Dihydronaphthofurans: synthetic strategies and applications

Abolfazl Olyaei* and Mahdieh Sadeghpour

Dihydronaphthofurans (DHNs) are an important class of arene ring-fused furans which are widely found in many natural and non-natural products and drug candidates with relevant biological and pharmacological activities. Furthermore, vinylidene-naphthofurans exhibit photochromic properties when exposed to UV or sun light at room temperature. For these reasons, a vast array of synthetic procedures for the preparation of dihydronaphthofurans including annulation of naphthols with various reagents, cycloaddition reactions ([3 + 2], [4 + 1] and Diels–Alder), intramolecular transannulation, Friedel–Crafts, Wittig, Claisen rearrangement, neophyl rearrangement and other reactions under various conditions have been developed over the past decades. This review aims to describe the different strategies developed so far for the synthesis of dihydronaphthofurans and their applications. After a brief introduction to the types of dihydronaphthofurans and their biological activities, the different synthetic approaches such as chemical, photochemical, and electrochemical, methods are described and organized on the basis of the catalysts and the other reagents employed in the syntheses. The subsequent section focuses on biological and pharmacological applications and photochromic properties of the target compounds.

1. Introduction

Furans are five-membered aromatic heterocycles containing one oxygen atom that are commonly found in many important compounds such as natural products, pharmaceuticals and polymers. Moreover, furans can be utilized as synthetic intermediates to access other useful compounds. The synthesis of this fundamental structural building block has received significant attention and a wide variety of approaches are available to the synthetic practitioner.1 Arene ring-fused furan derivatives such as dihydronaphthofurans (DHNs) have attracted widespread interest in view of their presence in many important natural and non-natural products. Natural products

Associate Professor Dr Abolfazl Olyaei was born in Tabriz, Iran in 1975. He received his B.Sc. degree in pure chemistry from the University of Tabriz in 1999. He received his M.Sc. in 2001 and his PhD in 2007 in organic chemistry under the supervision of Professor Mohammad Raouf Darvich and Professor Mehdi Ghandi, both at Tehran University, Tehran, Iran. He was an Assistant Professor in the University of Payame Noor in 2007 and now he is an Associate Professor at this University. His research interests include organic synthesis, organic materials, green chemistry, catalysis and organocatalysis and application of materials and organo materials in different sciences.

Associate Professor Dr Mahdieh Sadeghpour was born in Qazvin, Iran, in 1978. She received her B.Sc. degree in pure chemistry from Alzahra University, Tehran, Iran in 2001 and her M.Sc. in 2004 in organic chemistry under the supervision of Associate Professor Nikoo Sedighi from Tehran University, Tehran, Iran. She graduated in 2009 with a PhD in organic chemistry under the supervision of Professor Abbas Shokravi and Associate Professor Abolfazl Olyaei, from Kharazmi University, Tehran, Iran. Now she is an Associate Professor at the Islamic Azad University, Takestan Branch. Her research interests include organic synthesis, green chemistry and application of materials and nanomaterials in different sciences.
with DHN moieties have been shown to have a wide range of biological and pharmacological properties. For example, furaquinocins (A), consisting of highly oxygenated p-quinone rings, are antihypertensive, cytotoxic against HeLa S3 and B16 melanoma cells, and also inhibit platelet aggregation and coagulation. In contrast, (–)-nocardione (B) with an o-quinone moiety is a Cdc25B tyrosine phosphatase inhibitor with moderate antifungal and cytotoxic activity. Also, rubioncolin A (C) and rubioncolin B (D) were isolated from Rubia oncotricha in racemic forms. They are also found in Rubia cordifolia, which is used in traditional Korean medicine to treat coughs, bladder and kidney stones, joint inflammation, uterine hemorrhage, and uteritis. Interestingly, the electron rich catechol derivative aegyptinone (E) shows antibacterial and antifungal activity (Fig. 1).

Furthermore, some of the synthesized dihydronaphthofuran derivatives exhibit a variety of interesting biological and pharmacological properties including 5-lipoxygenase inhibitor, C17,20 lyase inhibitors, antitubercular activity against Mycobacterium tuberculosis H37Rv, anti-tyrosinase, antioxidant, and antibacterial, inhibitors of NF-κB activity, α-glucosidase inhibitors, inhibitor of α-chymotrypsin and anti cancer activities (liver tumor growth inhibitors). Moreover, vinylidene-naphthofurans are a new class of polycyclic compounds that exhibit photochromic properties when exposed to the UV or sunlight at room temperature and adsorbed in silica gel or dissolved in acidic alcoholic solutions (Fig. 2). This wide range of biological activities and properties has stimulated interest in the synthesis of dihydronaphthofuran derivatives. During the past decades, several synthetic approaches to 2,3-dihydronephtho[2,1-b]furan, 2,3-dihydronephtho[1,2-b]furan, 1,3-dihydronephtho[2,3-c]furan, 1,3-dihydronephtho[1,2-c]furan and vinylidene-1,2-dihydronephtho[2,1-b]furan derivatives (F–K) (Fig. 3) have been reported. The general methods used for the synthesis of these compounds include chemical, photochemical and electrochemical methods have been described and organized on the basis of the catalysts and the other reagents. To the best of our knowledge, there is no review on synthesis of dihydronaphthofuran derivatives. Hence, the main purpose of this review is to show all types of reactions for the synthesis of these heterocyclic compounds, such as annulation of naphthols with various reagents, cycloaddition reactions ([3 + 2], [4 + 1] and Diels–Alder), intramolecular transannulation, Friedel–Crafts, Wittig, Claisen rearrangement,
neophyl rearrangement and the other reactions in various conditions and their biological, pharmacological and photochromic properties.

2. Synthesis of dihydronaphthofurans

2.1. Base-catalyzed synthesis

The first synthesis of 1,2-dihydronaphtho[2,1-b]furan has been reported by Mckusick in 1948. Sodium methoxide and potassium iodide promoted condensation of 2-naphthol with β-methyl allyl chloride in methanol at room temperature for several days afforded β-methylallyl-2-naphthyl ether (1). Claisen rearrangement of 1 led to the formation of intermediate 2. The latter underwent cyclization to provide 1,2-dihydro-2,2-dimethyl[2,1-b]naphtho[2,1-b]furan (3) in 36% yield (Scheme 1).21

Guss and Jules reported that the reaction of 2-(2-hydroxy-1-naphthyl)-2-phenylethanol (4) with phthalic anhydride in the presence of pyridine in dioxane at room temperature for 72 h, led to the formation of acid phthalate 5. By heating in 5% sodium bicarbonate and 10% sodium hydroxide at 50–60 °C for 30 min the acid phthalate 5 was converted into the cyclized product, 1-phenyl-1,2-dihydronaphtho[2,1-b]furan (6) (Scheme 2).22

In a similar fashion, phenol–alcohols 7 and 8 were converted into the acid phthalates 9 and 10 by allowing a solution of the phenol alcohols, phthalic anhydride, pyridine and dioxane to stand at room temperature for 48 hours. Then, addition of weaker solution of sodium hydroxide to the bicarbonate solution of the esters 9 and 10 and the slurry were heated at reflux temperature for 1 hour afforded 1,2-dihydronaphtho[2,1-b]furans 11a–b, 6 and 2,3-dihydronaphtho[1,2-b]furans 12 in 88.2–99.3% and 87.4–99.3% yields, respectively (Scheme 3).23

In 1994, Kito et al. explored the reaction of 2-naphthol with glyoxal in the presence of KOH in aqueous media at 30 °C for 4.5 h, which furnished 1,2-dihydronaphtho[2,1-b]furan-1,2-diol (14) in 98% yield. Hemiacetal 14 was obtained via cyclization of intermediate 13 (Scheme 4).24

In a similar manner, dihydronaphthofuran 14 could be obtained via treatment of 2-naphthol with aqueous glyoxal (40%) in aqueous solution of KOH at 18–21 °C for 4.5 h in 90.2% yield. Moreover, 1,2-diacetoxy-1,2-dihydronaphtho[2,1-b]furan (15) was efficiently achieved from 14 in acetic anhydride and pyridine under reflux for 24 h (Scheme 5).25
Saidi et al. reported that the reaction of 2-naphthol with alkanyl halide in acetone in the presence of K₂CO₃ and KI gave the corresponding naphthyl ethers and . Naphthyl ethers in N,N-diethyl aniline (N,N-DEA) and sodium methoxide under reflux for 0.5–8 h afforded dihydronaphthofurans 17 and 3 in 65 and 64% yields, respectively. In order to prepare trimethylsilyl-substituted dihydronaphthofurans 18 and 20, dihydronaphthofurans 17 and 3 were treated with n-BuLi and then with chlorotrimethylsilane (TMS-Cl) in diethyl ether at room temperature for 6 h (Scheme 6).

A one-step synthesis of ethyl 1,2-dihydronaphtho[2,1-b]furan-2-carboxylates 23 from substituted naphthols and ethyl 2,3-dibromopropionate in the presence of K₂CO₃ in refluxing acetone for 18 h has been reported by Merour et al. First, ethyl 2,3-dibromopropionate is easily transformed in situ into ethyl-2-bromoacrylate with potassium carbonate in refluxing acetone. Then, a Michael-type addition of the naphthalenolate to the 2-bromoacrylate generates the C–C bond forming intermediate 21. Aromatization and formation of the 2-naphthalenolate anion gives the intermediate 22. This is followed by an intramolecular nucleophilic substitution on the carbon bearing the bromo atom in 22 affording the corresponding product 23 in 35–83% yields. Following the same methodology, the reaction of 2-naphthol with 2-chloroacrylonitrile and 3,4-dibromobutan-2-one in refluxing acetonitrile for 18 h afforded 24 and 25 in 75 and 60% yields, respectively (Scheme 7).

Treatment of 1-naphthol derivatives with ethyl 2,3-dibromopropionate in the presence of K₂CO₃ in refluxing acetone for 28 h led to the formation of the expected ethyl 2,3-dihydronaphtho[1,2-b]furan-2-carboxylates 26 in 0–31% yields and unexpected ethyl 4′-oxospiro[cyclopropane-1,1′(4′H)-naphthalene]-2-carboxylates in 0–71% yields besides starting materials. Also, the reaction of 1-naphthols with 3,4-dibromobutan-2-one by applying the same methodology gave 2,3-dihydronaphtho[1,2-b]furan-2-yl ketones 27 in 0–25% yields and unexpected products in 16–32% yields (Scheme 8).

An efficient procedure for the conjugate addition of methyl acetoacetate to 2-(methoxycarbonyl)-1,4-naphthoquinone using K₂CO₃ has been developed. The reaction was carried out in
CH₂Cl₂ at room temperature for 12 h yielded 61% of a mixture of cis and trans (20:80) 2,3-dihydronaphtho[1,2-b]furan derivatives 28 (Scheme 9).

Alla et al. noted that one-pot reaction of 2-amino-4H-pyran derivatives 29 with N-chlorosuccinimide and a base (piperidine or aqueous KOH) in alcohol medium at room temperature for 8–9 h gave dihydronaphthofurans 30 in 68–90% yields. Plausible mechanism for the formation of 30 has been arrived at Scheme 10. Initially aminopyran undergoes oxidative difunctionalization with NCS in the presence of an alcohol solvent. Subsequent addition of base to the aminopyran leads to proton abstraction from the amino group. This leads to a cascade pyran ring opening by the cleavage of the (C₂–O₁) bond, and ring closure of the (O₁–C₃) bond to dihydrofuran via elimination of HCl. The sequential elementary processes lead to formation of the ring contracted dihydrofuran carbimidate ester 30. In a similar manner, highly functionalized pyran derivatives 31 were treated with methanolic KOH (1 N) at room temperature for 36 h to obtain the products 32 in good yields (70–75%) (Scheme 10).

Base-mediated cyclization reactions of 2-(5-hydroxy-1-pentynyl)benzonitriles 33 to 4-amino-2,3-dihydronaphtho[2,3-b]furans 34 have been reported by Wu et al. Treatment of 33 with NaOMe in DMSO at 140 °C for 0.5 h gave the desired products 34 in 45–75% yields (Scheme 11). The proposed mechanism for the cyclization of 33a to 34a is shown in Scheme 12. The first step is the deprotonation of 33a with base to form an alcohol 35 that would undergo intramolecular 5-exo-dig cyclization to form the vinyl anion 36. The vinyl anion 36 could undergo direct proton transformation to give 37. Deprotonation of 37 with base to form anion 38. Then, the electrocyclic ring closure reaction to give 39. Finally protonation of 39 to give imine 40 and following the imine–enamine tautomerization, to convert the imine 40 to the final product 34a. Also, cyclization reaction of 41 with NaH in DMSO at 140 °C for 15 min afforded product 42 in 58% yield (Scheme 13). Several reports on the synthesis of hemiacetals of dihydronaphthofurans have been described by Dibble et al. 1,3-Dihydro-1-hydroxynaphtho[2,3-c]furan (43) and 1,3-dihydro-1-hydroxynaphtho[1,2-c]furan (44) could be successfully prepared in 77% and 85% yields, respectively. In this reaction, treatment of bromonaphthalene methanol (45) in dry diethyl ether with n-butyllithium in hexane at −78 to 0 °C for 30 min afforded 3-
(hydroxymethyl)-2-naphthaldehyde 46, which on treatment with dry DMF at 0 °C for 10 h led to dihydronaphthofuran 43 (Scheme 14). In a similar manner, dihydronaphthofuran 44 was prepared from bromonaphthalene methanol 47 in 85% yield as shown in Scheme 15.22

Scheme 15 Preparation of dihydronaphthofuran 44.

Treatment of 1-naphthol with alkenyl halide in acetone in the presence of K₂CO₃ and KI gave the corresponding allyl naphthyl ethers 45a–b. Heating of 45 in N,N'-diethyl aniline (N,N'-DEA) and sodium methoxide under reflux for 0.5–8 h afforded 2,3-dihydronaphtho[1,2-b]furan derivatives 46 and 47 via Claisen rearrangement in 60 and 47% yields, respectively (Scheme 16).26

Scheme 16 Synthesis of 2,3-dihydronaphtho[1,2-b]furan derivatives 46 and 47.

2.2. Acid-catalyzed synthesis

In 1971, Martini reported that preparation of dihydronaphthofuran 3 was accomplished by the treatment of 2-naphthol with isobutylaldehyde using HCl in EtOH at 80 °C for 0.5 h in 74.6% yield (Scheme 17).13

In a similar fashion, synthesis of 2,3-dihydro-2,2-dimethylnaphtho[1,2-b]furan (47) in 43.1% yield has been accomplished by the treatment of 1-naphthol with isobutylaldehyde using H₂SO₄ in toluene at 90–160 °C for 3 h (Scheme 18).33

Similarly, dihydronaphthofuran 47 was obtained via the reaction of isobutyraldehyde with 1-naphthol in the presence of catalytic amount of p-TSA under closed vessel solvent-free microwave irradiation conditions at 180 °C for 5 min in 80% yield (Scheme 19).34

Treatment of 4 with p-toluenesulfonic acid monohydrate in benzene under reflux condition for one hour with simultaneous removal of 50 cm³ of benzene containing the water formed, gave dihydronaphthofuran 6 in 80.6% yield (Scheme 20).22

Scheme 19 p-TSA-catalyzed synthesis of dihydronaphthofuran 47.

Scheme 20 Acid-catalyzed synthesis of 1-phenyl-1,2-dihydronaphtho[2,1-b]furan (6).
It was also shown that dihydronaphthofuran 6 was obtained by the reaction of styrene oxide with 2-naphthol in refluxing benzene for 1 h in 48.8% yield (Scheme 21). This reaction proceeded via the acid-catalyzed unimolecular ring opening of styrene oxide, followed by nucleophilic attack of naphthol to the resulting adduct 48 and cyclization, then elimination of water afforded the final product 6.

In 1953, Guss et al. have obtained 1,2-diphenyl-1,2-dihydronaphtho[2,1-b]furan (49) in 69.9% yield from the reaction of 2-naphthol and trans-stilbene oxide by using p-toluenesulfonic acid monohydrate as catalyst in 105 °C for 15 min under solvent-free condition. Presumably a phenol–alcohol was first formed and then cyclized under these reaction conditions to the desired product 49 (Scheme 22).

Miller and Lin noted that rearrangement of 1-acetoxy-1-allyl-2-naphthalenone (51) in 10% sulfuric acid in acetic acid at room temperature for 4 days, or in boron trifluoride etherate at room temperature for one week, gave 2-methyl-1,2-dihydronaphtho[2,1-b]furan (52) as the only product. Similarly, attempted thermal rearrangement at 150 °C for 3 days in the absence of solvent afforded 52 (Scheme 23).

Matsunaga et al. developed a strategy for the synthesis of 1,2-dihydronaphtho[2,1-b]furan 53. The reaction was carried out via the key intermediate 54 as shown in Scheme 24. Allylation of 6-bromo-2-hydronaphthalene followed by a Claisen rearrangement at 190 °C gave the 1-allyl-2-naphthol 54. Ozonolysis of 54 followed by treatment with NaBH4 afforded the diol 55 and intramolecular dehydration under acidic conditions provided 56. Lithiation of 1,2-dihydronaphthofuran 56 and then addition to the imidazolyl isopropyl ketone furnished 1,2-dihydronaphtho[2,1-b]furan 53 in 48% yield.

Hydrobromic acid-catalyzed Friedel–Crafts type reactions of 2-naphthols with allyl iodide in CH3CN at 60 °C for 8 and 24 h led to the formation of dihydronaphthofuran 57 and 7-bromo-2-(iodomethyl)-1,2-dihydronaphtho[2,1-b]furan (58) in 52% and 72% yields, respectively. Formation of products by reaction of 2-naphthols with allyl iodide is assumed to proceed via allylation of naphthols followed by iodocyclization to produce the corresponding products (Scheme 25).

A simple and highly efficient one-pot protocol for the synthesis of novel polysubstituted 1,2-dihydronaphtho[2,1-b]
Furans 59 in 87–91% yields has been developed by three-component coupling reaction of 2-aminopyridines, naphthols and aqueous glyoxal in the presence of guanidinium chloride as a polyfunctional organocatalyst under solvent-free conditions at 80 °C for 25–70 min (Scheme 26). A plausible mechanism for this conversion is shown in Scheme 27. The formation of products can be rationalized by the initial formation of intermediate 60 via condensation of amine with glyoxal. Subsequent addition of 2-naphthol to 60 affords intermediate 61 followed by intramolecular nucleophilic addition of naphthoxy ion 62 generated in situ by guanidinium chloride to activated imine group led to the formation of the desired products 59.

A set of new 1-vinylidene-1,2-dihydroraphtho[2,1-b]furans 63 in 19–47% yields was unexpectedly obtained in the reaction of 2-naphthol with readily available 1,1,4,4-tetraarylbut-2-yn-1,4-diol 64 in the presence of 4-toluenesulfonic acid monohydrate in CHCl₃ at room temperature for 1 h. This reaction may be assumed to proceed via Claisen rearrangement, enolization and rotation dehydration as shown in Scheme 28.¹⁵

In a similar fashion, vinylidene-naphthofurans 65 are a new class of photochromic molecules, easily synthesized by reaction of 1,1,4,4-tetraphenylbut-2-yn-1,4-diol with naphthols in the presence of 4-toluenesulfonic acid monohydrate in CHCl₃ at room temperature for 1–24 h in 37–49% yields (Scheme 29).¹⁶

Coelho et al. observed that the treatment of ethyl 6-hydroxy-2-naphthoate with diols 66 under acid catalysis in CHCl₃ at room temperature for 1 day, followed by reduction with LiAlH₄ in THF at room temperature for 4 h afforded the vinylidene-naphthofurans 67 in good yields (52–81%). The later compounds 67 were silanized with 3-(triethoxysilyl) propyl isocyanate (ISOTES) in THF at 50–60 °C for 7 days afforded the respective silanized products 68 as the photoactive molecules (Scheme 30).¹⁹
In a similar manner, a series of novel photochromic vinylidene-naphthofurans \(69\) was synthesized by reaction of 2-naphthols with tetraarylbut-2-yn-1,4-diol (70) in the presence of p-TSA in CHCl\(_3\) at room temperature for 5 h in 73–97% yields. This one-pot reaction occurs via a domino reaction (Scheme 31): under acid-catalysis the diol 70 is converted into a propargylic carbocation 71, which upon reaction with 2-naphthol provides a propargylic aryl ether 72. Then, this intermediate performs a [3,3]-sigmatropic Claisen rearrangement followed by enolization and acid-catalyzed intramolecular dehydration affording the final vinylidene-naphthofuran 69.\(^{20}\)

4-Formyl-5-hydroxy-2-(2'-oxoethyl)2,3-dihydronaphtho[1,2-b]furan (73) was readily achieved in 50% yield by acid induced fragmentation of the Diels-Alder adduct 74 in 90% aqueous THF at room temperature for 20 min (Scheme 32).\(^{20}\)

Smith et al.\(^{32}\) synthesized 1,3-dihydro-3-hydroxynaphtho[1,2-c]furan (75) in 84% yield from the reaction of 1-(hydroxymethyl)-2-(dimethoxymethyl)naphthalene with HOAc in water and \(p\)-dioxane at room temperature for 2 h (Scheme 33).

In 2007, Lafrance et al.\(^{41}\) have obtained dihydronaphthofuran 3 in 79% yield via the reaction of 1-bromo-2-(tert-butoxy)naphthalene in the presence of Pd(OAc)\(_2\) (5 mol\%), PCy\(_3\), HBF\(_4\) (6 mol\%) in conjunction with Cs\(_2\)CO\(_3\) as base and 2,2-dimethylpropionic acid (pivalic acid, 30 mol\%) as additive in mesitylene at 150 °C for overnight (Scheme 35).

A simple procedure for the preparation of 2-methyl-1,2-dihydronaphtho[2,1-b]furan (52) in 32% yield by allylation of 2-naphthol with allyl tosylate in the presence of...
[\text{Rh(nbd)}(\text{CH}_3\text{CN})_2]\text{PF}_6\text{ as catalyst in toluene at room temperature for 1 h was described by Tsukada \text{et al.} (Scheme 36).}\text{42}

Similarly, 2-methyl-2,3-dihydronaphtho[1,2-b]furan (77) in 10% yield was obtained via the above reaction condition (Scheme 37).

Mild, efficient, and economical Ag(i)-catalyzed sequential C–C/C–O bond formations between 2-naphthol and dienes in dichloroethane at 40 and 80 °C for 1–3 days were developed to afford a variety of 1,2-dihydronaphtho[2,1-b]furans 78a–c in 60–96% yields (Scheme 38). A plausible mechanism for formation of products 78a is shown in Scheme 39. Activation of the diene by coordination to Ag(i) is followed by intermolecular nucleophilic attack by the arene. The reactions of 2-naphthol with 1-substituted-1,3-diene substrates occur by either 1,2- or 1,4-addition. The resulting Ag–C bond is protonated to give 2-allylphenol intermediate then recoordination of C–C π-bond by Ag(i) activates the olefin toward intramolecular nucleophilic attack by the phenolic oxygen. Subsequent proton transfer produces the final product and regenerates the Ag(i) catalyst.

In a similar fashion, reusable scandium/ionic liquid catalyst system for sequential C–C and C–O bond formations between 2-naphthol and dienes with atom economy has been reported for the synthesis of 78a–c in toluene at 60 and 100 °C for 18–24 h in 60–95% yields (Scheme 40).

It was also shown that air-and moisture-stable Cu(OTf)$_2$-bipy catalyze the addition of 2-naphthol to 1,3-diene in dichloroethane at 50 °C for 18 h in a tandem hydroalkoxylation-rearrangement-hydroalkylation sequence, furnishing O-heterocycles such as 2-isopropyl-2-methyl-1,2-dihydronaphtho[2,1-b]furan (78a) in 60% yield (Scheme 41).

Palladium chloride-catalyzed intramolecular activation of electroneutral arylecyclopropane 79 in the presence of benzoquinone as oxidant in dioxane at 80 °C for 12 h resulted 2-ethyl-2-methyl-1,2-dihydronaphtho[2,1-b]furan (80) in 64% yield via cyclopropane isomerization followed by a Wacker oxidation (Scheme 42).
Tripathi et al. investigated reaction of dihydronaphthofuran 57 with NaN₃ in the presence of Cu-powder in DMF at 80 °C gave 2-(azidomethyl)-1,2-dihydronaphtho[2,1-b]furan (81) in 89% yield. [3 + 2] Cycloaddition of 81 with different alkynes in the presence of sodium ascorbate and CuSO₄·5H₂O (1 mol%) in 2:1 mixture of tert-butyl alcohol and water at 90 °C for 6 h afforded dihydronaphthofurans 82 in 64–95% yields (Scheme 43).

Kitamura et al. developed Rh₂(OAc)₄-catalyzed synthesis of dihydronaphthofurans 83 in 24–83% yields by the cycloaddition reaction of diazonaphthoquinones 84 with enol ethers in dichloroethane at 80 °C for 0.75–1.5 h. A possible reaction mechanism is illustrated in (Scheme 44). Initially, Rh₂(OAc)₄ reacts with 84 to form RhII carbene complex 85. Nucleophilic attack by the enol ether on carbene complex 85 proceeds to form 86. Then, aromatization drives the cyclization to form naphthofuran 83 with release of Rh₂(OAc)₄.

In a similar fashion, synthesis of 2,3-dihydronaphtho[1,2-b]furan derivatives 85 in 11–86% yields has been achieved by the cycloaddition reaction of diazonaphthoquinones 86 with enol ethers in CH₂Cl₂ at 30 °C for 0.5–21.5 h (Scheme 45).

Reaction of vinylidene-naphthofuran derivatives 87a–c with boronic acid in the presence of Pd(PPh₃)₄ and K₂CO₃ in refluxing toluene for 4–5 h afforded photostable vinylidene-naphthofurans 88a–c in 79–85% yields. The reaction of 88c with BBr₃ in dry CH₂Cl₂ at room temperature for 5 h afforded photostable vinylidene-naphthofuran 89 in 76% yield (Scheme 46).

PtCl₂-catalyzed cyclization of o-diethynylbenzene derivatives 90 bearing a hydroxyethyl group in toluene under an argon atmosphere at 80 °C for 1–40 h afforded dihydronaphthofuran derivatives 93a–c in 11–76% yields. Formation of 93 can be rationalized by initial intramolecular cyclization of the hydroxy group to an activated ethynyl group in 91 to form intermediate 92, followed by attack of the second ethynyl group to give 93 (Scheme 47).

Lee and Xia described a novel approach for the synthesis of diverse dihydronaphtho[1,2-b]furans 94 in 11–96% yields from 1,4-naphthoquinones 95 and olefins 96 in the presence of ceric ammonium nitrate in CH₂CN at room temperature for 20–30 min via formal [3 + 2] cycloaddition reaction (Scheme 48). This methodology was also used successfully to synthesize the biologically important natural product furomollugin in only 2

Scheme 41. Cu(OTf)₂-bipy catalyzed synthesis of dihydronaphthofuran 78a.

Scheme 42. PdCl₂-catalyzed synthesis of dihydronaphthofuran 80.

Scheme 43. Preparation of dihydronaphthofurans 81 and 82.

Scheme 44. Rhodium-catalyzed synthesis of dihydronaphthofurans 83.

Scheme 45. Rhodium-catalyzed synthesis of 2,3-dihydronaphtho[1,2-b]furan derivatives 85.

Scheme 46. PtCl₂-catalyzed cyclization of o-diethynylbenzene derivatives 90.
steps. The formation of 94 can be explained by the mechanism proposed in Scheme 49. The methyl 1,4-dioxo-1,4-dihydronaphthalene-2-carboxylate (95a) first forms complex 97 in the presence of CAN. The vinyl group of ethyl vinyl ether then attacks 97 to give another intermediate 98. Isomerization of 98 followed by intramolecular cyclization then gives the final product 94a.

Similarly, 2,3-dihydronaphtho[1,2-b]furans 99 were synthesized in 38–96% yields by the reaction of 2-acetylnaphthalene-1,4-dione (95b) with olefins in the presence of cerium(IV) ammonium nitrate (5.0 mol%) as catalyst in CH$_3$CN at room temperature for 20 min (Scheme 50).

Also, Lee et al. have described the reaction of 1,4-dihydroxynaphthalene-2-carboxylate 95a and the corresponding olefins in MeCN in the presence of cerium(IV) ammonium nitrate (5.0 mol%) at room temperature for 20 min via [3 + 2] cycloaddition reaction afforded dihydronaphthofuran derivatives 100 in 30–96% yields (Scheme 51).

Recently Katukojvala et al. found that 2,3-dihydronaphtho[1,2-b]furans 101 could be prepared in 62–93% yields from
intramolecular transannulation of ((2-alkynyl)aryl)cyclopropyl ketones **102** in the presence of AgOTf (20 mol%) as catalyst in toluene at 100 °C for 14 h (Scheme 52). As shown in Scheme 53, a plausible mechanism for the transannulation reaction was proposed. The first step involves Ag(I)-catalyzed, neighbouring carbonyl group directed regioselective hydration of the alkyne moiety of **102** via the benzo[c]-pyrylium cation **104** to give the intermediate diketone **103**. In the next step, Ag(I)-catalyzed regioselective ring expansion of the donor–acceptor cyclopropyl ring of **103** leads to the transient 2,3-dihydrofuran **105**. Subsequent intramolecular benzannulation of **105** via either aldol condensation or π-π-electrocyclization of trienol **106** leads to the 2,3-dihydronaphtho[1,2-b]furan **101**.

The cascade reaction of alkynols **107** with alkynes **108** under combined Sc(OTf)3 and rhodium catalyst, Cu(OAc)2 and HOAc in dichloroethane under nitrogen atmosphere at 80 °C for 24 h led to the formation of 2,3-dihydronaphtho[1,2-b]furans **109** in 50–86% yields (Scheme 54).

**ortho**-Carbonylarylacetylenols **110** have been employed for the synthesis of 2,3-dihydronaphtho[2,3-b]furans **111** and **113**.

The reaction mechanism of this transformation was then proposed as shown in pathway A of Scheme 56. First, alkyne was activated by Ag-catalyst with the assistance of **ortho**-carbonyl neighboring group to form oxo-carbenium ion intermediate **114**. After downstream process, this intermediate was then converted to intermediate **115** which further collapsed to give 1,5-diketone **116**. Under the presence of mild Ag-Lewis acid, this intermediate was activated and underwent the cyclization to obtain dihydrofuran intermediate **117**. Next, the second cyclization proceeded followed by tautomerization and dehydration providing 2,3-dihydronaphtho[2,3-b]furan product **111a**. Moreover, the mechanism in pathway B is also possible and cannot be ruled out. In pathway B, intermediate **115** underwent the cyclization to give spiro acetal **118** which could be converted to...
dihydrofuran intermediate 117. This intermediate could also be transformed to the desired product via the reaction mechanism in pathway A.55

2.4. Iodine-assisted synthesis

Tripathi et al.54 demonstrated that synthesis of 2-(iodomethyl)-1,2-dihydronaphtho[2,1-b]furan (57) in 80% yield by reaction of 1-allyl-2-naphthol with iodine in water at 80 °C for 4 h (Scheme 57).

Similarly, an efficient method was developed for the synthesis of dihydronaphthofuran 57 in 80% yield by the treatment of allyl naphthol with molecular iodine in the presence of NaHCO₃ in CH₂Cl₂ at room temperature for 24 h. The key step involve iodocyclization. In a similar manner, ortho-allylnaphthol on reaction with molecular iodine in CH₃CN under reflux condition for 4 h gave dihydronaphthofuran 57 in 62% yield (Scheme 58). This reaction is assisted by the hydroxyl group, involves formation of iodonium ion 119 and proceeds through non radical mechanism pathway.55

A number of 2-(iodomethyl)-1,2-dihydronaphtho[2,1-b]furan derivatives 120 in 71–85% yields have been synthesized from the corresponding allylhydroxy naphthalene precursors 121 involving N-iodosuccinimide in acetonitrile at 0–5 °C and then at room temperature for 2 h or by employing molecular iodine in aqueous micelle using CTAB as surfactant at 0–5 °C and then at room temperature for 6 h. At first the allylhydroxy precursor 121 may generate the iodonium intermediate 122, which undergoes 5-exo-trig cyclization to from the cyclized product 120 (Scheme 59).56

Recently Deng et al.57 found that dihydronaphthofurans 123 in 67–93% yields could be prepared from readily available 1-(2-nitrovinyl)naphthalen-2-ol 124 and maleonitrile esters 125 in the presence of I₂ (10 mol%), NaHCO₃ and TBHP as oxidant in THF at 30 °C for 24 h to 8 days (Scheme 60). A tentative mechanism is proposed in Scheme 61. As depicted in Scheme 61, I₂ could be transformed into hypoiode [IO]⁻ under basic conditions initially, then, which is further oxidized by TBHP to form the

Scheme 56 Proposed reaction mechanism for the synthesis of 111a.

Scheme 57 Synthesis of 2-(iodomethyl)-1,2-dihydronaphtho[2,1-b]furan (57).

Scheme 58 Synthesis of dihydronaphthofuran 57 in the presence of I₂.

Scheme 59 Synthesis of dihydronaphthofurans 120.

Scheme 60 Iodine-catalyzed synthesis of dihydronaphthofurans 123.
iodite [IO$_2$]$^-$. The Michael adduct formed by the reaction of malonate ester 125 and nitroalkene 124 could possibly react with the in situ formed reactive species [IO$_2$]$^-$ to give the intermediate 126, which could be captured by intramolecular phenolic hydroxyl to construct dihydronaphthofuran 123 and releasing hypoiolate species [IO] for the next catalytic cycle.

An efficient method was developed for the synthesis of 2-(iodomethyl)-2,3-dihydronaphtho[1,2-b]furan (127) in 80% yield by the reaction of 2-allyl-1-naphthol 128 with molecular iodine in the presence of NaHCO$_3$ in CH$_2$Cl$_2$ at room temperature for 24 h (Scheme 62).$^{38}$

Scheme 62 Synthesis of 2-(iodomethyl)-2,3-dihydronaphtho[1,2-b]furan (127) in the presence of I$_2$.

Regioselective iodocyclization of a series of allyldihydroxy naphthalene precursors 129 involving N-iodosuccinimide (method A) and environment friendly green approach associated with surfactant (CTAB)-promoted molecular-iodine-mediated (method B) 5-exo-trig cyclization strategies has been explored. Method A: the reaction mixture in CH$_3$CN was magnetically stirred for 150 minutes at 0–5 $^\circ$C and then at room temperature for further 30 minutes afforded dihydronaphthofurans 130 in 70–76% yields. Method B: the reaction mixture in water was stirred at room temperature for an additional period of 8 h gave dihydronaphthofurans 130 in 80–88% yields. The transformation is believed to proceed via the iodonium intermediate 131 (Scheme 63).$^{39}$

Scheme 63 Tentative mechanism for the formation of 123.

2.5. Syntheses via phosphorus, nitrogen and sulfur ylides

Taylor et al.$^{60}$ described practical synthesis of functionalized 1,2-dihydronaphtho[2,1-b]furans 132 from substituted 2,4-

Scheme 64 Synthesis of 1,2-dihydronaphtho[2,1-b]furans 132.

Scheme 65 Synthesis of dihydronaphthofuran derivatives 136–139.
dihydonaphtho[2,1-c][1,2]dioxines 133 and stabilised phosphorus ylides. Interaction of 133 in anhydrous chloroform or dichloromethane under a nitrogen gas atmosphere with ylide at a temperature of 60 °C or ambient temperature for 3–7 days resulted in the formation of E and Z isomers of 132 in 3–69% yields (Scheme 64).

Rose bengal bis(triethylammonium) salt sensitized photooxidation of 1-vinylnaphthalenes gave the 1,2-dioxines 134. 1,2-Dioxines 134 underwent rearrangement when allowed to react with DABCO to afford the 1-(β-keto)-2-naphthols 135 in excellent yield. Reaction of the naphthols 135 with methyl (triphenylphosphoranylidene) acetate afforded the requisite dihydronaphthofurans 136 in 74–94% yields via a Wittig/oxygen-Michael sequence. Saponification of the esters 136 afforded the acids 137 in 62–85% yields and LiAlH4 reduction of 136 gave the alcohols 138 in 88–92% yields. Reaction of dihydronaphthofurans 136 with nitric acid in glacial acetic acid at room temperature for 1 h afforded 1,2-dihydronaphtho[2,1-b]furan derivatives 139 in 31–81% yields (Scheme 65).63

1-(2,2-Diphenylvinylidene)-2,2-diphenyl-1,2-dihydronaphtho[2,1-b]furan-7-carbaldehyde (140) in 69% yield could be prepared by the reaction of dihydronaphthofuran 141 in the presence of pyridinium chlorochromate in CH2Cl2 at room temperature for overnight. 1,2-Dihydronaphtho[2,1-b]furans 142 were prepared in 36–89% yields by the Wittig reaction of 140 with triarylphosphonium salt in the presence of n-BuLi in THF at room temperature for 2.5 h (Scheme 66).17

Diastereoselective synthesis of 1,2-dihydronaphtho[2,1-b]furans 143 in 34–90% yields has been developed by the reactions of o-quinoine methides 144 from 2-naphthol Mannich base 145 with pyridinium methyldienes 146 in the presence of 1,1,3,3-tetramethylguanidine (TMG) or DBU in refluxing CH3CN or EtOH under an argon atmosphere for 3–12 h (Scheme 67).64 A mechanistic rationale portraying the probable sequence of events is given in Scheme 68. The first step is the formation of the two reaction intermediates. o-QM 144 is formed by the thermal decomposition of the Mannich base and deprotonation of the pyridinium salt 147 gives ylide 146. The second step is a Michael-type addition of a pyridinium ylide 146 to the electron-deficient o-QM to afford the zwitterion intermediate 148 which react further to give products 143.

In a similar manner, 2-aryl-1,2-dihydronaphtho[2,1-b]furans 149 in 29–45% yields were synthesized by the reaction of 2-naphthol Mannich base and pyridinium salts 150 in refluxing DMF for 5 h under an argon atmosphere (Scheme 69).52

Spasov et al.62 have shown the reaction of 1-((dimethylamino)methyl)naphthalen-2-ol (151) and 1-[2-(3-hydroxyadamantan-1-yl)-2-oxoethyl]pyridin-1-ium bromide (152) in refluxing a mixture of acetonitrile-DMF (3:1) for 10 h afforded 1,2-dihydronaphtho[2,1-b]furan 153 in 69% yield. In a similar manner, the reaction of 151 with 1-(2-(4-hydroxyphenyl)-2-oxoethyl)pyridin-1-ium bromide (154) in DMF at 90 °C for

Scheme 66 Synthesis of photochromic 1-vinylidenenaphthofurans 142.

Scheme 67 Diastereoselective synthesis of trans-1,2-dihydronaphtho[2,1-b]furans 143.

Scheme 68 Proposed mechanism for the formation of 143.
15 h gave 1,2-dihydronaphtho[2,1-b]furan 155 in 50% yield (Scheme 70).

1,2-Dihydronaphtho[2,1-b]furan (11b) could also be obtained in 50% yield from the Mannich base methiodide of 2-naphthol via the corresponding quinone methide in the presence of dimethyl sulfoxonium methide in dimethyl sulfoxide (DMSO) and base (B = Na⁻·CH₂SOCH₃) (Scheme 71).⁶⁴

In a similar manner, dihydronaphthofuran 11b was obtained by the reaction of Mannich bases, Mannich base methiodides, and Mannich base N-oxides derived from 1-naphthols with diazomethane in CH₂Cl₂ at 3°C for 24 h or with dimethylsulfoxonium methylide in DMSO at 60–70°C for 2–16 h (Scheme 73).⁶⁴

A simple and general route to the synthesis of 1,2-dihydronaphtho[2,1-b]furans 157, substituted in position 2 by an acyl or aryl group, starting from phenolic Mannich base methiodides and the carbonyl-stabilized sulphonium ylide in CH₃CN has been developed. The reaction proceeds readily at room temperature for 12 h and usually affords desired products 157 in 65–75% yields (Scheme 74). The formation of the
products can be rationalised by assuming the known behaviour of stabilised sulphonium ylides towards system bearing an electrophilic centre and a nucleophilic heteroatom.\textsuperscript{65}

The work of Yan et al.\textsuperscript{66} demonstrated that annulation reaction of $\beta$-naphthols with (2-bromoethyl)diphenylsulfonium trifluoromethanesulfonate salt (158) in the presence of K$_2$CO$_3$ in CH$_3$CN at 0 °C under an argon atmosphere for 16–24 h led to the formation of dihydronaphthofurans 159 in moderate to good yields (54–92%) (Scheme 75). A tentative reaction mechanism is outlined in Scheme 76. The reaction begins with the generation of a vinylsulfonium salt 160 via the elimination of hydrogen bromide from 158. The vinylsulfonium salt 160 reacts with $\beta$-naphthols to give sulfonium ylides 161, which then tautomerize to intermediates 162. After a proton transfer, the zwitterions 163 are formed. The subsequent intramolecular SN$_2$ reaction led to the formation of products 159 and eliminates diphenyl sulfide.

2.6. Enantioselective synthesis

Chen et al.\textsuperscript{67} described synthesis of enantiopure 1,2-dihydronaphtho[2,1-b]furanyl-2-hydroxylamine derivatives 164 in 52–67% yields with 99.5% ee and products 165 by the asymmetric Michael-type Friedel–Crafts alkylation of 2-naphthols with nitroolefins in toluene in the presence of bifunctional thiourea-tertiary amine organocatalyst at $-50$ °C for 144 h (Scheme 77).

The work of Zhang et al. demonstrated that 2-methyl-2-vinyl-1,2-dihydronaphtho[2,1-b]furan (166) was synthesized in 92% yield with enantioselectivity 54% ee (Scheme 79).

Asymmetric organocatalytic synthesis of optically active dihydronaphthofurans 168a–c has been reported. Treatment of trans-2-nonenal 169 with H$_2$O$_2$ in CH$_2$Cl$_2$ at room temperature for 24 h afforded 2,3-epoxy aldehyde 170. Then, the reaction of 2,3-epoxy aldehyde 170 with BnNH$_2$ at room temperature in the presence of DBU at room temperature led to the formation of dihydronaphthofurans 168 in 57–83% type cyclizations of o-substituted allyl naphthol in the presence of Pd(CF$_3$COO)$_2$/tetraoxazoline as ligand (Pd/ligand 1 : 1) and p-benzoquinone in methanol at 60 °C for 24 h (Scheme 78).\textsuperscript{68}

In a similar fashion, 2-methyl-2-vinyl-2,3-dihydronaphtho[1,2-b]furan (167) was synthesized in 88% yield and enantioselectivity 54% ee (Scheme 79).\textsuperscript{68}

Asymmetric organocatalytic synthesis of optically active dihydronaphthofurans 168a–c has been reported. Treatment of trans-2-nonenal 169 with H$_2$O$_2$ in CH$_2$Cl$_2$ at room temperature for 24 h afforded 2,3-epoxy aldehyde 170. Then, the reaction of 2,3-epoxy aldehyde 170 with BnNH$_2$ at room temperature led to the formation of dihydronaphthofurans 168 in 57–83% type cyclizations of o-substituted allyl naphthol in the presence of Pd(CF$_3$COO)$_2$/tetraoxazoline as ligand (Pd/ligand 1 : 1) and p-benzoquinone in methanol at 60 °C for 24 h (Scheme 78).\textsuperscript{68}

In a similar fashion, 2-methyl-2-vinyl-2,3-dihydronaphtho[1,2-b]furan (167) was synthesized in 88% yield and enantioselectivity 54% ee (Scheme 79).\textsuperscript{68}

Asymmetric organocatalytic synthesis of optically active dihydronaphthofurans 168a–c has been reported. Treatment of trans-2-nonenal 169 with H$_2$O$_2$ in CH$_2$Cl$_2$ at room temperature for 24 h afforded 2,3-epoxy aldehyde 170. Then, the reaction of 2,3-epoxy aldehyde 170 with BnNH$_2$ at room temperature led to the formation of dihydronaphthofurans 168 in 57–83% type cyclizations of o-substituted allyl naphthol in the presence of Pd(CF$_3$COO)$_2$/tetraoxazoline as ligand (Pd/ligand 1 : 1) and p-benzoquinone in methanol at 60 °C for 24 h (Scheme 78).\textsuperscript{68}

In a similar fashion, 2-methyl-2-vinyl-2,3-dihydronaphtho[1,2-b]furan (167) was synthesized in 88% yield and enantioselectivity 54% ee (Scheme 79).\textsuperscript{68}
yields and excellent enantioselectivities (94–97% ee) (Scheme 80). 69

Moreover, 2,3-dihydronaphtho[1,2-b]furan 173 in 60% yield and excellent enantioselectivity (93% ee) was obtained via the same reaction conditions that it has been reported for the synthesis of 168 (Scheme 81). 69

In a similar fashion, reaction of 2,3-epoxy aldehyde 170 with naphthols in the absence of BnNH2 and DBU gave dihydronaphthofurans 174 in 39 and 74% yields and excellent enantioselectivities (96 and 97% ee). Also, dihydronaphthofuran 174a (X: OH) via the Wittig reaction, using the stabilized phosphorus ylide, and subsequent base-induced ox-

Michael addition proved successful, thus affording access to the dihydrobenzofuran 175 in 36% yield and 97% ee (Scheme 82). 69

Asymmetric synthesis of trans-dihydroarylfurans 176 in 45–94% yields and excellent ee’s (up to 97%) via a Friedel-Crafts/substitution domino reaction of (Z)-bromonitroalkenes and 2-naphthols in the presence of squaramide as catalyst and co-base (sodium acetate) in CHCl3 at 0°C for 16–40 h has been reported (Scheme 83). 70

Also, a chiral multiple catalysis with two chiral units has been proved effective in the domino Friedel-Crafts alklylation of 2-naphthols with α-bromonitroalkenes. This efficient domino reaction affords chiral 1,2-dihydronaphtho[2,1-b] furans 176 in good to high yields (up to 93% yield) and high enantioselectivities (91% enantiomeric excess) (Scheme 84). 71
The diastereo- and enantioselective synthesis of 2,3-disubstituted trans-2,3-dihydronaphthofuran (95 : 5 dr, 95 : 5 er) via intramolecular Michael addition has been developed using keto-enone substrate and a bifunctional tertiary amine-thiourea catalyst (5 mol%) in toluene at 50 °C for 20 h in 93% yield (Scheme 85).

A copper-catalyzed asymmetric [3 + 2] cycloaddition of 3-trimethylsilylpropargylic esters with 2-naphthols has been realized and proceeds by a desilylation-activated process. Under the catalysis of Cu-(OAc)$_2$·H$_2$O in combination with a structurally optimized ketimine P,N,N-ligand and iPr$_2$NEt in MeOH at −40 °C for 24 h a wide range of optically active 1,2-dihydronaphtho[2,1-b]furans were obtained in good yields (48–98%) and with high enantioselectivities (up to 93% ee). Hydrogenation of (R)-2-methylene-1-phenyl-1,2-dihydronaphtho[2,1-b]furans were obtained in good yields (48–98%) and with high enantioselectivities (up to 93% ee). Hydrogenation of (R)-2-methylene-1-phenyl-1,2-dihydronaphtho[2,1-b]furans were obtained in good yields (48–98%) and with high enantioselectivities (up to 93% ee).

A reaction pathway for the preparation of 179 is proposed as shown in Scheme 87. In the first step, a copper complex forms the π-complex 181 with 182. A copper-promoted Si–C(sp) bond cleavage of 181, followed by the elimination of an acetoxyl moiety, affords the copper allenylidene complex 183 or its resonance structure 184. The intramolecular Cu–Si exchange by the elimination of AcO$i'$SiMe$_3$ proceeds more readily than the intermolecular base-assisted reaction with terminal propargylic esters for the formation of copper acetylide complex 185, which should be answered for the observed activation. The nucleophilic attack of the C$_u$ atom of β-naphthol at the C$_g$ atom of the allenylidene complex 183 gives the copper acetylide complex 186, which is then converted into the copper π-alkyne complex 187. Intramolecular nucleophilic attack of the hydroxy group on the C$_β$ atom of 187 generates an alkenyl complex 188, which is
transformed into the copper π-alkene complex 189. The starting 181 is then regenerated from 189 by liberating 179 through ligand exchange with another 182.

Wang and Tong demonstrated that phosphine-catalyzed asymmetric [3 + 2] annulations of δ-acetoxy allenoates 190 with 2-naphthols in the presence of K2CO3 in toluene at 0 °C for 12 h afforded 1,2-dihydronaphtho[2,1-b]furans 191 in moderate to excellent yields (27–99%) and with high enantioselectivity (83–93%) (Scheme 88). In the presence of phosphine catalyst, allenoate 190 can be readily converted into 3-phosphonium-2,4-dienoate 192 via 1,4-addition of phosphine and subsequent 1,2-elimination of acetate group. For 192, the αC-position has more steric hindrance than the δC-position. Therefore, to minimize the steric repulsion, 2-naphthol would preferentially attack intermediate 192 at its δC-position via a Friedel–Crafts type process to afford intermediate 193, which underwent oxo-Michael addition via a half-chair conformation, thus finally leading to product 191 (Scheme 89).

Similarly, phosphine-catalyzed asymmetric [3 + 2] annulation of δ-acetoxy allenoate with 1-naphthol afforded 2,3-dihydronaphtho[1,2-b]furan derivative 194 in 43% yield with high enantioselectivity (93% ee) (Scheme 90).

The enantioselective synthesis of naphtho-annulated oxaheterocycle dihydronaphthofuran 195 in 72% yield was accomplished by using β-hydroxy-α-tosyloxy esters 196 and 197 as chiral building blocks, which are easily accessible through the regioselective α-tosylation of Sharpless asymmetric dihydroxylation-derived syn-2,3-dihydroxy ester 198. Treatment of dihydronaphthofuran 195 with methylmagnesium iodide in refluxing ether for 4 h followed addition of tetrabutylammonium fluoride (TBAF) at 0 °C and stirring for 5 h afforded (2S,3S)-2-(1-hydroxy-1-methyl-ethyl)-1,2-dihydronaphtho[2,1-b]furan-1-ol (199) in 74% yield (Scheme 91).

2.7. Microwave-assisted synthesis

The reaction of 2,2-dialkylacetaldehydes with electron-rich 2-naphthols in the presence of p-TSA under closed-vessel solvent-free microwave irradiation condition at 180 °C for 5 min resulted in the formation of corresponding 1,2-dihydronaphtho
[2,1-b]furans 200 in 44–92% yields (Scheme 92). The reaction was carried out via oxidative annulation process. In several cases, small amounts of 14-alkyl-14-H-dibenzo[a,j]xanthenes were also formed. The proposed mechanism using isobutyraldehyde and 2-naphthol as starting materials is shown in Scheme 93. Nucleophilic C attack of 2-naphthol led to formation of a secondary alcohol intermediate 201 which formed a secondary benzylic carbocation 202 through corresponding oxonium ion 203 under catalytic amount of p-TSA. 1,2-Hydride shift leading a tertiary carbocation 204 followed by nucleophilic attack by the naphthol oxygen led to formation of 200a. Namboothiri et al. exploited [3 + 2] annulation of 2-naphthol with hydrazinonitroalkene 205 in the presence of Cs2CO3 in CH3CN under microwave radiation at 100 °C for 10 min afforded trans-1,2-dihydropnaphtho[2,1-b]furans 206 in 53–93% yields. The proposed mechanism, taking 2-naphthol as the representative arenol, envisages Cs2CO3 mediated addition of naphthol to MBH adduct 205 in a Michael fashion leading to the formation of intermediate 207 which forms an acyliminium type intermediate 208 with the loss of nitro group. Enolization of 208 and intramolecular 5-exo-trig cyclization gives rise to product 206 (Scheme 95). Also, trans-2,3-dihydropnaphtho[1,2-b]furans 209 was obtained in 34–52% yields via the reaction of 1-naphthol with hydrazinonitroalkene 205 (Scheme 95). Freire et al. have shown that synthesis of novel photochromic 1-(2,2-diphenylvinylidene-2,2-diphenyl-1,2-dihydropnaphtho[2,1-b]furan-7-yl)methyl (3-(triethoxysilyl)propyl) carbamate (210) was accomplished by the treatment of 211 with IsoTES 212 by a microwave-assisted reaction in the presence of dibutyltin dilaurate as catalyst in acetone at 80 °C during 45 min (Scheme 96).

2.8. Photochemical methods
Rossi et al. published synthesis of 1,2-dihydropnaphtho[2,1-b] furans 213a-c in very good yields by SRN1 photostimulated reactions in liquid ammonia from adequate 2-(allyloxy)-1-halonaphthalene and Me3Sn, Ph3P, and CH3NO2 anions. The mixture of 2-(allyloxy)-1-chloronaphthalene in EtOH, liquid ammonia and Me3SnCl in dried diethyl ether and Na was irradiated for 120 min using two medium-pressure mercury lamps emitting maximally at 366 nm gave 1,2-dihydropnaphtho[2,1-b] furan 213a in 84% yield. The reaction of 2-(allyloxy)-1-bromonaphthalene was performed by a procedure similar to that described for the other two nucleophiles, Ph3P and Na in t-BuOH and CH3NO2, t-BuOK in acetone afforded 1,2-dihydropnaphtho[2,1-b]furans 213b-c in 98% and 85% yields.
respectively (Scheme 97). The propagation steps of an SRN1 mechanism are presented in Scheme 98.

A mixture of naphtho[b]furans 214–215 and dihydronaphthofurans 216–217 were obtained from allyl halonaphthyl ethers employing photo induced radical cyclization with 100 W high-pressure mercury lamp in CH₃CN under Ar atmosphere for 0.5–3 h (Scheme 99). In addition, observations made in this effort suggest that a plausible mechanism for these photoreactions (Scheme 100) begins with homolytic C–halogen bond cleavage in the triplet states of the substrates to generate radical pairs, which undergo 5-exo type cyclization and halogen atom capture to produce the initially formed 2-halomethyl substituted naphthodihydrofurans 216 similar to atom-transfer radical cyclizations. Subsequently, photoinduced dehydrohalogenation of 216 takes place to generate alkylidene dihydrofuran intermediates 218 that undergo tautomerization to generate the naphthofuran product 214. In the case of R₁ = CH₃, R₂ = CH₃, the photochemical dehydrohalogenation leads to the respective formation of 218 and the regioisomeric product 217, which is photochemically tautomerized to 215.

2.9. Electrochemical methods

Treatment of 2-naphthol with 1,2-dimethoxy-4-propenylbenzene in the electrochemical oxidation using iodo benzene bis-trifluoroacetate (PhI(O₂CCF₃)₂) as oxidant in CH₃CN, gave a very low yield of 1,2-dihydronaphtho[2,1-b]furan 219 (Scheme 101).

Anodic oxidation of 4-methoxynaphthol and electron-rich styrenes gave 2,3-dihydronaphtho[1,2-b]furan derivatives 220

Scheme 97 Photostimulated synthesis of 1,2-dihydronaphtho[2,1-b]furans 213.

Scheme 98 Propagation steps of an SRN1 mechanism.


Scheme 100 Plausible mechanism for the preparation of 214–217.

Scheme 101 Electrochemical synthesis of dihydronaphthofuran 219.
in 35–76% yields. Reactions were conducted with a current density of 40–80 mA for 150–180 min in 8:1 CH3CN/HOAc using a platinum anode and cathode and perchlorate as supporting electrolyte (Scheme 102).

The electrochemical reduction of 2-(allyloxy)-1-bromonaphthalene under CO2 pressure (1 atm) allows the synthesis of dihydroxynaphthofurans 221 and 222 in 8 and 47% yields, respectively. This novel intramolecular cyclization-carboxylation reaction is carried out in single-compartment cells (Mg/C as the electrodes) at 20 °C and is catalyzed by [Ni(cyclam)Br2 2BF4]. In this method, three types of products 221–223 were obtained as indicated in Scheme 103. A catalytic cycle is proposed in Scheme 104. The electrochemical reduction of Ni(cyclam)2+ affords NiI species. Oxidative addition of the NiI species (coordinated to CO2) to the C-(aryl)-halogen bond of 224. After oxidative addition, the formation of NiIII intermediate species 225 is proposed. This NiIII intermediate induces a radical character to the aryl moiety, resulting in a rapid intramolecular cyclization on the double bond in the side chain, leading to 226. Further one-electron reduction of NiIII intermediate species 226 should form an allylnickel(II) species 227, able to undergo CO2 uptake, forming a nickel(II) carboxylate. Competitive protonation of 227 by the electrolytic medium (solvent) affords cyclized, noncarboxylated 222. In the one-compartment cell procedure with a magnesium anode, the presence of the magnesium ions issued from the anodic oxidation process, enables the formation of a magnesium carboxylate 228 liberating the nickel species for further recycling. Magnesium carboxylate 228 is stable under the reaction conditions, it accumulates during electrolysis and it is simply hydrolyzed to 221 at the end of the reaction. In a competitive reaction, intermediate 225 can also be directly reduced and carboxylated to the corresponding carboxylic acid derivatives 223 via intermediate 229.

2.10. Synthesis by radical methods
The work of Hayashi and Lawson demonstrated that various dihydroxynaphthofurans 230–232 were prepared by reaction of naphthofuran carboxylic acids 233–235 with sodium amalgam in alkali solution of NaOH at room temperature for 7 and 18 h led to the formation of dihydroxynaphthofuran carboxylic acids 236–238. Then, dihydroxynaphthofuran carboxylic acids were treated with an excess of ethereal diazomethane at 0 °C to give 230–232 in 95, 76 and 15.2% yields, respectively (Scheme 105). Cyclization of 1-bromo-2-(prop-2-enyloxy)naphthalene was employed by Beckwith et al. to the synthesis of 1-methyl-1,2-dihydroxynaphtho[2,1-b]furan (222) in 64% yield. The reaction was carried out in the presence of Bu3SnH and AIBN as initiator in dry benzene under reflux condition for 16 h (Scheme 106).
Presumably the mechanism involves generation of the radical 239 from 1-bromo-2-(prop-2-enyloxy)naphthalene followed by cyclization of radical 239 to 240 and transfer of a hydrogen atom from Bu3SnH to the primary radical 240 afforded the final product 222 according to the pathway given in Scheme 107.\[^8^3\]

Similarly, it was noted that reaction of ethyl 1-bromo-2-hydroxynaphthalene (241) with ethyl-4-bromocrotonate and \(\text{K}_2\text{CO}_3\) in dry acetone under reflux for overnight afforded ethyl 4-(1-bromo-2-naphthyl)but-2-enoate (242) in 37% yield. The reaction of compound 242 with Bu3SnH and AIBN in refluxing dry benzene for 30 min gave ethyl 1,2-dihydronaphtho[2,1-b]furan-3-acetate (243) in 97% yield. Treatment of 243 with KOH in water-ethanol (1:1 v/v) at room temperature for 2 h resulted 1,2-dihydronaphtho[2,1-b]furan-3-acetic acid (244) in 99% yield. The conversion of 244 into thiohydroxamate 245 can be efficiently performed in refluxing benzene using oxalyl chloride and then in dry ether using 3-hydroxy-4-methylthiazole-2(3H)-thione, pyridine and DMAP at room temperature for 20 min (Scheme 108).\[^8^5\]

Clive and Wang\[^4^4\] demonstrated that 1-methyl-1,2-dihydronaphtho[2,1-b]furan (222) in 63% yield and 2,3-dihydro-1H-naphtho[2,1-b]pyran (246) in 31% yield were synthesized by radical cyclization of 2-(allyloxy)-1-bromonaphthalene in the presence of stannane and AIBN in refluxing benzene for 6 h (Scheme 109).

Triarylaminium salt was disclosed as an efficient initiator for the novel Friedel–Crafts alkylation/annulation cascade reaction between chalcone epoxides 247 and 2-naphthols in CHCl\(_3\) at room temperature for 0.5 h to construct diastereomer poly-substituted 1,2-dihydronaphtho[2,1-b]furans 248 in 61–83% yields (Scheme 110). In this process, chalcone epoxides 247 acted as valuable halogen-free pre-electrophiles.\[^8^5\]
An efficient chemoselective tandem Friedel–Crafts alkylation/cyclization reaction of glycidic esters with 2-naphthol derivatives in CH₂Cl₂ at ambient temperature for 0.5 h initiated by stable radical cation triarylaminium salt [tris(4-bromophenyl)aminium hexachloroantimonate, TBPA⁺SbCl₆⁻] (0.5 mol%) led to the formation of the mixture of trans/cis-dihydronaphthofurans 249 in 51–70% yields (Scheme 111). A plausible mechanism for formation of 249 is depicted in Scheme 112. The glycidic ester (250) was first activated by single electron oxidation to give distonic radical cation intermediate 251. 2-Naphthol (as an example) was then attacked by the benzylic cation of intermediate 251 to form the dihydrofurylium distonic radical cation intermediate 252. Then oxygen radical combined with the carbocation to construct radical cation intermediate 253. Then the radical cation intermediate 254 was formed by eliminating a molecule of water from intermediate 253. Intermediate 254 would then undergo single electron transfer from substrate 250 to produce the major product 249 and regenerate intermediate 251 at the same time. Chain propagation continued until all substrates were converted into the products. 86

Wang et al. 87 concluded that tandem reaction between chalcone epoxides and 2-naphthyl ethers in the presence of stable triarylaminium salt (5 mol%) in CHCl₃ at room temperature for 0.5 h afforded dihydronaphthofurans 255 (Scheme 113). And after subsequent aerobic oxidative aromatization in one pot, a series of polysubstituted naphtho[2,1-b]furans were delivered. It should be noted that compounds 255 have not isolated. The reaction mechanism similar to the proposed mechanism for the synthesis of 249.

2.11. Other synthetic methods
Thermolysis of [methoxy(2-methoxy-1-naphthyl)methyl]trimethylsilane (256) at 610 °C/0.05–0.10 mm yields 1,2-dihydro-naphtho[2,1-b]furan (11b) in 64% yield presumably by

Scheme 110  TBPA⁺SbCl₆⁻-catalyzed synthesis of 1,2-dihydronaphtho[2,1-b]furans 248.

Scheme 111  TBPA⁺SbCl₆⁻-catalyzed synthesis of trans/cis-dihydronaphthofurans 249.

Scheme 112  Proposed mechanism for the synthesis of 249.

Scheme 113  TBPA⁺SbCl₆⁻-catalyzed synthesis of dihydronaphthofurans 255.

Scheme 114  Thermolysis of compound 256 to 1,2-dihydro-naphtho[2,1-b]furan (11b).
insertion of 2-methoxy-1-naphthylmethylene (257) into a C–H bond of its o-methoxy group (Scheme 114). 88

2-Bromo-1-(1,2-dihydronaphtho[2,1-b]furan-2-yl)ethanone (258) in 58% yield and 2-bromo-1-(2,3-dihydronaphtho[1,2-b]furan-2-yl)ethanone (259) in 50% yield have been synthesized from compounds 236 and 237 with SOCl₂ at 35–40 °C for 3 h. Subsequently, the crude acid chlorides in diethyl ether were treated with diazomethane for 3 h and after that with LiBr in HOAC (80%) at 0–5 °C for 10 min (Scheme 115).

Admas et al. 7 demonstrated that N-hydroxyurea derivative of dihydronaphthofuran 260 has been prepared in 12% yield from the corresponding ketone in three steps, oximation, reduction, and hydroxyurea formation (Scheme 116).

In a similar fashion, N-hydroxyurea derivative of dihydronaphthofuran 261 could be prepared in 18% yield from the corresponding ketone 262 in three steps, oximation, reduction, and hydroxyurea formation (Scheme 117).

Canesi et al. 89 demonstrated that treatment of 2-naphthol with allylsilane in hexafluoroisopropanol (HFIP) for 30 s in the presence of iodobenzene diacetate gave ((1,2-dihydronaphtho[2,1-b]furan-2-yl)methyl)trimethylsilane (263) in 44% yield. This reaction proceed via formal [2 + 3] cycloaddition is based on a common electrophilic intermediate 264 generated by an environmentally benign hypervalent iodine reagent in perfluorinated protic solvents. This intermediate can react with different sufficiently reactive allylsilane to lead in one step to different heterocyclic rings such as dihydronaphthofuran 263 (Scheme 118).

The Diels–Alder addition of naphthoquinone 265 to 1-trimethylsilyloxybuta-1,3-diene in CH₂Cl₂ at −78 °C and 0 °C for 1 h afforded Diels–Alder adducts 266. Individual treatment of adducts 266 with tin(IV) chloride in CH₂Cl₂ at 0 °C for 10 min or with tetrabutyl ammonium fluoride in THF for 30 min afforded 2,3-dihydronaphtho[1,2-b]furan 267 in 49–85% yields (Scheme 119).

A series of 2,3-dihydronaphtho[1,2-b]furan-2-carboxylic acid N-substituted phenyl amide analogs 268 were synthesized by...
Kwak et al.14 A mixture of 2-((1-(benzyloxy)naphthalen-2-yl)methyl)oxirane, 10% Pd/C, K₂CO₃, Et₃N (catalytic amount) and MeOH was stirred for 8 h at room temperature afforded (2,3-dihydronaphtho[1,2-b]furan-2-yl)methanol (269) in 93.7% yield. Treatment of 269 with TEMPO and BAIB in CH₃CN/H₂O at room temperature for 5–6 h gave 2,3-dihydronaphtho[1,2-b]furan-2-carboxylic acid (270) in 65.8% yield. Stirring a mixture of 270 and 1,1₀-carbodiimidazole in anhydrous THF for 1 h followed by addition of substituted aniline to the reaction mixture at room temperature and stirring for 12–16 h afforded 2,3-dihydronaphtho[1,2-b]furan-2-carboxylic acid N-(substituted phenyl)amide analogs 268 and 272.

Hong and coworkers reported that synthesis of N-(3,5-bis(trifluoromethyl)phenyl)-5-chloro-2,3-dihydronaphtho[1,2-b]furan-2-carboxamide (NHDC) (273) from 1-naphthol through a series of reactions including o-allylation, Claissen rearrangement, o-benzylation, epoxidation of allyl compound, debenzylation followed by cyclization, oxidation with TEMPO and NaOCl, and amide coupling with 3,5-trifluoromethylphenylamide for 12–16 h (Scheme 121).14

2,3-Dihydronaphtho[2,3-b]furan derivative 274 was synthesized as shown in Scheme 122. Bromination of 2,3-dihydro-1-benzofuran followed by formylation gave aldehyde 275, which was converted to 276 by treatment with acetal ester. Reduction of 276 by LAH afforded 2,3-dihydronaphtho[2,3-b]furan-2-carboxylic acid N-(substituted phenyl)amide derivatives 277 in 48% yield (Scheme 122).14

Interaction of 43 with absolute ethanol in the presence of Dowex 50W-X8 resin under reflux condition for 10 h gave...
1-ethoxy-1,3-dihydronaphtho[2,3-c]furan (281) in 92% yield. Also, treatment of 43 in a flask equipped with a Dean–Stark trap in refluxing toluene for 8 h afforded 1-[(3-formyl-2-napthalenyl)methoxy]-1,3-dihydronaphtho[2,3-c]furan (282) in 71% yield (Scheme 123).\textsuperscript{32}

3. Dihydronaphthofuran applications

3.1. Biological activities

Dihydronaphthofuran derivatives have received considerable attention in view of the interesting biological and pharmacological properties associated with this heterocyclic scaffold. For example, N-hydroxyurea derivatives of dihydronaphthofurans \textsuperscript{260} and \textsuperscript{261} were weaker inhibitors of 5-lipoxygenase, with IC\textsubscript{50} values in excess of 10 \textmu M in human whole blood.\textsuperscript{7} A series of dihydronaphthofuran derivatives such as \textsuperscript{53} and \textsuperscript{274} evaluated as C\textsubscript{17,20}-lyase inhibitors. 1,2-Dihydronaphtho[2,1-b]furan \textsuperscript{53} showed equipotent C\textsubscript{17,20}-lyase inhibition activities on rate and human 26 and 25, respectively, and 11\beta-hydroxylase activity on rate 77. Also, 2,3-dihydronaphtho[2,3-b]furan \textsuperscript{261} showed equipotent C\textsubscript{17,20}-lyase inhibition activities on rate and human 21 and 23, respectively, and 11\beta-hydroxylase activity on rate 350.\textsuperscript{8} Many functionalized dihydronaphthofurans \textsuperscript{81} and \textsuperscript{82} are widely employed as antitubercular activity against \textit{Mycobacterium tuberculosis} \textit{H}_{\text{37}Rv}. 2-Azidomethyldihydronaphtho-

3.2. Photochromic properties

Vinylidene-naphthofurans are a new class of photochromic molecules, with a unique structure combining an allene group linked to a dihydrofuran ring. These uncoloured molecules show acidochromism in solution and photochromic properties when adsorbed in silica gel or dissolved in acidic alcoholic solutions but not in common solvents or in the solid state. Mechanism of the photochromic behaviour for those compounds is thermally reversible. For example, vinylidenenaphthofuran \textsuperscript{63} exhibit photochromism at room temperature when adsorbed in silica gel. UV or sunlight irradiation leads, in a few seconds, to the formation of intense pink/violet to green colors that bleach completely in a few minutes in the dark (Scheme 124). Also, compound \textsuperscript{63} show acidochromic properties: addition of TFA to an uncolored solution of compound \textsuperscript{63} leads to the immediate development of an intense violet
coloration 283 that bleaches immediately when a weak base (NEt₃) is added (Scheme 125).¹⁵

Vinylidene-naphthofurans 63 exhibit acidochromic properties in TFA solutions. They are converted into stable cationic species in strong acidic medium and bleach back to the uncoloured closed form upon neutralisation with Et₃N. A mechanism for their thermally reversible photochromic behaviour is proposed based on NMR analysis of UV-irradiated CH₃OD + THF-d₈ acidified solutions: the UV light promotes the addition of methanol to the naphthofuran affording non-coloured photoprodct 284. In the presence of acid, the later is quickly converted into a cationic violet dye 283 that returns thermally to the initial closed naphthofuran in the dark. This photochromic system switches between the uncoloured and violet state under UV or sunlight exposure (15 s) and returns thermally to the initial uncoloured state in 2–8 min, in the dark, at room temperature (Scheme 126).¹⁶

The introduction of a styryl chain in the structure of the vinylidene-naphthofurans such as 140–142 leads to a new set of uncoloured photochromic compounds that afford grey/brown colourations upon exposure to the UV or sunlight, at room temperature and returning to the uncoloured state, in the dark, in several minutes. The photochromic properties of these smart dyes are very sensitive to the chemical environment, specially their acidity being faster in THF/HCOOH solution than in silica gel. The amount of formic acid influences the kinetics of the fading reaction as a low concentration leads to a faster system but with a lower colourability. A good compromise was obtained in THF/HCOOH (2/0.5) solutions. The substituents in the styryl group influences the kinetic of the fading process: electron-withdrawing groups like Br or CF₃ increases the fading rate leading to fast switching compounds but confers an initial yellowish colour to the solution before irradiation (Scheme 127).¹⁷

The photochromic properties of the ormosil materials 68 showed a strong dependence on the nature of the silanes, spacer, acid and curing conditions. The functionalization of the vinylidene-naphthofurans with a reactive siloxane group was essential to avoid their precipitation after curing. The best results were obtain using a mixture of TEOS, MTES, PTES, 1,2-ethanodiol, water, chloroacetic acid and vinylidene-naphthofurans (68: R = OMe) cured at 50 °C for 7 days. This uncoloured material is transparent and develops an intense green colouration, characterized by two absorption bands at 460 and 640 nm, after 2 min under UV light. When the light source is removed a mono-exponential colour decay occurs due to the spontaneously ring closure reaction that afford the initial molecule. These hybrids showed a fast thermal bleaching kinetics, losing almost their total colouration in 20 min in the dark (Fig. 4).¹⁹

A series of photochromic vinylidene-naphthofurans 88 and 89 with extended conjugation, embedded in ormosil matrices affording solid and transparent materials that acquire different colourations (violet, green, bluish), reversibly, when exposed to the UV (sun) light, for 2 min, at room temperature. The presence of an extra phenyl ring in some positions affects both the λmax of absorption of the photochromic compounds in the uncoloured closed and open coloured form. After removal of the light source the materials lose progressively their colouration returning to the initial uncoloured state in less than 15 min at

![Scheme 125](https://example.com/scheme125.png)

Scheme 125 Acidochromism of 1-vinylidenenaphtho[2,1-b]furan 63.

![Scheme 126](https://example.com/scheme126.png)

Scheme 126 Mechanism of photochromism for 1-vinylidene-naphthofuran 63.

![Scheme 127](https://example.com/scheme127.png)

Scheme 127 Photochromic equilibrium for 7-styryl-1-vinylidene-naphthofurans 142.

![Fig. 4](https://example.com/fig4.png)

Fig. 4 Structure of vinylidene-naphthofuran 68b.
naphthofuran immobilization strategy (adsorption that silica surface acidity and the type of vinylidene-photochromic behavior of these new nanoparticles indicates 

to fabricate tailor-made photochromic materials. The photochromic behavior of these new nanoparticles indicates that silica surface acidity and the type of vinylidene-naphthofuran immobilization strategy (adsorption vs. covalent grafting) were crucial factors for the occurrence of photochromism in the vinylidene-naphthofuran-based SiO2 NPs. Upon direct UV (λ = 365 nm) or sunlight exposure during 1 min, only the SiO2@211 nanomaterials prepared by direct vinylidene-naphthofuran adsorption onto SiO2 NPs with pH\text{pzc} ≈ 6.0 showed direct and reversible photochromic properties, developing fast (in seconds) and intense salmon and violet coloration in less than 10 min. Furthermore, they presented with fast rate constants, which were responsible for the loss of coloration in less than 10 min. Therefore, they presented very good resistance to fatigue, showing reversibility between the colored/uncolored states without significant loss of their performance for at least 8 successive UV/dark cycles. Scheme 128 has been represented of the proposed mechanism responsible for the photochromic behavior of 211 onto SiO2 NPs.18

**4. Conclusions**

In this review, wide range of synthetic strategies of dihydronaphthofurans (DHNs) as an important class of arene ring-fused furans has been discussed. We have started with chemical, photochemical and electrochemical methods for the synthesis of DHNs, followed by presenting of their diverse biological, pharmacological activities and photochromic properties. In general, naphthol derivatives play an important role and work well in construction of DHNs. Moreover, different types of reactions such as annulation of naphthols and naphthoquinones, [3 + 2] and [4 + 1] cycloaddition, Friedel–Crafts and Diels–Alder reactions, Claisen and neophyl rearrangement, cyclization of allyl naphthols and etc. were demonstrated for synthesis of DHNs. We believed that the reported methods could be of interest in material science, medicinal, photochromic compounds and natural products synthesis and their use has been growing rapidly.

**Conflicts of interest**

There are no conflicts to declare.

**Acknowledgements**

The authors thank the Research Council of Payame Noor University.

**Notes and references**


S. W. Youn, Synlett, 2007, 3050–3054.


