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Naphthaldehydes

A F Pozharskii

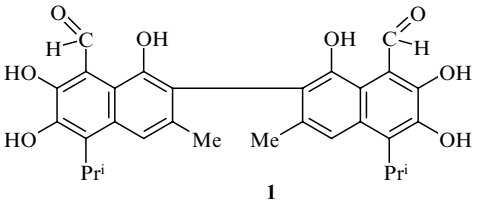
Contents

I.	Introduction	447
II.	Synthesis of naphthaldehydes	447
III.	Structures and physicochemical properties of naphthaldehydes	459
IV.	Reactions	466

Abstract. Data on methods for the preparation of naphthaldehydes, their physicochemical properties, structural characteristics and reactivities are generalised. Particular attention is given to procedures for formylation of naphthalenes and *peri*-interactions involving the aldehyde group in the α-position. The bibliography includes 201 references.

I. Introduction

Naphthaldehydes [1–3] play a very important role in naphthalene chemistry, much as other aldehydes play a significant part in the chemistry of other classes of organic compounds, which is associated primarily with the diversity of reactions involving these compounds. The high reactivity of the formyl group is widely utilised in the synthesis of complex natural compounds containing the naphthalene fragment. In addition, naphthaldehydes and, primarily, α-naphthaldehydes possess specific features, which receive the continuing attention of both synthetic and theoretical chemists. Among these features are, in particular, different manifestations of *peri*-interactions [4–6] and the possibility of performing *peri*-cyclisation.[7] Interest in naphthaldehydes has increased substantially after isolation of gossypol (**1**), *viz*., 2,2′-binaphthyl polyphenol dialdehyde, from cotton seeds. This compound appeared to be the first efficient contraceptive pill for men.[8]



1

Gossypol also exhibits antitumor and antiviral activity and, in spite of substantial toxicity, is registered in some countries for use as a pharmaceutical. It was established that the toxicity of gossypol is associated with the presence of aldehyde groups. However, all attempts to replace these groups by other functionalities led only to the disappearance of biological activity (the history of the discovery of gossypol and its chemical and pharmacological properties were surveyed in a review).[8]

The published data on the chemistry of naphthaldehydes are voluminous and scattered throughout various sources. These data have not been generalised, except for outdated information summarised in the monogrpahs,[9, 10] which causes great inconvenience for researchers. This fact gave impetus to the present review. Since it is practically impossible to cite all studies concerning naphthaldehydes, emphasis is given to main trends associated with the synthesis, reactions and physicochemical characteristics of these compounds. Most attention is concentrated on the preparation of naphthaldehydes by direct formylation of naphthalenes or naphthalene carbanions (organometallic compounds), *peri*-interactions, *peri*-cyclisation reactions involving the α-formyl group, characteristic features of the molecular structures of these compounds and their relationship with physicochemical properties and reactivity. Other aspects of the chemistry of naphthaldehydes are considered as necessary.

II. Synthesis of naphthaldehydes

Naphthaldehydes can be prepared according to virtually all procedures generally used in the synthesis of aromatic aldehydes.[1–3, 11] In addition to direct formylation, these methods involve oxidation of methyl-, hydroxymethyl- and halomethyl-substituted naphthalenes, reduction of nitriles and naphthalenecarboxylic acid chlorides, *etc*. Data on these methods published up to the mid-1950s are generalised in the monograph.[9] Since then, almost all the above-mentioned synthesis methods have been improved primarily due to the use of new reagents. Generally, this enables one to use milder conditions of reactions and enhance their selectivity. The most typical examples are considered below.

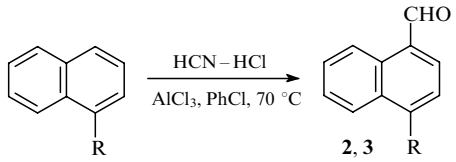
1. Formylation of naphthalenes

a. Naphthalene and alkylnaphthalenes

Gattermann formylation (under the action of a mixture of HCN and HCl in the presence of $AlCl_3$, $CuCl_2$ or other Lewis acids) of naphthalene [12] and α-methylnaphthalene [13] afforded α-naphthaldehyde (**2**) and its 4-methyl derivative **3**. The modification of this reaction consists in replacing HCN by less toxic $Zn(CN)_2$ (Adams method)[14] or *sym*-triazine.[15] Thus, the synthesis with the use of *sym*-triazine afforded aldehyde **2** in 57% yield.

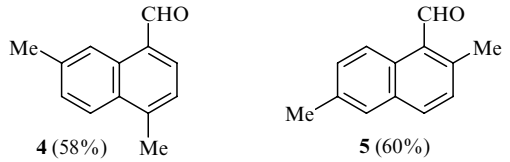
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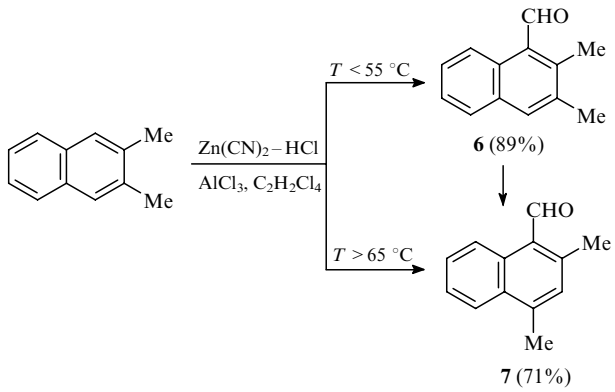


Compound	R	Yield (%)
2	H	60
3	Me	51

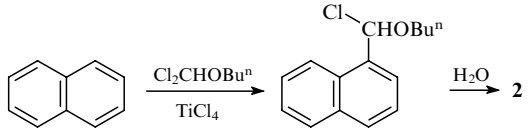
Under the conditions of the Gattermann reaction, 1,6- and 2,6-dimethylnaphthalenes gave aldehydes **4** and **5**, respectively.[12]



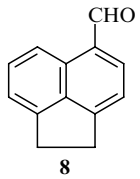
Formylation of 2,3-dimethylnaphthalene should be carried out with thorough control over the reaction temperature. Thus, 'normal' product **6** was generated in good yield only at a temperature below 55 °C, whereas it was transformed into 2,4-dimethyl-1-naphthaldehyde (**7**) at a temperature above 65 °C.[16, 17]



Naphthalene is readily subjected to formylation by dichloromethyl n-butyl ether in the presence of $TiCl_4$ (Rieche method).[18] Apparently, this procedure is among the simplest approaches to α-naphthaldehyde **2** (79% yield).



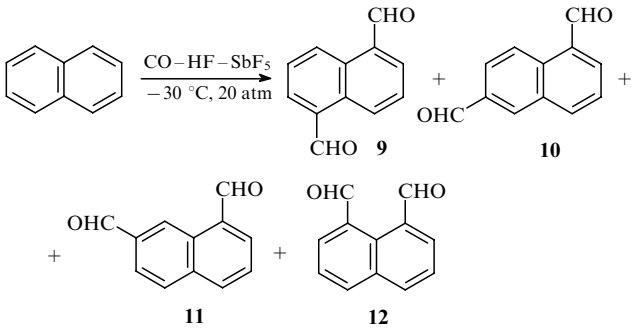
Naphthalene does not react with the milder formylating Vilsmeier reagent [19, 20] (a mixture of $POCl_3$ with *N*,*N*-dimethylformamide or other formamide derivatives, for example, with *N*-methylformanilide). However, the reaction of acenaphthene performed under these conditions afforded acenaphthene-5-carbaldehyde (**8**) (81% yield).[21, 22]



Recently, a convenient procedure was proposed for the preparation of aldehyde **8** by microwave irradiation of a mixture of acenaphthene and the Vilsmeier complex on a support (DMF – $POCl_3$ – SiO_2, 300 W, 2 min, 89% yield).[23] Naphthalene, like acenaphthene, is formylated by the modified Vilsmeier complex in which phosphorus oxychloride is replaced by trifluoromethanesulfonic anhydride.[20] The reaction proceeded under very severe conditions (130 °C, 48 h) to give aldehydes **2** and **8** in 50% and 90% yields, respectively.

Under standard conditions of the Gattermann – Koch reaction (CO – HCl, $AlCl_3$), naphthalene does not undergo formylation.[24] However, aldehyde **2** was prepared with the use of the CO – HF – BF_3 system under high pressure.[25] It was demonstrated that formyl fluoride served as the true formylating agent in this reaction.[26] In the presence of BF_3, the latter compound reacted (CS_2, 0 – 10 °C, 3 – 5 h) with naphthalene to form a mixture of α- and β-naphthaldehydes in 20% and 67% yields, respectively. Considering the traditionally higher reactivity of the α positions in naphthalene compared to the β positions, the formation of β-naphthaldehyde as the major product under such mild conditions seems to be surprising. However, this fact was not commented in the study [26] and the review.[27]

The modified Gattermann – Koch reaction with the use of the stronger Lewis catalyst SbF_5 instead of BF_3 can lead to diformylation of naphthalene.[28] This reaction afforded a mixture of 1,5- (**9**), 1,6- (**10**), 1,7- (**11**) and 1,8-diformylnaphthalenes (**12**) in a total yield of 80% in a ratio of **9** : **10** : **11** : **12** = 51 : 6 : 27 : 16. It should be noted that the positions of substituents in formylation products of naphthalene differ substantially from those in nitration products. It is known that nitration gives rise to 1,8- and 1,5-dinitronaphthalenes in a ratio of ~7 : 3.[9] By contrast, 1,5-dialdehyde prevails among diformylation products, the second highest yield was observed for the 1,7-isomer. Apparently, the first step of this reaction affords β-naphthaldehyde in a noticeable amount and further formylation of the latter at the free α positions of the unsubstituted ring gives dialdehydes **10** and **11**.



When studying Gattermann – Koch (CO – HF – SbF_5) and Friedel – Crafts (HCOF – HF – SbF_5) formylation of α-methylnaphthalene, Tanaka and co-workers [29, 30] found that the rate and regioselectivity of the Gattermann – Koch reaction depend on the SbF_5 : α-methylnaphthalene molar ratio (Table 1). The authors attributed this fact to a superposition of two mechanisms

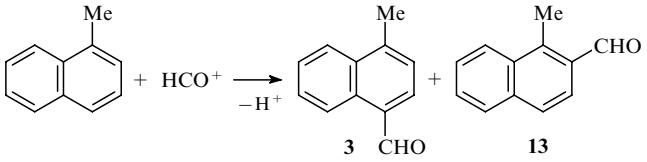
Table 1. Results of Gattermann – Koch (GK) and Friedel – Crafts (FC) formylation of α-methylnaphthalene.[30]

Molar ratio SbF_5 : α-methylnaphthalene	Reagent	Temperature /°C	Time /h	Product ratio **3** : **13**	Reaction type
1 : 1	CO	0	2	100 : 0	GK
1.25 : 1.00	CO	0	0.15	68 : 32	*ditto*
1.25 : 1.00	CO	−40	2	64 : 36	"
1 : 1	HCOF	0	1	93 : 7	FC
1.25 : 1.00	HCOF	0	1	94 : 6	*ditto*
1.25 : 1.00	HCOF	−40	1	94 : 6	"
2 : 1	HCOF	−40	1	94 : 6	"

Note. Reaction conditions: 10 mmol of 1-methylnaphthalene, 500 mmol of HF; CO pressure was 20 atm (GK reaction); 80 mmol of HCOF (FC reaction).

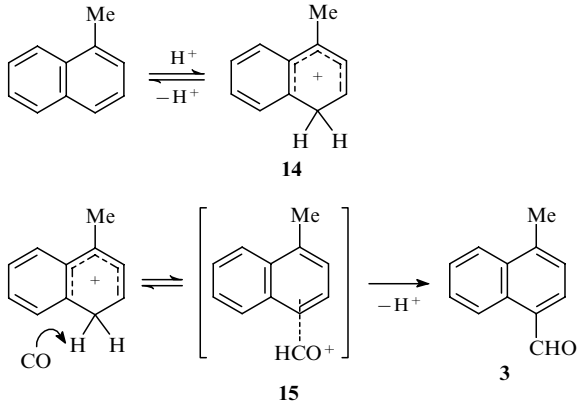
of electrophilic substitution, *viz*., conventional and non-conventional (intracomplex). In the course of formylation by a conventional mechanism, the electrophilic species (HCO^+), which is generated through the reaction of the reagent acting as a proto-electrophile (CO or HCOF) with protic (HF) or Lewis (SbF_5) acid, attacks the aromatic substrate at the *ortho* or *para* positions with respect to the methyl group to form the corresponding σ-complexes, which give aldehydes **3** and **13**.

$$CO \xrightarrow[SbF_5]{HF} HCO^+ + SbF_6^-;$$



In the naphthalene series, σ-complexes corresponding to α substitution are more stable than σ-complexes corresponding to β substitution. Hence, *para* isomer **3** is generally produced in higher yield than *ortho* isomer **13**.

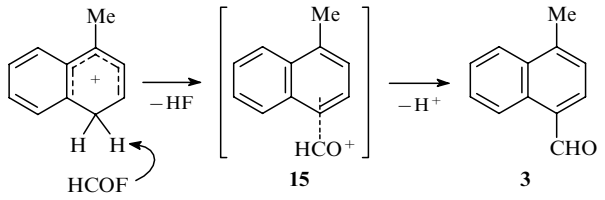
The first step of formylation according to an alternative mechanism involves protonation of the substrate giving rise exclusively to methylnaphthenium cation **14**. The latter donates a proton to the protoelectrophile (CO) thus transforming it into the active electrophile. If the electrophile and substrate in the *para*-oriented π-complex **15** thus produced have no time to move apart, their interaction gives rise to the *para*-σ-complex and finally (after proton elimination) to *para*-aldehyde **3**.



If the substrate and electrophile in complex **15** are separated, the reaction mechanism consists of the usual electrophilic attack.

The highest regioselectivity of the Gattermann–Koch reaction is observed at the SbF_5 : α-methylnaphthalene molar ratio of 1 : 1. Since the HF–SbF_5 system acts as a superacid, this reagent ratio allows the substrate to be completely protonated to give methylnaphthenium cation **14**. As a result, the reaction proceeds by an intracomplex mechanism to give *para* isomer **3** as the only product. In the presence of a larger amount of SbF_5 and, consequently, a larger amount of the superacid, carbon monoxide molecules are also subjected to protonation to give the HCO^+ cations. Since the reaction of the latter with cation **14** is unlikely, the contribution of the conventional mechanism of formylation increases and, as a consequence, the yield of *ortho* isomer **13** increases.

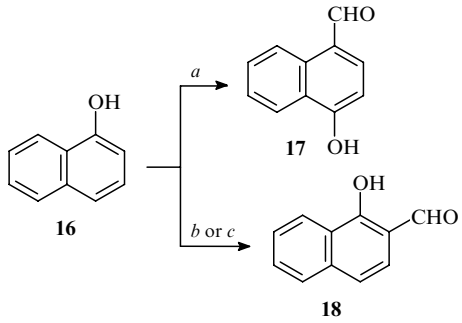
Since the basicity of formyl fluoride is lower than that of carbon monoxide, the dependence of the Friedel–Crafts reaction on the amount of SbF_5 is less pronounced and the constancy of the *para*/*ortho* regioselectivity most likely indicates that the reaction proceeds predominantly by the intracomplex mechanism.



Formylation of naphthalene and its 1- and 2-methyl derivatives was also performed with the use of triformamide $N(CHO)_3$ in the presence of $AlCl_3$. However, these reactions afforded aldehydes **2** and **3** and 2-methyl-1-naphthaldehyde in low yields (18%–30%).[31]

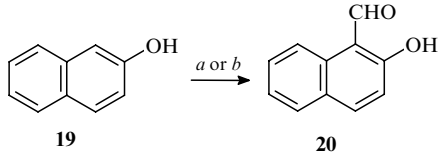
b. Naphthols and alkoxy- and alkylthionaphthalenes

Depending on the nature of the formylating agent, α-naphthol (**16**) is formylated at either *ortho* or *para* position with respect to the hydroxy group. For example, the reaction of compound **16** with the HCN–$AlCl_3$ system (Gattermann reaction) afforded 4-hydroxy-1-naphthaldehyde (**17**) in high yield,[14,32,33] whereas the Reimer–Tiemann reaction (70–80 °C, $CHCl_3$–NaOH) gave rise to its *ortho* isomer **18** in ~ 40% yield.[34] Apparently, one of the best methods for the synthesis of the latter compound involves the reaction of α-naphthol with orthoformic ester in the presence of $AlCl_3$ producing aldehyde **18** in almost quantitative yield.[35] The reaction of α-naphthol with α,α-dichlorodimethyl ether in the presence of $TiCl_4$ (Rieche method) afforded a mixture of aldehydes **17** and **18** in 68% and 10% yields, respectively.[35]



(*a*) HCN–$AlCl_3$ (> 90%); (*b*) $CHCl_3$–NaOH (38%–48%); (*c*) $HC(OEt)_3$–$AlCl_3$ (97%).

Formylation of β-naphthol (**19**) gave rise to 2-hydroxy-1-naphthaldehyde (**20**) regardless of the method used. The Gattermann reaction with the use of the HCN–$ZnCl_2$ system[33] or the $Zn(CN)_2$–HCl system[14] produced aldehyde **20** in virtually quantitative yield. However, even in spite of lower yields, this hydroxy aldehyde is much more convenient to prepare by the Duff[36] (with the use of urotopine and acetic acid), Rieche,[35] Vilsmeier[37] and, particularly, Reimer–Tiemann reactions.[38]

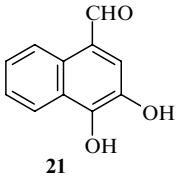


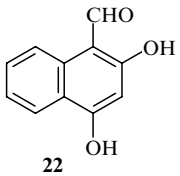
(*a*) $(CH_2)_6N_4$–AcOH (76%); (*b*) $CHCl_3$–NaOH (40%).

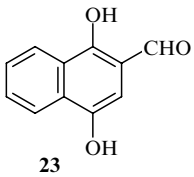
Recently, the $(CH_2O)_n$–$MgCl_2$–Et_3N system in acetonitrile was proposed for *ortho*-formylation of phenols.[39] In this reaction, β-naphthol gave aldehyde **20** (72%) and 1-methoxymethyl-2-naphthol (9%).

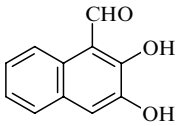
Gattermann formylation (HCN–$ZnCl_2$, ether, 20 °C) of 1,2-dihydroxy-, 1,3-dihydroxy-, 1,4-dihydroxy-, 2,3-dihydroxy-, 1,5-dihydroxy-, 2,6-dihydroxy- and 2,7-dihydroxynaphthalenes

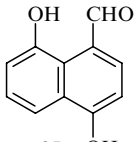
afforded aldehydes **21** – **27**, respectively, as the only products.[40, 41] Aldehyde **25** can also be synthesised by Rieche formylation of 1,5-dihydroxynaphthalene. However, the latter reaction is accompanied by the formation of impurities, which are difficult to separate.[42]

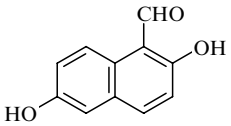

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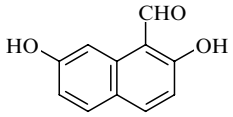

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24

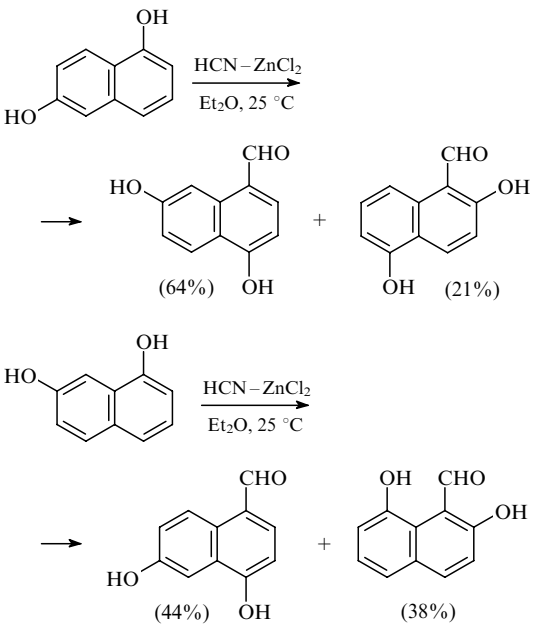

25

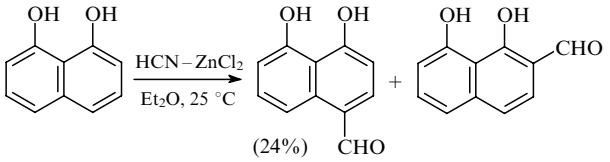

26


27

Compound	Yield (%)	Ref.
21	21	40
22	42	40
23	13	40
24	62	40
25	not given	40, 41
26	*ditto*	40, 41
27	70	40
27	100	41

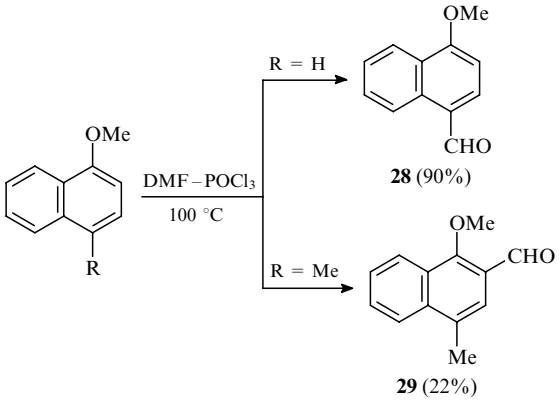
Unlike the above-mentioned dihydroxy derivatives of naphthalene, Gattermann formylation of 1,6- , 1,7- and 1,8-dihydroxynaphthalenes afforded two isomeric aldehydes in all cases.[40]





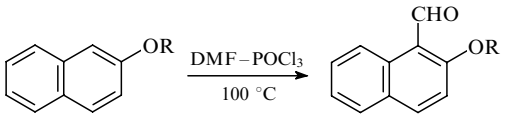
3-Hydroxy-2-naphthoic acid is subjected to Vilsmeier formylation at position 4.[19]

Formylation of alkoxynaphthalenes proceeds much as that of naphthols, although there are some exceptions. For example, Gattermann [43] or Vilsmeier [44] formylation of 1-methoxynaphthalene gave 4-methoxy-1-naphthaldehyde (**28**) in nearly quantitative yield (the reaction with the use of triformamide as the formylating agent, aldehyde **28** was prepared in only 42% yield).[31] If position 4 is occupied by the methyl group, the aldehyde group is added at the α position with respect to the more electron-donating methoxy substituent to form compound **29**.



28 (90%)
29 (22%)

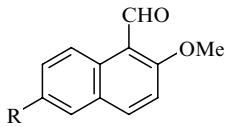
2-Alkoxynaphthalenes were smoothly formylated at position 1 to give aldehydes **30a**,**b** in good yields.[45 – 47]



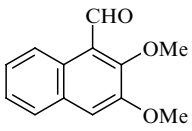
30a,**b**

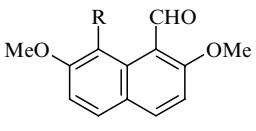
Compound	R	Yield (%)	Ref.
a	Me	90	45, 46
b	Et	74 – 84	46, 47

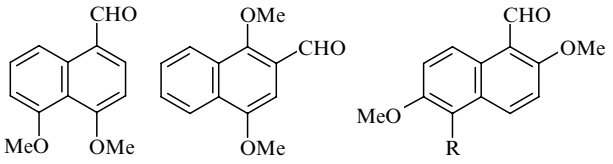
Under the same conditions, 6-alkyl-2-methoxynaphthalenes produced aldehydes **31**.[48 – 50]


31

Vilsmeier formylation of dimethoxynaphthalenes giving rise to aldehydes **32** – **36** was carried out in the studies.[44, 51 – 55]


32

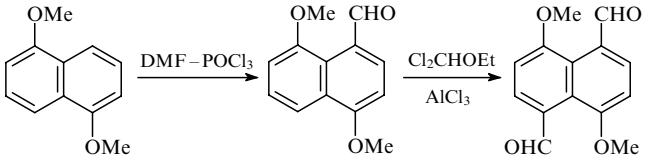

33a,**b**



34 **35** **36a,b**

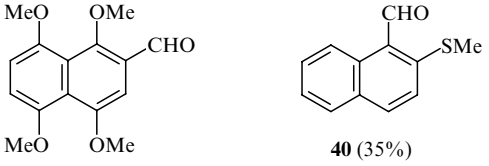
Compound	R	Yield (%)	Ref.
32	–	23	51
33a	H	82	44
33b	Me	82	44
34	–	23	52
34	–	88	53
35	–	42	54
35	–	88	55
36a	H	80	44
36b	Me	40	54

The Vilsmeier reaction of 1,5-dimethoxynaphthalene afforded 4,8-dimethoxy-1-naphthaldehyde (**37**) with a small impurity of dialdehyde **38**.[56] It was demonstrated [42] that the latter can also be synthesised by Rieche formylation of monoaldehyde **37** (93% yield).



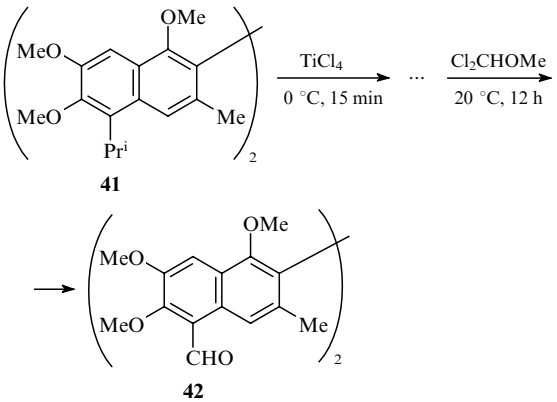
37 **38**

Vilsmeier formylation of 1,4,5,8-tetramethoxynaphthalene gave aldehyde **39** in quantitative yield. The latter was used as the starting compound in the synthesis of natural compounds.[57–59] Formylation of 2-methylthionaphthalene produced aldehyde **40**, which is one of a few known sulfur-containing naphthaldehydes.[60]



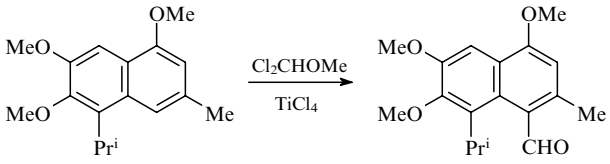
39 **40** (35%)

A rare example of *ipso*-formylation with the substitution of the isopropyl group was observed in attempting to subject 2,2′-binaphthyl derivative **41** to the Rieche reaction in the presence of $TiCl_4$. Dialdehyde **42** was obtained in 79% yield.[61]



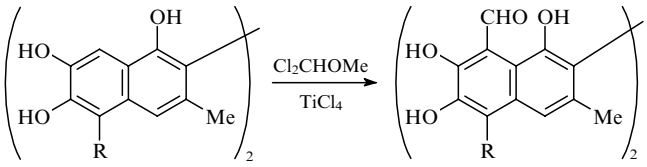
41 **42**

Interestingly, the reaction of monomeric substrate **43** performed under analogous conditions afforded 'normal' formylation product **44** in quantitative yield.[62]



43 **44**

Formylation of compounds **45a** (apogossypol) and **45b** giving rise to gossypol **1** [61,63] and its ethyl analogue **46**, respectively,[61] follows another pathway compared to the above-mentioned reactions involving polymethoxy derivatives **41** and **43**. Apparently, the hydroxy groups, which can form hydrogen bonds with an electrophile, efficiently stabilise the transition state corresponding to aldehydes **1** and **46**.

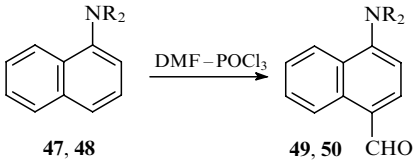


45a,b **1, 46**

R = Pr^i (**45a**, **1**), Et (**45b**, **46**).

c. Aminonaphthalenes and aminonaphthols

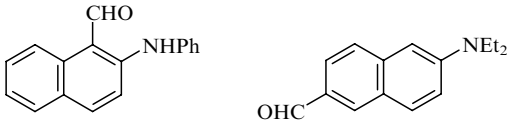
Aminonaphthalenes exhibit much higher reactivity in formylation compared to naphthols and alkoxynaphthalenes. However, the orientation effects in both series of compounds are virtually identical. For example, the Vilsmeier reactions of 1-dimethylamino- (**47**) [64,65] and 1-diethylaminonaphthalenes (**48**) [66] afforded the corresponding 4-dialkylamino-1-naphthaldehydes **49** and **50**.



47, 48 **49, 50**

R = Me (**47**, **49**), Et (**48**, **50**).

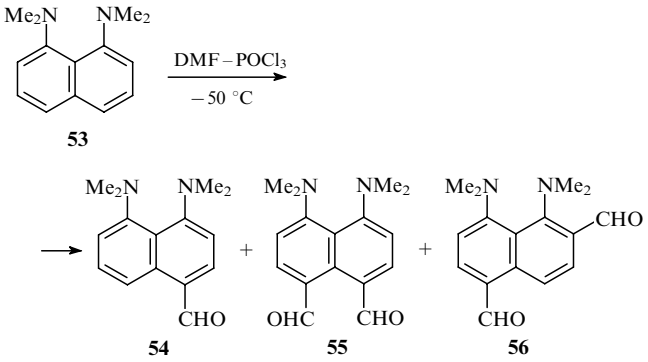
2-Anilinonaphthalene was formylated at position 1 to give aldehyde **51** (48% yield).[67] 2-Diethylaminonaphthalene was formylated at the *amphi* position with respect to the NEt_2 group to form aldehyde **52**.[66]



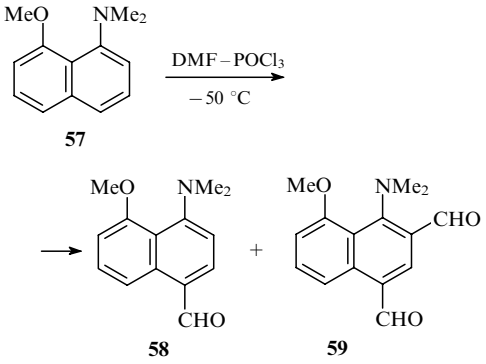
51 **52**

1,8-Bis(dimethylamino)naphthalene (**53**) known under the name of 'proton sponge' exhibits high reactivity with respect to formylating agents. This diamine reacts with the Vilsmeier reagent ($DMF-POCl_3$) already at −50 °C.[68] The results of this reaction depend substantially on the diamine **53** : Vilsmeier reagent molar ratio. Apparently, the proton abstracted upon formylation is bound by a highly basic (pK_a 12.1) compound **53** to form a cation, which is not involved in formylation. Hence, 2 equiv. of diamine **53** per equivalent of the $DMF-POCl_3$ mixture should be used for the preparation of monoaldehyde **54**. As a result, more than 50% of the starting compound is regenerated and aldehyde **54** is produced in 70% yield with respect to bis(dimethylamino)naphthalene **53** consumed. In the reaction of diamine **53** with the Vilsmeier reagent taken in a ratio of 1 : 1, the yield of monoaldehyde **54** decreased to 16.5%, *peri*-dialdehyde **55** was produced as the main reaction product (50%), and unsymmetrical dialdehyde **56** was generated as an impurity (all yields are given with respect to

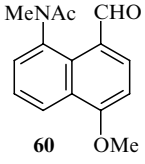
compound **53** consumed). Diamine **53** was also subjected to formylation by chloral in pyridine, but aldehyde **54** was obtained in a yield of no higher than 7%.[68] Unlike compound **53**, its tetraethyl analogue is difficult to formylate and 4,5-bis(diethylamino)-1-naphthaldehyde was isolated in only 13% yield.[69] Apparently, due to strong steric hindrances in the 4,5-bis(diethylamino)-1-naphthaldehyde molecule, the electron-donating effect of two *peri*-NEt_2 groups with respect to the naphthalene system is much weaker than that in the 'proton sponge.'



1-Methoxy-8-dimethylaminonaphthalene **57** exhibits reactivity as high as that of diamine **53**.[70] This compound readily reacts with the Vilsmeier reagent at -50 °C to form monoaldehyde **58** in 85% yield with an insignificant (2.5%) impurity of dialdehyde **59** (the yields are given with respect to amine **57** consumed in the reaction, about one-half of the latter being involved in the formation of inert cations and regenerated). The formation of compound **59** is the first example of the introduction of two aldehyde groups into the same ring of the naphthalene system. Interestingly, the yield of dialdehyde increased substantially when the reaction was performed at -10 °C and the **58** : **59** product ratio was 3 : 1.

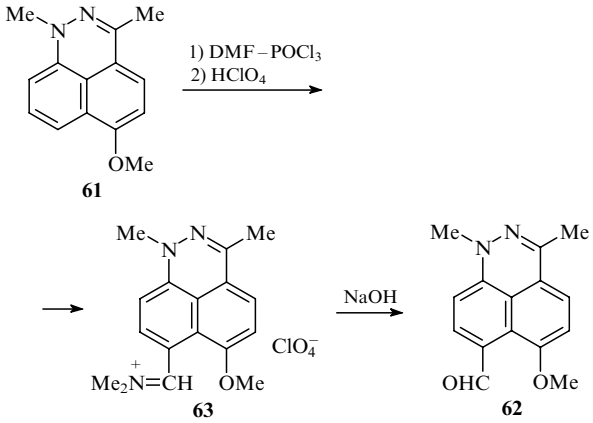


In 1-methoxy-5-(*N*-methylacetamido)naphthalene, the methoxy group exhibits a stronger activating effect in contrast to compound **57**. Formylation (Rieche method) afforded aldehyde **60** as the only product (yield 60%).[71]



d. Naphthalene-based heterocyclic systems

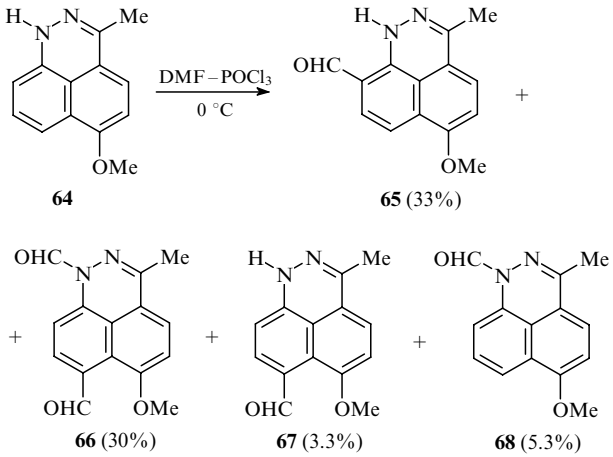
Formylation of *peri*-fused heterocyclic systems based on naphthalene was carried out in a series of studies. These systems are of interest because the heterocycle in these compounds serves as a special kind of substituent exerting a substantial effect on the degree of activation of the naphthalene system with respect to the electrophilic substitution as well as on the orientation effects. It was demonstrated[72] that 6-methoxy-1,3-dimethyl-1*H*-1,2-diazaphenalene (**61**) rapidly reacted with the Vilsmeier reagent even at 0 °C to give 7-carbaldehyde **62** as the only product (87% yield). In this experiment, intermediate immonium salt **63** was isolated as a perchlorate. The ease of formylation results from π-excessiveness of the heterocycle in diazaphenalene **61**, which formally contains 7 π electrons. The partial shift of the excessive Hückel electron from the heterocycle in molecule **61** induces substantial negative π-charges in the *ortho* and *para* positions of the naphthalene fragment.



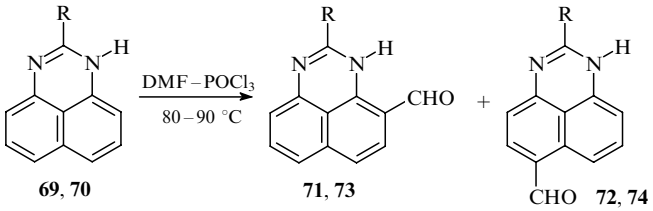
Formylation of 1,2-diazaphenalene **64** containing the unsubstituted NH group proceeds less selectively. In this reaction, the sterically non-hindered *ortho* position and the pyrrole nitrogen atom are subjected to electrophilic attack along with the *para* position with respect to the NH group. The reaction afforded aldehyde **65** and dialdehyde **66** as the major products. In addition, formyl derivatives **67** and **68** were isolated in low yields (Scheme 1).

Since heterocyclic 1,2-diazaphenalenes are characterised by very low basicity ($pK_a < 3$), they are present in reaction mixtures predominantly as bases, which, evidently, undergo formylation. A different situation occurs in the case of much more basic ($pK_a > 5.5$) 1,3-diazaphenalenes (perimidines). Perimidine (**69**) and 2-methylperimidine (**70**) are very difficult to formylate. A large excess of the Vilsmeier reagent and prolonged heating at 80–90 °C are required for the latter reactions to proceed. However, the yields of 4(9)- (**71**) and 6(7)-formylperimidines (**72**) produced under these conditions were also no higher than 10%. Aldehydes **73** and **74** derived from 2-methylperimidine were

Scheme 1

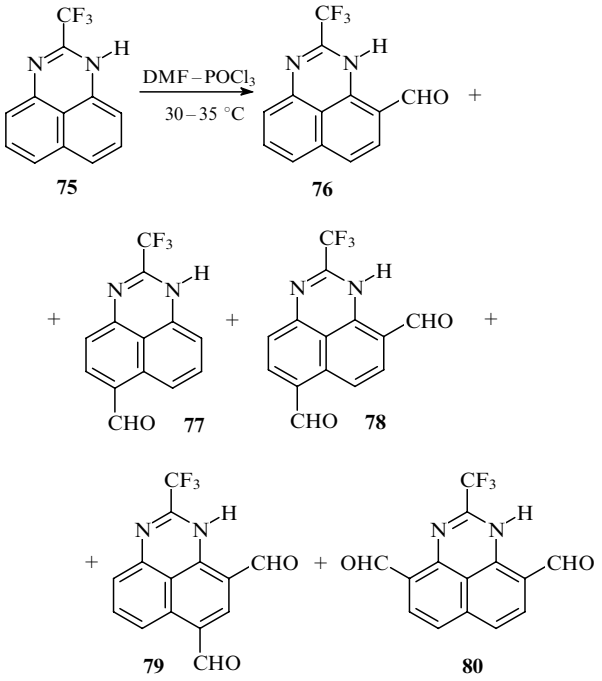


prepared in only 1% – 2% yields.[73] Since the 1,3-dimethylperimidinium cation does not undergo formylation at all, it can be concluded that perimidines **69** and **70** are virtually completely protonated under the conditions of the Vilsmeier reaction and the reaction proceeds through formation of the free base, which is present in the reaction mixture in a low equilibrium concentration.

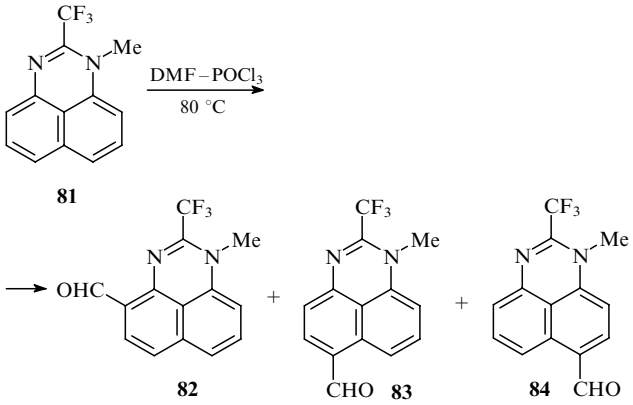


R = H (**69**, **71**, **72**), Me (**70**, **73**, **74**).

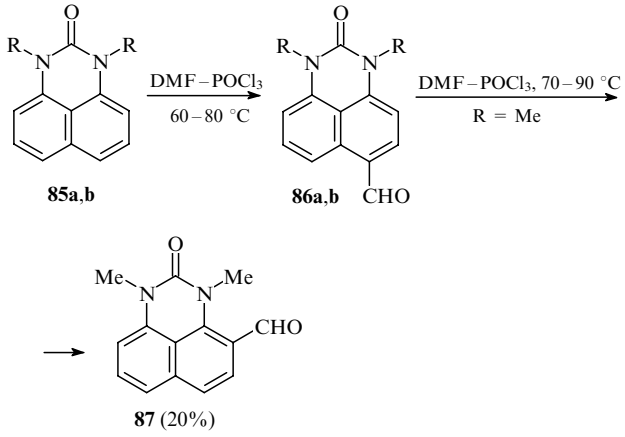
An important role of the basicity of the substrate is evidenced by the fact that 2-trifluoromethylperimidine (**75**) of low basicity is readily subjected to formylation.[74] This reaction afforded 4(9)-carbaldehyde **76** (yield 42%) and 6(7)-carbaldehyde **77** (22%) as the major products along with small amounts of dialdehydes **78** – **80**. It should be noted that formation of the latter product is the only example of diformylation of the naphthalene ring at two β positions.



It should be noted that 1-methyl-2-trifluoromethylperimidine (**81**) is much more difficult to formylate than its non-methylated analogue **75**.[74] For example, the reaction of compound **81** proceeded at a noticeable rate only at 80 °C, and the total yield of aldehydes **82** – **84** was 46% after 3.5 h, whereas formylation of perimidine **75** was completed within 2.5 h even at 35 °C. In addition, perimidines containing the unsubstituted NH group were formylated predominantly at positions 4(9), whereas an analogous reaction of *N*-methylated derivative **81** gave rise predominantly to 6- and 7-carbaldehydes (product ratio **82** : **83** : **84** = 22 : 20 : 58). It can be hypothesised that the NH group in molecule **75** is efficiently involved in stabilisation of the transition complex corresponding to *ortho*-formylation (this is, to a large extent, true also for 1,2-diazaphenalene **64** and other analogous compounds).



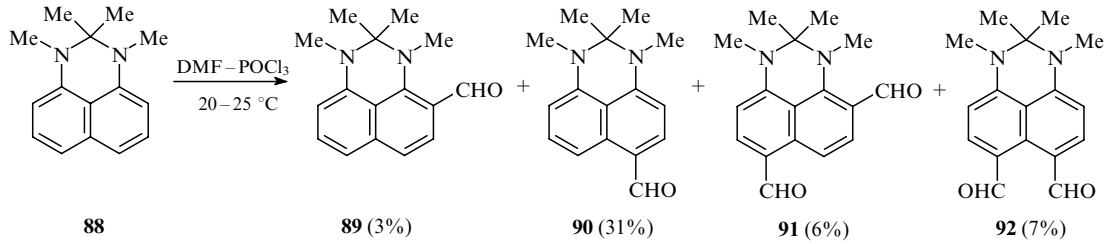
1,3-Dialkylperimidones **85a**,**b**, which are less basic than 2-trifluoromethylperimidines, were smoothly formylated at position 6 to form aldehydes **86a**,**b** in 85% yield.[74] In attempting to perform further formylation, compound **86a** underwent isomerisation to 4-carbaldehyde **87**. The fact that the second formyl group is difficult to introduce can be attributed to the lower π-donating ability of the heterocycle in perimidones due to the electron-withdrawing effect of the carbonyl group. This is also evidenced by the fact that formylation requires high temperature.



85, **86**: R = Me (**a**), Et (**b**).

The electronic structure of 1,2,2,3-tetramethyl-2,3-dihydroperimidine (**88**) is more similar to that of 1,8-bis(dimethylamino)-naphthalene (**53**) rather than to that of perimidines **69** and **70**. Being in addition a weak base, compound **88** is readily formylated (Scheme 2) to give monoaldehydes **89** and **90** and dialdehydes **91**

Scheme 2

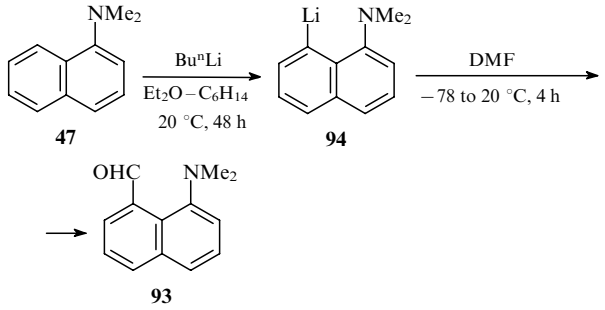


and **92**.[74] These results are very similar to those observed upon formylation of 'proton sponge' **53**, with the only difference that the formation of mono-*ortho*-aldehyde was not observed in the latter case.

2. Organometallic syntheses

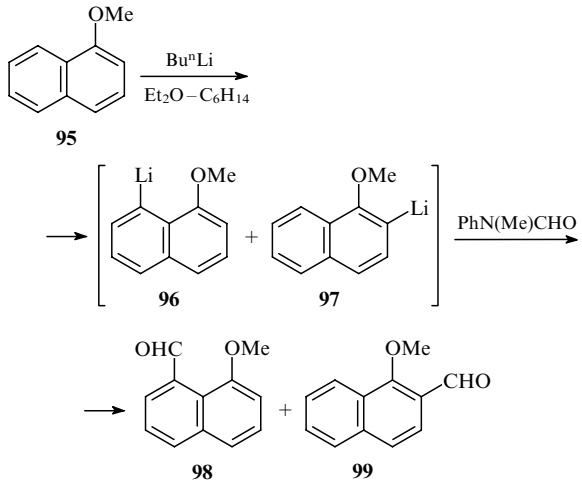
Not all aldehydes of the naphthalene series can be prepared by electrophilic formylation of naphthalenes. One of the typical limitations concerns compounds in which the CHO group and an electron-donating substituent are present in different benzene rings. In such cases, the problem can be solved by performing formylation of organometallic compounds of the naphthalene series with the use of DMF, *N*-methylformanilide or *N*-formylpiperidine. These organometallic compounds are synthesised by either direct metallation of the corresponding naphthalenes or replacement of the halogen atom by metal.

Direct metallation of C—H bonds in naphthalenes generally gives good results for molecules containing a group with a lone electron pair. Due to preliminary coordination with a metallating reagent, this group directs metallation and subsequent formylation at the *ortho* or *peri* position. A characteristic example is 1-dimethylaminonaphthalene (**47**) from which 8-dimethylamino-1-naphthaldehyde (**93**) was prepared as the only product (67% yield) according to the following scheme.[75,76]

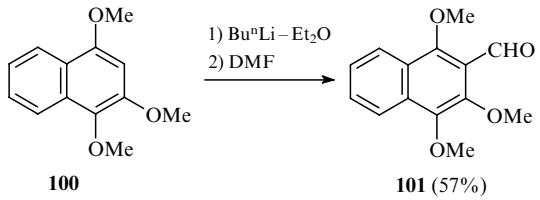


Apparently, metallation at position 8 (rather than at position 2) of the naphthalene system can be explained as follows. Due to steric hindrances, the NMe_2 group is twisted so that the lone electron pair of the nitrogen atom is oriented toward the *peri*-proton. Consequently, after coordination of this pair to the lithium ion, the Bu^- anion appears to be adjacent to the hydrogen atom at position 8, which is eliminated first to form 8-lithium derivative **94**.

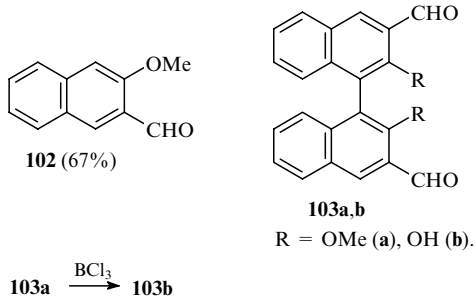
In the case of 1-methoxynaphthalene (**95**) in which the MeO group is conformationally more labile, the situation is not so unambiguous. This compound is lithiated by n-butyllithium at both positions 8 and 2, the contribution of *ortho*-metallation being much higher. Treatment of the resulting mixture of lithium derivatives **96** and **97** with *N*-methylformanilide afforded 8-methoxy-1-naphthaldehyde (**98**) in only 9% yield and 1-methoxy-2-naphthaldehyde (**99**) in 38% yield.[77,78] Nevertheless, in spite of such a low yield, this procedure for the preparation of *peri*-aldehyde **98** is preferable to alternative multistep syntheses. It was demonstrated that metallation of compound **95** depends substantially on the nature of both the metallating agent and solvent.[79] Thus, the addition of tetramethylethylenediamine completely shifted the reaction toward *ortho*-metallation, whereas the use of *tert*-butyllithium instead of n-butyllithium led to the predominant formation of *peri*-metallation product **96**.[79] (The latter observation is consistent with the data on the reaction of *tert*-butyllithium with 1,4-dimethoxynaphthalene.[80]) Treatment of 8- and 2-lithium derivatives thus prepared with dimethylformamide afforded *peri*- and *ortho*-naphthaldehydes **98** and **99** in a ratio of 2 : 1.



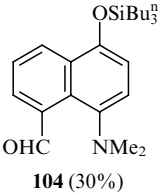
Neither of the two accessible *peri* positions was subjected to metallation upon treatment of 1,2,4-trimethoxynaphthalene (**100**) with n-butyllithium. The reaction proceeded at position 3 with high selectivity due, apparently, to its activation simultaneously by two methoxy groups. Treatment of the 3-lithium derivative with dimethylformamide gave aldehyde **101** as the only product.[55]



Interestingly, 2-methoxynaphthalene was also metallated at position 3 rather than at position 1. Subsequent formylation afforded aldehyde **102**.[77] Analogously, dialdehyde **103a** was generated from 2,2′-dimethoxy-1,1′-binaphthyl. Demethylation of **103a** with BCl_3 gave rise to dialdehyde **103b**.[81]

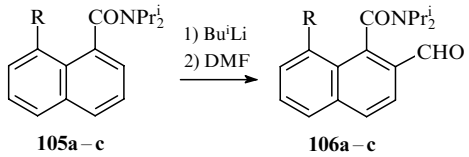


The dimethylamino group exerts a stronger orienting action in the course of metallation compared to the alkoxy group. Treatment of 4-dimethylamino-1-tributylsilyloxynaphthalene with *tert*-butyllithium followed by the addition of DMF produced aldehyde **104** as the only product.[80]



The carbamoyl group possesses an even higher metal-orienting ability than the NMe_2, CH_2NMe_2 or OMe groups. This is

evidenced by the transformation of compounds **105a–c** into aldehydes **106a–c**.[82]

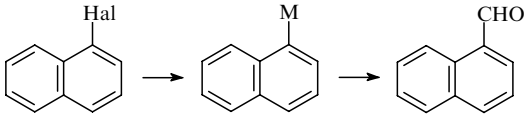


105a–c **106a–c**

R = NMe_2 (**a**), CH_2NMe_2 (**b**), OMe (**c**).

If metallation of C–H bonds in naphthalenes is either hindered or does not provide the required reaction pathway, naphthaldehydes are synthesised with replacement of the halogen atom by metal followed by formylation. For example, treatment of α-naphthylmagnesium bromide with dimethylformamide, *N*-formylpiperidine, *N*-formylmorpholine or 2-(*N*-formyl-*N*-methyl)aminopyridine afforded α-naphthaldehyde **2** in good yields (Table 2). For this purpose, 1-tributylstannylnaphthalene was also used. The latter was transformed into α-naphthaldehyde under the action of α,α-dichlorodimethyl ether in the presence of anhydrous $AlCl_3$. Analogously, β-naphthaldehyde was generated from 2-tributylstannylnaphthalene.[87] The reaction of 6-methoxy-2-naphthylmagnesium bromide with DMF gave 6-methoxy-2-naphthaldehyde in 80% yield.[88]

Table 2. Organometallic syntheses of α-naphthaldehyde.

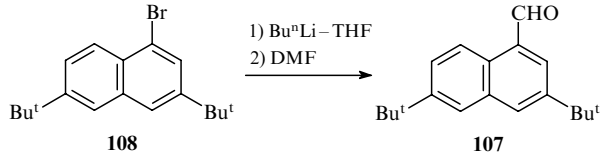


2

M	Formylating agent[a]	Reaction conditions	Yield (%)	Ref.
MgBr	DMF	Et_2O, 0–20 °C	87	83
MgBr	NFP	Et_2O, 0 °C	94	84
MgBr	NFM	Et_2O, 0 °C	92	85
MgBr	NMFAP	THF, 0 °C	76	86
$SnBu_3^n$	Cl_2CHOMe	$AlCl_3$, −78 to 20 °C	80	87

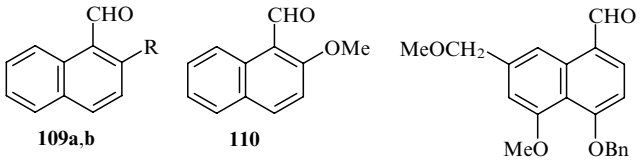
Note. The following notations are used: NFP is *N*-formylpiperidine, NFM is *N*-formylmorpholine, NMFAP is 2-(*N*-methyl-*N*-formyl)aminopyridine.

Lithiated naphthalenes, which are generated upon treatment of bromonaphthalenes with butyllithium, have found wide use in the synthesis of naphthaldehydes. The synthesis of 3,6-di-*tert*-butyl-1-naphthaldehyde (**107**) from bromide **108**[89] is a typical example.



108 **107**

Aldehydes **49**,[90] **109a,b**[91] and **110**[91,92] were prepared analogously. In these reactions, DMF or *N*-formylpiperidine generally serve as the formylating agents. However, the synthesis of aldehyde **111** was carried out with the use of *N*-methoxy-*N*-methylformamide.[93]



109a,b **110** **111**

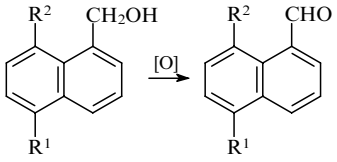
109: R = CH_2OH (**a**), $CH(OMe)_2$ (**b**).

3. Oxidation of alcohols and alkylnaphthalenes

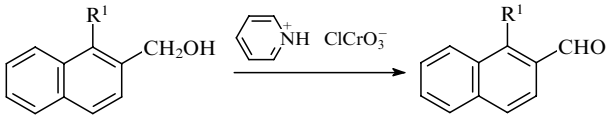
Various oxidising agents are presently used for the preparation of aldehydes from alcohols. These oxidising agents provide good yields, high selectivity and rather mild reaction conditions preventing further oxidation of aldehydes to carboxylic acids. In addition to a traditional oxidising agent (manganese dioxide), *N*-chlorosuccinimide, pyridinium chlorochromate, pyridinium dichromate, methylammonium chlorochromate deposited on silica gel,[94] the DMSO–oxalyl chloride–Et_3N system (Swern oxidation) and some other reagents also meet these requirements. Examples of their use in the synthesis of substituted α-naphthaldehydes are given in Table 3.

Catalytic procedures were developed for oxidation of alcohols of the naphthalene series to aldehydes. Thus, good results were obtained in oxidation of 1-hydroxymethylnaphthalene by molecular oxygen in the presence of heterogeneous catalysts based on transition metal salts (Ru, Co).[99] Bis(pentafluorophenyl)borinic acid $(C_6F_5)_2BOH$–Bu^{t}CHO–$MgSO_4$ was proposed as an efficient catalyst for homogeneous Oppenauer oxidation of the same alcohol to 1-naphthaldehyde.[100]

Table 3. Synthesis of selected naphthaldehydes by oxidation of alcohols.



98, **112**–**118**



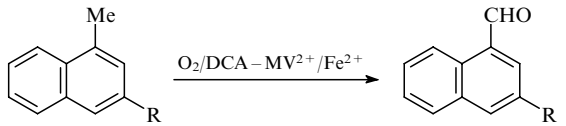
119, **120**

Aldehyde	R^1	R^2	Oxidant [O][a]	Yield (%)	Ref.
98	H	MeO	MnO_2	88	95
112	H	Br	NCS	85	96
113	H	I	NCS	70	96
114	Cl	Cl	NCS	78	96
115	Cl	Me	PDC	83	97
116	Br	Me	PDC	88	97
117	PhS	Me	DMSO–OxCl–Et_3N	88	97
118	$PhSO_2$	Me	DMSO–OxCl–Et_3N	78	97
1 (*S*-gossypol)	–	–	DMSO–OxCl–Pr_2^iNEt	81	63
119	Br	–	PCC	79	91
120	OMe	–	PCC	–	98

Note. The following notations are used: NCS is *N*-chlorosuccinimide; PDC is pyridinium dichromate; PCC is pyridinium chlorochromate; DMSO is dimethyl sulfoxide; OxCl is oxalyl chloride.

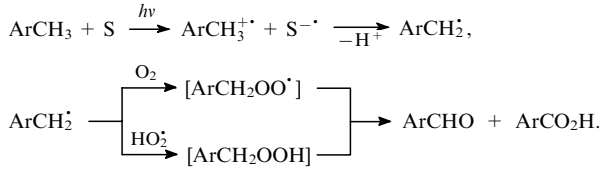
Many studies, including patents,[100–103] were devoted to the synthesis of naphthaldehydes by catalytic oxidation of methylnaphthalenes. Scheme 3 gives an insight into the mechanism of these transformations. This scheme shows photochemical oxidation of 1-methyl- and 1,3-dimethylnaphthalenes to aldehydes **2** and **121**, respectively.

Scheme 3



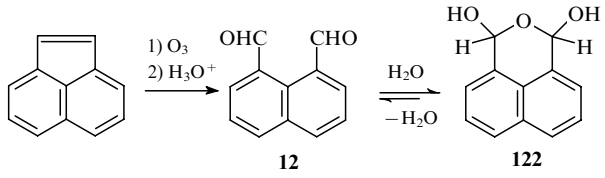
Compound	R	Yield (%)
2	H	69
121	Me	70

The reaction proceeds by the following mechanism:

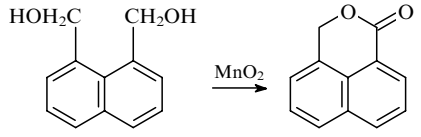


The process is carried out in the presence of 9,10-dicyanoanthracene (DCA) serving as a sensitising agent (S), methyl viologen (MV^{2+}) and divalent iron ions.[104] These reactions often afford naphthalenecarboxylic acid as a by-product. However, this drawback can be remedied by using modern reagents, such as *o*-iodoxybenzoic acid, as an oxidising agent.[105]

Vinylnaphthalenes[106] and acenaphthylene were also proposed as the starting compounds for the preparation of naphthaldehydes. Ozonolysis of acenaphthylene afforded 1,8-diformylnaphthalene (**12**) in 73% yield.[107] Due, apparently, to Coulombic repulsions between two closely spaced carbonyl groups, this dialdehyde is very readily hydrated and transformed into cyclic hydrate **122** under normal conditions. The latter exists as two stereoisomers with melting points (T_m) of 140.0–141.5 °C and 106–107 °C (its *cis-meso* form is shown below). Upon sublimation in hard vacuum, this hydrate loses the water molecule and is transformed into non-hydrated form **12** (T_m = 124–125 °C).[108]

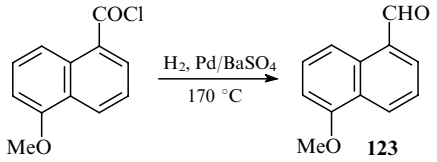


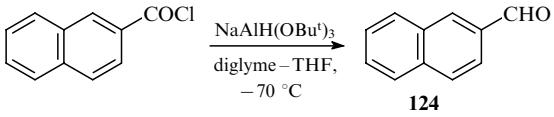
Interestingly, an attempt to prepare dialdehyde **12** by oxidation of 1,8-dihydroxymethylnaphthalene with manganese dioxide[108] led only to the formation of naphthopyranone.



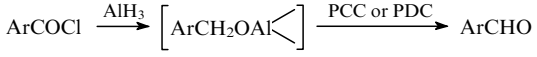
4. Syntheses from naphthalenecarboxylic acid derivatives

First data on syntheses of naphthaldehydes by reduction of naphthalenecarboxylic acid derivatives date back to the beginning of the 20th century. For example, 5-methoxy-1-naphthaldehyde (**123**) was prepared by the Rosenmund reaction.[109] Since that time, new more efficient reagents for reducing carboxylic acid chlorides were found. In our opinion, sodium tris(*tert*-butoxy)-aluminium hydride (STBA) is a reagent of choice. This reagent allows one to perform the reaction at low temperature and prepare 1- and 2-naphthaldehydes (in particular, aldehyde **124**) in nearly quantitative yields.[110] The lithium analogue of STBA can also be used, for example, in the synthesis of dialdehyde **103b**.[111] However, the reactions with the use of the latter reagent generally afford aldehydes in lower yields.[110]



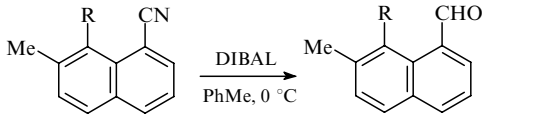


Recently, Korean chemists have developed an original procedure for the redox transformation of aroyl chlorides into aldehydes.[112] First, the reaction of aroyl chloride with aluminium chloride was carried out to obtain the corresponding aluminium alkoxide, which was immediately oxidised with pyridinium chlorochromate or pyridinium dichromate to prepare aldehyde. This method made it possible to synthesise 1- and 2-naphthaldehydes in virtually quantitative yields.



This approach was also extended to the synthesis of aldehydes from carboxylic acids,[113] esters[114] and directly from primary alcohols.[115]

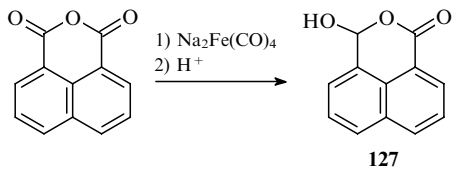
Reduction of acid nitriles is yet another procedure widely used for the preparation of naphthaldehydes. The list[116] of reducing reagents used for this purpose consists of more than ten compounds, including tin dichloride and a number of complex hydrides. For example, the use of lithium diisobutylaluminium hydride (DIBAL) as the reducing agent gave good results in the synthesis of aldehydes **125a**,**b** from nitriles **126a**,**b**.[117,118]

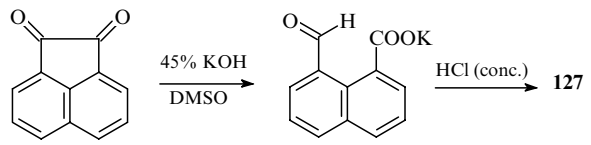


R = H (**a**), Br (**b**).

In recent years, high requirements have been imposed upon the selectivity of the process. For instance, potassium 9-(pentan-2-yl)-9-boratabicyclo[3.3.1]nonane[119] and lithium tris(dihexylamino)aluminium hydride[116] were proposed as reagents for reduction of aryl cyanides in the presence of aliphatic acid nitriles. These reducing reagents were also successfully used for the synthesis of naphthaldehydes.

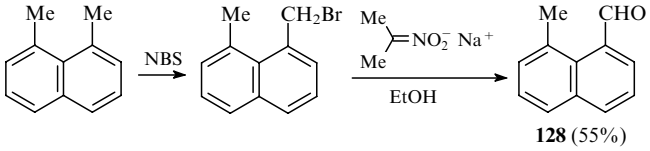
Reduction of 1,8-naphthalic anhydride in the presence of the $Na_2Fe(CO)_4$ complex[120] or treatment of acenaphthenequinone with alkali in DMSO[121] afforded 8-formylnaphthalene-1-carboxylic acid (existing in cyclic form **127**) in good yields.





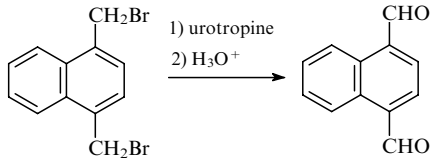
5. Syntheses based on halomethylnaphthalenes

The use of bromomethyl- and dibromomethylnaphthalenes in the synthesis of naphthaldehydes seems to be very attractive because they are readily accessible reagents prepared by free-radical bromination of methylnaphthalenes with *N*-bromosuccinimide (NBS). For example, 8-methyl-1-naphthaldehyde (**128**) was synthesised in two steps from commercial 1,8-dimethylnaphthalene. The bromomethyl group was oxidised with 2-nitropropane.[122]

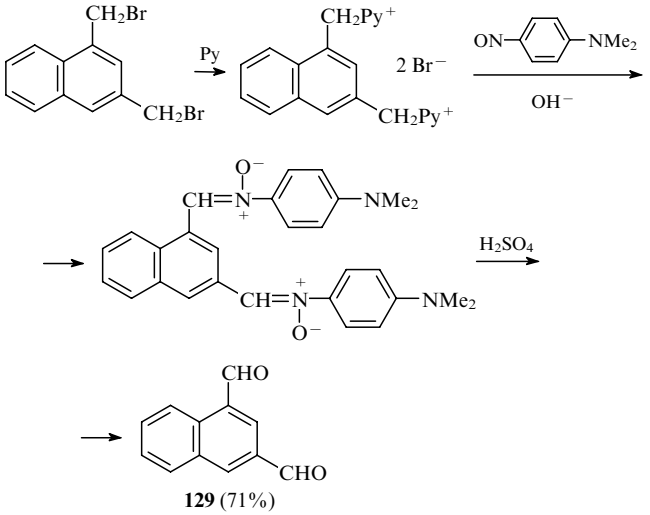


128 (55%)

1,4-Naphthodialdehyde was prepared from 1,4-bis(bromomethyl)naphthalene by the Sommelet reaction.[123]



Isomeric 1,3-, 1,5-, 1,6-, 1,7-, 2,6- and 2,7-dialdehydes as well as 1,3,5-, 1,3,6-, 1,3,7- and 1,4,6-trialdehydes of the naphthalene series were synthesised according to the Kröhnke method.[123] This method involves the preliminary transformation of halomethyl derivatives of naphthalene into pyridinium salts and then into nitrones, which are subjected to acid hydrolysis, as exemplified by the synthesis of 1,3-naphthodialdehyde (**129**).

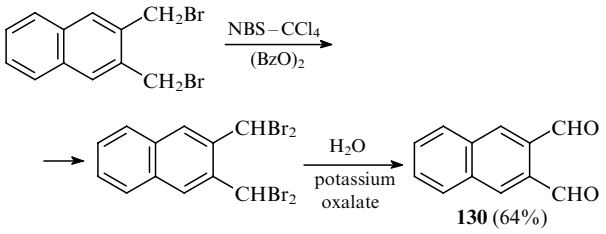


129 (71%)

Kochergin and co-workers [124] developed a procedure for the preparation of aromatic aldehydes, including naphthaldehydes, based on transformations of chloromethylarenes into nitrates and decomposition of the latter under the action of sodium ethoxide.

$$ArCH_2Cl \xrightarrow[MeCN]{AgNO_3} ArCH_2ONO_2 \xrightarrow[EtOH]{EtONa} ArCHO + NaNO_2 + H_2O$$

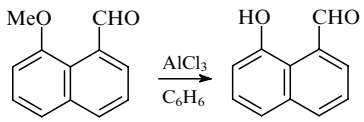
In some cases, naphthaldehydes were synthesised with the use of dibromomethylnaphthalenes as the starting compounds, which were subjected to hydrolysis. In particular, this method was used for the preparation of *peri*-dialdehyde **12**,[108] 1,1′-binaphthyl-2,2′-dicarbaldehyde [111] and naphthalene-2,3-dicarbaldehyde (**130**).[125]



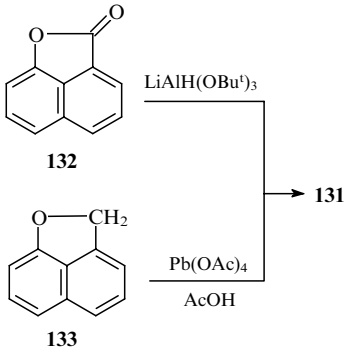
130 (64%)

6. Functionalisation of substituents in naphthaldehydes

Functionalisation of substituents in naphthaldehyde molecules as well as the introduction of new groups (for example, by electrophilic substitution) is used when target compounds are difficult to prepare according to other methods. For example, demethylation of 8-methoxy-1-naphthaldehyde (**98**) with aluminium chloride afforded aldehyde **131**,[77,95] which is a very valuable reagent from the preparative standpoint. This compound can also be synthesised by reduction of naphtholactone **132** with lithium tri(*tert*-butoxy)aluminium hydride (75% yield) [126] or by oxidation of 2*H*-naphtho[1,8-*b*,*c*]furan (**133**) with lead tetraacetate (30% yield).[95,127] However, the latter reaction is complicated by the formation of by-products. Compound **133** and its 2- and 4-methoxy derivatives are slowly transformed into *peri*-hydroxynaphthaldehydes even in air.[95,127]

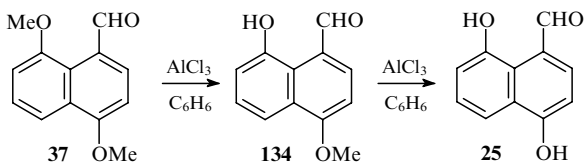


98 **131**

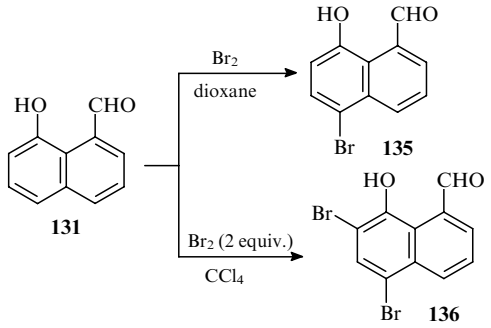


132 **133**

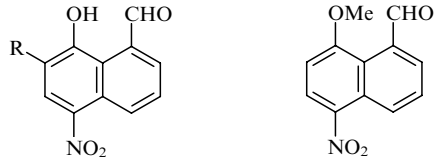
Heating of 4,8-dimethoxy-1-naphthaldehyde **37** with 1 equiv. of anhydrous $AlCl_3$ in benzene [42] or with BBr_3 in dichloromethane [56] led to selective demethylation of the methoxy group at position 8 to give *peri*-hydroxyaldehyde **134** in good yield. The reaction with the use of 2 equiv. of $AlCl_3$ afforded dinaphthol **25**.[42] This method was used also for the synthesis of hemigossypol and its analogues from methoxy precursors [8] (see also the transformation **103a** → **103b**).[81]



Bromination of aldehyde **131** produced its bromo derivatives **135** and **136**.[128]



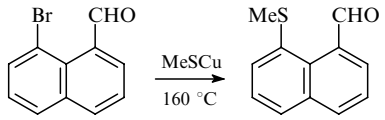
Nitration of aldehyde **131** with nitric acid (ρ = 1.35 g cm^{-3}) afforded nitro derivatives **137a**,**b**.[128] Analogously, the reaction of *peri*-methoxynaphthaldehyde **98** gave rise to 8-methoxy-5-nitro-1-naphthaldehyde (**138**), whose treatment with aqueous alkali produced 8-hydroxy-5-nitro-1-naphthaldehyde (**137b**).[128]



137a,**b** **138**

R = NO_2 (**a**), H (**b**).

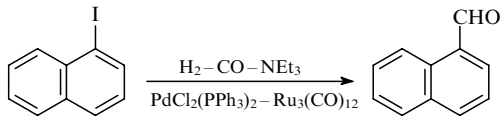
The synthesis of 8-methylthio-1-naphthaldehyde (**139**) from bromide **112** (72% yield)[96] provides an example of functionalisation based on the nucleophilic substitution.



112 **139**

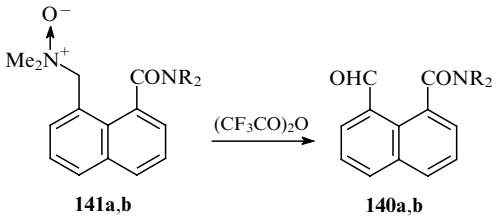
7. Other methods

The synthesis of aldehydes based on formylation of radical anions of polycyclic arenes was described. Thus, the reactions of sodium naphthalenide with ethyl formate or *N*,*N*-dibutylformamide afforded naphthaldehyde **2** in 55% yield.[129] Aromatic aldehydes can also be synthesised by formylation of aryl iodides under homogeneous catalysis conditions.[130]



2 (53%)

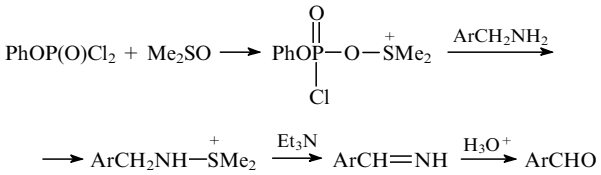
In some cases, naphthaldehydes are synthesised by the Polonovski reaction in spite of the fact that the products are generally obtained in low yields. The preparation of 8-formyl-1-naphthamides **140a**,**b** from *N*-oxides **141a**,**b**[82] provides a typical example.



141a,**b** **140a**,**b**

Compounds **140**, **141**	R	Yield **140** (%)
a	Et	19
b	Pr^i	40

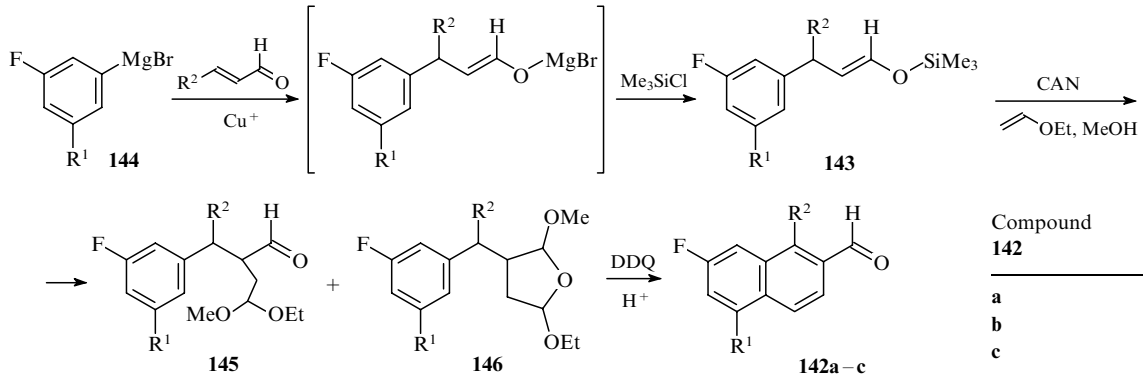
Treatment of benzylamines with phenyl dichlorophosphate and DMSO followed by the successive addition of triethylamine and oxalic acid made it possible to prepare both aromatic ketones and aldehydes.[131] For example, 1-aminomethylnaphthalene was transformed under these conditions into α-naphthaldehyde in 78% yield. This reaction is a modification of the Pfitzner–Moffat oxidation and involves preliminary activation with DMSO.



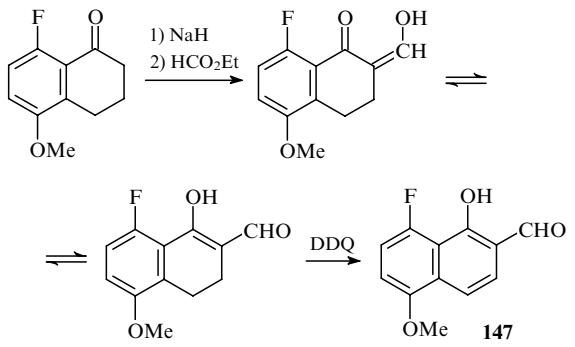
In several studies, naphthaldehydes were prepared by cyclisation. Recently, Italian chemists have developed a procedure for the synthesis of fluorinated 2-naphthaldehydes **142a**–**c** based on oxidative annelation of the benzene ring to *O*-trimethylsilyl 2-benzylvinyl ethers **143** (Scheme 4).[132] In addition to the organometallic synthesis of the ethers (**144** → **143**), the procedure involves carbon–carbon chain growth through the addition of ethyl vinyl ether to compounds **143** and acid-oxidative cyclisation of isomeric acetals **145** and **146** under the action of dichlorodicyanobenzoquinone (DDQ). The former reaction requires the use of cerium ammonium nitrate (CAN) and proceeds, most likely, by a radical mechanism. Aldehydes **142** were prepared in satisfactory total yield (~ 40%) with respect to the starting fluorophenylmagnesium bromide.

Tetralones were proposed as the starting compounds for the synthesis of substituted 1-hydroxy-2-naphthaldehydes, in particular, of compound **147**. Tetralones are subjected to successive formylation (through the formation of enolates) and aromatisation under the action of DDQ.[133]

Scheme 4



Compound **142**	R^1	R^2
a	H	Me
b	F	H
c	F	Me



147

III. Structures and physicochemical properties of naphthaldehydes

In this section, attention is focused on such physicochemical properties that allow one to obtain information on the conformation of the aldehyde group and the character of its electronic interactions with the core and other substituents.

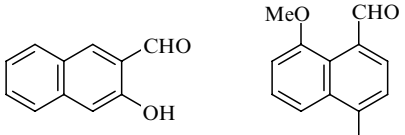
1. Infrared, ultraviolet and mass spectra

Based on the stretching absorption band of the C=O bond ($\nu_{C=O}$) as the characteristic band in the IR spectra of unsubstituted α- and β-naphthaldehydes **124** (1700 cm^{-1} in CCl_4), it can be seen from Table 4 that the low-frequency shift of this band ($\Delta\nu_{C=O}$) is favoured by the involvement of the aldehyde group in intramolecular hydrogen bonding, different electronic interactions of this group with other substituents and steric factors. For example, $\Delta\nu_{C=O}$ in the spectra of *o*-hydroxynaphthaldehydes **18** and **20** is -50 cm^{-1} due, apparently, to intramolecular hydrogen bonding. In the spectrum of 3-hydroxy-2-naphthaldehyde (**148**), this shift is smaller ($\Delta\nu_{C=O} = -32$ cm^{-1}). Apparently, the intramolecular hydrogen bond in the latter compound is weaker due to the larger C(β)–C(β) bond length and, consequently, to the larger distance between the CHO group in position 2 and the OH group in position 3 of the naphthalene ring. Interactions between the substituents in *peri*-hydroxynaphthaldehyde **131** are of particular interest. Formally, the OH and CHO groups are not conjugated and the intramolecular hydrogen bond cannot be as strong as those in aldehydes **18** and **20** because the seven-membered chelate ring rather than the six-membered ring is closed in **131**. Actually, $\Delta\nu_{C=O}$ in the IR spectrum (in $CHCl_3$) of compound **131** (-30 cm^{-1}) is even smaller than that in the spectrum of aldehyde **148**. In a solution of compound **131** in THF, the hydrogen bridge is, apparently, partially broken and the IR spectrum has two $\nu_{C=O}$ bands one of which (at 1660 cm^{-1}) can be assigned to the form containing an intramolecular hydrogen bond and another band (at 1680 cm^{-1}) can be attributed to the form without an intramolecular hydrogen bond.

Table 4. Position of the $\nu_{C=O}$ band in the IR spectra of selected naphthaldehydes.

Compound	Position of CHO groups	Other substituents	Solvent	$\nu_{C=O}$ /cm^{-1}	Ref.
2	1	–	CCl_4	1700	134
2	1	–	see [a]	1691	87
124	2	–	CCl_4	1702	134
124	2	–	see [a]	1690	87
20	1	2-OH	CCl_4	1649; 1638 [b]	134
18	2	1-OH	CCl_4	1651; 1637 [b]	134
148	2	3-OH	CCl_4	1668	134
131	1	8-OH	$CHCl_3$	1670	95
131	1	8-OH	THF	1680; 1660	95
134	1	8-OH, 4-OMe	see [c]	1650	56
12	1, 8	–	see [a]	1672	108
49	1	4-NMe_2	CCl_4	1685	65
93	1	8-NMe_2	$CHCl_3$	1660	76
54	1	4,5-$(NMe_2)_2$	CCl_4	1685	68
55	1, 8	4,5-$(NMe_2)_2$	$CHCl_3$	1665; 1635	68
56	1, 6	4,5-$(NMe_2)_2$	CCl_4	1670; 1635	68
149	1	4-OH, 8-OMe	see [c]	1640	56
35	2	1,4-$(OMe)_2$	see [a]	1675	55
150	2	1,4-$(OMe)_2$, 3-Me	see [a]	1680	55
151	2	1,4-$(OMe)_2$, 3-Br	see [a]	1693	55

[a] In KBr pellets. [b] The assignment of this peak to the aldehyde group is doubtful. [c] Data on the solvent were not reported in the study.[56]

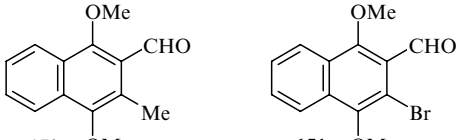


148 149

A record decrease in $\nu_{C=O}$ (to 1610 cm^{-1}) is observed in the IR spectra of gossypol **1** and its analogue **46**.[61,135] This fact suggests that the aldehyde group in compounds **1** and **46** is chelated with the *o*-OH group rather than with the *peri*-OH group (*cf.* ^{1}H NMR spectra and results of X-ray diffraction analysis discussed in Sections III.2 and III.6). In the IR spectrum of aldehyde **149**, $\Delta\nu_{C=O}$ is -60 cm^{-1}.

A decrease in the frequency of absorption of the carbonyl group due to its conjugation with the electron-donating substituents is smaller than one would expect (see, for example, Table 4, compounds **2**, **49** and **54**). A small value of $\Delta\nu_{C=O}$ for *peri*-dialdehyde **55** prepared from the 'proton sponge' is particularly surprising, the more so that other physicochemical characteristics of this compound, in particular, the dipole moments (see below), are indicative of very strong conjugation in its molecule.

Substituents facilitating the twist of the CHO group with respect to the plane of the naphthalene system cause a decrease in conjugation as a result of which $\nu_{C=O}$ increases [see Table 4, aldehyde **35** and its 3-methyl- (**150**) and 3-bromo derivatives (**151**)].



150 151

α-Naphthaldehyde **2** and *peri*-dialdehyde **12** are colourless compounds, and the long-wavelength absorption band in their UV spectra is observed at 300 nm (Table 5). However, the presence of even one electron-donating substituent in the *para* position with respect to the formyl group causes a strong bathochromic shift of this band and the corresponding compounds become coloured. Aldehydes **49** and **54**–**56** containing the NMe_2 groups are typical examples. The conjugation is particularly pronounced in *peri*-dialdehyde **55**, which occurs as dark-orange crystals with metallic lustre. α-Naphthaldehyde derivatives containing substituents with the lone electron pair (OH, OMe, $NAlk_2$) in position 8 are also yellow or orange in colour. The fact that aldehyde **93** is coloured was attributed to *peri*-interactions between the substituents (see Section III.6) resulting in an increase in the energy of the highest occupied molecular orbital (HOMO) involving the lone electron pair of the O or N atoms of the electron-donating group.[76] In our opinion, an alternative explanation can be put forward, according to which the electron-donating (NMe_2) and electron-withdrawing (CHO) substituents are independently conjugated with the π-system of the ring, which facilitates an increase in the energy of the HOMO and a decrease in the energy of the lowest unoccupied molecular orbital

Table 5. Position of the long-wavelength band in the UV spectra of selected naphthaldehydes.

Compound	Position of CHO groups	Other substituents	Solvent	λ_{max} /nm (log ε)	Colour	Ref.
2	1	–	MeOH	312 (3.39); 328, sh[a] (3.36)	colourless	136
12	1, 8	–	dioxane	296 (3.80)	*ditto*	108
49	1	4-NMe_2	MeOH	369 (3.75)	pale-yellow	136
54	1	4,5-$(NMe_2)_2$	MeOH	407 (3.74)	yellow	136
55	1, 8	4,5-$(NMe_2)_2$	MeOH	449 (3.52)	dark-orange	136
56	1, 6	4,5-$(NMe_2)_2$	MeOH	403 (3.67)	yellow	136
131	1	8-OH	cyclohexane	394 (3.52)	orange	95
131	1	8-OH	H_2O – MeOH, 3 : 1	350 (3.45)	*ditto*	95

[a] Shoulder.

(LUMO). A narrowing of the energy gap between these orbitals leads to a shift of the absorption band to the visible region. To study this problem in more detail, it would be of interest to record the UV spectra of 5-methoxy- and 5-dimethylamino-1-naphthaldehydes.

It should be noted that UV spectra played a large role in the determination of the structure of gossypol yellow in colour (λ_{max} = 277, 289 and 364 nm).[137]

Mass-spectrometric data for naphthaldehydes are scarce. Mezheritskii and co-workers[42] studied the fragmentation pathways of 4,8-dihydroxy-1,5-naphthodialdehyde in detail. In the mass spectrum of this compound, the molecular ion peak is most intense (100%). The character of fragmentation led the authors of the cited study[42] to the conclusion that both cyclic and acyclic forms of this dialdehyde are present in the gas phase, and decomposition of each form follows its own pathway. In particular, the fragmentation of the molecular ion of the dialdehyde form begins with elimination of the $^{\bullet}$CHO radical followed by liberation of two CO molecules. By contrast, the intensity of the molecular ion peak in the mass spectrum of 8-dimethylamino-1-naphthaldehyde is 60%, whereas the $[M^{+\bullet}-CO]$ peak is most intense.[76]

The electron affinities (*EA*) of 1- and 2-naphthaldehydes, which were measured by high-pressure pulse mass spectrometry, are 0.68 and 0.64 eV, respectively (for comparison, *EA* of naphthalene, 1-nitronaphthalene and 2-nitronaphthalene are −1.12, +1.23 and +1.18 eV, respectively; the negative electron affinity of naphthalene reflects the instability of its radical anion).[138]

2. NMR spectra

The most useful information on conformations of the formyl group, which can be obtained from ^{1}H NMR spectra of naphthaldehydes, involves chemical shifts of the protons of the CHO group and also of the nearest-neighbourhood protons, primarily, of *peri*-H. The chemical shifts of the proton of the CHO group for selected naphthaldehydes, which do not contain intramolecular hydrogen bonds, are given in Table 6.

If a molecule contains no bulky substituents adjacent to the formyl group, the latter can be located virtually in the ring plane (see Section III.6). In this case, the signal for the proton of the CHO group is generally observed at δ 10 (see Table 6). If the aldehyde group is twisted with respect to the naphthalene system, its proton is in the region of the diamagnetic component of the ring current and the corresponding signal shifts downfield. In addition, the chemical shift of the proton of the formyl group depends substantially on the anisotropic effect of the adjacent group, particularly, if it contains the lone electron pair. These phenomena can be observed in the ^{1}H NMR spectra of 8-substituted naphthaldehydes in which the chemical shifts of the proton of the CHO group reach 11 ppm and can be even higher (see Table 6). The rotation of the CHO group can be caused by both steric factors and electronic interactions between the substituents. For example, if a substituent in position 8 of the naphthalene system contains an

Table 6. Chemical shifts of the proton of the CHO group (δ_{CHO}) in the ^{1}H NMR spectra of selected naphthaldehydes.

Compound	Position of the CHO group	Other substituents	Solvent	δ_{CHO}	Ref.
2	1	–	CCl_4	10.24	86
2	1	–	$CDCl_3$	10.10, 10.38	87, 139
124	2	–	$CDCl_3$	9.99, 10.12	87, 139
30a	1	2-OMe	$CDCl_3$	10.85	139
49	1	4-NMe_2	$CDCl_3$	10.14	65
54	1	4,5-$(NMe_2)_2$	CCl_4	9.96	68
55	1, 8	4,5-$(NMe_2)_2$	$CDCl_3$	9.78[a]	68
56	1, 6	4,5-$(NMe_2)_2$	$CDCl_3$	10.18[a]	68
93	1	8-NMe_2	$CDCl_3$	10.65	75
128	1	8-Me	$CDCl_3$	10.81	122
112	1	8-Br	$CDCl_3$	11.32	96
139	1	8-SMe	$CDCl_3$	11.10	96
28	1	4-OMe	$CDCl_3$	10.12	140
149	1	4-OH, 8-OMe	DMSO-d_6	11.12	56
35	2	1,4-$(OMe)_2$	$CDCl_3$	10.86	55
150	2	1,4-$(OMe)_2$, 3-Me	$CDCl_3$	11.03	55
151	2	1,4-$(OMe)_2$, 3-Br	$CDCl_3$	10.86	55

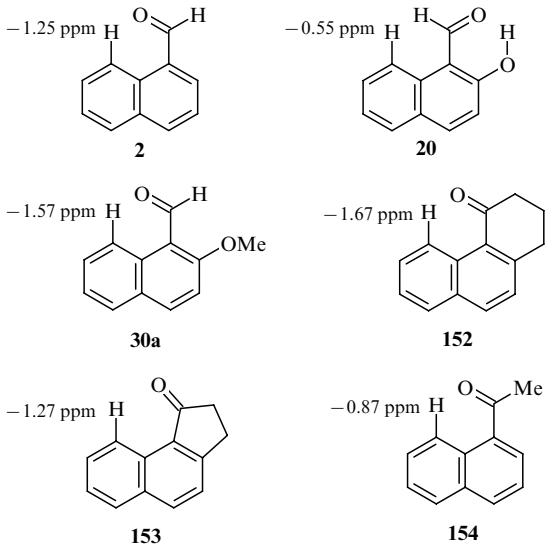
[a] 2H.

atom with the lone electron pair (NMe_2, OMe, SMe), the latter tends to attack nucleophilically the carbonyl carbon atom, which requires rotation of the CHO group with respect to the ring plane by a large angle τ (see Section III.6). Apparently, when τ is close to 90°, the signal for the proton of the CHO group is observed at $\delta \sim 11.0$. The arrangement of the ring and formyl group in a single plane is apparently characterised by the chemical shift $\delta_{CHO} \sim 9.8$.

It is known that the carbonyl group possesses a substantial anisotropic effect. The protons located in the magnetic cone in the vicinity of the oxygen atom are subjected to strong deshielding and their signal shifts substantially downfield. This effect influences also the protons adjacent to the carbonyl carbon atom (however, to a much lesser degree). α-Naphthaldehyde **2** and its 2-hydroxy derivative **20** are characteristic examples. Taking into account the presence of an intramolecular hydrogen bond in compound **20**, the orientation of the CHO group is beyond question. Hence, a substantially larger downfield shift of the signal for the H(8) proton in the ^{1}H NMR spectra of α-naphthaldehyde indicates that its carbonyl group is directed toward the *peri*-proton (*Z* conformation). The occupancy of the *Z* conforma-

tion in 2-methoxy-1-naphthaldehyde (**30a**) is even higher due, apparently, to the supporting effect of the methoxy group.

According to estimates made in the studies [141, 142] based, in particular, on a comparison of the chemical shifts of the signal for the H(8) proton in the spectra of α-naphthaldehyde (δ 9.23) and model compound **152** (δ 9.51), the CHO group in molecule **2** is non-coplanar with the ring (the corresponding angle is 22°). Judging from the data for cyclic ketones **152** and **153**, the formyl group in molecule **154** containing the even bulkier acetyl group should be even more non-coplanar. For a series of carbonyl derivatives of naphthalene,[139] the diamagnetic shifts of the signal for the proton at the *peri* position with respect to the aldehyde group (relative to the corresponding signal in the ^{1}H NMR spectrum of naphthalene) under the influence of the anisotropic effect of the C=O group are shown below.



2 **20** **30a** **152** **153** **154**

Data on deshielding of the *ortho*- and *peri*-protons in naphthaldehydes containing the NMe_2 groups in their cores are presented in Table 7. The downfield shifts of the signals for the *peri*- and *ortho*-protons in the ^{1}H NMR spectra of dimethylaminonaphthaldehydes relative to the corresponding signals for compounds **47** (for **49**) and **53** (for **54**–**56**) are shown below.[65, 68] (The atomic numbering scheme for the hydrogen atoms in compounds **47** and **53** used here and in Table 7 is arbitrary.)

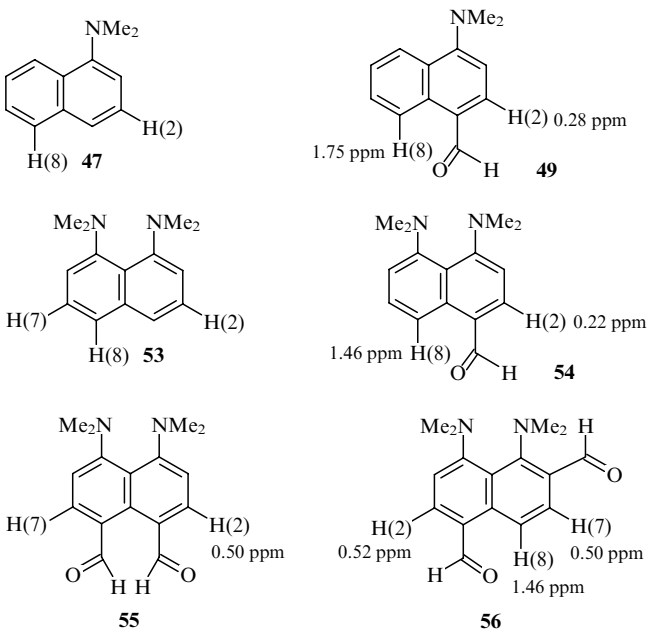


Table 7. Chemical shifts (δ) of the protons experienced the anisotropic effect of the carbonyl group in the ^{1}H NMR spectra (in $CDCl_3$) of dimethylaminonaphthaldehydes.[65, 68]

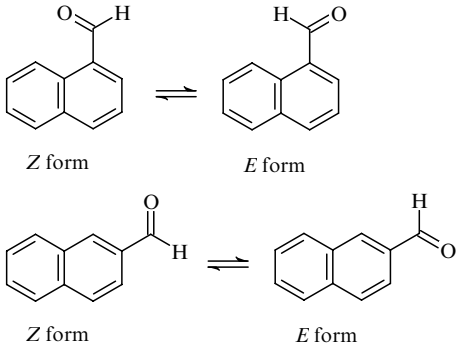
Compound	δ		
	H(2)	H(7)	H(8)
47	7.50	–	7.60
53	7.33	–	7.39
49	7.78	–	9.35
54	7.55	–	8.85
55	7.83	7.83	–
56	7.83	7.85	8.85

Conclusions about the orientations of the groups in dialdehydes **55** and **56** were made based on the results of X-ray diffraction analysis (see Section III.6). The degree of deshielding of the H(8) proton in monoaldehyde **54** is equal to that in dialdehyde **56**. This indicates that the carbonyl oxygen atom in molecule **54** is also directed toward the *peri*-proton. The same is true for monoaldehyde **49** in which the deshielding of the *peri*-proton is even more substantial. It should be noted that weak deshielding of the *ortho*-protons is observed even if the carbonyl oxygen atom is oriented toward these protons, the more so that this deshielding is, undoubtedly, associated with the electron-withdrawing ability of the CHO group.

Analysis of the ^{1}H NMR (see Ref. 142) and ^{13}C NMR (see Ref. 92) spectra and the nuclear Overhauser effect in combination with theoretical MM2 calculations [143] demonstrated that the occupancy of the *Z* conformation in α-naphthaldehyde is, on the average, 80%–90% regardless of the conditions, whereas the *E* conformer is more favourable for β-naphthaldehyde to the same extent (Table 8). It was believed [144] that both conformers are stabilised through a more efficient conjugation between the *trans*-arranged C=O group and the C(1)=C(2) bond characterised by a higher multiplicity. In addition, a weak intramolecular hydrogen bond can occur between the carbonyl oxygen atom and the H(8) proton in 1-naphthaldehyde.[145]

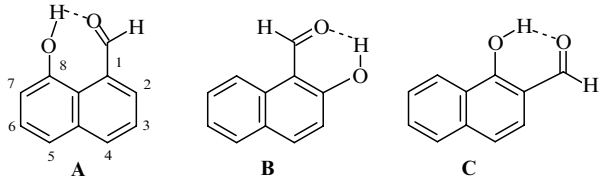
The free activation energies of rotation of the CHO group in α- and β-naphthaldehydes determined by dynamic ^{13}C NMR spectroscopy are 26.8 and 34.4 kJ mol^{-1}, respectively. The introduction of the methoxy substituent at position 4 of molecule **2** and at

Table 8. Content of the *Z* form in α- and β-naphthaldehydes.



Position of the CHO group	Content of the *Z* form (%)	Conditions	Ref.
1	77	$CDCl_3$, 25 °C	142
1	85	$CDCl_3$, 25 °C	143
1	90	freon, −134 °C	92
2	14	$CDCl_3$, 25 °C	142
2	12	$CDCl_3$, 25 °C	143
2	20	freon, −108 °C	92

Table 9. Chemical shifts (δ) of the protons of the CHO and OH groups in the ^{1}H NMR spectra of hydroxynaphthaldehydes containing an intramolecular hydrogen bond.

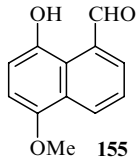


A **B** **C**

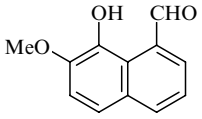
Compound	Type of aldehyde	Substituents	Solvent	δ_{CHO}	δ_{OH}	Ref.
131	**A**	–	$CDCl_3$	9.76	11.60	95
131	**A**	–	THF-d_6	10.39	10.72	95
134	**A**	4-OMe	$CDCl_3$	11.16	12.06	56
134	**A**	4-OMe	DMSO-d_6	10.66	9.5	56
155	**A**	5-OMe	$CDCl_3$	9.87	10.97	127
156	**A**	7-OMe	$CDCl_3$	10.08	10.75	127
135	**A**	5-Br	$CDCl_3$	9.84	11.65	128
136	**A**	5,7-Br_2	$CDCl_3$	9.93	12.07	128
137b	**A**	5-NO_2	$CDCl_3$	9.87	10.97	128
20	**B**	–	$CDCl_3$	10.78	13.15	139
157	**A**, **B**	2,3,8-$(OH)_3$, 4-Pr^i, 6-Me (hemigossypol)	$CDCl_3$	11.50	14.95	146
1	**A**, **B**	2,3,8-$(OH)_3$, 4-Pr^i, 6-Me [(*S*)-gossypol]	$CDCl_3$	11.11	15.11	63
18	**C**	–	$CDCl_3$	–	12.61	147

position 6 of molecule **124** increases the rotation barrier by 4.6 and 2.9 kJ mol^{-1}, respectively.[92]

The ^{1}H NMR spectra of naphthaldehydes in which the CHO group is involved in intramolecular hydrogen bonding have some characteristic features. Among these compounds are *peri*- and *ortho*-hydroxynaphthaldehydes (Table 9). Evidently, the formyl group in 8-hydroxy-1-naphthaldehyde (**131**) is virtually coplanar with its aromatic core, and the carbonyl oxygen atom is directed toward the hydroxy substituent. This is evidenced primarily by the chemical shift of the proton of CHO (δ 9.76) and the position of the signal of OH (δ 11.60) characteristic of the hydroxy group involved in intramolecular hydrogen bonding. Analogous patterns are observed in the spectra of 5-methoxy (**155**), 7-methoxy (**156**), 5-bromo (**135**), 5,7-dibromo (**136**) and 5-nitro derivatives (**137b**) of *peri*-hydroxyaldehyde.



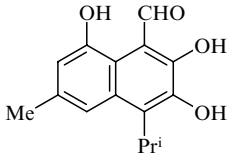
155



156

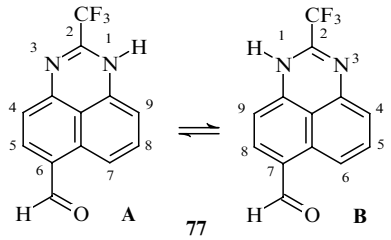
The spectrum of 8-hydroxy-4-methoxy-1-naphthaldehyde (**134**) differs substantially from those mentioned above. The unexpectedly large (δ 11.16) chemical shift of the proton of CHO in the spectrum of this compound can be attributed only to a sharp change in the conformation of the formyl group (for example, to its substantial rotation about the $C_{Ar}-CHO$ bond) necessary for the nucleophilic attack of the hydroxy group on the carbonyl carbon atom (see Section III.6) or its transformation into the *E* form. In the latter case, the proton of the CHO group is located in the diamagnetic field of simultaneously two benzene rings and its signal should be shifted substantially downfield, as was observed for the α-protons of naphthalene (δ 7.81) compared to the β-protons (δ 7.46). However, the role of the 4-methoxy group remains unclear.

As a result of the transformation into the *E* form, the signal for the proton of the CHO group in 2-hydroxy-1-naphthaldehyde (**20**) also undergoes a substantial diatropic shift (δ 10.78). The presence of an intramolecular hydrogen bond in this compound leads to closure of the more stable six-membered ring, as evidenced by the position of the signal for the proton of OH in the ^{1}H NMR spectrum of aldehyde **20** (δ 13.15) compared to that in the spectrum of aldehyde **131** (δ 11.60) containing the seven-membered chelate ring. In this connection, gossypol (**1**) and hemigossypol (**157**) are of interest. In these compounds, intramolecular hydrogen bonds can occur between the 1-CHO and OH groups both in positions 2 and 8. The data from Table 9 provide unambiguous evidence in favour of the former type of hydrogen bonding, *i.e.*, in favour of the six-membered ring closure and *E* conformation of the aldehyde functional group in molecules **1** and **157**. The record chemical shift of the proton of CHO in the spectrum of hemigossypol suggests that the aldehyde proton in this compound is, presumably, also involved in intramolecular hydrogen bonding with the oxygen atom of the OH group in position 8 (the assumption that the formyl group can act as an H donor in hydrogen bonding has been made recently in the study [148]).



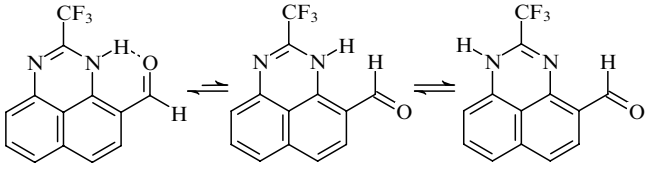
157 (hemigossypol)

On the whole, the same is true for the signals of the formyl group in the NMR spectra of aldehydes based on naphthalene-containing heterocyclic systems, but there are some specific features associated with annular tautomerism and the presence of heteroatoms. Thus, the ^{1}H NMR spectrum of 6(7)-formyl-2-trifluoromethylperimidine (**77**) in $CDCl_3$ has signals of both annular tautomers **A** and **B**, the aldehyde group occurring in the *Z* form in both tautomers.[149, 150] This is evidenced by a substantial deshielding of the adjacent *peri*-proton whose signal is observed at δ 8.77 and 8.82 for the tautomers **A** and **B**, respectively. The signals for the aldehyde proton are observed at δ 10.04 and 9.97, respectively. This is characteristic of the *Z* conformation of the CHO group, which is virtually coplanar with the naphthalene core (see Section III.6).



A **77** **B**

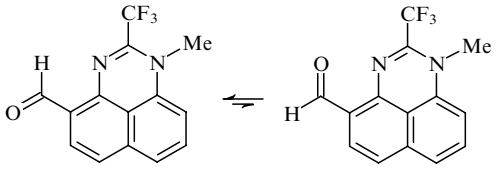
Due to the formation of a strong intramolecular hydrogen bond between the proton of the NH group and the oxygen atom of the formyl group, perimidine-4(9)-carbaldehydes, in particular, compound **76**, occur in non-polar solvents and in the solid state exclusively in the chelated 9-CHO-form **A**.[73] However, in polar media, for example, in DMSO, the solvent competes with the aldehyde group for the proton of the NH group, an intramolecular hydrogen bond is partially cleaved and different conformers and tautomers, including the forms **B** and **C**, can either coexist or undergo rapid interconversions. For example, the ^{1}H NMR spectrum of aldehyde **76** in DMSO-d$_6$ at 25 °C has two signals for the proton of CHO at δ 9.90 and 10.45 with the intensity ratio of $\sim$1 : 3. The former signal belongs, apparently, to the chelated 9-CHO group and the latter signal can be assigned to the 4-CHO group in the tautomer **C**. Upon heating, both peaks coalesce into one signal at δ 10.20, whereas the peak of the proton of NH disappears, which is indicative of the rapid interconversion of the tautomers



A (*Z* form) **B** (*E* form) **C** (*E* form)

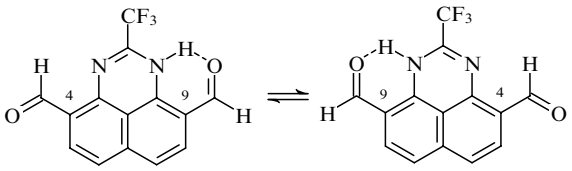
76

The spectra of 1-R-4-formylperimidines, for example, of compound **82**, have a signal for the proton of the CHO group at abnormally low field ($\delta_{CHO} \sim 10.8$). Since the aldehyde group in these compounds does not experience steric hindrances and its non-coplanarity with the ring is unlikely, this position of the signal indicates that compounds of type **82** adopt the *E* conformation **A** in which the hydrogen atom of the formyl group is deshielded by the adjacent nitrogen atom of the pyridine type. In addition, the *Z* conformation **B** can be destabilised due to repulsion between the lone electron pairs of the oxygen and nitrogen atoms.



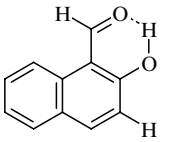
A (*E* form) **82** **B** (*Z* form)

Interesting conformational transitions were observed for 2-trifluoromethylperimidine-4,9-dicarbaldehyde (**80**).[73] Judging from the ^{1}H NMR spectrum in $CDCl_3$, under these conditions the CHO group in position 9 is fixed in the *Z* conformation (δ_{CHO} 9.93), whereas the 4-formyl substituent occurs in the *E* conformation (δ_{CHO} 10.83). In DMSO-d$_6$, the spectral pattern changes sharply. This spectrum has only two two-proton doublets corresponding to aromatic protons and one singlet of two equivalent CHO groups. Symmetrisation of the spectrum indicates that the polar solvent easily cleaves the intramolecular hydrogen bond resulting in rapid prototropism between the degenerate tautomers **A** and **B**.



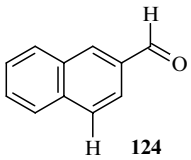
A **80** **B**

The conformers of naphthaldehydes can be reliably identified based on the long-range spin–spin coupling constants between the formyl proton and the *meta*-proton of the ring, $^5J_{H-CHO}$,[73, 142] whose values are given below. Generally, these constants are not observed in the spectra of the *Z* forms, but are pronounced in the spectra of the *E* conformations. Their values are generally in the range of 0.4–0.9 Hz. It can be readily seen that the necessary condition for the manifestation of the constants $^5J_{H-CHO}$ is the *trans*-arrangement of the coupling hydrogen atoms with respect to the $C_{Ar}-CHO$ bond.



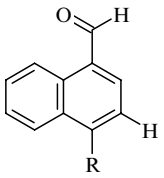
20

$^5J_{H-CHO}$ = 0.46 Hz

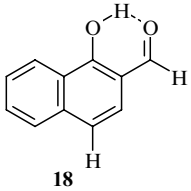


124

$^5J_{H-CHO}$ = 0.37 Hz

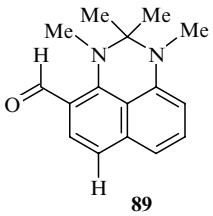


$^5J_{H-CHO}$ = 0 Hz



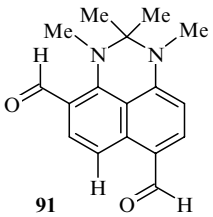
18

$^5J_{H-CHO}$ = 0 Hz



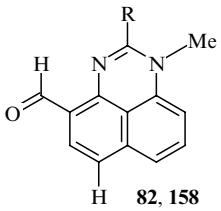
89

$^5J_{H-CHO}$ = 0.88 Hz



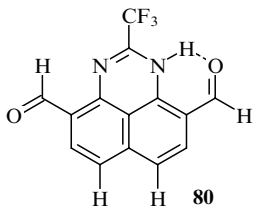
91

$^5J_{H-CHO-4}$ = 0.88 Hz;
$^5J_{H-CHO-7}$ = 0 Hz



82, **158**

158 (R = H): $^5J_{H-CHO}$ = 0.48 Hz;
82 (R = CF_3): $^5J_{H-CHO}$ = 0.70 Hz



80

$^5J_{H-CHO-4}$ = 0.40 Hz;
$^5J_{H-CHO-9}$ = 0 Hz

In principle, the conformations of naphthaldehydes can also be established based on analysis of the ^{13}C NMR spectra. For example, it was noted that the ^{13}C signal of the *ortho*-carbon atom in the *cis* position with respect to the carbonyl carbon atom shifts downfield, on the average, by $\sim$8 ppm compared to the signal for another *ortho*-carbon atom.[92] (The detailed data on the ^{13}C NMR spectra of naphthaldehydes were reported in the studies.[63, 140, 144, 151, 152]) The ^{17}O NMR spectrum of 4-methoxy-1-naphthaldehyde was studied.[140] This spectrum has a signal for the carbonyl oxygen atom at δ 552.3 and a signal for the oxygen atom of the methoxy group at δ 66.0.

The above-considered data lead to the following important conclusion. Naphthalenes have four types of formyl groups, which are subjected to different action of the diamagnetic component of the ring current. These groups correspond to the *E* and *Z* conformations of α- and β-naphthaldehydes. Each group in the planar form is characterised by different chemical shifts of the proton of the formyl group. The proton of CHO in the *E* form of α-naphthaldehyde is characterised by the most substantial deshielding, whereas the chemical shifts for the remaining three forms are much smaller and differ only slightly from each other. In

substituted naphthaldehydes, the situation is complicated because the chemical shifts of the proton of the CHO group are influenced by steric and electronic factors.

3. Dipole moments

To estimate the polarity and degree of conjugation between the CHO and NMe_2 groups in aldehydes **49**, **54** and **55**, their dipole moments were measured (Table 10). A comparison of the dipole moments of α-naphthaldehyde (**2**), 1-dimethylaminonaphthalene (**47**) and 4-dimethylamino-1-naphthaldehyde (**49**) demonstrated that the additional dipole π moment (μ_{tc}^{π}) in compound **49** induced by the so-called 'through-conjugation' is 0.35 D, which is almost three times smaller than that in 4-dimethylaminobenzaldehyde ($\mu_{tc}^{\pi} \approx 1$ D). Presumably, this is a consequence of steric hindrances to the planar arrangement of the CHO and NMe_2 groups, on the one hand, and the naphthalene π-system, on the other, caused by the *peri*-protons. However, the situation sharply changes on going to 4,5-bis(dimethylamino)-1-naphthalene-1,8-dialdehyde (**54**) and, particularly, to 4,5-bis(dimethylamino)-1,8-naphthodialdehyde (**55**). The unexpectedly large dipole moments of these compounds indicate that the conjugation between the CHO and NMe_2 groups becomes at least as efficient as that in 4-dimethylaminobenzaldehyde. The additional π moments in monoaldehyde **54** and *peri*-dialdehyde **55** are ~1.4 and 2.3 D, respectively. This is consistent with the X-ray diffraction data for dialdehyde **55**. These data are indicative of a sharp increase in the distance between the NMe_2 groups compared to the corresponding distance in 'proton sponge' **53**, which is favourable for the strong through-conjugation. Considering the dipole moment (9.21 D), *peri*-dialdehyde **55** is similar to ionic substances. Actually, unlike most of 'proton sponge' derivatives, dialdehyde **55** is noticeably water-soluble, has a rather high melting point (162–164 °C) and exhibits metallic lustre. Strong conjugation decreases the positive charges on the carbon atoms of the formyl groups, pushes them apart and is favourable for stabilisation of the molecule. This is a fundamental difference between *peri*-dialdehyde **55** and dialdehyde **12**, which exists as a cyclic hydrate **122** under ordinary conditions.

Table 10. Dipole moments (μ) of selected naphthaldehydes and model compounds.[136]

Compound	μ /D	Compound	μ /D
2	2.87	**53**	1.19
47	1.19	**54**	5.44
49	4.41	**55**	9.21

The Kerr constants and dipole moments of 1- and 2-naphthaldehydes **2** and **124** were determined and compared with those of 1- and 2-acetylnaphthalenes.[153] The Kerr constants for aldehyde **2** indicate that the CHO group is rotated with respect to the plane of the naphthalene system by 15°. However, these data do not allow one to make a conclusion as to which conformation (*Z* or *E*) is more favourable. The Kerr constants for aldehyde **124** are consistent with the planar *E* form.

Quantum-chemical calculations in the π approximation of dipole moments of two planar conformers of α- and β-naphthaldehydes and a comparison of these values with the experimental values μ did not lead to reliable conclusions about which form is favourable because of the similarity of the experimental and theoretical values.[154, 155] The dipole moment of 2-naphthaldehyde (**124**) in CCl_4 (3.26 D) is smaller than that of its 1 : 1 complex with phenol (4.6 D).[156]

4. Basicity

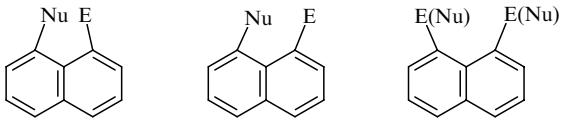
Like other carbonyl compounds, naphthaldehydes belong to bases and can be protonated by strong acids at the oxygen atom of the carbonyl group. The ionisation constants (pK_a) of 1- and 2-naphthaldehydes determined by spectrophotometry in aqueous H_2SO_4 are −6.34 and −6.68, respectively.[157] Therefore, both these aldehydes are somewhat more basic than benzaldehyde (pK_a −6.99) but less basic than 1- and 2-acetylnaphthalenes (pK_a −5.86 and −6.04, respectively). The basicities of aromatic aldehydes, including naphthaldehydes, can also be measured by IR and ^1H NMR spectroscopy.[158]

5. Electrochemical reduction

Electroreduction of 1- and 2-naphthaldehydes in DMF and acetonitrile was studied by cyclic voltammetry.[159] Radical anions were generated as primary reduction products, which rapidly disappeared due to subsequent dimerisation. It was found that the reactivity of the radical anions decreases in the series benzaldehyde > 2-naphthaldehyde > 1-naphthaldehyde.

6. Results of X-ray diffraction studies

The structural data for the crystal structures of more than 20 derivatives of 1- and 2-naphthaldehydes, including gossypol (**1**) and its numerous crystal solvates, are available in the Cambridge Structural Database (April 2002). These data were used primarily for studying the conformational effects and *peri*-interactions involving the α-formyl group. There are three main types of displacements of the *peri*-substituents.



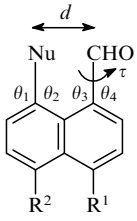
A **B** **C**

If one substituent is an electrophile (among which is the CHO group), whereas another substituent is a nucleophile, their interaction can cause these substituents to either approach each other (type **A**) or incline in the same direction (type **B**). If both substituents are either electrophiles or nucleophiles, they are pushed apart (type **C**). The type of interaction in each particular case can be judged from the distance (d) between the atoms of the substituents directly bound to the naphthalene ring and from the angles (θ) between the C—Nu and C—E bonds, on the one hand, and the adjoining bonds of the naphthalene ring, on the other (Table 11). It is very important to take into account the angle of rotation (τ) of the aldehyde group with respect to the ring plane.

The interaction of type **A** leads finally to the formation of covalent bonds. For naphthaldehydes existing in the aldehyde rather than cyclic form, such interactions have not been observed so far. All interactions of the CHO group with nucleophilic substituents in position 8 belong to type **B** (see Table 11). The type **B** displacement is most pronounced in 8-dimethylamino-1-naphthaldehyde (**93**). This is evidenced by the bond angles $\theta_1 - \theta_4$ and a shortened distance between the nitrogen atom and the carbon atom of the carbonyl group. Although both substituents in molecule **93** are inclined in the same direction, the angle of inclination of the NMe_2 group is larger than that of the CHO group due to which the distance between these substituents decreases. In addition, noteworthy is the large angle τ, which is a prerequisite to the attack of the lone electron pair of the amine nitrogen atom on the carbonyl carbon atom. One can conclude that this is the initial phase of the nucleophile–electrophile interaction and covalent binding.[5, 6]

In spite of the fact that both *peri*-substituents in 8-methoxy-1-naphthaldehydes **159** and **160** are also inclined in the same direction, the distances between these substituents are substantially larger and the angle of rotation of the formyl group with respect to the ring plane is too small to provide the necessary trajectory of attack of the methoxy oxygen atom on the carbonyl carbon atom. It is believed that the leaning effect in molecules **159** and **160** is associated with weak Coulombic attraction between the oxygen atom of the OMe group and the hydrogen atom of the aldehyde group. Apparently, it is this interaction that is responsible for the *E* conformation of the CHO group in both aldehydes.

Table 11. Geometric parameters characterising *peri*-interactions between the formyl and nucleophilic (Nu) groups in 8-substituted 1-naphthaldehydes.



93, **159**–**161**

Compound	Nu	R^1	R^2	d /Å	τ /deg	θ_1 /deg	θ_2 /deg	θ_3 /deg	θ_4 /deg	Ref.
93	NMe_2	H	H	2.489	65.8	124.3	116.0	122.2	118.5	160
159	OMe	OMe	OTs	2.628	23.9	123.4	115.1	126.4	114.9	5
160	OMe	H	OTs	2.644	32.9	123.5	115.3	124.7	115.8	5
161	OCOPh	OMe	H	2.823	12.8	117.6	118.8	125.5	115.9	5

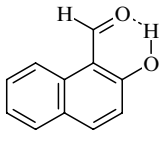
In molecule **161**, the benzoyloxy group is too bulky and the nucleophilicity of the oxygen atom of the ester group is too small to be attracted to the formyl group. That is the reason why this aldehyde is characterised by a large distance (d) between the *peri*-substituents, and the plane of the aldehyde group is nearly coplanar with the ring plane. As a consequence, the arrangement of the *peri*-substituents in this compound corresponds to type **C**. This structural type is even more pronounced in *peri*-dialdehyde **55** based on a 'proton sponge'.[136] The distance between the carbonyl carbon atoms (2.99 Å) in its molecule is much larger than the distance between the carbon atoms of the methyl groups in 1,8-dimethylnaphthalene (2.56 Å). Both aldehyde groups in molecule **55** exist in the sterically less strained *E* conformation and the angles of their rotation with respect to the plane of the naphthalene ring are relatively small ($\tau = 20.1°$ and $-27.3°$). All these geometric features are favourable for conjugation between the CHO and NMe_2 groups in this *peri*-dialdehyde.

According to the results of X-ray diffraction analysis, the conformations of the *para*- and *ortho*-aldehyde groups in the 2,5-diformyl derivative of 'proton sponge' **56** are virtually identical with those in 1- and 2-naphthaldehydes, respectively. The former group occurs in the *Z* conformation and is located virtually in the plane of the ring ($\tau = 6.8°$). The latter group occurs in the *E* conformation and the angle of its rotation ($\tau = 32.9°$) is substantially larger due to the presence of the adjacent NMe_2 group.[136] The *Z* form is typical also of the CHO group in trifluoromethylperimidine-6(7)-carbaldehyde (**77**).[149] Hence, it can be concluded that if there are no substituents adjacent to the α-formyl group in the naphthalene ring, the oxygen atom of this group is always directed toward the *peri*-proton.

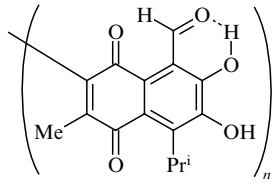
X-Ray diffraction studies, as well as ^{1}H NMR spectra, demonstrated that an intramolecular hydrogen bond involving the β-hydroxy group in 2-hydroxy-1-naphthaldehyde (**20**),[161] hemigossypolone (**162a**),[162] gossypolone (**162b**)[162] and gossypol (**1**)[163–166] stabilises the CHO group in the *E* conformation not only in solution but also in crystals. The geometric parameters of this intramolecular hydrogen bond are given in Table 12.

X-Ray diffraction studies of dialdehyde **56** and compounds **148**,[167] **163a**,[168] **163b**,[169] **164**[170] and **165**[171] showed that the β-formyl group tends to adopt the *E* conformation not only in solution (see Table 8) but in the crystalline state as well. The exception is binaphthyl dialdehyde **166** for which the *Z* form was observed.[172] Apparently, this is attributed to destabilisation of the *Z* conformer due to Coulombic repulsion between the oxygen carbon atom and the oxygen atoms of the substituent in position 3. Evidently, one CHO group in naphthalene-2,3-dicarbaldehyde (**167**) occurs in the *E* conformation, whereas another CHO group exists in the *Z* form for the same reason.[173]

Table 12. Geometric parameters of an intramolecular hydrogen bond in naphthaldehyde derivatives **20**, **162a** and **162b**.



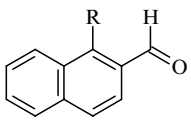
20



162a,**b**

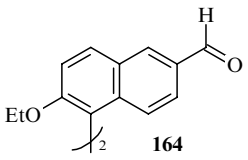
$n = 1$ (**a**), 2 (**b**).

Compound	d /Å			Angle O–H···O /deg	Ref.
	O···O	O–H	H···O		
20	2.567	1.070	1.59	148.9	161
162a	2.55	0.73	1.89	150.4	162
162b	2.54	1.03	1.71	134.7	162

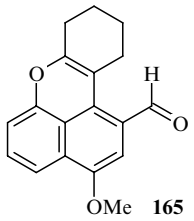


163a,**b**

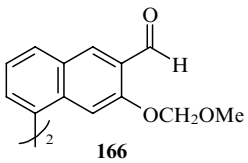
R = Br (**a**),
2,4,6-$Pr^i_3C_6H_2S(O)$ (**b**).



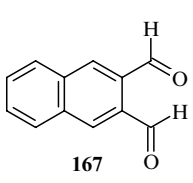
164



OMe **165**



166

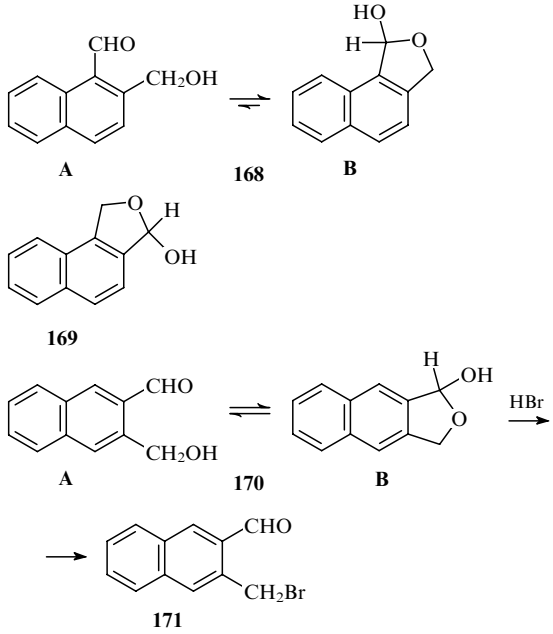


167

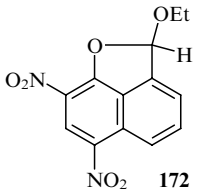
7. Ring-chain tautomerism

If a naphthaldehyde molecule has the OH-, NH- or SH-containing substituent adjacent to the aldehyde group, ring-chain tautomerism can take place due to the intramolecular nucleophilic addition of the O, N or S atoms of this substituent to the carbonyl group. 1,8-Naphthaldehydic acid existing under ordinary conditions in the naphthopyran form **127** serves as an example. Analogously, 2-hydroxymethyl-1-naphthaldehyde (**168**) occurs in the cyclic form **B** both in solution and in the solid state, whereas 1-hydroxymethyl-2-naphthaldehyde exists in form **169**.[91] Crystalline 3-hydroxymethyl-2-naphthaldehyde (**170**) also occurs in the cyclic form **B** (the $\nu_{C=O}$ band is absent in the IR spectrum), but its tautomers **A** and **B** in $CDCl_3$ co-exist in equilibrium, in which the

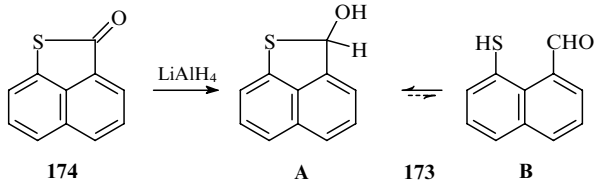
acyclic form **A** prevails (77%). It is this form of aldehyde **170** that is involved in reactions as evidenced by the formation of 3-bromomethyl derivative **171** upon treatment of compound **170** with hydrobromic acid.[91]



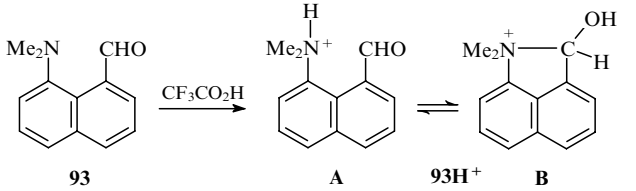
8-Hydroxy-1-naphthaldehyde (**131**) and its derivatives with electron-donating substituents in the naphthalene core are not prone to conversion into the cyclic form in neutral or acidic media although the presence of small amounts of this form in solutions cannot be ruled out.[7] Heating of 8-hydroxy-5,7-dinitro-1-naphthaldehyde in ethanol afforded cyclic acetal **172**.[128]



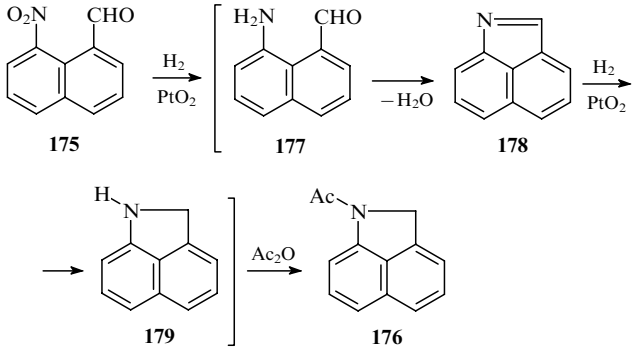
Unstable 8-mercapto-1-naphthaldehyde (**173**) prepared by reduction of 2-oxo-2*H*-naphtho[1,8-*b*,*c*]thiophene (**174**) with lithium aluminium hydride or diborane exists exclusively in the cyclic form **A**.[174]



As mentioned above (see Section III.6), there are pronounced attractions between the substituents in 8-dimethylamino-1-naphthaldehyde (**93**). Treatment of this aldehyde with acids led to its partial cyclisation, both forms of hydrate **93H**$^+$ (**A** and **B**) being clearly seen in the ^{1}H NMR spectrum.[76]



Catalytic reduction of 8-nitro-1-naphthaldehyde (**175**) followed by treatment of the reaction mixture with acetic anhydride afforded 1-acetyl-1,2-dihydrobenzo[*c*,*d*]indole (**176**).[175] Apparently, the initially formed *peri*-aminonaphthaldehyde **177** immediately underwent cyclisation to give compound **178**, which was subjected to further hydrogenation to form unstable benzoindoline **179**. The latter can be isolated only as the more stable acetylated derivative **176**.

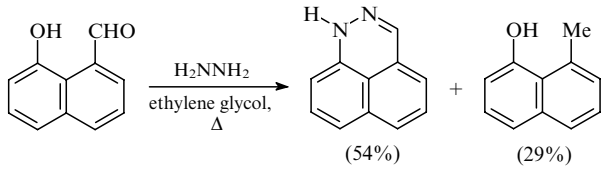


IV. Reactions

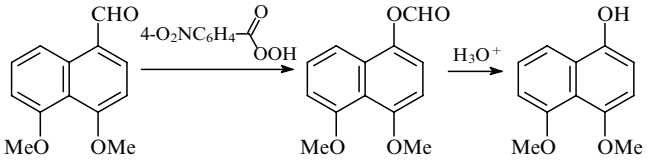
Naphthaldehydes are involved in all reactions typical of aromatic aldehydes. In addition, *peri*-substituted α-naphthaldehydes undergo specific transformations, primarily, cyclisations, due to the presence of closely spaced *peri*-substituents. For this series of compounds, the formation of thiosemicarbazones,[44] 2,4-dinitrophenylhydrazones,[68] oximes (which are then transformed into nitriles)[68, 176, 177] and azomethines,[68] including polydentate ligands based on 1,1′-binaphthyl dialdehydes of type **103a**,**b**,[81, 111, 178, 179] was described. Reduction of naphthaldehydes with complex metal hydrides afforded primary alcohols.[65, 69, 70, 180] These reactions with the use of lithium tritide and lithium trimethoxyborotritide gave rise to tritium-labelled alcohols.[181] Reduction of 2-naphthaldehyde with the $TiCl_4$–$Bu_4N^+I^-$ system afforded 1,2-binaphthylethanediol.[182] Procedures were developed for the enantioselective addition of diethylzinc[183] and other organometallic compounds[184] to 2-naphthaldehyde with the participation of chiral catalysts or auxiliary groups involved in the substrate. For other naphthaldehydes, analogous reactions were documented.[58, 185] Naphthaldehydes gave condensation products with compounds containing the active methylene group, *viz*., diethyl malonate ester,[122, 186] malononitrile,[186–188] esters of cyanoacetic[186] and other carboxylic acids,[89] benzyl cyanides,[52, 187] γ-picoline,[98] barbituric acid,[189] trinitrotoluene,[60] *etc*.

The transformation of 4,8-difluoro-1-naphthaldehyde into the corresponding naphthalenecarboxylic acid under the action of $KMnO_4$ or the Jones reagent[118] can serve as an example of oxidation of naphthaldehydes. The Angeli's salt (sodium trioxodinitrate, $Na_2N_2O_3$) can be used as an oxidising agent. In the latter case, the reaction proceeds by a very complex mechanism involving [2 + 2]-cycloaddition between the N=N bond of the oxidising agent and the C=O group of the aldehyde.[190] Milder reagents can oxidise other groups, the aldehyde group remaining intact. For example, gossypol was converted into gossypolone **162b** (47% – 69% yield) under the action of an aqueous solution of $FeCl_3$.[191]

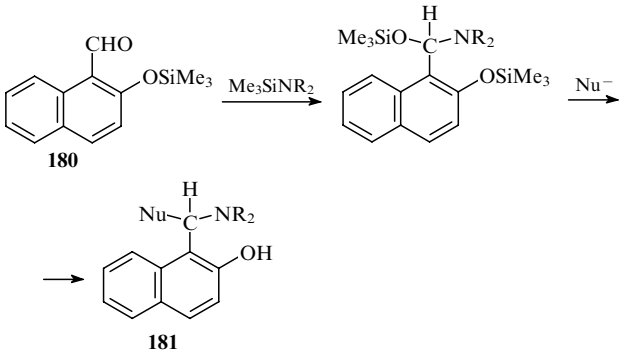
Attempts to prepare hydrazones by treating naphthaldehydes with hydrazine were often unsuccessful and led to the formation of the corresponding azines.[68, 192] Nevertheless, the *in situ* formation of hydrazones was used for the conversion of naphthaldehydes into methylnaphthalenes (Kishner – Wolff reaction)[44, 52] and *peri*-heterocyclic compounds.[176]



p-Toluenesulfonylhydrazones of α-naphthaldehydes were synthesised and then treated with alkali to prepare naphthyldiazomethanes.[96,97] Naphthaldehydes are involved in the Baeyer–Villiger reaction accompanied by the replacement of the formyl group by the hydroxy group.[53] Examples of such transformations were given in the Refs 55, 56, 117.

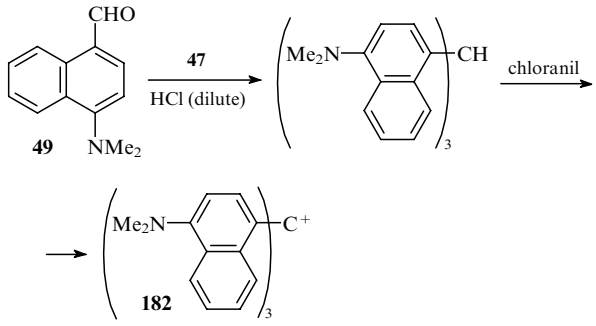


The tandem reactions of 2-trimethylsilyloxy-1-naphthaldehyde (**180**) with various trimethylsilyldialkylamines and nucleophiles afforded naphthols **181**.[193]

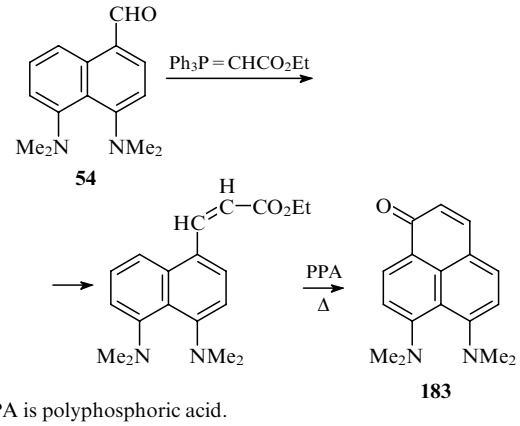


Nu = Me, CH_2CO_2Et, $CH_2CH=CH_2$, AlkC≡C; R = Alk.

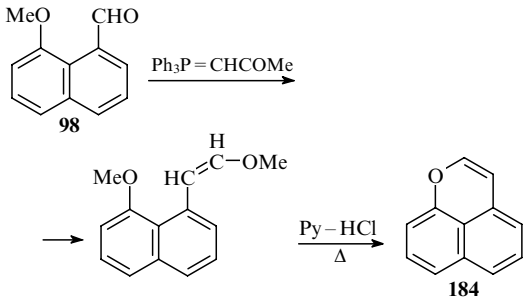
Under the conditions of acid catalysis, naphthaldehydes react with aromatic CH-nucleophiles, for example, with arylamines. This reaction was used, in particular, for the preparation of the dye Victoria Blue (**182**) from 4-dimethylamino-1-naphthaldehyde (**49**) and 1-dimethylaminonaphthalene (**47**).[90]

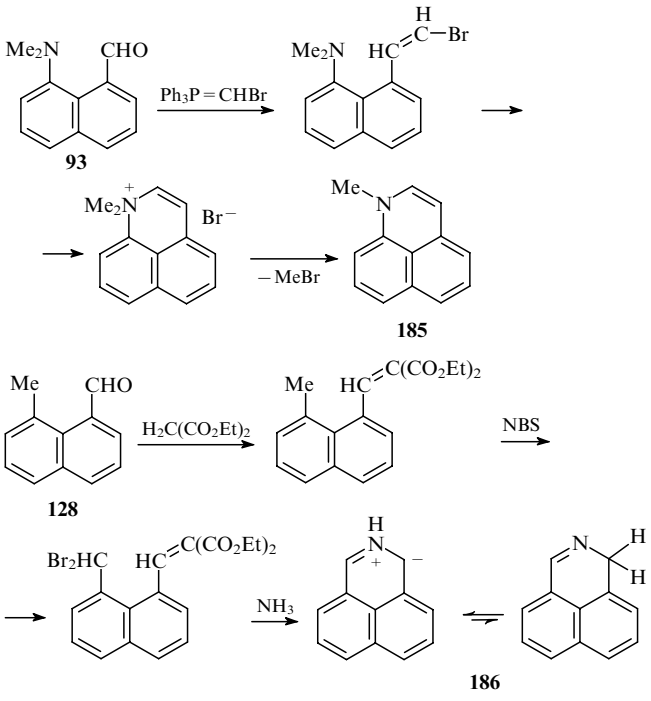


The Wittig[75,77,78,107,160,194] and Wittig–Horner reactions[133,195] of naphthaldehydes were studied in detail. These reactions afford alkenes, which are generally used for subsequent cyclisations, including the synthesis of natural compounds,[196] biologically active substances[133] and synthetic precursors of fullerene.[197] The syntheses of 6,7-bis(dimethylamino)phenalenone (**183**),[186] naphtho[1,8-*b*,*c*]pyran (**184**)[78] (a modification of this synthesis was described in the study[198]), 1-methylbenzo[*d*,*e*]quinoline (**185**)[160] and benzo[*d*,*e*]isoquinoline (**186**)[122] provide only a few examples of such transformations. An analogous approach was used for the synthesis of linear and angular naphthofurans and benzocoumarins.[77]

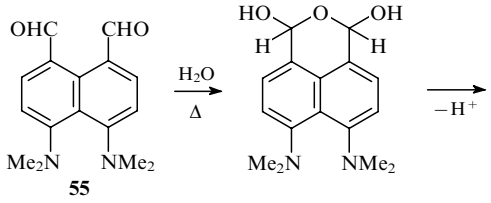


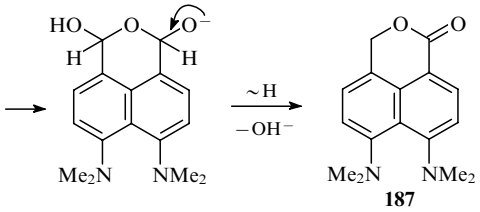
PPA is polyphosphoric acid.





peri-Dialdehyde **55** derived from the 'proton sponge' underwent the intramolecular Cannizzaro reaction upon refluxing in water to form 6,7-bis(dimethylamino)naphtho[1,8-*c*,*d*]pyran-1-one (**187**).[68] Interestingly, this process, unlike the classical procedure, does not require the use of alkali. Apparently, the necessary alkalinity of the medium is provided by the high alkalinity of the 'proton sponge' by itself.

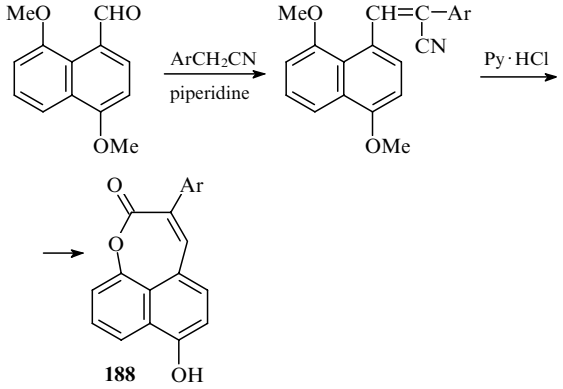


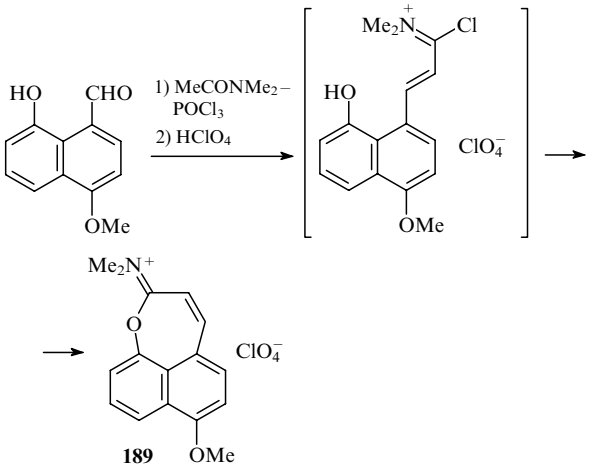


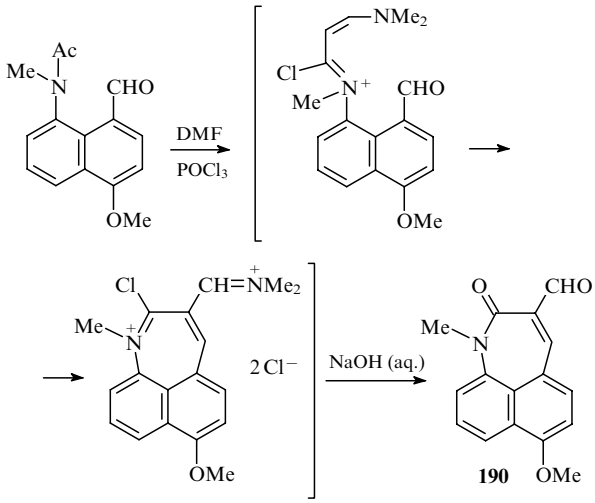
187

Naphthalene-1,8-dicarbaldehyde is also involved in the analogous reaction with the only difference that the latter reaction does require alkali.[199]

Buu-Hoi *et al.*[187] and then Mezheritskii and co-workers[7, 71, 200] demonstrated that the seven-membered heterocycles can be built up based on *peri*-hydroxy- and *peri*-aminonaphthaldehydes to form naphtho[1,8-*b*,*c*]oxepine and naphtho[1,8-*b*,*c*]-azepine derivatives **188**–**190**.







In some studies, heterocyclisation was carried out with the use of 2-hydroxy-1-naphthaldehydes.[188, 201]

* * *

The data surveyed in the present review provide evidence that naphthaldehydes play a very important role in the chemistry of naphthalene. These compounds serve as important starting reagents for the preparation of complex organic compounds, including biologically active and natural substances. Substituted naphthaldehydes are used for studying the effects of *peri*-interactions, in particular, these compounds model the transition state of the nucleophilic addition to the carbonyl group. This gives insight into the action of enzymes in living organisms. Studies of direct formylation of naphthalene derivatives are not only of great preparative importance but also provide a better understanding of the factors responsible for the reactivity of polynuclear arenes. Undoubtedly, these lines of investigation will be extensively developed in the coming years.

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References

1. S Patai *The Chemistry of the Carbonyl Group* (London: Wiley, 1966)
2. J Falbe *Methoden der Organischen Chemie (Houben-Weyl)* Bd. E3 (Stuttgart: Thieme, 1983)
3. J March *Advanced Organic Chemistry* (4th Ed.) (New York: Wiley, 1992)
4. V Balasubramaniyan *Chem. Rev.* **66** 567 (1966)
5. J C Gallucci, D J Hart, D G J Young *Acta Crystallogr., Sect. B* **54** 73 (1998)
6. J O'Leary, P C Bell, J D Wallis, W B Schweizer *J. Chem. Soc., Perkin Trans. 2* 133 (2001)
7. V V Mezheritskii, V V Tkachenko *Adv. Heterocycl. Chem.* **51** 1 (1990)
8. D L Van Jagt, L M Deck, R E Royer *Curr. Med. Chem.* **7** 479 (2000)
9. N Donaldson *The Chemistry and Technology of Naphthalene Compounds* (London: Arnold, 1957)
10. E Josephy, F Radt (Eds), in *Elsevier's Encyclopedia of Organic Chemistry. Carbocyclic Condensed Compounds* Vol. 12B (New York: Elsevier, 1950) p. 2189
11. R C Larock, in *Comprehensive Organic Transformations: a Guide to Functional Group Preparations* (2nd Ed.) (New York: Wiley, 1999) p. 1197
12. L E Hinkel, E E Ajing, J H Beynon *J. Chem. Soc.* 339 (1936)
13. R Robinson, H W Thompson *J. Chem. Soc.* 2016 (1932)
14. R Adams, I Levine *J. Am. Chem. Soc.* **45** 2373 (1923)
15. A Kreutzberger *Arch. Pharm.* **304** 362 (1971)
16. R C Fuson, E C Horning, M L Ward, S P Powland, J L Marsh *J. Am. Chem. Soc.* **64** 30 (1942)
17. F M Aslam, P H Gore, M Jehangir *J. Chem. Soc., Perkin Trans. 2* 892 (1972)
18. A Rieche, H Gross, E Hoeft *Chem. Ber.* **93** 88 (1960)
19. V I Minkin, G N Dorofeenko *Usp. Khim.* **29** 1301 (1960) [*Russ. Chem. Rev.* **29** 599 (1960)]
20. A G Martinez, R M Alvarez, J O Barcina, S M Cerero, E T Vilar, A G Fraile, M Hanack, L R Subramanian *J. Chem. Soc., Chem. Commun.* 1571 (1990)
21. L F Fieser, J E Jones *J. Am. Chem. Soc.* **64** 1666 (1942)
22. G Saint-Ruf, N P Buu-Hoi, P Jacquignon *J. Chem. Soc.* 48 (1958)
23. S Paul, M Gupta, R Gupta *Synlett* 1115 (2000)
24. J Dewar, H O Jones *J. Chem. Soc.* **85** 212 (1904)
25. US P. 2 485 237; *Chem. Abstr.* **44** 2027 (1950)
26. G A Olah, S J Kuhn *J. Am. Chem. Soc.* **82** 2380 (1960)
27. G A Olah, L Ohannesian, M Arvanaghi *Chem. Rev.* **87** 671 (1987)
28. M Tanaka, Y Souma *J. Chem. Soc., Chem. Commun.* 1551 (1991)
29. M Tanaka, M Fujiwara, H Ando, Y Souma *Chem. Commun.* 159 (1996)

30. M Tanaka, M Fujiwara, Q Xu, Y Souma, H Ando, K K Laali *J. Am. Chem. Soc.* **119** 5100 (1997)
31. W Kantlehner, M Vettel, A Gissel, E Hang, G Ziegler, M Ciesielski, O Scherr, R Haas *J. Prakt. Chem.* **342** 297 (2000)
32. L Gattermann, W Berchelman *Chem. Ber.* **31** 1765 (1898)
33. L Gattermann, Th Horlacher *Chem. Ber.* **32** 284 (1899)
34. In *Sintezy Organicheskikh Preparatov* T. 3 (Moscow: Izd. Inostr. Lit., 1952) p. 365 [Translation from *Organic Syntheses* Vols 20–25 (New York: Academic Press, 1940–1945)]
35. H Gross, A Rieche, G Matthey *Chem. Ber.* **96** 308 (1963)
36. C F H Allen, G W Leubner *Org. Synth. Coll.* **4** 866 (1963)
37. Germ. P. 519 444; *Chem. Abstr.* **25** 2734 (1931)
38. In *Preparativnaya Organicheskaya Khimiya* (Preparative Organic Chemistry) (Moscow: Izd. GNTIKhim. Lit., 1959) p. 326
39. N U Hofslokken, L Skattebol *Acta Chem. Scand.* **53** 258 (1999)
40. C T Morgan, D C Vining *J. Chem. Soc.* **119** 177 (1921)
41. L Gattermann *Annalen* **357** 313 (1907)
42. N G Tregub, A P Knyazev, V V Mezheritskii *Zh. Org. Khim.* **26** 168 (1990) [a]
43. R Adams, E Montgomery *J. Am. Chem. Soc.* **46** 1518 (1924)
44. N P Buu-Hoi, D Lavit *J. Chem. Soc.* 2776 (1955)
45. N P Buu-Hoi, N Hoan, M R Knenissi *J. Chem. Soc.* 2307 (1951)
46. L Gattermann *Annalen* **357** 367 (1907)
47. In *Sintezy Organicheskikh Preparatov* T. 3 (Moscow: Izd. Inostr. Lit., 1952) p. 74 [Translation from *Organic Syntheses* Vols 20–25 (New York: Academic Press, 1940–1945)]
48. N P Buu-Hoi, D Lavit, J Collard *J. Org. Chem.* **23** 542 (1958)
49. W J Traynelis, J J Miskel, J K Sowa *J. Org. Chem.* **22** 1269 (1957)
50. N P Buu-Hoi, D Lavit *J. Org. Chem.* **22** 912 (1957)
51. N P Buu-Hoi, D Lavit *J. Org. Chem.* **21** 21 (1956)
52. N P Buu-Hoi, D Lavit *J. Chem. Soc.* 2412 (1956)
53. K A Parker, T Iqbal *J. Org. Chem.* **45** 1149 (1980)
54. N P Buu-Hoi, D Lavit *J. Chem. Soc.* 1743 (1956)
55. L Syper, K Mlochkowski, K Kloc *Tetrahedron* **39** 781 (1983)
56. R L Hannan, R B Barber, H Rapoport *J. Org. Chem.* **44** 2153 (1979)
57. A Terada, Y Tanoue, A Hatada, H Sakamoto *Bull. Chem. Soc. Jpn.* **60** 205 (1987)
58. A Terada, Y Tanoue, A Hatada, H Sakamoto *J. Chem. Soc., Chem. Commun.* 987 (1983)
59. V L Novikov, N N Balaneva, A M Moiseenkov, G B Elyakov *Izv. Akad. Nauk, Ser. Khim.* 1901 (1992) [b]
60. N P Buu-Hoi, N Hoan, D Lavit *J. Chem. Soc.* 485 (1953)
61. P C Meltzer, P H Bickford, G J Lambert *J. Org. Chem.* **50** 3121 (1985)
62. A Mamade, P Herlihy, J Quick, R P Duffley, M Burgos, A P Hoffer *Experientia* **39** 1276 (1983)
63. A I Meyers, J J Willemsen *Tetrahedron* **54** 10 493 (1998)
64. A Vilsmaier, A Haack *Chem. Ber.* **60** 119 (1927)
65. O V Vinogradova, E A Filatova, N V Vistorobskii, A F Pozharskii, in *Tez. Dokl. II Mezhdunarodnoi Konferentsii Molodykh Uchenykh po Aktual'nym Tendentsiyam v Organicheskom Sinteze na Poroge Novoi Ery, S Peterburg, 1999* [Abstracts of Reports of the IIth International Conference of Young Scientists on Current Trends in Organic Synthesis on the Threshold of New Era, St Petersburg, 1999] p. 189
66. Br. P. 607 908; *Chem. Abstr.* **43** 2232 (1949)
67. N P Buu-Hoi, P Jacquignon, C T Long *J. Chem. Soc.* 505 (1957)
68. N V Vistorobskii, A F Pozharskii *Zh. Org. Khim.* **25** 2154 (1989) [a]
69. N V Vistorobskii, O V Vinogradova, A F Pozharskii *Izv. Akad. Nauk, Ser. Khim.* 348 (1997) [b]
70. A F Pozharskii, N V Vistorobskii, M I Rudnev, A I Chernyshev *Izv. Akad. Nauk, Ser. Khim.* 2039 (1996) [b]
71. V V Mezheritskii, L G Minyaeva *Zh. Org. Khim.* **22** 2394 (1986) [a]
72. V V Mezheritskii, D M Elisevich, G N Dorofeenko *Zh. Org. Khim.* **17** 2444 (1981) [a]
73. E A Filatova, Candidate Thesis in Chemical Sciences, Rostov State University, Rostov-on-Don, 2001
74. A F Pozharskii, E A Filatova, N V Vistorobskii, I V Borovlev *Khim. Geterotsikl. Soedin.* 365 (1999) [c]
75. A J Kirby, F O'Carrol *J. Chem. Soc., Perkin Trans. 2* 649 (1994)
76. A J Kirby, J M Percy *Tetrahedron* **44** 6903 (1988)
77. N S Narasimhan, R S Mali *Tetrahedron* **31** 1005 (1975)
78. N S Narasimhan, R S Mali *Synthesis* 796 (1975)
79. D A Shirley, C F Cheng *J. Organomet. Chem.* **20** 251 (1969)
80. G A Kraus, J Kim *J. Org. Chem.* **67** 2358 (2002)
81. H Brunner, H Schiessling *Bull. Soc. Chim. Belg.* **103** 119 (1994)
82. J Clayden, C S Frampton, C McCarthy, N Westlund *Tetrahedron* **55** 14 161 (1999)
83. G A Olah, G K S Prakash, M Arvanaghi *Synthesis* 228 (1984)
84. G A Olah, M Arvanaghi *Angew. Chem., Int. Ed. Engl.* **20** 878 (1981)
85. G A Olah, L Ogannesian, M Arvanaghi *J. Org. Chem.* **49** 3856 (1984)
86. D Comins, A I Meyers *Synthesis* 403 (1978)
87. M Niestroj, W P Neumann *Chem. Ber.* **129** 45 (1996)
88. C Tard, H Lapin, A Horeau *C. R. Seances Acad. Sci., Ser. C* **246** 3644 (1958)
89. K Goto, T Kubo, K Yamamoto, K Nakasuji, K Sato, D Shiomi, T Takui, M Kubota, T Kobayashi, K Yakusi, J Quyang *J. Am. Chem. Soc.* **121** 1619 (1999)
90. S G R Guinot, J D Hepworth, M Wainwright *J. Chem. Soc., Perkin Trans. 2* 297 (1998)
91. J G Smith, P W Dibble, R E Sandborn *J. Org. Chem.* **51** 3762 (1986)
92. T Drakenberg, J Sandstrom, J Seita *Org. Magn. Reson.* **11** 246 (1978)
93. B H Lipshutz, S S Pfeiffer, W Christman *Tetrahedron Lett.* **40** 7889 (1999)
94. X Yin, X Wei, Z Zong, Q Lin *Meitan Zhuanhua* **24** 93 (2001); *Chem. Abstr.* **135** 154 326 (2001)
95. D Berry, D C C Smith *J. Chem. Soc., Perkin Trans. 1* 699 (1972)
96. R J Bailey, P J Card, H Shechter *J. Am. Chem. Soc.* **105** 6096 (1983)
97. M J Fritz, E L Ramos, M S Platz *J. Org. Chem.* **50** 3522 (1985)
98. Eur. P. 1 138 328; *Chem. Abstr.* **135** 272 763 (2001)
99. T Matsushita, K Ebitani, K Kaneda *Chem. Commun.* 265 (1999)
100. K Ishihara, H Kirihara, H Yamamoto *J. Org. Chem.* **62** 5664 (1997)
101. Jpn. P. 06 135 879; *Chem. Abstr.* **121** 179 275 (1994)
102. Jpn. P. 08 143 503; *Chem. Abstr.* **125** 142 304 (1996)
103. Jpn. P. 09 316 019; *Chem. Abstr.* **128** 48 066 (1997)
104. J Santamaria, R Iroundi *Tetrahedron Lett* **32** 4291 (1991)
105. K C Nicolaou, P S Baran, Y-L Zhong *J. Am. Chem. Soc.* **123** 3183 (2001)
106. Jpn. P. 03 227 951; *Chem. Abstr.* **116** 58 959 (1992)
107. J K Stille, R T Foster *J. Org. Chem.* **28** 2703 (1963)
108. S Hauptmann, P Hunger, A Blaskovits *J. Prakt. Chem.* **37** 72 (1968)
109. J B Shoesmith, H Rubli *J. Chem. Soc.* 3241 (1926)
110. J S Cha, H C Brown *J. Org. Chem.* **58** 4732 (1993)
111. H Brunner, J Goldbrunner *Chem. Ber.* **122** 2005 (1989)
112. J S Cha, J M Kim, J H Chun, O O Kwon, S Y Kwon, S W Han *Org. Prep. Proced. Int.* **31** 204 (1999)
113. J S Cha, J M Kim, J H Chun, S Y Kwon, J C Lee *Bull. Korean Chem. Soc.* **19** 730 (1998)
114. J S Cha, J M Kim, J H Chun, S Y Kwon, S D Cho *Bull. Korean Chem. Soc.* **19** 1301 (1998)
115. J S Cha, M J Kim, J M Kim, O O Kwon, J H Chun, S D Cho *Bull. Korean Chem. Soc.* **19** 724 (1998)
116. J S Cha, S E Lee, H S Lee *Org. Prep. Proced. Int.* **24** 331 (1992)
117. S V Kolotuchin, A I Meyers *J. Org. Chem.* **64** 7921 (1999)
118. J R Tagat, S W McCombie, D V Nazareno, C D Boyle, J A Kozlowski, S Chackalamannil, H Josieu, Y Wong, G Zhou *J. Org. Chem.* **67** 1171 (2002)
119. J S Cha, M S Yoon *Tetrahedron Lett.* **30** 3677 (1989)
120. Y Watanabe, M Yamashita, T Mitsudo M Igami, Y Takegami *Bull. Chem. Soc. Jpn.* **48** 2490 (1975)
121. H Badger, Y H Chiang *Synthesis* 249 (1976)
122. C-K Sha, D-C Wang *Tetrahedron* **50** 7495 (1994)
123. W Ried, H Bodem, U Ludwig, H Neidhardt *Chem. Ber.* **91** 2479 (1958)
124. P M Kochergin, L S Blinova, G A Karpov *Khim.-Farm. Zh.* **28** 63 (1994) [d]
125. W Ried, H Bodem *Chem. Ber.* **89** 708 (1956)
126. C A Elliger *Org. Prep. Proced. Int.* **17** 419 (1985)
127. T Horaguhi, T Abe *Bull. Chem. Soc. Jpn.* **51** 2068 (1978)

128. Yu M Chunaev, N M Przhiyaglovskaya, L N Kurkovskaya, M A Gal'bershtam *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.* **25** 278 (1982)
129. M Periasamy, M R Reddy, P Bharathi *Synth. Commun.* **29** 677 (1999)
130. Y Misumi, Y Ishii, M Hidai *J. Mol. Catal.* **78** 1 (1993)
131. H-J Liu, J M Nyangulu *Synth. Commun.* **19** 3407 (1989)
132. J-P Gourvès, R Ruzziconi, L Villarroig *J. Org. Chem.* **66** 617 (2001)
133. W M Owton *J. Chem. Soc., Perkin Trans. 1* 2131 (1994)
134. I M Hunsberger *J. Am. Chem. Soc.* **72** 5626 (1950)
135. R T O'Connor, P Von der Haar, E F DuPre, L E Brown, C H Pominski *J. Am. Chem. Soc.* **76** 2368 (1954)
136. A F Pozharskii, G G Aleksandrov, N V Vistorobskii *Zh. Org. Khim.* **27** 1536 (1991) [a]
137. V L Frampton, J D Edwards, H R Henze *J. Am. Chem. Soc.* **70** 3944 (1948)
138. T Heinis, S Chowdhury, P Kebarle *Org. Mass Spectrom.* **28** 358 (1993)
139. R H Martin, N Defay, F Geerts-Evrard *Tetrahedron* **20** 1505 (1964)
140. S Perumal, G Vasuki, D A Wilson, D W Boykin *Magn. Reson. Chem.* **30** 320 (1992)
141. J Niwa *Bull. Chem. Soc. Jpn.* **50** 979 (1977)
142. R Benassi, D Iarossi, U Folli, L Schenetti, F Taddei *J. Chem. Soc., Perkin Trans. 2* 228 (1981)
143. L Lunazzi, G Placucci, D Macciantelli *Tetrahedron* **47** 9125 (1991)
144. J Seita, T Drakenberg, J Sandstrom *Org. Magn. Reson.* **11** 239 (1978)
145. W B Smith, D L Deavenport, A M Ihring *J. Am. Chem. Soc.* **94** 1959 (1972)
146. L V Metlitskii, A S Sadykov, A K Karimdzhanov, A I Ismailov, R A Mukhamedova, M Kh Avazkhodzhaev, F T Kamaev *Dokl. Akad. Nauk SSSR* **218** 1472 (1974) [e]
147. P E Hansen *Magn. Reson. Chem.* **31** 23 (1993)
148. E A Corey, J J Rohde *Tetrahedron Lett.* **38** 37 (1997)
149. E J Filatova, I V Borovlev, A F Pozharskii, Z A Starikova, N V Vistorobskii *Mendeleev Commun.* 178 (2000)
150. A F Pozharskii, E A Filatova, I V Borovlev, N V Vistorobskii *Khim. Geterotsikl. Soedin.* 796 (2001) [c]
151. G Razniewska-Lazecka, A Dambska, A Janowski *Magn. Reson. Chem.* **24** 365 (1986)
152. D Strohl, S Thomas, E Kleinpeter, R Radeglia, J Brunn *Monatsh. Chem.* **123** 769 (1992)
153. R I W Le Fevre, A Sundaram *J. Chem. Soc.* 4756 (1962)
154. G Khibaum, N Tyutyulkov, M Ivanova *Teor. Eksp. Khim.* **6** 595 (1970) [f]
155. B Klabuhn, E Clausen, H Goetz *Tetrahedron* **29** 1153 (1973)
156. T Gramstad *Acta Chem. Scand.* **47** 68 (1993)
157. G Culbertson, R Pettit *J. Am. Chem. Soc.* **85** 741 (1963)
158. N M Somera, L Do Amaral *An. Assoc. Bras. Quim.* **44** 36 (1995); *Chem. Abstr.* **123** 256 052 (1995)
159. W R Fawcett, A Lasia *Can. J. Chem.* **59** 3256 (1981)
160. D R W Hodgson, A J Kirby, N Feeder *J. Chem. Soc., Perkin Trans. 1* 949 (1999)
161. W Maniukiewicz, M Bukowska-Strzyzewska *Acta Crystallogr., Sect. C, Cryst. Struct. Commun.* **48** 1324 (1992)
162. S A Talipov, B T Ibragimov, K M Beketov, Sh Yu Islambekov, R G Mardanov, A I Ismailov *Khim. Prir. Soedin.* 814 (1995) [g]
163. S A Talipov, B T Ibragimov, G N Tishchenko, T F Aripov, G B Nazarov, B V Strokopytov, K M Polyakov *Kristallografiya* **33** 384 (1988) [h]
164. B T Ibragimov, S A Talipov, M Gdaniec *J. Inclusion Phenom. Mol. Recognit. Chem.* **8** 409 (1990)
165. M Gdaniec, B T Ibragimov, S A Talipov *J. Inclusion Phenom. Mol. Recognit. Chem.* **8** 431 (1990)
166. B T Ibragimov, S A Talipov, T F Aripov, A S Sadykov *J. Inclusion Phenom. Mol. Recognit. Chem.* **8** 323 (1990)
167. J M Fernandez, G Espinosa-Perez *J. Chem. Cryst.* **24** 151 (1994)
168. B Koppenhoefer, J W Bats *Acta Crystallogr., Sect. C, Cryst. Struct. Commun.* **42** 1612 (1986)
169. S Nakamura, H Yasuda, Y Watanabe, T Toru *J. Org. Chem.* **65** 8640 (2000)
170. H-J Deussen, C Boutton, N Thorup, T Geisler, E Hendrickx, K Bechgaard, A Persoons, T Bjørnholm *Chem. Eur. J.* **4** 240 (1998)
171. J-P Buisson, P Demerseman, N Platzer *J. Heterocycl. Chem.* **32** 17 (1995)
172. Y Tachi, S Nakayama, F Tani, G Ueno, Y Naruta *Acta Crystallogr., Sect. C, Cryst. Struct. Commun.* **55** 1351 (1999)
173. D Britton *Acta Crystallogr., Sect. C, Cryst. Struct. Commun.* **55** 978 (1999)
174. D G Hawthorne, Q N Porter *Aust. J. Chem.* **19** 1909 (1966)
175. G Spiteller *Monatsh. Chem.* **90** 721 (1959)
176. P H Lacy, D C C Smith *J. Chem. Soc., Perkin Trans. 1* 419 (1975)
177. J S Yadav, B V S Reddy, C Madan *J. Chem. Res. (S)* 190 (2001)
178. H Brunner, H Schiessling *Angew. Chem., Int. Ed. Engl.* **33** 125 (1994)
179. H-C Zhang, W-S Huang, L Pu *J. Org. Chem.* **66** 481 (2001)
180. A F Pozharskii, N V Vistorobskii *Izv. Akad. Nauk, Ser. Khim.* 1016 (1996) [b]
181. E M Zippi, H Anders, H Morimoto, P G Williams *Synth. Commun.* **25** 2685 (1995)
182. T Tsuritani, S Ito, H Shinokubo, K Oshima *J. Org. Chem.* **65** 5066 (2000)
183. J Priego, O G Mancheño, S Cabrera, J C Carretero *J. Org. Chem.* **67** 1346 (2002)
184. S Nakamura, H Yasuda, Y Watanabe, T Toru *Tetrahedron Lett.* **41** 4157 (2000)
185. O V Ryabtsova, A F Pozharskii, V A Ozeryanskii, N V Vistorobskii *Izv. Akad. Nauk, Ser. Khim.* 817 (2001) [b]
186. N V Vistorobskii, A F Pozharskii *Zh. Org. Khim.* **27** 1543 (1991) [a]
187. N P Buu-Hoi, G Saint-Ruf, J C Perche *J. Chem. Soc. C* 1327 (1970)
188. A A Fadda, M T Zeimaty, M M Gerges, H M Refat, E R Biehl *Heterocycles* **43** 23 (1996)
189. B S Jursic *J. Heterocycl. Chem.* **38** 655 (2001)
190. L Torun, T Mohammad, H Morrison *Tetrahedron Lett.* **40** 5279 (1999)
191. R H Haas, D A Shirley *J. Org. Chem.* **30** 4111 (1965)
192. V V Mezheritskii, V V Tkachenko, O N Zhukovskaya, D M Elisevich, G N Dorofeenko *Zh. Org. Khim.* **17** 627 (1981) [a]
193. M R Saidi, H R Khalaji *J. Chem. Res. (S)* 340 (1997)
194. N V Vistorobskii, A F Pozharskii *Izv. Akad. Nauk, Ser. Khim.* 2297 (1996) [b]
195. T Kobayashi, T Eda, O Tamura, H Ishibashi *J. Org. Chem.* **67** 3156 (2002)
196. B Kesteleyn, L Van Puyvelde, N De Kimpe *J. Org. Chem.* **64** 438 (1999)
197. Z Marcinow, P W Rabideau *J. Org. Chem.* **65** 5063 (2000)
198. J P Buisson, R Royer *J. Heterocycl. Chem.* **25** 539 (1988)
199. K Bowden, A M Butt, M Streater *J. Chem. Soc., Perkin Trans. 2* 567 (1992)
200. V V Mezheritskii, V V Tkachenko, A L Pikus *Zh. Org. Khim.* **22** 1487 (1986) [a]
201. L Yu Ukhin, V N Komissarov *Zh. Org. Khim.* **27** 885 (1991) [a]

[a] — *Russ. J. Org. Chem. (Engl. Transl.)*
[b] — *Russ. Chem. Bull., Int. Ed. (Engl. Transl.)*
[c] — *Chem. Heterocycl. Compd. (Engl. Transl.)*
[d] — *Pharm. Chem. J. (Engl. Transl.)*
[e] — *Chem. Dokl. (Engl. Transl.)*
[f] — *Theor. Exp. Chem. (Engl. Transl.)*
[g] — *Chem. Nat. Compd. (Engl. Transl.)*
[h] — *Crystallogr. Rep. (Engl. Transl.)*