

Review

Schiff Bases: A Short Survey on an Evergreen Chemistry Tool

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Received: 10 August 2013; in revised form: 18 September 2013 / Accepted: 23 September 2013 /
Published: 8 October 2013

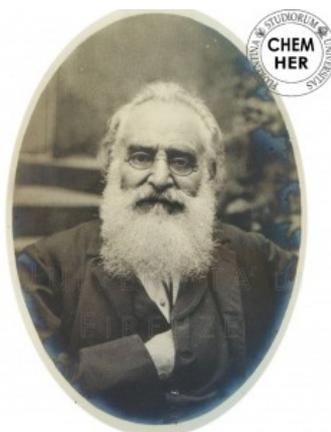
Abstract: The review reports a short biography of the Italian naturalized chemist Hugo Schiff and an outline on the synthesis and use of his most popular discovery: the imines, very well known and popular as Schiff Bases. Recent developments on their “metallo-imines” variants have been described. The applications of Schiff bases in organic synthesis as partner in Staudinger and hetero Diels-Alder reactions, as “*privileged*” ligands in the organometallic complexes and as biological active Schiff intermediates/targets have been reported as well.

Keywords: imines; Schiff bases; metallo-imines; salen complexes; bio-active-imines

1. Introduction

1.1. Ugo Schiff (Frankfurt, 26 April 1834-Florence, 8 September 1915): A Brief Biography

Ugo (Hugo) Joseph Schiff (Figure 1), one of the founders of modern chemistry, was born in Frankfurt on the 26 April 1834, into a wealthy Jewish family of merchants, Joseph Moses Schiff (1784–1852) and Henriette Trier (1798–1888).

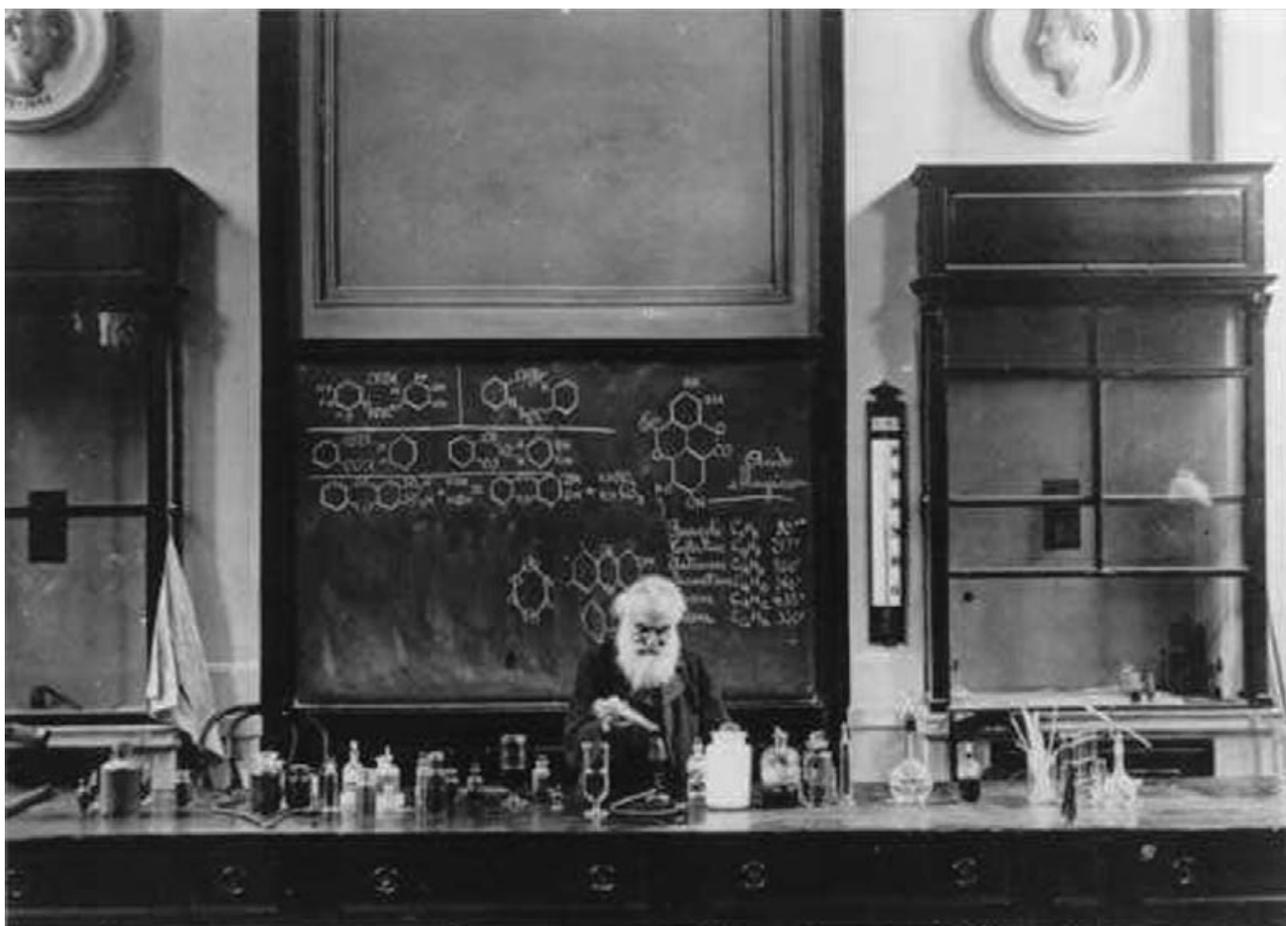
Figure 1. A portrait of Hugo Schiff.

He was the eighth son out of ten, of which only four, Moritz, Hugo, Bertha and Clementine reached adulthood [1]. He studied chemistry and physics in Frankfurt with Professors Böttenger and Löwe, and continued his studies in Göttingen, where he got his degree in 1857 under the supervision of professor Wöhler. Professor Wöhler was, in turn, student of Berzelius in Stockholm and was the first chemist to synthesize urea, an organic molecule, starting from inorganic compounds: the birth of modern organic chemistry is taught to start from this experiment, which, once and for all, excluded the presence of “*vis-vitalis*” (vital strength residing in the organic matter) demonstrating that there is no metaphysical difference between organic and inorganic substances. This was the origin of organic chemistry and the beginning of a new type of scientific research. Professor Schiff was used to say to his pupils: “*Remember that you descend from Berzelius, because Berzelius taught Chemistry to the old Wöhler and the old Wöhler taught me.*” [2]. In 1856 Ugo Schiff moved out of Germany because of his Jewish origins and political ideas and spent six years in Bern before reaching Italy where he remained for the rest of his career. On this base Professor Schiff must be fully considered an Italian Chemist. Schiff retained his liberal views and was a cofounder of the socialist Italian newspaper *L’Avanti* in 1894 (Figure 2).

Figure 2. A commemorative Postal card celebrating the 150th anniversary of Ugo Schiff’s birth.

He started by teaching chemistry as assistant professor at the University of Pisa and in 1864 was nominated professor at the *Regio Istituto di Studi Superiori Pratici e di Perfezionamento* of Florence, the future University of Florence, where he was the first chemistry teacher. Between 1864 and 1915, Ugo Schiff spent his entire career in Florence and continued teaching until 1915, the year of his death (Figure 3).

Figure 3. Hugo Schiff, 24 April 1915.



He devoted his interest to organic and inorganic chemistry, physical and analytical chemistry, mineralogy, and natural substances. His studies on Schiff bases, target of this Review, are very popular. The name “Organic Bases” appears in a paper entitled “*A New Series of Organic Bases*” (“*Eine neue Reihe organischer Basen*”) [3]. The designation of these compounds as bases, although they are not used as bases in the conventional sense, has persisted up to the present time [4]. In the meantime, boric ethers, glucosides, arbutin, tannin and gallic acid, aromatic carboxylic acids and asparagine, urea and its derivatives were also studied by Schiff. He developed the analytical methodology, later used by Sørensen, to determine amino acids in urine, and he devised the Schiff fuchsin aldehyde test [5], still in use nowadays [6]. Thionyl chloride must also be cited as one of his important discoveries [7].

1.2. Schiff Bases: Physical-Chemical Properties

Imines, known even as azomethines or Schiff bases [3,8–14] are compounds that are represented by the general formula $R_3R_2C=NR_1$. The substituents R_2 and R_3 may be alkyl, aryl, heteroaryl, hydrogen. The substituent at the *N*-imino ($C=N$) may be alkyl, aryl, heteroaryl, hydrogen or metallo (usually Si, Al, B, Sn). The physical properties and reactivity of imines are and continue to be studied by more than a hundred years [15]. Physical-chemical properties (IR, Raman, 1H -NMR, ^{13}C -NMR) of a large variety of Schiff bases are easily found in any current dedicated textbook.

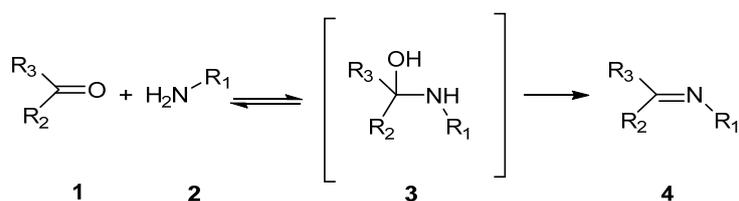
2. Preparations of Imines

2.1. Preparation of *N*-Aryl or Alkyl Substituted Imines

2.1.1. Reaction of Aldehydes and Ketones with Amines

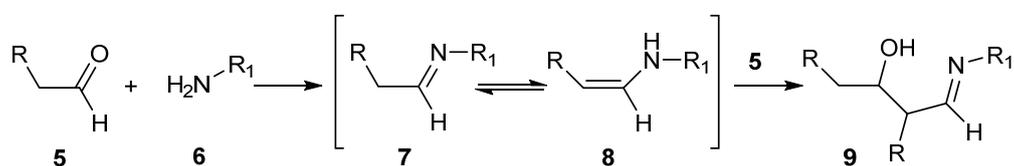
The most common method for preparing imines is the original reaction discovered by Schiff [3,5,11,16,17]. Basically it consists in the reaction of an aldehyde (respectively a ketone) with a primary amine and elimination of one water molecule (Scheme 1). This reaction can be accelerated by acid catalysis and is generally carried out by refluxing a mixture of a carbonyl compound **1** and an amine **2**, in a Dean Stark apparatus in order to remove the water. This removal is important as the conversion of aminal **3** into the imine **4** is reversible (Scheme 1). From this point several dehydrating agents have been successfully used including sodium sulphate and molecular sieves [18]. Alternatively, some *in situ* methods, involving dehydrating solvents such as tetramethyl orthosilicate or trimethyl orthoformate, have been reported as well [19,20]. As far as the use of acid catalyst is required [21–27], mineral acids, like H_2SO_4 or HCl , organic acids such as *p*-toluene sulphonic acids or pyridinium *p*-toluenesulphonate, acid resin, montmorillonite or even Lewis acids like $ZnCl_2$, $TiCl_4$, $SnCl_4$, BF_3Et_2O , $MgSO_4$, $Mg(ClO_4)_2$, *etc.*, have been reported.

Scheme 1. Schiff reaction for the preparation of imines.



In the course of the preparation of imines, if aliphatic aldehydes are used, a known competitive reaction, due to the formation of a condensation product arising from an aldol type reaction, can occur as well (Scheme 2).

Scheme 2. Aldol like condensation of aliphatic aldehydes.

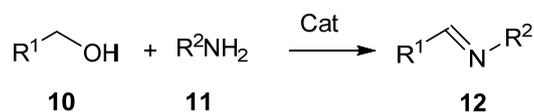


Aliphatic ketones react with amines to form imines more slowly than aldehydes, therefore, higher reaction temperatures and longer reaction time are required. Acid catalysts and water removal from the reaction mixture can significantly increase the reaction yields, which can reach 80%–95% values. Aromatic ketones are less reactive than aliphatic ones and require harsh conditions to be converted into imines [28]. Recently, several new techniques to produce imines have been published, including solvent-free, clay, microwave irradiation, water suspension medium, liquid crystals, molecular sieves, infrared and ultrasound irradiation [29–36].

2.1.2. Aerobic Oxidative Synthesis in the Preparation of Schiff's Bases

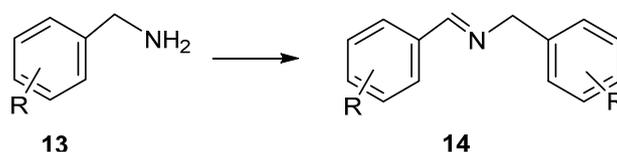
Since aldehydes and ketones are mostly obtained from the corresponding alcohols via oxidative process, a straightforward preparation of imines from amines and alcohols, through tandem oxidative processes, have recently been developed (Schemes 3 and 4) [37–44].

Scheme 3. Oxidative synthesis of imines from alcohols and amines.



Following this general approach a mild and efficient method of amine oxidation has been reported by Huang and Largeron (Scheme 4) [39,45].

Scheme 4. Oxidative synthesis of imines from amines.

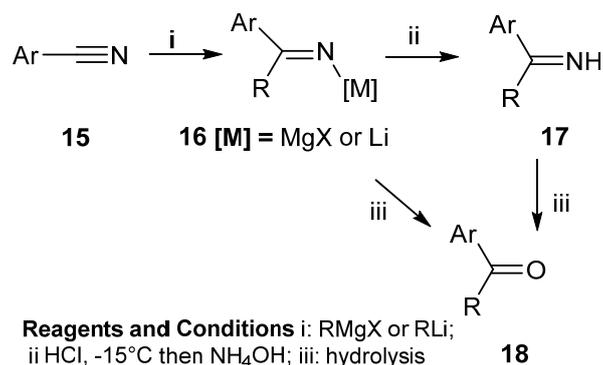
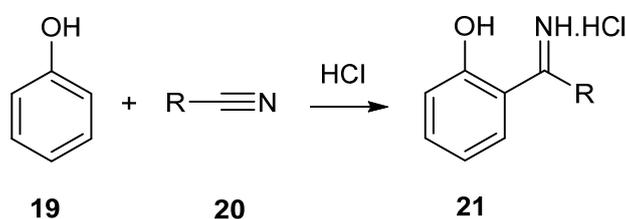


2.1.3. Addition of Organometallic Reagents to Cyanides

Addition of Grignard or organolithium reagents to aryl cyanides can lead to unsubstituted ketimines which, in turn, can be elaborated to the corresponding ketones depending on the hydrolysis conditions used to decompose the metallo imine intermediate **16** (Scheme 5). The reaction has also been extended to aliphatic cyanides [46], producing very high yields of ketimines, provided that the Mg-imine intermediate is treated with anhydrous methanol [47]. The use of heteroaryl lithium reagents affording the corresponding ketimines has also been reported [48].

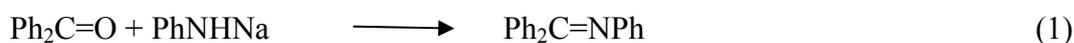
2.1.4. Reaction of Phenols and Phenol-Ethers with Nitriles

Alkyl and aryl cyanides react smoothly with phenols and their ethers producing ketimines in very good yields in the presence of an acid catalyst (Scheme 6) [49–51]. The reaction is performed by mixing the nitrile and phenol in ether and saturating the solution with gaseous HCl, whereas, for less reactive phenols, ZnCl₂ must be used.

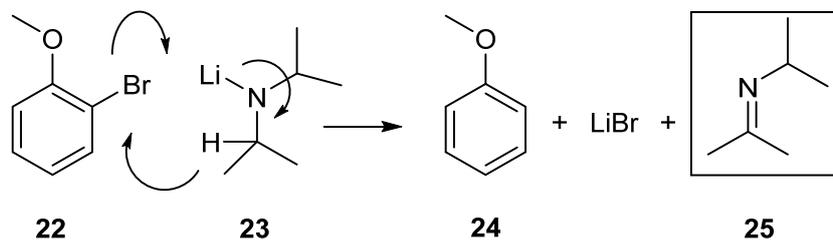
Scheme 5. Addition of organometallic reagents to cyanides.**Scheme 6.** Synthesis of ketimines from phenols and nitriles.

2.1.5. Reaction of Metal Amides

Ketimine has been produced by the addition reactions of alkali metal (or calcium amine salts) to aromatic ketones [Equation (1)]. The scope of this reaction has been widely extended [52]:

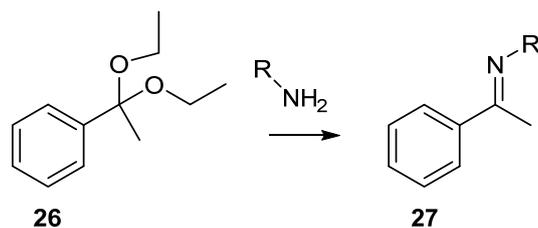


An interesting reaction is the oxidation of metalloamines bearing an α -hydrogen by 2-bromoanisole [53] to yield imines (Scheme 7).

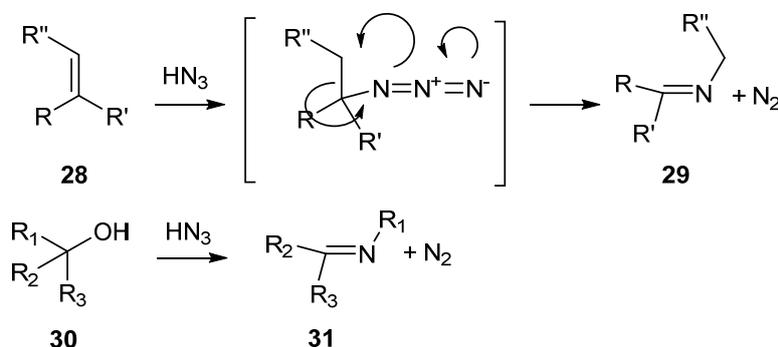
Scheme 7. Oxidation of metal amines to imines by 2-bromoanisole.

2.1.6. Other Methodologies

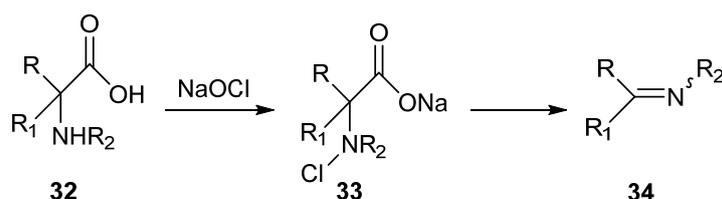
Ketimine can be prepared in high yield using aryl ketone diethyl ketals and arylamines, while alkylamines give only low yields (Scheme 8) [54]. Similarly, imines can react with higher boiling point amines to give the exchange products. The latter can be distilled driving the equilibrium towards the formation of the desired product [55].

Scheme 8. Synthesis of ketimines from ketals.

Olefins and tertiary alcohols can be converted into ketimines [56] by reaction of hydrazoic acid in sulfuric acid (Scheme 9).

Scheme 9. Reaction of olefins and tertiary alcohols with hydrazoic acid.

Imines can also be formed by reaction of amino acids with sodium hypochlorite (Scheme 10). The first step of this reaction is the formation of a chloramine intermediate that gives rise to the imine via elimination of carbon dioxide and sodium chloride [57].

Scheme 10. Conversion of α -amino acids into imines.

2.2. Preparation of *N*-Metallo-Imines as Stable Synthetic Equivalents of *N*-Unsubstituted Schiff Bases [58]

N-metallo-imines constitute a young family of organometallic compounds congeners of Schiff bases [59]. They have been found synthetic applications in the last few decades as relatively stable analogues of the corresponding Schiff bases. Their elaborations to azadiene have been fully explored by the Barluenga [60–62], Ghosez [63,64] and Panunzio groups [65–69]. Generally speaking, they are monomeric compounds reasonably stable under anhydrous conditions. Since the metal-nitrogen bond is easily hydrolysed, the *N*-metalloimines may be considered a protected, stabilized form of the corresponding elusive imines of ammonia, which are known to be very unstable readily trimerizing to triazines [11]. Although some metalloimines, e.g., the silylimines of certain aldehydes, can be isolated in a pure form by distillation under reduced pressure, for synthetic purposes it is in general more

convenient to prepare them *in situ* just before the use. In this case it is possible to ascertain their structure by a combined use of IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$ and mass spectroscopic techniques.

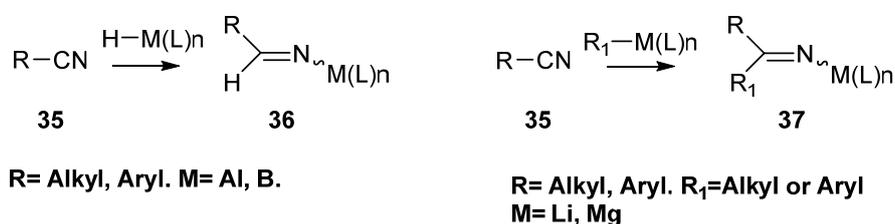
2.2.1. Preparation of Certain *N*-Metallo Imines (Metallo = B, Al, Si, Sn) [70]

2.2.1.1. Preparation of *N*-Boryl [71–73] and *N*-Aluminium Imines [74–78]:

Addition of an Organometallic Reagents or a Metallo Hydride to a Nitrile [59,79–82]

Scheme 11 illustrates the general procedure used to prepare metalloimines starting from nitriles **35** and a suitable organometallic reagent either by hydrometallation to give compounds of general formula **36** or by alkylation to give compounds of general formula **37**.

Scheme 11. Preparation of *N*-metalloimines from nitriles.

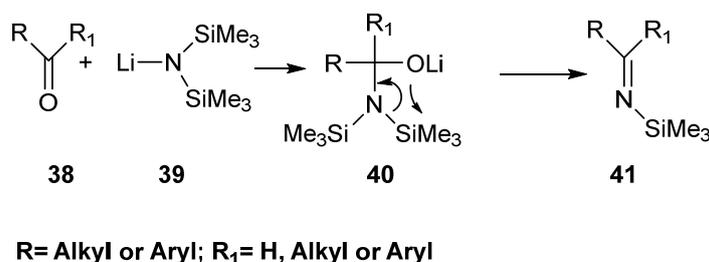


2.2.1.2. Preparation of *N*-Silylimines

2.2.1.2.1. Via Reaction of the Hexalkyldisilylamide of Group I Metals (Li, Na, K) with an Aldehyde or a Nonenolizable Ketones [83–86]

Among different metalloimines, *N*-trialkylsilyl imines must be considered the most popular and the most used intermediates in the preparation of nitrogen containing organic compounds, with special emphasis to the potentially bioactive ones [67,86]. Silyl imines have been prepared, for the first time, by Rochow [84] starting from aromatic aldehydes and nonenolizable ketones by treatment of the carbonyl compounds with one equivalent of lithium hexamethyldisilylamide in tetrahydrofuran [86]. The reaction proceeds by an addition-elimination sequence probably involving a four centers cyclic transition state (Scheme 12).

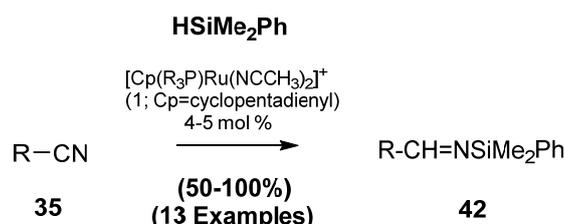
Scheme 12. Preparation of *N*-silylimines via reaction of lithium hexalkyldisilylamide.



Ketones, bearing a hydrogen atom in α -position to the carbonyl group, failed to produce the silylimines since in this case the strongly basic organometallic reagent attacks an α -hydrogen affording the corresponding lithium enolate. Enolizable aldehydes were supposed to behave in the same way [85].

This notwithstanding the preparation of such silyl imines is easier than one might expect [87]. Few competitive methods, to the above cited, have been reported in the last few years on the preparation of *N*-alkylsilyl imines. Very recently Nikonov and co-workers [88] reported an elegant preparation of *N*-silyl-aldimines **42** via a chemoselective hydrosilylation of nitriles **35** catalysed by ruthenium complex (Scheme 13).

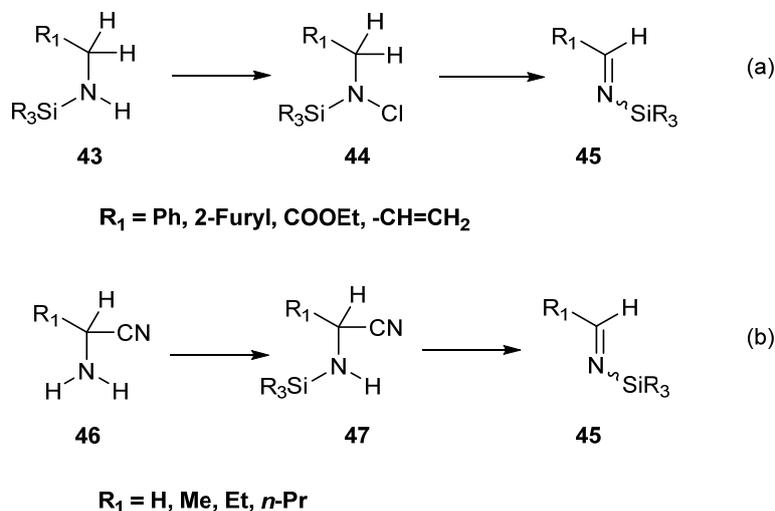
Scheme 13. *N*-alkylsilyl imines via hydrosilylation of nitrile.



2.2.1.2.2. Preparation of *N*-Silylimines via Base-Induced Elimination of Vicinal Substituent from *N*-Silyl Amines [89,90]

In analogy of classical preparation of Schiff Bases silyl-imines **45** may be prepared by elimination of vicinal substituents as shown in (Scheme 14).

Scheme 14. Formation of silylimines via elimination of vicinal groups. (a) from *N*-chloro silylamines; (b) from α -cyano silylamines.

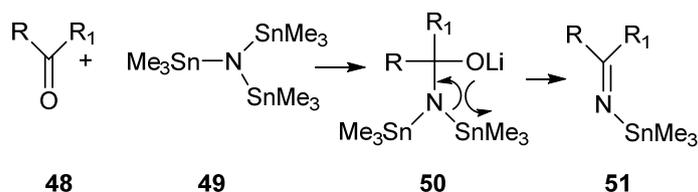


2.2.1.3. Preparation of *N*-tin-Imines via Reaction of Carbonyl Compounds with Tris(trimethylstannyl)amine [91]

This method allows the preparation of tin imines from enolizable and non enolizable aldehydes and ketones, in good yield and under very mild conditions (Scheme 15) [91]. The reaction involves an addition-elimination reaction of the type discussed for the Rochow's procedure. The organometallic reagent is, in this case, the tris(trimethylstannyl)amines which can be easily prepared from trimethyl tin chloride and lithium amide. Since the tris(trimethylstannyl)amine does not show strong basic properties, the α -deprotonation is completely suppressed thus allowing a facile preparation of

tin-imines even in the case of enolizable ketones and aldehydes. An interesting feature of the tin-imines is the possibility to undergo transmetallation reactions with trialkylsilyl chlorides (e.g., chloro *tert*-butyldimethylsilane) to give the corresponding *N*-silylimine and tris(trimethyltin)onium chloride that spontaneously precipitates from the solution. Removal of this precipitate by filtration allows the preparation of almost pure solution of silylimines [91].

Scheme 15. Synthesis of *N*-tin imines.



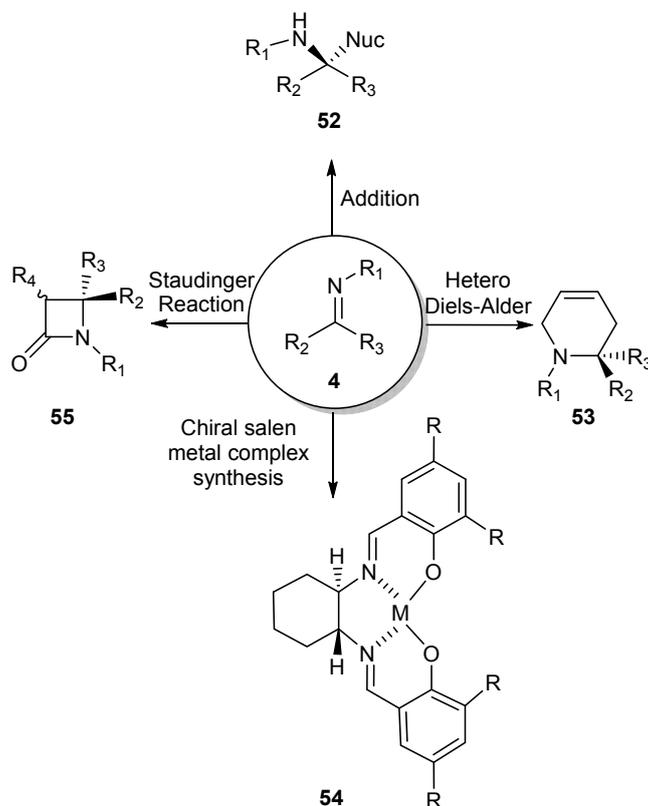
R= Alkyl or Aryl; R₁= H, Alkyl or Aryl

3. Importance of Schiff Bases in Organic Synthesis, Bio-Processes and Pharmaceutical Chemistry

3.1. Schiff Bases as Precursors of Countless Versatile Organic Processes for the Production of Intermediates/Products

As a versatile precursor for organic syntheses, we can identify, in an oversimplification, four different types of reactions in which Schiff bases have been found extremely important applications: (a) addition of organometallic reagents or hydride to C=N bond to afford compounds of structure **52**; (b) hetero Diels-Alder reaction to furnish six membered nitrogen containing heterocyclic compounds of general formula **53**; (c) skeletons for the building-up scaffolds, as the very famous *salen scaffold*, to be used as “*privileged ligand*” [92] for the formation of the corresponding *chiral salen metal complexes* **54**; (d) Staudinger reaction with ketene to furnish biologically important β -lactam ring **55** (Chart 1). It must be underlined for point (c) that we are reporting only the applications of chiral salen complexes [92–96]. For different complex catalysts, as salophen [97,98], or for the use of Schiff bases, different from salen backbone, we refer the interested reader to the following up-to-date survey of extremely good and dedicated reviews on the subject authored by specialists in the field [92,99–105].

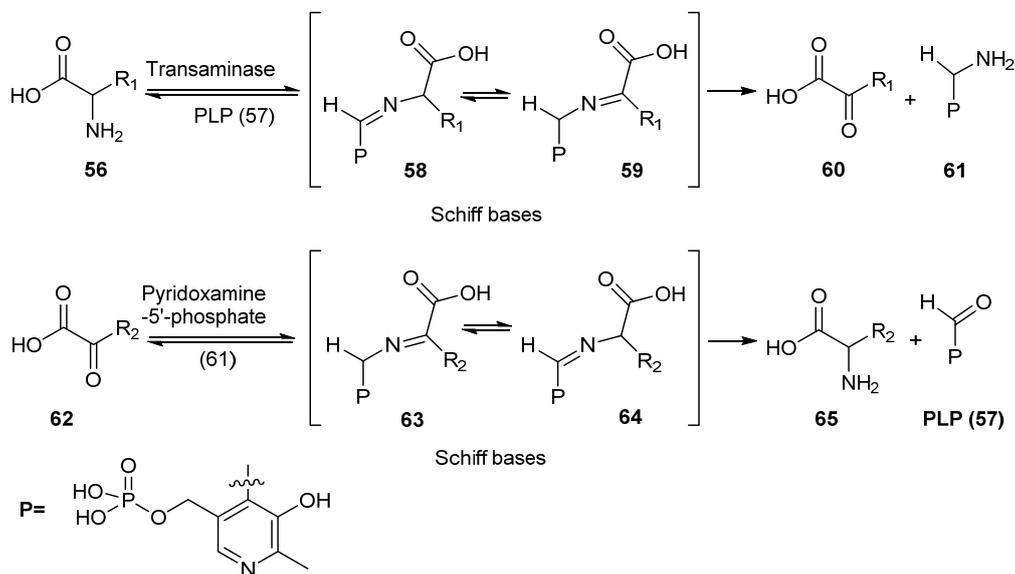
The same criteria have been used for all the applications reported in Chart 1. Accordingly we have grouped the references reported in: (a) Reduction of C=N bond, focused on asymmetric formation of carbon-carbon bond [60,106–109]; (b) Hetero Diels-Alder reactions with the formation of heterocyclic compounds [110–116]; (c) Use of chiral salen metal complexes in the asymmetric synthesis [92–96,117,118]; (d) Staudinger reactions for the preparation of β -lactams [4,119–122]. In the following paragraphs we will emphasize the importance of imines, first discovered by the Ugo Schiff, providing the reader with relevant information highlighting the importance of Schiff bases and their applications in a wide range of organic and pharmaceutical chemistry fields.

Chart 1. Applications of Schiff bases in organic synthesis.

3.2. Schiff Bases as Intermediate of Bio-Processes

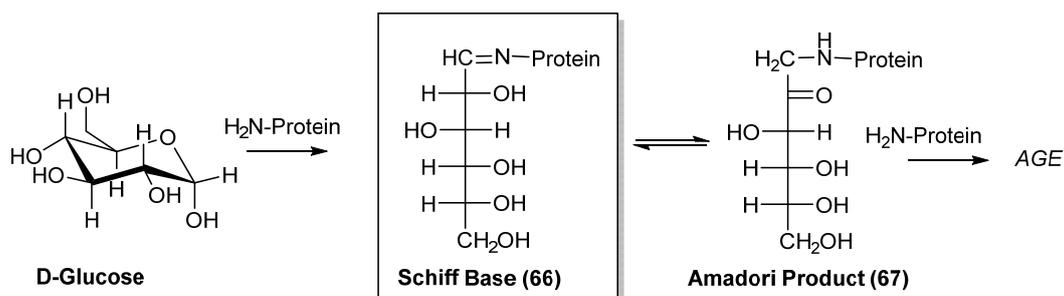
The importance of Schiff bases as intermediates in bio-processes is very well established: suffice it to mention one of the very basic process of life: the transamination reaction (Scheme 16) [123].

Scheme 16. Transamination reaction through Schiff bases from amino-acid to ketoacid and *vice versa*.



Other important bio-processes, that lately are attracting the interest of chemists and biologists, are related to the glycation of albumin that leads to the formation of important biomarkers, which are predictive of type II diabetes [124] or to the reaction between sugars and biologically relevant amines with the formation of Schiff bases. These intermediates Schiff bases **66**, in turn, evolve to Advanced Glycation Endproducts (*AGE*) through Amadori compounds (Scheme 17).

Scheme 17. Protein glycation by glucose.

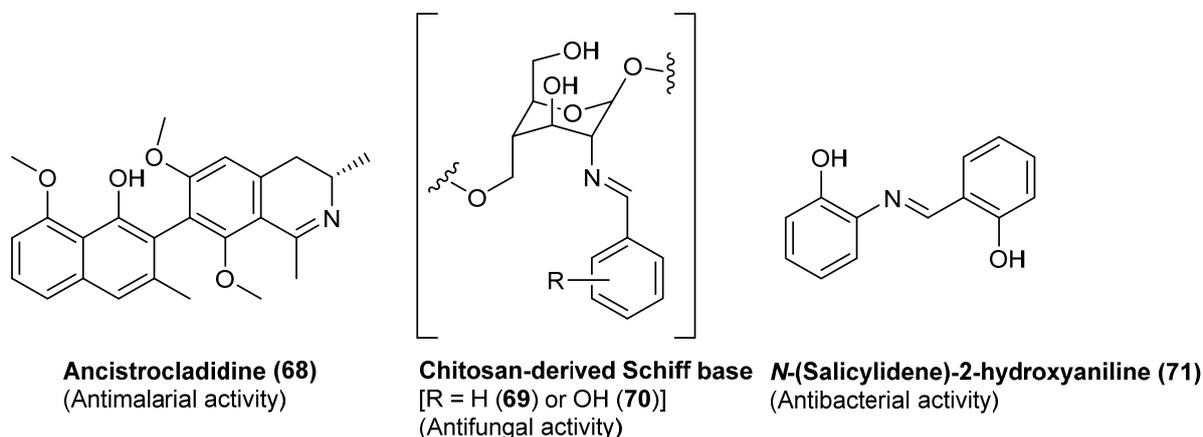


AGEs are involved in many pathological conditions such as cardiovascular disease [125], Alzheimer [126] and so on. Although these compounds are very important a depth discussion would take the reader into specific scientific area that goes behind the scope of this review. The following paragraphs will focus on the importance of Schiff discovery and present some examples of compounds featuring the Schiff bases as pharmaceutical garrisons.

3.3. Some Application of Schiff Bases in Pharmaceutical Research

There are numerous publications covering the use of Schiff bases in therapeutic or biological applications either as potential drug candidates or diagnostic probes and analytical tools. The activity of Schiff bases as anticancer compounds [127,128] including radioactive nuclide complexes, antibacterial [129–135], antifungal [25,136,137], antiviral agents [138], has been extensively studied. Moreover, Schiff bases are present in various natural, semi-synthetic, and synthetic compounds (see Figure 4 for some examples) and have been demonstrated to be essential for their biological activities [139,140].

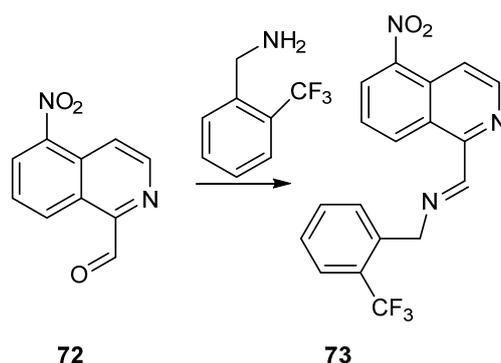
Figure 4. Some examples of biologically active Schiff bases.



3.3.1. Antiparasitic Schiff Bases

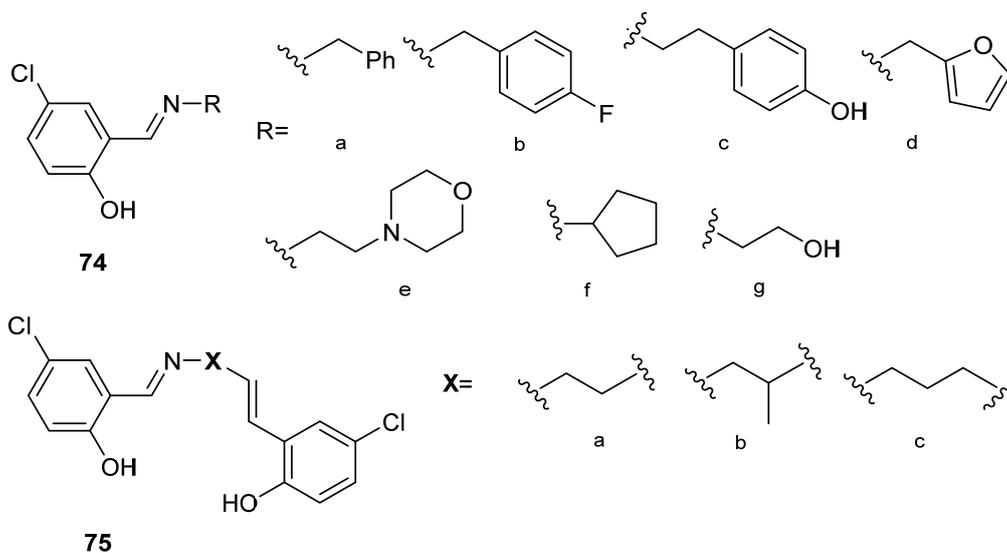
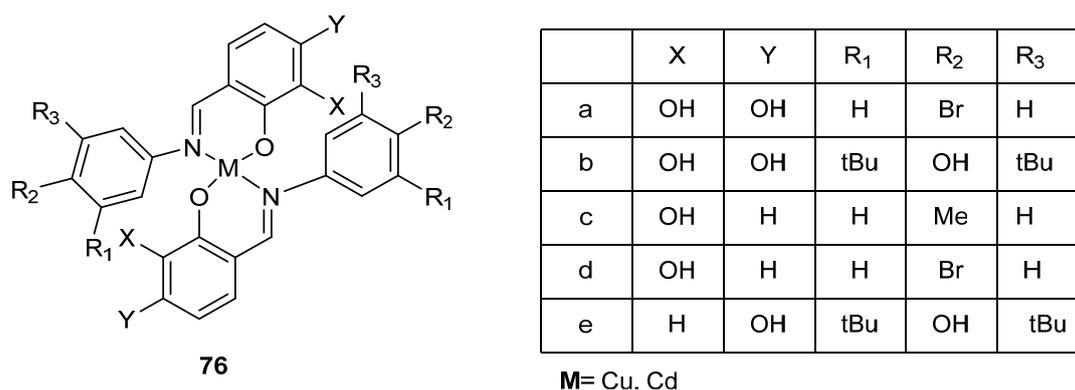
Malaria is a severe morbidity of humans and other animals. It is caused by protozoa of the genus *Plasmodium*. It is initiated by a bite from an infected female *Anopheles* mosquito, which introduces the *Plasmodium* through saliva into the circulatory system. In the blood, the protists travel to the liver to mature and reproduce. Typical symptoms of malaria include fever and headache, which, in severe cases, can progress to coma and eventually death. The imino-group of Schiff bases has been shown to be valuable function to confer antimalarial activity. For example, ancistrocladidine (**68**, Figure 4), a secondary metabolite produced by plants belonging to the families *Ancistrocladaceae* and *Dioncophyllaceae*, features an imine group in its structure. The compound has shown potent activity against *P. falciparum* K1. Some novel aldimine and hydrazone isoquinoline derivatives, prepared by reacting 1-formyl-5-nitroisoquinoline with amines (Scheme 18), showed activity against a chloroquine-resistant *Plasmodium falciparum* strain (ACC Niger). In particular the corresponding Schiff base of formyl-5-nitroisoquinoline (*E*)-*N*-((5-nitroisoquinolin-1-yl)-methylene)-1-(2-(trifluoromethyl)-phenyl)methanamine (**73**, Scheme 18) showed an IC₅₀ of 0.7 µg/mL against *P. falciparum* [137].

Scheme 18. Synthesis of some 5-nitroisoquinolines Schiff bases.



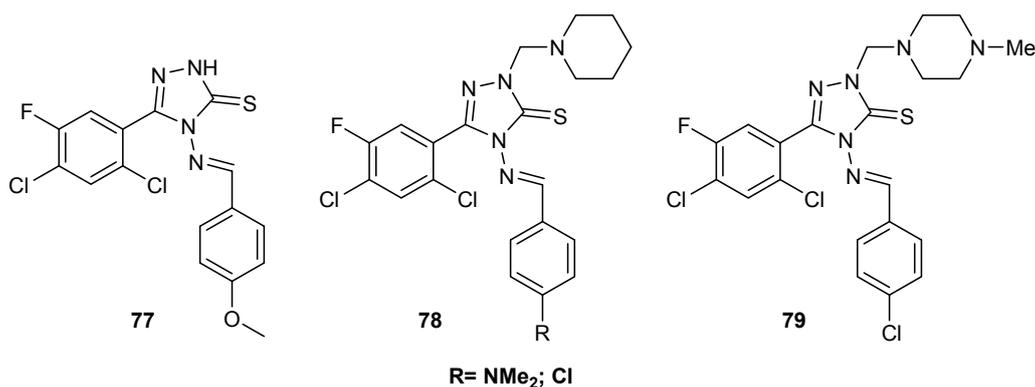
3.3.2. Salicylidene Amines as Bioactive Compounds

Salicylidenebenzylamine derivatives have been studied extensively for their biological activities [121–123]. Schiff base complexes derived from 4-hydroxysalicylaldehyde and amines have strong anticancer activity, e.g., against Ehrlich ascites carcinoma (EAC) [141]. *N*-(salicylidene)-2-hydroxyaniline, in turn, showed activity against *Mycobacterium tuberculosis* H37Rv [136]. The antibacterial activity of a series of 5-chlorosalicylaldehyde-Schiff bases (Scaffolds **74** and **75** Figure 5) was studied against several strains including *Escherichia coli* and *Staphylococcus aureus* [142]. Cu(II) and Cd(II) complexes **76** (Figure 6) of more highly functionalized salicylidenebenzylamines present higher activity with respect to the free molecules [143].

Figure 5. 5-chloro-salicylaldehyde-Schiff bases.**Figure 6.** Cu(II) and Cd(II) complexes of salicylidenebenzylamines.

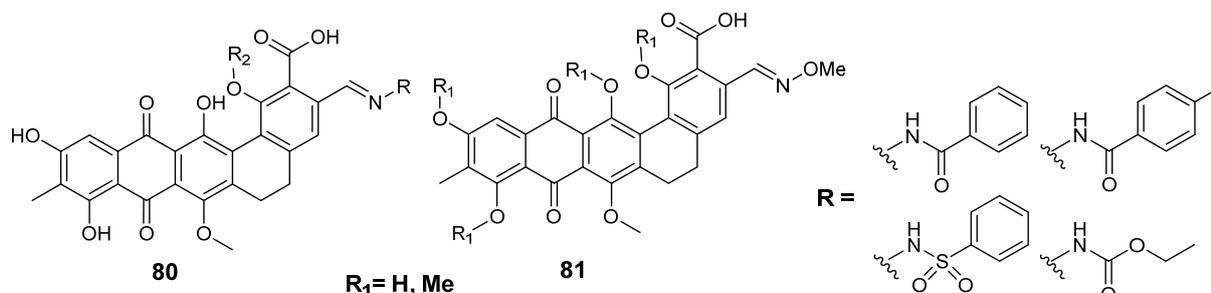
3.3.3. Other Antibacterial Schiff Bases

Schiff bases characterized by a 2,4-dichloro-5-fluorophenyl moiety (Figure 7) completely inhibited the growth of *S. aureus*, *E. coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae* with MIC values ranging from 6.3 to 12.5 $\mu\text{g/mL}$, which are comparable to ciprofloxacin [134].

Figure 7. Chemical structure of 2,4-dichloro-5-fluorophenyl Schiff bases.

The secondary metabolites of the plant *Actinomadura rubra*, madurahydroxylactones, have been transformed into the corresponding Schiff bases **80** (Figure 8) [144]. Madurahydroxylactone-derived compounds inhibited *in vitro* *B. subtilis*, *Micrococcus flavus*, *Sarcina lutea*, and *S. aureus* giving MIC values varying from 0.2 to 3.1 $\mu\text{g/mL}$ [145].

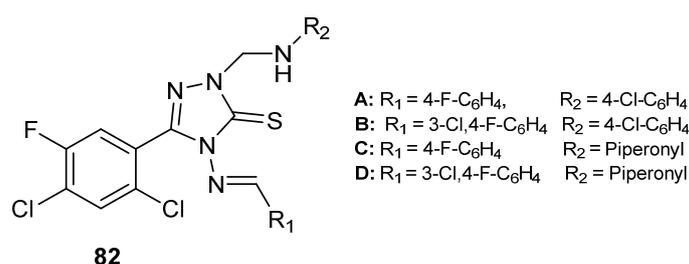
Figure 8. Madurahydroxy lactones Schiff bases.



3.3.4. Antifungal Schiff Bases

Schiff bases of chitosan **69** and **70** (See Figure 4) have shown antifungal activity against *Botrytis cinerea* and *Colletotrichum lagenarium* [140]. Imine derivatives having a 2,4-dichloro-5-fluorophenyl moiety (see Figure 7) and the Schiff bases **82**, reported in Figure 9, inhibited the growth of fungal clinical isolates, such as *Aspergillus fumigatus*, *Aspergillus flavus*, *Penicillium marneffeii*, *Trichophyton mentagrophytes*. The compounds showed MIC values in the range of 6.3–12.5 $\mu\text{g/mL}$, which is comparable to that of fluconazole [134]. The isatin-derived Schiff bases **83–86** (Figure 10) showed an interesting activity against *Microsporum audouinii* (MIC range 2.4–9.7 $\mu\text{g/mL}$) and *Microsporum gypseum* (MIC range 1.2–9.7 $\mu\text{g/mL}$) [43].

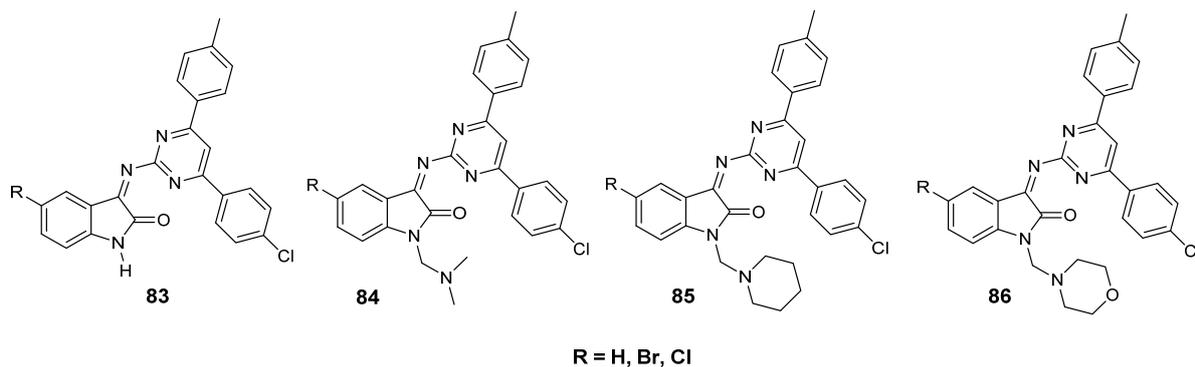
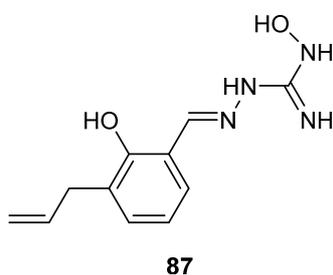
Figure 9. Antifungal Schiff bases derived from 2,4-dichloro-5-fluorophenyl scaffold.



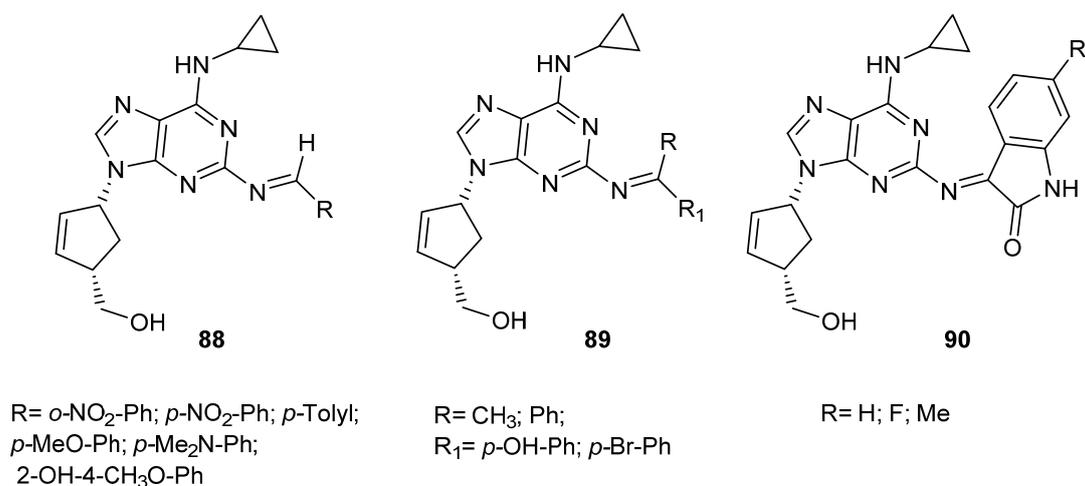
The compounds reported inhibited also *Candida albicans*, *Aspergillus niger*, *Cryptococcus neoformans*, *T. mentagrophytes*, *E. floccosum*, and *Histoplasma capsulatum* (MIC range 10–79 $\mu\text{g/mL}$) [146].

3.3.5. Antiviral Schiff Bases

The Schiff bases of modified 3-hydroxyguanidines [147,148], have been prepared and tested against mouse hepatitis virus (MHV), in particular, compound **87** (Figure 11) inhibited the viral replication by 50% when used at a concentration of 3.2 μM .

Figure 10. *Isatin* derived Schiff bases.**Figure 11.** Modified 3-hydroxyguanidines antiviral Schiff base.

Similarly, a set of imine derivatives of abacavir [148] have been prepared and tested for their antiviral activity. Compounds **88–90** in Figure 12 were highly effective against the human immunodeficiency virus-type 1 (HIV-1). The molecules, which are reported to be Abacavir prodrugs, showed a 50% protection of human leukemic cells (CEM) at micromolar and even nanomolar concentration (compound **87**, $EC_{50} = 50$ nM).

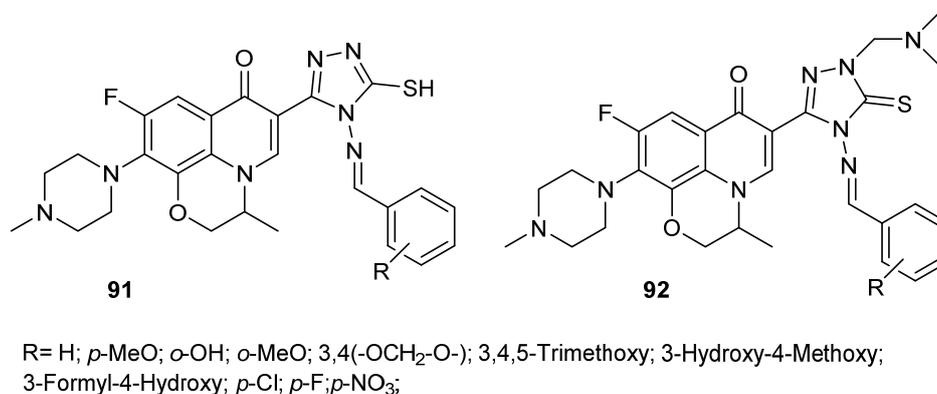
Figure 12. Schiff bases of abacavir.

3.3.6. Hybrid Structures

The use of hybrid structures to achieve new pharmacological activities is widely used in medicinal chemistry. In an attempt to achieve novel antitumor compounds, Schiff and Mannich bases of

fluoroquinolones have been prepared and tested in cell line [149] (Figure 13). In particular compounds **92** depicted in Figure 13 showed potent activity against L1210, HL60 and CHO tumor cells in the MTT assay.

Figure 13. Chemical structure of hybrid fluoroquinolone-Schiff bases.



4. Conclusions

On typing “Schiff bases” in any chemistry database a countless number of records appears as proof of the importance of such derivatives in chemistry. They are present as reactants in umpteen synthetic organic processes, as important scaffolds in organometallic chemistry, as backbones of precious catalysts and as pharmaceutical presidiums against a series of different diseases and pathological states. According to the scope of this review we have tried to give simple headlines not pretending to account the multidisciplinary applications of Schiff Bases. The short section on *N*-metalloimines has been included because they must be considered as synthetic equivalents of the Schiff base arising from aldehydes/ketones and the simplest amine: ammonia. Our final goal has been to celebrate the name of an Italian (by adoption) founder of modern Organic Chemistry: Professor Hugo Schiff from the University of Florence.

Acknowledgments

S.L. and W.L.Q. thank China Scholarship Council (CSC) for Scholarships (2009–2012 and 2010–2013, respectively).

Conflicts of Interest

The authors declare no conflict of interest.

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