

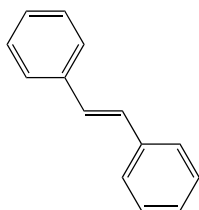
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Stilbenes Preparation and Analysis

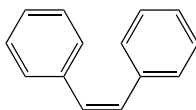
1.1

General

The name for stilbene (1,2-diphenylethylene) was derived from the Greek word *stilbos*, which means shining. There are two isomeric forms of 1,2-diphenylethylene: (*E*)-stilbene (*trans*-stilbene), which is not sterically hindered, and (*Z*)-stilbene (*cis*-stilbene), which is sterically hindered and therefore less stable.



trans-stilbene



cis-stilbene

(*E*)-Stilbene has a melting point of about 125 °C, while the melting point of (*Z*)-stilbene is 6 °C. Stilbene is a relatively unreactive colorless compound practically insoluble in water [1]. *trans*-Stilbene isomerizes to *cis*-stilbene under the influence of light. The reverse path can be induced by heat or light. The stilbene feature is associated with intense absorption and fluorescence properties, which correspond to the excitation of π -electrons of the conjugated ethenediyl group into π^* orbitals, as well as some other dynamic processes. The excited singlet state behavior of *trans*-stilbene is governed by fluorescence from the S_1 state that effectively competes with isomerization. This phenomenon of photochromism, namely, *trans*-*cis* photoisomerization of stilbene derivatives, can be readily monitored by a single steady-state fluorescence technique. A necessary stage in the olefinic photoisomerization process, in the singlet or triplet excited state, involves twisting (about the former double bond) of stilbene fragments relative to one another. The chemistry and photochemistry of stilbenes have been extensively investigated for decades and have been reviewed [2–25].

Stilbene derivatives are synthesized relatively easily, are usually thermally and chemically stable, and possess absorption and fluorescence properties that are

convenient for monitoring by relevant optical techniques. Stilbenes are widely used in the manufacture of industrial dyes, dye lasers, optical brighteners, phosphor, scintillator, and other materials. They are playing an increasingly prominent role in the area of photophysical, photochemical, biophysical, and biomedical investigations.

Hydroxylated derivatives of stilbene (stilbenoids) are secondary products of heartwood formation in trees that can act as phytoalexins (antibiotics produced by plants).

Because of the chemical stability of phenyl moiety of 1,2-diphenylethylene, stilbene is not a suitable starting compound for synthesis of stilbene derivatives. In order to form more complex molecules, it is necessary to introduce more reactive functional groups.

1.2 Classical Methods and Their Development

Many synthetic routes to stilbene derivatives have been reported, and only most important methods, which were used in the total synthesis, will be considered in this section. Figure 1.1 summarizes the five most important methods for forming the C=C bond of the 1,2-ethenediyl unit in stilbenes.

The following classical methods will be described in this section:

1. Aldol-type condensation
2. Siegrist method
3. Wittig–Horner reaction
4. Heck reaction
5. Negishi–Stille reactions
6. Barton–Kellogg–Staudinger reaction
7. McMurry reaction
8. Perkin reaction

1.2.1 Aldol-Type Condensation

Aldol-type condensation of an aromatic aldehyde with activated methylene or phenylacetic acid is a useful reaction for preparing stilbene derivatives. Starting from *para*-substituted toluenes or *para*-substituted aromatic aldehydes, one can obtain 4,4'-disubstituted stilbenes. This reaction is relatively simple but has low yield. As an example, condensation of 2,4-dinitrotoluene and 4-nitrophenylacetic acid with aromatic aldehyde was studied [26]. The reaction involves carbanion addition to the carbonyl group. The carbanion is formed by the extraction of proton from the active methylene group of 2,4-dinitrotoluene by the base (usually, piperidine). The carbanion then adds to carbon atoms of the carbonyl group of the aldehyde. The reaction will therefore be facilitated by the ease of both the formation of the

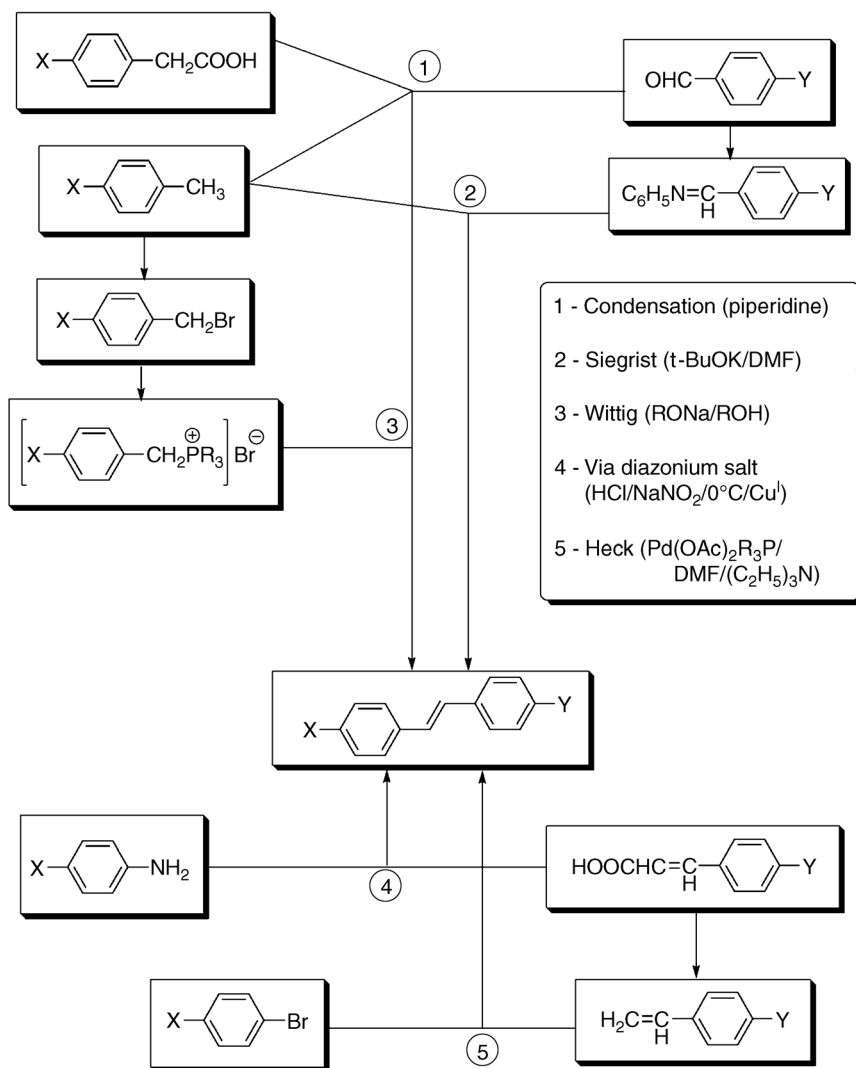


Figure 1.1 The most important synthetic routes to stilbene compounds. (Reproduced with permission from Ref. [24].)

relatively stable carbanion and the formation of the carbonium ion, which is obtained by the migration of p-electrons from carbonyl to the oxygen atom.

1.2.2

Siegrist Method

The total yield of the Siegrist method (Figure 1.1) [27] is often inferior to those of the other four methods – its main advantage is its remarkably high selectivity.

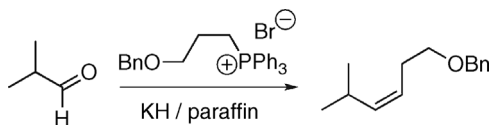


Figure 1.2 Wittig reaction using potassium hydride in paraffin. (Reproduced with permission from Ref. [30].)

For example, the synthesis of 4-methoxy-4-methyl stilbene showed that the selectivity of *cis*-configuration is 100 times more [28]. The decisive factor here in this reaction is the anti-elimination (E2) from the least energetic conformation.

1.2.3

Wittig Reaction

The Wittig reaction is the reaction of an aldehyde or ketone with a triphenyl phosphonium ylide to give an alkene and triphenylphosphine oxide. The Wittig reaction was discovered in 1954 by Georg Wittig and described in his pioneering publication titled “Über Triphenyl-phosphin-methylene als olefinbildende Reagenzien I” [29]. A recent example of the Wittig reaction is shown in Figure 1.2.

The Wittig reaction has proved to be quite versatile in the preparation of different substituted stilbenes [31–36]. This reaction is not sensitive to atmospheric oxygen, thus allowing simpler experimental procedures. It furnishes the *trans*-isomer in the stereospecific reaction. Moreover, the *trans*-isomer can be separated from the *cis*-isomer in the course of reaction because it is less soluble in the reaction solvent (usually, methanol, if sodium/lithium methoxide is used as a base) and precipitates on standing.

The Horner–Wadsworth–Emmons reaction (or HWE reaction) is the reaction of stabilized phosphonate carbanions with aldehydes (or ketones) to produce predominantly *E*-alkenes. In 1958, Horner published a modified Wittig reaction using phosphonate-stabilized carbanions [32]. Wadsworth and Emmons further defined the reaction [33]. Compared to phosphonium ylides used in the Wittig reaction, phosphonate-stabilized carbanions are more nucleophilic and more basic. Likewise, phosphonate-stabilized carbanions can be alkylated, unlike phosphonium ylides. The dialkylphosphate salt by-product is easily removed by aqueous extraction. A reliable and versatile synthesis of a stilbene derivative, 2,2-aryl-substituted cinnamic acid esters, using the Wittig reaction was reported [34–36] (Figure 1.3).

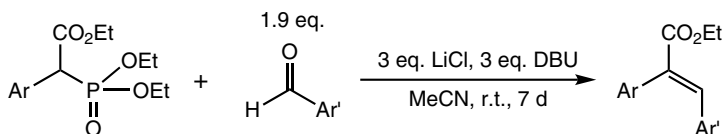


Figure 1.3 Scheme of synthesis of 2,2-aryl-substituted cinnamic acid esters. (Reproduced with permission from Ref. [36].)

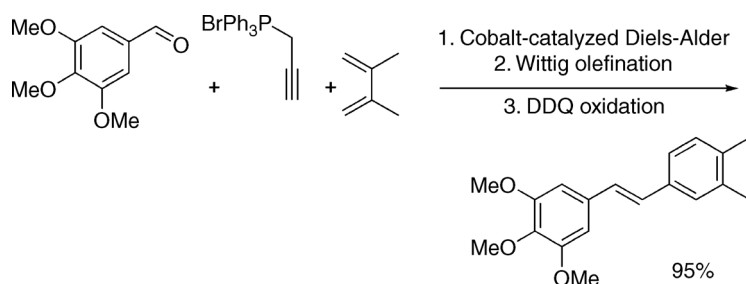


Figure 1.4 Scheme of cobalt-catalyzed Diels–Alder/Wittig olefination reaction. (Reproduced with permission from Ref. [37].)

A concise synthesis of substituted stilbenes from propargylic phosphonium salts by a cobalt-catalyzed Diels–Alder/Wittig olefination reaction has been described (Figure 1.4) [37]. It was shown that the cobalt(I)-catalyzed Diels–Alder reaction of propargylic phosphonium salts and alkyne-functionalized phosphonium salts with 1,3-dienes led to dihydroaromatic phosphonium salt intermediates that were directly used in a one-pot Wittig-type olefination reaction with aldehydes. Subsequent oxidation led to styrene- and stilbene-type products with the formation of three new carbon–carbon bonds. The reaction gives predominantly the *E*-configured products.

A convenient procedure to effect the Wittig and Horner–Wadsworth–Emmons reactions employing guanidine TBD and MTBD as base promoters was developed. Mild reaction conditions highly efficiently facilitated isolation of the final products (Figure 1.5) [38]. Further developments of the Wittig reaction have been reported [39, 40].

1.2.4

Heck Reaction

The Heck reaction (Mizoroki–Heck reaction) is the reaction of an unsaturated halide (or triflate) with an alkene and a strong base and palladium catalyst to form a substituted alkene [41, 42]. The reaction is performed in the presence of an organo-palladium catalyst. The halide or triflate is an aryl, benzyl, or vinyl compound, and the alkene contains at least one proton and is often electron deficient, such as acrylate ester or an acrylonitrile. The catalyst can be tetrakis(triphenylphosphine)palladium

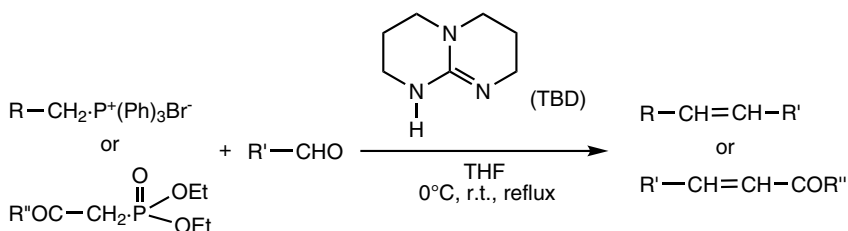


Figure 1.5 Horner–Wadsworth–Emmons reactions base-promoted with guanidine. (Reproduced with permission from Ref. [38].)

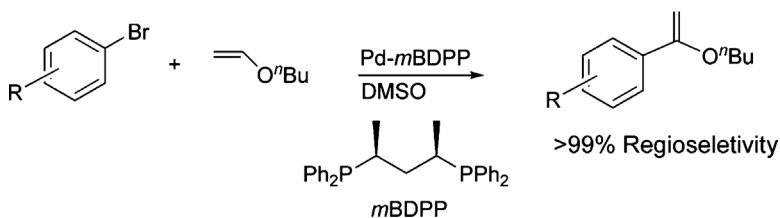


Figure 1.6 Pd-*m*BDPP-catalyzed regioselective internal arylation of electron-rich olefins by aryl halides. (Reproduced with permission from Ref. [43].)

(0), palladium chloride, or palladium(II) acetate. The ligand can be triphenylphosphine. The base is triethylamine, potassium carbonate, or sodium acetate.

An example of the Heck reaction is shown in Figure 1.6. Several reviews on this topic have been published [44–46].

A proposed mechanism of Heck reaction and other reactions using palladium compounds as catalysts and running via surface transient organometallic (STO) intermediates is presented in Figure 1.7. The formation of only one STO intermediate in all the Heck-, Suzuki-, Sonogashira-, and Stille-type coupling reactions during their reaction sequences was stressed.

The palladium(0) compound required in this cycle is generally prepared *in situ* from a palladium(II) precursor [48]. Further modifications of the Heck reaction are described in Ref. [49]. Among these modifications, the following can be considered. In the ionic

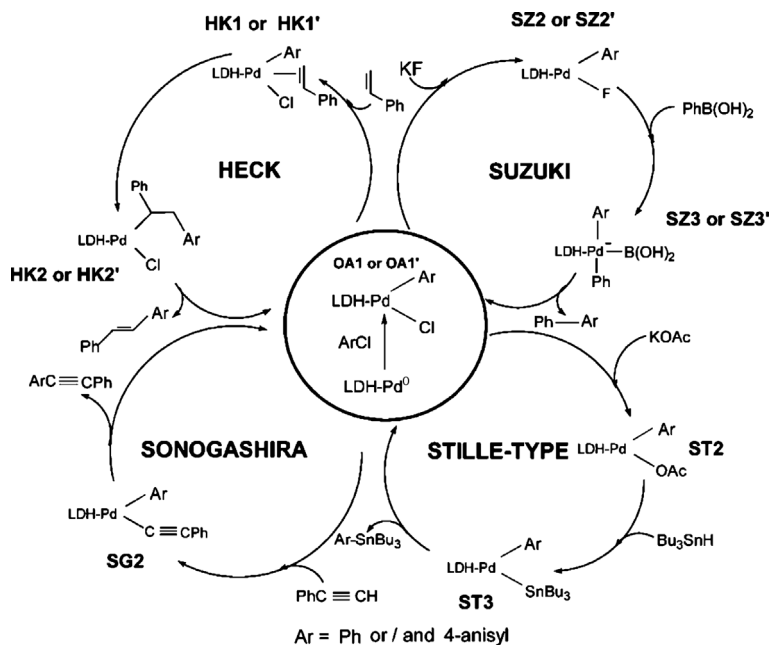


Figure 1.7 Proposed validated mechanistic cycle for the coupling reactions. (Reproduced with permission from Ref. [47].)

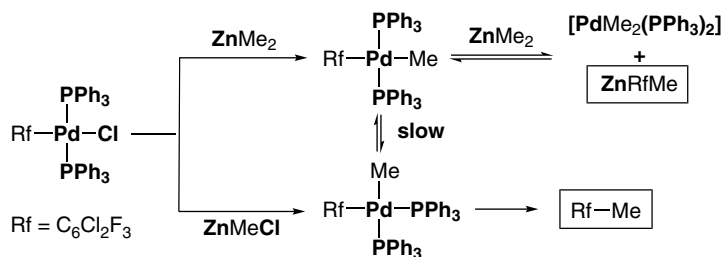


Figure 1.8 The Negishi coupling reaction and concentration/time data for the reaction 1 + ZnMe₂ obtained by ¹⁹F NMR, in THF at 298 K. Starting conditions: [1] = 1.65 × 10⁻² M. (Reproduced with permission from Ref. [52].)

liquid Heck reaction, palladium acetate and the ionic liquid (bmim)PF₆ were immobilized inside the cavities of reversed-phase silica gel. In this way, the reaction proceeded in water and the catalyst was reusable [50]. In the Heck oxyarylation modification, the palladium substituent in the *syn*-addition intermediate was displaced by a hydroxyl group, and the reaction product contained a tetrahydrofuran ring [49]. In the amino-Heck reaction, a nitrogen-carbon bond was formed. The catalyst used was tetrakis(triphenylphosphine)palladium(0) and the base was triethylamine [51].

1.2.5

Negishi–Stille Coupling

The Negishi coupling is a cross-coupling reaction between organozinc and alkenyl or aryl halide or triflate promoted by Pd catalyst (Figure 1.8).

The Stille coupling is the palladium-catalyzed cross-coupling between organotin and alkenyl or aryl halide or triflate [53–56].

In the Stille reaction mechanism (Figure 1.9), the first step in this catalytic cycle is the reduction of the palladium catalyst to the active Pd(0) species. The oxidative

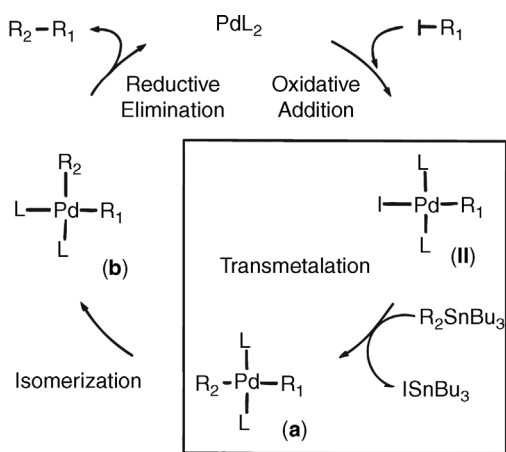


Figure 1.9 The Stille coupling mechanism [54].

addition of the organohalide gives a *cis* intermediate that rapidly isomerizes to the *trans* intermediate. Transmetalation with organostannane forms intermediate, which produces the desired product and the active Pd(0) species after reductive elimination. The oxidative addition and reductive elimination retain the stereochemical configuration of the respective reactants.

An interesting development in Stille coupling by using only catalytic amounts of tin was reported [56].

1.2.6

Barton–Kellogg–Staudinger Reaction

The Barton–Kellogg reaction (diazo-thioetone coupling) is a reaction between a ketone and a thioetone through a diazo intermediate forming an alkene [57–60]. In Ref. [59], the authors presented a new methodology to prepare sterically overcrowded alkenes by using the Barton–Kellogg method (Figure 1.10).

As versatile synthetic intermediates with a tetramethylindanylidane (stiff-stilbene) core, the *cis* and *trans* isomers of 5,16-dibromo-2,2,13',13'-tetramethylindanylidanes were synthesized by the Barton–Kellogg coupling [60].

1.2.7

McMurry Reaction

The McMurry reductive coupling reaction is an organic reaction in which two ketone or aldehyde groups are coupled to an alkene in the presence of titanium(III) chloride and a reducing agent [61, 62]. As an example, intramolecular reductive McMurry coupling reactions of bis(formylphenoxy)-substituted calix[4]arene diols mediated by titanium(IV) chloride and activated zinc followed by cyclocondensation of the diols with tetra- and penta(ethylene glycol) bistosylates provided stilbene- and crown ether-bridged calix[4]arenes. For the synthesis of stilbenes, some authors use the

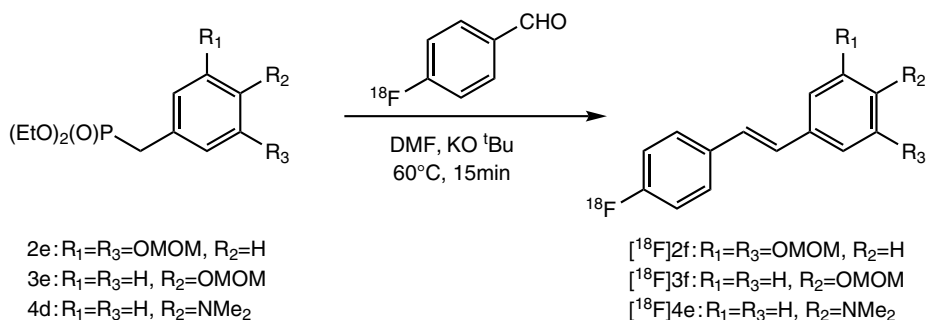
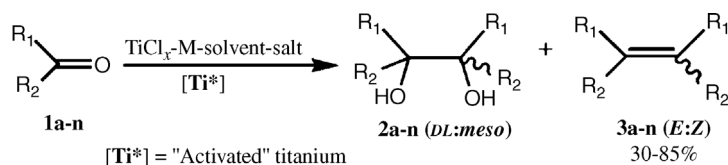


Figure 1.10 Scheme of the Barton–Kellogg reaction for modified diazo–thioetone coupling for the synthesis of overcrowded alkenes. (Reproduced with permission from Ref. [59].)



TiCl_x x = 3, 4

M (reducing metal) = Li, Mg

Solvent = THF, DME

Salt = LiCl, LiI, KCl, CsCl, MgCl₂, ZnCl₂

Aromatic carbonyls

a: R₁ = Ph, R₂ = Me

b: R₁ = 2-naphthyl, R₂ = Me

c: R₁ = 4-MeC₆H₄, R₂ = Me

d: R₁ = 4-*iso*-PrC₆H₄, R₂ = Me

e: R₁ = 4-*t*-BuC₆H₄, R₂ = Me

f: R₁ = R₂ = Ph

g: R₁ = Ph, R₂ = H

h: R₁ = 4-ClC₆H₄, R₂ = H

i: R₁ = 4-MeOC₆H₃, R₂ = H

j: R₁ = (3,4-CH₂O₂)C₆H₃, R₂ = H

Aliphatic carbonyls

k: R₁ = R₂ = *cyc*-Hex

l: R₁ = R₂ = *cyc*-Pent

m: R₁ = PhCH₂, R₂ = H

n: R₁ = *n*-C₆H₁₃, R₂ = H

Figure 1.11 McMurry olefination. (Reprinted from [64].)

Suzuki–Miyaura coupling that is the reaction of an aryl- or vinylboronic acid with an aryl or vinyl halide catalyzed by a palladium(0) complex (Figure 1.1) [63].

A combination of alkali metal salts, particularly potassium chloride, with low-valent titanium reagents generated from titanium chlorides with lithium or magnesium in either THF or DME are effective reagents for stereoselective McMurry coupling reactions of aldehydes and ketones to substituted alkenes (Figure 1.11).

1.2.8

Perkin Reaction

The Perkin reaction is an organic reaction developed by William Henry Perkin that can be used to make cinnamic acids by the aldol condensation of aromatic aldehydes and acid anhydrides in the presence of an alkali salt of the acid [65, 66].

A mild and convenient one-pot two-step synthesis of hydroxystilbenes (*E*)-4-chloro-4'-hydroxy-3'-methoxystilbene from 4-hydroxy-3-methoxybenzaldehyde and 4-chlorophenylacetic acid with *trans* selectivity developed through a modified Perkin reaction between benzaldehydes and phenylacetic acids was recently reported (Figure 1.12) [67].

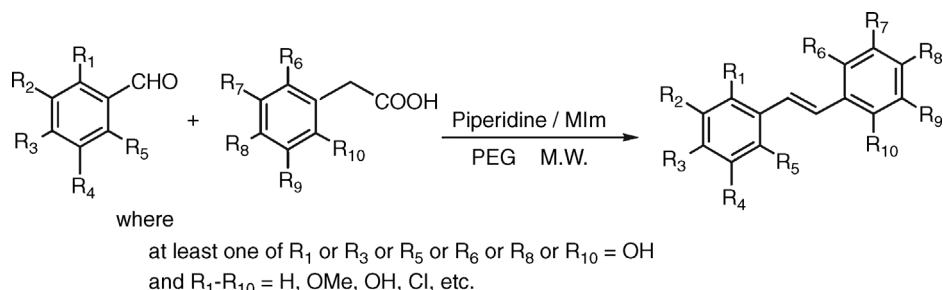


Figure 1.12 Scheme of the modified Perkin reaction. (Reprinted from [67].)

The observation of a simultaneous condensation–decarboxylation leading to the unusual formation of hydroxystilbenes in lieu of α -phenylcinnamic acid reveals an interesting facet of the classical Perkin reaction.

1.3

Miscellaneous Chemical Methods of Stilbene Synthesis

1.3.1

Palladium-Catalyzed Reactions

Pd-catalyzed cross-coupling reactions were studied in one-pot multicatalytic processes to synthesize disubstituted alkenes and alkanes from carbonyl derivatives [68]. The use of Cu-catalyzed methylenation reactions was the key starting reaction to produce terminal alkenes that are not isolated but submitted to further structure elongation (hydroboration followed by Suzuki cross-coupling) (Figure 1.13). These processes have been used to synthesize methoxylated (*E*)-stilbenoids (i.e., (*E*)-1,3-dimethoxy-5-(4-methoxystyryl)benzene).

Synthesis of symmetrical *trans*-stilbenes by a double Heck reaction of (aryloxy) amines with vinyltriethoxysilane has been reported [69]. A detailed procedure of the method for the synthesis of *trans*-4,4'-dibromostilbenes was described. Bis-stilbene (I) was obtained using the Heck reaction with catalyst generated *in situ* from equimolar amount of Pd acetate and corresponding phosphine [70]. Due to its relatively low melting point, this compound formed a smectic mesophase and was readily soluble in dioxane, THF, CH₂Cl₂, and CHCl₃. Palladium-catalyzed stereoselective synthesis of (*E*)-stilbenes via organozinc reagents and carbonyl compounds has been reported [71]. In the presence of a catalytic amount of PdCl₂(PPh₃) and a silylating agent, organozinc halides reacted with carbonyl compounds to give the corresponding (*E*)-stilbenes, in good to excellent yields under mild conditions. Two types of domino reactions from the same internal alkynes and hindered Grignard reagents based on carbopalladation, Pd-catalyzed cross-coupling reaction, and a C–H activation strategy were described [72]. The reaction was used in Pd(OAc)₂-catalyzed domino carbopalladation cross-coupling of PhC≡CPh and mesitylmagnesium bromide in the presence of BrCH₂CH₂Br and PPh₃ (4 equiv) in refluxing THF to give 71% *cis*-stilbene II (Figure 1.14).

Synthesis of polyhydroxylated ester analogues of the stilbene resveratrol was accomplished using decarbonylative Heck couplings [73]. Levulinate- and

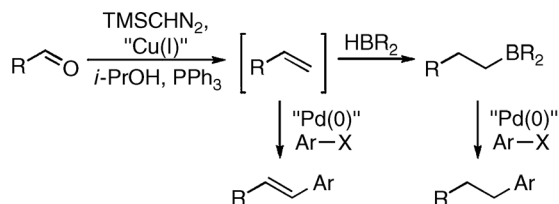


Figure 1.13 One-pot multicatalytic processes. (Reproduced with permission from Ref. [68].)

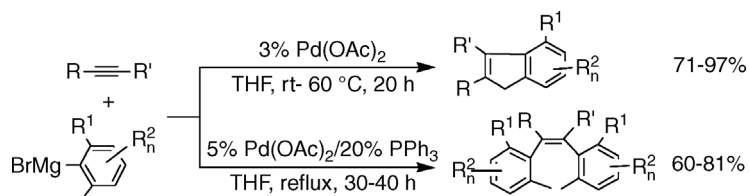
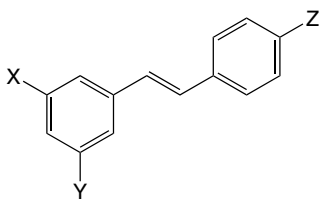


Figure 1.14 Pd(OAc)₂-catalyzed domino carbopalladation cross-coupling. (Reproduced with permission from Ref. [72].)

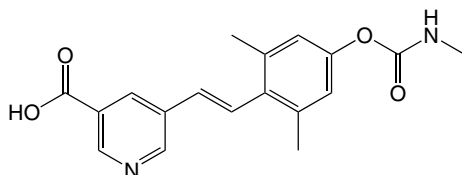
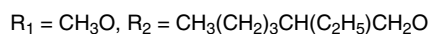
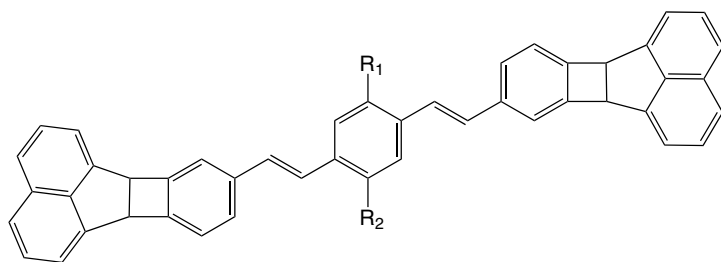
chloroacetate-protected 3,5-dihydroxybenzoyl chlorides were coupled with styrenes, H₂C:CHC₆H₄X-4 (X = OH, OAc, OCOCH₂Cl, OCOCH₂CH₂COMe, F), to give hydroxylated stilbenes, analogues of resveratrol I (X = Y = Z = OH).



Levulinate and chloroacetate protecting groups allowed selective production of mono- and diacetate variations under palladium-*N*-heterocyclic carbene (NHC) catalyzed decarbonylative coupling conditions. Fluorinated analogues, such as I (X = F, Y = Z = OH; X = Y = OH, Z = F; X = Y = F, Z = OH; X = Y = Z = F), were also produced using Heck conditions with bromofluorobenzenes. Luminescent stilbenoid chromophores with diethoxysilane end groups were prepared via Heck reactions [74]. Diethoxysilane-substituted styrenes were used as vinylic components, thus allowing the combined connection of the chromophore to the silane moiety with an extension of the π -system. Monodisperse oligo(phenylenevinylene)s of different conjugation lengths and bromine or iodine as reactive sites were used as coupling partners.

It was shown [75] that CuI-mediated substitution of 2-bromopyridine with sodium 4-bromophenylsulfinate in DMF followed by Pd-catalyzed coupling with (*E*)-2-(4-fluorophenyl)vinylboronic acid gave pyridinylsulfonyl stilbene. In the palladium-catalyzed Heck vinylation performed in nonaqueous ionic liquids, catalytic amounts of ligand-free PdCl₂ yielded stilbene from chlorobenzene and styrene in high yield [76]. The reaction occurred without the need for further promoting salt additives such as tetraphenylphosphonium chloride. The heterodinuclear Ru–Pd complex photocatalyst that catalyzes selective reduction of toluene to produce *cis*-stilbene without added H₂ was designed [77]. The photocatalyst contained a photoactive Ru(II) fragment as a light absorber, a PdCl₂ unit coordinated to the other end as a catalytic center, and a bridging unit connecting the two metal centers. It was suggested that intramolecular photoinduced electron transfer in the heterodinuclear complex facilitates the photocatalytic reactions.

Novel photoswitchable chiral compounds having an axis chiral 2,2'-dihydroxy-1,1'-binaphthyl (BINOL)-appended stiff-stilbene, *trans*-(*R,R*)-**1** and *trans*-(*S,S*)-**1**, were synthesized by palladium-catalyzed Suzuki–Miyaura coupling (forming aryl–aryl bond) and low-valence titanium-catalyzed McMurry coupling as key steps [78]. The Suzuki–Miyaura reaction of aryl halides with *trans*-(2-phenylvinyl)boronic acid using a series of related *in situ* generated *N*-heterocyclic carbene palladium(II) complexes was studied [79]. The nature of the substituents of the carbene ligand was found to be critical. Specifically, the presence of alkyl groups on the *ortho* positions of the Ph substituents was a requisite for obtaining the most efficient catalyst systems. The synthesis by Heck and/or Wittig reactions and characterization of a new class of molecules based on 6b,10b-dihydrobenzo[*j*]cyclobut[*a*]acenaphthylene (DBCA) with potentially interesting optical and electronic properties were described [80]. The new compounds contain one or two DBCA units linked via a double bond to an aromatic system.



The synthesis of several aza-stilbene derivatives similar to was carried out (Figure 1.15) [81]. The compounds were tested for their c-RAF enzyme inhibition.

Convenient methods for highly stereoselective synthesis of unsymmetrical stilbenoids were accomplished [82]. Cross-metathesis of 4-chlorostyrene with (vinyl)

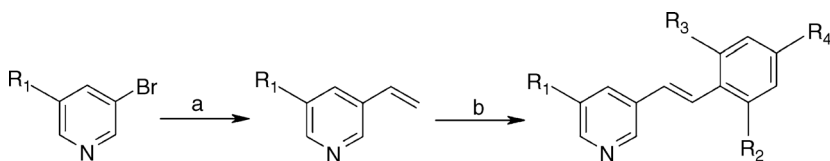


Figure 1.15 Synthesis of several aza-stilbene derivatives. Reagents and conditions: (a) tributylvinyl tin, LiCl, BHT, Pd(PPh₃)₂Cl₂, DMF, 70 °C; (b) aryl bromide(iodide), Pd₂dba₃, TEA, P(*o*-tol)₃, DMF, 95 °C [81]. (Reproduced with permission from Elsevier.)

silane derivatives in the presence of second generation of Grubbs catalyst $[\text{Cl}_2(\text{PCy}_3)(\text{IMesH}_2)\text{Ru}(\text{=CHPh})]$ or silylative coupling in the presence of $[\text{RuH}(\text{Cl})(\text{CO})(\text{PPh}_3)_3]$ followed by palladium-catalyzed Hiyama coupling has been proved.

1.3.2

Horner–Wadsworth–Emmons and Wittig–Horner Olefination Reactions

The synthesis of ^{18}F -labeled stilbenes $[^{18}\text{F}]2\text{g}$, $[^{18}\text{F}]3\text{g}$, and $[^{18}\text{F}]4\text{e}$ (*E*-isomers) by the Horner–Wadsworth–Emmons reaction was accomplished [83]. This carbonyl-olefination reaction was performed via a “multistep/one-pot” reaction by the coupling of benzylic phosphonic acid esters (3,5-bis-methoxymethoxybenzyl)-phosphonic acid diethyl ester, (4-methoxymethoxybenzyl)phosphonic acid diethyl ester, and (4-dimethylaminobenzyl)phosphonic acid diethyl ester with 4- $[^{18}\text{F}]$ fluorobenzaldehyde. The radiochemical yields ranged from 9 to 22%. Three new polyfluorinated compounds ($[(E)\text{-}4\text{-}(4\text{-bromostyryl})\text{-}2,3,5,6\text{-tetrafluorobenzonitrile}]_x\text{-}[(E)\text{-}4\text{-}(4\text{-bromo-}2,3,5,6\text{-tetrafluorostyryl})\text{-}benzonitrile]_{1-x}$) were obtained by the Horner–Wadsworth–Emmons approach to study intermolecular interactions in the crystal state and the formation of cocrystals [84].

Three new coordination polymers, $[\text{Cd}(\text{SCN})_2\text{L}_2]_n$, $[\text{CdHg}(\text{SCN})_4\text{L}_2]_n$, and $[\text{MnHg}(\text{SCN})_4\text{L}_2]_n$, were prepared by the self-assembly of L with the corresponding metal salts and NaSCN (L is a new functional rigid imidazole ligand, *trans*-4-imidazolyl-4'-(*N,N*-diethylamino)stilbene) [85]. The crystal structures of the coordination polymers were detected by single-crystal X-ray diffraction.

A recent example of Horner–Wadsworth–Emmons reaction has been reported in Ref. [86]. A modified Wittig–Horner reaction and a rearrangement in the presence of *t*-BuOK in toluene under mild conditions have been developed for the synthesis of stilbenes bearing electron-withdrawing group(s) by using benzils and arylmethyl-diphenylphosphine oxides [87]. The authors suggested that this approach could be readily applied to a facile synthesis of biologically important natural products, resveratrol and its derivatives, such as (*Z*)- and (*E*)-trimethoxystilbenes. A reaction of α -selenylation and Wittig–Horner olefination of benzylphosphonates was developed [88]. The reaction between $(\text{EtO})_2\text{P}(\text{O})\text{CH}_2\text{Ph}$ and PhSeCl gave $(\text{EtO})_2\text{P}(\text{O})\text{CH}(\text{SePh})\text{Ph}$, which gave vinylselenides $\text{RCH}:\text{C}(\text{Ph})\text{SePh}$ (**6a–h**; R = Ph, 4-MeC₆H₄, PhCH:CH, 4-MeOC₆H₄, 4-ClC₆H₄, *n*-Pr, *i*Pr, H) by reaction with aldehydes RCHO. Selenium–lithium exchange of **6a–d** through the reaction with *n*-BuLi followed by capture with several electrophiles (H₂O, PhCHO, *i*PrCHO, DMF) gave *trans*-stilbene, (*Z*)-allyl alcohols, and (*E*)- α -phenyl- α,β -unsaturated aldehydes. Seventeen derivatives of stilbenes, including resveratrol, were synthesized using a scheme.

1.3.3

Other Synthetic Reactions

Bichromophoric photochromes based on the photoinduced opening and thermal closing of a [1,3]oxazine ring were designed [89]. In particular, by incorporating fused 3*H*-indole and 4-nitrophenoxy fragments, the compound containing stilbenylvinyl

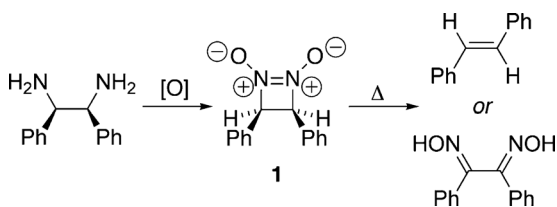


Figure 1.16 Possible products from the decomposition of diazetine dioxides **1**. (Reproduced with permission from Ref. [91].)

groups was prepared. The photoinduced process simultaneously generates a 4-nitrophenolate anion and a 3*H*-indolium cation. A series of liquid crystal stilbene derivatives containing 1,2-dienylalkoxy chains **1** ($n = 7, 9, 11$) have been synthesized [90]. The mesomorphic properties of stilbenes have been measured by polarizing optical microscopy, differential scanning calorimetry, and absorption spectroscopy. The effect of terminal alkoxy chain length and polymerizable function on the mesomorphic behavior was discussed. In the work [91], diazetine dioxide has been prepared in a single step via oxidation of *meso*-2,3-diphenyl-1,2-ethanediamine with dimethyldioxirane, albeit in low yield (7%). Thermal decomposition of 1,2-diazetine *N,N'*-dioxide afforded predominantly *trans*-stilbenes (Figure 1.16).

The reactions of $[\text{ReCl}_3(\text{MeCN})(\text{PPh}_3)_2]$ with benzil $\text{PhC}(\text{O})\text{C}(\text{O})\text{Ph}$ and with a natural 1,2-naphthoquinone derivative, β -lapachone, resulted in oxidative addition with the formation of Re(V) complexes with stilbenediolate, $[\text{ReCl}_3(\text{PhC}(\text{O})=\text{C}(\text{O})\text{Ph})(\text{PPh}_3)]$ (**1**) [92]. General procedures for the preparation of thiol end-capped stilbenes and oligo(phenylenevinylene)s with *tert*-butyl- and acetyl-protected thiol termini have been developed (Figure 1.17) [93]. These reactions proceed via

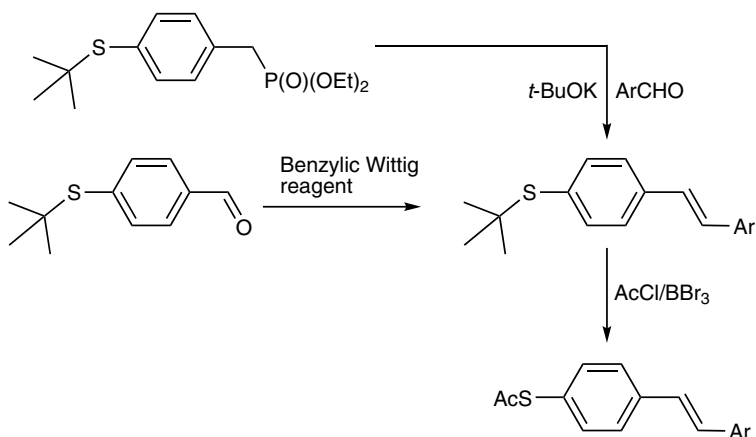


Figure 1.17 General procedures for the preparation of thiol end-capped stilbenes and oligo(phenylenevinylene)s. (Reproduced with permission from Ref. [93].)

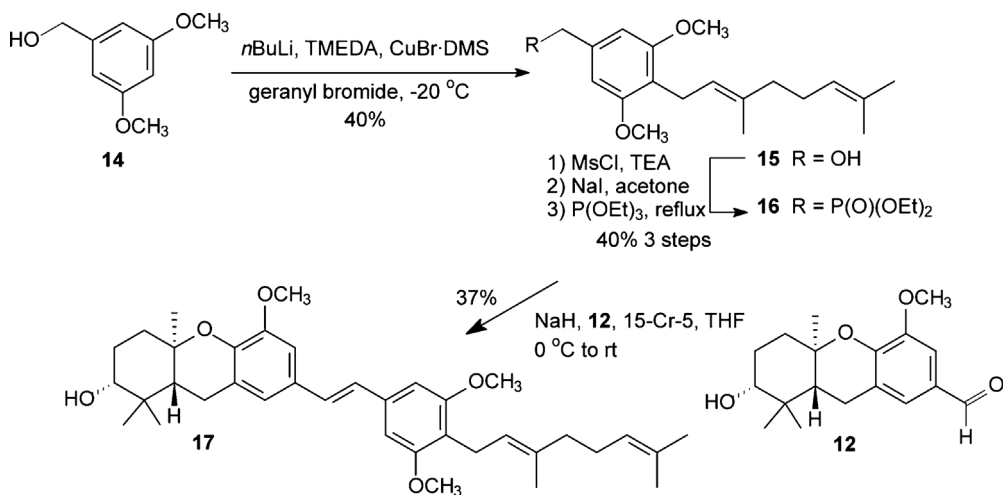
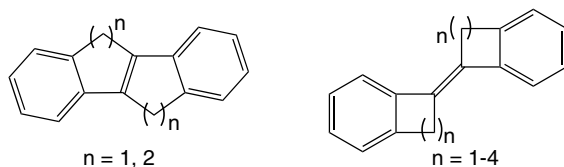


Figure 1.18 Synthesis of deoxyschweinfurthin. (Reproduced with permission from Ref. [96].)

Br/Li exchange, McMurry, and Wittig-type reactions. The reprotection of the thiol group is accomplished by means of acetyl chloride and boron tribromide.

New labeled stilbene derivatives, such as *cis*-3,5-dimethoxy-4'-[¹¹C]methoxystilbene, *cis*-3,4',5-trimethoxy-3'-[¹¹C]methoxystilbene, *trans*-3,5-dimethoxy-4'-[¹¹C]methoxystilbene, *trans*-3,4',5-trimethoxy-3'-[¹¹C]methoxystilbene, *cis*-3,5-dimethoxy-4'-[¹⁸F]fluorostilbene, and *trans*-3,5-dimethoxy-4'-[¹⁸F]fluorostilbene, were designed and synthesized [94]. The synthesis of (*E*)-tris-*O*-methylresveratrol and (*E*)-3,5-dimethoxystilbene via the Miyaura–Suzuki coupling was described [95]. This reaction has been carried out in air without solvent/substrate purification and in the absence of additional free ligand. Figure 1.18 shows a scheme of deoxyschweinfurthin synthesis accomplished in Ref. [96].

The synthesis, structural and spectroscopic characterization, and photophysical and photochemical properties of cyclic *trans*-stilbenes have been carried out [97].



A method of stilbene synthesis via homocoupling of aryl aldehyde tosylhydrazones in the presence of lithium *tert*-butoxide and trimethyl borate under reflux in THF has been described.

Series of stilbenes were prepared in good yields via homocoupling of aryl aldehyde tosylhydrazones in the presence of lithium *tert*-butoxide and trimethyl borate under reflux in THF (Figure 1.19) [98].

Synthesis of *trans*- and *cis*-3,4',5-trihydroxystilbene from 3,5-dimethoxybenzaldehyde and 4-methoxyphenylacetonitrile via condensation reaction to form stilbene

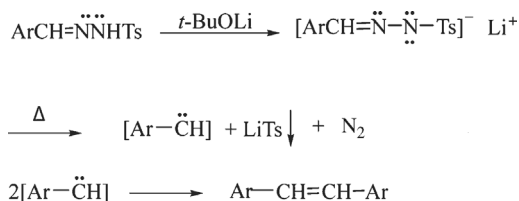
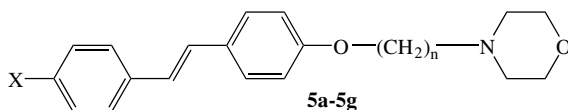


Figure 1.19 Synthesis of homocoupling stilbenes [98]. (Reproduced with permission from Elsevier.)

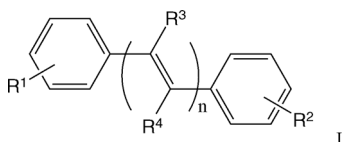
skeleton, after hydrolysis, decarboxylation, and demethylation to obtain *trans*-3,4',5-trihydroxystilbene was accomplished [99]. Highly functionalized (*E*)-stilbenes and 4-aryl-6-styrylpyran-2-ylideneacetonitriles were prepared and delineated through the ring transformation of 3,4-disubstituted 6-aryl-2*H*-pyran-2-ones with (*E/Z*)-4-phenyl-3-buten-2-one without using any catalyst [100]. Synthesis of 21 new (*E*)-4-[piperidino (4'-methylpiperidino-,morpholino-) *N*-alkoxy]stilbenes of chemical structure (where



- | | |
|-------------------|--------------------------------|
| a X=H n=2; | e X=NO ₂ n=3 |
| b X=H n=3; | f X=NO ₂ n=4 |
| c X=H n=4; | g X=NO ₂ n=5 |
| d X=H n=5; | |

$n = 3, 4, R = X = \text{H}; n = 4, 5, R = \text{H}, X = \text{NO}_2$) and their antimicrobial activities was reported [101].

A series of stilbene derivatives of formula ($R^1 = (\text{substituted}) \text{NH}_2, \text{OH}, \text{alkoxy},$



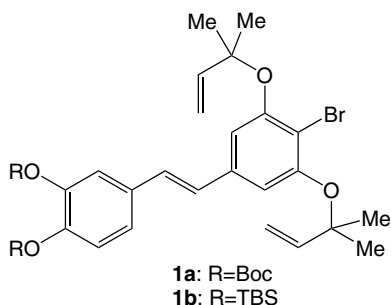
hydroxyalkyl; $R^2 = (\text{substituted}) (\text{OCH}_2\text{CH}_2)_q\text{-Z}; q = 1-10; \text{Z} = \text{halo}, \text{halobenzoyloxy}, \text{haloaryl}, \text{chelating group}, \text{and so on}; R^3, R^4 = \text{H}, \text{OH}, \text{NH}_2, \text{alkoxy}, \text{and so on}; n = 1-6$) were prepared [102].

A series of synthesis of stilbene derivatives was presented in Ref. [103]. In the work [104], another series of 4,4'-disubstituted organic-organometallic stilbenes were synthesized, that is, the 4'-substituted stilbenoid-NCN-pincer platinum(II) complexes $[\text{PtCl}(\text{NCN-R-4})]$ ($\text{NCN-R-4} = [\text{C}_6\text{H}_2(\text{CH}_2\text{NMe}_2)_2\text{-2,6-R-4}]^-$ in which $R = \text{C}_2\text{H}_2\text{C}_6\text{H}_4\text{-R}'\text{-4}'$ with $R' = \text{NMe}_2, \text{OMe}, \text{SiMe}_3, \text{H}, \text{I}, \text{CN}, \text{NO}_2$) (1-7). In these compounds, the PtCl grouping can be considered to be present as a donor substituent. Their synthesis involved a Horner-Wadsworth-Emmons reaction of $[\text{PtCl}(\text{NCN-CHO-4})]$ (9) with the appropriate phosphonate ester derivatives (8a-g). Under these reaction conditions, the C-Pt bond in aldehyde 9 was not affected, and the platinated stilbene products were obtained in 53-90% yield. The solid-state

structures of complexes **1**, **2** and **5–7** were detected by single-crystal X-ray diffraction, which revealed interesting bent conformations for **2**, **5**, and **7**. Linear correlations were found between both the $^{13}\text{C}\{^1\text{H}\}$ (C ipso to Pt) and the $^{195}\text{Pt}\{^1\text{H}\}$ NMR chemical shifts and the Hammett σ_p value of the R' substituent; therefore, these NMR shifts can be used as a qualitative probe for the electronic properties of the delocalized π -system to which it is connected. Platinum–stilbene complexes were investigated for charge transfer (CT) properties in solvents of different polarities.

Three novel organic optical materials, 4'-(*N,N*-dihydroxyethylamino)-4-(pyridine-4-vinyl)stilbene, *N*-((4-*N,N*-dihydroxyethylamino)benzylidene)-4-(pyridine-4-vinyl)aniline, and 4'-(*N,N*-dihydroxyethylamino)-4-(pyridine-4-vinyl)azobenzene, were synthesized [105]. Tolunitriles reacted with donor-substituted aromatic aldehydes in high yielding reactions of the synthesis of donor–acceptor cyanostilbenes without the need of inert atmosphere. The keys to this reaction were the use of anhydride DMF solvent and the phase transfer agent – tris(3,6-dioxaheptyl)amine (TDA). High yields of stilbenes were also obtained with amino-substituted aromatic aldehydes [106].

According to Ref. [107], the addition of diphenylacetylene (110 °C, 3 h) to the hydrido acyl complex $\text{Ru}(\text{H})\{2\text{-PPh}_2\text{C}_6\text{H}_4\text{C}(\text{O})\}(\text{CO})_2(\text{PPh}_3)$ afforded the novel complex $\text{Ru}\{2\text{-PPh}_2\text{C}_6\text{H}_4\text{C}(\text{O})\text{PhC:CHPh}\}(\text{CO})\{\text{PPh}_3\}$, incorporating the newly assembled *o*-(diphenylphosphino)phenyl (*E*)-stilbenyl ketone ligand. The α,β -unsaturated ketone moiety of the latter was bound to the metal in an η^4 coordination mode involving both a side-on coordination of the carbonyl group and a classical η^2 linkage of the olefinic bond. A series of unsymmetrical *trans*-stilbenes have been prepared using the sequential coupling reactions of bromobenzenesulfonate with formylarylboronic acids, benzylphosphonates, and arylmagnesium bromides [108]. The nickel-catalyzed reactions of stilbene sulfonates with aryl Grignard reagents produced the corresponding stilbenes via the nucleophilic aromatic substitution of the neopentylsulfonyl group by aryl nucleophiles. The high chemoselectivity of the alkyloxysulfonyl group allowed the stepwise construction of unsymmetrical *trans*-stilbenes possessing terphenyl moieties. Total synthesis of stilbene artochamins **F** (I),



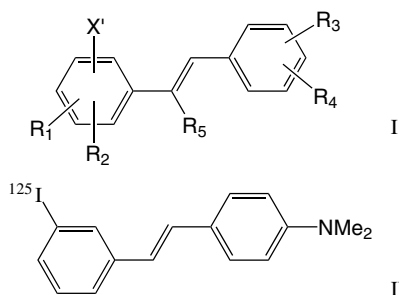
H (II), I (III), and J(IV) has been achieved through a flexible and expedient strategy that features a cascade sequence involving two concurrent [3,3] sigmatropic rearrangements and an unusual intramolecular formal [2 + 2] thermal cycloaddition reaction between an electron-rich stilbene and a prenyl group [109].

The photochemical coupling of various stilbenes (**S**) and chloranil (**Q**) was effected by the specific charge transfer activation of the precursor electron donor–acceptor (EDA) complex [**S**, **Q**] [110]. The [2 + 2] cycloaddition was established by X-ray structure elucidation of the crystalline *trans*-oxetanes formed selectively in high yields.

It was shown [111] that intramolecular reductive McMurry coupling reactions of bis(formylphenoxy)-substituted calix[4]arenediols mediated by titanium(IV) chloride and activated zinc followed by cyclocondensation of the diols with tetra- and penta(ethylene glycol) bistosylates provided the stilbene- and crown ether-bridged calix[4]arenes. Two synthesized analogues with two ethoxyethoxyethoxy substituents replacing the crown ether moiety and two calix[4]arene crown ethers with methoxy groups replacing the bridging stilbene moiety were tested for their extraction of alkali metal cations from aqueous solutions into chloroform. Stilbene-bridged calix[4]arenes with bridging tetra(ethylene glycol) ethers selectively extracted potassium ion over other alkali metal cations, while stilbene-bridged calix[4]arenes with bridging penta(ethylene glycol) ethers favor the complexation of cesium cation over other alkali metal cations.

To investigate the gelation ability of novel oxamide-based derivatives bearing a stilbene as a photoresponsive unit, oxamide-based derivatives, containing one or two oxamide moieties coupled to the 4- or 4,4'-positions of *cis*- and *trans*-stilbenes, have been synthesized [112]. *trans*-4-Me(CH₂)₁₁C₆H₄CH:CHC₆H₄NHCOCOR (I, R = OEt, NH-L-Leu-OMe) was found to act as efficient gelators of various organic solvents.

Several synthesis on the basis of stilbenes as starting materials were reported. The paper [113] presented experimental data regarding some azo dyes synthesized by coupling of the diazonium salt of 4,4'-diamino-stilbene-2,2'-disulfonic acid with different acetoacetylides. Reaction products were purified and characterized by means of elemental analysis by UV-VIS, IR, ¹H-NMR, and ¹³C-NMR spectroscopy. A series of stilbene and fluorene compounds were prepared [114]. Compounds of



formula where X' is H, halo, C1–4 haloalkyl(amino), Sn(alkyl)₃, and so on; R¹, R², and R³ are independently H, OH, halo, C1–4 alkyl, C1–4 alkoxy, CN, and so on; R⁴ is C1–4 alkylthio, C1–4 alkylsulfonyl, OH, C1–4 alkoxy, NH₂ and derivatives, and so on; R⁵ is H and C1–4 alkyl; and their pharmaceutically acceptable salts were prepared.

These synthesized compounds were found to be useful for rescuing cells from beta-amyloid toxicity and in the treatment of Alzheimer's disease.

1.4

Physically Promoted Reactions

The microwave-promoted Heck reaction of aryl iodides and bromides with terminal olefins using a $\text{Pd}(\text{OAc})_2$ (0.05 mol%)/ K_3PO_4 catalytic system under ligand-free and solvent-free conditions was described [115]. Microwave radiation was used for synthesis of a number stilbene derivatives [115–117]. The reaction mixture was placed inside the cavity of the microwave reactor and irradiated at 300 W for 25 min. After the reaction mixture was cooled to room temperature, the solid was extracted with ethyl acetate and the solvent was evaporated in a vacuum. The residue was purified by flash-column chromatography on silica gel using ethyl acetate/hexane (1:20). *para/ortho*-Hydroxylated (*E*)-stilbenes have been synthesized by a metal-free protocol for decarboxylation of substituted α -phenylcinnamic acid derivatives in aqueous media [116]. The authors stressed a synergism between methylimidazole and aqueous NaHCO_3 in polyethylene glycol under microwave irradiation using discover[®] focused microwave (2450 MHz, 300 W).

A one-pot two-step synthesis of hydroxystilbenes with *trans* selectivity was developed through a modified Perkin reaction between benzaldehydes and phenylacetic acids bearing 4- or 2-hydroxy substitution at the aromatic ring [67]. The reaction was performed under mild conditions in the presence of piperidine–methylimidazole and polyethylene glycol under microwave irradiation. As a result, 71% yield of (*E*)-4-chloro-4'-hydroxy-3'-methoxystilbene from 4-hydroxy-3-methoxybenzaldehyde and 4-chlorophenylacetic acid was obtained. A microwave-induced one-pot process for the preparation of arylenes has been patented [118]. For the preparation of a series of arylenes (I; $\text{R}^1\text{--R}^5 = \text{H, OH, OMe, AcO, halo, NO}_2$; $\text{R}^1, \text{R}^3, \text{R}^5 = \text{OH, AcO}$; $\text{R} = \text{H, substituted aryl}$), reaction of 2- or 4-hydroxy substituted cinnamic acids or derivatives in the presence of a base, under reflux or microwave irradiation, has been used. For example, a mixture of α -phenyl-4-hydroxy-3-methoxycinnamic acid, NaHCO_3 , methylimidazole, and polyethylene glycol was microwaved at 200 W and 180 °C for 10 min to give 96% 4-hydroxy-3-methoxystilbene.

Ultrasound-assisted synthesis of *Z* and *E*-stilbenes by Suzuki cross-coupling reactions of organotellurides with potassium organotrifluoroborate salts has been reported [119]. Palladium-catalyzed cross-coupling reactions between potassium aryl- or vinyltrifluoroborate salts and aryl or vinyl tellurides proceeded to give stilbenes containing a variety of functional groups. For example, a suspension of *Z*-(2-butyl-tellanyl-vinyl)-benzene, potassium phenyltrifluoroborate ($\text{Pd}(\text{PPh}_3)_4$), and silver(I) oxide of methanol was irradiated in a water bath of an ultrasonic cleaner for 40 min.

1.5

Synthesis of Stilbene Dendrimers

Dendrimers are repeatedly branched molecules. The name comes from the Greek “δενδρον”/*dendron*, which means tree. A series of stilbene dendrimers with a stilbene core and benzyl ether type dendrons has been synthesized and investigated

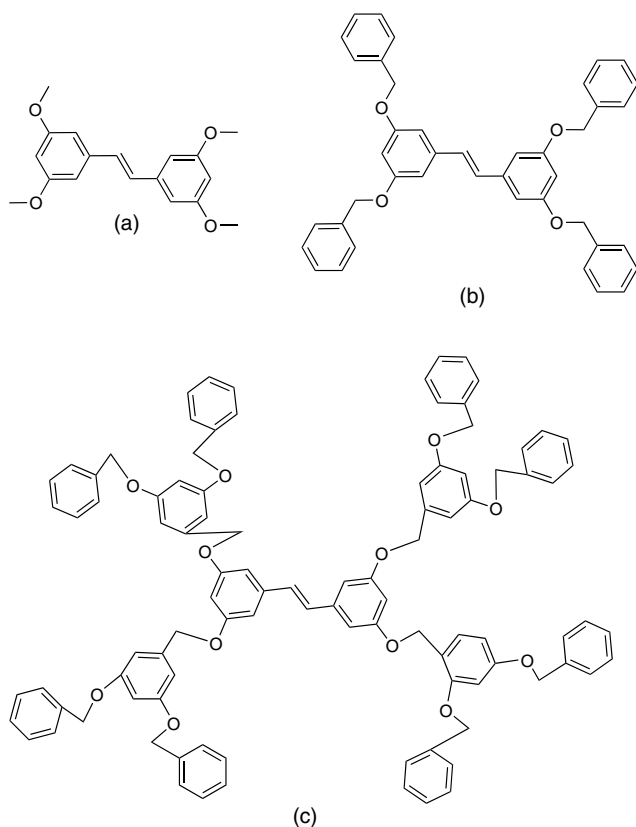


Figure 1.20 Dendrimers synthesized in the work [120].
(Reproduced with permission from Ref. [120].)

in an acetonitrile and 1,2-dichloroethane mixture (3: 1) to elucidate the dendrimer effects (Figure 1.20) [120]. It was shown that the quantum yield of the formation of stilbene core radical cation during the 308-nm TPI was independent of the dendron generation of the dendrimers, whereas the generation dependence of the quantum yield of the radical cation was observed during the 266-nm TPI, where both the stilbene core and the benzyl ether-type dendron were ionized, suggesting that the subsequent hole transfer occurs from the dendron to the stilbene core and that the dendron acts as a hole-harvesting antenna.

Stilbenoid dendrons with various donor and acceptor groups on the focal unit were synthesized by a Wittig–Horner reaction, starting from an aldehyde-functionalized dendron and various substituted phosphonic acid esters [121]. It was shown that the target molecules were composed of *meta*-branched arms, two of them with extended conjugation (distyrylbenzene) and three flexible dodecyloxy chains; the focal group consists of a donor- or acceptor-substituted styryl unit. The synthesized stilbenoid dendrons were photosensitive, and degradation of the supramolecular order proceeds even in the glassy liquid crystal state.

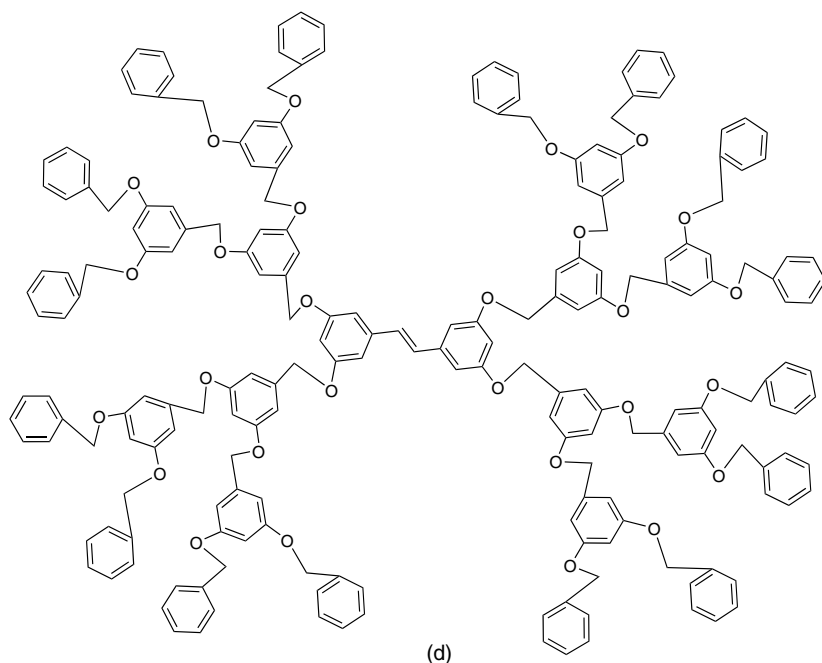
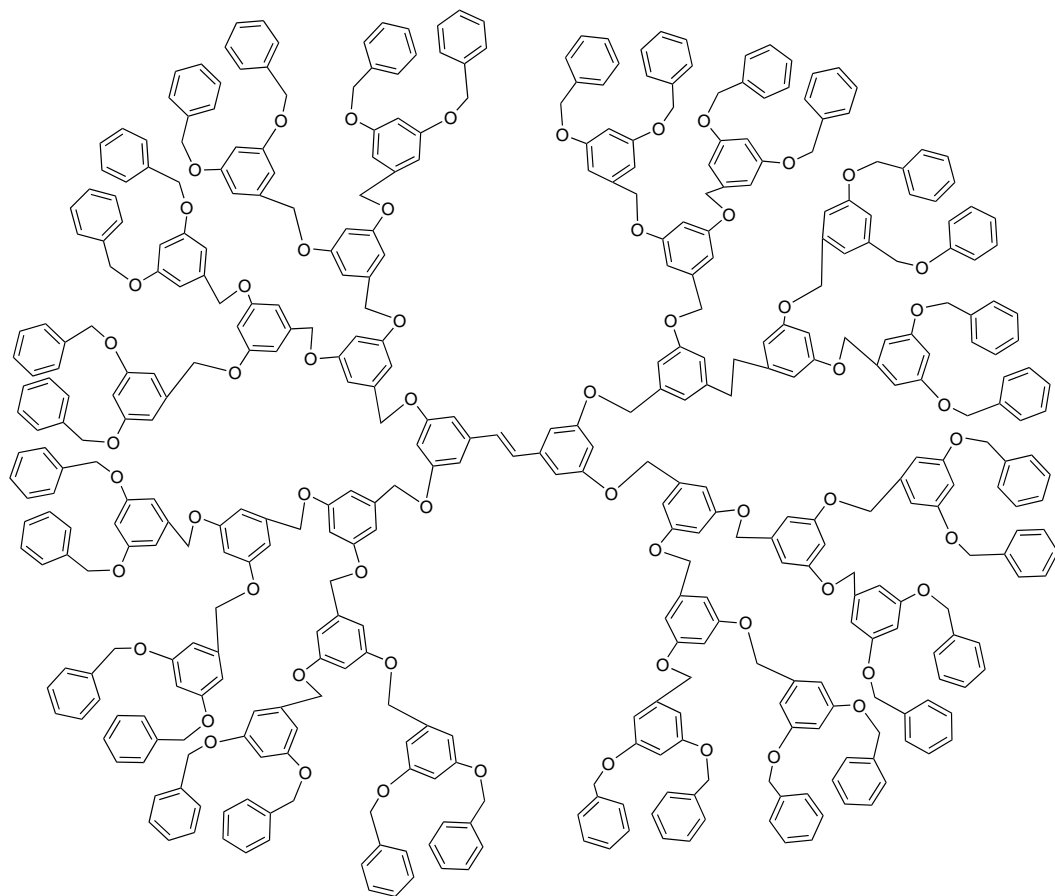


Figure 1.20 (Continued)

Polyamidoamine dendrimers, constructed on the surface of silica, were phosphonated by the Heck reaction using diphenylphosphinomethanol and complexed to form a palladium-dimethyl TMEDA [122]. This catalyst was found to be effective in the Heck reaction of aryl bromides with both butyl acrylate and styrene, affording coupling products in moderate to good yields. The heterogeneous palladium catalyst can also be recycled and reused with only moderate reduction in activity. Water-soluble self-assembly of amphiphilic pyrene-cored poly(aryl ether) dendrimers was prepared and its fluorescence properties were studied [123]. Dendron-conjugated branches of stilbene and 4-styrylstilbene groups have been attached to resorcinarene cores [124]. The optical properties of thin films were identical to those of the solutions indicating the absence of intermolecular interactions. Two generations of dendritic nanoparticles were prepared, which contain (*E*)-stilbene or (*E,E*)-1,4-distyrylbenzene chromophores in the 4 or 8 terminal positions of the propylene imine dendrons [125]. Two large π -conjugated dendrimers (G0 and G, molecular weight of 10 973 Da) employing the stilbenoid moiety as the bridge unit have been synthesized through the Suzuki and the Horner-Wadsworth-Emmons reactions [126]. Stilbene dendrimers were prepared by coupling 4,4'-dihydroxystilbene with first-, second-, third-, or fourth-generation benzyl ether-type dendrons [127]. All the generations of stilbene dendrimers underwent

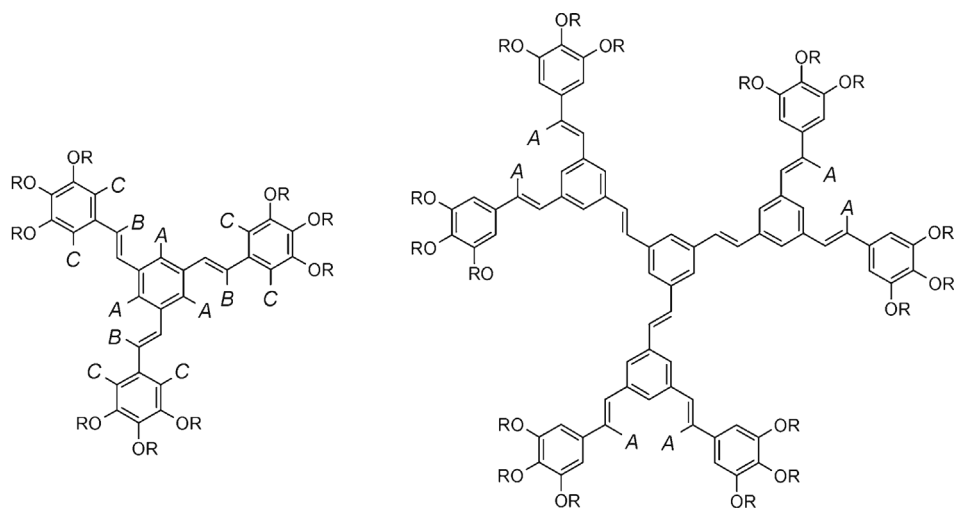


(e)

Figure 1.20 (Continued)

photoisomerization with the same efficiency as that of 4,4'-dimethoxystilbene. Dendrimers with terminal (*E*)-stilbene moieties based either on a hexamine core or on a benzenetricarboxylic acid core were synthesized [128]. Under irradiation, both types of dendrimers undergo photochemical reactions to yield cross-linked products lacking styryl moieties.

Photochemistry and mobility of the stilbenoid dendrimers [all-(*E*)-1,3,5-tris[2-(3,4,5-tridodecyloxyphenyl)ethenyl]benzene] and [all-(*E*)-1,3,5-tris(2-{3,5-bis[2-(3,4,5-tridodecyloxyphenyl)ethenyl]phenyl}ethenyl)benzene] in their neat phases were synthesized and investigated [129]. Selectively deuterated, dodecyloxy-substituted stilbenoid dendrimers of the first and second generations (Figure 1.21) were synthesized by a convergent synthesis, using the Wittig–Horner reaction. Molecules deuterated at the



1a $A-C = {}^1\text{H}$, $R = \text{C}_{12}\text{H}_{25}$

1b $A = {}^2\text{H}$, $B, C = {}^1\text{H}$, $R = \text{C}_{12}\text{H}_{25}$

1c $B = {}^2\text{H}$, $A, C = {}^1\text{H}$, $R = \text{C}_{12}\text{H}_{25}$

1d $C = {}^2\text{H}$, $A, B = {}^1\text{H}$, $R = \text{C}_{12}\text{H}_{25}$

1e $A-C = {}^1\text{H}$, $R = \text{C}^2\text{H}_2\text{C}_{11}\text{H}_{23}$

2a $A = {}^1\text{H}$, $R = \text{C}_{12}\text{H}_{25}$

2b $A = {}^2\text{H}$, $R = \text{C}_{12}\text{H}_{25}$

2c $A = {}^1\text{H}$, $R = \text{C}^2\text{H}_2\text{C}_{11}\text{H}_{23}$

Figure 1.21 Chemical structure of the stilbenoid dendrimers synthesized and investigated in Ref. [129]. (Reproduced with permission from Ref. [129].)

α -position of the alkoxy chains were used to study the photoreactions in the neat phases by ${}^1\text{H}$ NMR. No photoreactions occur in the crystal state. The mobility of the dendrimers was studied by means of ${}^2\text{H}$ solid-state NMR spectroscopy. The onset of the photochemistry for dendrimer 1 [all-(*E*)-1,3,5-tris[2-(3,4,5-tridodecyloxyphenyl)ethenyl]benzene] corresponds to the increasing mobility at the Cr/LC transition. The first-generation dendrimers still show large angle motion, whereas dendrimers of the second generation 2 [all-(*E*)-1,3,5-tris(2-{3,5-bis[2-(3,4,5-tridodecyloxyphenyl)ethenyl]phenyl}ethenyl)benzene] were restricted to librational motions. Photochemical conversion and fluorescence quenching for first- and second-generation dendrimers 1 and 2 were found to increase with increasing molecular motion and reach a maximum in the isotropic phase.

1.6

Stilbene Cyclodextrin Derivatives

Rotaxane is a mechanically interlocked molecular architecture consisting of a “dumbbell-shaped molecule” that is threaded through a “macrocycle.” The name

is derived from the Latin words for wheel (*rota*) and axle (*axis*). The synthesis of a novel rotaxane containing α -CD (α -cyclodextrin) as the macrocycle, stilbene as the “string,” and the isophthalic acid as stopper via a palladium-catalyzed Suzuki coupling reaction in water at room temperature and supramolecular self-assembly was reported [130]. The molar ratio of α -CD to the “string” was 1: 1 and the rotaxane was [2]rotaxane according to the results of ^1H NMR spectroscopy and mass spectrometry of rotaxane. The synthesis of homo- and hetero[3]rotaxanes with two π -system (dumbbell) components threaded through a single γ -cyclodextrin macrocycle has been accomplished [131]. The synthesis was carried out in two steps: first dumbbell was synthesized threaded through the macrocycle to give a [2]rotaxane and then a second dumbbell was prepared through the remaining cavity of the [2] rotaxane. A hetero[3]rotaxane with one stilbene and one cyanine dye threaded through γ -cyclodextrin has been synthesized. The stilbene [2]rotaxane intermediate in this synthesis was shown to have a high affinity for suitably shaped hydrophobic guests in aqueous solution, facilitating the synthesis of [3]rotaxanes and suggesting possible applications in sensors.

Two [2]rotaxanes (Figure 1.22), each comprising α -cyclodextrin as the rotor, stilbene as the axle, and 2,4,6-trinitrophenyl substituents as the capping groups, were prepared and their conformations were examined in solution and in solid state using ^1H NMR spectroscopy and X-ray crystallography, respectively [132]. In the solid state, the axles of rotaxanes form extended molecular fibers that are separated

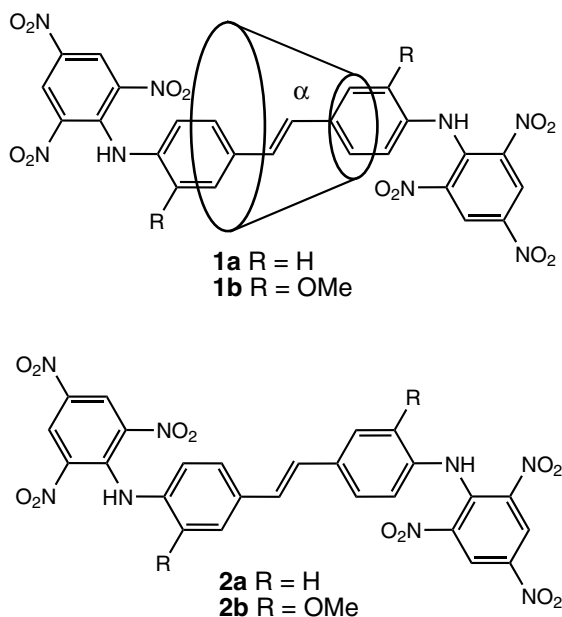


Figure 1.22 [2]Rotaxane comprising α -cyclodextrin as the rotor. (Reproduced with permission from Ref. [132].)

from each other and aligned along a single axis. The molecular fibers are strikingly similar to those formed by the axle component of one of the rotaxanes in the absence of the cyclodextrin, but in the latter case they are neither separated nor all aligned.

1.7

Stilbenes on Templates

A new catalyst system for Heck reaction, silica-supported poly- γ -aminopropylsiloxane palladium (Pd^{2+})-transition metal (Cu^{2+}) complex, has been designed [133]. The catalyst has been prepared from organic silica via immobilization on fumed silica, followed by treatment with $\text{Cu}(\text{OAc})_2$ and PdCl_2 in ethanol. The catalyst was efficient for Heck arylation of aryl iodides with alkene. Stilbene-based azo dyes were synthesized and poly(vinyl alcohol) polarizing films were prepared [134]. Two series of combined liquid crystal polyphosphates bearing dual photoreactive mesogenic units (stilbene and azobenzene/ α -methylstilbene and azobenzene) were synthesized by the solution polycondensation method [135]. Structures of the synthesized polymers were confirmed by various spectroscopic techniques. The photochemical response, photocross-linking reaction, and conversion of *trans* to *cis* form of azobenzene unit were investigated. The terminal substituents in the side chain affected the texture of liquid crystal phase for all the polymers. Poly[2- $\{$ bis(4-methoxyphenyl)amino $\}$ phenyl-5-(2-ethylhexyloxy)-1,4-phenylenevinylene] was prepared via the Gilch reaction of the *p*-bis(chloromethyl)benzene monomer, 2- $\{$ bis(4-methoxyphenyl)aminophenyl $\}$ - α,α' -dichloro-*p*-xylene [136]. 2,3-Bis[*N,N*-bis(4-methoxyphenyl)aminophenyl]stilbene 2 and its aminium diradical 2^+ were also prepared as model dimer compounds.

A new urethane acrylic monomer with stilbene in its structure, *trans*-4-(2-methacryloyloxyethylcarbamoyloxymethyl)stilbene (SUM), was synthesized to be further free radically copolymerized with methyl methacrylate (MMA) [137]. The structures of SUM and the resulting copolymer, *trans*-4-(2-methacryloyloxyethylcarbamoyloxymethyl)stilbene-*co*-methyl methacrylate (SUMMA), were characterized by a set of physicochemical methods. Morphological changes in the surface of the polymeric film during the photoisomerization were visualized by means of atomic force microscopy (AFM), and the newly formed cone-shaped structures from the irradiated surface were attributed to J-aggregates. In order to gain insight into the properties of the triplet excited states in platinum-acetylide polymers, four platinum complexes were synthesized in which the metal is linked to the *trans*-stilbene through acetylide bonds [138]. Comparison of the properties of these complexes provided information on the geometry of the π -conjugated acetylide ligands and the existence of the metal-to-ligand charge transfer (MLCT) state on the photophysics of these systems.

Three new coordination polymers, $[\text{Cd}(\text{SCN})_2\text{L}_2]_n$ (Figure 1.23), $[\text{CdHg}(\text{SCN})_4\text{L}_2]_n$, and $[\text{MnHg}(\text{SCN})_4\text{L}_2]_n$, were synthesized by the self-assembly of L with the corresponding metal salts and NaSCN (L is a functional rigid imidazole ligand, *trans*-4-imidazolyl-4'-(*N,N*-diethylamino)stilbene) [139]. It was shown that adjacent Cd(II)

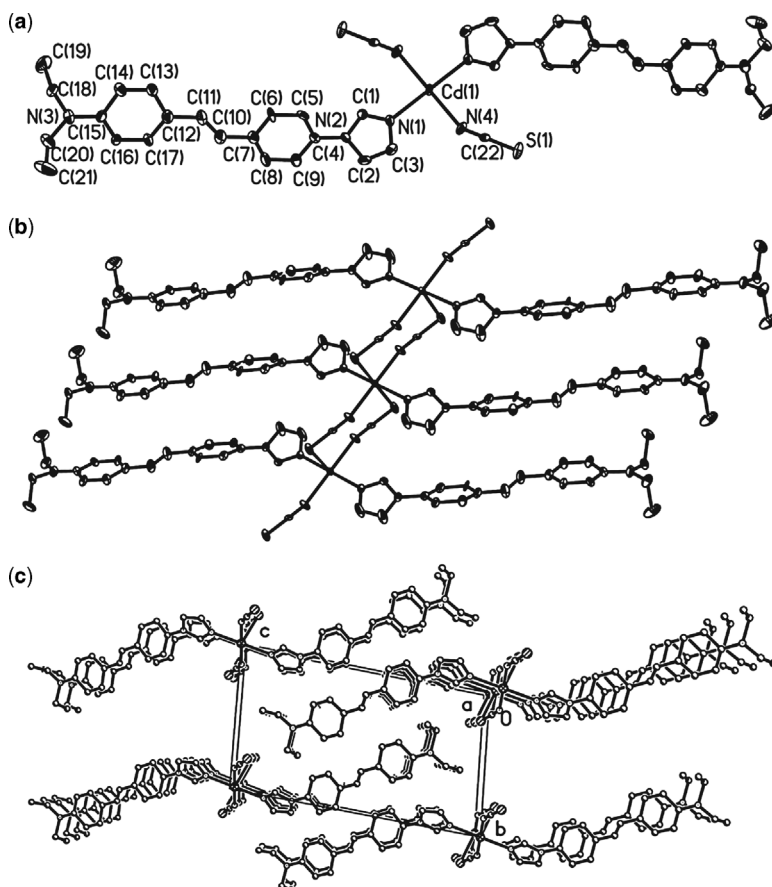


Figure 1.23 Structural unit of complex from coordination polymers $[\text{Cd}(\text{SCN})_2\text{L}_2]_n$ [139]. (Reproduced with permission from Elsevier.)

ions are bridged by SCN^- ligands to form infinite chains with the remaining two positions of six-coordinated $\text{Cd}(\text{II})$ ion occupied by two imidazole ligands. $\text{Cd}(\text{II})$ and $\text{Hg}(\text{II})$ centers were bridged by SCN^- ligands to form two-dimensional framework sheets. $\text{Cd}(\text{II})$ and $\text{Hg}(\text{II})$ ions were coordinated by six N atoms and four thiocyanate S atoms, respectively. $\text{Mn}(\text{II})$ and $\text{Hg}(\text{II})$ ions were linked by bridging NCS^- groups to form two-dimensional sheets. Figure 1.23 shows the structural unit of the complex from coordination polymers $[\text{Cd}(\text{SCN})_2\text{L}_2]_n$.

A cross-linkable embossed film containing polyester stilbene has been prepared [140]. The substrate film comprised a copolyester consisting of repeating units derived from stilbene dicarboxylic acid (1–40 mol%), 1,4-cyclohexane dicarboxylic acid (60–99 mol%), and 1,4-cyclohexane dimethanol (50–100 mol%). UV-curable polyesters containing stilbene structural unit with good thermal stability

have been synthesized [141]. The polymers consisted of (a) 1–40 mol% *trans* 3,3' or *trans* 4,4' of stilbene dicarboxylic acid, (b) 60–99 mol% *cis*, *trans* of 1,4-cyclohexane dicarboxylic acid, and (c) 50–100 mol% *cis*, *trans* of 1,4-cyclohexane dimethanol. A number of nanoparticle–monomer–receptor (NMR) sensors, where the nanoparticles were SiO₂ and ZnS: Mn/CdS core/shell quantum dots, the monomers were stilbene derivatives, and the receptors were isoquinoline and 3-aminohexafluoropropanol, have been synthesized [142]. Using these sensors, nerve gas analogues DCP and DMMP and acids such as HCl were detected with these NMR sensors by fluorescence change in the wavelength range 380–500 nm. Wang and Muralidharan [143] have synthesized 12 different stilbene-based monomers for the nanoparticle–monomer–nanomolecule–receptor (NMNR) and NMR sensors and investigated their efficacies for the detection of nerve gas analogues DCP and DMMP and acids such as HCl. Both NMNR sensors with Eu(dppz)₃ (dppz = dipyrido[3,2-*a*:2',3'-*c*]phenazine) complex and NMR sensors have been obtained with the stilbene-based monomers.

The synthesis of poly(MMA/2,2,2-trifluoroethyl methacrylate (3FMA)/benzyl methacrylate = 52.0/42.0/6.0 (w/w/w)) and poly(MMA/3FMA = 85.0/15.0 (w/w)) containing 2.8 wt% of *trans*-stilbene that exhibited birefringence close to zero was reported [144]. Zigzag polymers consisting of dithia[3.3](2,6)pyridinophane units were prepared [145]. The resulting polymer complex exhibited a high catalytic activity for the Heck coupling reaction. A perdeuterated *trans*-stilbene grafted polystyrene has been synthesized [146]. The effects of chromophore concentration, solvent polarity, excitation energy, chromophore aggregation, and UV irradiation on photophysical properties of this photoactive material have been investigated.

The paper [147] has reported the preparation and characterization of pure Langmuir and Langmuir–Blodgett (LB) films of a stilbene derivative containing two alkyl chains, 4-dioctadecylamino-4'-nitrostilbene. Mixed films incorporating docosanoic acid and stilbene derivatives were also studied. Brewster angle microscopy (BAM) analysis revealed the existence of randomly oriented 3D aggregates, spontaneously formed immediately after the spreading process of the stilbene derivative onto the H₂O surface. It was shown that monolayers were transferred undisturbed onto solid substrates with AFM revealing that the one-layer LB films are constituted by a monolayer of the stilbene derivative together with some three-dimensional aggregates.

The synthesis and properties of DNA minihairpin conjugates possessing stilbene capping groups have been investigated for two hairpin base sequences with three stilbene capping groups [148]. It was found that the two hairpin sequences 5'-TTTACCGAAA and 5'-ATTACCGAAT differ in the orientation of the terminal base pair, the latter forming the more stable hairpin. Conjugation of these hairpins with a 5'-stilbenecarboxamide capping group significantly increased hairpin stability and reduced the difference in stability observed for the unmodified hairpins. The synthesis and properties of nicked dumbbell and dumbbell DNA conjugates having A-tract base pair domains connected by rod-like stilbenedicarboxamide linkers were reported [149]. Structures of the nicked dumbbells and dumbbells (Figure 1.24) have been investigated using a combination of CD spectroscopy and molecular modeling.

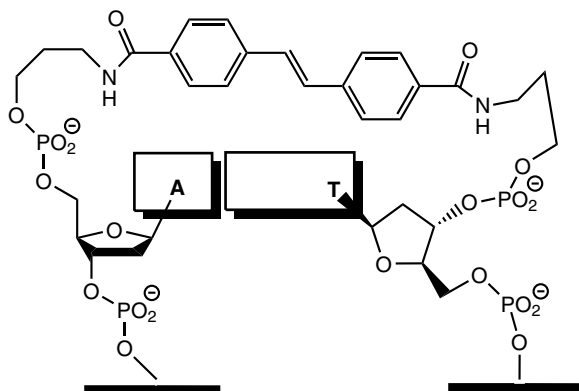


Figure 1.24 Structure of the hairpin loop region of synthetic hairpins having a stilbenedicarboxamide (SA) linker. (Reproduced with permission from Ref. [149].)

A synthesized dual stilbene–nitroxide probe was covalently immobilized onto the surface of a quartz plate as an eventual fiber-optic sensor (Figure 1.25) [150]. The immobilization procedure included a cyanogen bromide surface activation followed by smoothing with a protein tether. The rate of fluorescence change was monitored in aqueous glycerol solution of different viscosities and contents of ascorbic acid.

The attachment of *para*-NH₂-stilbene to the surface of the cowpea mosaic virus (CPMV) coat protein was performed with an indicating antibody–antigen interaction [151]. Antibody binding was subsequently blocked by the installation of polyethylene glycol chains. The authors claimed that these results typify the type of site-specific control that is available with CPMV and related virus building blocks. A preparation scheme of virus–stilbene conjugate is shown in Figure 1.26. The authors claimed that these results typify the type of site-specific control that is available with CPMV and related virus building blocks.

A complex antibody–donor–acceptor-substituted stilbene has been investigated (Figure 1.27) [152]. Photophysical and structural analyses indicated that antibody binding alters the excited-state behavior of stilbene. The authors suggested that such complexes may find *in vivo* application as fluorescent biosensors.

1.8

Stilbenes Analysis

1.8.1

Methods Using Liquid and Gas Chromatography

A method has been developed to detect residual stilbenes such as diethylstilbestrol (DES), dienestrol (DIS), and hexestrol (HS) in animal tissues using solid-phase extraction (SPE) and gas chromatography–mass spectrometry (GC–MS) [153]. The

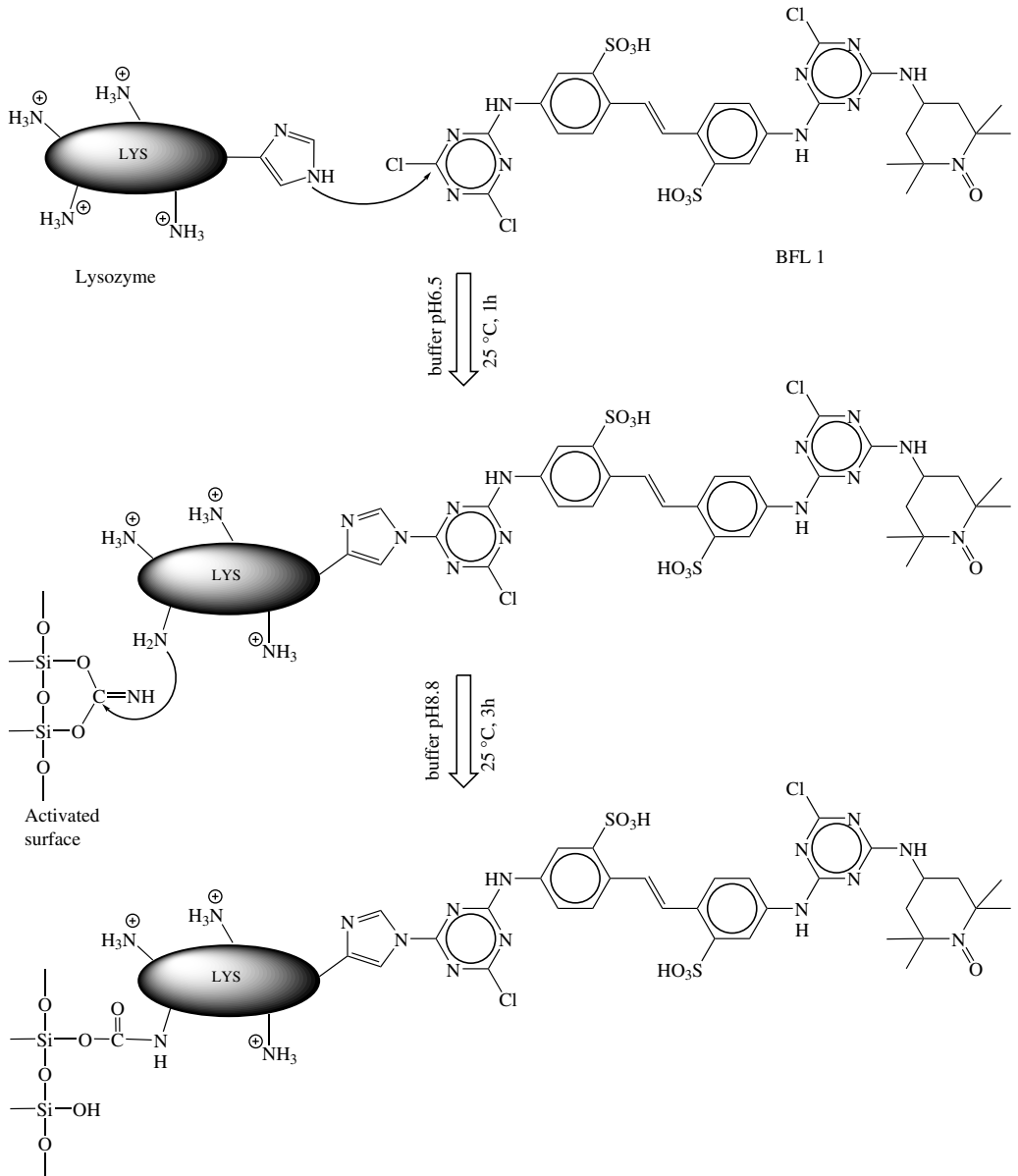


Figure 1.25 Scheme of immobilization of BFLT on quartz plate by BrCn with lysozyme as a tether [150]. (Reproduced with permission from Elsevier.)

analytes were detected by mass spectrometer with electron impact source in selected ion monitoring mode (EI/SIM) and quantified with an external standard calibration curve method. Linear calibration curves were obtained in the concentration ranges from 5 to 500 $\mu\text{g}/\text{l}$ for HS and from 10 to 1000 $\mu\text{g}/\text{l}$ for DES and DIS.

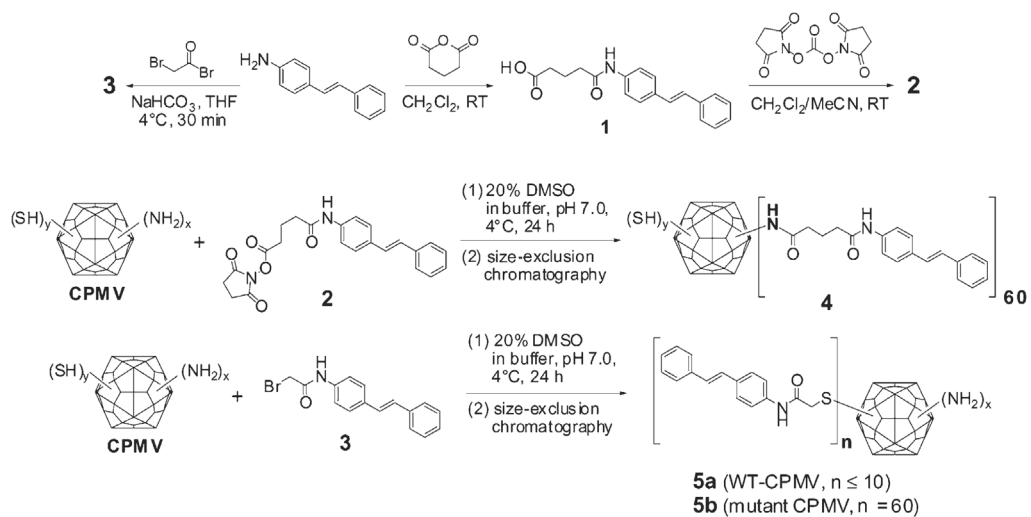


Figure 1.26 Preparation of virus–stilbene conjugate. (Reproduced with permission from Ref. [151].)

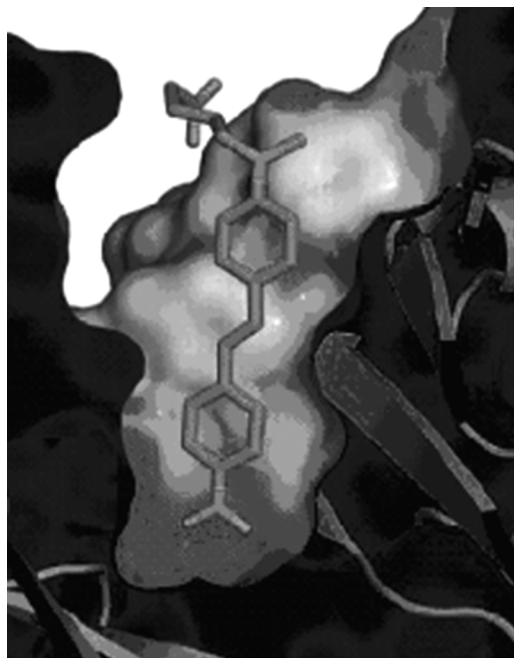


Figure 1.27 Antibody combining site of 11G10 in complex with hapten with electron density contoured at 1.5σ . Representation of the electrostatic surface [152].

A comprehensive method for the detection of four stilbene-type disulfonate agents and one distyrylbiphenyl-type fluorescent whitening agent (FWA) in paper materials (napkin and paper tissue) and infant clothes using the newly developed Oasis WAX (mixed mode of weak anion exchange and reversed-phase sorbent) solid-phase extraction cartridge was proposed [154]. The analytes were detected by ion-pair chromatography coupled with negative electrospray ionization-tandem mass spectrometry (HPLC-ESI-MS/MS), applying a di-*n*-hexyl-ammonium acetate (DHAA) as the ion-pairing reagent in mobile phase. The method was applied to commercial samples, showing that two stilbene-type disulfonates were predominant FWAs detected in napkin and infant cloth samples.

Three different sample preparation techniques, solid-phase extraction, reverse osmosis, and vacuum distillation, were studied and the recoveries were compared for detecting highly water-soluble stilbene sulfonic acids by liquid chromatography with photodiode array (PDA) and electrospray ionization-tandem mass spectrometry (LC-ESI-MS/MS) [155]. The detection limits were 1–28 µg/l with LC-ESI-MS. The sample collected from wastewater treatment plant contained 21.1, 13.3, 12.1, 41.8, and 9.9 µg/l of *cis*-4,4'-diaminostilbene-2,2'-disulfonic acid (*cis*-DASDA), *trans*-4,4'-diaminostilbene-2,2'-disulfonic acid (*trans*-DASDA), 3-amino acetanilide-4-sulfonic acid (3-AASA), 4-chloroaniline-2-sulfonic acid (4-CASA), and 2-chloroaniline-5-sulfonic acid (2-CASA), respectively. Reversed-phase high-performance liquid chromatography (RP-HPLC) with PDA and MS detection was employed to study the accumulation of stilbenes and other naturally occurring polyphenol intermediates of flavonoid pathway in tomato fruits of plants genetically modified to synthesize resveratrol [156]. The results of these analysis revealed that the genetic modification of the tomato plants originated from different levels of accumulation of *trans*- and *cis*-piceid and *trans*- and *cis*-resveratrol in their fruit depending on the stages of ripening. Determination of stilbenes in *Sicilian pistachio* by high-performance liquid chromatographic diode array (HPLC-DAD/FLD) was carried out [157]. The presence of several natural stilbenes in 12 samples of pistachios harvested from 10 different farms of Sicily (Bronte and Agrigento) was detected and two types of stilbenes in the samples of pistachios examined, *trans*-resveratrol and *trans*-resveratrol-3-*O*-β-glucoside (*trans*-piceid), were found. HPLC methods for the detection of 2,3,5,4'-teterahydroxystilbene-2-*O*-β-*D*-glucoside in Yangyan Pills were used [158]. The 2,3,5,4'-teterahydroxystilbene-2-*O*-β-*D*-glucoside sample showed a good linear relationship in the range of 0.05–0.40 mg/ml.

Determination of glyoxal (Go), and methylglyoxal (MGo), in the serum of diabetic patients by MEKC, using stilbenediamine as derivatizing reagent, was reported [159]. Uncoated fused silica capillary, effective length 50 cm × 75 µm i.d., applied voltage 20 kV, and photodiode array detection were used. Calibration was linear within 0.02–150 µg/ml with detection limits of 3.5–5.8 ng/ml. An HPLC method with photodiode array detection and ESI/MS detection was developed for the qualitative and quantitative analyses of stilbenes, stilbene glycosides, and other compounds in the dried rhizome of *Polygonum cuspidatum* [160]. Five samples of *Rhizoma polygoni cuspidati* from different regions were analyzed by this method. The major constituents piceid, resveratrol, emodin-8-*O*-β-*D*-glucoside, and emodin were

selected to provide an index for the quality assessment of the herbal drug. A simple, sensitive, and specific HPLC method was developed and applied for simultaneous detection of the six major active constituents in *Smilax china*, namely, taxifolin-3-O-glycoside, piceid, oxyresveratrol, engeletin, resveratrol, and scirpusin A [161]. The samples were separated on an Agilent Zorbax XDB-C18 column with gradient elution of acetonitrile and 0.02% (v/v) phosphoric acid at a flow rate of 1.0 ml/min and detected at 300 nm.

A liquid chromatography–andem mass spectrometry method was proposed for simultaneous detection of stilbenes, diethylstilbestrol, hexestrol, and dienestrol in animal tissue [162]. Sample cleanup and analyte enrichment was performed by automated solid-phase extraction (ASPE) with a silica gel cartridge. The recovery level of the method was 84–108% for DES and DIS between 0.5 and 5 ng/g, and 59–87% for HS between 0.25 and 2.5 ng/g. A facile method based on liquid chromatography coupled with electrospray ionization-tandem mass spectrometry has been established for the analysis of bioactive phenolic compounds in rhubarbs [163]. From six rhubarb species (*Rheum officinale*, *R. palmatum*, and *R. tanguticum* and unofficial *R. franzenbachii*, *R. hotaoense*, and *R. emodi*), a total of 107 phenolic compounds were identified or tentatively characterized based on their mass spectra. Stilbenes, which are the major constituents of unofficial rhubarbs, were found to be different among the species. Seven prenylated stilbenes were identified by combined HPLC-PAD-APCI/MSn analysis of an extraction of mucilage isolated from peanut (*Arachis hypogaea* L.) root tips [164]. The principal constituent was assigned the structure 4-(3-methyl-but-1-enyl)-3,5-dimethoxy-4'-hydroxy-*trans*-stilbene (I). The common name mucilagin A was proposed for this novel compound, with its concentration in the mucilage established at 250 µg/g (wet weight basis). The authors suggest that compounds detected in peanut mucilage may play a role in regulating root–soil pathogen interactions.

A combination of reversed-phase HPLC with UV-diode array detection and electrospray ionization-tandem mass spectrometry ion-trap detection was used for characterization of a photochemical mixture of *trans*-resveratrol and its derivatives, including oligomers and glucosides [165]. As the polyphenol source, the stems of three frost-hardy grapevine varieties (*Hasaine* (*Hasansky*) *sladki*, *Zilga*, and *Yubilei Novgoroda*) were used. A quantitative determination of stilbene oligomers in *Jin Que-gen* collected from different regions was performed [166]. An HPLC method has been developed for efficiently quantifying two stilbene tetramers, carasinol B (1) and kobophenol A (2), and one stilbene trimer, (+)- α -viniferin (3), in the plant. A simultaneous determination of the contents of two stilbene tetramers, carasinol B and kobophenol A, and one stilbene trimer, (+)- α -viniferin, in roots, tubers, and leaves of *Caragana sinica* in various seasons was performed using an improved HPLC method [167]. The contents of stilbene tetramers were maximal in winter while the contents of the stilbene trimer were maximal in summer.

A rapid analysis of resveratrol, *trans*- ϵ -viniferin, and *trans*- δ -viniferin from downy mildew-infected grapevine leaves by liquid chromatography–atmospheric pressure photoionization mass spectrometry was performed [168]. The characterization of unknown stilbene derivatives such as six resveratrol dimers, two dimethylated

resveratrol dimers, and a resveratrol trimer is reported. ^{13}C NMR spectroscopy in combination with HPLC and spectrophotometry was used to complement HPLC or spectrophotometry to analyze stilbene and anthocyanin metabolites in grape cell cultures [169]. The effect of various elicitors such as sucrose and methyl jasmonate and fungal elicitor on stilbene and anthocyanin biosynthesis was investigated. Methyl jasmonate and fungal elicitor strongly increased stilbene production through the activation of enzymes from phenylalanine ammonia lyase to stilbene synthase. A liquid chromatography–mass spectrometry method was employed to analyze total resveratrol (including free resveratrol and resveratrol from piceid) in fruit products and wine [170]. Samples were extracted using methanol, enzymatically hydrolyzed, and analyzed using reversed-phase HPLC with positive ion atmospheric pressure chemical ionization (APCI) mass spectrometric detection. Following APCI, the abundance of protonated molecules was recorded using selected ion monitoring of m/z 229. An external standard curve was used for quantitation, which showed a linear range of 0.52–2260 pmol of *trans*-resveratrol injected on-column. The extraction efficiency of the method was detected to be 92%. Resveratrol was detected in grape, cranberry, and wine samples. Concentration ranged from 1.56 to 1042 nmol/g in Concord grape products and from 8.63 to 24.84 $\mu\text{mol/l}$ in Italian red wine. Concentrations of resveratrol were found to be similar in cranberry and grape juice at 1.07 and 1.56 nmol/g, respectively.

1.8.2

Miscellaneous Analytical Methods

X-ray structure of 1-(methylthio)-*cis*-stilbene-2-thiol, $\text{Ph}(\text{SCH}_3)\text{C}:\text{C}(\text{SH})\text{Ph}(\text{HL})$, and 1-(benzylthio)-*cis*-stilbene-2-thiol, $\text{Ph}(\text{SCH}_2\text{Ph})\text{C}:\text{C}(\text{SH})\text{Ph}$, forming monomeric complexes with Sb^{3+} complex was established [172]. The structure of Moracin M, a stilbenoid extracted from the stem bark of *Milicia excelsa* (*Moraceae*), was obtained by a single-crystal X-ray analysis. A competitive ELISA method was developed for quantitative detection of hexestrol [173]. Polyclonal rabbit antisera, raised against protein conjugate hexestrol-mono-carboxyl-propyl-ethyl-bovine-serum-albumin (HS-MCPE-BSA), were used in immobilized antibody-based and competitive immunoassays. Assay conditions, including concentration of antisera and horseradish peroxidase (HRP)-HS, were optimized. The effects of incubation time, surfactant concentration, ionic strength, and pH of the medium were also investigated. The typical calibration curve gave an average IC_{50} value of 2.4 ng/ml, calibration range from 0.2 to 30.5 ng/ml, and a detection limit of 0.07 ng/ml.

Stilbene-related heterocyclic compounds including benzalphthalide, phthalazinone, imidazoindole, and pyrimidoisoindole derivatives were tested for their anti-HIV activity [174]. Assays based on recombinant viruses were used to evaluate HIV replication inhibition, and stably transfected cell lines were used to evaluate inhibition of Tat and NF- κB proteins. Some of the stilbene-related heterocyclic compounds analyzed displayed anti-HIV activity through interference with NF- κB and Tat function. Near-IR spectroscopy (NIRS) and artificial neural networks were employed for quantitative detection of four active constituents in rhubarb:

anthraquinones, anthraquinone glucosides, stilbene glucosides, and tannins and related compounds [175]. The authors proposed that this method can be used for detecting the active constituents in Chinese herbal medicine. Simultaneous determination of stilbene and anthraquinone compound in *Polygonum cuspidatum* by ultraviolet spectrophotometry was performed [176]. A method based on *in vivo* fluorescence using commercial spectrofluorometers that allowed fast and local assessment of stilbene content in grapevine leaves was tested [177]. Synthesis of stilbenes in grapevine *Vitis vinifera* var. Muscat Ottonel leaves was induced by *Plasmopara viticola* inoculation or UV-C irradiation. Fluorescence was measured from both the abaxial and adaxial sides of leaves; then, stilbene content was analyzed by HPLC. The authors concluded that significant regressions were found between HPLC stilbene content and the corresponding leaf UV-induced blue fluorescence. The authors suggested that *in vivo* fluorescence is a good tool for the rapid study of stilbene synthesis in grapevine leaves that can potentially be extended to other fluorescent molecules.

An online Raman analyzer to quantitatively track the levels of *trans*-stilbene, benzaldehyde, and α -methoxybenzyl hydroperoxide in a continuous flow ozonolysis reactor was described [178]. The analysis was carried out using spectral stripping in order to overcome baseline artifacts inherent to simple peak area detections and to incorporate prior knowledge into the analytical model. The performance of spectral stripping was compared to partial least squares (PLS) analysis. Two new dihydrostilbenes, stilbostemins H (1) and I (2), were isolated and identified from the roots of *Stemona sessilifolia*, together with known stilbostemins B, D, and G, and stemanthrenes A and C (4–8) [179]. Structures of new stilbenoids were established by 1D and 2D ^1H NMR and ^{13}C NMR.

A rapid and sensitive capillary electrophoretic method for analysis of resveratrol in wine was proposed [180]. The protocol consists of sample preparation using a C-18 solid-phase extraction cartridge. The limits of detection for *trans*- and *cis*-resveratrol were 0.1 and 0.15 $\mu\text{mol/l}$, respectively. These procedures were used to analyze the *trans*- and *cis*-resveratrol levels in 26 wines. It was found that the concentration of *trans*-resveratrol ranged from 0.987 to 25.4 $\mu\text{mol/l}$, whereas the concentration of *cis*-resveratrol was much lower. The adsorptive voltammetric behavior of resveratrol was studied at a graphite electrode in B-R buffer (pH 6.0) solution using adsorptive cyclic voltammetric technique [181]. The oxidation of resveratrol was an irreversible adsorption-controlled process. It was found that in the range from 8.0×10^{-9} to 2.0×10^{-6} mol/l, the currents measured by differential pulse voltammetries presented a good linear property as a function of the resveratrol concentration. The proposed method was also applied for the determination of resveratrol in Chinese patent medicine with good results.

An amperometric biosensor for *trans*-resveratrol determination in aqueous solutions by means of carbon paste electrodes modified with peroxidase basic isoenzymes (PBIs) from *Brassica napus* was developed [182]. Catalytic properties of PBIs from *Brassica napus* toward *trans*-resveratrol oxidation were demonstrated by conventional UV-vis spectroscopic measurements. The enzymatic reaction rate was studied and kinetics parameters were detected. An amperometric biosensor based on *Brassica*

napus PBIs to detect resveratrol was also proposed. The method employed a dialysis membrane covered, PBIs entrapped, and ferrocene (Fc)-embedded carbon paste electrode (PBIs-Fc-CP) and was based on the fact that the decreased amount of H₂O₂ produced by the action of PBIs was proportional to the oxidized amount of H₂O₂ in the solution. The lowest resveratrol value measured for a signal-to-noise ratio of 3: 1 was 0.83 μM.

Supported liquid membranes (SLMs) consisting of 5% tri-*n*-octylphosphine oxide (TOPO) dissolved in di-*n*-hexylether/*n*-undecane (1: 1) have been used in the simultaneous extraction of a mixture of three stilbene compounds (dienestrol, diethylstilbestrol, and hexestrol) in cow's milk, urine, bovine kidney, and liver tissue matrices [183]. The efficiencies obtained after the enrichment of 1 ng/l stilbenes in a variety of biological matrices of milk, urine, liver, kidney, and water were 60–70, 71–86, 69–80, 63–74, and 72–93%, respectively. A new method to contribute to the discrimination of polyphenols including resveratrol with synthetic pores was proposed [184]. The work [185] evaluated two types of commonly available chiral detectors for their possible use in chiral method development and screening: polarimeters and CD detectors. Linearity, precision, and the limit of detection (LOD) of six compounds (*trans*-stilbene oxide, ethyl chrysanthemate, propranolol, 1-methyl-2-tetralone, naproxen, and methyl methionine) on four common detectors (three polarimeters and one CD detector) were experimentally determined and the limit of quantitation calculated from the experimental LOD. *trans*-Stilbene oxide worked well across all the detectors, showing good linearity, precision, and low detection limits. However, the other five compounds proved to be more discriminating and showed that the CD detector performed better as a detector for chiral screens than the polarimeters.

As described in this chapter, stilbenes synthetic chemistry has been making gradual progress for the past two decades, paving the way for more fundamental uses and applications of stilbenes in research fields of both materials and life sciences. We could not give all details and references to cover this vast area in limited pages. Therefore, readers who want to study stilbenes chemistry further are recommended to consult relevant papers, reviews, and books cited in references.

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