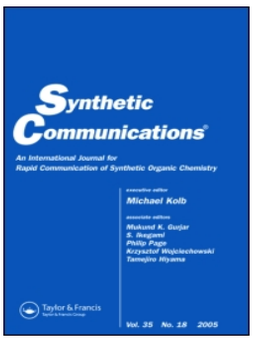

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SYNTHETIC COMMUNICATIONS REVIEWS

Diphenic acid derivatives: Synthesis, reactions, and applications

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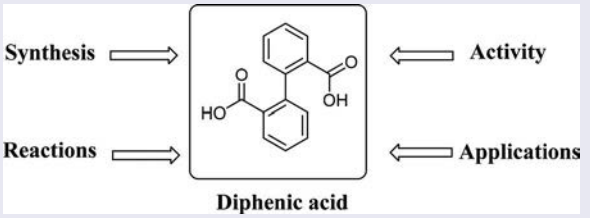
ABSTRACT

This review describes the synthesis and reactions of simple diphenic acid derivatives and to highlight the effects of compounds containing the diphenic acid moiety in important applications.

GRAPHICAL ABSTRACT



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KEYWORDS
Diphenic acid; electrophilic reaction; nucleophilic reactions

Introduction

Diphenic acid derivatives that possess useful therapeutic properties have attracted great attention for their widespread applications in many herbs and components of foods. Hexahydroxy diphenic acid ester (polyphenol) and its ellagic acid derivative (Fig. 1) are obtained from dried fruits of *Terminalia bellerica* (Bahera) that are reported to possess analgesic activity.[1,2] Many derivatives of these compounds are also found in blackberries, raspberries, and strawberries. The consumption of these fruits is shown to lower the risk of chronic diseases such as cancer, cardiovascular diseases, and other pathologies.[3–12]

Diphenyl-sugar moieties are present in several naturally occurring biologically active compounds.[13,14] Due to their important pharmaceutical[15] and agrochemical proprieties,[16] diphenyl-sugar units constitute attractive synthetic leads. Many efforts devoted to prepare analogues of molecular receptors[17] and redox[18] and antimalaria agents[19] have been reported in the past decade. Among them, the most attractive syntheses of diphenyl-sugar core-containing molecules regard the preparation of new antibiotics related to ristocetin A and teicoplanin,[20] two glycopeptides that belong to the family of

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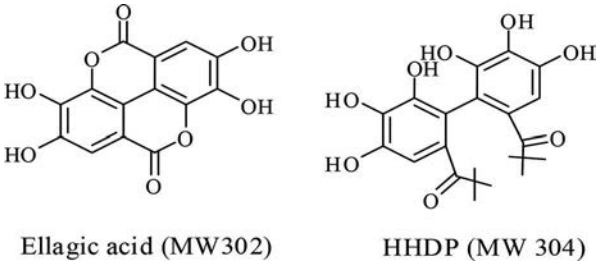


Figure 1.

ristocetin-type antibiotics.[21] The structure of these challenging molecules shows a conformationally stable axially chiral ortho trisubstituted diphenyl unit, glycosylated to a mannopyranoside. The ellagitannins are another vast family of biologically active compounds that gained a top position in research fields engendered by recent disclosures of their promising anticancer and antiviral activities. The structures of most ellagitannins are characterized by the presence of one or more axially chiral hexahydrodiphenoyl (HHDP) residues connected to a glucopyranose scaffold by ester functions[22] (Fig. 2).

There is an increasing awareness that health benefits of dietary polyphenols may be due to their role as modulators of cell signaling and gene expression, in addition to their antioxidant activities.[23,24] Kiely et al. explored the potential pharmacological role of some new diphenic acid monoamides. They are reported as leukotriene antagonists, 5-lipoxygenase, and mediator release inhibitors providing activity useful for treating asthma, cardiovascular diseases, migraines, and immune-inflammatory conditions.[25] Some novel diphenic acid monohydroxamides were equipotent to prototypical quinolone, nalidixic acid as DNA gyrase inhibitors, exhibiting potent antibacterial activity against *Escherichia coli*. They were preferentially devoid of the side effects on the central nervous system that has been reported for the members of quinolone series.[26] The biological importance of biaryl diphenic acids extended their vital role as phospholipase A_2 (PLA_2) inhibitors, owing to their carboxylate groups that linked to a hydrophobic biphenyl system.[27] PLA_2 are known mediators in inflammatory processes and their activity has been linked to many diseases such as asthma, arthritis, psoriasis, and pancreatitis. Further, PLA_2 has different physiological functions include their role in cell proliferation

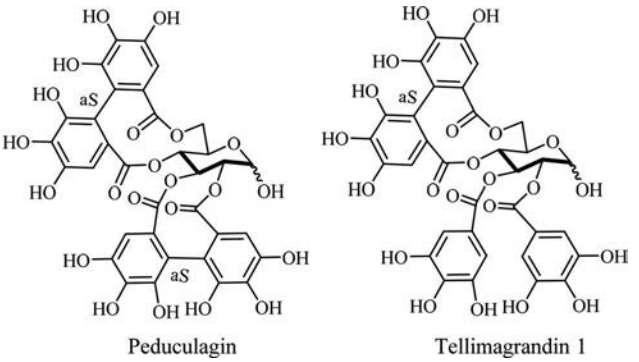


Figure 2. Structure of two naturally occurring ellagitannins.

and differentiation.[28] The vital biological activity extended to N-(4-methylphenyl)-diphenimide as antihyperlipidemic agent. In 1992, this compound successfully lowered serum lipids, very low-density lipoprotein and low-density lipoprotein with elevating high-density lipoprotein in balanced and hyperlipidemic diet-induced rats.[29] A reliable anticancer activity of some diphenic acid derivatives and diphenimides was reported against several human cancer cell lines, e.g., leukemia, non-small cell lung cancer and breast cancer.[30,31] Diphenic acid and its derivatives cannot be ignored as interesting moieties for studying the relation between the chemical structure and the physicochemical characters. Conformational analysis of some substituted diphenic acids and diphenimides was investigated. The preferred conformations were chosen by the comparison of experimental and theoretical values of dipole moments.[32,33]

Syntheses and reactions of simple diphenic acid derivatives

Synthesis

Reductive coupling of aromatic halides

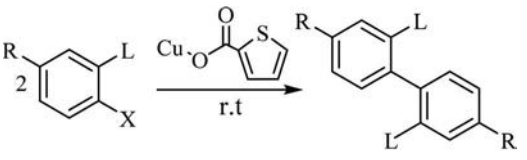
The most versatile method available for the synthesis of diphenic acid derivatives involves reductive coupling of aromatic halides, where copper is the most ancient transition metal used for the synthesis of biaryls[34] and it is still used nowadays[35,36] and Liebeskind et al.[37] have developed Ullmann-reductive coupling of substituted aromatic iodides and bromides to produce diphenic acid derivatives **1** using copper (I)-thiophene-2-carboxylate at room temperature (Scheme 1).

Meyers and Nelson[38,39] reported that a thermodynamically controlled resolution appeared to be operative under its reaction conditions so that diastereomerically enriched biaryls are formed (93(*S*)/7(*R*)) and may be readily purified to 100% diastereomeric purity. Mild conditions were required to hydrolyze the bis(oxazoline) (*S*)-**3** to enantiomerically pure diphenic acid (*S*)-**5** (Scheme 2).

Takagi et al.[40] have discovered the use of *N*-chlorosuccinimide (NCS) as the auxiliary oxidant. Using a molar ratio (ArZnI/NCS/Pd) 2/1.1/0.04, they prepared functionalized diphenic acid derivative **7** in good to excellent yields (Scheme 3).

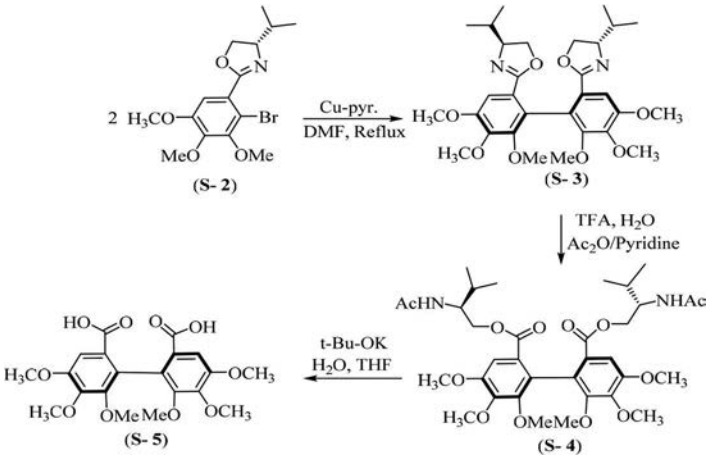
Diazotization of anthranilic acid

Barakat et al.[41] published a study of diazotization of anthranilic acid with a reducing mixture formed from ammoniacal cupric sulfate and alkaline hydroxylamine sulfate to give diphenic acid **1** (Scheme 4).

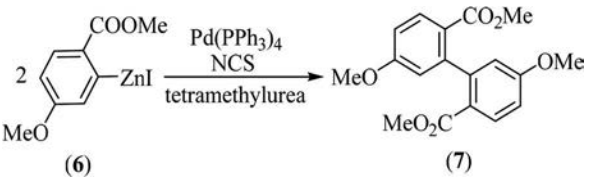


X=I or Br
R=H or OCH_3
L=CO_2H or CO_2CH_3

Scheme 1.



Scheme 2.



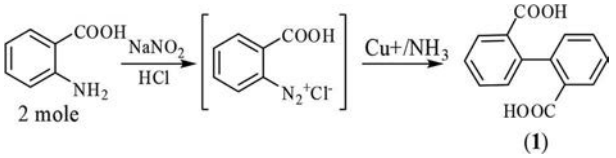
Scheme 3.

Basic hydrolysis of ellagic acid

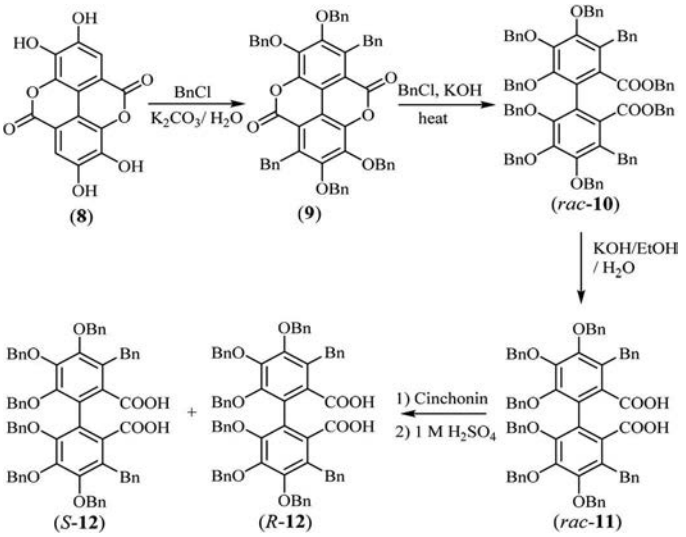
Khanbabaee et al.[42] have reported the reaction of ellagic acid **8** with benzyl chloride to afford bis-lactone **9**. The latter under strongly basic conditions with potassium hydroxide in the presence of benzyl chloride gave a racemic mixture **10**. Basic hydrolysis of *rac*-**10** under led to the formation of the corresponding biaryl dicarboxylic acid *rac*-**11** in a quantitative yield. At this stage, attempts to separate the racemic mixture *rac*-**11** into its enantiomerically pure atropisomers (a*R*)-**12** and (a*S*)-**12** using cinchonin was only effective for (a*R*)-**12** but unfortunately not for (a*S*)-**12** (Scheme 5).

Oxidation of phenanthrene

Recently, phenanthrene was oxidized into diphenic acid by peracetic acid. The overall reaction was reported by Zheng et al.[43] (Scheme 6).



Scheme 4.



Scheme 5.

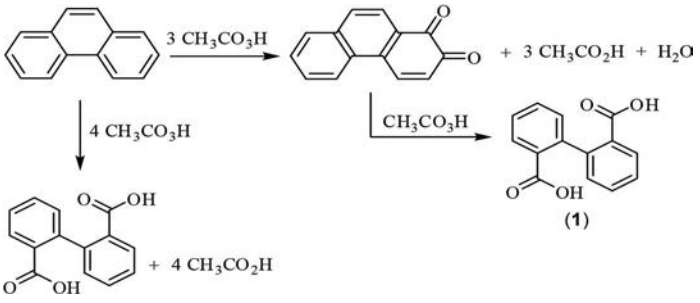
Bacterial degradation of pyrene

Mycobacterium as Gram-positive species has been most widely studied for degrading pyrene **13** by using it as a sole carbon and energy source.[44] A novel metabolite, 6,6′-dihydroxy-2,2′-biphenyl-dicarboxylic acid, was identified by Vila et al.[45] from the degradation of pyrene by *Mycobacterium* sp. strain AP1. Liang et al.[46] reported pyrene-4,5-dione formation and identified almost all the enzymes required during the initial steps of pyrene degradation in *Mycobacterium* sp. KMS. Kim et al.[47] identified 27 enzymes necessary for constructing a complete pathway for pyrene degradation from both genomic and proteomic data (Scheme 7).

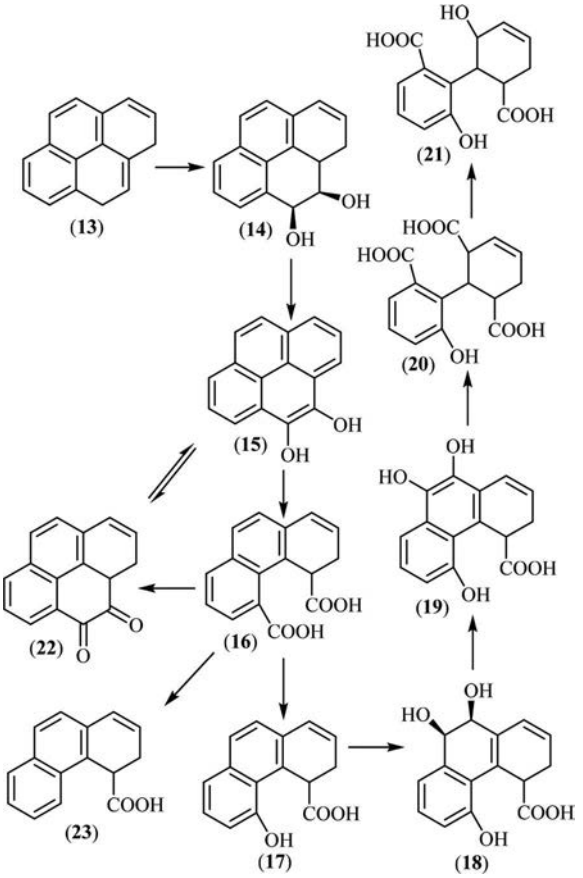
Reactions

Nucleophilic reactions

Aminolysis. Reaction of diphenic anhydride **24**[34] with ammonia afforded diphenamic acid **25**, which on cyclodehydration produced diphenimide **26**. Azepine **26** was then



Scheme 6.



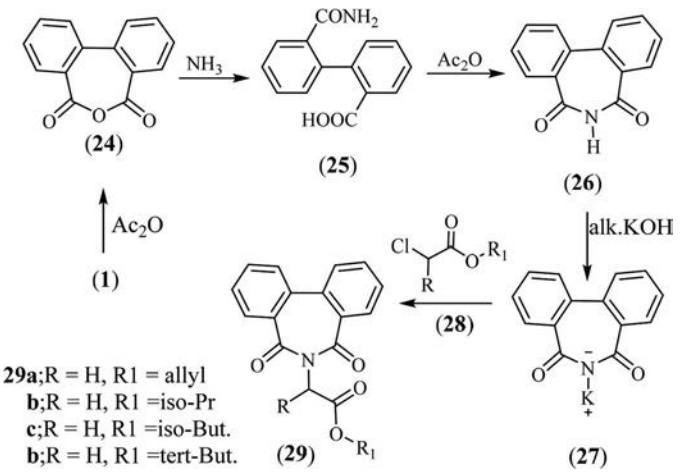
Scheme 7.

converted into its potassium salt **27** through treatment of **26** with an equivalent amount of ethanolic potassium hydroxide solution and pouring the resulting solution in drops on dry ether. Nucleophilic substitution reaction of diphenimide potassium salt **27** with the chloroacetates **28** in dimethyl-formamide produced the desired esters **29a–d**[48] (Scheme 8).

Treatment of diphenic anhydride **24** with the appropriate aryl and/or cyclohexylamine in dry xylene produced *N*-substituted diphenamic acids **30a–d**. They were cyclized under the effect of acetic anhydride in the presence of fused sodium acetate to give several new 6-(substituted)dibenz[*c*,*e*]azepine-5,7-diones **31a–d**,[34] (Scheme 9).

On the other hand, diphenic acid monoamides **33a–c** were obtained by Elzahabi et al.[49] through reaction of diphenic anhydride **24** with equimolar amounts of the appropriate aromatic amines **32a–c** under reflux condition. Also, Aminolysis of **24** by with heterocyclic amines **34** and **36** upon changing the ethanol to dioxane under reflux afforded the final monoamides **35** and **37**, respectively (Scheme 10).

Thin-layer chromatography (TLC) study of the reaction of diphenic anhydride **24** with 2-aminotriazole **38**[49] evidenced the presence of spot corresponding to unreacted starting compound **24**, so it was more convenient to start this reaction with two mole equivalents of **38** to get a single spot that represents the biphenyl dicarboxamide derivative **39**. Spectral



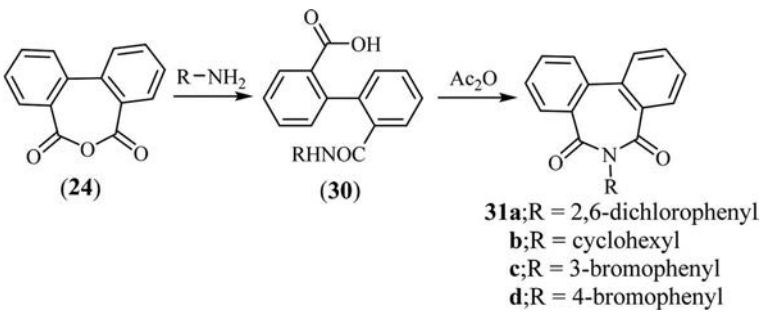
Scheme 8.

and elemental analysis were in agreement with the proposed structure and not **40** (Scheme 11).

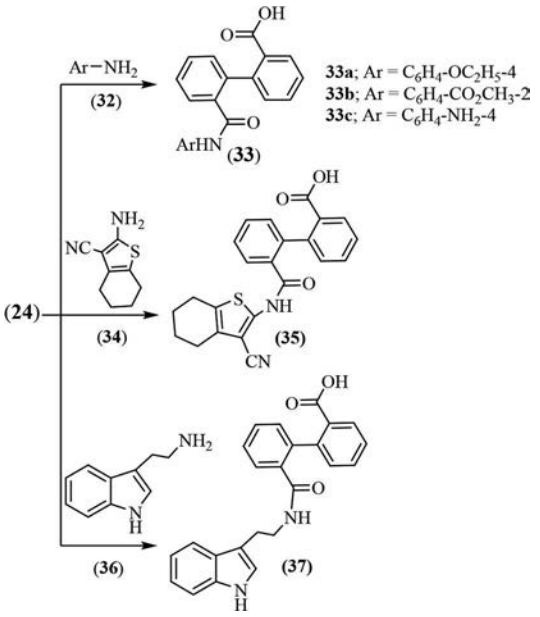
Diphenic amide derivative **33c** was used as a key intermediate for further synthesis of other target compounds. Thus when compound **33c** was reacted with chloroacetyl chloride afford chloroacetamide derivative **41** in a good yield, reaction of **41** with malononitrile in refluxing DMF afford the pyrolidinone derivative **43** through intramolecular cyclization intermediate **42**. Also, reaction of chloroacetamide derivative **41** with potassium thiocyanate in refluxing DMF was attempted to form the final thiazolidinone compound **45** as outlined in (Scheme 12).[49]

An extension of the substrate scope of the Flögel three-component reaction of lithiated alkoxyallenes, nitriles, and carboxylic acids is presented. As typical model substrates, diphenic acid **1** was used in combination with methoxyallene **46**, pivalonitrile **47** and/or thiophene-2-carbonitrile **48** in the three-component reaction, and bis(β-ketoenamides) **49**–**50** were isolated in reasonable yields of 15–28%[50] (Scheme 13).

After these successful multicomponent reactions, the authors investigated the intramolecular condensations of the bis(β-ketoenamides) **49, 50** to pyridine and pyrimidine derivatives. Enamide **49** were treated with trimethylsilyl trifluoromethanesulfonate and



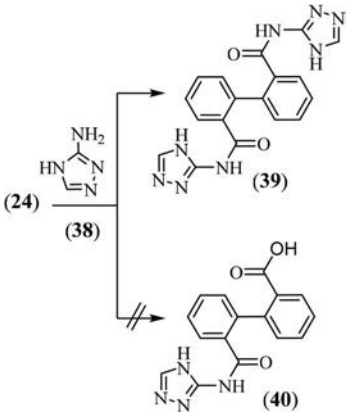
Scheme 9.



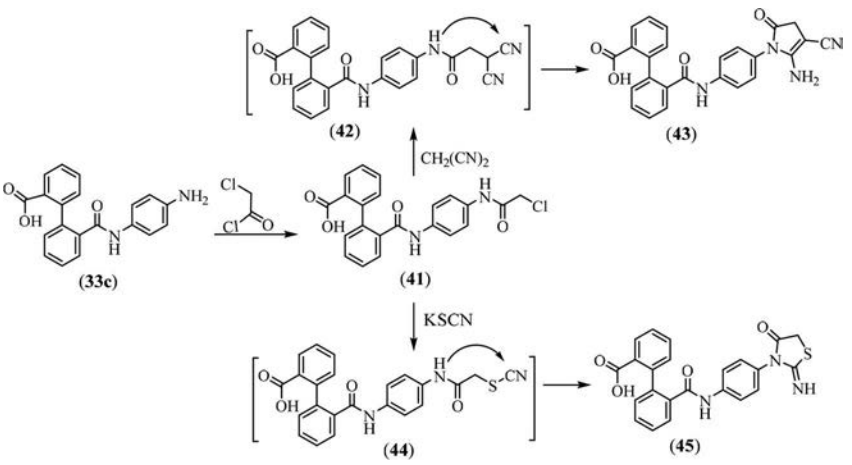
Scheme 10.

triethylamine to provide the bis(4-hydoxy-pyridines) **51** in 50% yield and **52** in 60% yield, respectively (Scheme 14). Also, cyclocondensation of bis(β-ketone-amides) **49, 50** to pyrimidines using ammonium acetate as ammonia source was investigated. When enamide **49** was cyclized under these optimized conditions, the conversion was nevertheless incomplete giving the desired bis(pyrimidine) derivative **53a** in 56% yield and the corresponding monopyrimidine **53b** in 23% yield. For enamide **50** however, the cyclization was complete under these conditions furnishing bis(pyrimidine) derivative **54** as a single product in 60% yield.[50]

Treatment of diphenic acid **1** with enantiomerically pure 2-amino alcohols **55** afforded bis(carboxiamides) **56**, the activation of the hydroxyl group of **56** was optimized, using



Scheme 11.



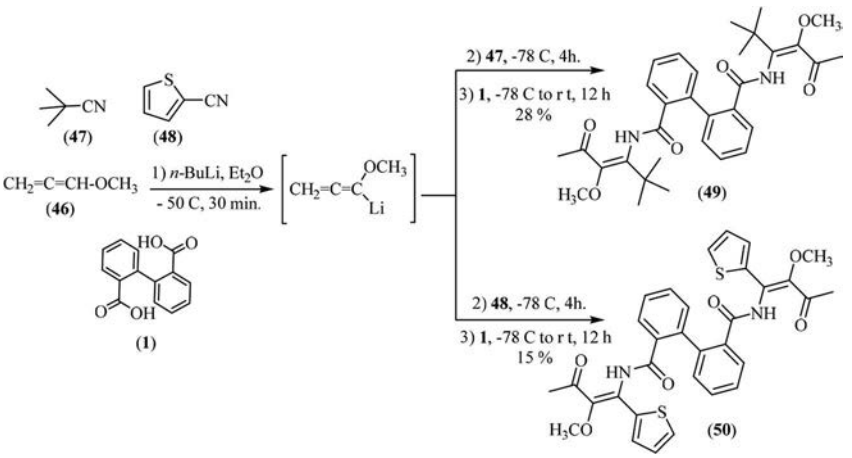
Scheme 12.

methanesulfonyl chloride, thionyl chloride to afford the chiral bis(oxazoline) derivatives **57**[51] (Scheme 15).

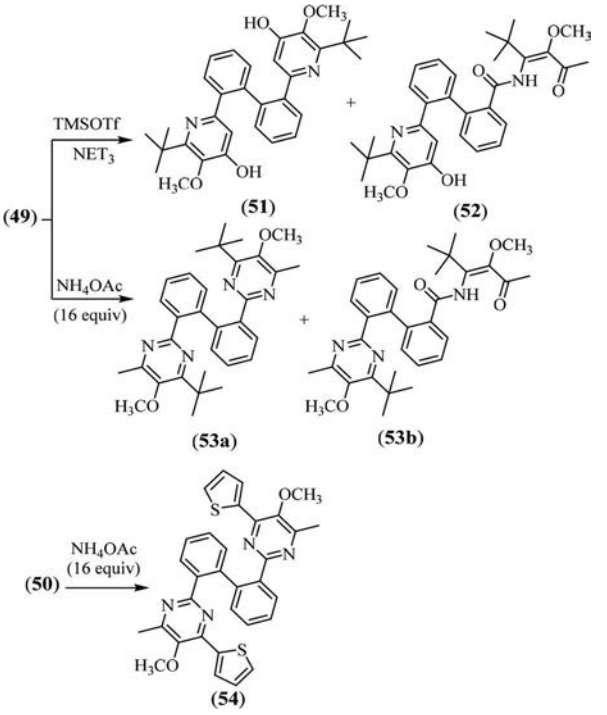
Similarly, enantiomerically pure (*R*)-**11** was treated with achiral amine **58** to give β-hydroxylamide (*R*)-**59**. The latter was then converted into the chiral oxazoline (*R*)-**60** by mesylation and spontaneous cyclization[42] (Scheme 16).

2-(*N*-imido)propanoic acid **62** was prepared as described in (Scheme 17) through two-step reaction of corresponding anhydride **24** with L-alanine at the first step followed by cyclodehydration of amide **61** using acetic anhydride and catalytic amount of anhydrous sodium acetate at the second step.[52]

Also, bihelical compound **64**[53] was obtained in two steps from the reaction of diphenic anhydride **24** with cystine di-OMe. The chirality of **64** largely arises from the L-cystine (Scheme 18).



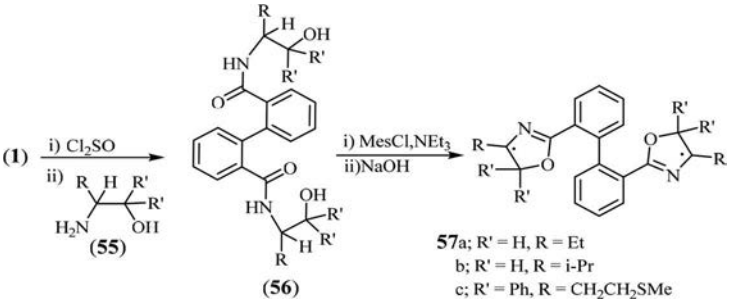
Scheme 13.



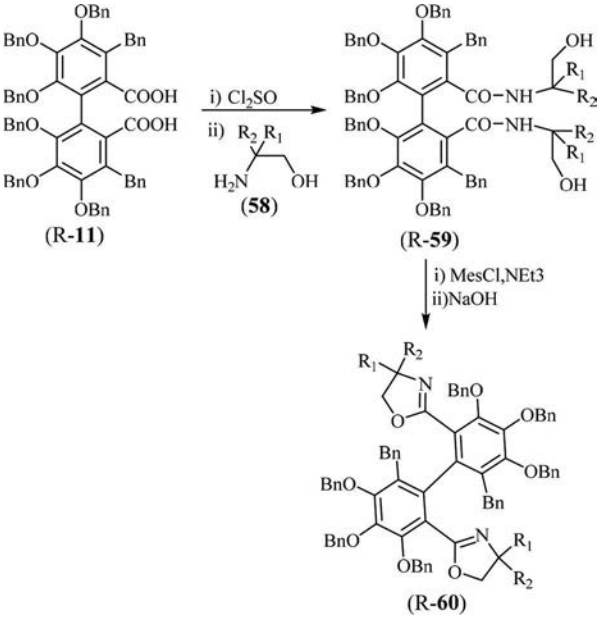
Scheme 14.

On the other hand, bihelical compound **65**[54] obtained from D-cystine di-OMe was found to be the perfect mirror image of **64** prepared from L-cystine based on X-ray crystallography, CD studies, and optical rotation (Scheme 19).

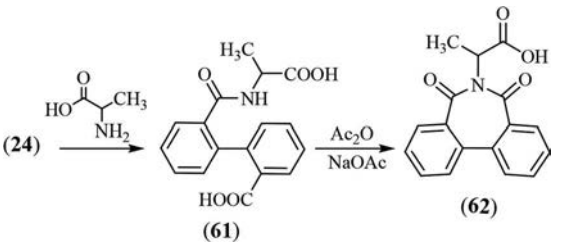
Diphenic acid monohydroxamides exhibited the inhibitory activities against the *E. coli* DNA gyrase supercoiling activity and their ability to facilitate the "cleavable complex" is reported.[55] The oxime **67** was synthesized through condensation of acetyl derivatives **66** with hydroxyl amine chloride under basic condition. Reduction of oxime **67** with sodium cyanoborohydride afforded the hydroxylamines **68**. The latter was reacted with diphenic anhydride **24** in THF to give monohydroxamide products **69** (Scheme 20).



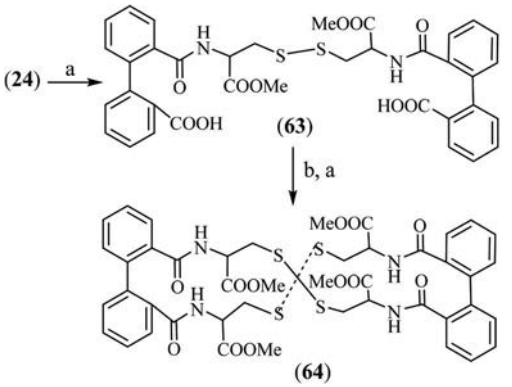
Scheme 15.



Scheme 16.

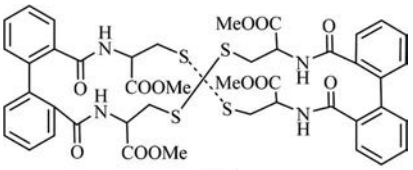


Scheme 17.



a = Cystine di-OMe, b = EDCI-HOBt

Scheme 18.



(65)

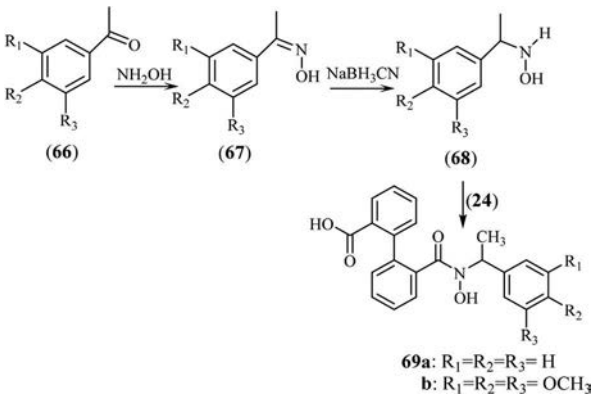
Scheme 19.

Ligands derived from 4,4′-dinitrobiphenyl containing aza-crown cavities in the 2,2′ position have been used in extraction and transport experiments of cations. Thus, Costero et al.[56] have reported that the synthesis of this ligand through the reaction of 4,4′-dinitrodiphenic acid **70** with thionyl chloride gives rise to the corresponding acid chloride that reacts with the commercially available macrocycle 1-aza-18-crown-6 to lead compound **71**. The asymmetric compound **74** was prepared in a similar way from the monomethylester of the 4,4′-dinitro-diphenic acid **73**. This ester was prepared from the same acid through the corresponding anhydride **72** (Scheme 21).

Diazocine derivative as a molecule with axial chirality has attracted attention recently because of their frequent occurrence in nature[57,58] and their numerous applications in asymmetric synthesis, catalysis.[59,60] Thus, the racemic cyclic monohydrazide 6,7-dihydro-dibenzo-[*d,f*][1,2]diazocine-5,8-dione (**75**) was prepared through reaction of diphenic anhydride **24** with hydrazine[61] (Scheme 22).

On the other hand, the 2-(4-chlorophenyl)-4-hydrazinyl-6-iodoquinazoline **(76)** was allowed to react with diphenic anhydride **24** to obtain the corresponding azepine derivative **77**[62] (Scheme 23).

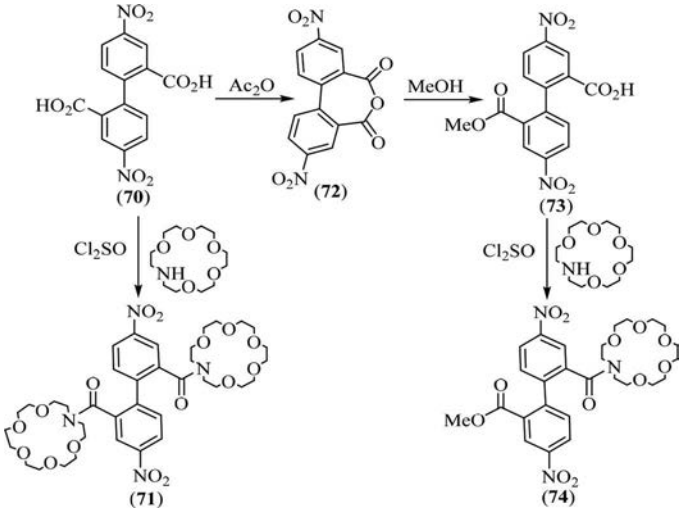
Esterification. Cercidinins **A** and **B** are the first published unusual ellagitannins, whose (*R*)-configured HHDP moieties are located at the 2,3-positions of the glucopyranoside core. Khanbabaee and Lötzerich[63,64] reported a total synthesis of the enantiomerically pure unusual ellagitannins (cercidinins **A** and **B**). Esterification reaction of racemic hexabenzyloxydiphenic acid **78** with the appropriate benzylidine sugar **79** afforded a racemic mixture of compounds (*S*)-diastereomer [(*S*)-D] **80** and (*R*)-diastereomer [(*R*)-D] **81** (Scheme 24).



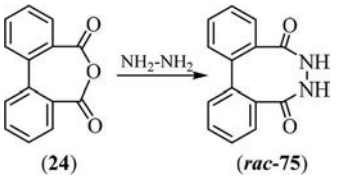
(66) (67) (68)

69a: $R_1=R_2=R_3=H$
b: $R_1=R_2=R_3=OCH_3$

Scheme 20.



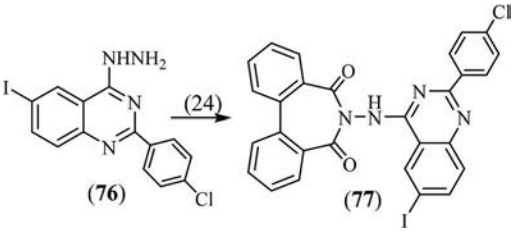
Scheme 21.



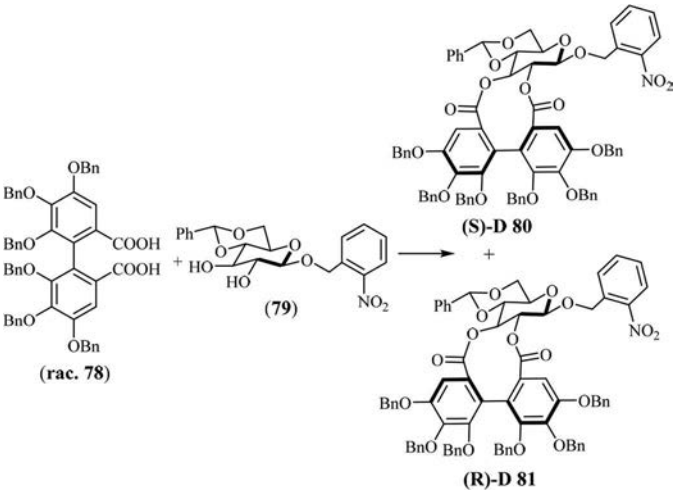
Scheme 22.

As per Itoh et al.'s[65] methodology for kinetic resolution of racemic hexamethoxydiphenic acid, alkaline hydrolysis of (*R*)-D **81** using anhydrous potassium hydroxide led to the optically pure (d)-hexabenzyloxydiphenic acid **82**. The removal of benzylidenacetal of (*R*)-D **81** under acidic conditions took place to afford the diol **83** in 86% yield. The esterification of diol **83** with tribenzylgallic acid yielded the sugar derivative (*R*)-D **84** (Scheme 25).

The (*R*)-D-**84** was subsequently subjected to irradiation and purification of the crude product was performed easily by column chromatography on silica gel to afford the anomerically deprotected derivative **73** in 88% yield. The debenzylation of compound **85** by



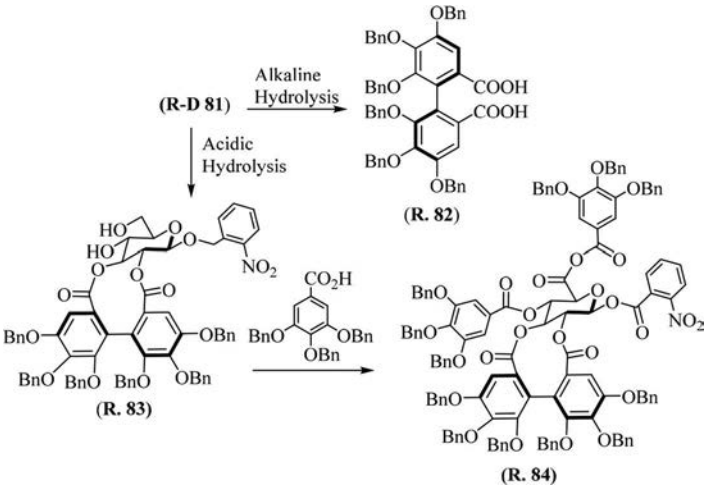
Scheme 23.



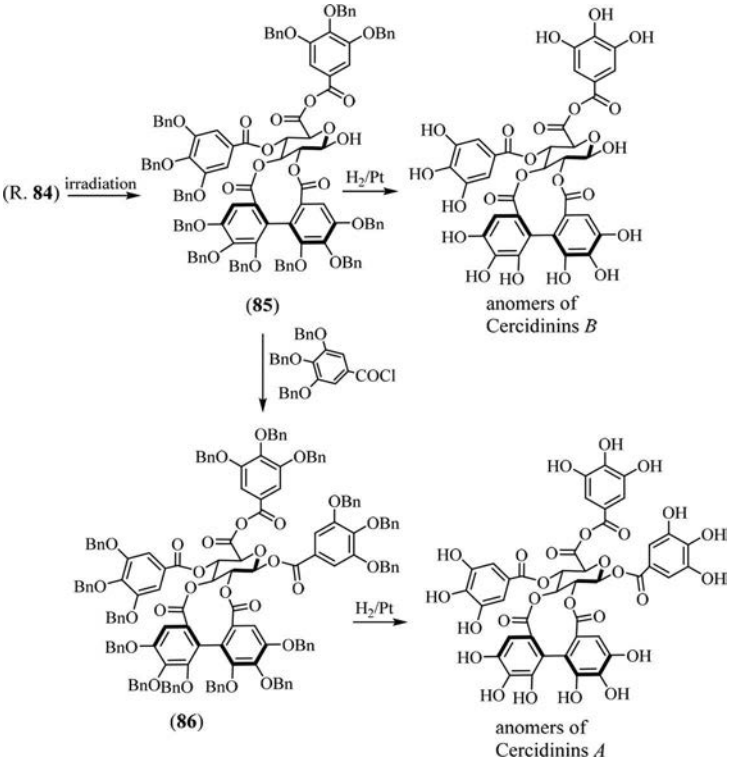
Scheme 24.

hydrogenolysis with H_2 and Pd/C also yielded a mixture of *R*, α, β-anomers of cercidinin **B**. Acylation of the α, β-anomeric mixture **85** with 3,4,5-tri-*o*-benzylgalloyl chloride under β-selective reaction conditions[22] in the presence of TEA led exclusively to the formation of the desired compound **86** in 69% yield. Finally, the cleavage of the benzyl ether groups of the β-galloyl anomer **86** by hydrogenolysis closed this synthetic sequence, affording the desired compound cercidinin **A** in 89% yield (Scheme 26).

Capozzi et al.[66] have reported a special study on the reaction of diphenic acid with a rhamnose and glucose template to afford unusual ellagitannin. Author was observed the chiral scaffold of glucose (diequatorial 2,3-hydroxyl groups) that exerts a remarkable stronger atropdiastereo selective effect onto the diphenoyl group than the rhamnose ring (axialequatorial 2,3-hydroxyl groups). Thus, the rhamnose template **87** was reacted under



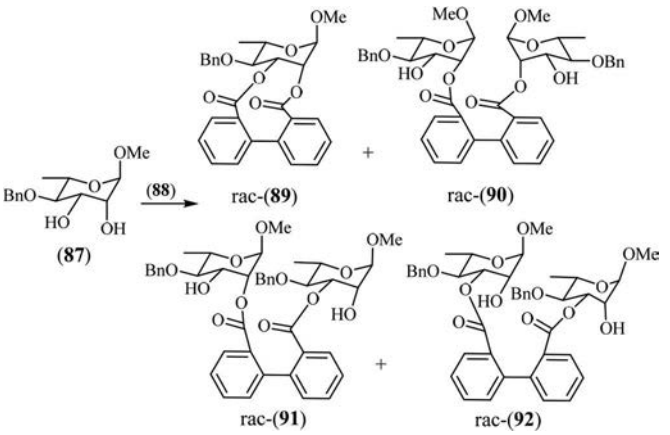
Scheme 25.



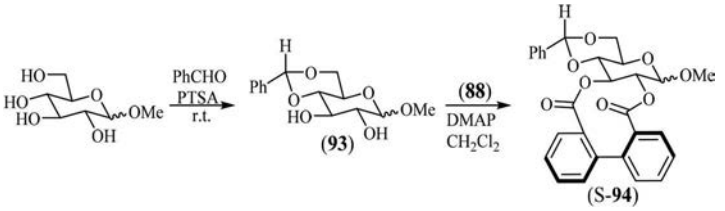
Scheme 26.

different conditions with the conformationally flexible diphenoyl chloride **88**. Independently of reaction conditions, five different products were formed: two cyclic diesters **89** and the flexible open-chain diesters[67] **90–92** (Scheme 27).

On the other hand, reaction of diphenoyl chloride **88** with a conformationally more rigid template **93** (prepared by treatment of methyl glucose with benzaldehyde in the



Scheme 27.



Scheme 28.

presence of *p*-toluenesulfonic acid) afforded only one atrop diasterioisomer **94**, meaning that the diesterification of **93** had occurred with total diasteroselectivity (Scheme 28).[67]

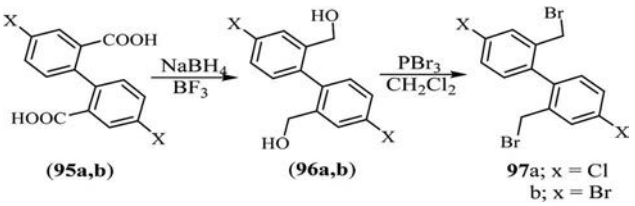
Reduction with sodium borohydride. Reduction of diphenic acids **95a,b** into the diol **96a,b** was obtained using sodium borohydride and $BF_3 \cdot Et_2O$ as the activating Lewis acid. The crude diol **96** was allowed to react with PBr_3 to obtain the dibenzyl dibromide[68] **97** in a yield of 48%[69] (Scheme 29).

It was shown that reduction of unsubstituted imide of diphenic acid **98a** by 2 moles of $NaBH_4$ in methanol results in forming the mixture of four products. Only the main reaction product which is the amide of 2′-hydroxymethylbiphenil-2-carboxylic acid (**99a**) was extracted individually. One more product of this reaction by the data of TLC is probably 7H-dibenzo[*c,e*]oxepine-5-one (**100**). *N*-substituted imides **98b–e** is reduced with 2 moles of $NaBH_4$ in methanol exclusively to acyclic *N*-substituted amides of 2′-hydroxymethylbiphenil-2-carboxylic acid (**99b–e**). While, the reduction of *N*-(antipyryl-4) imide of diphenic acid **98f** under similar conditions results in the removal of molecule of 4-aminoantipyrin and accompanied with the formation of 7H-dibenzo-[*c,e*] oxepine-5-one (**100**). It is obvious that relative *N*-(antipyryl-4) amidis formed nevertheless during the reaction, however, its existence turns out to be energy unfavorable may be owing to steric problems; then it dissociates forming two more stable molecules of 4-aminoantipyrin and 7H-dibenzo[*c,e*]oxepine-5-one (**100**)[70] (Scheme 30).

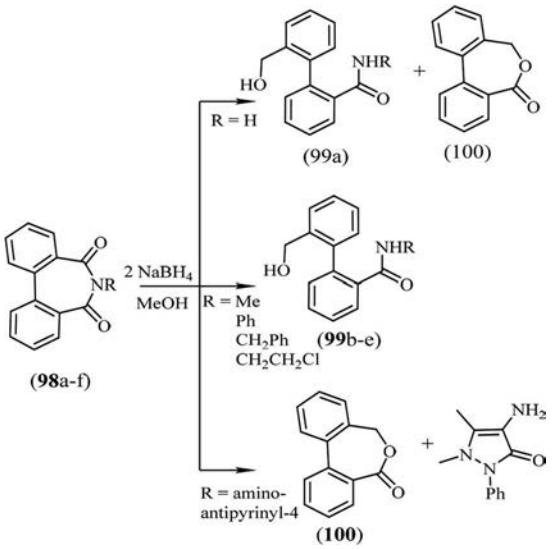
Electrophilic reactions

Nitration of diphenic acid. 4,4′-Diaminodiphenic acid (**103**) has received attention due to its importance for the synthesis of biologically active compounds.[71] Thus, Rubezhov[72] reported the direct nitration of diphenic acid **1** followed by catalytic hydrogenation to afford a mixture of 4,4′-diaminodiphenic acid **103** and 3-amino-5,6-dihyrobenz-[*c*] quinolin-l0-carboxylic acid (**104**) through dinitro derivatives **101** and **102** (Scheme 31).

Also, reduction of the diester derivative **105** by H_2/Pt afforded 2,2′-diamino-6,6′-dimethoxycarboxylbiphenyl (**106**) through the dihydroxamic acid intermediate.



Scheme 29.

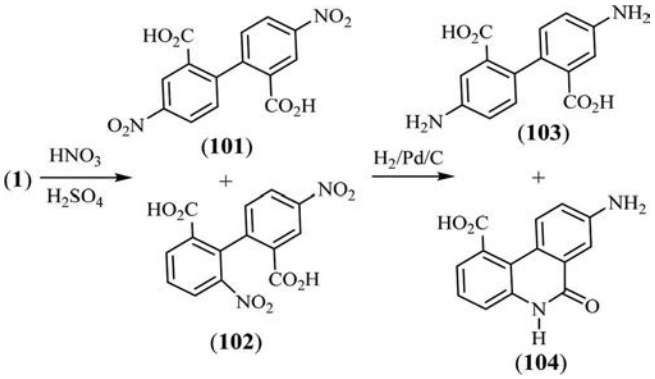


Scheme 30.

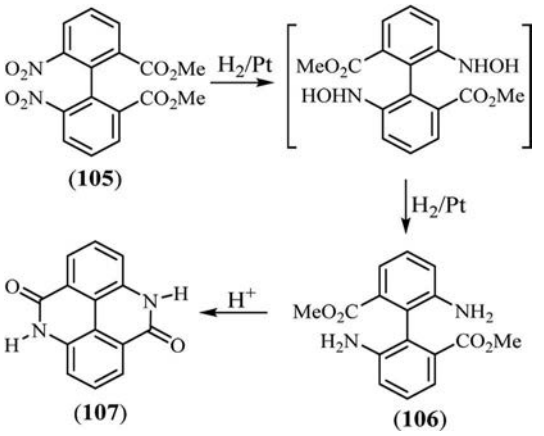
Compound **106** readily undergoes cyclization to 4,5,9,10-tetrahydro-4,9-diazapyrene (**107**) when heated with mineral acid[73] (Scheme 32).

Olefination. Direct olefination reactions on aromatic rings involving regioselective C–H bond cleavage have been developed to provide more simple synthetic routes for vinylarene derivatives.[74,75] Thus, ortho-olefination of diphenic acid can be achieved effectively through rhodium-catalyzed oxidative coupling with styrene to afford mixture of mono-**108** and di-olefinated product **109**[76] (Scheme 33).

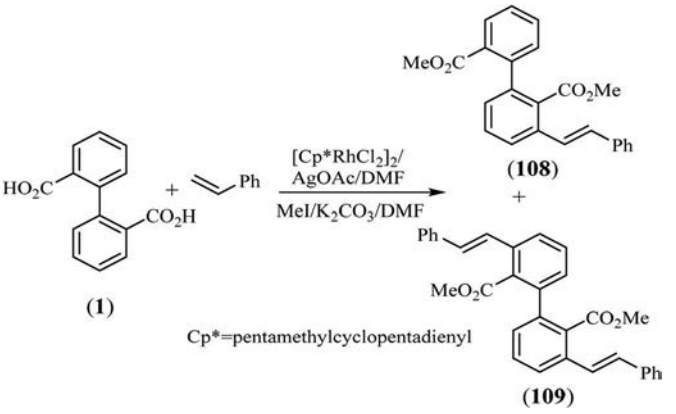
On the other hand, the intermolecular coupling of aromatic substrates with alkynes by transition metal catalysis was recognized to be a powerful tool to construct π-conjugated molecules.[77] Particularly, 3,3′,4,4′-tetrapropyl [8,8′-bi-1H-2-benzopyran-]-1,1′-dione (**111**) was obtained through rhodium-catalyzed oxidative coupling of diphenic acid with internal alkyne such as 4-Octyne **110**[78] (Scheme 34).



Scheme 31.

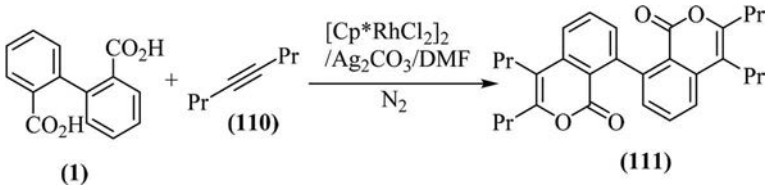


Scheme 32.



Scheme 33.

Formation of fluorenones. Treatment of diphenic acid **1** with sulfuric acid gives the corresponding fluorenone **112**.[79] Reaction of fluorenones **112** with excess phenol afforded 9,9-bis(4-hydroxyphenyl)-9H-fluorene-4-carboxylic acid (**113**). Also, poly(aryl ether ketone)s containing carboxyl acid group attached to fluorenyl **115** was prepared through the reaction of fluorene derivative **113** with bis(4-fluorophenyl)methanone **114** (Scheme 35).



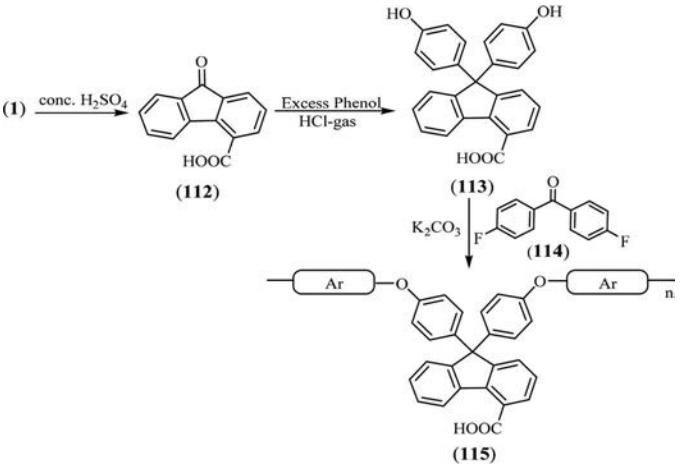
Scheme 34.

Syntheses and effects of compounds containing the diphenic acid moiety

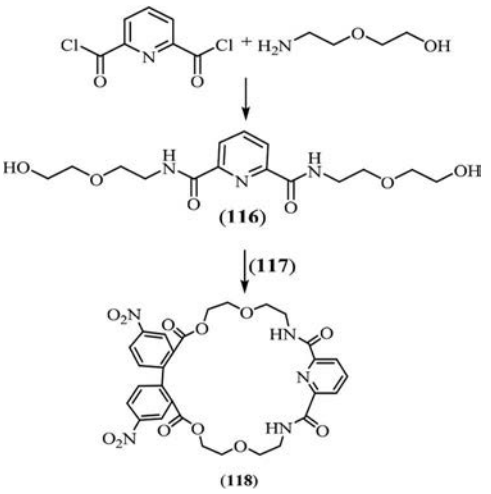
Synthesis of macrolactam

Biphenyl macrolactam was used as amide-based macrocyclic anion sensors in complexation of anion species and the selective colorimetric sensing of fluoride.[80] Reaction of bis-amide **116**[81] with the dichloride of 4,4′-dinitro-2,2′-diphenic acid **117** produced ligand **118** (Scheme 36).

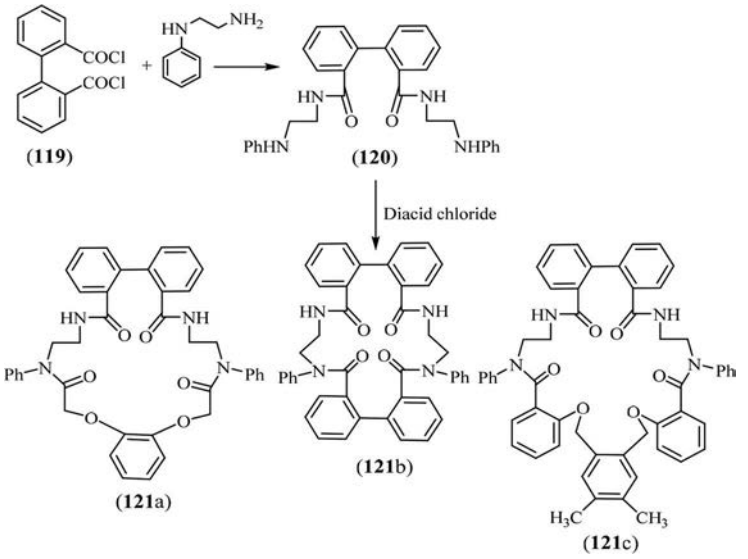
Tetra aza macrocyclic complexes have been screened for their biological activity.[82] Thus, diamide **120** was obtained in 60% yield by the reaction of diphenic acid chloride **119** with 2.1 equivalent of *N*-phenyl ethylene diamine in the presence of TEA. Also, cyclophane tetra-amides **121a–c** were obtained by the reaction of diamide **120** with diacid



Scheme 35.



Scheme 36.

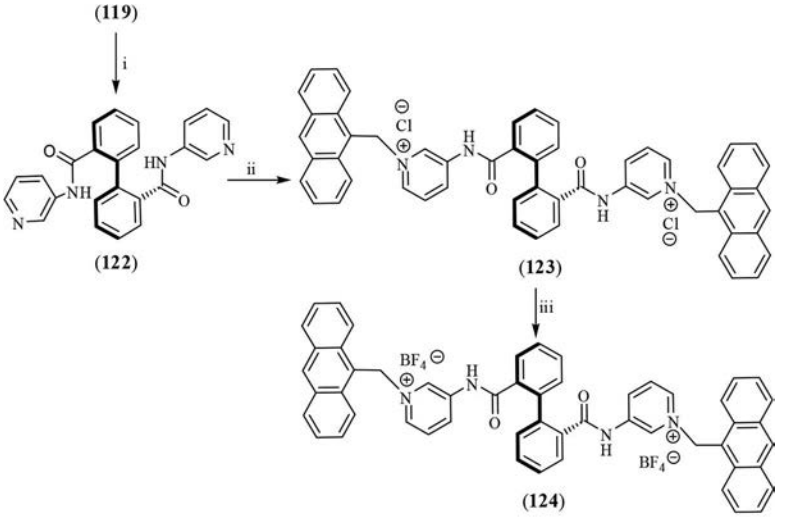


Scheme 37.

chlorides in the presence of triethyl amine under high dilution conditional reflux in chloroform[83] (Scheme 37).

Synthesis of fluorescent receptor

A fluorescent receptor for anion **124** built on biphenyl motif has been designed and synthesized according to Scheme 38. Initially, by the reaction of diphenoyl chloride **119** with 3-aminopyridine afforded the diamide **122**. On refluxing diamide **122** in the presence of



i: 3-aminopyridine,$SOCl_2$, ii: 9-chloroethylanthracene, iii: NH_4PF_6

Scheme 38.

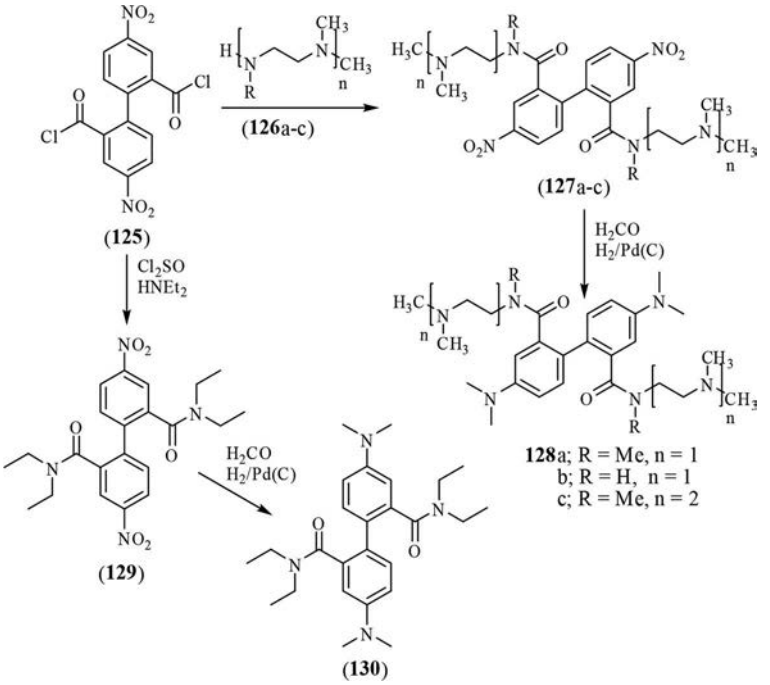
9-chloromethylanthracene, the chloride salt **123** was obtained, the anion exchange using NH_4PF_6 gave the receptor **124** as light yellow solid.[84]

A new polyazapodands containing a 4,4′-substituted biphenyl moiety has been synthesized by Costero et al.,[85] who clearly suggest that a modification in the dihedral angle between the biphenyl rings is an important factor in determining the fluorescent response of the molecule. The fluorescence is pH dependent, due to the formation of intramolecular hydrogen bonds between protonated aliphatic nitrogens and carbonyl oxygen. The synthesized ligands were prepared through treatment of 4,4′-dinitro-2,2′-diphenic acid chloride **125** with the corresponding polyamines **126a–c** provided compounds **127a–c**, which were converted into **128a–c**, respectively, by the reaction with formaldehyde under reducing conditions (H_2, Pd(C)). In addition, compound **130** was prepared for use in control experiments (Scheme 39).

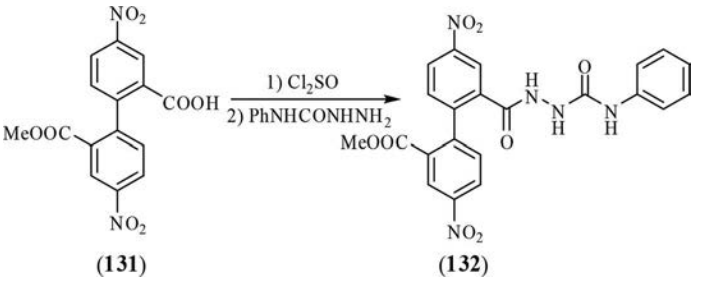
Also, as a further advancement in the field of colorimetric chemodo-simeters, Costero et al.[86] have reported the preparation of ligand **132** which is useful for the selective recognition of benzoate versus other aromatic carboxylates. The monomethylester of 4,4′-dinitro-2,2′-diphenic acid (**131**)[87] was transformed into its acyl chloride by the reaction with thionyl chloride. The subsequent treatment with 4-phenylsemicarbazide gave rise to compound **132** (Scheme 40).

Synthesis of polymer

Highly branched macromolecules including hyperbranched polymers have attracted considerable and increasing interest due to their fascinating unique structure, interesting



Scheme 39.



Scheme 40.

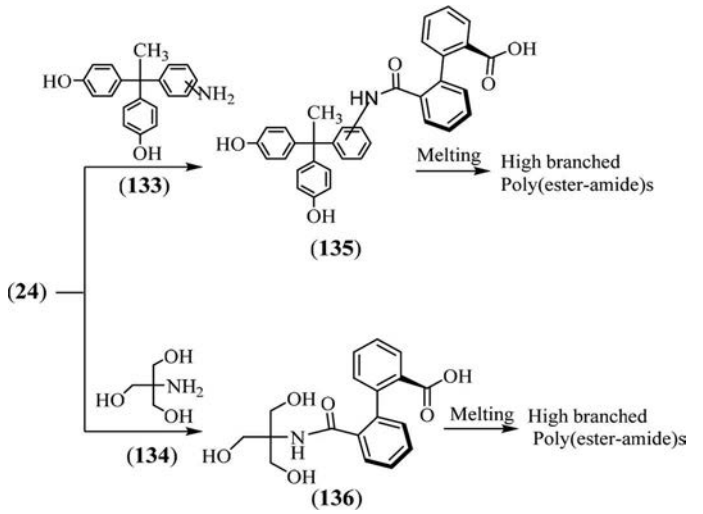
and versatile performance, and promising applications.[88–91] Li et al.[92] synthesized aromatic and semiaromatic hyperbranched poly(ester-amide)s **135** and **136** from the reaction of diphenic anhydride **24** with multihydroxyl primary amines **133** and **134** (Scheme 41).

Also, two-dimensional (2D) coordination polymer $[Zn\text{-}(ATZ)_2]_n$ (HATZ = 5-amino-1H-tetrazole) featuring a 2D + 2D → 2D pillar-layer array was synthesized, wherein two honeycomb-shaped $Zn(ATZ)_{1.5}$ sublayers can be stitched together by 2,2′-biphenyl-dicarboxylic acid bridging linkers of varied length and type to generate 4 three-dimensional (3D) isoreticular noninterperpentrated frameworks under solvothermal conditions.[93]

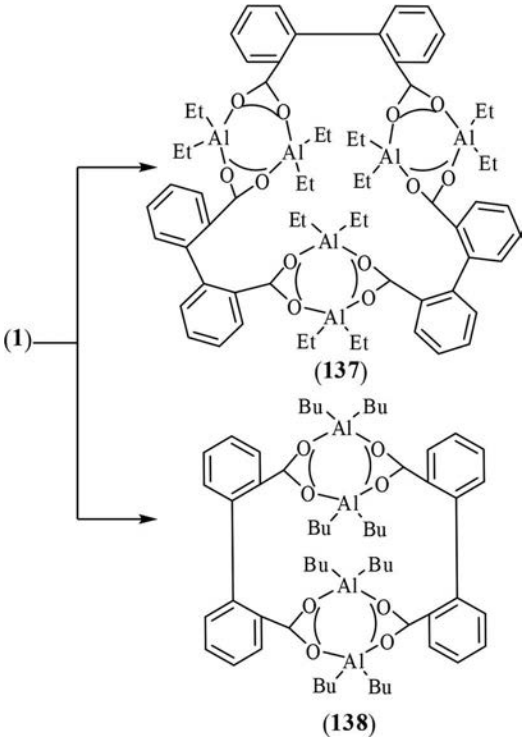
Complexation

Diphenic acid **1** reacted with R_3Al (R=Et, *i*-Bu) in a 1:2 molar ratio to produce the dialkylaluminum dicarboxylates $[Et_4Al_2(OOCC_{12}H_8COO)]_3$ (**137**) and $[i\text{-}Bu_4Al_2\text{-}(OOCC_{12}H_8COO)]_2$ (**138**) (Scheme 42). Compounds **137** and **138** were isolated in 55 and 40% yield, respectively.[94]

Cobalt metal–organic material of 2,2′-biphenyl dicarboxylic acid and benzimidazole has been synthesized under solvothermal conditions. On the addition of benzimidazole as a



Scheme 41.



Scheme 42.

neutral ligand to the reaction mixture, the dimentionality of the resulting coordination polymer increases, resulting a multilayered structures. The complex shows good thermal stability which was confirmed by thermal analysis.[95] Also, the complexes of diphenic acid with Co^{II} and Cu^{II} metals and diphenic acid/nicotinamide-mixed ligand with Co^{II} and Zn^{II} metals were synthesized and characterized by Sahin et al.[96] The pure ligand complexes of diphenic acid ($C_{14}H_{16}O_8Co$ (**139**), $C_{14}H_{16}O_8Cu$ (**140**)), and mixed ligand complexes of diphenic acid/nicotinamide ($C_{40}H_{38}N_4O_{14}Co$ (**141**), $C_{40}H_{38}N_4O_{14}Zn$ (**142**)) are similar to each other and they have $P2_1$,$P2_1/n$, and P1 space groups. The diphenic acid ligands in **139** and **140** complexes were coordinated to metal cations as dianionic bridge and in the others complexes (**141** and **142**), it was involved as monoanionic counterion.

References

[1] Kaur, S.; Jaggi, R. K. *Indian J. Exp. Biol.* **2010**, *48*, 925–930.
[2] Ali, M.; Bhutani, K. K. *Indian J. Nat. Prod.* **1991**, *7*, 16–17.
[3] Clifford, M. N.; Scalbert, A. *J. Sci. Food Agric.* **2000**, *80*, 1118–1125.
[4] Ayrton, A. D.; Lewis, D. F. V.; Walker, R.; Ioannides, C. *Food Chem. Toxicol.* **1992**, *30*, 289–295.
[5] Hirose, M.; Akagi, K.; Hasegawa, R.; Yaono, M.; Satoh, T., Hara, Y.; Wakabayashi, K.; Ito, N. *Carcinogenesis* **1995**, *16*, 217–221.
[6] Liu, T.; Mokuolu, A. O.; Rao, C. V.; Reddy, B. S.; Holt, P. R. *Gastroenterologica* **1995**, *109*, 1167–1172.
[7] Mertz, C.; Cheynier, V.; Gunata, Z.; Brat, P. *J. Agric. Food Chem.* **2007**, *55*, 8616–8624.

[8] Hollman, H. C. P.; Heltog, L. G. M.; Katan, B. M. *Food Chem.* **1996**, *57*, 43–46.
[9] Bravo, L. *Nutr. Rev.* **1998**, *56*, 317–333.
[10] Sellappan, S.; Akoh, C. C.; Krewer, G. J. *Agric. Food Chem.* **2002**, *50*, 2432–2438.
[11] Wang, Y. S.; Lin, S. H. *J. Agric. Food Chem.* **2000**, *48*, 140–146.
[12] Wada, L.; Ou, B. *J. Agric. Food Chem.* **2002**, *50*, 3495–3500.
[13] Charlton, J. L. *J. Nat. Prod.* **1998**, *61*, 1447–1451.
[14] Quideau, S.; Felman, K. S. *Chem. Rev.* **1996**, *96*, 475–504.
[15] Medda, S.; Mukhopadhyay, S.; Basu, M. K. *J. Antimicrob. Chemother.* **1999**, *44*, 791–794.
[16] Borejsza-Wysocki, W.; Lester, C.; Attygalle, A. B.; Hrazdina, G. *Phytochemistry* **1999**, *50*, 231–235.
[17] Kogan, P.; Dupré, B.; Keller, K. M.; Scott, I. L.; Bui, H.; Market, R. V.; Beck, P. J.; Voytus, J. A.; Revelle, B. M.; Scott, D. J. *J. Med. Chem.* **1995**, *38*(8), 4976–4984.
[18] Itoh, T.; Shirakami, S.; Nakao, Y.; Yoshida, T. *Chem. Lett.* **1998**, *27*, 979–980.
[19] Itoh, T.; Shirakami, S.; Ishida, N.; Yamashita, Y.; Yoshida, T.; Kim, H. S.; Wataya, Y. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 1657–1659.
[20] Pearson, A. J.; Heo, J. N. *Org. Lett.* **2000**, *2*, 2987–2990.
[21] Nicolaou, K. C.; Boddy, C. N. C.; Bräse, S.; Winssinger, N. *Angew. Chem. Int. Ed.* **1999**, *38*, 2096–2152.
[22] Haddock, E. A.; Gupta, R. K.; Al-Sha, S. M. K.; Layden, K.; Haslam, E.; Magnolato, D. *Phytochemistry* **1982**, *21*, 1049–1062.
[23] Williamson, G.; Manach, C. *Am. J. Clin. Nutr.* **2005**, *81*, 243S–255S.
[24] Williams, L. R.; Spencer, E. P. J.; Rice-Evans, C. *Free Radical Biol. Med.* **2004**, *36*, 838–849.
[25] Kiely, S.; John, H. S. *US Patent* **1986**, *4*, 786, 755.
[26] Ohemeng, K. A.; Podlogar, B. L.; Nguyen, V. N.; Bernstein, J. I.; Krause, H. M.; Hilliard, J. J.; Barrett, J. F. *J. Med. Chem.* **1997**, *40*, 3292–2396.
[27] Springer, D. M.; Bronson, J. J.; Mansuri, M. M.; Nettleton, D. O.; Tramposch, K. M. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2669–2672.
[28] Springer, D. M.; Luh, B. Y.; Bronson, J. J.; McElhone, K. E.; Mansuri, M. M.; Gregor, K. R.; Nettleton, D. O.; Stanley, P. L.; Tramposch, K. M. *Bioorg. Med. Chem.* **2000**, *8*, 1087–1109.
[29] Hall, I. H.; Wong, O. T.; Simlot, R.; Reynolds, D. *J. Pharm. Res.* **1992**, *9*, 1324–1329.
[30] Kong, X. W.; Zhang, Y. H.; Wang, T.; Lai, Y. S.; Peng, S. X. *Chem. Biodiversity* **2008**, *5*, 1743–1752.
[31] Ganjian, I.; Khorshidi, M.; Lalezari, I. *J. Heterocyclic Chem.* **1991**, *28*, 1173–1175.
[32] Botrel, P. A.; Guerillot, C. R. *J. Chim. Phys.* **1974a**, *71*, 1240.
[33] Botrel, P. A.; Guerillot, C. R. *J. Chim. Phys.* **1974b**, *71*, 1293.
[34] Ullmann, F. B. *J. Chem. Ber.* **1901**, *34*, 2174–2185.
[35] Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1470.
[36] Wang, D. H.; Cheng, S. Z. D.; Harris, F. W. *Polymer* **2008**, *49*, 3020–3028.
[37] Liebeskind, L. S.; Zhang, S.; Zhang, D. *J. Org. Chem.* **1997**, *62*, 2312–2313.
[38] Meyers, A. I.; Nelson, T. D. *Tetrahedron Lett.* **1994a**, *35*, 3259–3262.
[39] Meyers, A. I.; Nelson, T. D. *J. Org. Chem.* **1994b**, *59*, 2577–2580.
[40] Takagi, K.; Hossain, K. M.; Shibata, T. *Synlett* **2000**, *2000*, 1137–1138.
[41] Barakat, S.; El-Zahabi, M. A. A.; Abdel-Rahman, A. A.; Bayomi, A. H.; Ali, H. E.; Amin, M. A. *J. Med. Sci.* **2007**, *14*, 3–17.
[42] Khanbabaee, K.; Basceken, S.; Florke, U. *Tetrahedron: Asymmetry* **2006**, *17*, 2804–2812.
[43] Zheng, Q.; Liu, Z.; Wang, J. *Adv. Mater. Res.* **2013**, *112*, 634–638.
[44] Seo, J. S.; Keum, Y. S.; Li, Q. X. *Int. J. Environ. Res. Public Health* **2009**, *6*, 278–309.
[45] Vila, J.; Lopez, Z.; Sabate, J.; Minguillon, C.; Solanas, A. M.; Grifoll, M. *Appl. Environ. Microbiol.* **2001**, *67*, 5497–5505.
[46] Liang, Y.; Gardner, D. R.; Miller, C. D.; Chen, D.; Anderson, A. J.; Weimer, B. C.; Sims, R. C. *Appl. Environ. Microbiol.* **2006**, *72*, 7821–7828.
[47] Kim, S. J.; Kweon, O.; Jones, R. C.; Freeman, J. P.; Edmondson, R. D.; Cerniglia, C. E. *J. Bacteriol.* **2007**, *189*, 464–472.
[48] Barakat, E. S.; El-Zahabi, M. A.; Radwan, M. F. *Saudi Pharm J.* **2000**, *8*, 110–115.

[49] Elzahabi, H. S. A.; Salem, M. A.; Thabet, H. Kh. *Der Pharma Chem.* **2011**, *3*, 48–58.
[50] Bera, M. K.; Domínguez1, M.; Hommes, P.; Reissig, H. *Beilstein J. Org. Chem.* **2014**, *10*, 394–404.
[51] Gómez, M.; Jansat, S.; Muller, G.; Maestro, M. A.; Mahía, J. *Organometallics* **2002**, *21*, 1077–1087.
[52] El-Zahabi, M. A.; Gad, L. M.; Bamanie, F. H.; Al-Marzooki, Z. *Med. Chem. Res.* **2012**, *21*, 75–84.
[53] Karle, I. L.; Venkateshwarlu, P.; Ranganathan, S. *Biopolymers(Peptide Science)* **2006**, *84*, 502–507.
[54] Karle, I. L.; Venkateshwarlu, P.; Nagaraj, R.; Vijay, D.; Sastry, N. G.; Ranganathan, S. *Chemistry* **2007**, *13*, 4253–4263.
[55] Ohemeng, K. A.; Podlogar, B. L.; Nguyen, V. N.; Bernstein, J. I.; Krause, H. M.; Hilliard, J. J.; Barrett, J. F. *J. Med. Chem.* **1997**, *40*, 3292–3296.
[56] Costero, A. M.; Sanchis, J.; Peransi, S.; Gil, S.; Sanza, V.; Domenechb, A. *Tetrahedron* **2004**, *60*, 4683–4691.
[57] Bringmann, G.; Menche, D. *Acc. Chem. Res.* **2001**, *34*, 615–624.
[58] Hattori, T.; Shimazumi, Y.; Goto, H.; Yamabe, O.; Morohashi, N.; Kawai, W.; Miyano, S. *J. Org. Chem.* **2003**, *68*, 2099–2108.
[59] Vorogushin, A. V.; Wulff, W. D.; Hansen, H.-J. *J. Am. Chem. Soc.* **2002**, *124*, 6512–6513.
[60] Song, Y. C.; Okamoto, S.; Sato, F. *Tetrahedron Lett.* **2002**, *43*, 8635–8637.
[61] Lenev, D. A.; Lyssenko, K. A.; Golovanov, D. G.; Weingart, O.; Busc, V.; Kostyanovskya, R. G. *Tetrahedron: Asymmetry* **2004**, *15*, 537–543.
[62] Mosaad, S. M.; Mohammed, K. I.; Ahmed, M. A.; Abdel-Hamide, S. G. *J. Biol. Sci.* **2004**, *4*, 504–509.
[63] Khanbabaee, K.; Lötzerich, K. *Liebigs Ann.* **1997**, *7*, 1571–1575.
[64] Khanbabaee, K.; Lötzerich, K. *J. Org. Chem.* **1998**, *63*, 8723–8728.
[65] Itoh, T.; Chika, J.; Shirakami, S.; Ito, H.; Yoshida, T.; Kubo, Y.; Uenishi, J. *J. Org. Chem.* **1996**, *61*, 3700–3705.
[66] Capozzi, G.; Ciampi, C.; Delogu, G.; Menichetti, S.; Nativi, C. *J. Org. Chem.* **2001**, *66*, 8787–8792.
[67] Feldman, K. S.; Sahasrabudhe, K. *J. Org. Chem.* **1999**, *64*, 209–216.
[68] Ciszek, J. W.; Tour, J. M. *Tetrahedron Lett.* **2004**, *45*, 2801–2803.
[69] Tolbert, L. M.; Ali, M. Z. *J. Org. Chem.* **1982**, *47*, 4793–4795.
[70] Yanovskiy, V. A.; Baturin, D. M.; Yagovkin, A.; Yu.; Bakibaev, A. A. *Bull. Томск Polytech. Univ.* **2007**, *311*, 93–97.
[71] Ding, W. D.; Mitsner, B.; Krishnamurthy, G.; Aulabaugh, A.; Hess, C. D.; Zaccardi, J.; Cutler, M.; Feld, B.; Gazumyan, A.; Raifeld, Y.; Nikitenko, A.; Lang, S. A.; Gluzman, Y.; OHara, B.; Ellestad, G. A. *J. Med. Chem.* **1998**, *41*, 2671–2675.
[72] Rubezhov, A. *Org. Prep. Proced. Int.* **2006**, *38*, 401–404.
[73] Borovlev, I. V.; Demidov, O. P. *Chem. Heterocycl. Compd.* **2003**, *39*, 1417–1442.
[74] Karimi, B.; Behzadnia, H.; Elhamifar, D.; Akhavan, P. F.; Esfahani, F. K. *Synthesis* **2010**, *2010*, 1399–1427.
[75] Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624–655.
[76] Mochida, S.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2011**, *76*, 3024–3033.
[77] Balme, G.; Bouyssi, D.; Monteiro, N. Metal-catalyzed multicomponent reactions. In *Multicomponent Reactions*; J. Zhu, H. Bienaymé (Eds.); Wiley-VCH Verlag GmbH & Co. KGaA: Weinheim, FRG, 2005; pp. 224–276.
[78] Shimizu, M.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 3478–3483.
[79] Liu, B.; Hu, W.; Robertsona, G. P.; Guiver, M. D. *Mater. Chem.* **2008**, *18*, 4675–4682.
[80] Costero, A. M.; Ban˜uls, M. J.; Aurell, M. J.; Wardb, M. D.; Argentb, S. *Tetrahedron* **2004**, *60*, 9471–9478.
[81] Kumar, S.; Hundal, M. S.; Kaur, N.; Singh, R.; Singh, H.; Hundal, G.; Ripoll, M. M.; Aparicio, J. S. *J. Org. Chem.* **1996**, *61*, 7819–7825.
[82] Ashu, C.; Saurabh, D.; Ratan, S.; Singh, R. V. *J. Ind. Chem. Soc.* **2002**, *79*, 371–373.

[83] Rajakumar, P.; Abdul Rasheed, A. M.; Balu, P. M.; Murugesan, K. *Bioorg. Med. Chem.* **2006**, *14*, 7458–7467.
[84] Ghosh, K.; Sarkar, A. R.; Patra, A. *Tetrahedron Lett.* **2009**, *50*, 6557–6561.
[85] Costero, A. M.; Sanchis, J.; Gil, S.; Sanz, V.; Arelano, M. C. R.; Williams, J. A. G. *Supramol. Chem.* **2004a**, *16*, 435–446.
[86] Costero, A. M.; Peransi, S.; Gil, S. *Tetrahedron Lett.* **2006**, *47*, 6561–6564.
[87] Costero, A. M.; Sanchis, J.; Peransi, S.; Gil, S.; Sanz, V.; Domenech, A. *Tetrahedron* **2004b**, *60*, 4683–4691.
[88] Gao, C.; Yan, D. *Prog. Polym. Sci.* **2004**, *29*, 183–275.
[89] Harth, E. M.; Hecht, S.; Helm, B.; Malmstrom, E. E.; Fréchet, J. M. J.; Hawker, C. J. *J. Am. Chem. Soc.* **2002**, *124*, 3926–3938.
[90] Voit, B. *J. Polym. Sci., Polym. Chem.* **2000**, *38*, 2505–2525.
[91] Peng, H.; Luo, J.; Cheng, L.; Lam, J. W. Y.; Xu, K.; Dong, Y.; Zhang, D.; Huang, Y.; Xu, Z.; Tang, B. Z. *Opt. Mater.* **2003**, *21*, 315–320.
[92] Li, X.; Zhan, J.; Lin, Y.; Li, Y.; Li, Y. *Macromolecules* **2005**, *38*, 8235–8243.
[93] Zhang, H.; Sheng, T.; Hu, Sh.; Zhuo, Ch.; Li, Haoran; Fu, R.; Wen, Y.; Wu, X. *Cryst. Growth. Des.* **2016**, *16*, 3154–3162.
[94] Ziemkowska, W.; Cyranski, M.; Kunicki, A. *Inorg. Chem.* **2009**, *48*, 7006–7008.
[95] Vithiya, R. R.; Madhurambal, DR. G. *Int. J. Curr. Res. Chem. Pharma. Sci.* **2015**, *2*, 74–82.
[96] Sahin, Z. S.; Sahin, O.; Daglı, Ö.; Köse, D. A. *Polyhedron* **2016**, *117*, 214–223.