815 (2008)
23. V.Kumbaraci, D.Ergunes, M.Midilli, S.Begen, N.Talinli. *J. Heterocycl. Chem.*, **46**, 226 (2009)
24. N.J.Willis, C.D.Bray. *RSC Adv.*, **5**, 80212 (2015)
25. S.J.Gharpure, A.M.Sathiyanarayanan, P.Jonnalagadda. *Tetrahedron Lett.*, **49**, 2974 (2008)
26. M.A.Marsini, Y.Huang, C.C.Lindsey, K.-L.Wu, T.R.R.Pettus. *Org. Lett.*, **10**, 1477 (2008)
27. S.Arumugam, V.V.Popik. *J. Am. Chem. Soc.*, **133**, 5573 (2011)
28. K.Tanaka, K.Ueno, Y.Tanaka, N.Ohtsuka, Y.Asada, M.Kishimoto, S.Sunaga, Y.Hoshino, K.Honda. *Synlett*, **31**, 1197 (2020)
29. K.Tanaka, M.Kishimoto, N.Ohtsuka, Y.Iwama, H.Wada, Y.Hoshino, K.Honda. *Synlett*, **30**, 189 (2019)
30. A.F.Barrero, J.F.Quílez del Moral, M.M.Herrador, P.Arteaga, M.Cortés, J.Benites, A.Roselløn. *Tetrahedron*, **62**, 6012 (2006)
31. O.L.Chapman, C.L.McIntosh. *J. Chem. Soc., D*, 383 (1971)
32. T.Rosenau, W.D.Habicher, A.Potthast, P.Kosma. *Synlett*, 291 (1999)
33. E.Alden-Danforth, M.T.Scerba, T.Lectka. *Org. Lett.*, **10**, 4951 (2008)
34. F.Liebner, P.Schmid, C.Adelwöhrer, T.Rosenau. *Tetrahedron*, **63**, 11817 (2007)
35. Y.Luan, H.Sun, S.E.Schaus. *Org. Lett.*, **13**, 6480 (2011)
36. M.Deodhar, D.S.Black, N.Kumar. *Tetrahedron*, **63**, 5227 (2007)
37. A.k.Shaikh, A.J.A.Cobb, G.Varvounis. *Org. Lett.*, **14**, 584 (2012)
38. M.Uyanik, K.Nishioka, R.Kondo, K.Ishihara. *Nat. Chem.*, **12**, 353 (2020)
39. Z.Wang, J.Sun. *Org. Lett.*, **19**, 2334 (2017)
40. Z.Liu, Y.Meng, P.Yuan, Z.Wang, J.-M.Gao, H.Zheng. *Org. Lett.*, **22**, 520 (2020)
41. T.J.Doyon, J.C.Perkins, S.A.B. Dockrey, E.O.Romero, K.C.Skinner, P.M.Zimmerman, A.R.H.Narayan. *J. Am. Chem. Soc.*, **141**, 20269 (2019)
42. A.Gubu, L.Li, Y.Ning, X.Zhang, S.Lee, M.Feng, Q.Li, X.Lei, K.Jo, X.Tang. *Chem. – Eur. J.*, **24**, 5895 (2008)
43. C.Li, T.Dong, Q.Li, X.Lei. *Angew. Chem., Int. Ed.*, **53**, 12111 (2014)
44. X.Zhang, T.Dong, Q.Li, X.Liu, L.Li, S.Chen, X.Lei. *ACS Chem. Biol.*, **10**, 1676 (2015)
45. X.Zhang, S.-Q.Zhang, Q.Li, F.Xiao, Z.Yue, X.Hong, X.Lei. *Org. Lett.*, **22**, 2920 (2020)
46. Q.Li, T.Dong, X.Liu, X.Lei. *J. Am. Chem. Soc.*, **135**, 4996 (2013)
47. W.E. Noland, B.L.Kedrowski. *J. Org. Chem.*, **64**, 596 (1999)
48. G.Dyker, D.Hildebrandt, J.Liu, K.Merz. *Angew. Chem., Int. Ed.*, **42**, 4399 (2003)
49. R.M.Jones, C.Selenski, T.R.R.Pettus. *J. Org. Chem.*, **67**, 6911 (2002)
50. Y.-B.Shen, S.-S.Li, L.Wang, X.-D.An, Q.Liu, X.Liu, J.Xiao. *Org. Lett.*, **20**, 6069 (2018)
51. Y.-B.Shen, S.-S.Li, X.Liu, L.Yu, Q.Liu, J.Xiao. *Adv. Synth. Catal.*, **361**, 1453 (2019)
52. A.S.Makarov, A.E.Kekhvaeva, P.N.Chalikidi, V.T.Abaev, I.V.Trushkov, M.G.Uchuskin. *Synthesis*, **51**, 3747 (2019)

53. A.S.Makarov, A.E.Kekhvaeva, C.J.J.Hall, D.Price, I.V.Trushkov, M.G.Uchuskin. *Tetrahedron*, **73**, 7042 (2017)
54. M.S.Chauhan, F.M.Dean, D.Matkin, M.L.Robinson. *J. Chem. Soc., Perkin Trans. 1*, 120 (1973)
55. L.Xu, F.Liu, L.-W.Xu, Z.Gao, Y.-M.Zhao. *Org. Lett.*, **18**, 3698 (2016)
56. S.Rashid, B.A.Bhat, G.Mehta. *Tetrahedron Lett.*, **60**, 1122 (2019)
57. Y.Zhang, Y.Guo, Z.Li, Z.Xie. *Org. Lett.*, **18**, 4578 (2016)
58. T.-Z.Li, C.-A.Geng, X.-J.Yin, T.-H.Yang, X.-L.Chen, X.-Y.Huang, Y.-B.Ma, X.-M.Zhang, J.-J.Chen. *Org. Lett.*, **19**, 429 (2017)
59. Y.Sawama, T.Kawajiri, S.Asai, N.Yasukawa, Y.Shishido, Y.Monguchi, H.Sajiki. *J. Org. Chem.*, **80**, 5556 (2015)
60. E.E.Allen, C.Zhu, J.S.Panek, S.E.Schaus. *Org. Lett.*, **19**, 1878 (2017)
61. K.Stefańska, H.Jędrzejewska, M.Wierzbicki, A.Szumna, W.Iwanek. *J. Org. Chem.*, **81**, 6018 (2016)
62. J.Rodriguez, D.Bonne. *Chem. Commun.*, **55**, 11168 (2019)
63. X.Wu, L.Xue, D.Li, S.Jia, J.Ao, J.Deng, H.Yan. *Angew. Chem., Int. Ed.*, **56**, 13722 (2017)
64. S.Beppu, S.Arae, M.Furusawa, K.Arita, H.Fujimoto, M.Sumimoto, T.Imahori, K.Igawa, K.Tomooka, R.Irie. *Eur. J. Org. Chem.*, 6914 (2017)
65. J.-P.Lumb, K.C.Choong, D.Trauner. *J. Am. Chem. Soc.*, **130**, 9230 (2008)
66. T.Zhang, C.Ma, J.-Y.Zhou, G.-J.Mei, F.Shi. *Adv. Synth. Catal.*, **360**, 1128 (2018)
67. M.Ashram, D.O.Miller, P.E.Georghiou. *J. Chem. Soc., Perkin Trans. 1*, 1470 (2002)
68. Y.-C.Zhang, Q.-N.Zhu, X.Yang, L.-J.Zhou, F.Shi. *J. Org. Chem.*, **81**, 1681 (2016)
69. J.Zhou, M.Wang, X.Gao, G.Jiang, Y.G.Zhou. *Chem. Commun.*, **53**, 3531 (2017)
70. H.Hu, Y.Liu, J.Guo, L.Lin, Y.Xu, X.Liu, X.Feng. *Chem. Commun.*, **51**, 3835 (2015)
71. H.Lv, L.You, S.Ye. *Adv. Synth. Catal.*, **351**, 2822 (2009)
72. M.Spanka, C.Schneider. *Org. Lett.*, **20**, 4769 (2018)
73. S.Feng, B.Yang, T.Chen, R.Wang, Y.-H.Deng, Z.Shao. *J. Org. Chem.*, **85**, 5231 (2020)
74. Y.You, T.-T.Li, S.-P.Yuan, K.-X.Xie, Z.-H.Wang, J.-Q.Zhao, M.-Q.Zhou, W.-C.Yuan. *Chem. Commun.*, **56**, 439 (2020)
75. D.Mathur, A.K.Prasad, T.S.Cameron, A.Jha. *Tetrahedron*, **70**, 5608 (2014)
76. D.Zhou, X.Yu, J.Zhang, W.Wang, H.Xie. *Org. Lett.*, **20**, 174 (2018)
77. L.Jurd. *J. Heterocycl. Chem.*, **25**, 89 (1988)
78. E.Sh.Kagan, V.I.Mikhailov, V.D.Sholle, V.A.Smirnov, E.G.Rozantsev. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)*, 1458 (1978)
79. J.R.Mahajan, H.C.Araújo. *Synthesis*, 111 (1976)
80. A.V.Popova, G.P.Mrug, K.M.Kondratyuk, S.P.Bondarenko, M.S.Frasinyuk. *Chem. Nat. Compd.*, **52**, 1000 (2016)
81. E.G.Rozantsev, M.Dagonneau, E.S.Kagan, V.I.Mikhailov, V.D.Sholle. *J. Chem. Res. (S)*, **8**, 260 (1979)
82. M.Strandtmann, M.P.Cohen, J.Shavel Jr. *Tetrahedron Lett.*, **6**, 3103 (1965)
83. M.Strandtmann, M.P.Cohen, J.Shavel Jr. *J. Heterocycl. Chem.*, **7**, 1311 (1970)
84. L.Benameur, Z.Bouaziz, P.Nebois, M.-H.Bartoli, M.Boitard, H.Fillion. *Chem. Pharm. Bull.*, **44**, 605 (1996)
85. G.P.Mrug, K.M.Kondratyuk, S.P.Bondarenko, M.S.Frasinyuk. *Chem. Heterocycl. Compd.*, **52**, 460 (2016)
86. Y.-H.Zhu, M.Zhang, Q.-Y.Li, Q.Liu, J.Zhang, Y.-Y.Yuan, F.-J.Nan, M.-W.Wang. *Chin. Chem. Lett.*, **25**, 693 (2014)
87. L.Y.Ukhin, L.Belousova, V.Khrustalev. *Russ. Chem. Bull., Int. Ed.*, **52**, 700 (2003)
88. L.Y.Ukhin, L.Belousova, Z.I.Orlova, S.Shishkina, O.Shishkin. *Russ. Chem. Bull., Int. Ed.*, **51**, 1262 (2002)
89. V.A.Osyanin, D.V.Osipov, M.R.Demidov, P.E.Krasnikov, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **53**, 1310 (2017)
90. G.Ragaitė, M.Dagilienė, S.Krikstolaitytė, V.Martynaitis, A.Saskus. *J. Fluorine Chem.*, **182**, 34 (2016)
91. M.Dagilienė, V.Martynaitis, M.Vengris, K.Redeckas, V.Voiciuk, W.Holzer, A.Saskus. *Tetrahedron*, **69**, 9309 (2013)
92. B.Büyükkidan, M.Ceylan. *J. Chem. Res. (S)*, 749 (2003)
93. D.V.Osipov, V.A.Osyanin, L.G.Voskressensky, Yu.N.Klimochkin. *Synthesis*, **49**, 2286 (2017)
94. A.R.Katritzky, X.Lan. *Synthesis*, 761 (1992)
95. H.Sugimoto, S.Nakamura, T.Ohwada. *Adv. Synth. Catal.*, **349**, 669 (2007)
96. M.Yato, T.Ohwada, K.Shudo. *J. Am. Chem. Soc.*, **112**, 5341 (1990)
97. G.-Q.Xu, Z.-T.Feng, J.-T.Xu, Z.-Y.Wang, Y.Qin, P.-F.Xu. *Chem. – Eur. J.*, **24**, 13778 (2018)
98. T.Oguma, T.Katsuki. *Chem. Commun.*, **50**, 5053 (2014)
99. S.Saha, C.Schneider. *Org. Lett.*, **17**, 648 (2015)
100. S.Saha, C.Schneider. *Chem. – Eur. J.*, **21**, 2348 (2015)
101. J.-J.Zhao, S.-B.Sun, S.-H.He, Q.Wu, F.Shi. *Angew. Chem., Int. Ed.*, **54**, 5460 (2015)
102. M.-S.Tu, S.-J.Liu, C.Zhong, S.Zhang, H.Zhang, Y.-L.Zheng, F.Shi. *J. Org. Chem.*, **85**, 5403 (2020)
103. L.Kong, N.Thirupathi, J.Jia, Z.Xu. *Sci. China Chem.*, **62**, 80 (2019)
104. V.A.Osyanin, N.E.Sidorina, Yu.N.Klimochkin. *Russ. J. Gen. Chem.*, **81**, 115 (2011)
105. V.A.Osyanin, D.D.Borisov, D.V.Osipov, Yu.N.Klimochkin. *Russ. J. Org. Chem.*, **50**, 1590 (2014)
106. G.Decodts, M.Wakselman, M.Vilkas. *Tetrahedron*, **26**, 3313 (1970)
107. T.F.Spande, M.Wilchek, B.Witkop. *J. Am. Chem. Soc.*, **90**, 3256 (1968)
108. N.Douglas, C.J.Neef, R.A.Rogers, J.A.Stanley, J.Armitage, B.Martin, T.W.Hudnall, W.J.Brittain. *J. Phys. Org. Chem.*, **26**, 688 (2013)
109. P.Yang, W.Xu, R.Wang, M.Zhang, C.Xie, X.Zeng, M.Wang. *Org. Lett.*, **21**, 3658 (2019)
110. C.Lin, H.-J.Du, H.Zhao, D.-F.Yan, N.-X.Liu, H.Sun, X.Wen, Q.-L.Xu. *Org. Biomol. Chem.*, **15**, 3472 (2017)
111. S.L.Crawley, R.L.Funk. *Org. Lett.*, **5**, 3169 (2003)
112. L.Peng, D.Xu, X.Yang, J.Tang, X.Feng, S.-L.Zhang, H.Yan. *Angew. Chem., Int. Ed.*, **58**, 216 (2020)
113. T.Asai, K.Tsukada, S.Ise, N.Shirata, M.Hashimoto, I.Fujii, K.Gomi, K.Nakagawara, E.N.Kodama, Y.Oshima. *Nat. Chem.*, **7**, 737 (2015)
114. Y.Li, T.Liu, C.Liang. *Mol. Catal.*, **441**, 199 (2017)
115. S.Radomkit, P.Sarnpitak, J.Tummatorn, P.Batsomboon, S.Ruchirawat, P.Ploypradith. *Tetrahedron*, **67**, 3904 (2011)
116. K.Tangdenpaisal, K.Chuayboonsong, P.Sukjarean, V.Katesampao, N.Noiphrom, S.Ruchirawat, P.Ploypradith. *Chem. – Asian J.*, **10**, 1050 (2015)
117. P.Chen, K.Wang, W.Guo, X.Liu, Y.Liu, C.Li. *Angew. Chem., Int. Ed.*, **56**, 3689 (2017)
118. N.Thirupathi, C.H.Tung, Z.Xu. *Adv. Synth. Catal.*, **360**, 3585 (2018)
119. W.Chen, S.K.Park, W.Yu, A.Xiong, B.G.Sanders, K.Kline. *Eur. J. Med. Chem.*, **58**, 72 (2012)
120. J.A.Hyatt. *Synth. Commun.*, **38**, 8 (2008)
121. M.Ingold, G.V.López, W.Porcal. *ACS Sust. Chem. Eng.*, **2**, 1093 (2014)
122. Patent EP 1184378A1 (2002)
123. H.Wang, Y.Wang, K.-L.Han, X.J.Peng. *J. Org. Chem.*, **70**, 4910 (2005)
124. K.Wojciechowski, K.Dolatowska. *Tetrahedron*, **61**, 8419 (2005)
125. L.Giraud, A.Giraud. *Synthesis*, 1153 (1998)
126. S.Azuma, M.Ota, A.Ishida, K.Isozaki, H.Takaya, M.Nakamura, T.Sasamori, N.Tokitoh, K.Kuramochi, K.Tsubaki. *Chem. Lett.*, **42**, 1531 (2013)

127. K.Chandrasenan, R.H.Thomson. *J. Chem. Soc. C*, 123 (1966)
128. L.I.Smith, R.W.H.Tess, G.E.Ullyot. *J. Am. Chem. Soc.*, **66**, 1320 (1944)
129. R.F.Moore, W.A.Waters. *J. Chem. Soc.*, 243 (1954)
130. D.V.Muslin, N.S.Lyapina. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)*, **33**, 1475 (1984)
131. K.Hultzsch. *J. Prakt. Chem.*, **159**, 180 (1941)
132. L.Jurd. *Tetrahedron*, **33**, 163 (1977)
133. T.Rosenau, A.Potthast, T.Elder, P.Kosma. *Org. Lett.*, **4**, 4285 (2002)
134. T.Rosenau, A.Potthast, T.Elder, T.Lange, H.Sixta, P.Kosma. *J. Org. Chem.*, **67**, 3607 (2002)
135. M.S.Chauhan, D.M.McKinnon. *Can. J. Chem.*, **59**, 2223 (1981)
136. X.Wang, J.A.Kalow. *Org. Lett.*, **20**, 1716 (2018)
137. Y.Tanoue, K.Sakata, M.Hashimoto, Sh.Morishita, M.Hamada, N.Kai, T.A.Nagai. *Tetrahedron*, **58**, 99 (2002)
138. M.Matsumoto, K.Kuroda, Y.Suzuki. *Tetrahedron Lett.*, **22**, 3253 (1981)
139. P.Supsana, P.G.Tsoungas, A.Aubry, S.Skoulika, G.Varvounis. *Tetrahedron*, **57**, 3445 (2001)
140. W.W.Sullivan, D.Ullman, H.Shechter. *Tetrahedron Lett.*, **10**, 457 (1969)
141. T.R.Kasturi, A.B.Mandal, P.A.Reddy, K.B.G.Prasad, B.Rajasekhar. *Tetrahedron*, **47**, 5245 (1991)
142. G.Catterall. *J. Chem. Soc., Chem. Commun.*, 41 (1974)
143. L.W.Schenck, K.Kuna, W.Frank, A.Albert, C.Asche, U.Kucklaender. *Bioorg. Med. Chem.*, **14**, 3599 (2006)
144. Y.Tan, Z.Zhao, Z.Chen, S.Huang, S.Jia, L.Peng, D.Xu, W.Qin, H.Yan. *Org. Lett.*, **22**, 4461 (2020)
145. D.A.Bolon. *J. Org. Chem.*, **35**, 715 (1970)
146. D.Liao, H.Li, X.Lei. *Org. Lett.*, **14**, 18 (2012)
147. D.V.Osipov, V.A.Osyanin, Yu.N.Klimochkin. *Synlett*, **23**, 917 (2012)
148. Y.Xiong, H.Xia, H.W.Moore. *J. Org. Chem.*, **60**, 6460 (1995)
149. T.Rosenau, A.Potthast, A.Hofinger, P.Kosma. *Angew. Chem., Int. Ed.*, **41**, 1171 (2002)
150. F.Bures. *RSC Adv.*, **4**, 58826 (2014)
151. Z.Dzambaski, M.Baranac-Stojanović. *ChemistrySelect*, **2**, 42 (2017)
152. D.V.Dar'in, P.S.Lobanov. *Russ. Chem. Rev.*, **84**, 601 (2015)
153. L.Rene. *Synthesis*, 69 (1989)
154. A.V.Lukashenko, V.A.Osyanin, D.V.Osipov, Yu.N.Klimochkin. *J. Org. Chem.*, **82**, 1517 (2017)
155. A.V.Lukashenko, D.V.Osipov, V.A.Osyanin, Yu.N.Klimochkin. *Russ. J. Org. Chem.*, **52**, 1817 (2016)
156. A.V.Lukashenko. Candidate Thesis in Chemical Sciences, Samara State Technical University, Samara, 2019
157. D.V.Osipov, I.V.Melnikova, V.A.Osyanin, A.V.Lukashenko, Yu.N.Klimochkin. *J. Fluorine Chem.*, **202**, 71 (2017)
158. A.V.Lukashenko, V.A.Osyanin, D.V.Osipov, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **52**, 711 (2016)
159. D.V.Osipov, A.A.Artyomenko, V.A.Osyanin, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **55**, 261 (2019)
160. K.S.Korzhenko, D.V.Osipov, V.A.Osyanin, P.E.Krasnikov, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **54**, 940 (2018)
161. G.P.Mrug, N.V.Myshko, S.P.Bondarenko, V.M.Sviripa, M.S.Frasinyuk. *J. Org. Chem.*, **84**, 7138 (2019)
162. W.Wei, Y.Wang, J.Yin, J.Xue, Y.Li. *Org. Lett.*, **14**, 1158 (2012)
163. A.V.Lukashenko, D.V.Osipov, V.A.Osyanin, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **56**, 529 (2020)
164. V.A.Osyanin, A.V.Lukashenko, D.V.Osipov, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **50**, 1528 (2015)
165. A.V.Lukashenko, D.V.Osipov, V.A.Osyanin, Yu.N. Klimochkin. *Chem. Heterocycl. Compd.*, **53**, 1369 (2017)
166. A.V.Lukashenko, D.V.Osipov, V.À.Osyanin, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **56**, 521 (2020)
167. M.V.Reddy, G.D.Reddy, J.T.Kim, Y.T.Jeong. *Tetrahedron*, **72**, 6484 (2016)
168. P.Padmaja, J.S.Anireddy, P.N.Reddy. *Chem. Heterocycl. Compd.*, **54**, 812 (2018)
169. J.Zhang, X.Liu, S.Guo, C.He, W.Xiao, L.Lin, X.Feng. *J. Org. Chem.*, **83**, 10175 (2018)
170. K.Tangdenpaisal, K.Chuayboonsong, S.Ruchirawat, P.Ploypradith. *J. Org. Chem.*, **82**, 2672 (2017)
171. S.J.Gharpure, A.M.Sathiyanarayanan, P.K.Vuram. *RSC Adv.*, **3**, 18279 (2013)
172. G.Zhou, J.Zhu, Z.Xie, Y.Li. *Org. Lett.*, **10**, 721 (2008)
173. V.A.Osyanin, E.A.Ivleva, Yu.N.Klimochkin. *Synth. Commun.*, **42**, 1832 (2012)
174. V.A.Osyanin, E.A.Ivleva, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **46**, 1011 (2010)
175. V.A.Osyanin, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **47**, 242 (2011)
176. V.A.Osyanin, D.V.Osipov, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **47**, 1601 (2012)
177. G.P.Mrug, N.V.Bondarenko, S.P.Bondarenko, M.S.Frasinyuk. *Chem. Nat. Compd.*, **54**, 654 (2018)
178. Y.Chen, M.G.Steinmetz. *Org. Lett.*, **7**, 3729 (2005)
179. Y.Chen, M.G.Steinmetz. *J. Org. Chem.*, **71**, 6053 (2006)
180. V.A.Osyanin, D.V.Osipov, S.A.Pavlov, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **50**, 11951 (2014)
181. V.A.Osyanin. Doctoral Thesis in Chemical Sciences, Samara State Technical University, Samara, 2014; http://d21221705.samgtu.ru/sites/d21221705.samgtu.ru/files/osya-ninv.pdf
182. V.A.Osyanin, N.E.Sidorina, E.L.Golub. *Vestn. SamGU — Estestvennonauch. Ser.*, **46** (6/1), 195 (2006)
183. X.Chen, M.Nagata, K.Tanaka, F.Yoneda. *J. Chem. Soc., Chem. Commun.*, 44 (1989)
184. X.-Y.Yu, J.-R.Chen, Q.Wei, H.-G.Cheng, Z.-C.Liu, W.-J.Xiao. *Chem. – Eur. J.*, **22**, 6774 (2016)
185. A.Gervais, K.E.Lazarski, J.A.Porco Jr. *J. Org. Chem.*, **80**, 9584 (2015)
186. H.-M.Huang, X.-Y.Wu, B.-R.Leng, Y.-L.Zhu, X.-C.Meng, Y.Hong, B.Jiang, D.-C.Wang. *Org. Chem. Front.*, **7**, 414 (2020)
187. A.Yu.Rulev. *Russ. Chem. Rev.*, **71**, 195 (2002)
188. L.R.Domingo, E.Chamorro, P.Pérez. *J. Org. Chem.*, **73**, 4615 (2008)
189. K.K.Balasubramanian, S.Selvaraj. *J. Org. Chem.*, **45**, 3726 (1980)
190. Y.Zhou, K.-D.Zhou, X.-P.Xu, Y.-N.Zhu, Z.Wu, S.-J.Ji. *Tetrahedron*, **70**, 9644 (2014)
191. C.G.S.Lima, F.P.Pauli, D.C.S.Costa, A.S.Souza, L.S.M.Forezi, V.F.Ferreira, F.C.Silva. *Eur. J. Org. Chem.*, 2650 (2020)
192. J.-Y.Wang, W.-J.Hao, S.-J.Tu, B.Jiang. *Org. Chem. Front.*, **7**, 1743 (2020)
193. A.Parra, M.Tortosa. *ChemCatChem*, **7**, 1524 (2015)
194. P.Chauhan, U.Kaya, D.Enders. *Adv. Synth. Catal.*, **359**, 888 (2017)
195. W.Li, X.Xu, P.Zhang, P.Li. *Chem. – Asian J.*, **13**, 2350 (2018)
196. Z.-P.Zhang, K.-X.Xie, C.Yang, M.Li, X.Li. *J. Org. Chem.*, **83**, 364 (2018)
197. G.-H.Yang, Q.Zhao, Z.-P.Zhang, H.-L.Zheng, L.Chen, X.Li. *J. Org. Chem.*, **84**, 7883 (2019)
198. J.-R.Wang, X.-L.Jiang, Q.-Q.Hang, S.Zhang, G.-J.Mei, F.Shi. *J. Org. Chem.*, **84**, 7829 (2019)
199. N.Maripally, V.R.Reddy, R.Donthi, R.Mutyala, R.Chandra. *Tetrahedron Lett.*, **61**, 151554 (2020)
200. L.Zhang, Y.Liu, K.Liu, Z.Liu, N.He, W.Li. *Org. Biomol. Chem.*, **15**, 8743 (2017)
201. J.-P.Tan, H.Zhang, Z.Jiang, Y.Chen, X.Ren, C.Jiang, T.Wang. *Adv. Synth. Catal.*, **362**, 1058 (2020)
202. Z.Ye, L.Bai, Y.Bai, Z.Gan, H.Zhou, T.Pan, Y.Yu, J.Zhou. *Tetrahedron*, **75**, 682 (2019)

203. M.Huo, J.Zhou, L.Bai, Q.Xu, Z.Zhou, H.Zhou, G.Liang. *Tetrahedron*, **75**, 130752 (2019)
204. Y.-X.Wang, Y.-N.Lu, L.-L.Xu, F.-T.Sheng, J.-P.Zhang, W.Tan, F.Shi. *Synthesis*, **52**, 2979 (2020)
205. Y.Han, Y.Zhu, P.Zhang, W.Li, P.Li. *ChemistrySelect*, **2**, 11380 (2017)
206. K.Zhao, Y.Zhi, T.Shu, A.Valkonen, K.Rissanen, D.Enders. *Angew. Chem., Int. Ed.*, **55**, 12104 (2016)
207. S.Roy, S.Pradhan, K.Kumar, I.Chatterjee. *Org. Chem. Front.*, **7**, 1388 (2020)
208. Z.Cao, G.-X.Zhou, C.Ma, K.Jiang, G.-J.Mei. *Synthesis*, **50**, 1307 (2018)
209. J.-Y.Zhou, C.Ma, Y.-Z.Zhang, Q.Wu, F.Shi. *Org. Biomol. Chem.*, **16**, 9382 (2018)
210. Z.-H.Wang, X.-Y.Zhang, Y.You, J.-Q.Zhao, M.-Q.Zhou, X.-M.Zhang, X.-Y.Xu, W.-C.Yuan. *Tetrahedron*, **75**, 3456 (2019)
211. X.-L.Jiang, S.-F. Wu, J.-R.Wang, G.-J.Meia, F.Shi. *Adv. Synth. Catal.*, **360**, 4225 (2018)
212. A.A.Golovanov, I.S.Odin, S.S.Zlotskii. *Russ. Chem. Rev.*, **88**, 280 (2019)
213. F.Göricke, S.Haseloff, M.Laue, M.Schneider, T.Brumme, C.Schneider. *J. Org. Chem.*, **85**, 11699 (2020)
214. D.V.Osipov, I.V.Melnikova, K.S.Korzhenko,V.A.Osyanin, Yu.N.Klimochkin. *Chem. Heterocycl. Compd.*, **56**, 990 (2020)
215. S.-F.Wu, M.-S.Tu, Q.-Q.Hang, S.Zhang, H.Ding, Y.-C.Zhang, F.Shi. *Org. Biomol. Chem.*, **18**, 5388 (2020)
216. M.Xiang, C.-Y.Li, X.-J.Song, Y.Zou, Z.-C.Huang, X.Li, F.Tian, L.-X.Wang. *Chem. Commun.*, **56**, 14825 (2020)
217. V.A.Osyanin, D.V.Osipov, I.V.Melnikova, K.S.Korzhenko, I.A.Semenova, Yu.N.Klimochkin. *Synthesis*, **52**, 3604 (2020)