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Polycyclic *peri*-hydroxycarbonyl compounds and their derivatives

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Abstract. Data on the methods of synthesis, structure and properties of polycyclic aromatic aldehydes, ketones, carboxylic acids and their derivatives containing free or substituted hydroxy or oxo group in the *peri*-position to the carbonyl group are generalized. The attention is focused on the intramolecular interactions between these *peri*-substituents and heterocyclizations involving them in comparison with heterocyclizations of similar *ortho*-substituted carbonyl compounds. The bibliography includes 305 references.

I. Introduction

Derivatives of naphthalene and other polycyclic aromatic compounds containing carbonyl and hydroxy or substituted hydroxy group in the *peri*-position play an important role as potential precursors of *peri*-annulated heterocyclic systems.[1–3] In addition, they are unique models for studying so-called '*peri*-effects'[4,5] (hydrogen bonding, electrophile–nucleophile interactions, ring–chain tautomerism, *etc*.) occurring between *peri*-arranged substituents.[2–13]

A huge amount of knowledge on the methods of synthesis, structure and properties of these compounds has been accumulated to date; however, this knowledge has not been generalized as yet. Some data concerning *peri*-hydroxynaphthaldehydes as representatives of naphthaldehydes are contained in the review by Pozharsky,[5] and some heterocyclizations of *peri*-hydroxycarbonyl compounds are encountered in the review by Mezheritskii and Tkachenko [1] devoted to the synthesis of *peri*-annulated heterocycles.

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II. Synthetic approaches to the construction of *peri*-R-oxycarbonyl group

1. Electrophilic substitution in the aromatic nucleus

The most convenient general approach to the construction of *peri*-hydroxycarbonyl aromatic compounds is direct introduction of a carbonyl group into the corresponding R-oxy derivatives by acid-catalyzed Vilsmeier, Rieche, Friedel–Crafts acylation reaction, *etc*. A necessary condition for implementing this approach is the presence of an electron-donating substituent in the aromatic ring, which directs the entering carbonyl group to the *peri*-position relative to the R-oxy group that is already present in the molecule to be acylated.

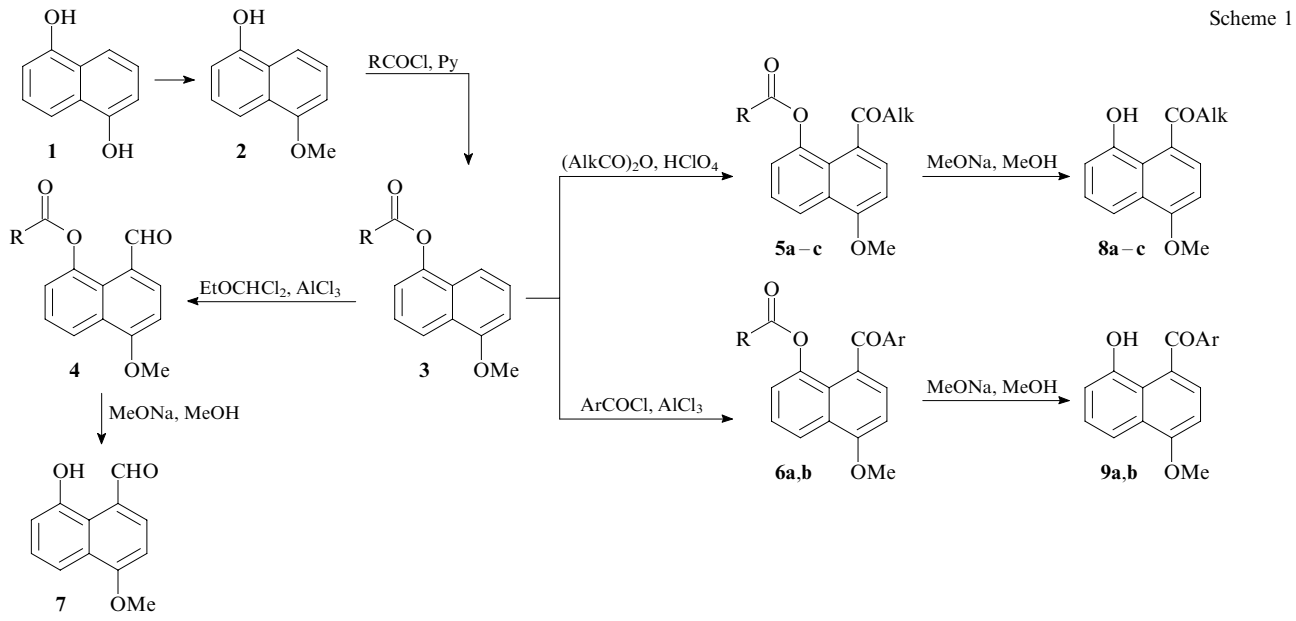
Naphthalene-1,5-diol (**1**) is a universal template for the construction of these compounds. This is due to the convenient arrangement of hydroxy groups in its molecule where the carbon atom located in the *para*-position to one of them is simultaneously in the *peri*-position to the other one. Apart from naphthalene-1,5-diol, its derivatives **2** and **3** are applicable. When these derivatives react with formylating and acylating agents, *peri*-hydroxy- or *peri*-R-oxycarbonyl compounds are formed in one step (Scheme 1).

Thus acylation of 1-acyloxy-5-methoxynaphthalenes **3** with appropriate electrophilic reagents first gives *peri*-acyloxycarbonyl compounds **4**–**6** (yields 50%–90%). After cleavage of the ester group, these are converted to *peri*-hydroxycarbonyl derivatives **7**–**9** in nearly quantitative yields.[14–19]

peri-Acyloxynaphthyl alkyl ketones **5** can also be obtained by treatment of 5-methoxy-1-naphthol (**2**) with aliphatic acid anhydrides in the presence of perchloric acid; however, the yields of the final products are much lower (~30%). Also, in this case, C-acylation is preceded by O-acylation.

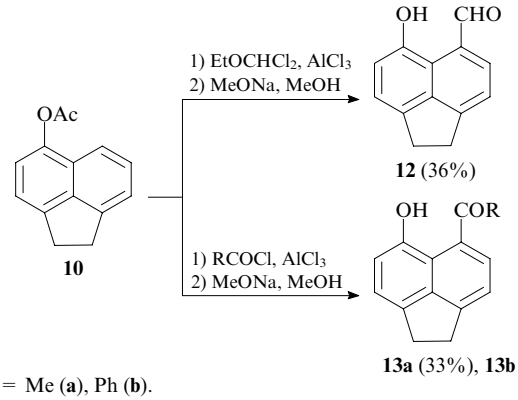
The same strategy was used in the synthesis of *peri*-hydroxycarbonyl derivatives of acenaphthene and naphtho[1,8-*bc*]furan. Thus acid-catalyzed acylation (formylation) of 5-acetoxyacenaphthene (**10**) and substituted 5-acetoxynaphtho[1,8-*bc*]furans (**11a**,**b**) with subsequent cleavage

Scheme 1



Alk = Me (**8a**), Et (**8b**), Bn (**8c**); Ar = Ph (**9a**), 4-MeOC$_6$H$_4$ (**9b**).

of the ester group results in *peri*-hydroxycarbonyl acenaphthene (**12**, **13**) [20] and naphthofuran (**14**, **15**) derivatives.[21–23]

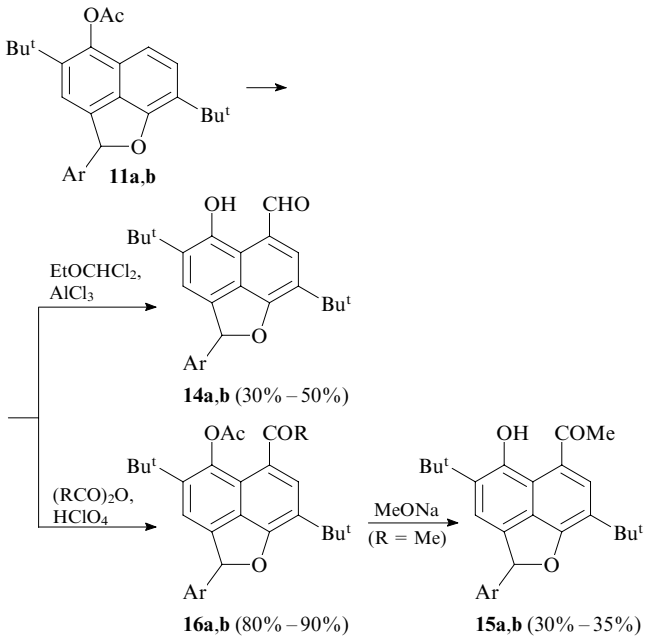


R = Me (**a**), Ph (**b**).

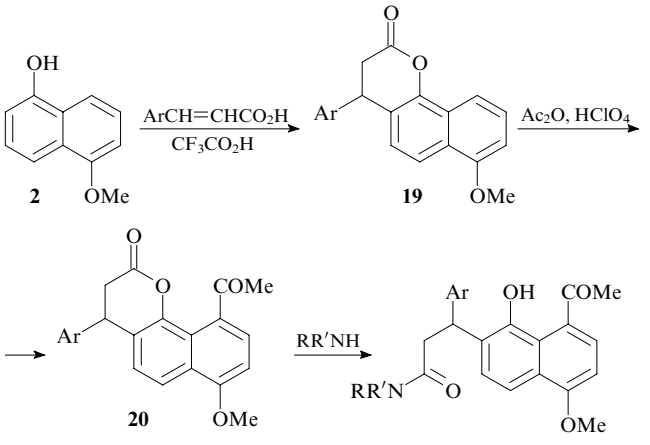
Derivatives **11a**,**b** were obtained by treating 2,6-di(*tert*-butyl)naphthalene-1,5-diol with morpholinals of aromatic aldehydes followed by acetylation of the 5-hydroxy group. the Rieche formylation of 4,8-di(*tert*-butyl)-2-aryl-5-acetoxynaphtho[1,8-*bc*]furans (**11**) gives immediately *peri*-hydroxy aldehydes **14**, whereas in the formylation of 5-acetoxyacenaphthene (**10**), the *peri*-acetoxy group is retained; sodium methoxide is used to cleave this group. Acylation of compounds **11a**,**b** affords *peri*-acetoxy ketones **16a**,**b**, which are converted to *peri*-hydroxy ketones **15a**,**b** on treatment with sodium methoxide. As side products of acenaphthene **10** acylation, 3- and 8-acyl-5-hydroxyacenaphthenes are formed.

The reaction of 1-aroyloxy-5-methoxynaphthalenes **17** with trifluoroacetic anhydride in the presence of boron trifluoride etherate gives *peri*-hydroxy ketones **9a**–**c** rather than the expected trifluoromethyl ketone (**18**) (Scheme 2).[24] Presumably, the key steps of this process are attack of the carbonyl-group oxygen by the trifluoroacetyl cation and subsequent heterocyclization.

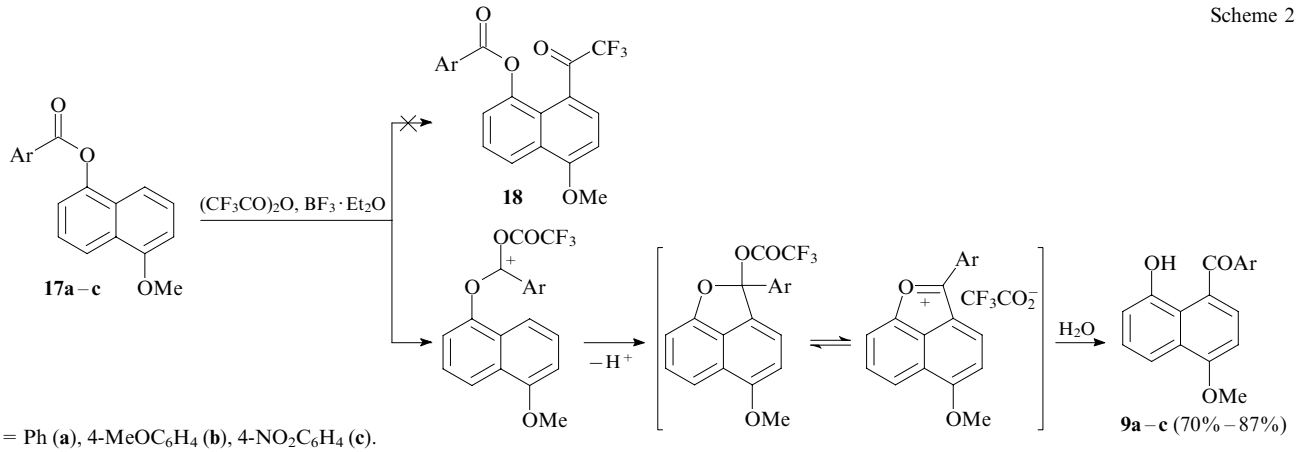
By acetylation of pyran-2-ones **19** formed on refluxing 5-methoxy-1-naphthol (**2**) with cinnamic acids, cyclic *peri*-acyloxy ketones **20** were obtained. The cleavage of the ester fragment in compounds **20** under the action of amines



Ar = Ph (**a**), 4-MeOC$_6$H$_4$ (**b**); R = Me, Et.



Scheme 2



Ar = Ph (**a**), 4-$MeOC_6H_4$ (**b**), 4-$NO_2C_6H_4$ (**c**).

affords compounds having a substituent with the amide group in the *ortho*-position to the hydroxy group. The introduction of this substituent considerably extends the possibilities of functionalization of *peri*-hydroxy ketones.[25]

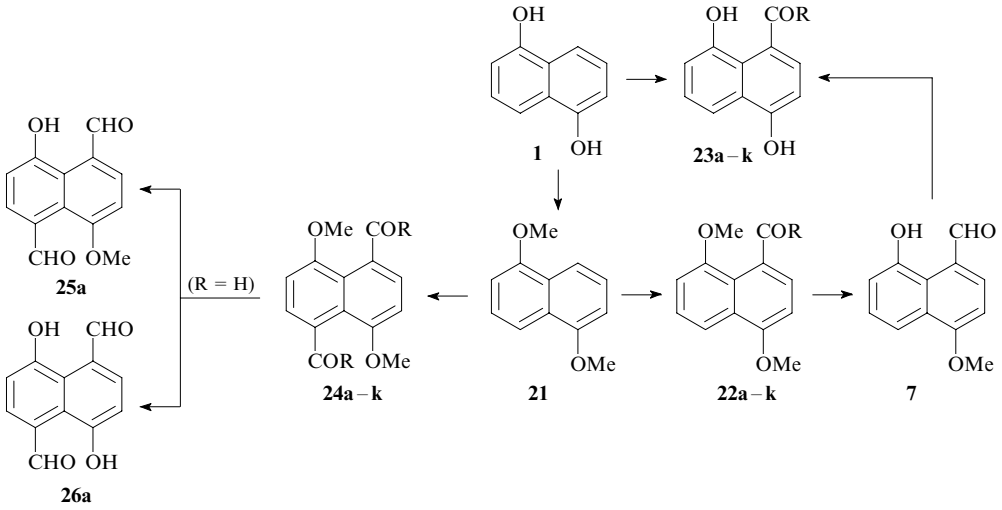
peri-Hydroxy-substituted mono- and dicarbonyl naphthalene derivatives can be obtained by direct formylation or acylation of naphthalene-1,5-diol (**1**) or its dimethyl ether **21**. In the latter case, the preparation of *peri*-hydroxy derivatives requires cleavage of the *peri*-methoxy group,

Table 1. Conditions of synthesis of 1,5-dimethoxynaphthalene (**21**) and some *peri*-methoxy- (**22**, **24**) and *peri*-hydroxy-substituted (**7**, **23**, **25**, **26**) mono- and dicarbonyl naphthalene derivatives.

Starting compound	Reaction conditions	Reaction product	Yield (%)	Ref.
1	MeOH, H_2SO_4, 60 °C, 4.5 h	**21**	100	26
	Me_2SO_4, K_2CO_3, Me_2CO, 60 °C, 24 h	**21**	98	27
21	HCONMePh, $POCl_3$, PhMe, 100 °C, 6 h	**22a**	90	28–30
	MeCOCl, $AlCl_3$, $PhNO_2$, 20 °C, 10 h	**22b**	82	30
	EtCOCl, $AlCl_3$, $PhNO_2$, 20 °C, 10 h	**22c**	67	30
	$ClCH_2COCl$, $AlCl_3$, CH_2Cl_2, 20 °C, 48 h	**22d**	66	31, 32
	$(CH_2CO)_2O$, $AlCl_3$, TCE,[a] 20 °C, 48 h	**22e**	70–80	33–35
	$(CH_2CH_2CO)_2O$, $AlCl_3$, TCE,[a] 20 °C, 48 h	**22f**	not indicated	33, 34
	4-MeC_6H_4COCl, $AlCl_3$, 20 °C, 4 h	**22g**	not indicated	36
	4-BrC_6H_4COCl, $AlCl_3$, $PhNO_2$, 20 °C, 24 h	**22h**	82	37
	$C_6H_4(CO)_2O$, $AlCl_3$, TCE,[a] 20 °C, 48 h	**22i**	75	38
	$ClSO_2NCO$, PhMe, 20 °C, 24 h	**22j**	93	39
1	HCN, $ZnCl_2$, Et_2O, 25 °C	**23a**	not indicated	40–43[b]
	$EtOCHCl_2$, $AlCl_3$, TCE,[a] 0 °C, 2 h	**23a**	47	44
7	$AlCl_3$, TCE,[a] 80 °C, 40 min	**23a**	84	44
22a	$AlCl_3$, TCE,[a] 80 °C, 40 min	**23a**	93	44
	$AlCl_3$, PhH, 80 °C, 15 min	**7**	61	44
	BBr_3, CH_2Cl_2, −60, −75 °C, 1 h	**7**	82–91	28, 29, 45, 46
1	$MeCO_2H$, $SnCl_4$, reflux, 5 h	**23b**	29	47
22e	$AlCl_3$, TCE,[a] 60 °C, 30 min	**23e**	not indicated	33, 34
22f	$AlCl_3$, TCE,[a] 60 °C, 30 min	**23f**	not indicated	33, 34
22a	$EtOCHCl_2$, $AlCl_3$, TCE,[a] 0 °C, 2 h	**24a**	93	44
21	$EtOCHCl_2$, $AlCl_3$, TCE,[a] 0 °C, 2 h	**24a**	41	44
	$EtOCHCl_2$, $TiCl_4$, $(CH_2Cl)_2$, 20 °C, 2 h	**24a**	85	48
	HCONMePh, $POCl_3$, PhMe, 100 °C, 6 h	**24a**	4	30, 49
	MeCOCl, $AlCl_3$, $PhNO_2$, 20 °C, 10 h	**24b**	2.5	30
	$(MeCO)_2O$, $HClO_4$, 20 °C, 15 min	**24b**	2.5	50
	PhCOCl, $AlCl_3$, TCE,[a] 20 °C, 10 h	**24k**	90	51, 52
	4-MeC_6H_4COCl, $AlCl_3$, $(CH_2Cl)_2$, 20 °C, 10 h	**24g**	46	27, 53
	4-BrC_6H_4COCl, $AlCl_3$, $PhNO_2$, 20 °C, 24 h	**24h**	9	37
	$C_6H_4(CO)_2O$, $AlCl_3$, TCE,[a] 20 °C, 24 h	**24i**	19	38
	$ClSO_2NCO$, MeCN, 20 °C, 48 h	**24j**	80	39
24a	$AlCl_3$, TCE,[a] 80 °C, 40 min	**25a**	83	44
	$AlCl_3$, TCE,[a] 100 °C, 2 h	**26a**	48	44
	BBr_3, CH_2Cl_2, −78 → 20 °C	**26a**	not indicated	48

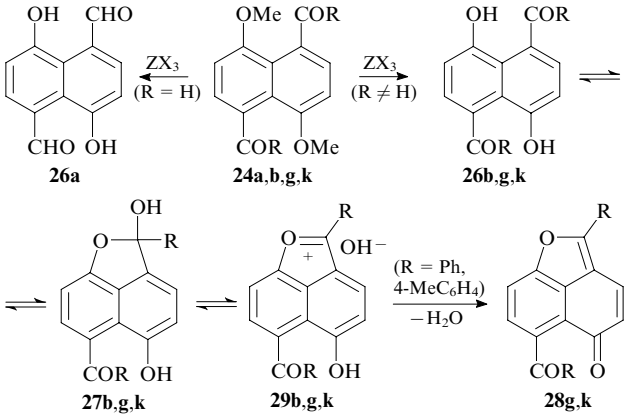
[a] TCE is tetrachloroethane; [b] the melting point of compound **23a** postulated by the authors[40–43] as 4,5-dihydroxynaphthaldehyde differs from the melting point of this compound obtained in another work.[44]

Scheme 3



R = H (**a**), Me (**b**), Et (**c**), CH_2Cl (**d**), $(CH_2)_2CO_2H$ (**e**), $(CH_2)_4CO_2H$ (**f**), 4-MeC_6H_4 (**g**), 4-BrC_6H_4 (**h**), 2-$HO_2CC_6H_4$ (**i**), $NHSO_2Cl$ (**j**), Ph (**k**).

which can be effected by aluminium chloride or boron tribromide. Table 1 presents the conditions of synthesis of 1,5-dimethoxynaphthalene (**21**), certain *peri*-methoxy- (**22**) and *peri*-hydroxycarbonyl (**7**, **23**) naphthalene derivatives and 1,5-dicarbonyl naphthalene derivatives (**24**–**26**), containing hydroxy or methoxy groups in the *peri*-positions to two carbonyl groups (Scheme 3).

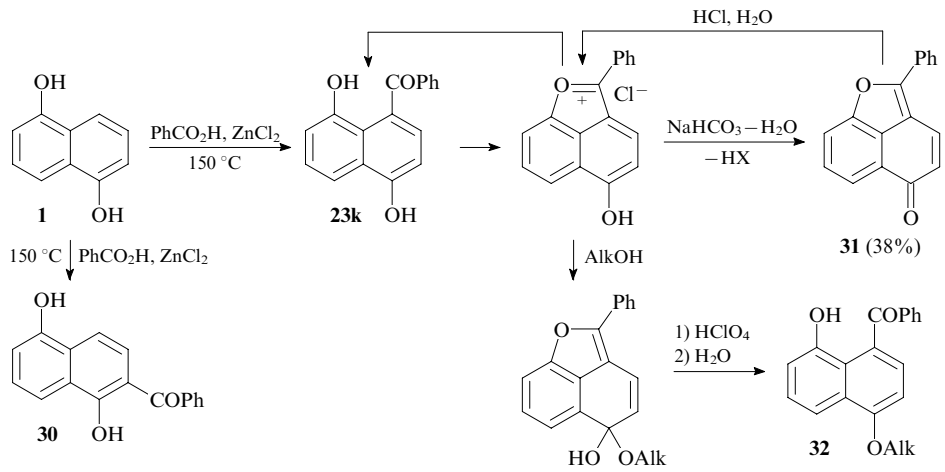


R = H (**a**), Me (**b**), 4-MeC_6H_4 (**g**), Ph (**k**); Z = Al, B; X = Cl, Br.

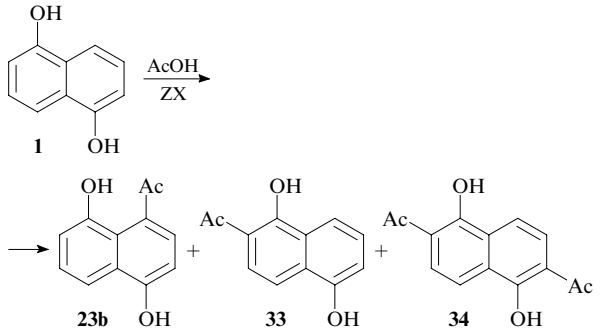
Whereas demethylation of 1,5-diformyl-4,8-dimethoxynaphthalene (**24a**) gives rise to 1,5-diformyl-4,8-dihydroxynaphthalene (**26a**), demethylation of dimethoxy diketones **24b**,**g**,**k** affords cyclic products **27b** and **28g**,**k**, respectively.[27, 50, 52] The observed differences in the structures of final products **27b** and **28g**,**k** are attributable to the greater ability of the 2-aryl substituent to delocalize the positive charge in the naphtho[1,8-*bc*]furylium cations **29g**,**k** as compared with the 2-methyl substituent in cation **29b**.

Stirring of a melt of naphthalene-1,5-diol (**1**), benzoic acid and zinc chloride produces *peri*-hydroxy ketone **23k** containing an *ortho*-hydroxy ketone **30** impurity (Scheme 4).[54] *peri*-Hydroxy ketone **23k** is heterocyclized under the reaction conditions giving the 5-hydroxynaphtho[1,8-*bc*]furylium cation. This product is deprotonated in the weakly alkaline solution, being converted to phenylnaphtho[1,8-*bc*]furan-5-one (**31**). In the acidic medium, the reverse reaction takes place, namely, transformation of naphthofuranone **31** to *peri*-hydroxy ketone **23k** (yield 72%).[55] When naphthofuranone **31** was kept in alcohol solutions in the presence of catalytic amounts of perchloric acid and then the mixture was diluted with water, 4-alkoxy-substituted *peri*-hydroxy ketones **32** were formed in high yields (see Scheme 4).[56]

Scheme 4



The reactions of naphthalene-1,5-diol with acetic acid taking place on refluxing in the presence of various Lewis acids were studied.[47] This always gave a mixture of three products: compounds **23b**, **33** and **34** whose ratio considerably depended on the nature and amount of the condensing agent. The highest yield of *peri*-hydroxy ketone **23b** (29%) was attained by using tin chloride at a molar ratio **1** : $SnCl_4$: AcOH equal to 1 : 6.6 : 12. Diketone **34** was obtained in the maximum yield (~4%) under the same conditions. *ortho*-Hydroxy ketone **33** was formed in the highest yield (56%) when zinc chloride was used and the **1** : $ZnCl_2$: AcOH molar ratio was 1 : 1.5 : 6.

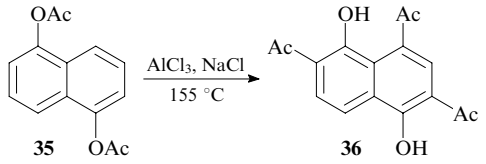


ZX = $ZnCl_2$, $AlCl_3$, $SnCl_4$, $TiCl_4$, $BF_3 \cdot Et_2O$.

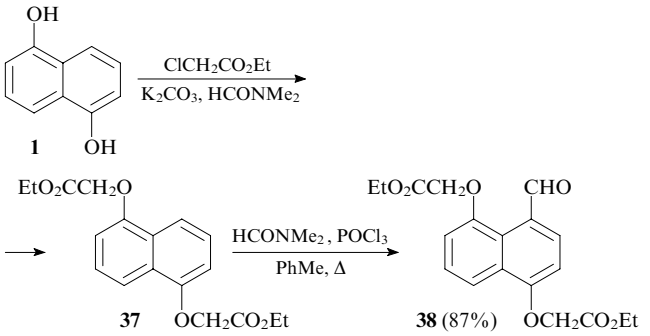
Thamizharas and Reddy[57] reported the synthesis of *peri*-hydroxy ketone **23b** in 70% yield by refluxing equimolar amounts of naphthalene-1,5-diol, zinc chloride and acetic acid in tetrahydrofuran. However, neither the melting point, nor elemental analysis data, nor the spectral characteristics of the obtained compound correspond to any of the three compounds shown above whose structures are beyond doubt.

Heating of naphthalene-1,5-diol and its monomethyl ether with phthalic anhydride and aluminium chloride in a melt or in tetrachloroethane leads to acylation of only the carbon atoms located in the *ortho*-position relative to the hydroxy groups, whereas 1,5-dimethoxynaphthalene is converted only to *peri*-substituted mono- and diketones **22i** and **24i** under the same conditions (see Table 1).[38]

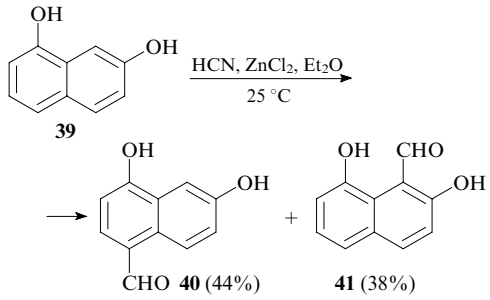
Apparently, acid-catalyzed reaction of naphthalene-1,5-diol or its monomethyl ether with acylating agents gives initially esters, which then rearrange to *ortho*- and *peri*-hydroxynaphthoyl compounds or their mixture; this is in agreement with the above-described reactions and with the results of the Fries rearrangement of 1,5-diacetoxynaphthalene (**35**) to 2,4,6-triacetylnaphthalene-1,5-diol (**36**) (the yield is not indicated).[58]



The Vilsmeier formylation of compound **37** obtained from naphthalene-1,5-diol and ethyl chloroacetate gives aldehyde **38**,[59] the high yield of which indicates that replacement of the hydrogen atom in the methoxy groups by electron-withdrawing ethoxycarbonyl group has almost no effect on the electron-donating properties of the methoxy groups.

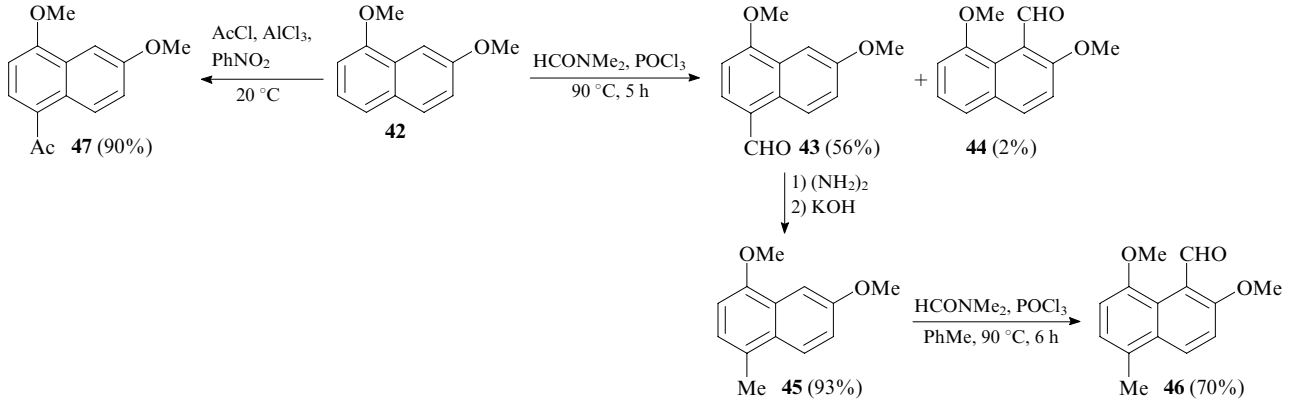


The Gattermann formylation of naphthalene-1,7-diol (**39**) follows an ambiguous route, resulting in a mixture of two isomeric *para*- (**40**) and *peri*-dihydroxynaphthaldehydes (**41**) where *peri*-hydroxynaphthaldehyde **41** is the minor product.[41] The structure of the products is postulated in the original study relying only on the data from elemental analysis.



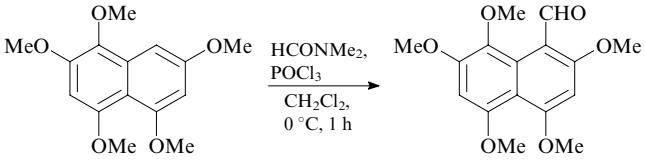
The Vilsmeier formylation of 1,7-dimethoxynaphthalene (**42**) involves predominantly the *para*-position to the 1-methoxy group yielding compound **43** (*peri*-methoxynaphthaldehyde **44** is formed in a very low amount) (Scheme 5), whereas formylation of 4-methyl-1,7-dimeth-

Scheme 5



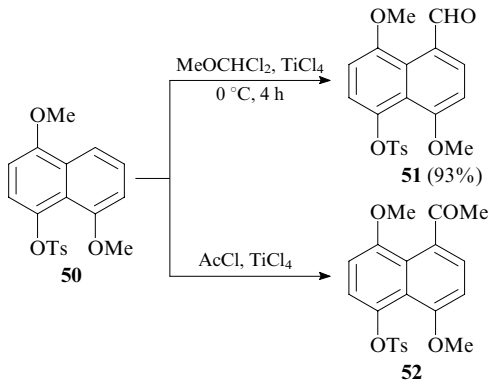
oxynaphthalene (**45**) involves only the *peri*-position to the 1-methoxy group, which is simultaneously an *ortho*-position to the 7-methoxy group, giving rise to product **46**.[60] Upon the Friedel–Crafts acetylation of 1,7-dimethoxynaphthalene (**42**), only one product, 1-acetyl-4,6-dimethoxynaphthalene (**47**), was isolated.

The Vilsmeier formylation of 1,2,4,5,7-pentamethoxynaphthalene (**48**) gives *peri*-methoxynaphthaldehyde **49**.[61,62] Unlike the previous case where the formylation required heating, this reaction occurs at 0 °C, which is due to the considerable increase in the electron-donating properties of the naphthalene ring as a result of electron density 'pumping' by five methoxy groups.



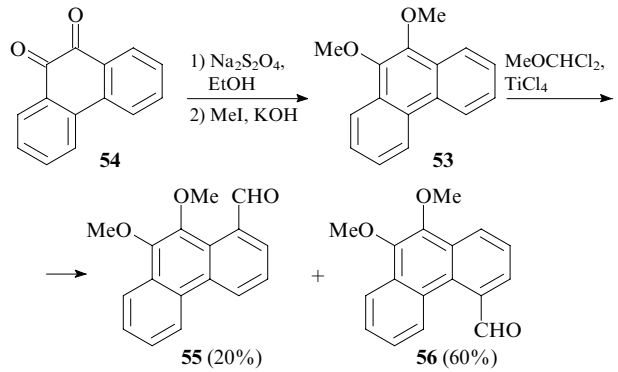
48 **49** (83%)

The formylation of 1,5-dimethoxy-4-tosyloxynaphthalene (**50**) yields *peri*-methoxynaphthaldehyde **51**[63] and acetylation of **50** affords *peri*-methoxy ketone **52**.[8]



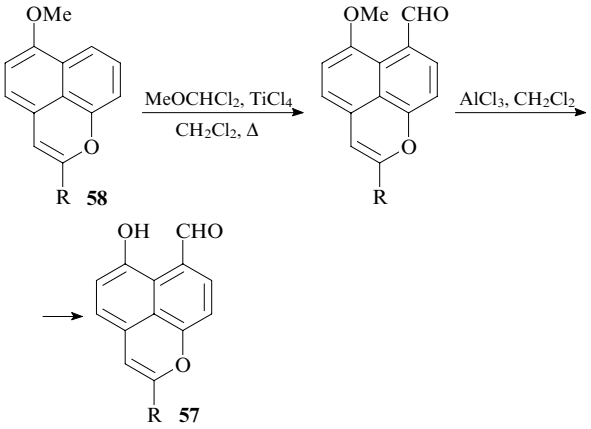
50 **51** (93%) **52**

The formylation of dimethoxyphenanthrene **53** obtained from phenanthrenequinone **54** furnishes a mixture of isomeric aldehydes **55** and **56** where the latter predominates.[64]



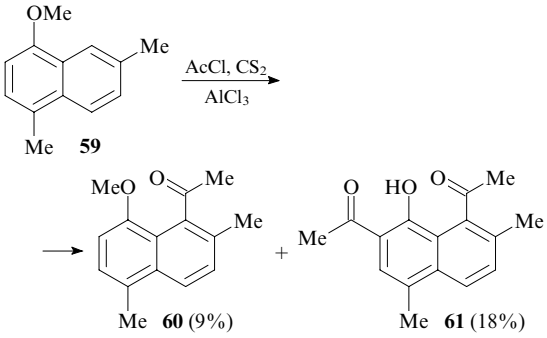
54 **53** **55** (20%) **56** (60%)

The synthesis of 1,6- and 1,8-dioxapyrenes by *peri*-heterocyclization of *peri*-hydroxyformyl derivatives of naphtho[1,8-*bc*]pyran (**57**) has been described.[59,65–68] The latter compounds were prepared by formylation of 5-methoxy derivatives of naphtho[1,8-*bc*]pyran (**58**)[65–68] or diethyl (naphthalene-1,5-diyldioxy)diacetate.[59] As the initial compounds, 1,5-dihydroxy-, 1-hydroxy-5-methoxy- or 1,5-dimethoxynaphthalenes were used in these syntheses.

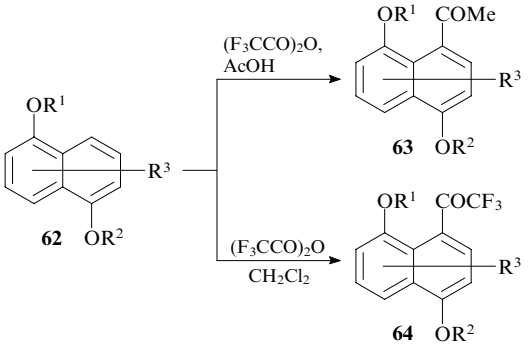


R = COAlk, CO_2Alk, CO_2Ar, $CONH_2$.

The acylation of 4,7-dimethyl-1-methoxynaphthalene (**59**) afforded a mixture of ketones from which *peri*-methoxy and *peri*-hydroxy ketones, compounds **60** and **61**, respectively, were isolated.[69]

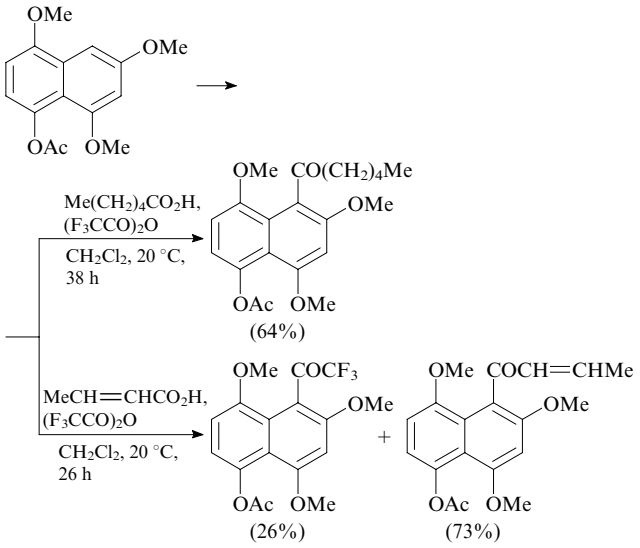


On long-term (24–48 h) keeping of naphthalenediol with the general formula **62** in a mixture of acetic acid and trifluoroacetic anhydride at 20 °C, acetylation products (compounds **63**) are formed, whereas in the absence of acetic acid, acylation with trifluoroacetic anhydride takes place (compound **64**).[70–73]

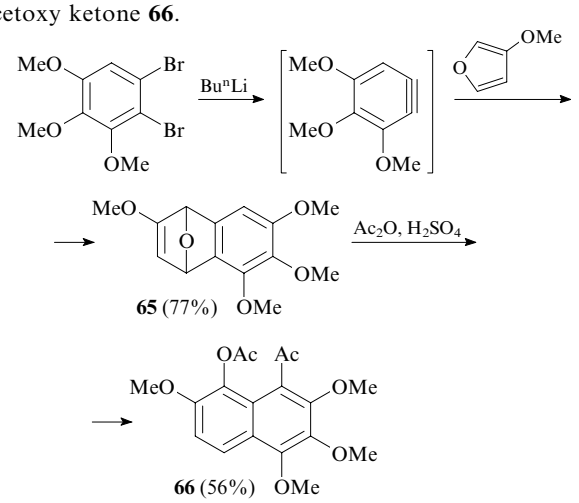


$R^1 = R^2$ = Me, Pr^i, Bn; R^3 = H, Me, OAlk, OAc.

Instead of acetic acid, other aliphatic and unsaturated carboxylic acids can be used as acylating agents.[73] In this case, the reactions are also carried out in the presence of trifluoroacetic anhydride.



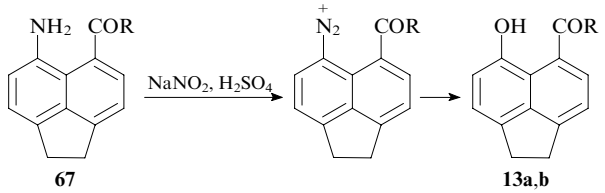
An original way for constructing the *peri*-acetoxycarbonyl group has been proposed.[74] Trimethoxydehydrobenzene used as the starting compound reacts with 3-methoxyfuran to give adduct **65**. On treatment with acetic anhydride, adduct **65** undergoes acid-catalyzed isomerization with subsequent O- and C-acylation yielding *peri*-acetoxy ketone **66**.



Trimethoxydehydrobenzene was prepared by treatment of 4,5-dibromo-1,2,3-trimethoxybenzene with butyllithium.

2. Nucleophilic substitution in the aromatic nucleus

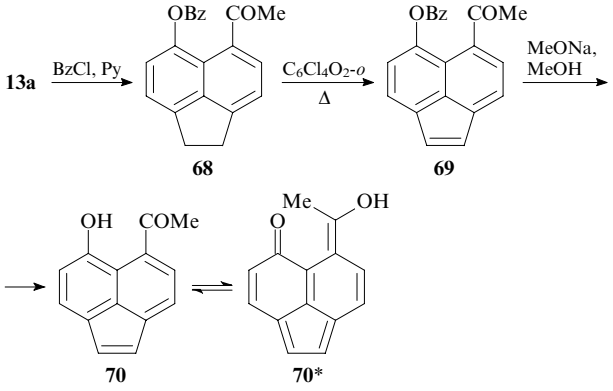
A hydroxy group can enter the *peri*-position to the carbonyl group by substituting an electron-deficient group. Thus diazotization of acenaphthene *peri*-amino ketone **67** resulted in the synthesis of acenaphthene *peri*-hydroxy ketones **13a**,**b**.[75]



R = Me (**a**), Ph (**b**).

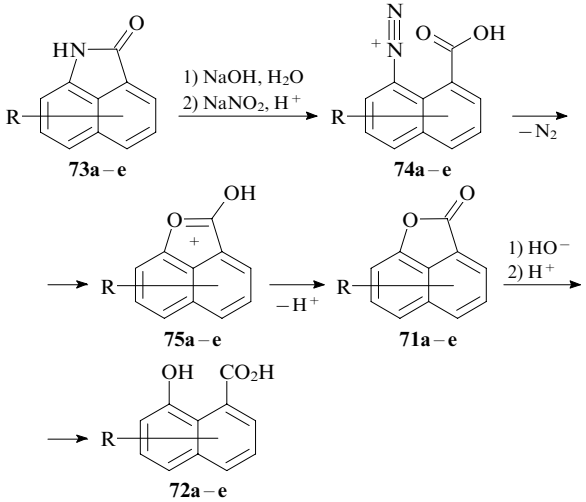
A similar transformation in the series of naphthalene *peri*-amino-substituted aldehydes and ketones is impossible as they cyclize during the reaction to benzo[*cd*]indoles;[76–78] the presence of the dimethylene unit in compound **67** prevents this process.

The dehydrogenation of hydroxy-protected derivative of **13a**, acenaphthene *peri*-benzoyloxy ketone **68**, with chloranil afforded acenaphthylene *peri*-benzoyloxy ketone **69**, which was deprotected to give *peri*-hydroxy ketone **70**.[79] Compound **70** refers to a new class of compounds in which the hydroxy and carbonyl groups are conjugated *via* the acenaphthylene π-system, which imparts qualitatively new properties to them; in particular, they are capable of benzenoid–quinonoid tautomerism (**70** ⇄ **70***), which is impossible for *peri*-hydroxy-substituted naphthalene and acenaphthene aldehydes and ketones.



The general route to *peri*-hydroxynaphthoic acids is replacement of the functional substituent (amino or sulfo group or halogen atom) located in the *peri*-position to the carboxy group by a hydroxy group.

Naphtholactones **71**, which are potential precursors of *peri*-hydroxynaphthoic acids **72**, are prepared most conveniently from naphtholactams **73** by alkaline cleavage of the heterocycle followed by diazotization of the resulting *peri*-aminonaphthoic acid.[80–85]

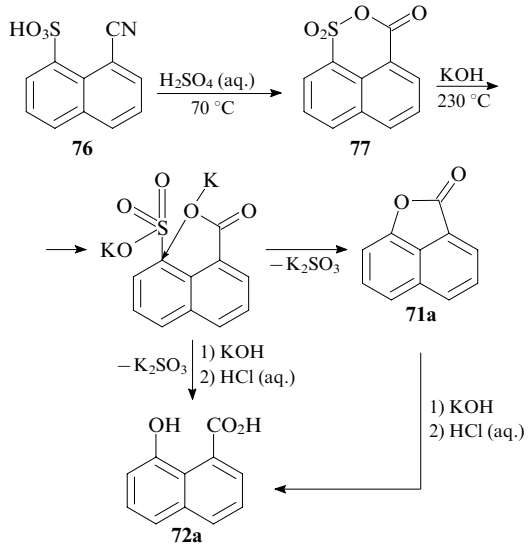


R = H (**a**), 3-OMe (**b**), 6-NO_2 (**c**), 3-Br (**d**), 5-Bz (**e**).

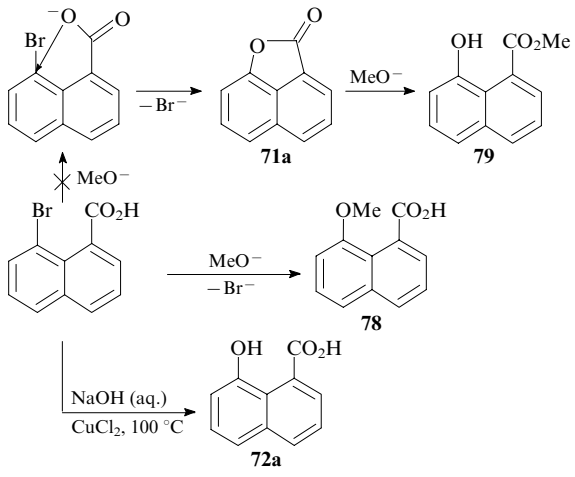
It is believed[2] that the heterocycle closure (**74** → **75** transformation) occurs through displacement of a nitrogen

molecule as a result of intramolecular nucleophilic attack of the *peri*-carbon atom attached to the diazonium ion by the carbonyl oxygen atom of the carboxy group; this assumption is supported by the experimental fact that 1,8-hydroxynaphthoic acid **72a** is not lactonized in acidic media.[2] *peri*-Hydroxynaphthoic acids **72a–e** are formed on treatment of naphtholactones **71a–e** first with an alkali and then with an acid.

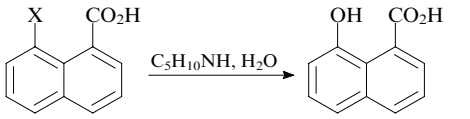
Heating of *peri*-cyanonaphthalenesulfonic acid (**76**) with dilute sulfuric acid gives rise to sulfonaphthoic anhydride **77**, which is converted to *peri*-hydroxynaphthoic acid **72a** on fusion with alkali and treatment first with alkali and then with acid.[26,86] Presumably, displacement of the sulfo substituent is intramolecular and is effected by oxygen of the carboxylate anion, although one cannot rule out the alternative mechanism, namely, the direct attack by potassium hydroxide of the naphthalene carbon atom bonded to the sulfo group, thus bypassing the formation of naphtholactone **71a**.



The fact that displacement of the *peri*-substituent in the *peri*-substituted naphthoic acids can bypass the intermediacy of naphtholactone **71a** is supported by the formation of product **78** rather than **79** in the reaction of 8-bromonaphthoic acid with sodium methoxide.[87] (The displacement of bromine by alkoxy groups is substantially facilitated when a nitro group is present in the *para*-position to bromine.[88]) On refluxing 8-bromonaphthoic acid with aqueous alkali in the presence of copper(II) chloride, *peri*-hydroxynaphthoic acid **72a** is formed (yield 50%).[87]

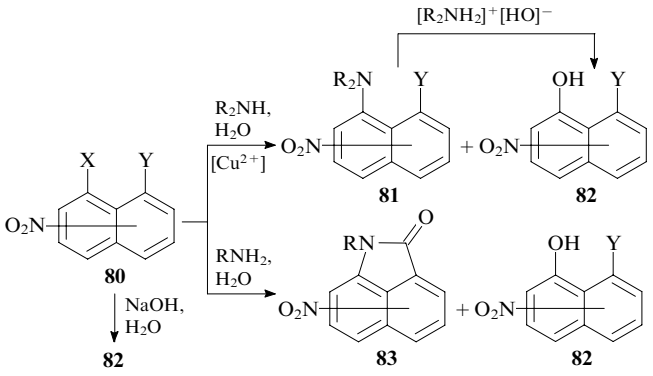


The reaction of *peri*-halonaphthoic acid with the hydroxide anion generated in a 13% aqueous solution of piperidine, resulting in *peri*-hydroxynaphthoic acid **72a**, has been studied.[89–92] The ease and the rate of the reaction were found to increase in the series Cl < Br < I, although the yields of acid **72a** are nearly equal. Indeed, the replacement of chlorine requires the presence of the $CuCl_2$ catalyst and refluxing for an hour, whereas bromine is replaced at room temperature in the presence of the same catalyst, and replacement of iodine does not require a catalyst and occurs on moderate heating (50 °C). The activity of copper catalysts was found to decrease in the order $Cu^{II} > Cu^{I} > Cu^{0}$.



X = Cl, Br, I.

Various aspects of the reaction (kinetics, substituent effects and nature of the amine, catalyst and halogen atom) of 4- and 5-nitro-substituted 1,8-halonaphthoic acids **80** with amines have been studied.[93–98]

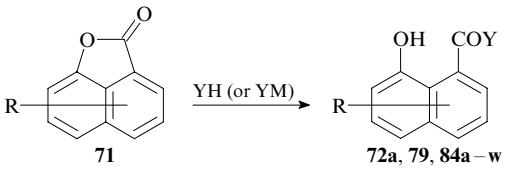


X = Cl, Br, I; Y = CO_2H; R = Alk, Ar, N⬡Z (Z = CH_2, O).

In the absence of water and copper catalysts, compounds **80** reacted with secondary amines to give *peri*-dialkylamino-substituted nitronaphthoic acids **81**, while in aqueous solutions in the presence of copper catalysts, a mixture of *peri*-amino and *peri*-hydroxy derivatives **81** and **82** is formed, the *peri*-hydroxy acid resulting from replacement of both the halogen atom and the dialkylamino group, which was established in a separate experiment. In aqueous solutions of primary amines, *peri*-halonaphthoic acids **80** are converted to a mixture of naphthostyryls **83** and *peri*-hydroxy acids **82**. The formation of *peri*-hydroxy acids **82** was confirmed by their alternative synthesis from *peri*-halo acids **80** and alkali.

3. Syntheses based on naphtholactones

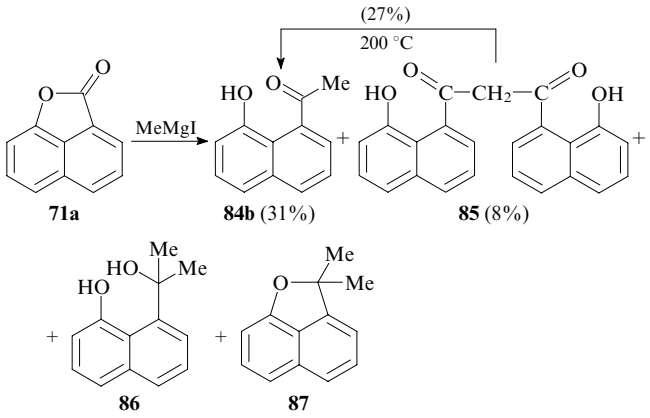
Cleavage of the five-membered heterocycle in naphtho[1,8-*bc*]furan-2-ones (naphtholactones) **71** induced by various nucleophilic reagents (YH) may be considered to be a versatile route to constructing the *peri*-hydroxycarbonyl group.



Along this route, various *peri*-hydroxy-substituted aldehydes, ketones, carboxylic acids and esters or amides of these acids were obtained in one step (Table 2). High reactivity of naphtholactones with respect to nucleophilic reagents is due to the strain in the furan ring caused by the distortion of the bond angles in this ring.

The low yields of *peri*-hydroxy-substituted ketones **84b**,**f** and diketones **84g**,**h** (see Table 2) formed upon the reaction of naphtholactone **71a** (R = H) with the corresponding organometallic reagents are associated with side reactions, resulting in a product mixture. For instance, the reaction of naphtholactone **71a** with methylmagnesium iodide gives also compounds **85**–**87** apart from the major product **84b**.[2]

Along with the one-step syntheses of *peri*-hydroxynaphthoyl derivatives from naphtholactones **71** summarized in Table 2, there are more complicated synthetic routes to these products.[2] For example, *peri*-hydroxyacetonaphthone **84b** can be obtained from naphtholactone **71a** by its reaction with ethyl bromoacetate followed by saponification and decarboxylation of acid **88** or by its reaction with sodium methanesulfinylmethylide followed by desulfurization (Scheme 6).[2] In addition, *peri*-hydroxyacetonaphthone **84b** is also formed upon thermal cleavage of diketone **85**. In this case, naphtholactone **71a** is formed as the second product.

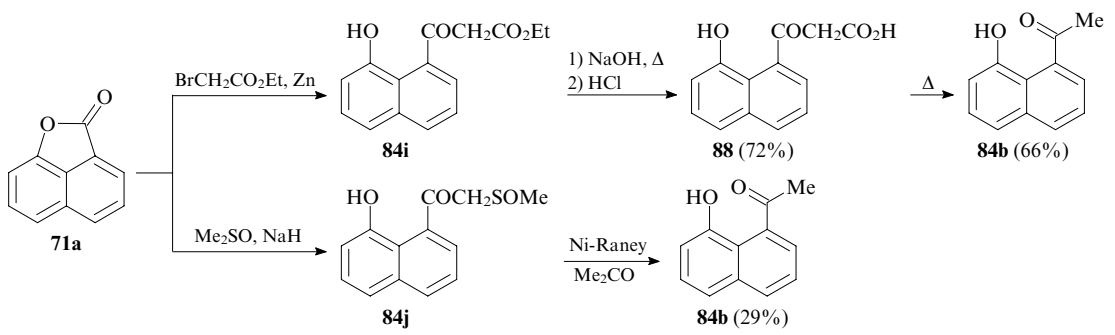


Apart from naphtholactones **71**, naphtho[1,8-*bc*]pyran-2,3-diones **89** in which the six-membered pyran ring is easily cleaved under the action of nucleophiles to give functional

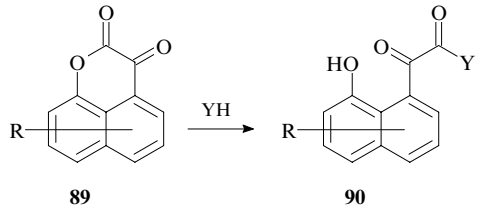
Table 2. Synthesis of *peri*-hydroxycarbonyl naphthalene derivatives from naphtholactones **71**.

Compound	Y	R	Reagents, conditions	Yield (%)	Ref.
72a	OH	H	NaOH, H_2O, 100 °C, 12 h	84	81, 99
79	OMe	H	MeONa, MeOH, 60 °C, 3 h	59	6, 99
			MeONa, MeOH, 20 °C, 4 h	72	82
			MeOH, H_2SO_4, 60 °C, 3 h	98	2
			MeOH, 20 °C, 96 h	85	100
84a	H	H	$LiAlH(OBu^t)_3$, THF, 20 °C	75	101
84b	Me	H	MeMgI, Et_2O, PhH, N_2, 20 °C	31	2
			MeLi, THF, N_2, −75 °C	62	102
84c	Me	5-$OCONR_2$ (R = Alk, Ar)	MeLi, THF, N_2, 0 °C	55–65	103–105
84d	Et	H	EtMgBr, THF, N_2, −75 °C	33	102, 106
84e	Et	2,4-$(OBn)_2$,3-Me	EtLi, Et_2O, 0 °C, 1 h	100	107
84f	Ph	H	PhMgI, THF, PhH, N_2, 20 °C	42	2
84g	CH_2COMe	H	Me_2CO, Me_2SO, NaH, N_2, 20 °C	46	2
84h	CH_2COPh	H	PhCOMe, Me_2SO, NaH, N_2, 20 °C	10	2
84i	CH_2CO_2Et	H	$BrCH_2CO_2Et$, Zn, THF, 70 °C	70	2
84j	CH_2SOMe	H	Me_2SO, NaH, 0 → 20 °C	100	2
84k	OMe	3-OMe	MeONa, MeOH, 20 °C, 4 h	95	82
84l	OMe	6-NO_2	MeOH, H_2SO_4, 60 °C, 3 h	100	84
84m	OEt	H	EtOH, H_2SO_4, 80 °C, 5 h	70	2
84n	OPr^i	H	Pr^iOH, H_2SO_4, 90 °C, 4 h	77	2
84o	OBu^t	H	Bu^tOK, Me_2SO, 20 °C, 1 h	89	2
84p	$N(CH_2CH_2)_2$	H	$(CH_2CH_2)_2NH$, PhH, 20 °C, 10 h	59	2
84q	NH_2	H	NH_3, Et_2O, 20 °C, 20 min	100	108
84r	NMe_2	H	Me_2NH, PhMe, Δ	100	6, 108
			Me_2NH, MeOH–THF, 20 °C, 4 h	77	100
84s	NHPh	H	$PhNH_2$, PhMe, 110 °C, 5 min	97	108
84t	$N(CH_2CH_2)_2O$	H	$O(CH_2CH_2)_2NH$, PhMe, 110 °C, 5 min	100	108
84u	NMePh	H	PhMeNH, PhMe, 110 °C, 5 min	87	108
84v	NPr^i_2	H	Pr^i_2NLi	—	109
84w	2-C_8H_5NTs	H	2-lithio-1-tosylindole	—	110

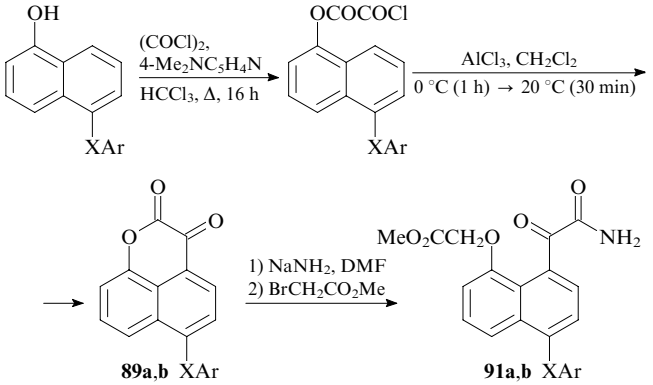
Scheme 6



derivatives **90** can be used to synthesize *peri*-hydroxy ketones.

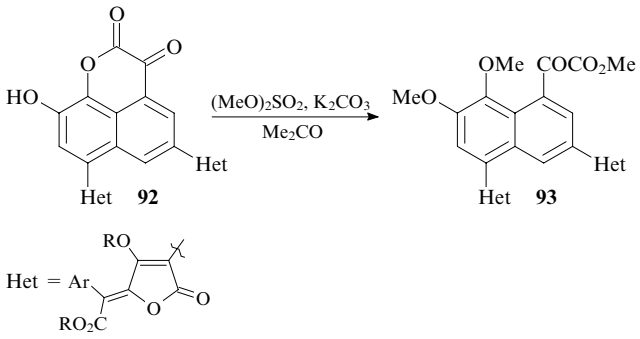


For example, a patent was granted for the preparation of 6-benzyl- (**89a**) and 6-aryloxynaphtho[1,8-*bc*]pyran-2,3-diones (**89b**) and their conversion to *peri*-hydroxy-substituted naphthylglyoxamides **91a**,**b** and their derivatives, which have antiseptic action.[111]

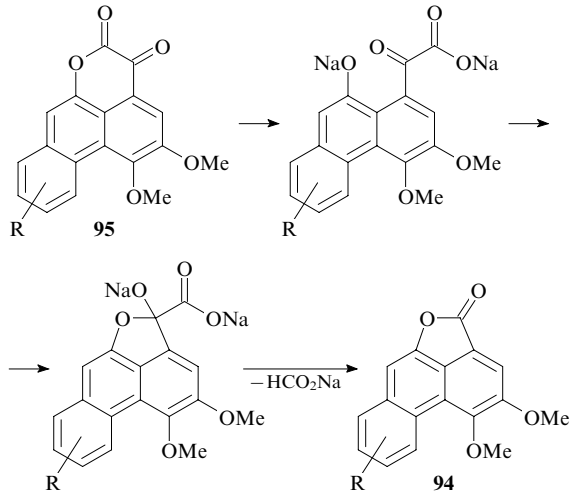


X = CH_2 (**a**), O (**b**).

Naphtho[1,8-*bc*]pyrandione **92** isolated from the plant *Xerocomus badius* reacts with dimethyl sulfate under base catalysis to give specific *peri*-methoxy ketone **93** containing a $COCO_2Me$ fragment.[112]

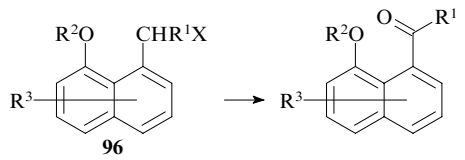


The synthesis of lactones of *peri*-hydroxycarboxylic acid **94**, which are potential precursors of aristolactams, natural compounds related to aporphines,[113,114] includes opening of the pyran ring in pyrandione **95** followed by recyclization.



4. Oxidative generation of carbonyl group

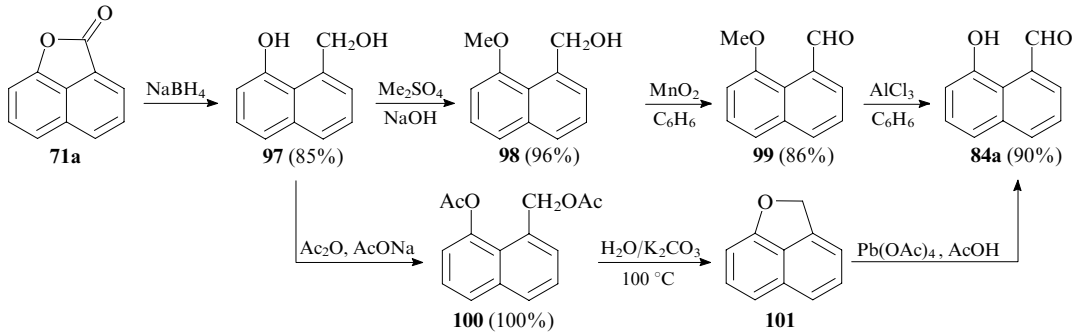
The transformation of the methylene group in compounds with the general formula **96** to a carbonyl group under the action of oxidants is employed in the synthesis of a number of *peri*-substituted aldehydes (R^1 = H) and ketones (R^1 = Alk, Ar).



X = OH, OAc, CO_2H.

The parent *peri*-hydroxycarbonyl compound, *viz*., *peri*-hydroxynaphthaldehyde (**84a**), was first prepared in 1972 starting from naphtholactone **71a** by a four-step synthesis (Scheme 7).[3] The key steps of this synthesis are the reduction of naphtholactone **71a** to 8-hydroxymethyl-1-naphthol (**97**), methylation of 8-hydroxy group (compound **98**) and the subsequent oxidation of alcohol **98** in *peri*-methoxynaphthaldehyde (**99**). Despite the rather high overall yield

Scheme 7

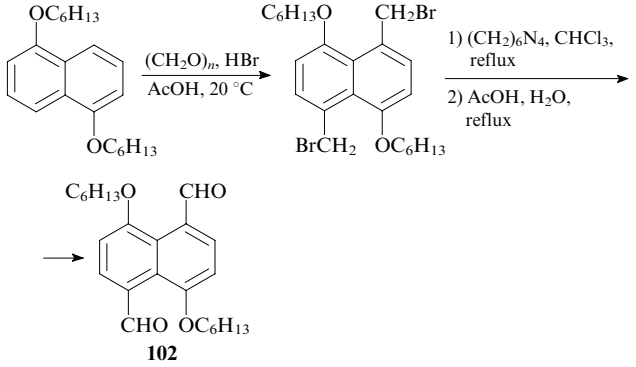


of the target product, this method is rather laborious. The reduction of naphtholactone **71a** with lithium tri(*tert*-butoxy)aluminium hydride providing *peri*-hydroxynaphthaldehyde (**84a**) in 75% yield in one step is considered to be more promising (see Table 2).[101] In this case, owing to the presence of three bulky *tert*-butoxy groups and only one active hydrogen atom in the reducing agent, it is possible to avoid the formation of alcohol **97**, which is formed upon more extensive reduction of naphtholactone **71a**.

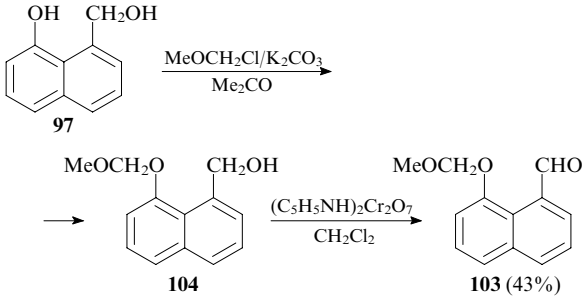
Yet another method for the synthesis of *peri*-hydroxynaphthaldehyde **84a** includes preparation of diacetate **100**, its conversion to naphtho[1,8-*bc*]furan (**101**) upon steam distillation over potassium carbonate and oxidation of **101** with lead tetraacetate.[3] In this case, the overall yield of naphthaldehyde **84a** was 44% in relation to naphtholactone **71a**. Oxidation proceeds ambiguously. In addition to the target aldehyde, a number of dimeric products were isolated from the reaction mixture; their exact composition was not determined.

Oxidation of 6- and 8-methoxy naphtho[1,8-*bc*]furan derivatives in air afforded 5- and 7-methoxy-substituted *peri*-hydroxynaphthaldehydes in moderate yields.[115]

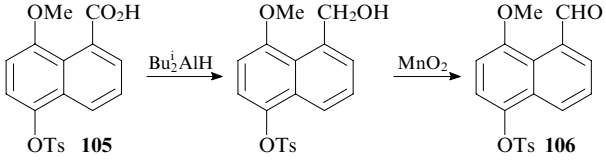
Bromomethylation of 1,5-di(hexyloxy)naphthalene furnishes 4,8-bis(bromomethyl)-1,5-di(hexyloxy)naphthalene, which reacts with urotropine (the Sommelet reaction) to be converted to *peri*-substituted dialdehyde **102**.[116, 117]



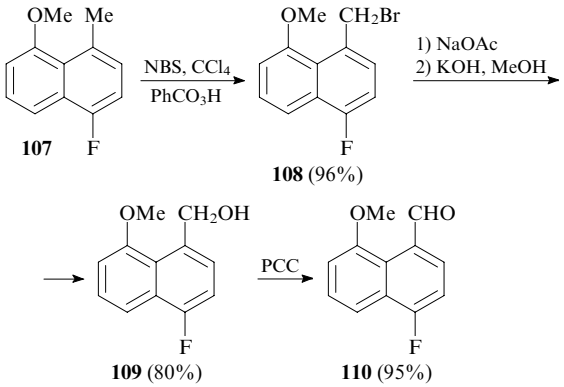
peri-Substituted aldehyde **103** is formed upon alkylation of 8-hydroxymethyl-1-naphthol (**97**) with chloromethyl methyl ether followed by oxidation of the reaction product **104** (without isolation) by pyridinium dichromate.[102, 106]



By reduction and oxidation transformations of *peri*-methoxycarboxylic acid **105**, *peri*-methoxynaphthaldehyde **106** was obtained.[8]

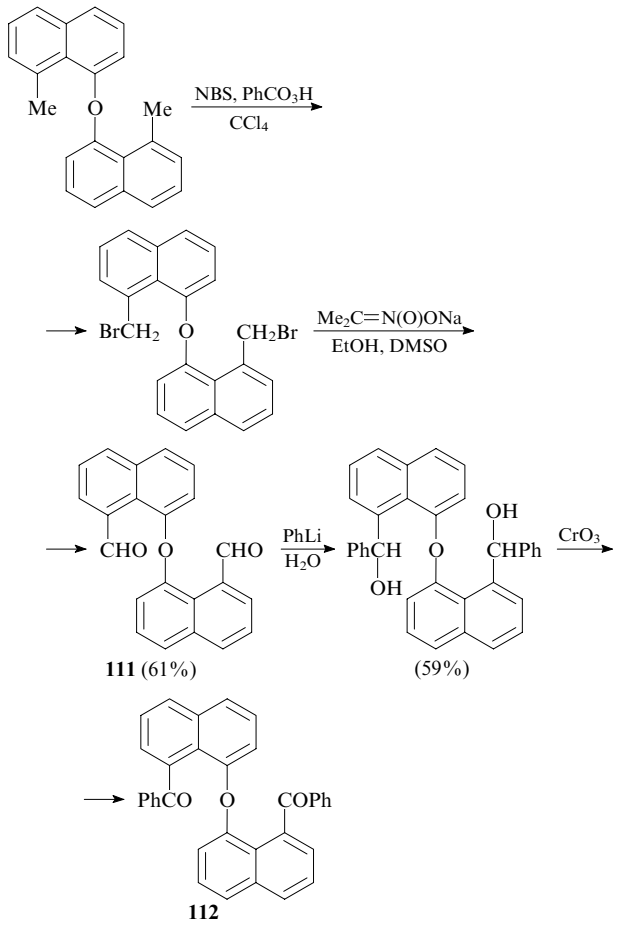


A route for transformation of the *peri*-methoxymethyl group to the *peri*-methoxyformyl group was proposed.[118] To this end, 4-fluoro-8-methoxy-1-methylnaphthalene (**107**) is treated with *N*-bromosuccinimide (NBS) and the resulting bromomethyl derivative **108** is converted to alcohol **109**, which is then oxidized to aldehyde **110** with pyridinium chlorochromate (PCC, $C_5H_5N \cdot HCl \cdot CrO_3$).

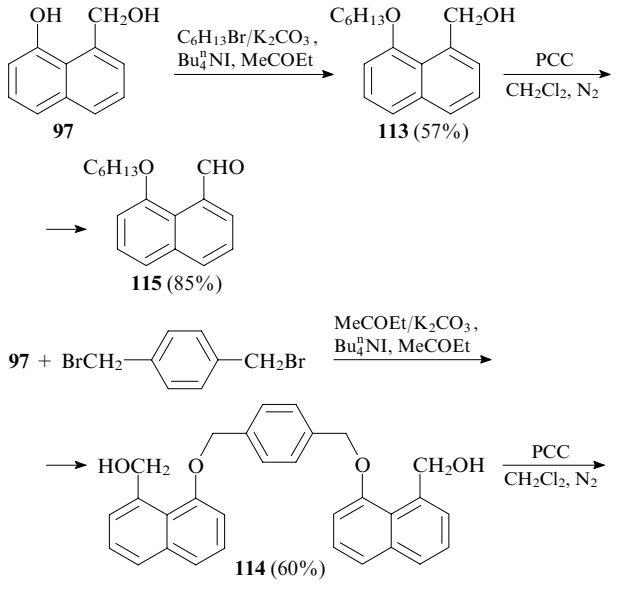


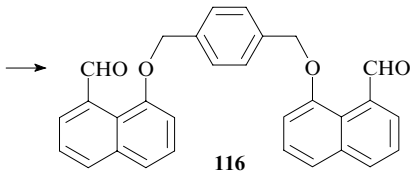
A similar strategy was used to prepare dialdehyde **111**, the only difference being that instead of pyridinium chlorochromate, the sodium salt of nitropropane aci-form in dimethyl sulfoxide was used as the oxidant to convert the

bromomethyl group to the aldehyde group.[119] The reaction of dialdehyde **111** with phenyllithium followed by oxidation gives *peri*-substituted diketone **112** (the yield was not indicated).

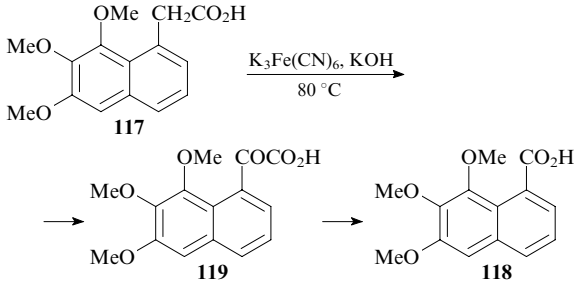


Pyridinium chlorochromate was used also for oxidation of alcohols **113** and **114** in *peri*-R-oxy-substituted naphthaldehydes **115** and **116**, respectively.[120]





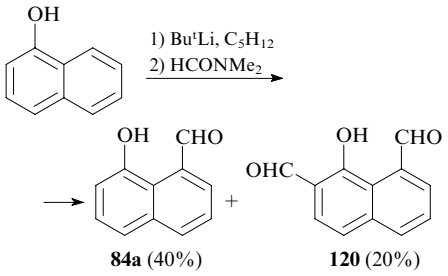
The oxidation of 6,7,8-trimethoxynaphthalene-1-ylacetic acid (**117**) affords *peri*-methoxynaphthoic acid **118**. The reaction proceeds obviously *via* intermediate **119**, which is decarbonylated under these conditions.[121]



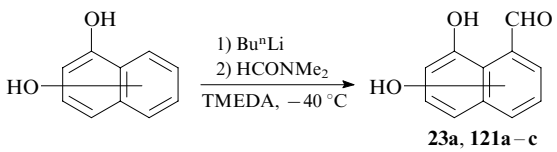
5. Syntheses using metal-containing aromatic compounds

Yet another general pathway to *peri*-R-oxy-substituted carbonyl compounds is based on reactions of lithium- or other metal-containing aromatic substrates with formylating, acylating or carboxylating reagents. Aromatic organolithium compounds can be prepared by replacing hydrogen or halogen atom in aromatic compounds by lithium in the reaction with aliphatic organolithium reagents. A necessary condition for the formation of *peri*-R-oxycarbonyl group is the presence of an R-oxy group in the α-position of the naphthalene nucleus.

Thus treatment of α-naphthol with *tert*-butyllithium and then with dimethylformamide produces a mixture of *peri*-hydroxy-substituted mono- (**84a**) and dialdehydes (**120**).[122]

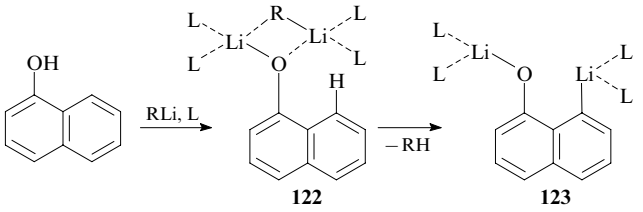


Similarly, on treatment of naphthalene-1,3-, -1,4-, -1,5- and 1,6-diols first with n-butyllithium and then with dimethylformamide, the corresponding *peri*-hydroxynaphthaldehydes **23a**, **121a**–**c** are formed in high yields.[123]



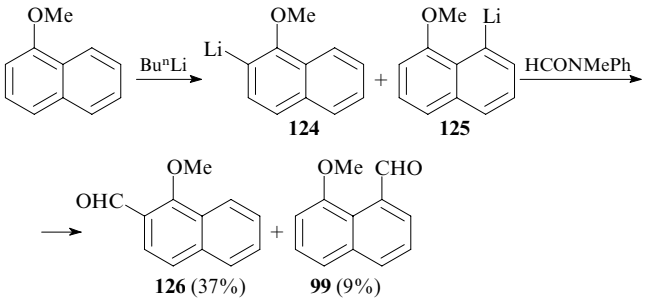
Compound	**23a**	**121a**	**121b**	**121c**
Positions of OH groups	4,8	5,8	3,8	6,8
Yield (%)	96	85	65	60

Using semiempirical computations, it was found that the key step of C-lithiation is the formation of complex intermediate **122**, which is converted to intermediate **123**. In this reaction, *peri*-lithiation is preferred over *ortho*-lithiation.[123]

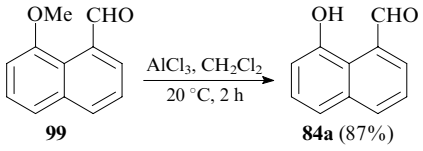


R = Alk, L is the solvent ligand.

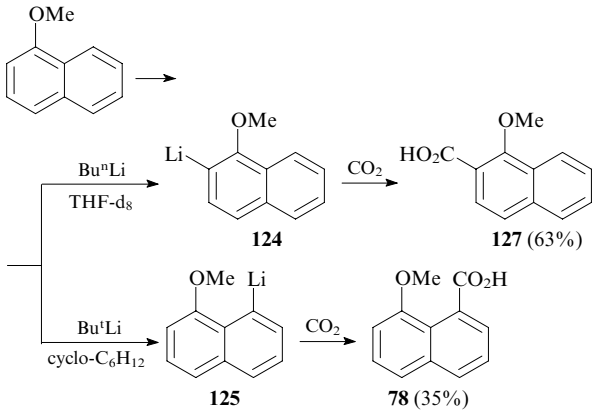
The directing effect of the methoxy group in the lithiation differs from the effect of the hydroxy group. Thus lithiation of 1-methoxynaphthalene with n-butyllithium results in a mixture of *ortho*- (**124**) and *peri*-lithiomethoxynaphthalenes (**125**). The subsequent formylation of this mixture results in *ortho*- (**126**) and *peri*-methoxynaphthaldehydes (**99**) where the former considerably predominates.[124, 125]



Demethylation of *peri*-methoxynaphthaldehyde (**99**) with aluminium chloride affords *peri*-hydroxynaphthaldehyde (**84a**).[124, 125]

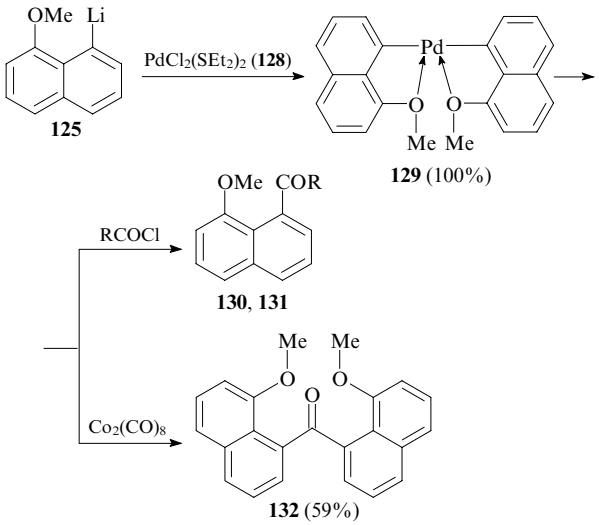


Using ^{1}H NMR spectra and quantum chemical calculations, the lithiation route of 1-methoxynaphthalene as a function of the nature of the lithiation reagent, the solvent, and the temperature regime was studied.[126]



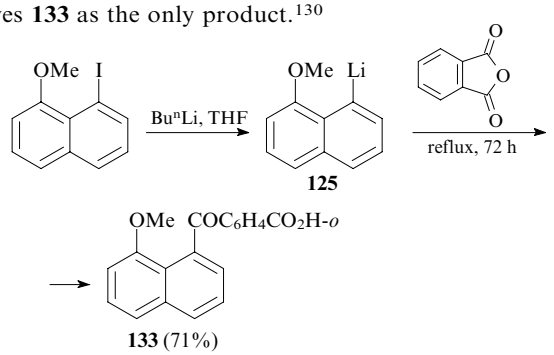
The lithiation carried out in an NMR tube showed that the reaction of 1-methoxynaphthalene with n-butyllithium in THF-d_8 affords *ortho*-derivative **124** in 92% yield, whereas the reaction of 1-methoxynaphthalene with *tert*-butyllithium in cyclohexane gives *peri*-isomer **125** in 52% yield. It was established that the *peri*-isomer is formed in the thermodynamically controlled reaction, while the *ortho*-isomer is the kinetically controlled product. The preparative lithiation followed by pouring the reaction mixture onto solid carbon dioxide gives the corresponding carboxylic acids **78** and **127**.

Treatment of *peri*-lithiomethoxynaphthalene **125** with palladium reagent **128** gives organopalladium chelate **129**,[127] which reacts with carbonyl-containing electrophiles in toluene over a period of 5–10 min at room temperature to give *peri*-methoxynaphthyl ketones **130**–**132**.[128] The direct reaction of lithium derivative **125** with acetic anhydride or dimethylacetamide gives *peri*-methoxyacetylnaphthalene **130** in very low yields (10% and 5%, respectively).[129]



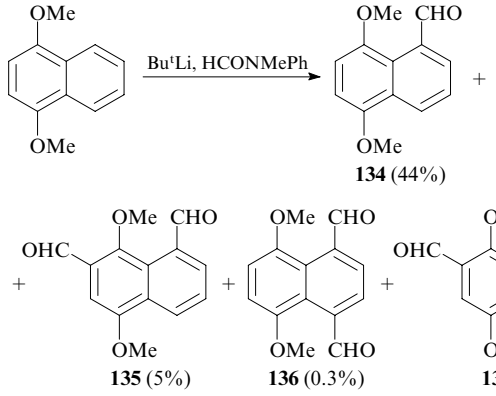
R = Me (**130**, 49%), Ph (**131**, 40%).

It may seem that the formation of *ortho*-methoxy-substituted aldehydes, ketones and acids can be avoided by using *peri*-halomethoxynaphthalenes for lithiation. Indeed, on long-term refluxing with phthalic anhydride, *peri*-lithiomethoxynaphthalene **125** obtained from *peri*-iodomethoxynaphthalene is converted to *peri*-methoxycarbonyl derivatives **133** as the only product.[130]

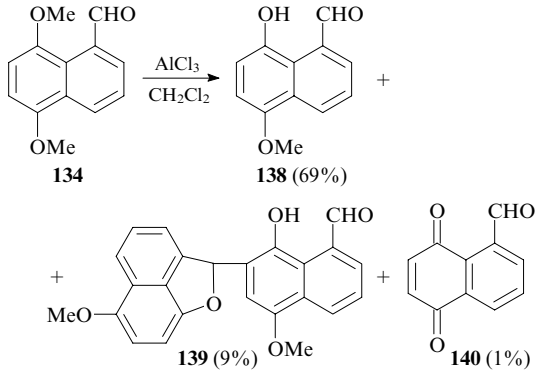


However, the fact that, as shown above, the *ortho*- and *peri*-lithium isomers occur in dynamic equilibrium makes the expected result not that unambiguous. The formylation of lithiated 1,4-dimethoxynaphthalene leads to a mixture of

products **134**–**137** three of which (compounds **134**–**136**) are *peri*-methoxynaphthaldehydes.[67, 131]

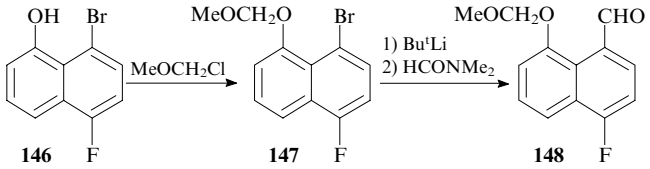


On treatment of *peri*-methoxynaphthaldehyde **134** with aluminium chloride, *peri*-hydroxynaphthaldehyde **138** was obtained together with the products of its self-condensation (compound **139**) and oxidation (compound **140**). The authors note[131] that compound **140** they obtained is the first representative of the class of *peri*-oxoquinonealdehydes.

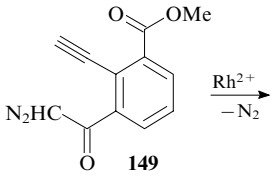


From 1,5-dimethoxynaphthalene (**21**), three types of dibromo derivatives were obtained: compounds **141**–**143**.[132] The lithiation and then formylation of compounds **141**–**143** gave three types of dimethoxydialdehydes: compounds **24a**, **144** and **145**.[132] A surprising fact is that under very similar bromination conditions, the authors isolated only one of the three possible bromo derivatives. It cannot be ruled out that all three types of bromo derivatives are formed in each case, the more so, because the yields of isolated individual compounds are far from being quantitative. The isolation of one of the isomers and the 'loss' of two other isomers may take place in crystallization stage; however, this is not mentioned in the paper cited. Later, the synthesis of dialdehydes **24a** and **144** was repeated by other researchers[133] (Scheme 8).

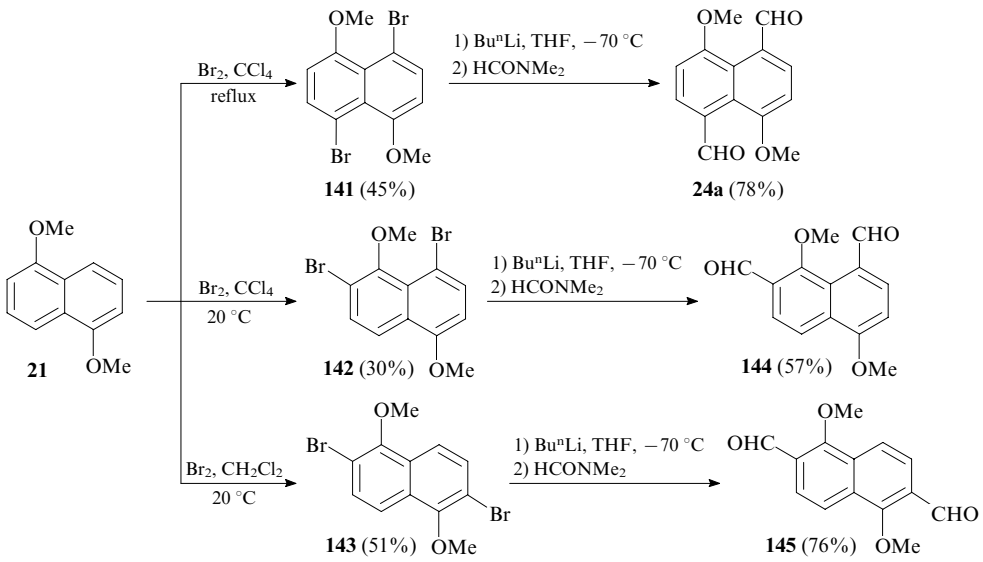
The reaction of 2-bromo-4-fluoro-1-naphthol **146** with chloromethyl methyl ether yields compound **147**, which is lithiated with replacement of the bromine atom. The subsequent treatment of the lithiated compound with dimethylformamide results in *peri*-(methoxymethoxy)naphthaldehyde **148**.[134]

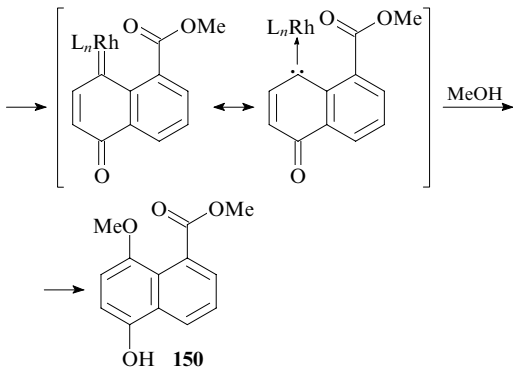


The transformation of *o*-ethynylphenyl diazomethyl ketone **149** to *peri*-methoxycarboxylate **150** induced by rhodium salts in methanol has been reported.[135] The *peri*-methoxycarbonyl group is formed upon substitution of the methoxy group for rhodium in the rhodium-containing aromatic intermediate during the reaction.[135]



Scheme 8





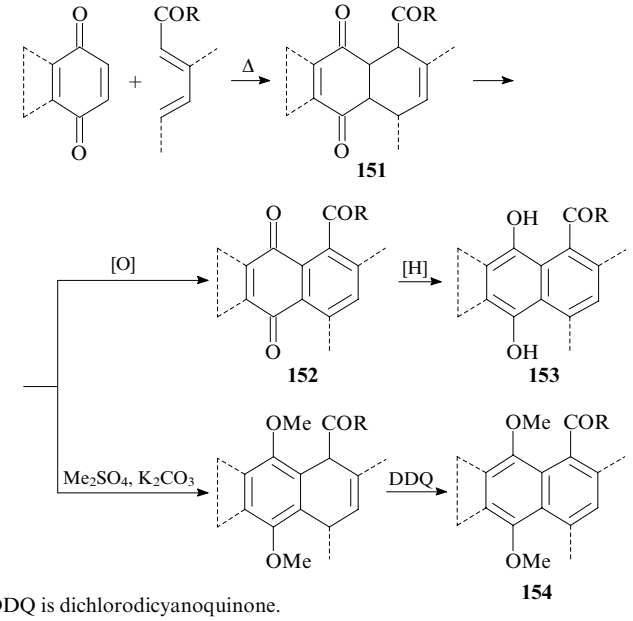
The authors assumed that the rhodium-containing intermediate has a carbenoid structure stabilized by rhodium.

6. The Diels – Alder reaction in the synthesis of *peri*-R-oxycarbonyl compounds

The Diels – Alder reaction is often used as the key step in the synthesis of *peri*-R-oxy-substituted aldehydes, ketones, carboxylic acids and their derivatives. This reaction affords bi- or polycyclic adducts whose further transformations provide the target compounds containing the desired group. *p*-Quinones or *in situ* generated dehydroarenes are used most often as dienophiles, while derivatives of butadiene, furan, isobenzofuran (phthalide), *etc*. containing the appropriate substituents are employed as dienes. These reactions often produce *p*-quinones containing *peri*-oxocarbonyl group. Being components of a redox system, the latter compounds are easily and reversibly converted to phenols (in this case, to *peri*-hydroxycarbonyl compounds); therefore, it is not without reason that they are subjects of discussion in this review.

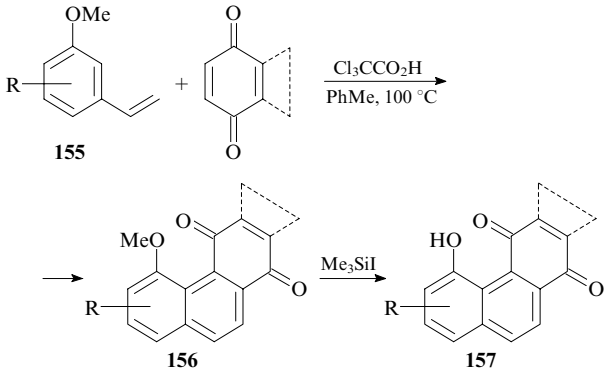
The reaction of *p*-quinones with acyl butadiene derivatives gives first adducts **151**, which undergo oxidative aromatization under the action of atmospheric oxygen or specially added oxidants under the Diels – Alder reaction conditions.[136–158] The *peri*-oxocarbonyl compounds **152** thus formed are readily reduced to the corresponding *peri*-hydroxycarbonyl compounds **153**, for example, by means of sodium dithionite ($Na_2S_2O_4$).[140] It is noteworthy that aromatic 1,4-diols **153** are unstable and are fast converted in air to quinones **152**. In order to avoid this, adducts **151** are converted to stable *peri*-methoxycarbonyl compounds **154** (Scheme 9).[159–161]

Scheme 9

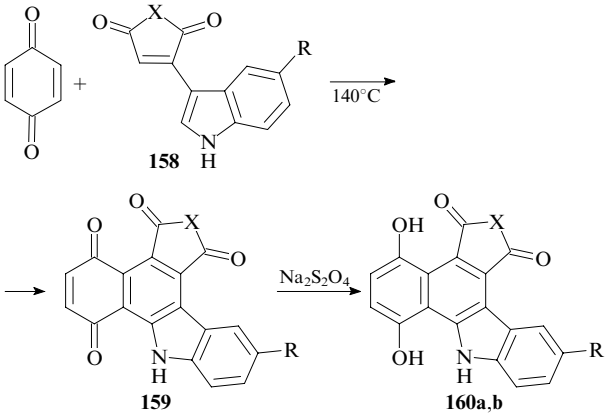


DDQ is dichlorodicyanoquinone.

This principle operates also when styrene derivatives are used as dienes. Thus the reaction of methoxystyrenes **155** with an excess of quinones gives immediately *peri*-methoxyphenanthrenequinones **156**.[162–165] The excess of quinone functions as an aromatizing reagent with respect to the initially formed hydrogenated adduct. Demethylation of methoxyquinones **156** with trimethylsilyl iodide gives *peri*-hydroxyphenanthrenequinones **157**.

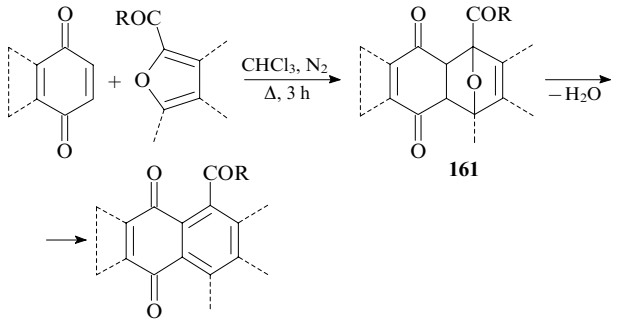


Coupling of benzoquinone with dienes **158** in which the two double bonds belong to different heterocycles immediately yields aromatic compounds **159**.[166] The reaction is carried out with heating in a sealed tube without adding an oxidant. The reduction of compounds **159** with sodium dithionite gives *peri*-hydroxy-substituted anhydrides **160a** (X = O) or imides **160b** (X = NH).

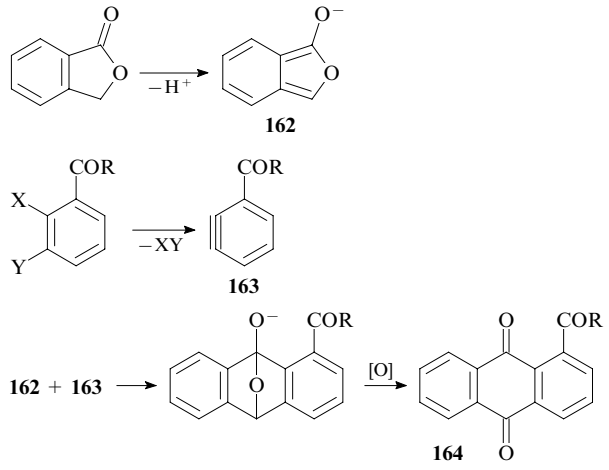


X = O (**160a**), NH (**160b**).

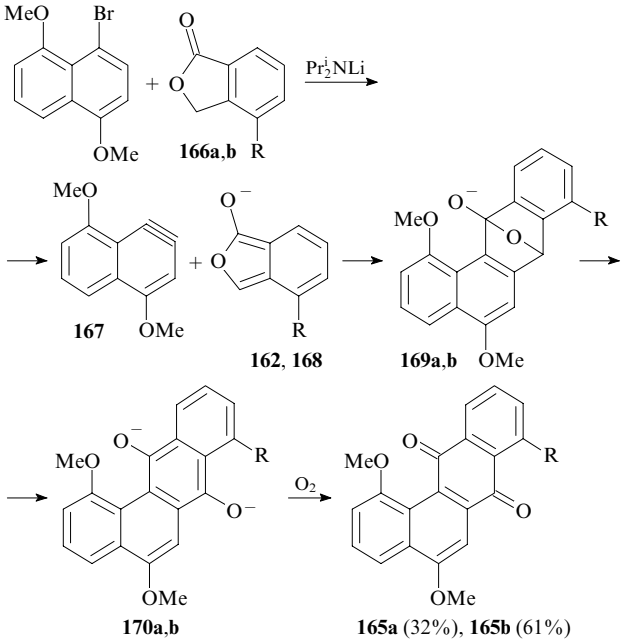
p-Quinones react with 2-acylfuran derivatives to give initially adducts **161**, which represent epoxy derivatives; under the reaction conditions, they eliminate a water molecule to be converted to *peri*-oxocarbonyl compounds.[167, 168]



On treatment with strong bases, phthalides produce isobenzofuran anions **162**, which can undergo the Diels–Alder reaction with acyl-substituted dehydroarenes **163** generated under the action of the same bases to give epoxy adducts, which are converted to *peri*-quinonecarbonyl compounds **164** under the reaction conditions.[169, 170]



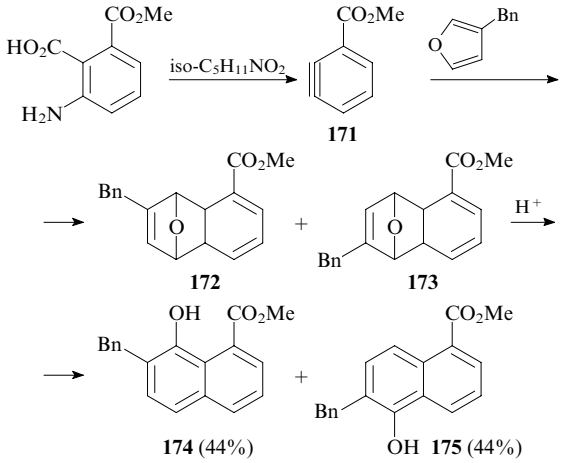
A similar approach was used to synthesize so-called angucyclins **165a**,**b** [171, 172] from 1-bromo-4,8-dimethoxynaphthalene and phthalides **166a**,**b**. The reaction occurs *via* dehydronaphthalene **167**, which reacts with phthalide enolates **162**, **168** yielding adducts **169a**,**b**. These products converted to dianionoid intermediates **170a**,**b**, which are oxidized with atmospheric oxygen under the reaction conditions to angucyclins **165a**,**b**.[171, 172]



R = H (**a**), MeO (**b**).

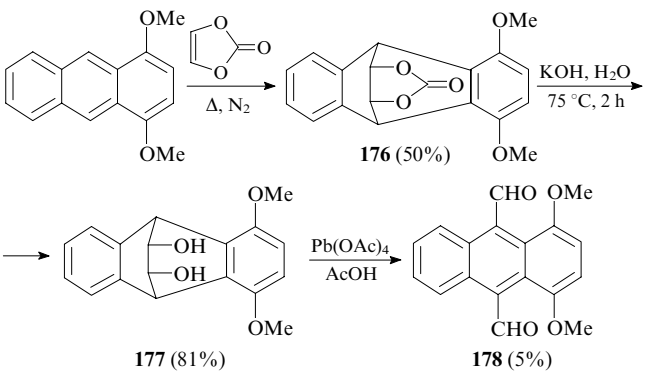
This method is widely used for the synthesis of other angucyclin antibiotics containing a similar *peri*-methoxyquinone group.[173–182]

Methyl dehydrocarboxylate **171** reacts with 3-benzylfuran to afford a mixture of epoxides **172** and **173** (1 : 1) in an overall yield of 72%. The unseparated mixture was treated with concentrated hydrochloric acid with heating to give a mixture of hydroxynaphthylcarboxylates **174** and **175**, which was separated into individual compounds by flash chromatography.[183] Isomerization of epoxides **172** and **173** to the corresponding hydroxy derivatives is stereoselective giving only one of the two possible hydroxynaphthylcarboxylates, which is due to participation of the benzyl group in delocalization of the positive charge arising upon protonation of epoxides.



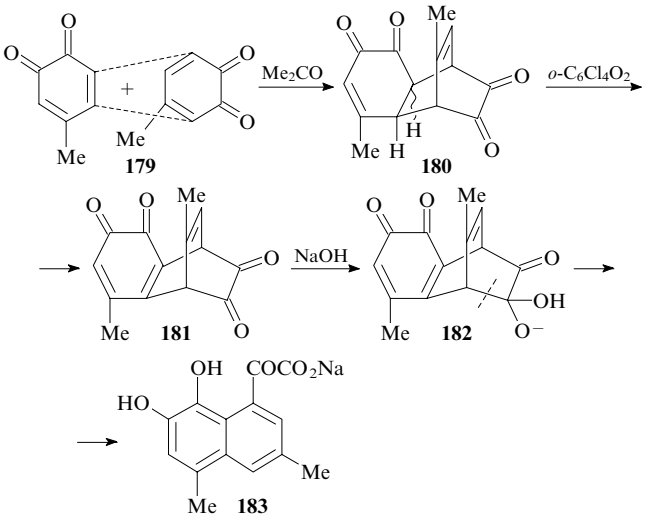
7. Other electrocyclic reactions used in the synthesis of *peri*-R-oxycarbonyl compounds

An original method for the introduction of the *peri*-methoxyformyl group into the anthracene nucleus is based on the cycloaddition of vinylene carbonate to 1,4-dimethoxyanthracene, the subsequent hydroxylation of adduct **176** and oxidation of diol **177** resulting in bis(*peri*-methoxyaldehyde) **178** (although in a very low yield).[184–186]

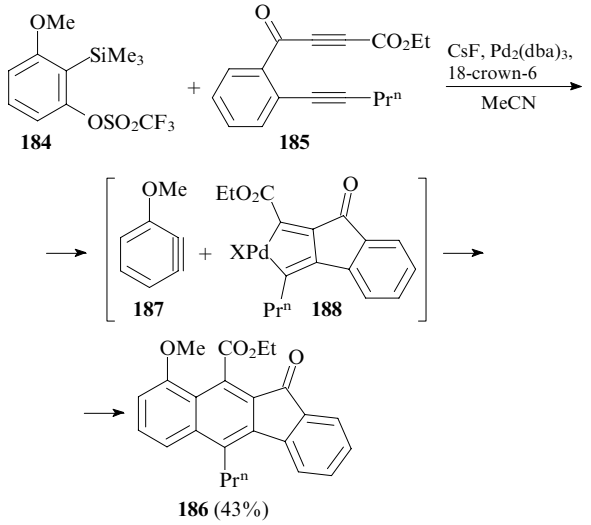


The introduction of the *peri*-hydroxy(carboxycarbonyl) group to the naphthalene nucleus is based on dimerization of 1,2-benzoquinone **179** resulting in adduct **180**. Dehydro-

genation of adduct **180** followed by alkaline treatment of cage *o*-quinone **181** gives intermediate **182**, which is converted to sodium *peri*-hydroxy-substituted carboxy ketone **183** upon a sigmatropic rearrangement.[187]

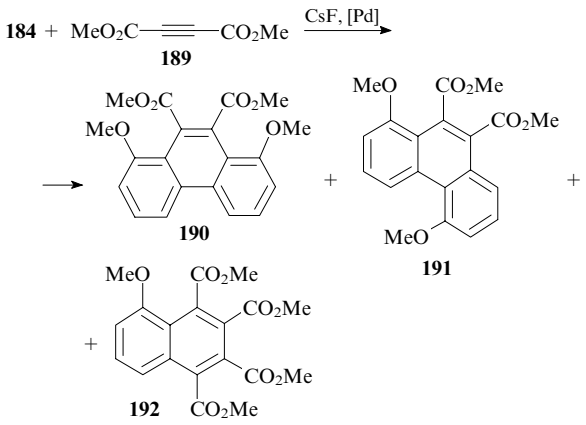


The reaction of compound **184** containing trimethylsilyl and triflate groups at vicinal carbon atoms with diethynyl ketone **185** occurs as palladium-catalyzed [2 + 2 + 2]-cycloaddition under argon at room temperature in the presence of a palladium complex to give *peri*-methoxy carboxylate **186**.[188] Presumably, the reaction proceeds *via* intermediates **187** and **188**.

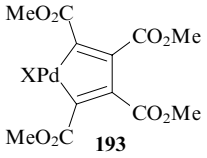


dba is dibenzylideneacetone.

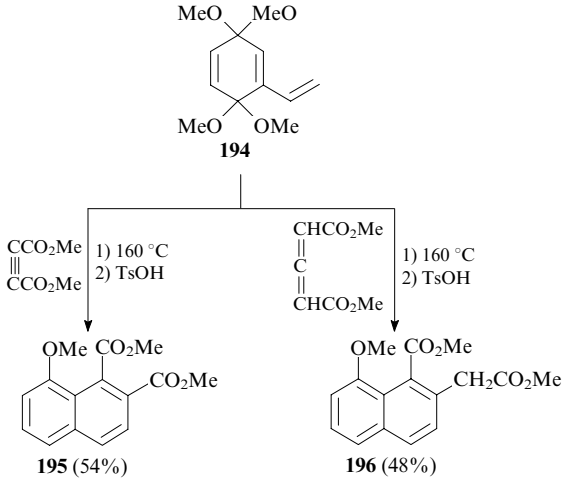
The reaction of compound **184** with dimethyl acetylenedicarboxylate (**189**) in the presence of caesium fluoride and palladium catalyst produces a mixture of *peri*-methoxy-substituted methyl carboxylates with phenanthrene (compounds **190** and **191**) or naphthalene (compound **192**) cores.[189] The product ratio is controlled by the type of the palladium catalyst. Indeed, in the presence of $Pd(PPh_3)_4$ as the catalyst, the yields of products **190**, **191** and **192** were 23%, 60% and 6%, respectively, whereas with $Pd_2(dba)_3$, these yields are 3%, 11% and 82%, respectively.



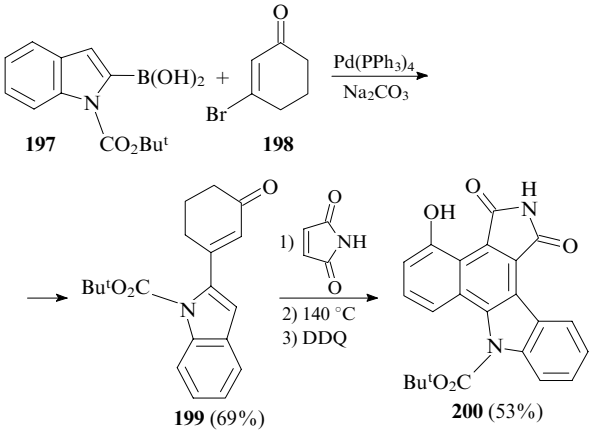
Pena *et al.*[189, 190] believe that naphthalene derivative **192** is formed from palladium complex **193**.



Methyl acetylene- and allenedicarboxylates undergo the Diels–Alder reaction with vinylquinone **194** bis-ketal at 160 °C. The adducts formed in this reaction undergo acid-catalyzed aromatization to give *peri*-methoxycarboxylates **195** and **196**, respectively.[158]



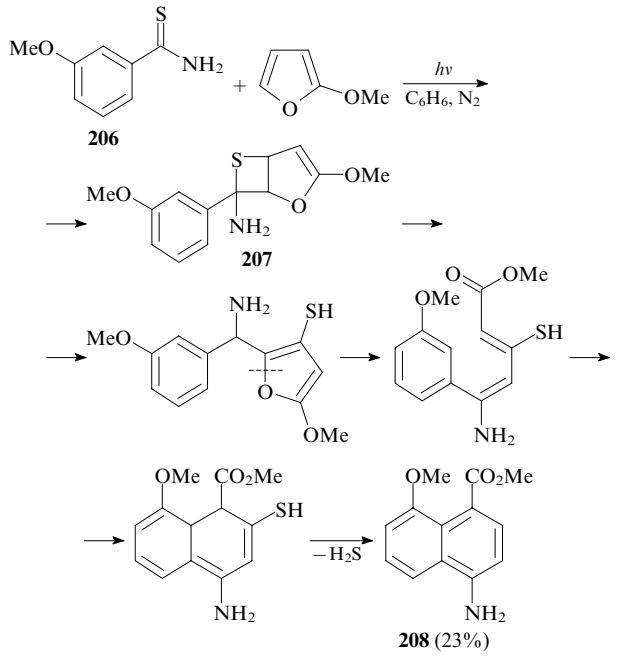
The reaction of indolylboronic acid **197** with 3-bromocyclohex-2-enone (**198**) gives diene **199** the reaction of which



with maleimide followed by aromatization of the resulting adduct furnish *peri*-hydroxy carboxamide **200**.[166]

In the modelling of approaches to the synthesis of the natural antibiotic fredericamycin, a new method for the design of functional derivatives of naphthalene was developed. The key steps of the synthesis include coupling of cyclic thioacetal of dimethoxybenzaldehyde **201** with 6-iodo-1-trimethylsilylhex-1-yne giving adduct **202** and intramolecular oxidative [4 + 2]-cyclization of compound **203**, the protected product of oxidation of adduct **202**. Deprotection and O-acylation of the cyclization product **204** produce the target *peri*-methoxy carboxylate **205** (Scheme 10).[191]

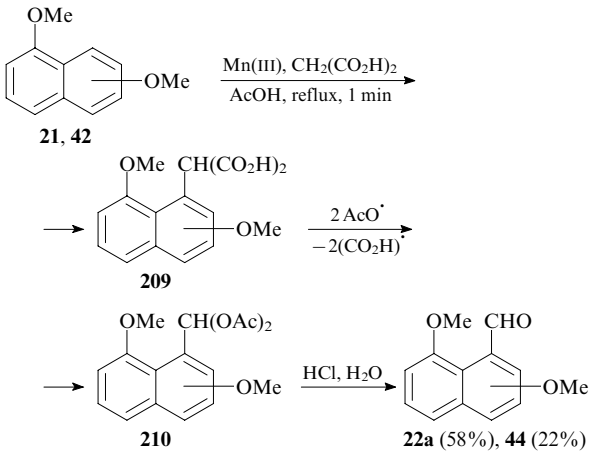
Irradiation of a benzene solution of a mixture of thioamide **206** and 2-methoxyfuran with a mercury lamp under nitrogen induces [2 + 2]-cycloaddition to give adduct **207**, which is converted to *peri*-methoxy carboxylate **208** after a series of intramolecular rearrangements.[192]



8. Miscellaneous methods

This Section considers the methods for constructing the *peri*-R-oxy- and *peri*-oxocarbonyl groups based on reactions that are not covered by the general patterns described above.

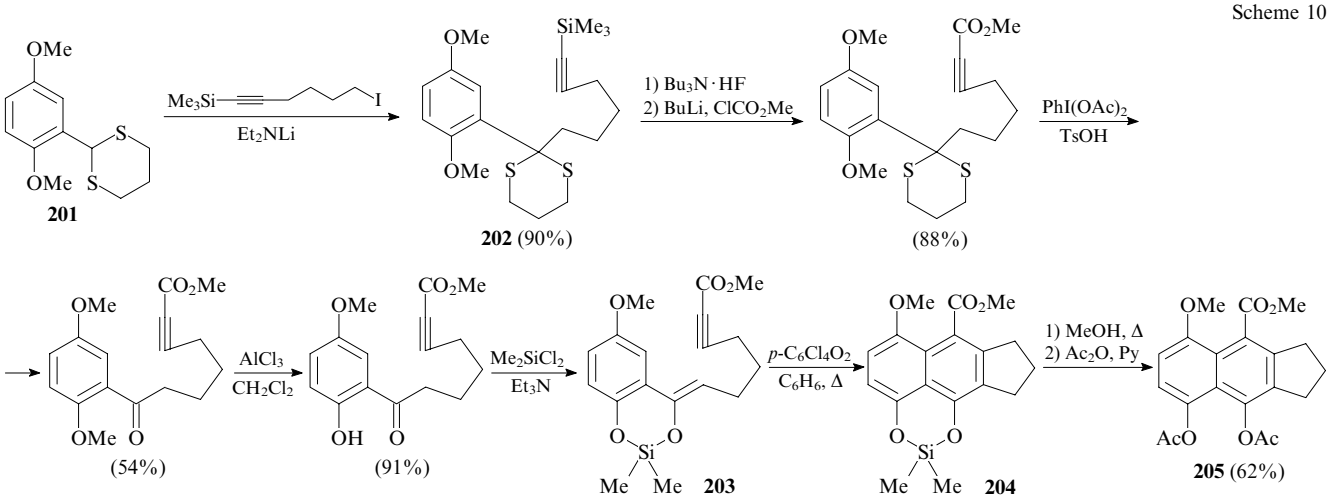
Nishino *et al.*[193] proposed an original method for the synthesis of *peri*-methoxynaphthaldehydes based on the reaction of dimethoxynaphthalenes with malonic acid in the presence of a Mn(III) catalyst. The reaction was assumed to follow a free-radical mechanism involving a dicarboxymethyl radical $^{\bullet}CH(CO_2H)_2$, which attacks the 1,5- (**21**) or 1,7-dimethoxynaphthalene (**42**) molecule to give intermediate **209**. Under the reaction conditions, two carboxyl radicals are successively eliminated from this intermediate, while two acetoxyl radicals are added to give acylal **210**, which is hydrolyzed upon acidification to give the corresponding aldehyde **22a** or **44**.[193] It was noted that the dicarboxymethyl radical attacks the aromatic nucleus at the position having the highest electron density, this process being most effective when the ionization potential of the aromatic substrate is lower than 7.8 eV.



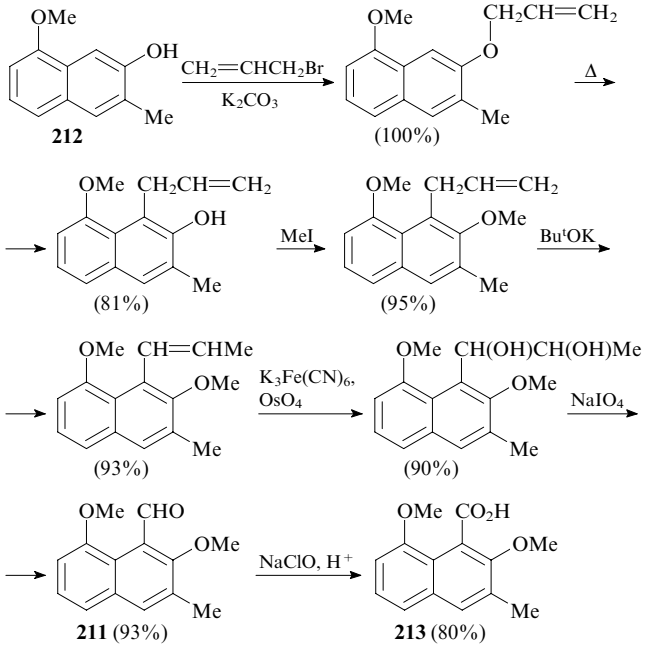
Mn(III) = $[Mn_3O(OAc)_7 \cdot (AcOH)] \cdot 5\,H_2O$.

A multistep synthetic approach was proposed for preparing *peri*-methoxynaphthaldehyde **211**. This approach uses 8-methoxy-3-methyl-2-naphthol (**212**) as the starting compound. The process comprises several rearrangements and oxidative transformations. At the final step, aldehyde

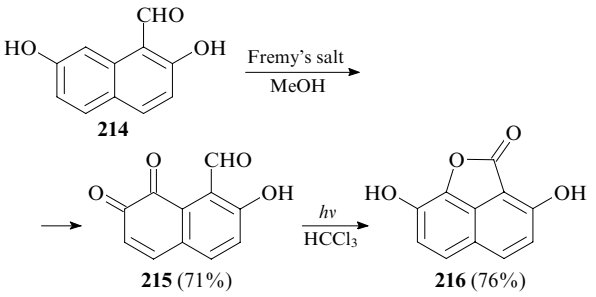
Scheme 10



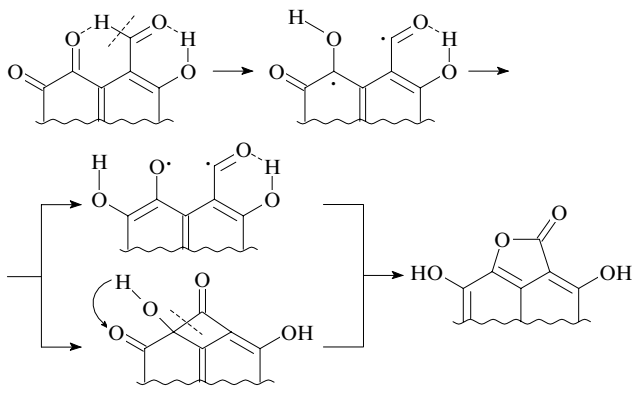
211 is converted to natural *peri*-methoxynaphthoic acid **213**.[194]



Free-radical oxidation of hydroxyaldehyde **214** with Fremy's salt results in *peri*-oxonaphthaldehyde **215**. When this is kept in chloroform for several hours at natural light and room temperature, redox reaction takes place to give ultimately naphtholactone **216**.[195] This route was used to prepare some natural naphtholactones.[195, 196]

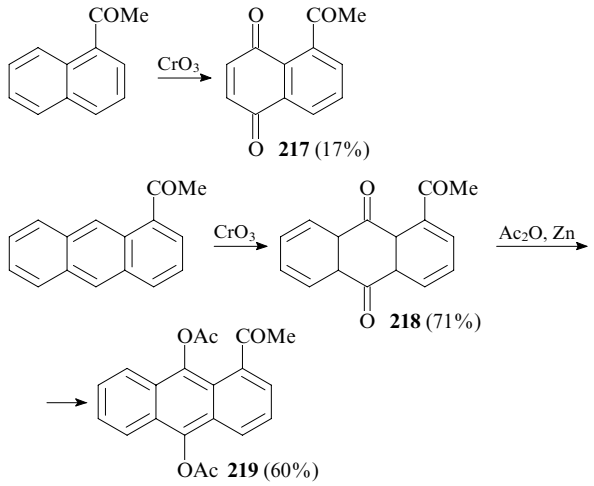


The redox transformation is assumed to proceed through homolytic cleavage of the H—CO bond; this is facilitated by the planar conformation of *ortho*-hydroxy-*peri*-oxoaldehyde **215** stabilized by intramolecular hydrogen bonds O—H···O and C—H···O. The free radical intermediates

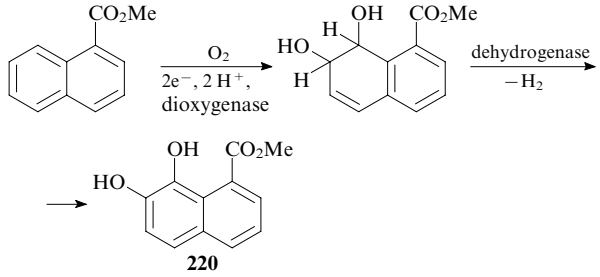


thus formed isomerize to naphtholactone according to one of the possible alternative mechanisms.[195]

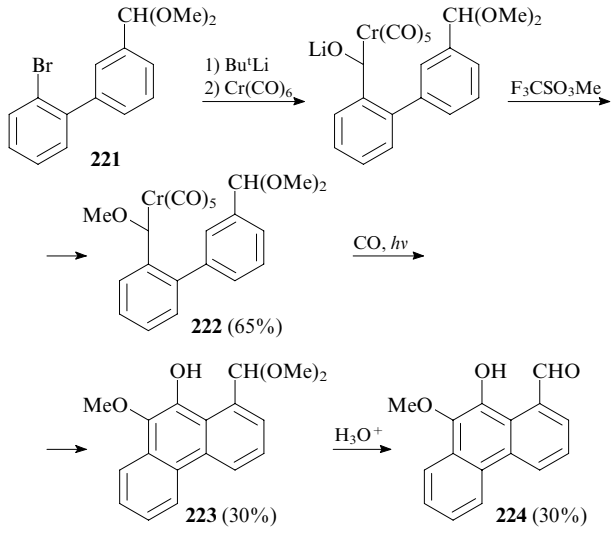
The oxidation of 1-acetylnaphthalene and 1-acetylanthracene with chromic anhydride yields *peri*-oxo-substituted acetylnaphthoquinone **217** and acetylanthraquinone **218**, respectively.[197] The latter is converted to *peri*-acetoxy ketone **219** upon reduction by zinc in acetic anhydride.[198]



A biochemical method for the construction of the *peri*-hydroxycarboxylate group was reported. Thus oxidative bioconversion of methyl 1-naphthoate by means of recombinant strains of *Escherichia coli* containing naphthalene dioxygenase and dehydrogenase genes afforded *peri*-hydroxycarboxylate **220** in a high yield.[199, 200]



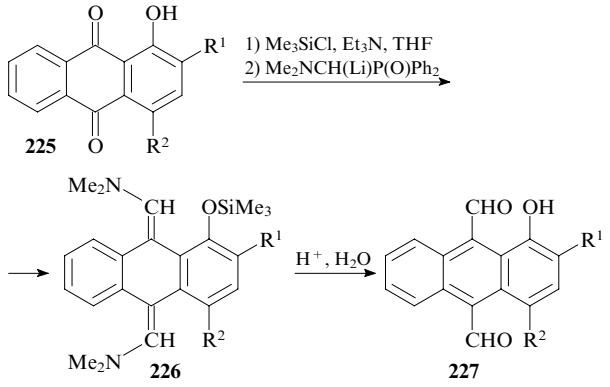
An original method for the synthesis of *peri*-hydroxyphenanthraldehyde was proposed.[201] As the starting compound, biaryl **221** was used. After lithiation, treatment with



hexacarbonylchromium and methylation, this compound was converted to pentacarbonylorganochromium intermediate **222**. The latter photochemically reacts with carbon oxide to give *peri*-hydroxy acetal **223**, which is hydrolyzed to give aldehyde **224**.

The synthesis of *peri*-hydroxy anthraldehydes starting from *peri*-hydroxy anthraquinones was patented.[185, 186]

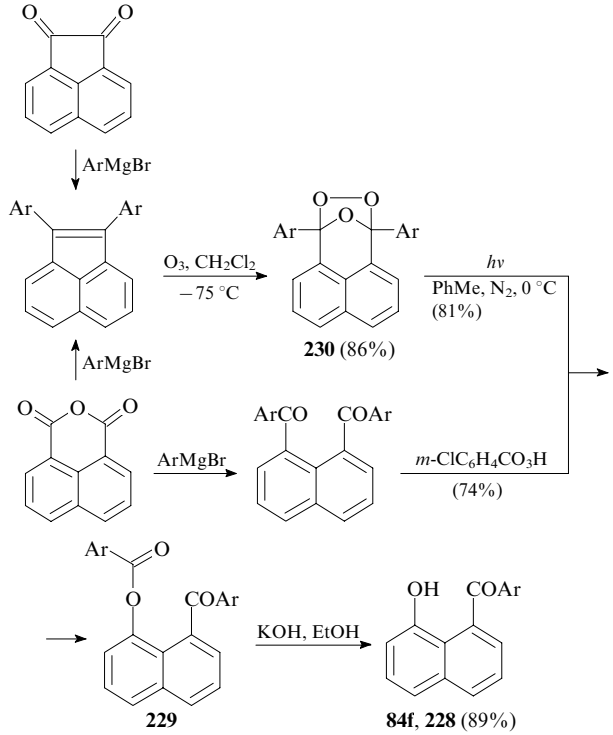
peri-Hydroxyanthraquinones **225** are introduced into the Wittig reaction, after protection of the hydroxy group, resulting in the formation of imines **226**. These products are hydrolyzed to give *peri*-hydroxyanthraldehydes **227** (the yield was not indicated).[185, 186]



225 **226** **227**

Acenaphthoquinone and naphthalic anhydride were used to prepare *peri*-hydroxy ketones **84f** and **228** (Scheme 11).[202, 203] After reaction with the Grignard reagent and oxidation, acenaphthoquinones and naphthalic anhydride were converted to *peri*-aroyloxy ketones **229**, which were converted to final products **84f** and **228** after saponification of the aroyloxy group.

Scheme 11

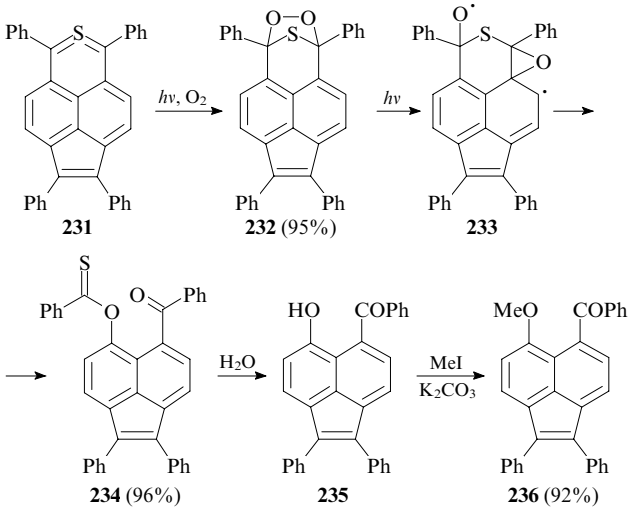


230 (86%) **229** **84f**, **228** (89%)

Ar = Ph (**84f**), *p*-$MeOC_6H_4$ (**228**).

In the case of acenaphthoquinone, ozone was used as the oxidant and in the case of naphthalic anhydride, *m*-chloroperbenzoic acid was used. For converting ozonide **230** to *peri*-aroyloxy ketone **229**, irradiation was used (the Wieland rearrangement).

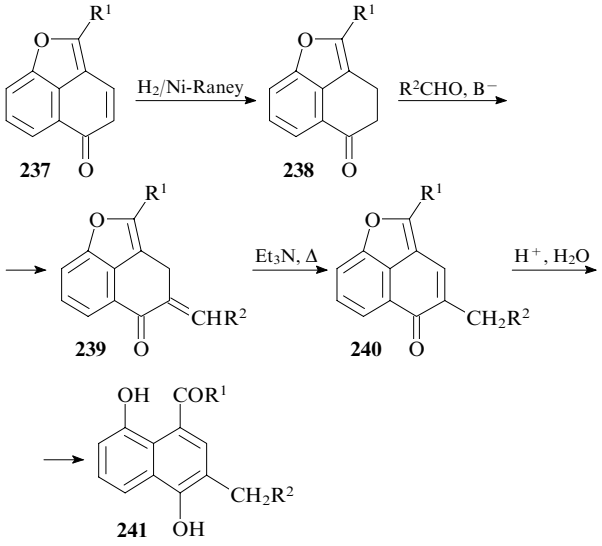
The photochemical addition of oxygen to λ^4-thiopyran (**231**) fused to acenaphthylene results in thioozonides **232**. On irradiation, their O—O bond undergoes homolytic cleavage to give biradical intermediate **233**. This product rearranges to *peri*-thioacyloxy ketone **234**.[204] Ketone **234** was transformed to acenaphthylene *peri*-hydroxy- and *peri*-methoxy-substituted ketones **235** and **236**. The synthesis of the starting thiopyrans was reported.[205–209]



231 **232** (95%) **233**

234 (96%) **235** **236** (92%)

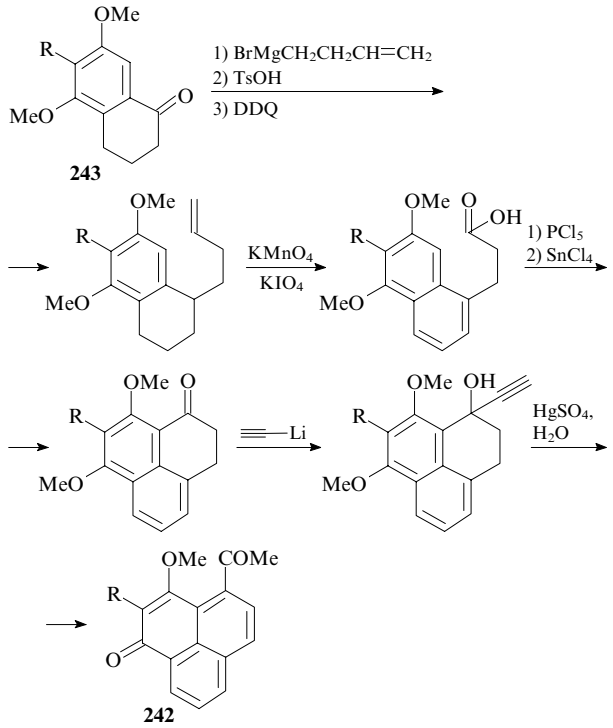
A series of works [54, 55, 210–214] devoted to the synthesis of tetracyclines propose an original method for the preparation of *peri*-hydroxy ketones based on reduction of the double bond in the quinonoid naphthofuran **237** followed by condensation of the resulting dihydronaphthofuranone **238** with aldehydes. The resulting α,β-unsaturated ketone **239** is isomerized on refluxing in anhydrous triethylamine yielding compound **240** with the quinonoid structure. Compounds **240** are latent form of *peri*-hydroxy ketones **241**, which are readily formed from **240** in acidic medium.



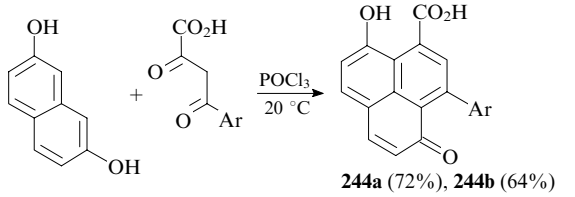
237 **238** **239** **240** **241**

B^- is base.

A multistep synthesis of phenalenone **242** containing a *peri*-methoxy ketone group starting from benzocyclohexanone **243** was proposed.[215]

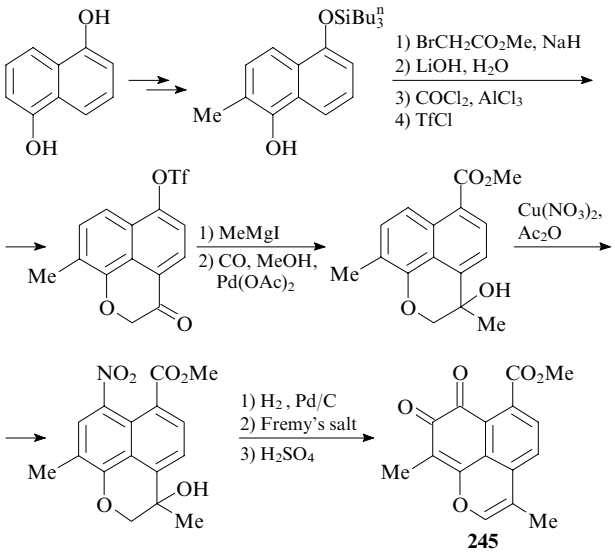


Phenalenones with *peri*-hydroxycarboxyl group (compounds **244a**,**b**) were obtained by condensation of naphthalene-2,7-diol with aroylpyruvic acids.[216]

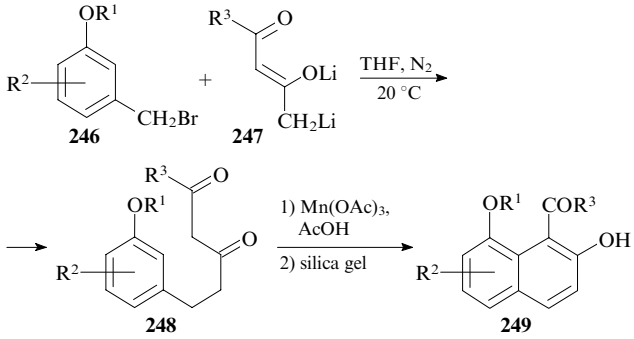


Ar = Ph (**a**), *o*-$MeOC_6H_4$ (**b**).

Naphtho[1,8-*bc*]pyran with a *peri*-oxocarboxylate group (compound **245**) was synthesized by a multistep synthesis from naphthalene-1,5-diol.[217]



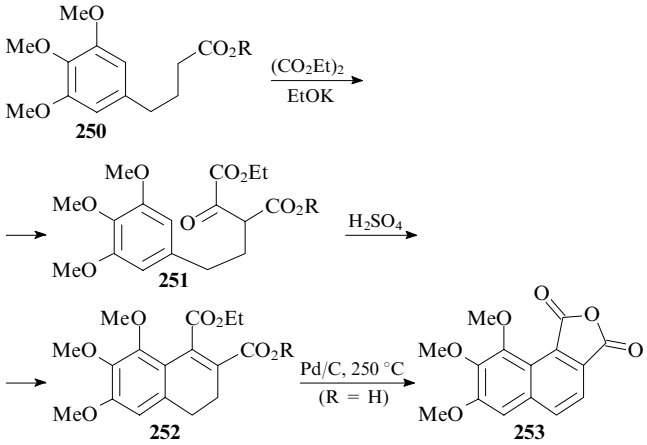
Substituted benzyl bromides **246** react with the dilithium enolates of β-dicarbonyl compounds **247** giving aryl-substituted β-diketones or β-ketocarboxylates **248**, which first undergo manganese triacetate-induced free-radical oxidative cyclization and then treatment of intermediate tetralones with silica gel induces aromatization to afford *o*-hydroxy-*peri*-alkoxy-substituted carbonyl naphthalene derivatives **249**.[218–220]



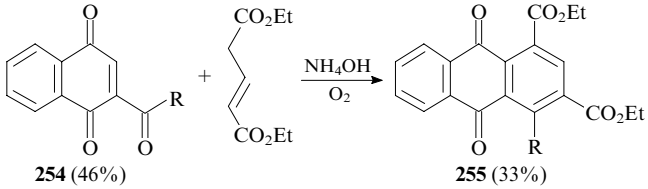
R^1 = Alk; R^2 = H, OH, OMe; R^3 = Alk, OAlk.

This approach was employed to construct polycyclic *peri*-hydroxycarbonyl compounds.[221, 222]

Acylation of compound **250** with diethyl oxalate and subsequent intramolecular acid-catalyzed cyclization of the product **251** thus formed leads to *peri*-methoxycarboxylate **252**. On heating with palladium on carbon, compound **252** is converted to *peri*-methoxy-substituted anhydride **253**. The latter was utilized in the synthesis of the natural pigment purpurogallone.[121]

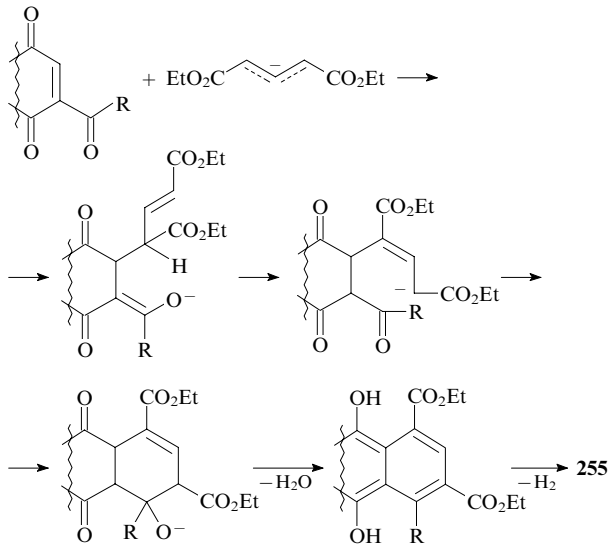


Base-catalyzed condensation of acylnaphthoquinone **254** with diethyl glutaconate results in anthraquinone **255** containing a *peri*-oxocarboxyl group.[223]

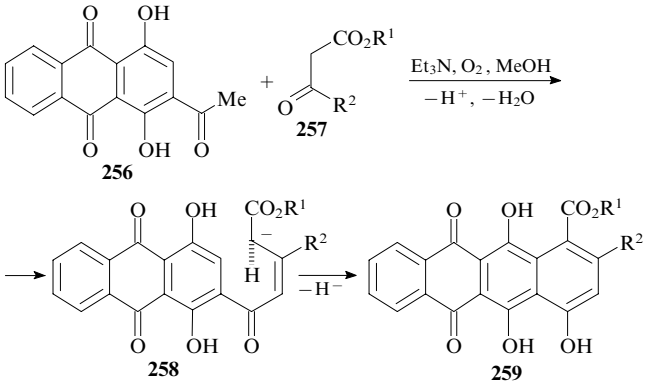


The reaction mechanism is shown in Scheme 12.

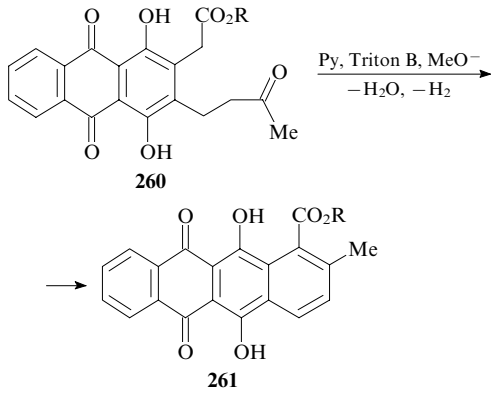
Scheme 12



In the authors' opinion,[224,225] the reaction of dihydroxyacetylanthraquinones **256** with β-keto esters **257** involves the formation of hypothetical intermediates **258** whose cyclization followed by aromatization ends in the formation of tetracyclic *peri*-hydroxycarboxylates **259**.

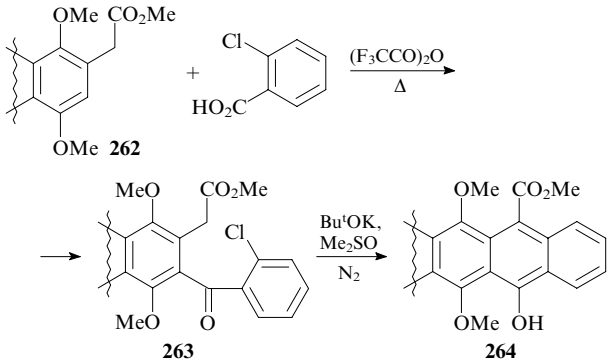


The intranolecular crotonic condensation of keto acid **260**, which is accompanied by aromatization, also ends in the formation of tetracyclic *peri*-hydroxycarboxylic acid or its esters, compounds **261**.[226]

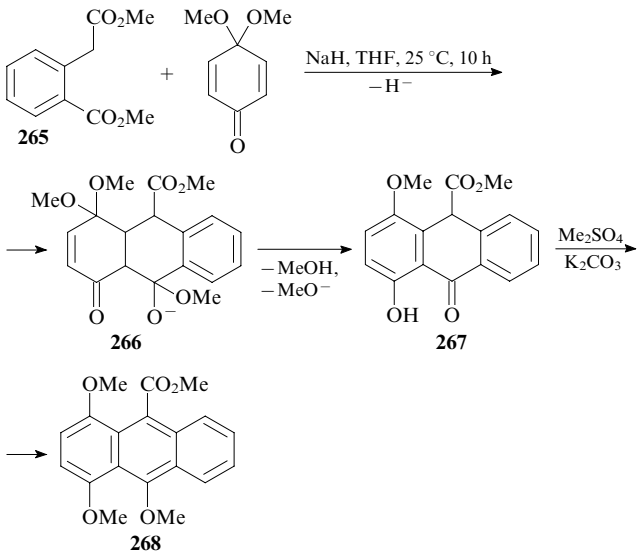


R = H, Alk.

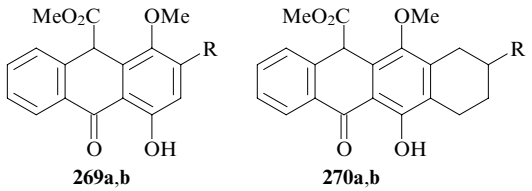
Methyl arylacetate **262** undergoes the Friedel–Crafts reaction on long-term heating with *o*-chlorobenzoic acid to give diaryl ketone **263**, which is converted to *peri*-methoxymethylcarboxylate **264** upon intramolecular nucleophilic substitution induced by treatment with potassium *tert*-butoxide.[227]



The Michael condensation of dimethyl homophthalate **265** with quinone dimethylacetal leads to intermediate **266**, which is aromatized under reaction conditions to give methyl *peri*-methoxycarboxylate **267**.[228,229]

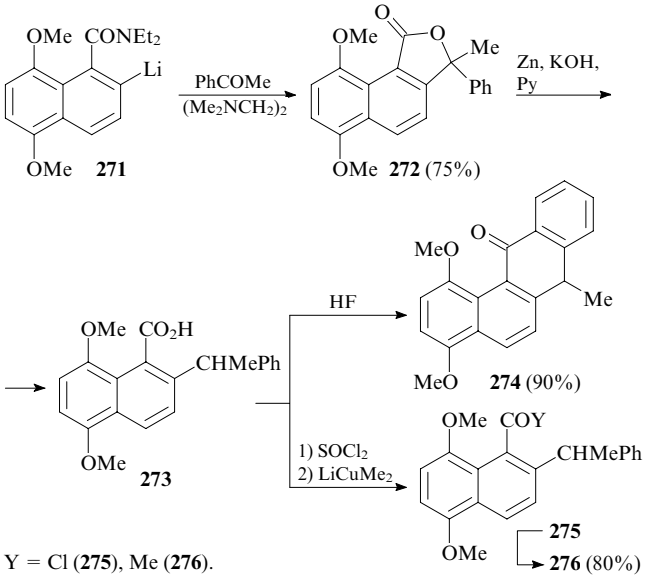


Although methylation of compound **267** yields aromatic structure **268**, the authors believe that methyl methoxycarboxylate exists in the oxo-form **267** rather than in the hydroxy form. Methyl *peri*-methoxycarboxylates **269a**,**b** and **270a**,**b** were prepared in this way in 20%–60% yields.



R = Me (**a**), Br (**b**). R = H (**a**), COMe (**b**).

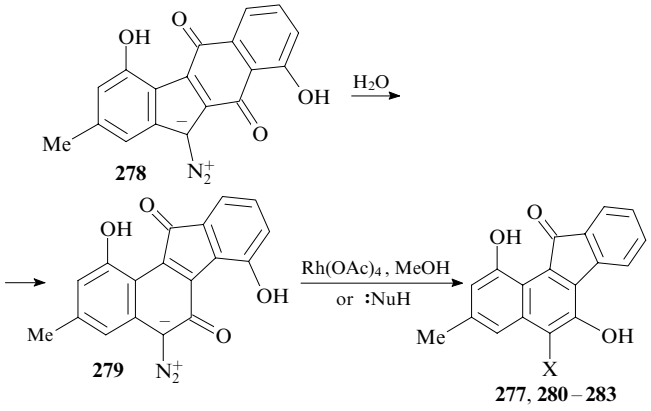
The lithiated derivative *peri*-methoxycarboxamide **271** reacts with acetophenone to give lactone **272**, which is reduced to *peri*-methoxynaphthoic acid **273** (yield 79%).



Y = Cl (**275**), Me (**276**).

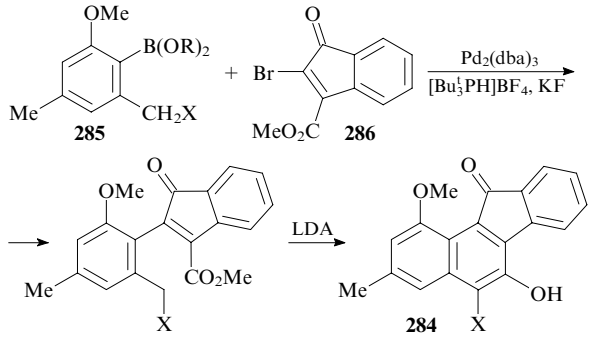
Treatment of acid **273** with hydrogen fluoride produced tetracyclic *peri*-methoxy ketone **274**, while the reaction of the chloride of this acid, compound **275**, with lithium dimethylcuprate affords *peri*-methoxy ketone **276**.[230]

The synthesis of *peri*-hydroxy ketone **277** from diazobenzo[*b*]fluorene **278** was reported. First, compound **278** is isomerized under the action of water to diazobenzo[*a*]fluorene **279**, which eliminates a nitrogen molecule under the action of rhodium tetraacetate being converted to *peri*-hydroxy ketone **277**.



X = H (**277**), NNOEt (**280**), OH (**281**), Me (**282**), Ar (**283**).

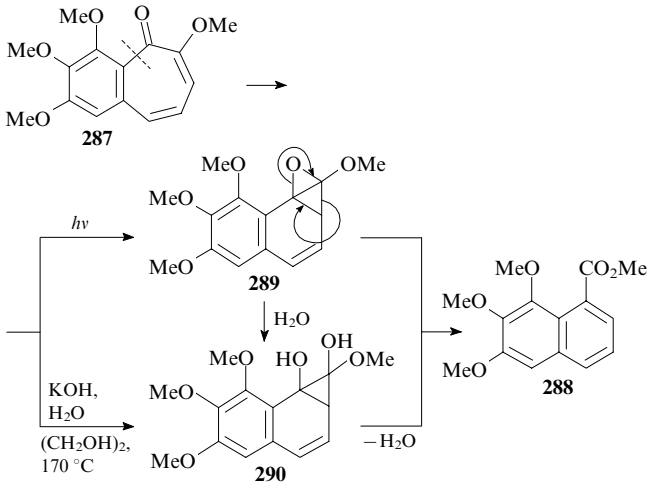
Some transformations of diazo ketone **279** involving the diazo group and resulting in *peri*-hydroxy ketones **280**–**283**



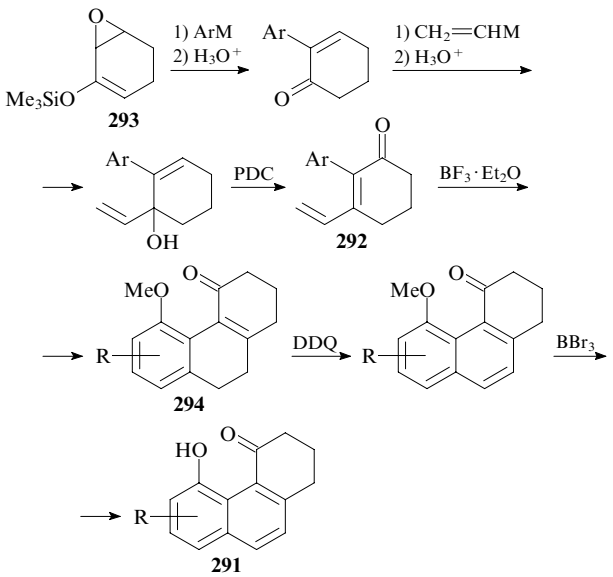
X = CN, $CONH_2$, *etc*.

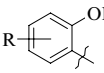
were studied.[231,232] More recently, *peri*-methoxy ketones **284** with benzo[*a*]fluorene carbon skeleton were synthesized from compound **285** and methyl 2-bromo-3-oxoindanecarboxylate (**286**).[233]

On heating with potassium hydroxide or on exposure to light, tetramethoxybenzotropone **287** is converted to methyl 6,7,8-trimethoxynaphthoate (**288**).[234] Using labelled atoms, it was shown that these transformations involve water.[235] Water can add both to the starting tropone **287** and to intermediate **289**, resulting in new intermediate **290**, which is converted to final product **288** *via* sigmatropic rearrangement and elimination of water.

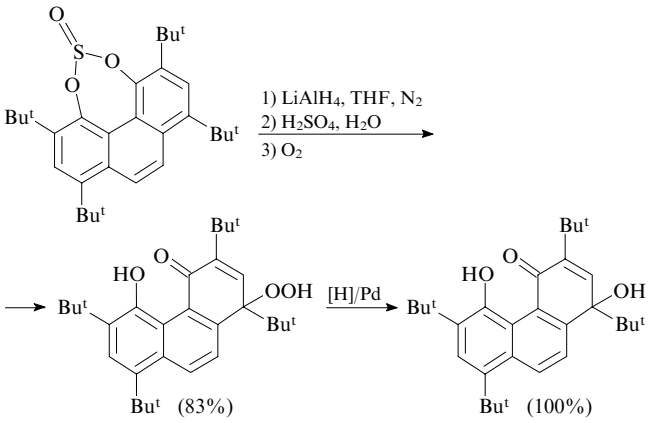


peri-Hydroxy ketone **291** with the phenanthrene carbon skeleton was synthesized using 3-vinylcyclohex-2-enone **292**, which was obtained in several steps from epoxide **293**. Diene **292** undergoes intramolecular cycloalkylation under the Friedel–Crafts reaction conditions to give dihydrophenanthrene **294**.[236] After dehydrogenation followed by demethylation, **294** is converted to *peri*-hydroxy ketone **291**.

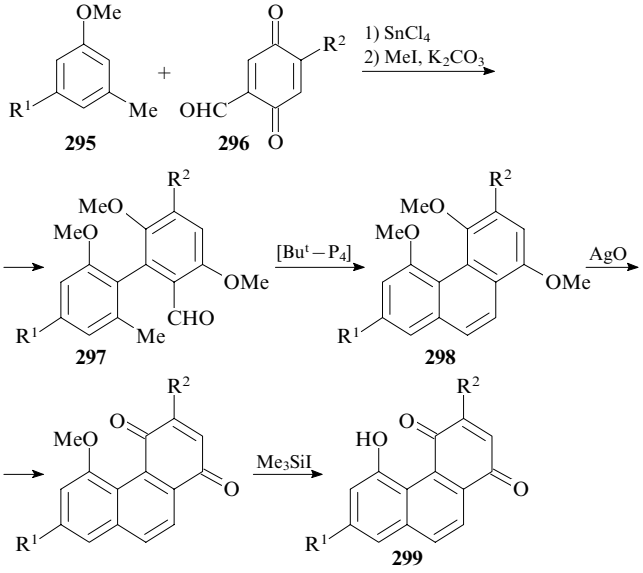


Ar =  ; M = Li, MgBr; PDC is pyridinium dichromate.

Yet another method for the preparation of *peri*-hydroxy ketone with a phenanthrene carbon skeleton was described.[237, 238]



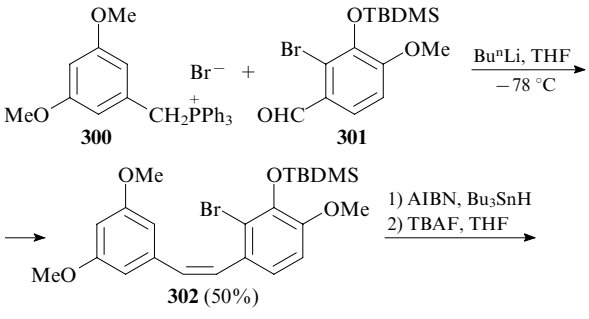
Tin chloride-catalyzed coupling of *m*-methylanisole derivatives **295** with formylbenzoquinones **296** and subsequent reductive methylation affords biphenyl derivative **297**, which undergoes intramolecular crotonic cyclocondensation to give compound **298** with a phenanthrene skeleton. The latter is converted to *peri*-hydroxyphenanthrenequinone **299** upon oxidation and demethylation.[239–243]



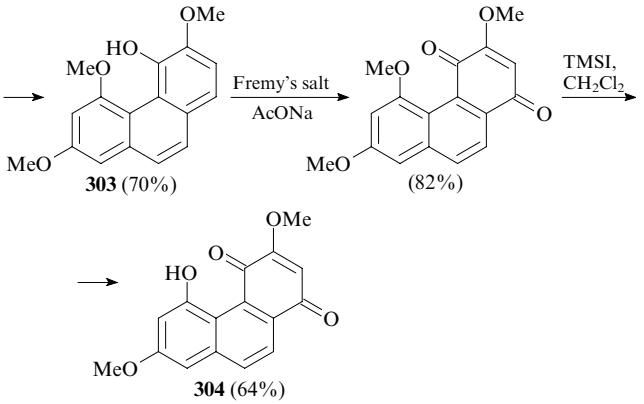
295 **296** **297** **298** **299**

[But–P4] = But NP[NP(NMe2)3]3.

The Wittig reaction of substituted benzylphosphonium salt **300** with substituted benzaldehyde **301** furnishes *cis*-stilbene **302**,[244] which is transformed to hydroxyphenanthrene **303** upon free-radical cyclization. The oxidation and the subsequent demethylation of compound **303** lead to *peri*-hydroxyphenanthrenequinone **304**.



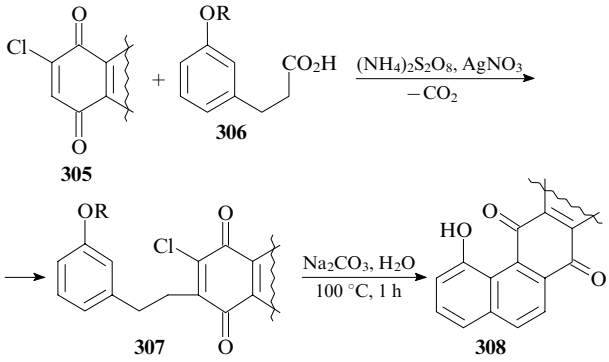
300 **301** **302** (50%)



303 (70%) (82%) **304** (64%)

TBDMS = $SiMe_2Bu^t$, AIBN is azobis(isobutyronitrile), TBAF = Bu_4NF, TMS = $SiMe_3$.

One more route for the construction of the *peri*-hydroxyquinone group is based on free-radical C-alkylation of chloroquinones **305** with β-arylpropionic acids **306** followed by cyclization of alkylation products **307** to *peri*-hydroxyquinones **308**.[245]



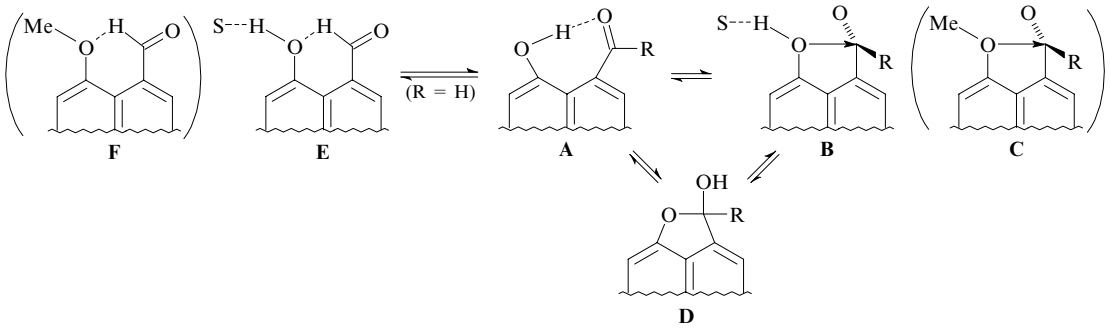
305 **306** **307** **308**

III. Types of interaction and conformations of *peri*-arranged substituents

Scheme 13 shows the possible types of intramolecular interactions of *peri*-substituents in the considered class of compounds.[246]

These interactions include the classical intramolecular hydrogen bond (structure **A**).[247] The rupture of this bond induced by polar solvents (S) produces intermolecular hydrogen bond with the solvent and creates conditions for implementation of another effect that can be considered as intramolecular attractive electrophile–nucleophile interaction of *peri*-arranged substituents (structure **B**) where the free electron pair of the hydroxyl oxygen atom is electrostatically 'attracted' to the electron-deficient carbon atom of the carbonyl group. This interaction also exists as the only one possible interaction in *peri*-methoxycarbonyl derivatives (structure **C**) and can be regarded as an initial stage of addition of O-nucleophile to the carbonyl group. Both types of intramolecular interactions of *peri*-substituents giving structures **A** and **B** can be the driving force of the reaction, resulting in the closure of a five-membered heterocycle (structure **D**). These interactions model the acid or

Scheme 13



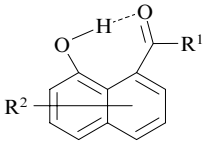
base catalysis of the reaction of the carbonyl group with nucleophiles. If an aldehyde group acts as the carbonyl function, one more type of interaction is possible: the hydrogen atom of the CH-acidic formyl group interacts electrostatically with the free electron pair of the *peri*-located oxygen atom of the hydroxy (structure **E**) or methoxy group (structure **F**). This type of interaction can be regarded as the formation of weak intramolecular hydrogen bond.[247, 248]

In solutions of *peri*-hydroxycarbonyl compounds, structures **A** ⇄ **B** and **A** ⇄ **E** exist in dynamic equilibrium, which is reflected in the IR, UV and NMR spectra.

This Section deals with spectroscopic, X-ray diffraction and quantum chemical investigations of *peri*-hydroxy- and *peri*-methoxycarbonyl compounds; in addition, attention is paid to the effect of rigidity of the polycyclic system (the presence of the ethylene or vinylene bridge) on the strength of interactions between the *peri*-located substituents.

1. Hydrogen bond

The presence and strength of the intramolecular hydrogen bond (IntraHB) in the seven-membered H-ring of *peri*-hydroxycarbonyl compounds



can be judged considering the change of the carbonyl stretching band ($\nu_{C=O}$) in the IR spectra recorded for solutions in various solvents.

The formation of an intramolecular hydrogen bond (structure **A**) is indicated by a lower-frequency shift of the $\nu_{C=O}$ band (to about 1640 – 1650 cm^{-1}), while the formation of an intermolecular hydrogen bond (InterHB, structure **B**) is indicated by a higher-frequency shift (to about 1690 – 1700 cm^{-1}). If the solution contains both forms **A** and **B**, two bands occur in the IR spectrum; if there is only one form, there is a single band. The equilibrium position is dictated by the solvent basicity. For equal molar concentrations of various *peri*-hydroxycarbonyl compounds, the intensity ratio of the absorption bands (peak heights) reflects the ratio of conformers **A** and **B** (**A** and **E**) present in this solvent (see Scheme 13). The stronger the IntraHB, the higher the content of conformer **A** in solution and the more intense the band corresponding to this species. Thus, the intensity ratio of the carbonyl bands in basic and neutral solvents can be used to qualitatively or semiquantitatively estimate the relative strengths of the intramolecular hydrogen bonds (Table 3).

A comparison of the ratios of conformers **A** and **B** in solutions in carbon tetrachloride, chloroform and tetrahydrofuran taken from the literature[2, 3, 20, 79, 246] permits one to arrange compounds presented in Table 3 in the order of decreasing the IntraHB strength as follows:

12 > **13a** > **70** > **84a** > **72a** > **84p** > **84m** > **79** > **84n** > > **84o** > **84b** > **84f**.

The numerical values obtained by this measurement method are dictated by the activation energy of **A** → **B** or **A** → **E** 'conformerization' rather than by the IntraHB energy in the ground state of conformer **A**. It is clear that the values found by this simplified method should not be identified with the results of another, more rigorous experimental estimate of the hydrogen bond strength (energy) based on the correlations between the position, width and intensity of the O – H vibration band.[247, 249]

As follows from the data presented in Table 3, high-frequency mode $\nu_{C=O}$ in tetrahydrofuran has a lower value for *peri*-hydroxynaphthaldehyde **84a** (1680 cm^{-1}) than for *peri*-hydroxynaphthyl methyl ketone **84b** (1708 cm^{-1}) and is equal to that for *peri*-methoxynaphthaldehyde;[3, 246] this may be attributed to the existence of *peri*-methoxy- and *peri*-hydroxynaphthaldehydes in conformations **F** and **E**, respectively, in which the coplanar arrangement of the aldehyde group and the naphthalene nucleus is maintained by an IntraHB between the formyl hydrogen atom and the hydroxyl (or methoxyl) oxygen atom.

The conclusion about the strength of IntraHB in *peri*-hydroxynaphthoic acid **72a** based on the intensity ratio of the absorption bands corresponding to forms **A** and **B** should be drawn with some caution, because intermolecular associates and some other structures can be formed due to the presence of the carboxy group.

It follows from the data presented in Table 3 that the dimethylene (or vinylene) bridge connecting the carbon atoms in positions 4 and 5 contributes to strengthening of IntraHB. The acenaphthene *peri*-hydroxyaldehyde **12** shows only the low-frequency band at 1660 cm^{-1} in both inert (CCl_4, $CHCl_3$) and highly basic (THF) solvents. The IR spectra of *peri*-acetyl-(hydroxy)acenaphthene (**13a**) and -acenaphthylene (**70**) in carbon tetrachloride also exhibit only the low-frequency band at 1640 cm^{-1} corresponding to form **A**; however, in THF, ~10% – 12% of molecules exist in form **B** (**A** : **B** = 7 : 1), which is accompanied by the appearance of a weak high-frequency band at 1700 cm^{-1}.

Table 3. Position and intensity of the carbonyl absorption band in the IR spectra of *peri*-hydroxycarbonyl compounds in solutions in carbon tetrachloride, chloroform and tetrahydrofuran.[2, 3, 20, 79, 246]

Compound	R^1	R^2	Form	CCl_4		$CHCl_3$		THF	
				$\nu_{C=O}$ / cm^{-1}	intraHB form (**A** : **B** ratio)[a] (%)	$\nu_{C=O}$ / cm^{-1}	IntraHB form (**A** : **B** ratio)[a] (%)	$\nu_{C=O}$ / cm^{-1}	IntraHB form (**A** : **B** ratio)[a] (%)
12	H	4,5-CH_2CH_2	**A**	1660	100	1660	100	1660	100
			B	–		–		–	
13a	Me	4,5-CH_2CH_2	**A**	1640	100			1640	88
			B	–				1700	(7 : 1)
70	Me	4,5-CH=CH	**A**	1640	100			1640	88
			B	–				1700	(7 : 1)
84a[b]	H	H	**A**	1660	100	1660	100	1660	~50–60
			B	–		–		1680	(~2 : 1)
72a	OH	H	**A**	1659	43	1660	33	1671	60
			B	1694	(3 : 4)	1687		1732	(3 : 2)
						(1 : 2)			
84p	C_4H_8N	H	**A**	1608	100	1583	100	1590	33
			B	–		–		1642	(1 : 2)
84m	EtO	H	**A**	1677	100	1676	89	1675	33
			B	–		1720		1737	(1 : 2)
						(8 : 1)			
79	MeO	H	**A**	1687	100	1679	83	1680	20
			B	–		1721		1741	(1 : 4)
						(5 : 1)			
84n	Pr^iO	H	**A**	1674	100	1665	91	1669	17
			B	–		1710		1730	(1 : 5)
						(10 : 1)			
84o	Bu^tO	H	**A**	1674	100	1670	89	1671	17
			B	–		1710		1729	(1 : 5)
						(8 : 1)			
84b	Me	H	**A**	1660	86	1660	75	–	0
			B	1694	(6 : 1)	1698		1708	
						(3 : 1)			
84f	Ph	H	**A**	1639	80	1637	50	–	0
			B	1678	(4 : 1)	1673		1681	
						(1 : 1)			

Note. The measurements were carried out for 0.5% solutions and for 1 mm-thick layer. [a] Intensity ratio of bands (peak heights). [b] The absorption band $\nu_{C=O}$ corresponding to the InterHB is manifested as an inflection on the $\nu_{C=O}$ band corresponding to IntraHB; hence, **A** : **B** ≈ 2 : 1.

The shift of the low-frequency $\nu_{C=O}$ band in the IR spectra of compounds **13a** and **70** (1640 cm^{-1}) by 20 cm^{-1} from its position in the spectrum of *peri*-hydroxynaphthyl methyl ketone **84b** (1660 cm^{-1}) is also caused by enhancement of IntraHB upon the appearance of the ethylene or vinylene bridge, which is related to the accompanying changes in the geometry of the seven-membered H-ring (bond angles and bond lengths, distances between the nonbonded atoms, torsion angles). These structural features will be considered below in the discussion of X-ray diffraction and quantum chemical data.

The stretching frequency of the *peri*-hydroxy group is also sensitive to the strength of IntraHB in conformer **A** and its content in the equilibrium mixture of conformers **A** and **B** or **A** and **E** (see Scheme 13). The more stable the seven-membered H-ring and the higher the content of conformer **A** in solution, all other factors being the same, the lower ν_{OH}.[2, 3, 20, 79, 246]

Conformation transitions in *peri*-hydroxycarbonyl naphthalene compounds are accompanied by colour effects.

In polar solvents able to break IntraHB (alcohols, ethers, tetrahydrofuran, *etc*.), esters of *peri*-hydroxynaphthoic acid (compounds **79**, **84m**–**o**) as well as *peri*-hydroxymethyl (**84b**) and *peri*-hydroxyphenyl ketones (**84f**) (see Tables 2, 3) are colourless or nearly colourless.† However, in melts or in inert solvents (carbon tetrachloride, chloroform), they are yellow, except for amide **84p**. Replacement of an inert solvent by a polar one induces shifts of the absorption bands in the electronic spectra of these compounds.

The UV spectra of the above-listed compounds have been reported.[2] Table 4 presents the long-wavelength absorption maxima in the UV spectra of some *peri*-hydroxy-substituted aldehydes and ketones of the naphthalene, acenaphthene and acenaphthylene series.[2, 3, 246]

† Exceptions are provided by partially enolyzed diketones **84g**,**h** (see Table 2) and *peri*-hydroxynaphthoic acid **72a**, which form yellow or orange solutions in polar solvents.

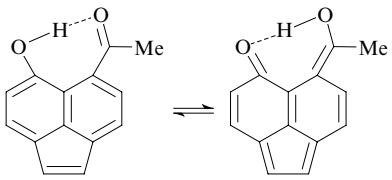
Table 4. Position of the long-wavelength absorption band in the UV spectra of some *peri*-hydroxy-substituted aldehydes and ketones.[2, 3, 246]

Compound	Solvent	λ_{max} /nm ($\log\varepsilon$)	Colour
84a	CCl_4	394 (3.52)	orange
	THF	350 (3.45)	"
12	CCl_4	414 (3.71)	red
	THF	406 (3.71)	"
84b	CCl_4	372 (3.37)	yellow
	THF	324 (3.58)	colorless
13a	CCl_4	405 (3.45) 500 (1.95)	red
	THF	399 (3.56) 500 (2.21)	"
70	CCl_4	378 (3.40) 503 (2.90)	"
	THF	374 (3.49) 417 (3.23) 500 (2.70)	"

As follows from the presented data, on passing from an inert solvent (carbon tetrachloride) to a highly basic solvent (tetrahydrofuran), in the spectra of both *peri*-hydroxynaphthaldehyde **84a** and *peri*-hydroxynaphthyl methyl ketone **84b**, the band is shifted hypsochromically from 394 to 350 nm and from 372 to 324 nm, respectively. Although the long-wavelength absorption maxima of compounds **84a**,**b** are below 400 nm, carbon tetrachloride solutions of these compounds have intense orange colour, because absorption also continues above this value. The colour of the solution of *peri*-hydroxy ketone **84b** is due to the presence of conformer **A**, whereas the solution of conformer **B** is colourless. A solution of aldehyde **84a** in tetrahydrofuran remains coloured because IntraHB is cleaved only in ~30% of the molecules (see Table 3), whereas in the case of *peri*-hydroxy ketone **84b**, conformer **A** is fully replaced by conformer **B** through intermolecular hydrogen bonding between the substrate and the solvent. In addition, the carbonyl group of conformer **E** of aldehyde **84a** remains in the naphthalene ring plane, owing to interaction of the formyl hydrogen atom with the lone pair of the *peri*-hydroxy group oxygen, and, hence, it is conjugated with the ring π-system, whereas the carbonyl group of conformer **B** of ketone **84b** is rotated through a substantial angle relative to the naphthalene ring plane and is almost completely removed from conjugation.[6]

The position of the long-wavelength absorption band (λ_{max}) in the UV spectra of acenaphthene *peri*-hydroxy aldehyde **12** and *peri*-hydroxy ketone **13a** is nearly the same in carbon tetrachloride and in tetrahydrofuran (see Table 4), which is in line with high (about 100%) content of conformer **A** in these solutions (IR spectroscopy data, Table 3). Solutions of compound **12** and **13a** in carbon tetrachloride and in tetrahydrofuran are intensely red coloured due to non-zero light absorption at 500 nm ($\log\varepsilon \approx 2$). The bathochromic shifts of the long-wavelength absorption maximum of acenaphthene *peri*-hydroxy aldehyde **12** and *peri*-hydroxy ketone **13a** relative to the position of this band in naphthalene derivatives **84a**,**b** are ~20 and 30 nm in carbon tetrachloride and ~55 and 75 nm, respectively, in tetrahydrofuran. This supports the conclusion based on analysis of IR spectroscopic data according to which a stronger IntraHB is formed if an ethylene unit is present between the carbon atoms in positions 4 and 5 of the naphthalene nucleus.

UV spectra of acenaphthylene *peri*-hydroxy ketone **70** differ considerably from the spectra of naphthalene and acenaphthene *peri*-hydroxy ketones **84b** and **13a**. The longest-wavelength maximum shifts to ~500 nm. However, the intensity of this band ($\log\varepsilon = 2.90$ in CCl_4 and 2.70 in THF) is much lower than that of the long-wavelength band (about 320–400 nm) of acenaphthene *peri*-hydroxy ketone **13a** (see Table 4). In the UV spectrum of compound **70** in a tetrahydrofuran solution, a band at ~420 nm appears as an inflection. The absorption ends at ~600 nm. The observed changes are undoubtedly caused by the presence of a vinylene bridge linking the carbon atoms in positions 4 and 5 of the naphthalene nucleus, which allows the *peri*-substituents to be conjugated through the naphthalene π-system, thus creating conditions for proton phototransfer from the hydroxyl to carbonyl oxygen atom and for implementation of the benzenoid–quinonoid tautomerism in the excited state. Note that a quantum chemical calculation showed[246] that in the ground state the quinonoid tautomer **70*** has no minimum on the potential energy curve and there is only one isomer of **70** with the O–H···O=C hydrogen bond.



70 **70***

The solvent effects observed in the electronic spectra are in agreement with the data from IR spectroscopy (see Table 3), which imply that the IntraHB in the *peri*-acetyl(hydroxy)acenaphthylene **70** molecule is stronger than that in *peri*-hydroxynaphthyl methyl ketone **84b** and is nearly equivalent to that in *peri*-acetyl(hydroxy)acenaphthene (**13a**).

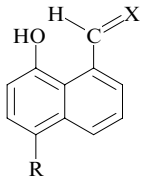
The chemical shift of the bridging proton ($\delta_{O-H\cdots O=C}$) in the ^1H NMR spectra of *peri*-hydroxycarbonyl compounds is considered[247] to be a sensitive measure of variation of the H-bond energy. Hydrogen bonding normally increases the chemical shift of this proton (deshielding), which reaches in some cases the critical range of δ_{OH} (>20 ppm). Although the degree of hydroxyl proton shielding in the NMR spectrum does not reflect unambiguously the strength of the H-bond,[247] nevertheless, the chemical shift of the proton involved in the IntraHB in the series of similar compounds is suitable for considering the energy of this bond at the qualitative and semiquantitative level.

Consider how the strength of the H-bond in *peri*-hydroxycarbonyl compounds depends on the acidity of the hydroxy group and the structure of the carbon skeleton. Table 5 presents the ^1H NMR chemical shifts of the OH and CHO groups involved in the construction of the seven-membered H-ring in *peri*-hydroxy-substituted naphthaldehydes **84a**, **138**, **309a**,**b**, acenaphthaldehyde (**12**) and *o*-hydroxynaphthaldehyde (**310**). For comparison, the proton chemical shifts of the OH and HC=NR groups in the

Table 5. ^{1}H NMR chemical shifts of hydroxy-substituted naphthaldehydes and acenaphthaldehydes and their azomethine analogues (from publications [3, 246, 250–252]).

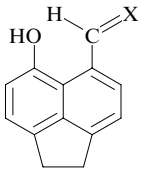
Compound	Solvent	δ_{CHO}	δ_{OH}	$\delta_{CH=N}$
84a	$CDCl_3$	9.76	11.60	
	THF	10.39	10.72	
12	$CDCl_3$	9.80	11.50	
138	$CDCl_3$	9.87	10.97	
309a	$CDCl_3$	9.84	11.65	
309b	$CDCl_3$	9.87	12.73	
310	$CDCl_3$	10.78	13.15	
311	$CDCl_3$		14.00	8.54
312	$CDCl_3$		14.40	8.54
313a	$CDCl_3$		14.60	8.60
313b	$CDCl_3$		14.70	8.30
313c	$CDCl_3$		14.83	8.56
313d	$CDCl_3$		15.10	8.25
314	$CDCl_3$			9.75

azomethine analogues **311**, **312**, **313a–d** and **314** are given in the same Table.



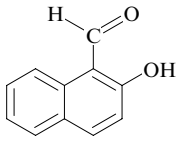
84a, **138**, **309a**,**b**, **311**, **312**, **315**

X = O: R = H (**84a**), OMe (**138**), Br (**309a**), NO_2 (**309b**); X = NPh: R = H (**311**), Br (**312**), NO_2 (**315**).

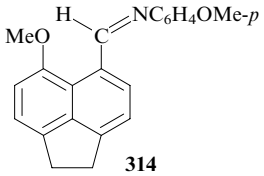


12, **313a–d**

X = O (**12**); X = NPh (**313a**), NBn (**313b**), NC_6H_4OMe-*p* (**313c**), NPr^i (**313d**).



310



314

Attention is attracted by the nearly equal values of the proton chemical shifts of the H–C=O group of compounds **138** and **309a**,**b** irrespective of the nature of the substituent R (indicating approximately equal degrees of shielding of this group) and different δ_{OH} values whose low-field shift corresponds to the increase in the acidity of the hydroxy group according to the Hammett constants of *para*-substituents,[250] which is especially obvious for 5-nitro derivative **309b**.

In the ^{1}H NMR spectra of *peri*-hydroxynaphthaldehyde **84a**, the chemical shifts of the formyl hydrogen (δ 9.76) and the *peri*-hydroxy group proton (δ 11.60) in deuteriochloroform [3] nearly coincide with those of its acenaphthene analogue **12** (δ 9.80 and 11.50, respectively).[246] However, apparently these data should not be interpreted as an indication of equal strengths of the IntraHB, which is determined by the energy required for its cleavage. As shown above, the relative strength of the IntraHB in *peri*-hydroxy aldehydes is well correlated with the ratio of conformers **A** and **E** (see Scheme 13) in solutions depending on the solvent basicity (polarity). In conformity with this characteristics, the IntraHB is stronger in acenaphthene aldehyde **12** than in naphthaldehyde **84a**. This conclusion is supported also by the calculated values of H-bond energy in compounds **84a** and **12**, which are 9 and 13 kcal mol^{-1}, respectively.[246]

If the statement that the low-field shift of the δ_{OH} value can serve as indication for the IntraHB strength is valid, then the H-bond in 2-hydroxy-1-naphthaldehyde (**310**) should be regarded as the strongest (δ_{OH} = 13.15, see Table 5).[253] However, this estimate should be treated with caution as the geometry of the six-membered H-ring in compound **310** considerably differs from the geometry of seven-membered H-ring in compounds **12** and **84a**, and, hence, the shielding and the proton chemical shift of the hydroxy group would also be different. (The chemical shifts of the hydroxyl protons in the series of salicylaldehyde derivatives fluctuate at about δ 11.[254]) One should also bear in mind the possibility of participation of the hydroxyl proton of *ortho*-substituted aldehydes and ketones in intramolecular exchange interactions, the most important manifestation of which is the benzenoid–quinonoid tautomerism, which strengthens the IntraHB and, possibly, promotes the low-field shift of the ^{1}H NMR signal of this proton. Recall that for *peri*-hydroxy-substituted carbonyl naphthalene derivatives, this type of tautomerism is in principle impossible due to specific features of their structure.

In a THF solution of *peri*-hydroxynaphthaldehyde **84a**, the signal of the formyl proton is shifted downfield (from 9.76 ppm in $CDCl_3$ to 10.39 ppm in THF) and the signal of the hydroxyl proton is shifted upfield (from δ 11.60 in $CDCl_3$ to δ 10.72 in THF), which is related to the transition of ~30% of molecules from conformation **A** with intramolecular hydrogen bond to conformation **E** with intermolecular hydrogen bond (IR spectroscopic data, see Table 3).

Proceeding from the chemical shifts of the OH-group protons, the IntraHB in the seven-membered H-ring becomes much stronger on going from *peri*-hydroxy aldehydes **84a**, **309a** and **12** to their azo analogues **311**, **312** and **313a** ($\delta_{azomethine} - \delta_{aldehyde}$ = 2.40–3.10 ppm, see Table 5).

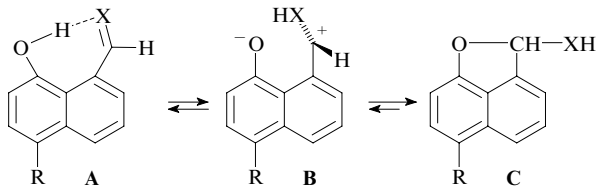
The low-field shift of the signal of the hydroxyl proton by 0.6 ppm on going from azomethine **311** to azomethine **313a** with an ethylene bridge can be interpreted as strengthening of the IntraHB. Furthermore, dependence of the IntraHB strength on the basicity of the imine nitrogen can be followed in the series of acenaphthene azomethines; this is accompanied by the low-field shift of the signals of the hydroxyl proton in the series **313a** < **313b** < **313c** < **313d**.

Thus, one can conclude that the strength of the seven-membered H-ring in the series of *peri*-hydroxy compounds presented in Table 5 depends on both the acidity of the hydroxy group proton and the basicity of the acceptor atom X, and also on either presence or absence of an ethylene unit in positions 4 and 5 of the naphthalene nucleus.

When the acidity of the hydroxy group considerably increases (for example, in 5,7-dinitro-*peri*-hydroxynaphthaldehyde), proton 'hopping' from the hydroxy group to oxygen of the aldehyde group with simultaneous closure of the five-membered heterocycle becomes possible.[250] This type of prototropism is even more characteristic of azomethines containing an electron-withdrawing substituent in the *para*-position to the hydroxy group, as in this case, apart from

enhancement of the acidity of the OH group, basicity of the acceptor atom (X) also increases.[251] For example, in azomethine **311** the equilibrium is completely shifted to form **A**, while in azomethine **312**, the **A** : **B** ratio is 1 : 2 and in azomethine **315**, only cyclic tautomer **C** is present (Scheme 14).[251]

Scheme 14

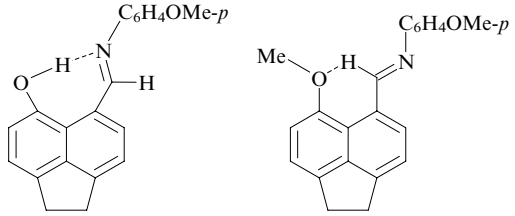


X = O, NAlk, NAr.

For acenaphthene derivatives **12** and **313a**, a similar ring–chain tautomerism is impossible due to the strain that should arise upon the closure of the second five-membered ring.

It is of interest that the chemical shifts of the methine proton in the naphthaldehyde or naphthazomethine series do not depend crucially on the nature of substituents in the naphthalene nucleus or on the geometry of the molecule as a whole; however, they differ by ~1.2 ppm on going from one series to the other (see Table 5).

The ^{1}H NMR spectrum of *peri*-methoxy-substituted azomethine **314** shows a downfield shift (1.19 ppm) of the signal for the imino-group methine proton compared with the *peri*-hydroxy analogue **313c** (see Table 5), which is related to the considerable conformational rearrangement of the *peri*-substituents accompanied by the formation of the IntraHB between the methane proton and the oxygen atom of the *peri*-arranged methoxy group. The intramolecular hydrogen bonds of this type are classified as weak H-bonds.[247]



313c **314**

The chemical shifts of the hydroxyl and methyl-group protons in the ^{1}H NMR spectra of *peri*-hydroxy-substituted naphthyl (**84b**), acenaphthenyl (**13a**) and acenaphthylenyl methyl ketones (**70**) are presented below:[246]

Compound	**84b**	**13a**	**70**
Solvent	CCl_4	$CDCl_3$	$CDCl_3$ ($DMSO\text{-}d_6$)
δ_{MeO}	2.40	2.80	2.90 (2.60)
δ_{OH}	11.50	11.60	12.90 (11.50)

Considering the downfield shift of the hydroxy-group proton as a criterion of the IntraHB strength, one can conclude that the strength of IntraHB in *peri*-hydroxy ketones **84b**, **13a** and **70** increases insignificantly in the series **84b** < **13a** < **70**. The downfield shift of the proton signals of the methyl group of these *peri*-hydroxy-substituted methyl ketones increases in the same order.

The conclusion about increase in the IntraHB strength on going from *peri*-hydroxynaphthyl methyl ketone **84b** to its acenaphthene (**13a**) and acenaphthylene (**70**) analogues, which follows from analysis of the ^{1}H NMR spectra, coincides, in principle, with the conclusion based on analysis of the IR spectra of these compounds in solutions (see Table 3).

Some disagreement of the conclusions that can be drawn upon comparison of the spectral characteristics of the acenaphthylene *peri*-hydroxy ketone **70** obtained by IR, UV and ^{1}H NMR spectroscopy is attributable to specific features of its electronic structure, which differs qualitatively from the structure of other *peri*-hydroxy ketones by the presence of conjugation between the hydroxy and carbonyl groups through the naphthalene ring π-system, which creates conditions for the existence of benzenoid–quinonoid tautomerism. The nature of the electronic effects of *peri*-substituents in compounds of this structure is largely obscure and calls for more in-depth investigations.

The structure of the seven-membered H-ring in the considered *peri*-hydroxycarbonyl compounds can be determined more strictly by means of X-ray diffraction studies. However, by the time this review was written, the Cambridge Crystallographic Data Centre did not contain data on the crystal structure of naphthalene *peri*-hydroxy aldehydes and ketones, bit did contain data on the crystal structure of acenaphthene *peri*-hydroxy aldehyde **12** and *peri*-hydroxy ketone **13a** (Table 6).[246]

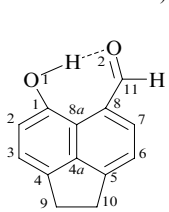
According to X-ray diffraction data, the hydrogen atom of the hydroxy group in molecules **12** and **13a** is involved in H-bonding that closes a planar seven-membered H-ring. The molecules of compounds **12** and **13a** have approximate C_s-symmetry with slight deviation from the planar structure [the O(2)C(11)C(8)C(8*a*) torsion angles for aldehyde **12** and ketone **13a** are 3.0° and 4.2°, respectively]. The O(1)HO(2) angle at the hydrogen atom is nearly linear (172.8° for compound **12** and 165.0° for compound **13a**), which attests to the strength of H-bond in the seven-membered H-rings.‡ This is a typical feature of seven-membered H-rings compared with analogous six-membered rings [the OHO angle in the six-membered H-ring of 2-hydroxy-1-naphthaldehyde molecule (**310**) was reported[255] to be 148.9°].

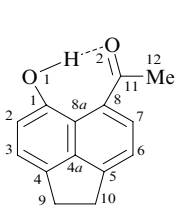
In *peri*-hydroxy ketone **13a**, the H-bond is somewhat stronger than that in aldehyde **12**; this is manifested, in particular, as shortening of the O(1)···O(2) distances in compound **13a** by ~0.08 Å (see Table 6). This effect is caused by steric factors, namely, repulsion of the methyl group and the hydrogen atom in position 7 of the naphthalene ring.

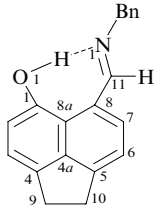
When the naphthaldehyde molecule contains two hydroxy groups in the *peri*- and *ortho*-positions to the formyl group, only the six-membered H-ring involving the formyl and *ortho*-hydroxy group is formed, as indicated by X-ray diffraction data for gossypol and its derivatives.[256,257] Unfortunately, no data on the crystal structure of acenaphthene derivatives in which the formyl group is located between the *peri*- and *ortho*-hydroxy groups are available from the Cambridge Crystallographic Data Centre. Another H-ring can be formed in this molecule.

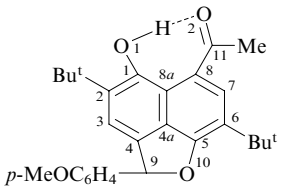
‡ It is known[247] that the strongest hydrogen bond is formed when the proton is located in the straight line between two electronegative atoms, hydrogen atom donor and acceptor.

Table 6. Bond angles, bond lengths and other interatomic distances in the seven-membered H-ring of compounds **12**, **13a**,[246] **313b** [252] and **15b** [22] according to X-ray diffraction and quantum chemical calculation data (the values in braces).[246]


12


13a


313b


15b

Angle (name)	Angle value /deg				Bond (name)	Length /Å			
	12	**13a**	**313b**	**15b**		**12**	**13a**	**313b**	**15b**
O(1)C(1)C(8*a*)	123.9(1) {125.0}	124.46(5) {125.4}	124.12	121.34	O(1)—H	0.992[a] {0.992}	0.995[a] {0.995}	1.014	1.098
C(1)C(8*a*)C(8)	130.1(1) {129.9}	131.29(5) {130.8}	130.01	132.50	O(2)···H or N(1)···H	1.600 {1.611}	1.538 {1.547}	1.560	1.402
C(8*a*)C(8)C(11)	127.5(1) {127.0}	126.09(4) {125.9}	128.26	126.15	O(1)···O(2) or O(1)···N(1)	2.587(2) {2.592}	2.511(1) {2.531}	2.566	2.492
C(9)C(4)C(4*a*)	109.8(1) {110.0}	110.03(4) {110.4}	109.83	107.31	O(1)···C(11)	3.142(2) {3.152}	3.181(1) {3.188}	3.168	3.148
C(4)C(4*a*)C(5)	111.2(1) {111.1}	110.34(4) {110.4}	111.11	109.77	C(1)···C(8)	2.610(2) {2.616}	2.639(1) {2.642}	2.614	2.650
C(4*a*)C(5)C(10) or C(4*a*)C(5)O(10)	109.3(1) {109.5}	110.03(4) {110.0}	109.19	110.51	C(4)···C(5)	2.333 {2.331}	2.320(1) {2.324}	2.334	2.284

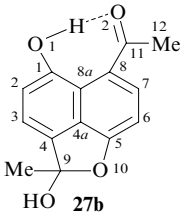
[a] The O(1)—H distances determined from X-ray diffraction data were normalized to the values obtained by quantum chemical calculation.

It is of interest to compare the X-ray diffraction data for *peri*-hydroxyacenaphthaldehyde **12** with the data for its azomethine analogue **313b** (see Table 6).[252] According to X-ray diffraction data, the seven-membered H-ring and the acenaphthene nucleus in the azomethine **313b** molecule, as in the acenaphthaldehyde **12** molecule, are nearly coplanar [the N(1)C(11)C(8)C(8*a*) torsion angle is 3.9°]. The hydrogen atom of the hydroxy group is located near the straight line connecting the O(1) and N(1) atoms [the O(1)HN(1) angle is 170.7°]. The O(1)—H bond length in the aldehyde **12** molecule is shorter than this bond in the azomethine **313b** molecule, which implies that the IntraHB is stronger in acenaphthene *peri*-hydroxyazomethine **313b** as compared with acenaphthene *peri*-hydroxy aldehyde **12**.

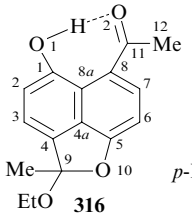
The contribution of steric effects to the strength of the H-bond in the studied systems is additionally illustrated by X-ray diffraction data for *peri*-hydroxy ketone **15b** with the naphtho[1,8-*bc*]furan nucleus (see Table 6).[22] The presence of *tert*-butyl substituent in the *ortho*-position to the hydroxy group in compound **15b** is responsible for shortening of the O(1)···O(2) distance to 2.492(2) Å.

It can be stated with a high degree of probability that the crystal structures of reported[50] naphtho[1,8-*bc*]furans **27b** and **316** would be identical to the structure of compound **15b** determined by X-ray diffraction analysis (see Table 6).[22] This is confirmed indirectly by similar positions of proton signals for methyl and hydroxy groups and the naphthalene ring in the ^{1}H NMR spectra of these compounds (Table 7).

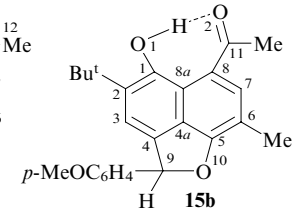
Table 7. ^{1}H NMR chemical shifts (δ) of compounds **27b**, **316** and **15b** (J/Hz).[27, 59]



27b



316



15b

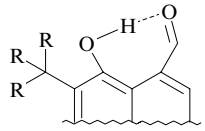
Compound	12-Me	H(2)	H(3)	H(6)	H(7)	1-OH
27b	2.52 s	7.04 d (7.77)	7.35 d (7.77)	6.63 d (8.09)	8.18 d (8.09)	12.77 s
316	2.80 s	7.13 d (7.67)	7.32 d (7.67)	6.65 d (8.13)	8.30 d (8.13)	12.80 s
15b	2.80 s		7.20 s		8.25 s	12.80 s

As can be seen from Table 6, the bond lengths in the naphthalene nucleus and in the adjacent five-membered carbocycle (heterocycle) and seven-membered H-ring of *peri*-hydroxy-substituted compounds **12**, **13a**, **15b** and azomethine **313b** considerably deviate from the classical values.

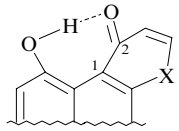
The greatest distortions are found for the angles at the C(8*a*) and C(4*a*) carbon atoms in the seven-membered H-ring and in the five-membered carbocycle (heterocycle), which differ by ~19–23°; this induces considerable changes in the non-bonding distances, C(1)···C(8) and C(4)···C(5), as compared with those in naphthalene (2.45 Å) and attests to considerable distortion of the naphthalene fragment in these molecules. This 'forced' deformation of molecules caused by the 'drawing together' effect of the five-membered ring provides exceptionally favourable conditions for the formation of a stable seven-membered H-ring by stabilizing it and neutralizing the 'pushing apart' effect arising between the oxygen atoms of the hydroxy and carbonyl groups or between the oxygen atom of the hydroxy group and the nitrogen atom of the imino group upon the formation of IntraHB.

Apparently, other acenaphthene and acenaphthylene *peri*-hydroxy aldehydes and ketones have a similar structure in the crystals. The same may be true for other related compounds having a diatomic bridge in the *peri*-position opposite to the *peri*-hydroxycarbonyl group.

Apart from the diatomic bridge, the formation of a seven-membered H-ring in the molecules of *peri*-hydroxycarbonyl compounds can be facilitated by other factors, for example, a bulky substituent in the *ortho*-position to the hydroxy group, which prevents this group from intermolecular interactions (structure **G**),[67] or by specific geometry of the carbonyl group, which prevents the oxygen atom of this group from deviating by a large distance from the hydroxyl oxygen atom through rotation along the C(1)—C(2)=O bond (the oxygen–oxygen van der Waals contact is ~3.2 Å) (structure **H**).[164, 258, 259] Both these factors also 'compel' the hydroxy and carbonyl groups to form the IntraHB.



G



H

X = O, C=O, CR_2.

In all other representatives of *peri*-hydroxynaphthoyl compounds without such steric hindrance that have been studied by X-ray diffraction, the proton of the hydroxy group of one molecule is involved in the intermolecular hydrogen bond with the carbonyl oxygen atom of another molecule or in other types of intermolecular interactions caused by molecular packing in the crystals.[6]

The structures of a number of *peri*-hydroxy-substituted aldehydes and methyl ketones of the naphthalene, acenaphthene and acenaphthylene series[246] were also investigated by quantum chemical calculations by the density functional theory methods B3LYP/6-31G** and B3LYP/6-311++G**.[246] The energy of the hydrogen bonds was calculated from the barrier to the O—H bond cleavage.

As shown by calculations, *peri*-hydroxy-substituted aldehydes **12**, **84a** and ketones **13a**, **70**, **84b** have a strong O—H···O bond with a nearly linear angle at the hydrogen atom; the energy of the H-bond is ~9–13 kcal mol^{-1} for **84a**,**b** and ~13–18 kcal mol^{-1} for **12**, **13a** and **70**. All molecules have C_s symmetry; the oxygen atoms of the hydroxy and carbonyl groups approach each other to ~2.5 Å.

According to calculations,§ in conformers **E** (see Scheme 2) of *peri*-hydroxy aldehydes **84a** and **12**, rather stable hydrogen bonds, O···H—C=O, are formed. The barrier to the reverse transition from conformer **E** to conformer **A** (R = H) is 5–7 kcal mol^{-1} (the lower barrier limit for a hydrogen bond). On passing from molecule **84a** to **12** and then to 6-hydroxy-5-formylacenaphthylene, this barrier increases. The data of quantum chemical calculations of the bond angles and interatomic distances in

§ The solvent (S) effect was not taken into account in the calculations.

molecules **12** and **13a** are summarized in Table 6. It can be seen that these data correlate well with X-ray diffraction data.

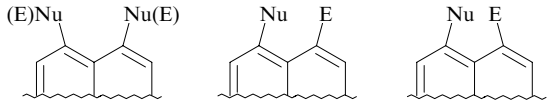
On the basis of analysis of spectral data (see Tables 3–5), X-ray diffraction data and results of quantum chemical calculations, the compounds in question can be arranged in the following order in terms of decreasing strength of the IntraHB:[246]

12 > **13a** ≡ **70** > **84a** > **84b**.

2. Intramolecular attractive electrophile – nucleophile interactions

Three types of mutual positions of *peri*-substituents in polycyclic aromatic compounds depending on their nature and size can be distinguished (Scheme 15).[6]

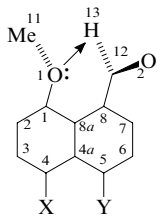
Scheme 15



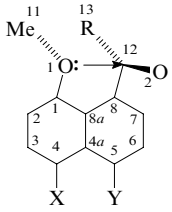
I **J** **K**

The presence of neutral bulky substituents (*e.g.*, alkyl) or substituents of the same nature [nucleophile — nucleophile (Nu–Nu) or electrophile — electrophile (E–E)] in the *peri*-positions results in them being pushed apart (conformation **I**), and the presence of substituents of different nature (nucleophile and electrophile) results in their interaction, either conformation **J** or **K** being formed depending on the strength of attractive interaction between them. It is these conformations that occur in *peri*-alkoxy- and *peri*-dialkylamino-substituted carbonyl compounds. A particular case of attractive interactions of this type is the interaction between the *peri*-substituents in *peri*-hydroxycarbonyl compounds (Scheme 13, conformations **B**, **C**, **E**, **F**).

This Section considers the results of X-ray diffraction studies and quantum chemical simulation of a number of *peri*-methoxy-substituted carbonyl compounds represented by naphthaldehydes (**51**, **106**),[8] naphthyl (**52**, **130**), acenaphthyl (**317**)[6,8,246] and acenaphthylene ketones (**318**)[246] and also naphthoic acid derivatives (**78**, **319**–**321**).[6,11]



51, **106**



52, **78**, **130**, **317**–**321**

Compound	R	X	Y
51	H	OTs	OMe
106	H	OTs	H
52	Me	OTs	OMe
130	Me	H	H
317	Me	$-CH_2CH_2-$	
318	Me	$-CH{=}CH-$	
78	OH	H	H
319	OH	OMe	H
320	OMe	OMe	H
321	NMe_2	H	H

Comparison of the structural data for these compounds (Table 8) indicates that the bond angles at the exocyclic bonds of *peri*-substituents with the naphthalene nucleus are similar, indicating equal leaning of these bonds in one and the same direction, so called 'leaning effect'. In naphthaldehydes **51** and **106**, this effect is caused by mutual repulsion of oxygen atoms of the methoxy and formyl groups with simultaneous attractive interaction of the formyl hydrogen with the lone electron pair of oxygen of the methoxy group. This gives rise to conformation **J**. The presence of only one of these effects would have produced either of conformations **I** and **K** (see Scheme 15).

The existence of a weak IntraHB in the molecules of *peri*-methoxynaphthaldehydes **51** and **106** is indicated by the shortened O(1)···H(13) distance (see Table 8), which is shorter than the sum of the van der Waals radii, and by small values of the torsion angle O(2)C(12)C(8)C(7) and the dihedral twist angle of the mean planes of the carbonyl group and the naphthalene ring relative to each other.

The 'leaning effect' observed in the series of ketones and naphthylcarboxylic acid derivatives has a different nature, being due to the balance of two oppositely directed forces, namely, the electrostatic attractive interaction of the lone electron pair of the methoxy-group oxygen with the electron-deficient carbonyl carbon atom and the steric pushing apart of two oxygen atoms, O(1) and O(2), incorporated in these substituents. The observed effect is interpreted as the initial phase of addition of a nucleophile to the carbonyl group.[6] The postulated character of attractive interaction in the series of ketones and naphthoic acid derivatives is supported by the nearly orthogonal mutual arrangement of the naphthalene ring and the carbonyl group planes, which is indicated by the O(2)C(12)C(8)C(7) torsion angle and the dihedral twist angle between the planes of the naphthalene ring and the carbonyl group (see Table 8).

The optimal value for the angle of nucleophile attack on the carbonyl group [the O(1)C(12)O(2) angle] is considered to be 95–105° (Ref. 260). Whereas in the molecules of *peri*-methoxynaphthyl methyl ketones **52**, **130** and 1-naphthoic acid derivatives **78**, **319**–**321**, this angle does not differ much from the optimal value, in acenaphthene derivative **317**, this angle is much greater (117.53°, see Table 8). The C(1)C(8*a*)C(8) and C(4)C(4*a*)C(6) bond angles at the *meso*-carbon atoms of the naphthalene ring in the compounds being compared differ to even a greater extent. In the molecules of naphthyl methyl ketones and 1-naphthoic acid derivatives, these angles are nearly equal, while in the molecule of acenaphthenyl methyl ketone **317**, they differ by 15.6°, which attests to considerable intraplane distortion of the carbon skeleton of the naphthalene nucleus of this molecule and accounts for the increase in the O(1)···C(12) distance.

The presented parameters imply a weaker electrophile–nucleophile attractive interaction for acenaphthene compound **317** as compared to naphthalene derivatives. This is also indicated by higher twist angles of the carbonyl group plane relative to the naphthalene ring plane (see Table 8).

Yet another important characteristics used to evaluate the electrophile–nucleophile interactions is the deflection of the C(12) carbon atom from the plane of the carbonyl group [C(8)O(2)C(13)] toward the nucleophile (*s* value), which attests to 'pyramidalization' of the carbonyl group under the attractive influence of the lone electron pair of the nucleophilic *peri*-substituent.

Table 8. Structural parameters of some *peri*-methoxycarbonyl compounds according to X-ray diffraction [26, 44] and quantum chemical calculation data [6, 8, 11, 246] (in curly brackets).

Parameter	Compound								
	106	**51**	**130**	**52**	**320**	**321**	**319**	**78**	**317**
Angles,[a] /deg									
C(2)C(1)O(1)	123.5	123.4	124.5 {123.8}	124.0	125.6	122.6	124.73	125.0	124.51 {124.1}
O(1)C(1)C(8*a*)	115.3	115.1	116.0 {115.1}	114.1	114.3	114.40	114.10	113.24	115.21 {115.5}
C(1)C(8*a*)C(8)	123.9	122.5	121.8 {123.4}	121.9	123.7	124.31	123.33	124.52	127.57 {128.0}
C(8*a*)C(8)C(12)	124.7	126.4	125.6 {125.0}	125.5	124.3	123.06	123.98	123.32	124.76 {125.3}
C(1)C(8)C(7)	115.8	114.9	115.4 {115.3}	115.3	115.6	115.12	114.99	116.02	116.56 {115.7}
C(4)C(4*a*)C(5)	121.5	124.2	121.6 {120.9}	124.4	121.6	123.12	121.76	121.91	111.99 {112.0}
C(1)C(12)O(2)	141.5	147.8	107.6	113.2	101.9	103.28	92.58	93.88	117.53 {120.7}
O(1)H(13)C(12)	102.4	106.3							
O(2)C(12)C(8)C(7)	30.8	22.2	72.6 {62.2}	62.8	82.34	77.90	77.7	92.86	60.8 {55.5}
C(11)O(1)C(1)C(1)	7.8	9.8	3.0	6.9	2.06	2.94	2.61	8.83	17.7 {3.7}
Twist	32.9	23.9	75.0	68.3			80.0		
Distances /Å									
O(1)···C(12)	2.644	2.628	2.610 {2.644}	2.578	2.588	2.597	2.566	2.560	2.778 {2.822}
C(1)···C(8)	2.530	2.514	2.500	2.496	2.515	2.511	2.493	2.511	2.566 {2.575}
C(4)···C(5)	2.478	2.526	2.495 {2.472}		2.475	2.509	2.469	2.462	2.333 {2.334}
C(1)−O(1)	1.360	1.361	1.341	1.359	1.363	1.369	1.369	1.351	1.368 {1.360}
C(12)−O(2)	1.172	1.176	1.228	1.207	1.199	1.224	1.266	1.230	1.215 {1.217}
C(12)−C(8)	1.492	1.479	1.487	1.513	1.505	1.519	1.500	1.500	1.500 {1.512}
O(1)···H(13)	2.220	2.162							
O(1)···O(2)	3.635	3.677	3.200	3.248	3.068	3.166	3.070	2.914	3.509

[a] The presented angles include the bond angles at the C(1), C(8), C(8*a*) and C(4*a*) atoms; the angle of attack of the nucleophile [O(1) atom] on the C(12)=O(2) carbonyl group [O(1)C(12)O(2) angle]; the O(1)H(13)C(12) angle in the six-membered H-ring; torsion angles at the C(8)−C(12) and C(1)−O(1) bonds; the dihedral angle between the mean plane of naphthalene and carbonyl group (twist).

Figure 1 shows the pattern of pyramidalization of the carbonyl group in *peri*-methoxy-substituted naphthalenyl (**130**) and acenaphthenyl methyl ketones (**317**). Contrary to expectations, a more pronounced pyramidalization occurs in molecule **317**, which in this case, rather reflects features of the crystal packing of this compound and not the energy of attractive electrophile–nucleophile interaction.¶

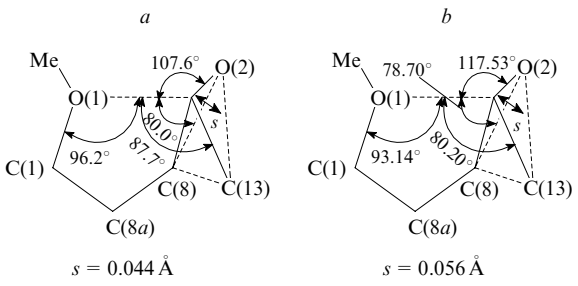


Figure 1. Schematic view of the electrophilic and nucleophilic fragments in molecules **130** (*a*) and **317** (*b*).
The dashed lines designate the plane of the carbonyl group, which passes through C(8), O(2) and C(13) atoms.

¶ It was found [7, 260–262] that pyramidalization of the carbonyl group is not always a consequence of attractive interaction but may be due only to molecular environment.

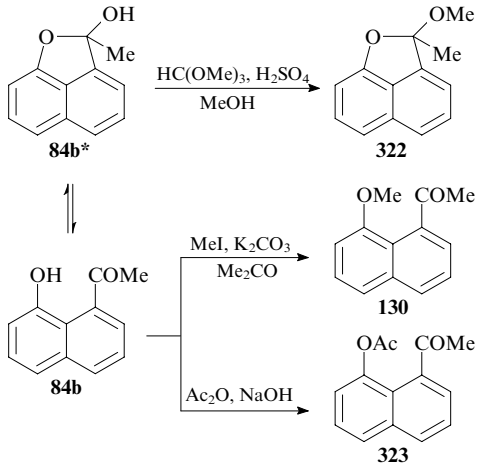
Indeed, the rotation angle of the methoxy group from the acenaphthene ring plane, C(11)O(1)C(1)C(2), in molecule **317** found by X-ray diffraction analysis differs from this angle found by quantum chemical calculations for isolated molecule **317** by 14° (see Fig. 1). The rotation angle found by X-ray diffraction analysis for compound **130** amounts to ~3°, *i.e.*, the methoxy group in this compound (unlike compound **317** in which this angle is 17.7°) lies almost in the naphthalene ring plane.

The geometric parameters and electrophile–nucleophile interaction energy in *peri*-methoxy-substituted methyl ketones of the naphthalene (**130**), acenaphthene (**317**) and acenaphthylene (**318**) series were calculated.[246] According to the calculation results, non-bonding O···C=O distances in these molecules are 2.644, 2.822 and 2.852 Å, respectively, which is shorter than the length of the van der Waals O···C contact (~3 Å). The calculated O···C=O interaction energy does not exceed 1.5 kcal mol^{-1} for compounds **317** and **318** and is 3 kcal mol^{-1} for the molecule of **130**. Thus, the strength of the intramolecular attractive oxygen–carbon interaction decreases in the order **130** > **317** > **318**.

3. Ring–chain tautomerism

Presumably, the two theoretically possible mechanisms of the closure of five-membered heterocycle (**A** → **D**) and (**B** → **D**) (see Scheme 13) in the molecules of compounds containing *peri*-hydroxycarbonyl group are reversible and, hence, these are examples of ring–chain tautomerism. Although no special kinetic studies of the ring–chain tautomerism were carried out, there is indirect evidence for

the existence of this process. The acid-catalyzed reaction of *peri*-hydroxynaphthyl methyl ketone **84b** with methyl orthoformate gives (obviously, *via* hemiacetal form **84b***) cyclic acetal **322**, whereas methylation and acetylation in alkaline media gives open-chain reaction products **130** and **323**.[2]



Sections II.1 (compounds **26**, **27**) and III.1 (Scheme 14) present some examples of ring–chain tautomerism. Other examples of this process considering the equilibrium between the open-chain and cyclic acetal, hemiacetal and amino acetal forms have also been reported. In a number of publications [2, 29, 50, 52, 250, 251] the conditions of existence and isolation of these species and the effect of the nature of substituents on the state of equilibrium are considered, the transformation of semiacetals to ring acetals is performed and the spectral characteristics of tautomers are discussed.

IV. Chemical transformations

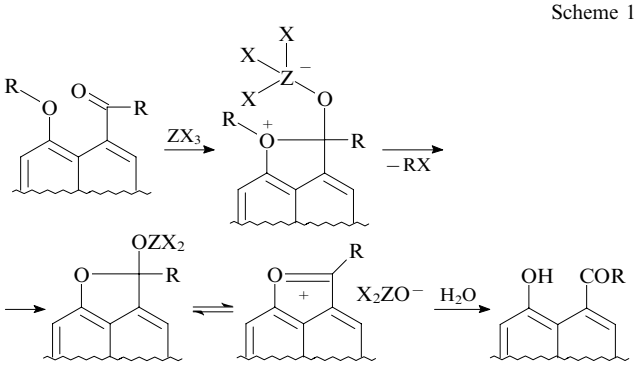
1. Reactions of *peri*-substituents

a. Reactions involving the hydroxy group

O-Alkylation,[2, 159, 161] O-acylation [75] and O-silylation [185, 186] of *peri*-hydroxycarbonyl compounds are carried out under usual conditions characteristic of α-naphthols. Methyl iodide or dimethyl sulfate are used as alkylating agents and carboxylic acid anhydrides and chlorides are used as acylating agents (under base catalysis).

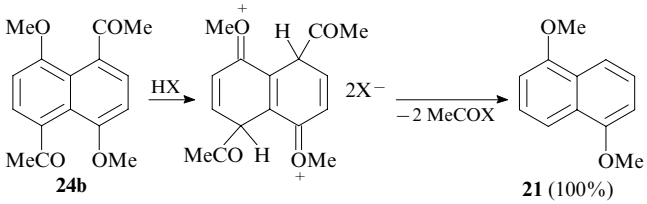
The removal of the ester group in *peri*-acyloxycarbonyl compounds can be effected by alkalis or dialkylamines,[14–19] while dealkylation of the *peri*-alkoxy group is performed by aluminium chloride or boron tribromide.[26, 33, 124, 125] The proposed mechanism of cleavage of the *peri*-alkoxy group under the action of Lewis acid differs basically from the generally accepted mechanism of cleavage of phenol ethers and *ortho*-alkoxycarbonyl compounds owing to the tendency of *peri*-hydroxycarbonyl group to close a five-membered heterocycle (Scheme 16).

Scheme 16



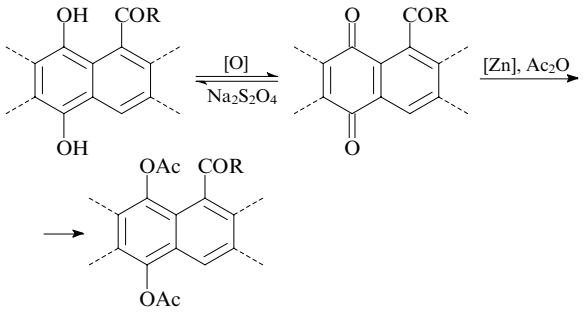
Z = Al, B; X = Cl, Br, F.

The attempt at demethylation of diacetyldimethoxynaphthalene **24b** by hydrobromic or hydroiodic acid used commonly to cleave phenol ethers and *ortho*-alkoxycarbonyl compounds leads, as a result of *ipso*-substitution, to unusual elimination of the acetyl group to give 1,5-dimethoxynaphthalene (**21**).[15] In this case, the ease of deacylation is, in our opinion, due to the removal of the carbonyl group from conjugation with the naphthalene ring caused by attractive interaction between *peri*-arranged substituents (see Section III.2).



X = Br, I.

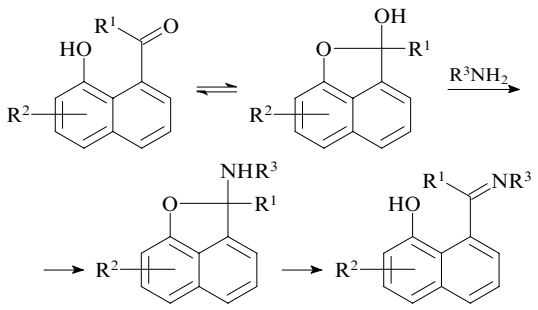
peri-Hydroxycarbonyl compounds containing one more hydroxy group in the *para*-position relative to the first one are converted to *p*-quinones under the action of oxidants or atmospheric oxygen. *p*-Quinones can be easily reduced to the initial *peri*-hydroxycarbonyl compounds. If the reduction of quinones is carried out in acetic anhydride, the corresponding acetates are formed.[67, 126, 169, 223]



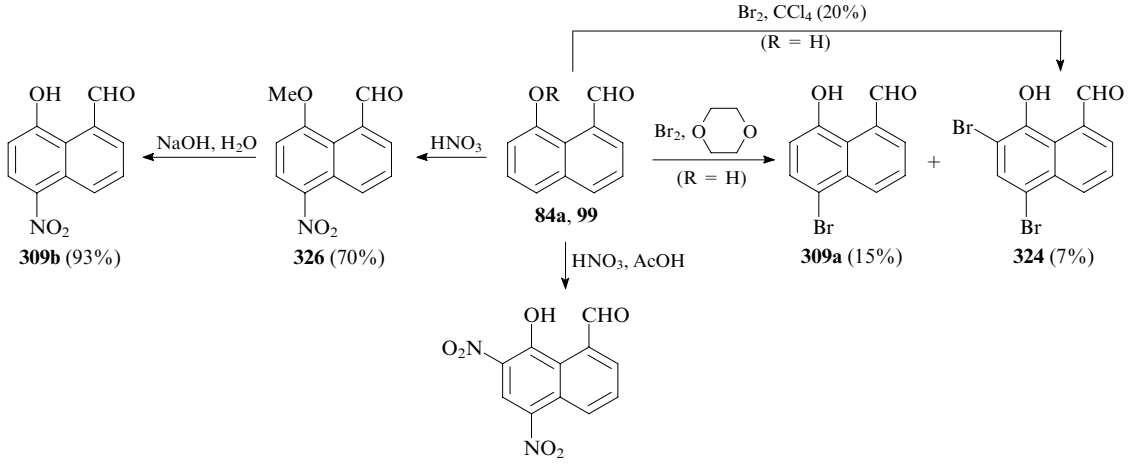
b. Reactions involving the carbonyl group

The carbonyl group of *peri*-hydroxy-substituted aldehydes and ketones readily reacts with amines (arylamines, hydrazines, hydroxyamines) to give azomethines,[251] hydrazones [16] and oximes,[263] respectively.

In our opinion, the ease of these transformations is related to the presence of cyclic hemiacetal tautomer, which reacts with amines by to the S_N2 mechanism.



Scheme 17



R = H (**84a**), Me (**99**).

2. Functionalization of the aromatic nucleus

The reaction of *peri*-hydroxynaphthaldehyde **84a** with dioxane dibromide yielded a mixture of mono- (**309a**) and dibrominated (**324**) derivatives (Scheme 17), whereas upon the reaction with bromine in carbon tetrachloride, only dibromide **324** was isolated.[250] In both cases, the yields of bromo derivatives were moderate. It was shown in the same study that the reaction of *peri*-hydroxynaphthaldehyde **84a** with nitric acid affords dinitro derivative **325**. Mononitro-substituted *peri*-hydroxynaphthaldehyde **309b** was prepared by nitration of *peri*-methoxynaphthaldehyde **99** followed by demethylation of product **326**.

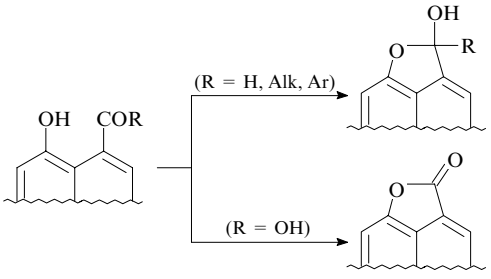
The bromination of 8-hydroxy-5-methoxy-1-naphthaldehyde gives 7-bromo-8-hydroxy-5-methoxy-1-naphthaldehyde.[29]

3. Heterocyclization of *peri*-hydroxynaphthoyl compounds

The structure of *peri*-hydroxycarbonyl compounds affects considerably the routes and mechanisms of heterocyclization (in some cases, heterocyclizations of *peri*-hydroxycarbonyl compounds are compared with heterocyclizations of analogous *ortho*-substituted derivatives).

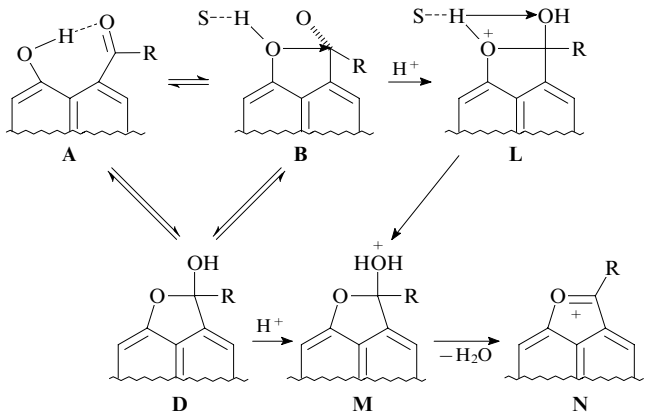
a. Naphtho[1,8-*bc*]furan derivatives

The simplest heterocyclization reaction of *peri*-hydroxycarbonyl compounds is closure of the five-membered heterocycle. Furthermore, aldehydes and ketones are converted to 2-hydroxynaphtho[1,8-*bc*]furans (R = H, Alk, Ar) and carboxylic acids are converted to naphtho[1,8-*bc*]furan-2-ones.[1, 2, 250, 251]



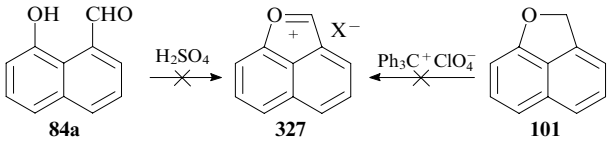
Acid-catalyzed closure of the five-membered heterocycle is the fastest kinetically controlled process, which starts from the attack by the proton on the carbonyl oxygen atom (**B** → **L**) and ends in the formation of the naphtho[1,8-*bc*]-furylium cation **N** (Scheme 18).

Scheme 18



The stability of the naphtho[1,8-*bc*]furylium cation **N** depends first of all on the electron-donating properties of the substituent R and on the nature of substituents in the naphthalene nucleus.

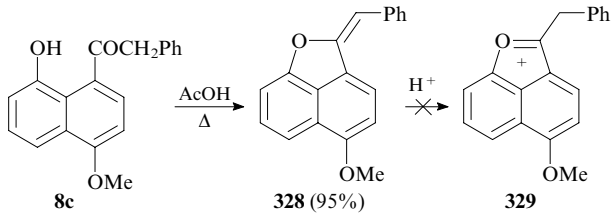
The simplest unsubstituted naphtho[1,8-*bc*]furylium cation (**327**) is unknown. Neither dissolution of *peri*-hydroxynaphthaldehyde (**84a**) in concentrated sulfuric acid nor dehydrogenation of naphtho[1,8-*bc*]furan (**101**) on treatment with trityl perchlorate resulted in the generation of this cation.[3]



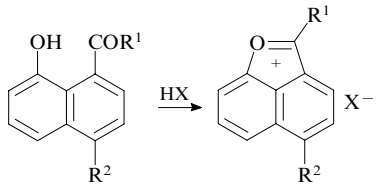
The simplest *peri*-hydroxynaphthyl methyl ketone **84b** is dissolved in sulfuric acid to give a yellow solution (λ_{max} = 399 nm, $\log \varepsilon$ = 4.05), the colour apparently being due to 2-methylnaphtho[1,8-*bc*]furylium sulfate stable under these conditions.[2]

peri-Hydroxynaphthyl benzyl ketone **8c** gives no crystalline salts on treatment with perchloric acid but on refluxing in anhydrous acetic acid it is converted to 2-benzylidene-5-methoxynaphtho[1,8-*bc*]furan (**328**); equal bond

lengths in the molecule of this product account for its low basicity, which prevents it from being protonated and forming cation (**329**).[18]

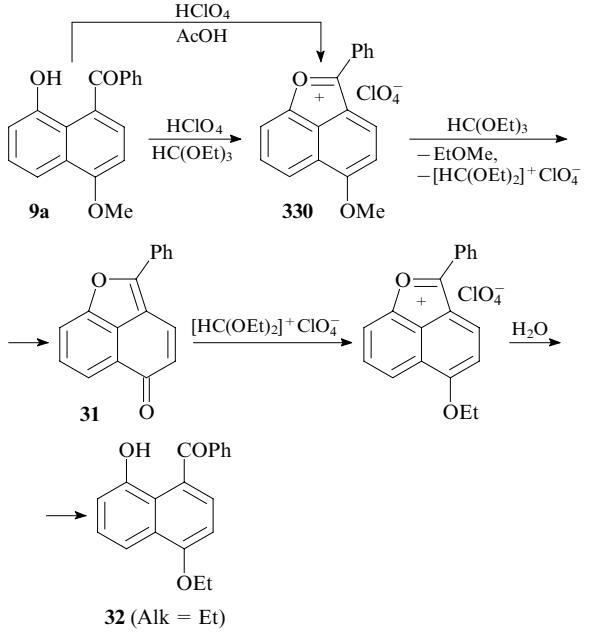


Stable naphtho[1,8-*bc*]furylium cations can be obtained and isolated as salts under acid catalysis in those cases where R^1 = Ar, CH=CHAr, CH=CHOR.[2, 15, 264–266]

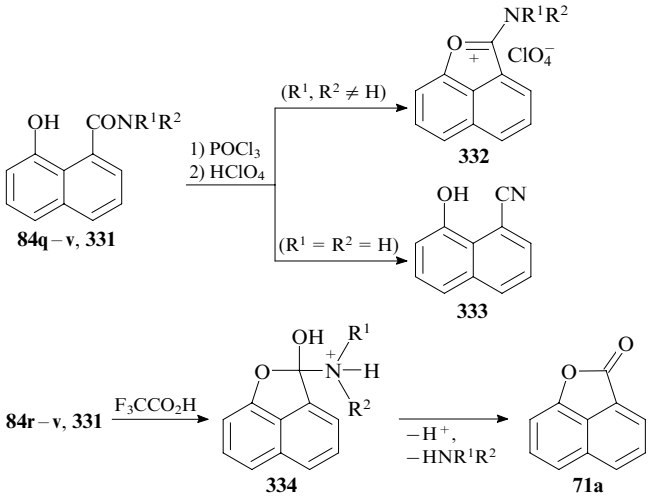


R^1 = Ar, CH=CHAr, CH=CHOAlk; R^2 = H, OMe.

peri-Hydroxynaphthyl phenyl ketone **9a** reacts with perchloric acid in acetic acid giving rise to 5-methoxy-substituted naphtho[1,8-*bc*]furylium perchlorate **330**, whereas the same reaction carried out in triethyl orthoformate leads to replacement of the 5-methoxy group by a 5-ethoxy group, which is due to the intermediate formation and subsequent O-ethylation of naphtho[1,8-*bc*]furan-5-one **31** with diethoxycarbenium perchlorate.[264]

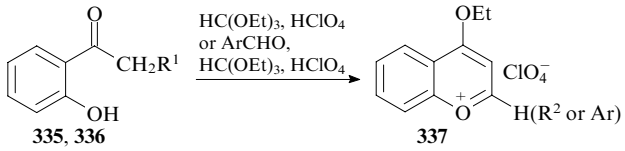


The naphtho[1,8-*bc*]furylium cation containing *N*-substituted amino group in position 2 has a high thermodynamic stability. Heating of *N*-substituted *peri*-hydroxycarboxamides **84r–v**, **331** (R^1, $R^2 \neq$ H) in phosphorus oxychloride or keeping it in a dimethylformamide–phosphorus oxychloride mixture at room temperature followed by adding dilute perchloric acid to the reaction mixture produced perchlorates **332**.[267] Unsubstituted *peri*-hydroxycarboxamide **84q** (R^1 = R^2 = H) is converted to *peri*-hydroxycarbonitrile **333** under these conditions. Heating of *peri*-hydroxycarboxamides **84r–v** and **331** in trifluoroacetic acid affords naphtholactone **71a** in a good yield. The reaction may involve intermediate **334**.[108]

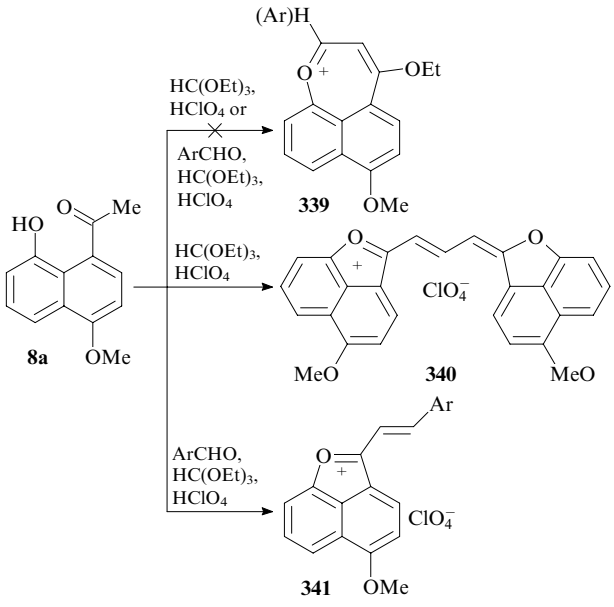


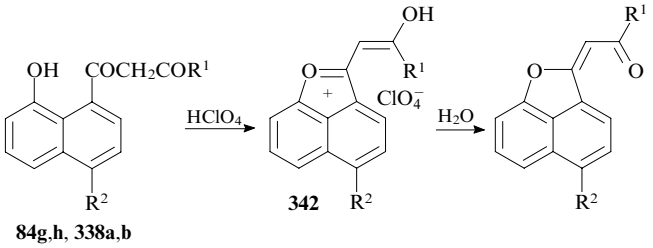
R^1, R^2 = H, Alk, Ar.

The reaction of *o*-hydroxyacetophenone (**335**) or its derivative, diketone **336**, with ethyl orthoformate and perchloric acid or with aromatic aldehydes together with the above reagents is known to give 4-ethoxybenzopyrylium salts **337**,[267–272] whereas the transformation of *peri*-hydroxynaphthyl methyl ketone **8a** and *peri*-hydroxy diketones **84g**,**h**, **338** under the same reaction conditions follows a different pathway: instead of the theoretically possible naphtho[1,8-*bc*]oxepinium cation **339**, naphtho[1,8-*bc*]furylium perchlorates **340–342** are formed.[2, 15, 265, 266, 273]



R^1 = H (**335**), COR^2 (**336**).

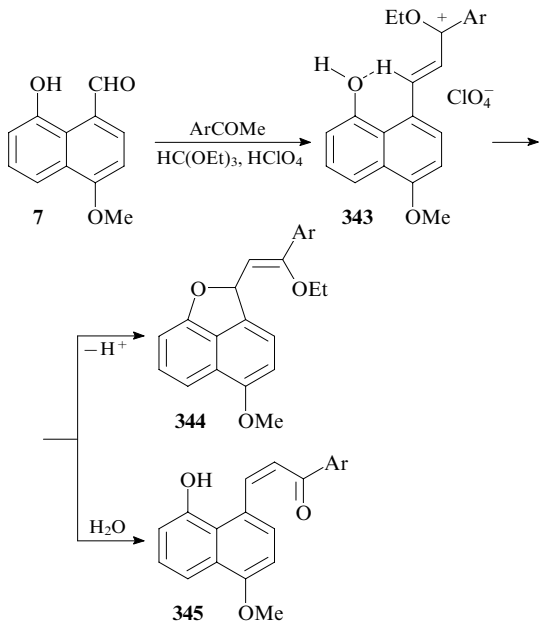




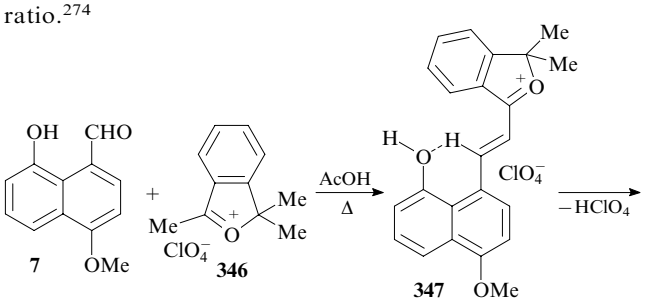
84g,**h**, **338a**,**b**

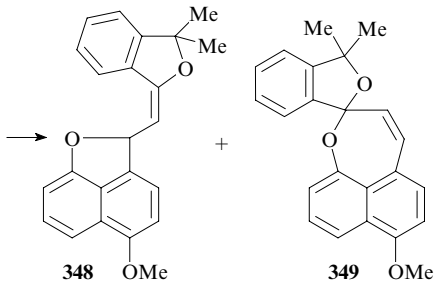
R^2 = H: R^1 = Me (**84g**), Ph (**84h**);[2]
R^2 = OMe: R^1 = Ph (**338a**), C_6H_4Me-*o* (**338b**).[273]

The outcome of acid-catalyzed condensation of 4-methoxy-8-hydroxy-1-naphthaldehyde (**7**) with aryl methyl ketones in ethyl orthoformate was even more surprising. Instead of the expected naphthoxepinium salt, the reaction gives stable open-chain perchlorate **343**, which is deprotonated to give naphthofuran derivative **344** or hydrolyzed to give chalcone **345**.[266] Probably, the formation of open-chain cation **343** in the conformation that prevents the closure of seven-membered heterocycle is considerably facilitated by the attractive interaction of the β-proton with the oxygen atom of *peri*-hydroxy group.



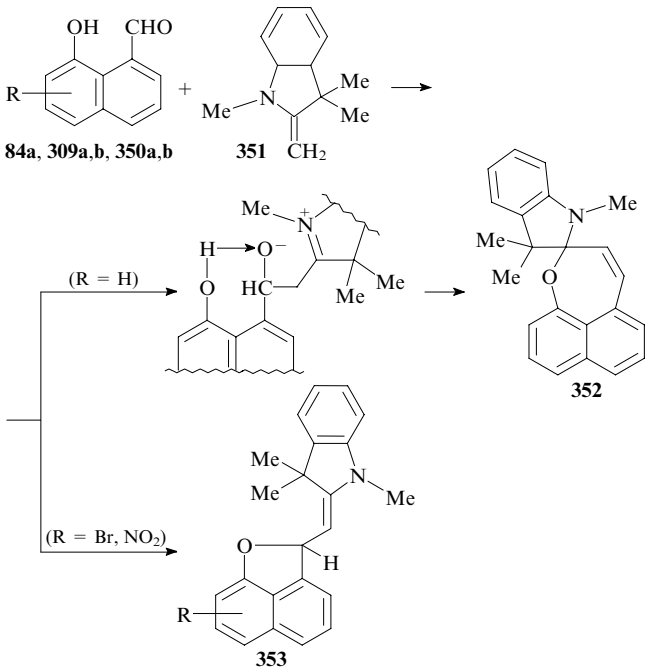
The reaction of *peri*-hydroxy aldehyde **7** with isobenzofurylium salt **346** affords compound **347**, which is isoelectronic to cation **343** and has the same conformation as **343**. However, deprotonation of cation **347**, unlike cation **343**, gives closure products, *viz*., five-membered (compound **348**) and seven-membered (compound **349**) heterocycles in 1 : 1 ratio.[274]





348 **349**

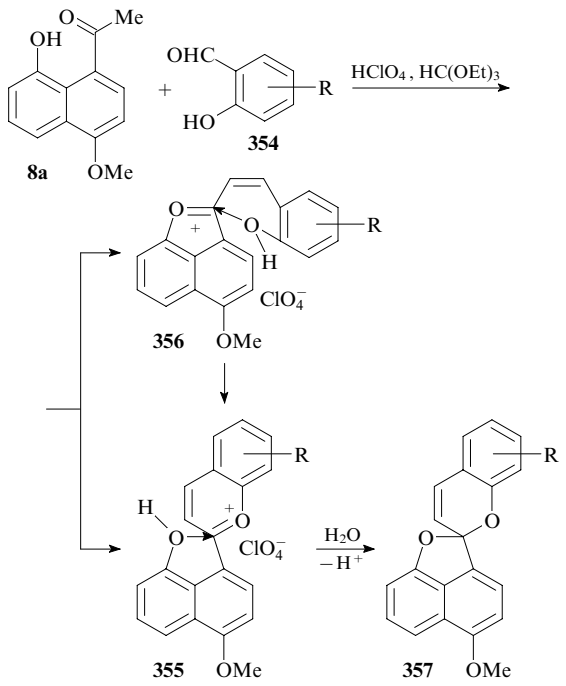
peri-Hydroxynaphthaldehydes **84a**, **309a**,**b** and **350a**,**b** show a different behaviour in the reaction with Fischer's base **351**. Compound **351** reacts with 8-hydroxy-1-naphthaldehyde (**84a**) to give only naphtho[1,8-*bc*]oxepine derivative **352**, whereas in the presence of electron-withdrawing substituents (Br and NO_2), conjugated with the hydroxy group, in positions 5 or 7 of the naphthalene nucleus, the reaction yields naphtho[1,8-*bc*]furan **353**.[251,275] Probably, the type of the final products is dictated by the presence or absence of cyclic hemiacetal (conformer **D**, see Scheme 13) in the reaction mixture, and the content of this species sharply increases in the presence of electron-withdrawing substituents. Hemiacetal **D** reacts with Fischer's base by the S_N2 mechanism, giving rise to isomer **353** with a five-membered heterocycle, whereas free aldehyde group (tautomer **A**) attacks the methylene unit of the enamine (the Stork reaction) followed by closure of a seven-membered heterocycle (compound **352**).



84a, **309a**,**b**, **350a**,**b** **351**

R = H (**84a**), 5-Br (**309a**), 5-NO_2 (**309b**), 7-Br (**350a**), 7-NO_2 (**350b**).

peri-Hydroxy ketone **8a** reacts with *o*-hydroxybenzaldehydes **354** and perchloric acid yielding benzopyrylium perchlorates **355**,[276] which are possibly the primary reaction products. However, another pathway where naphtho[1,8-*bc*]furylium cation **356** is initially formed and then undergoes recyclization to cation **355** appears more likely.



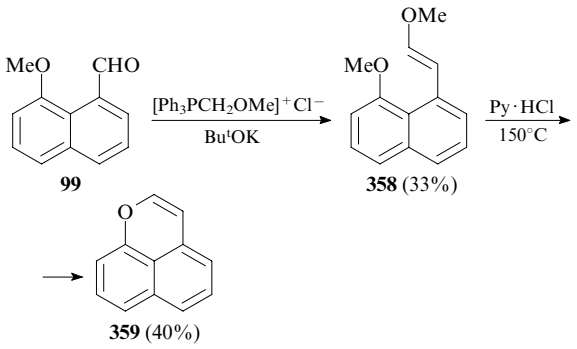
This assumption is based on the fact that kinetically controlled intramolecular closure of five-membered heterocycle is faster than other intramolecular and, all the more so, intermolecular transformations (see Scheme 18 and comments on it).

Relying on the X-ray diffraction data on the structure of *peri*-R-oxy ketones (see Section III.2), one can suggest that the planes of the naphthalene and pyrylium fragments would be orthogonal to each other and the exocyclic bonds of *peri*-substituents would lean towards each other (conformation **K**, Scheme 15). This structure of cations **355** is confirmed by the ease of their deprotonation even by weak bases such as water, resulting in spirochromenes **357**. Moreover, some spirochromenes are the only products formed under conditions of formation of perchlorates **355**, despite the presence of a strong acid in the medium.

The obtained spirochromenes are promising for the practical use, as upon irradiation they form long-lived photostable merocyanine dyes with high quantum yield of photocolouration.[277]

b. Naphtho[1,8-*bc*]pyran derivatives

The Wittig reaction of *peri*-methoxynaphthaldehyde **99** with methoxymethylenephosphorane gives vinyl ether **358**; upon heating **358** with pyridinium chloride, simplest naphtho[1,8-*bc*]pyran **359** was obtained.[125]

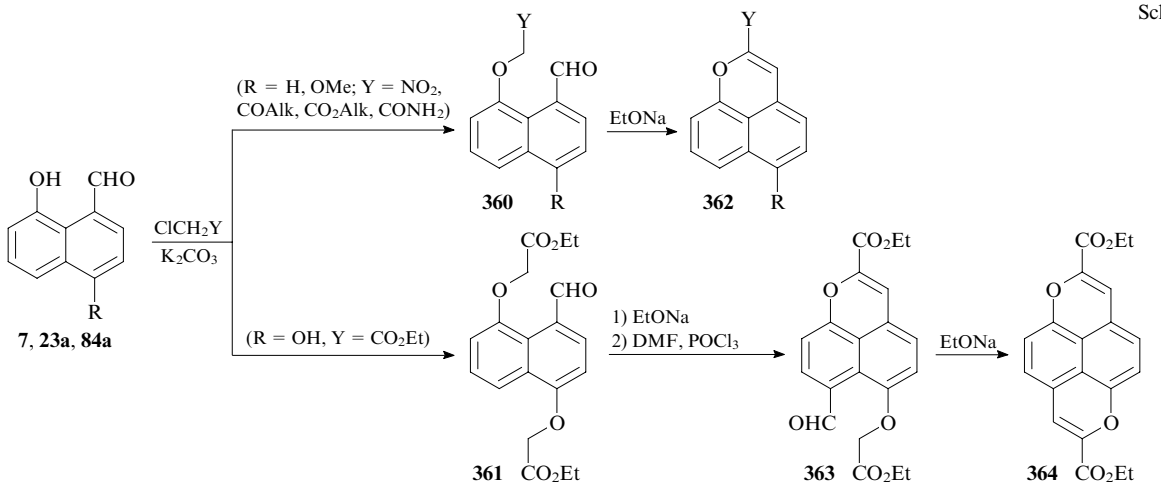


The *peri*-substituted derivatives with an electron-withdrawing group at the hydroxyl oxygen atom (compounds **360**, **361**) were prepared from chloromethyl compounds having electron-withdrawing groups and *peri*-hydroxynaphthaldehydes **7**, **23a** and **84a**. The intramolecular cyclization of **360** or **361** leads to mono- (**362**, **363**) and bis(naphtho[1,8-*bc*]pyrans) (**364**) (Scheme 19).[65–68, 278]

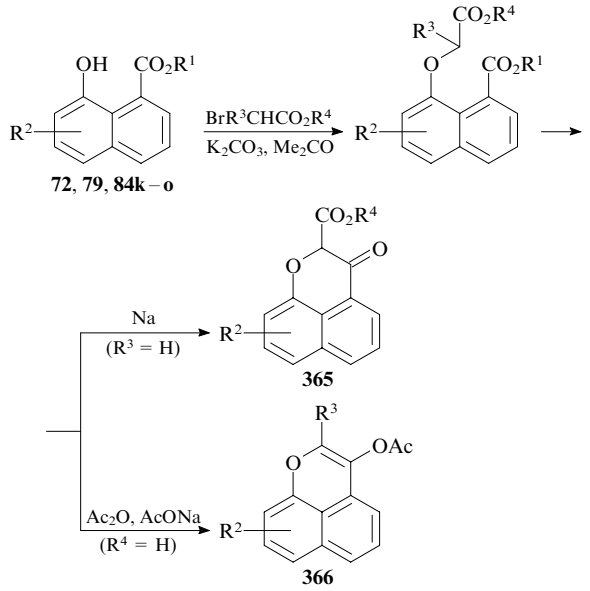
A similar intramolecular Dieckmann heterocyclization of *peri*-substituted naphthoic acids **72** or esters **79**, **84k–o** and other results in 3-oxonaphtho[1,8-*bc*]pyran-2-carboxylates **365**. If heterocyclization is accompanied by decarboxylation, other 2-substituted derivatives of this heterocyclic system are formed, *e.g.*, compound **366**.[82, 99, 279]

The negatively charged oxygen atom in the anionic intermediates **369** and **370** generated from *peri*-benzoyloxy ketones **367** and **368** attacks the α-carbon atom at the carbonyl group to produce 2-arylmethylidenenaphtho[1,8-*bc*]pyran-3-ones **371**.[19] No products resulting from the attack by the negatively charged oxygen atom on the β-carbon atom are formed. Since the carbonyl plane in the *peri*-R-oxy ketone molecules is orthogonal to the naphtha-

Scheme 19



R = H (**84a**), OMe (**7**), OH (**23a**); Y = NO_2, COAlk, CO_2Alk, $CONH_2$.

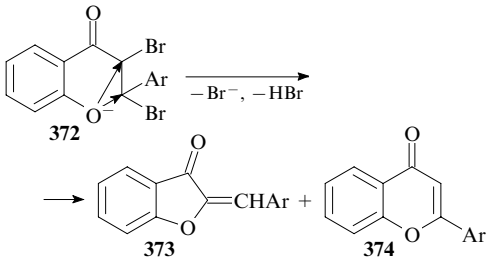


R^1 = H, Alk, Ar; R^2 = H, OMe, Br, NO_2, *etc.*; R^3 = H, Alk.

lene plane (see X-ray diffraction data, Section III.2), during the rotation of the carbonyl fragment, which precedes heterocyclization, the α-carbon atom will be the first to stand in the way of the phenoxide anion (Scheme 20).

In other words, the direction of heterocyclization is due not so much to electronic factors, which would lead to the attack on the β-carbon atom in the case of intermediate **369** or to the attack on both the α- and β-carbon atoms in the case of intermediate **370**, as to the geometry of the transition state, which is favourable for the closure of a six-membered ring.

The foregoing is indirectly confirmed by the fact that the phenoxide anion generated from *ortho*-hydroxy ketones **372** attacks with equal probability both the α- and β-carbon atoms in α,β-dibromo-β-arylethylene fragment of ketone **372** with closure of five- and six-membered heterocycles, respectively. This gives a mixture of 2-arylmethylidenebenzofuran-3-ones (aurones) **373** and benzopyran-4-ones (flavones) **374** in ~1 : 1 ratio.

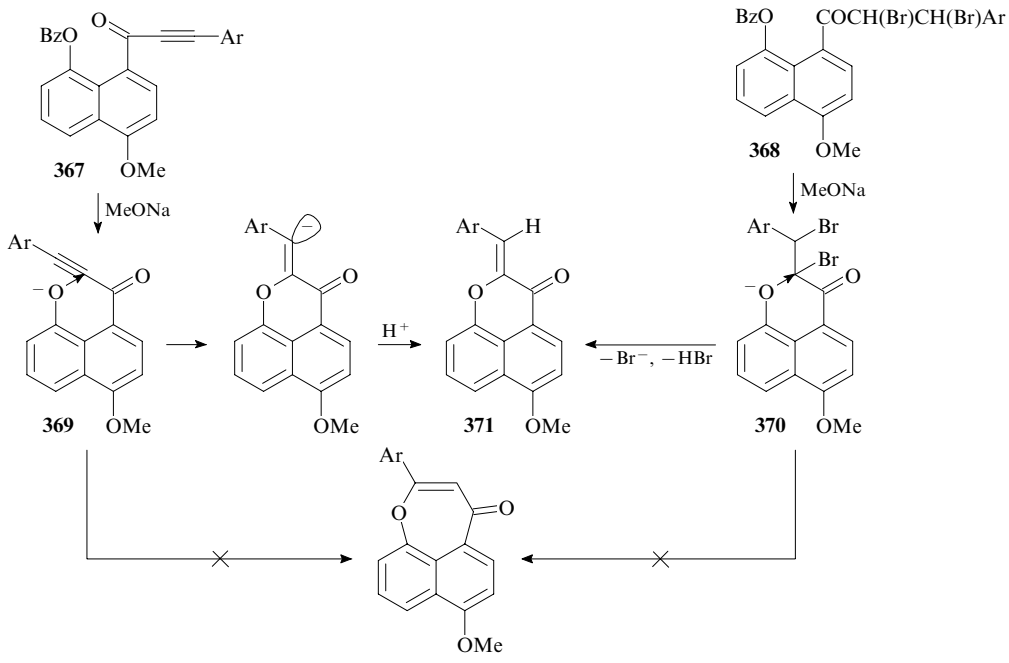


In an intermolecular reactions with esters of propiolic and phenylpropiolic acids, the phenoxide anion adds only to the β-carbon atom at the triple bond.[280]

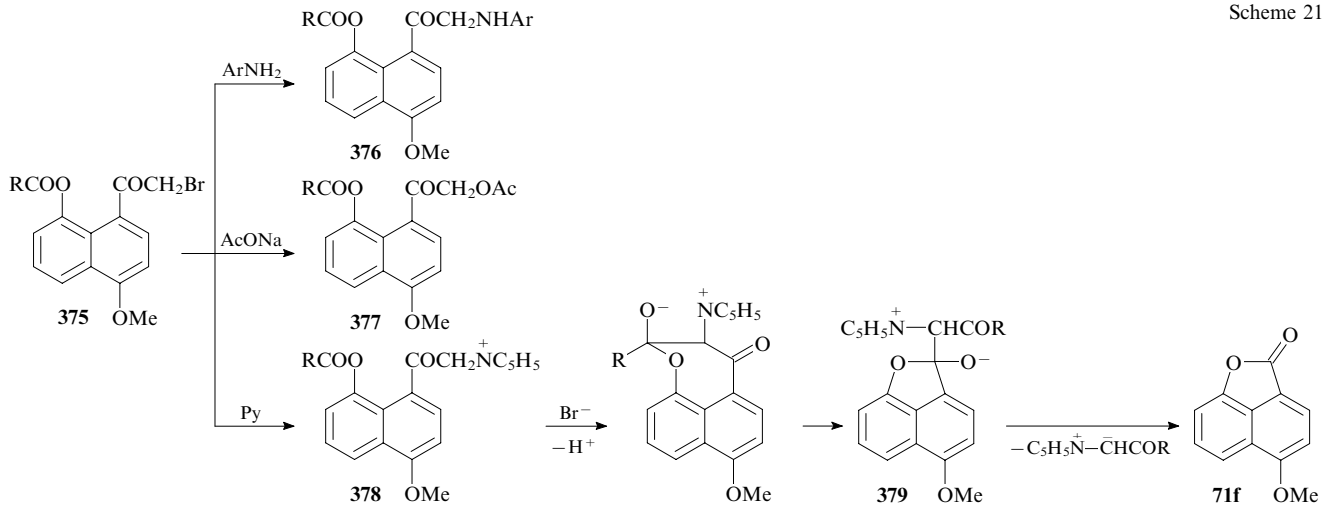
From comparison of the geometry of intermediates **370** and **372**, it follows that the position of the α-carbon atom in intermediate **370** is more favourable for the intramolecular attack by the phenoxide anion than the β-carbon atom position. For this attack, it is sufficient that the carbonyl group rotates around the C–C bond between the carbonyl carbon atom and the aromatic nucleus. As regards intermediate **372**, its geometry favours the closure of the five-membered ring; however, closure of the six-membered ring is more favourable from the thermodynamic standpoint. This competition produces a mixture of heterocycles **373** and **374**. In the case of intermediate **370**, both factors act in the same direction, resulting in only product **371** with a six-membered heterocycle.

A number of interesting transformations of *peri*-acyloxy-substituted bromomethyl naphthyl ketones proceeding in the presence of bases have been discovered. On treatment of *peri*-acyloxynaphthyl α-bromomethyl ketones **375** with low-basic aromatic amines or sodium acetate as a weak base, replacement of the bromine atom by arylamino or acetoxy group takes place giving rise to compounds **376** or **377**, respectively.[281] Pyridine is quaternized under the action of ketone **375** to give cation **378**. The latter first cyclizes and then rearranges to intermediate **379**, which

Scheme 20

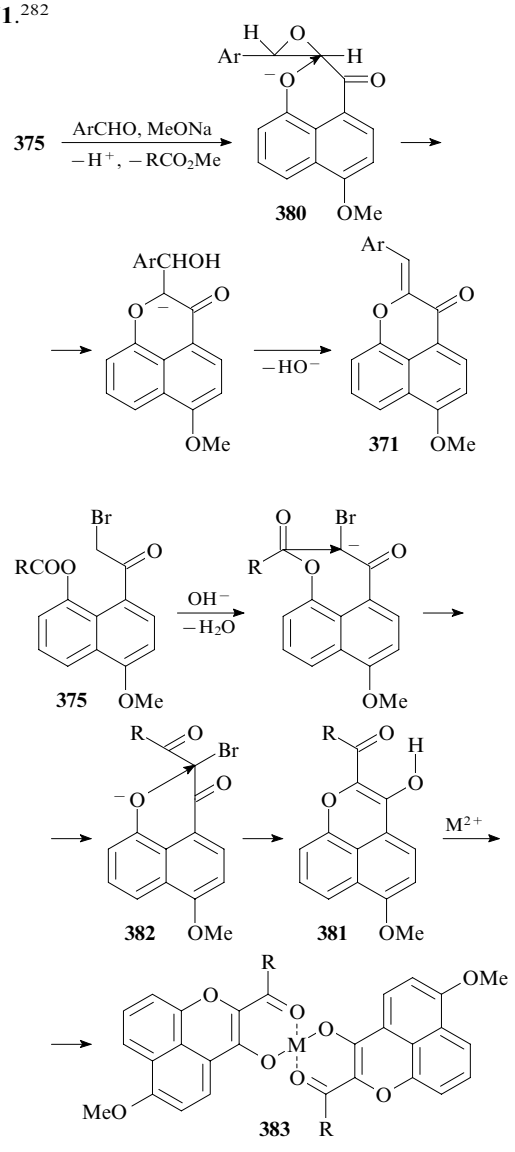


Scheme 21



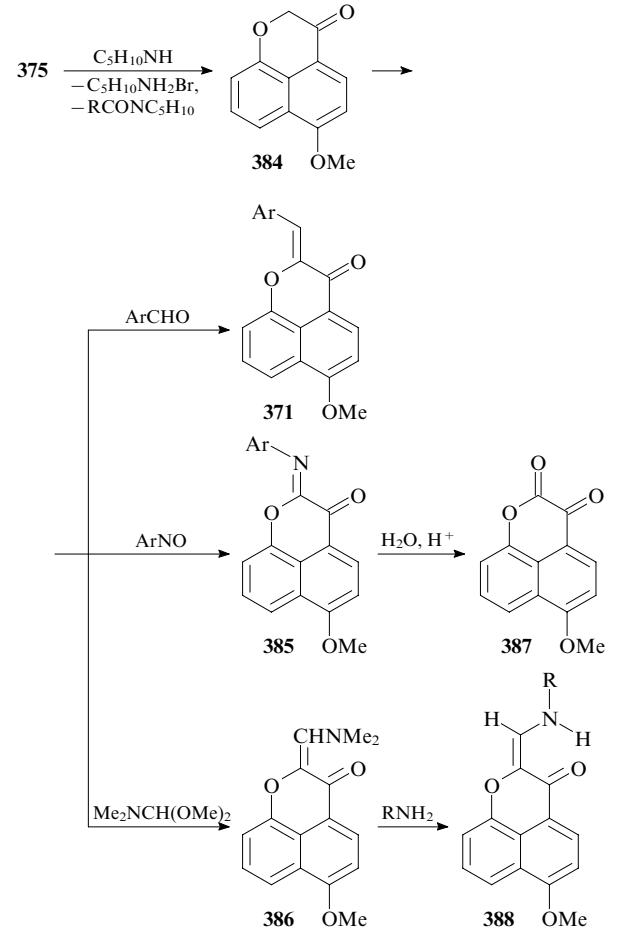
decomposes to pyridinium ylide and naphtholactone **71f** (R = 5-OMe) (Scheme 21).[281]

The reaction of ketones **375** with aromatic aldehydes in the presence of sodium methoxide gives first epoxide intermediates **380**, which are then converted to the above-described 2-arylmethylidenenaphtho[1,8-*bc*]pyran-3-ones **371**.[282]



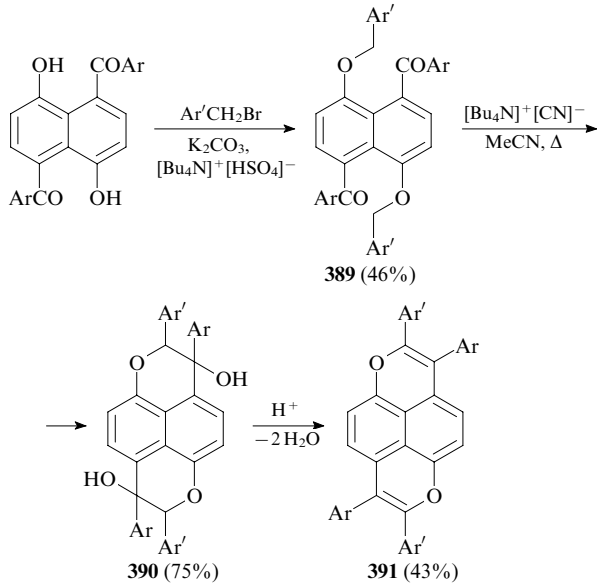
When treated with alkalis, ketones **375** rearrange to 2-acyl-3-hydroxynaphtho[1,8-*bc*]pyrans **381**.[283] The reaction also occurs *via* anionic intermediate **382**. Compounds **381** are chemosensing reagents for divalent metal ions, including toxic heavy metals. They form luminescent complexes **383** with copper, zinc, cadmium, nickel, *etc*. cations.[283]

Ketones **375** react with piperidine to be converted to naphtho[1,8-*bc*]pyran-3-ones **384**,[281] which readily react with aromatic aldehydes, nitroso compounds and dimethylformamide dimethyl acetal to give 2-arylmethylidene- (**371**), 2-arylimino- (**385**) and 2-dimethylaminomethylidenenaph-



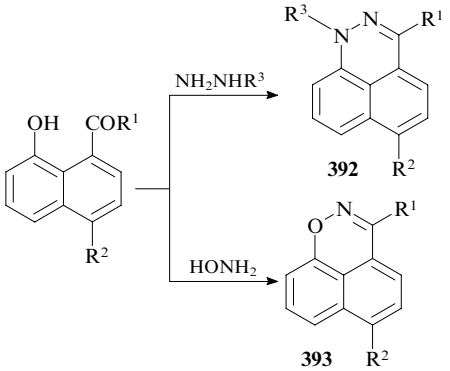
tho[1,8-*bc*]pyran-3-ones (**386**), respectively.[284] Hydrolysis of imines **385** affords naphtho[1,8-*bc*]-pyran-2,3-dione (**387**). Enamino ketones **386** and **388** can be used as new ligands for the synthesis of chelates.[284]

On long-term refluxing of diketone **389** with tetrabutylammonium cyanide, intramolecular aldol condensation takes place to give cyclic diol **390**, which eliminates water under acid catalysis to be converted to tetraaryl-substituted 1,6-dioxapyrene **391**.[32]



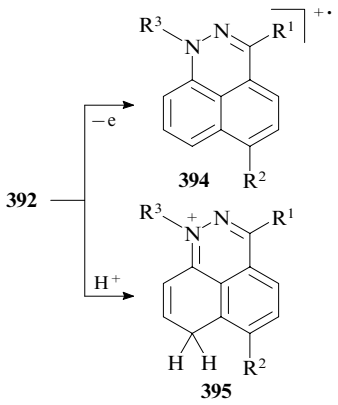
c. 1,2-Oxaza- and 1,2-diazaphenalene derivatives

The reaction of *peri*-hydroxy naphthaldehydes or naphthyl ketones with hydrazines or hydroxylamine produces 1,2-diazaphenalenes **392** or 1,2-oxazaphenalenes **393** (Refs 16, 263 and 285).

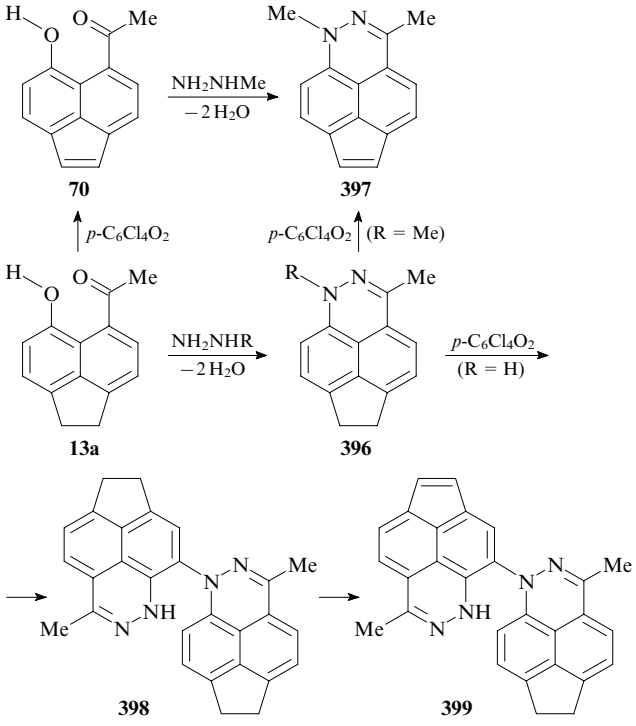


Diazaphenalenes **392** are very interesting *peri*-annulated heterocyclic systems. First, they have exceptionally high electron-donating ability and readily give off an electron to give rather stable radical cations **394**, which exist in air as salts with mineral acid anions without special protective measures.[286]

Yet another remarkable feature of these compounds is their protonation in the naphthalene nucleus to give stable salts **395**, despite the presence of highly basic 'pyridine type' nitrogen atom, although it is the 'pyridine' nitrogen atom that is alkylated.[16, 287] Finally, they are very potent antioxidants with almost no toxicity (it was impossible to determine their LD_{50} in experiments in animals).[288]

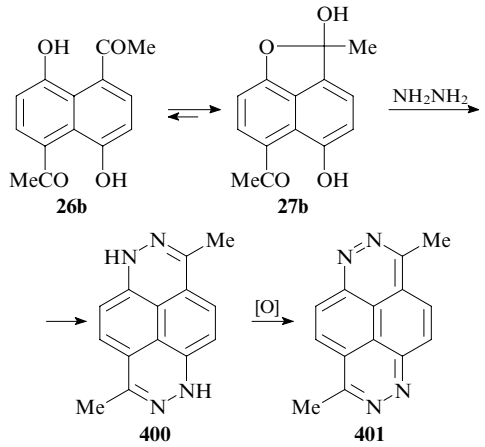


Starting from acenaphthene **13a**, diazaphenalene derivatives **396** with an ethylene bridge were obtained and their oxidative dehydrogenation was studied. It was shown that in the presence of a substituent at nitrogen [compound **396** (R = Me)], dehydrogenation on treatment with *p*-quinones involves the ethylene unit to give compound **397**, while in the absence of this substituent [compound **396** (R = H)], cross-linking takes place to give dimers **398** and **399**. The reactions follow a free radical mechanism.[289, 290] Acenaphthylene-detived diazaphenalene **397** was also obtained by an alternative synthesis from acenaphthylene *peri*-hydroxy ketone **70**.

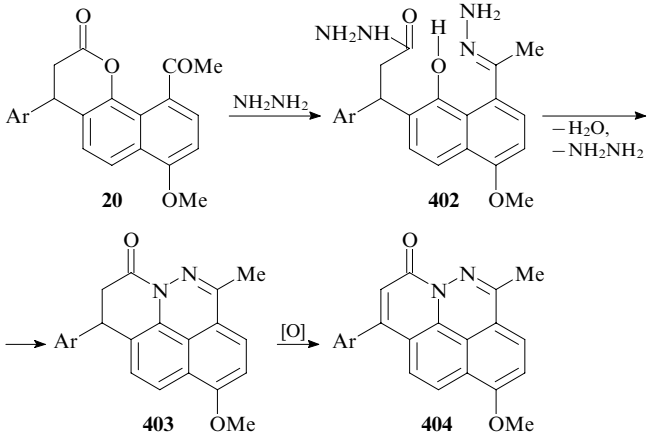


Other transformations of this interesting heterocyclic system were reported in a review.[291]

peri-Dihydroxy diketone **26b** existing in the hemiacetal form **27b** reacts with hydrazine to give first dihydrotetraazapyrene **400**, which is oxidized with atmospheric oxygen under the reaction conditions to give tetraazapyrene **401**.[50]

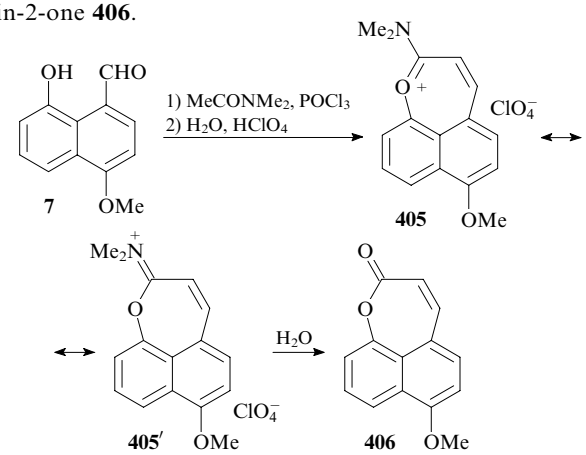


The reaction of *peri*-acyloxy ketone **20** with hydrazine affords intermediate **402**, which eliminates water and hydrazine molecules to be converted to dihydrodiazapyrenone derivative **403**. The latter is oxidized to give diazapyrenone **404**.[25]

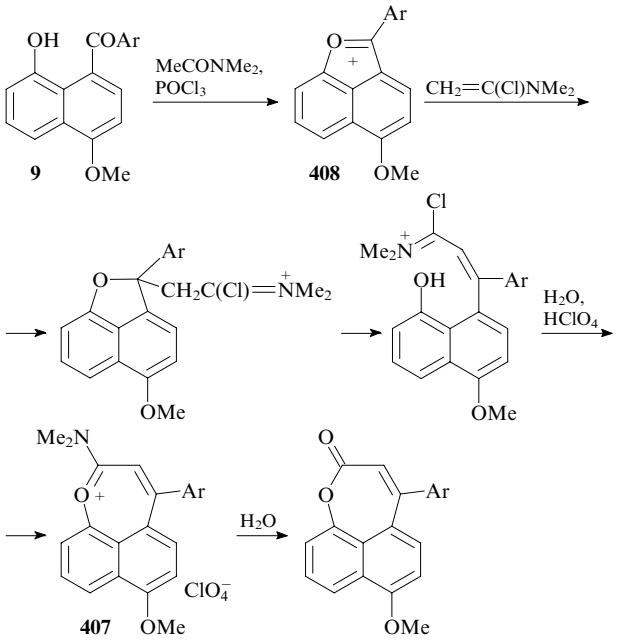


d. Naphtho[1,8-bc]oxepine derivatives

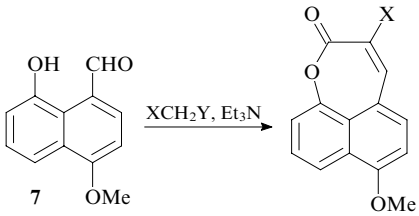
The Vilsmeier reaction of *peri*-hydroxy aldehyde **7** with dimethylacetamide produced salt **405**, which rather exists in the immonium (structure **405′**) than in the oxepine form (structure **405**).[292, 293] Hydrolysis of salt **405′** affords oxepin-2-one **406**.



Not only *peri*-hydroxyaldehydes but also *peri*-hydroxy ketones **9** are able to react with dimethylacetamide.[294] Although in this case, 2-dimethylaminonaphth[1,8-*bc*]oxepinium salts **407** were also obtained, the reaction pathways are different for compounds **7** and **9**. Probably, the first step of the reaction of dimethylacetamide with ketone **9** is the formation of naphtho[1,8-*bc*]furylium ion **408** rather than direct closure of a seven-membered ring, as in the reaction with aldehyde **7**.



Functionally substituted naphthoxepinones (X = CN, CO_2Et, Ar) are formed in the base-catalyzed reaction of *peri*-hydroxyaldehyde **7** with active methylene compounds containing electron-withdrawing groups.[295]

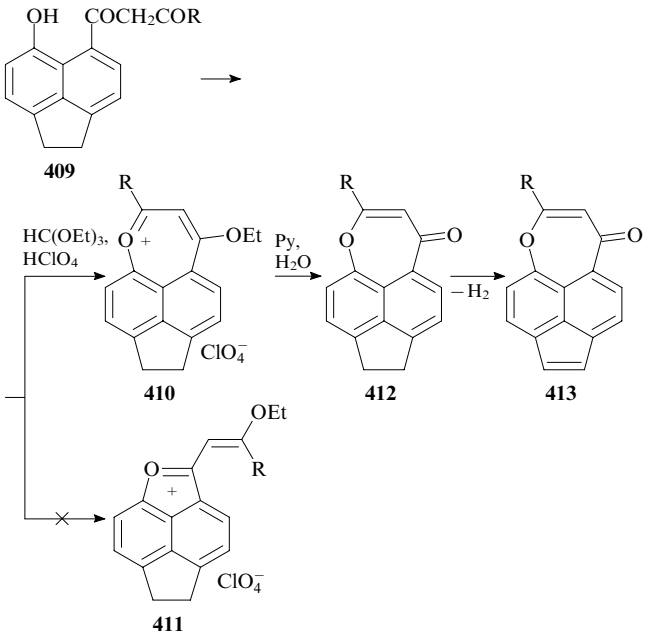


X = CN, CO_2Et, Ar; Y = CO_2Alk.

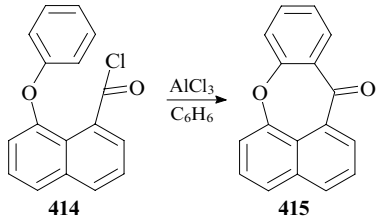
As shown above (see Section IV.3.a), *peri*-hydroxy naphthalene β-diketones (*e.g.*, compounds **84g**,**h**) are converted in acidic media to naphtho[1,8-*bc*]furylium cation **342**. In order to direct heterocyclization along a different pathway, namely, with closure of a seven-membered heterocycle, the process of five-membered ring closure should be suppressed. This can be attained by using, as the starting compound, *peri*-hydroxy-substituted carbonyl acenaphthene derivatives having already one five-membered ring in the *peri*-position of the naphthalene nucleus, which considerably hampers closure of the second five-membered heterocycle in the opposite *peri*-position.

Indeed, the introduction of an ethylene bridge in positions 4, 5 of the naphthalene nucleus directed the heterocyclization of acenaphthene *peri*-hydroxy diketones **409** along the pathway with closure of the seven-membered ring giving rise to acenaphth[5,6-*bc*]oxepinium perchlorate **410** rather than acenaphtho[5,6-*bc*]furylium cations **411**.[75, 296] Hydrolysis of perchlorates **410** leads to acenaphth[5,6-*bc*]oxepin-4-ones **412**,[75, 296] which are dehydro-

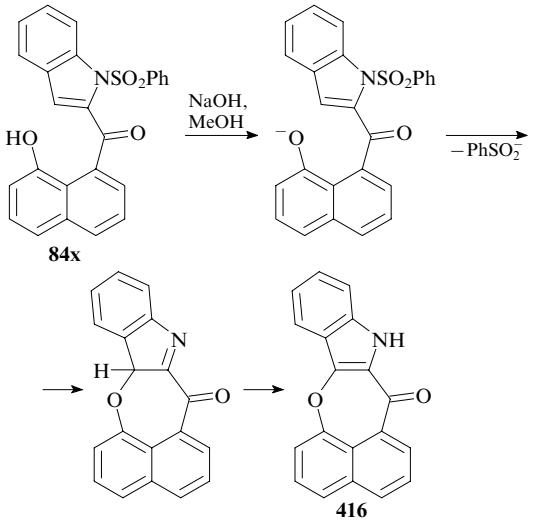
genated to produce the first representatives of a new heteroaromatic system **413**.[297]



peri-Phenoxynaphthoyl chloride **414** undergoes intramolecular heterocyclization under the action of aluminium chloride to give benzonaphth[1,8-*bc*]oxepin-4-one **415**.[298]



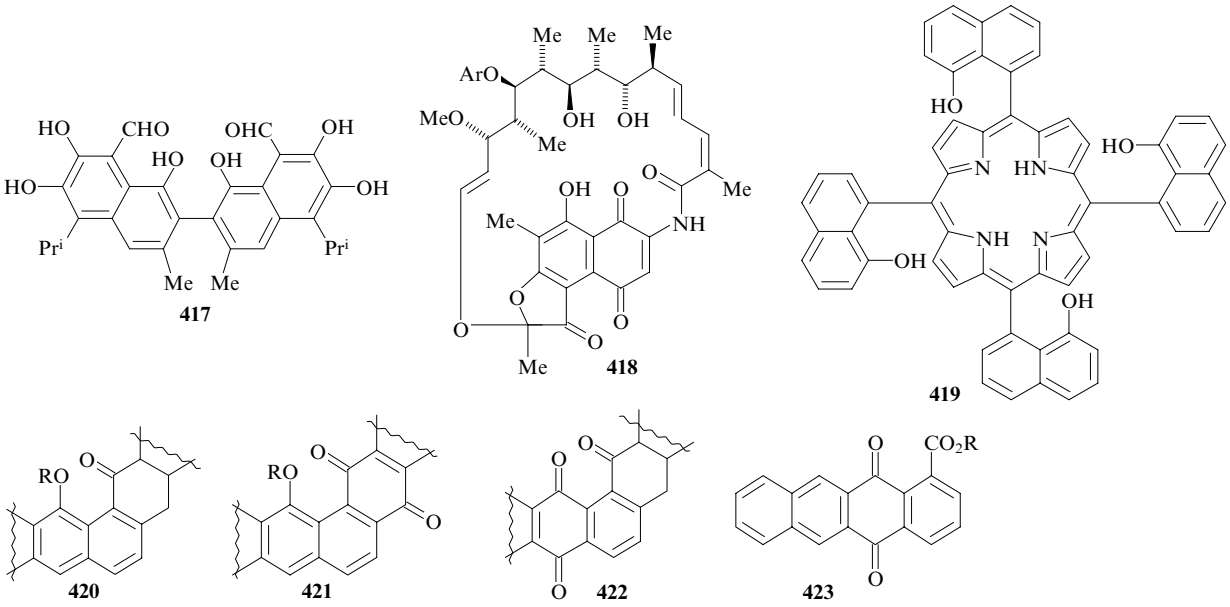
The heteroanalogue of naphth[1,8-*bc*]oxepin-4-one, compound **416**, was prepared by alkaline treatment of *N*-sulfonylindole *peri*-hydroxy ketone **84x**.[110]



V. Natural compounds

There is a group of natural compounds the molecules of which contain *peri*-R-oxy- or *peri*-oxocarbonyl group. The structures of some natural compounds described most often in the literature are presented below. These include gossypol (**417**), a representative of rifampicin antibiotics (compound **418**), porphyrin **419**, angucycline antibiotic fragments (structures **420**–**422**) and one anthracycline antibiotic (compounds **423**).

All of these compounds have been studied in detail; therefore, we mention only some literature sources from which full information on these compounds can be retrieved. In terms of the accumulated knowledge and the number of publications, the top position belongs to gossypol **417** isolated from cotton seeds and its numerous synthetic derivatives. Apart from the multitude of original publications devoted to the synthesis and investigation of gossypol and its derivatives, a number of survey works have been published, for example, Refs 299 and 300. The family of rifampicine antibiotics is considered in reviews,[301, 302] and publications [303–305] are devoted to porphyrins **419** with *peri*-hydroxynaphthyl groups.



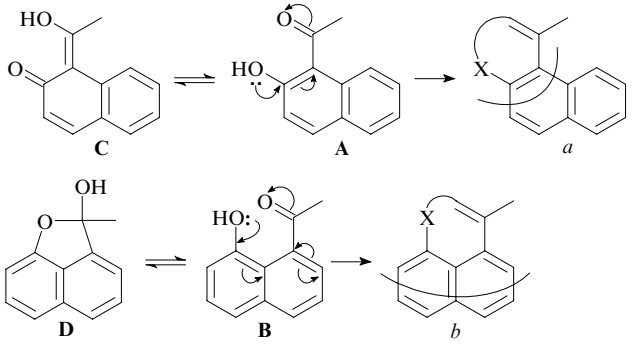
Angucycline (**420**–**422**) and anthracycline (**423**) antibiotics are described in a number of works.[138, 141, 143, 148–165]

VI. Conclusion

It should be noted that the synthesis of compounds containing a *peri*-R-oxy- or *peri*-oxocarbonyl group was not the final goal of the vast majority of works cited in this review but was rather accidental. These compounds were prepared among other compounds devoid of this group. Targeted systematic research of these compounds was started only in 1974 at the Research Institute of Physical and Organic Chemistry of the Rostov State University (currently Southern Federal University). Initially, this was an attempt to study heterocyclizations of *peri*-hydroxycarbonyl compounds, which were expected to behave in these reactions similarly to *ortho*-hydroxycarbonyl derivatives the properties of which are well-known. However, it was found that similar spatial structures of *ortho*- and *peri*-substituted compounds based on the neighbouring positions of hydroxy and carbonyl groups did not guarantee the similarity of their chemical behaviour. Heterocyclization of *ortho*-and *peri*-substituted carbonyl compounds gives *ortho*- and *peri*-annulated heterocyclic systems, respectively, the electronic and spatial structures of these systems being basically different.

In this connection, it is expedient to consider in more detail the structural features of *ortho*- (tautomer **A**) and *peri*-hydroxycarbonyl (tautomer **B**) compound and also *ortho*- (system *a*) and *peri*-annulated (system *b*) heterocyclic systems obtained from them (Scheme 22).

Scheme 22



The *ortho*- and *peri*-substituents differ in the direction of action on each other through the aromatic π-system: the directions of the mutual electronic effects of substituents in *ortho*-positions coincide (structure **A**), while in *peri*-positions they are opposite (structure **B**). In terms of the direction of mutual electronic effects, *peri*-substituted carbonyl compounds resemble *meta*-substituted compounds. This structural feature of *peri*-substituted compounds keeps them from being involved in transformations that are fundamental for aromatic systems such as benzenoid–quinonoid tautomerism (**A** ⇄ **C**), electrocyclic cycloaddion reactions, metal chelation processes, *etc*. Instead of benzenoid–quinonoid tautomerism, ring–chain tautomerism (**B** ⇄ **D**) is possible for *peri*-substituted compounds.

A specific feature of *ortho*-annulated derivatives of naphthalene and other aromatic fused systems is that the parent monoheterocycle is incorporated, as a structural unit, into fused system *a* with retention of the electronic structure and can formally be extracted from it without changing the spatial and electronic structure. Moreover, *ortho*-annulated heterocyclic compounds largely retain fundamental characteristics of the monoheterocyclic precursors such as π-excess or π-deficiency determined by the hybridization type of the heteroatom.

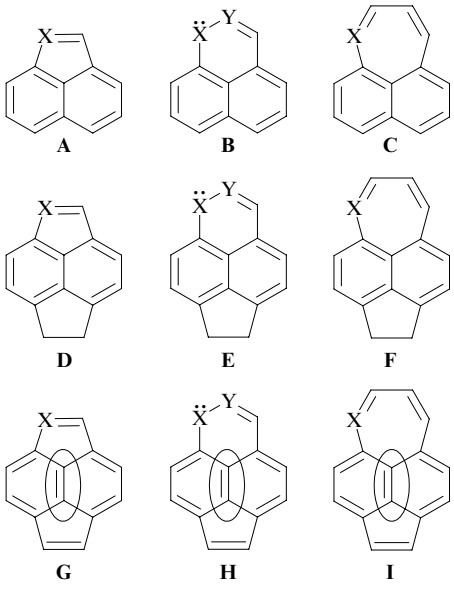
The specific character of *peri*-annulation is the lack of a structural element that could be defined as the parent monoheterocycle. Therefore, in this case, the primary structural unit is the tricyclic nucleus with a carbon atom common to the three rings (system *b*). By monoheterocycles, one means heterocyclic compounds with a closed endo-π-system; hence, the formally distinguished structural fragment *b* cannot be considered as such.

The further development of the line of research discussed in the review would presumably concern investigation of various aspects of the chemistry of *peri*-substituted naphthalene carbonyl compounds and *peri*-annulated heterocyclic systems based on it and investigations of so-called *peri*-effects (IntraHB, electrophile–nucleophile interactions, ring–chain tautomerism, *etc*.).

A qualitatively new stage in the development of this area of science would be related, in our opinion, to the study of *peri*-hydroxy-substituted carbonyl derivatives of acenaphthene and acenaphthylene and *peri*-annulated heterocyclic systems based thereon.

The appearance of an ethylene bridge in the *peri*-position opposite to the *peri*-hydroxycarbonyl group affects substantially the geometry of this group, the related *peri*-effects and the chemical transformations involving this group, first of all, heterocyclizations. The dehydrogenation of the ethylene unit in *peri*-acyl(hydroxy)acenaphthene molecules affords *peri*-hydroxycarbonyl acenaphthylene derivatives in which the hydroxy group can be involved in conjugation (unlike *peri*-hydroxycarbonyl derivatives of naphthalene and acenaphthene) with the carbonyl group along the double bond system of the acenaphthylene nucleus. Dehydrogenation of *peri*-annulated acenaphthene derivatives affords new heteroaromatic systems.

Among the family of *peri*-annulated heterocycles with a closed π-system, one should distinguish naphthalene (structures **A**–**C**) and acenaphthene (structures **D**–**F**) derivatives from acenaphthylene derivatives (structures **G**–**I**).



$\ddot{X}$ = O, NR; Y = CH, N; X = O^+, S^+, RN^+, N.

Systems **A**–**F**, although contain an aromatic naphthalene fragment, cannot generally be assigned to fully heteroaromatic molecular structures due to the odd number of π-electrons (13) in the peripheral contour. Acenaphthylene derivatives (structures **G**–**I**) with an even number of π-electrons in the peripheral contour can also be classified into two groups: structures with $4n+2$ peripheral π-electrons (system **G**) and $4n$ peripheral π-electrons (systems **H**, **I**). System **G** should apparently be assigned to antiaromatic, despite the fact that the whole molecule has 14 π-electrons, *i.e.*, $(4n+2)$ π-electrons, whereas systems **H** and **I** containing 16 π-electrons, *i.e.*, $4n$, are nevertheless aromatic. It is considered that it is the peripheral electrons that play the crucial role in determining either aromatic or antiaromatic character of the molecule.

Thus, the specific structure and unusual properties of *peri*-substituted and *peri*-annulated compounds often give a clue for a new understanding and supplementation of fundamental concepts and views of organic chemistry and heterocyclic chemistry. Nevertheless, organic chemistry and heterocyclic chemistry monographs do not include special chapters devoted to *peri*-substituted carbonyl and *peri*-annulated heterocyclic compounds, and this gives every ground for regarding them as new subjects that deserve systematic investigation.

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