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A Historical Perspective on the Structure, Synthesis, and Use of Azines

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Abstract: A general overview of the chemistry of 2,3-diaza-1,3-butadienes (azines) is provided in this article. We briefly overview azines before reviewing the literature on their Synthesis, characteristics, uses, and reactivity. We conclude by highlighting their importance and looking into their organometallic chemistry. Since it has not been offered before, a thorough analysis of the broad chemical properties of azine derivatives appears suitable.

INTRODUCTION

In chemistry, the word "azine" has two different meanings. In heterocyclic chemistry, azines are aromatic six-membered rings with one (pyridine) to six (hexazine) N atoms. Azines are substances produced by the reaction of two molecules of the same carbonyl compound (symmetrical azines 1) or, more frequently, two different carbonyl compound molecules (unsymmetrical azines 2) with hydrazine in alicyclic chemistry (Fig. 1). Depending on whether the carbonyl component is an aldehyde or a ketone, the compounds are referred to as aldazines or ketazines, respectively.

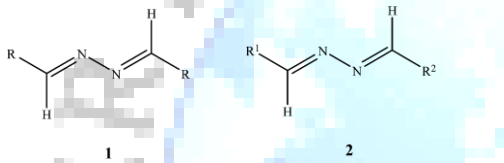
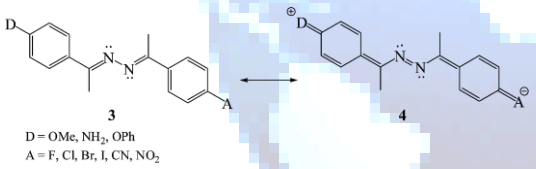
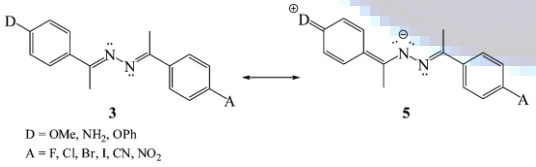


Fig. 1 Structures of symmetrical and unsymmetrical azines.



Scheme 1

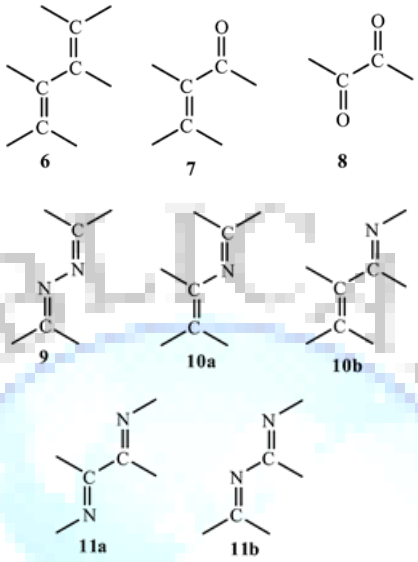


Scheme 2

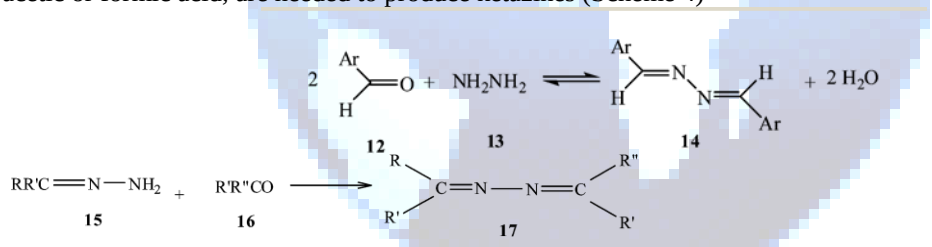
Azines that are 2,3-diaza analogues of 1,3-butadiene are N-N-linked diimines. The two imine bonds that make up the azine moiety can be considered polar acceptor groups with opposite orientations, including an N-N link. They are a class of molecules with intriguing chemical properties that go through numerous chemical processes. Third, given their connection to butadiene, electronic delocalization may be anticipated. In Scheme 1, resonance structures 3 and 4 illustrate delocalization. However, there is scant proof of delocalization inside the azine backbone regarding crystallographic information, nuclear magnetic resonance (NMR) spectroscopic studies, and theoretical computations. Accordingly, it was determined that an azine bridge, often known as a "conjugation stopper," between two conjugated systems prevents delocalization, as demonstrated by the resonance structure 5 (Scheme 2). The study of systems with two or more components has been one of the active areas of organic chemistry over the past few years. Double bonds that are coupled. Three types of molecules have drawn the most significant interest within this general family of compounds: 1,3-dienes 6, enones 7, and 1,2-diones

Azines 9, enimines 10a and 10b, and 1,2-diamines 11a and 11b make up numerous more types of compounds with two conjugated double bonds in addition to the molecules indicated above. The bifunctionality of hydrazine causes two different sorts of complex scenarios in the mechanisms of hydrazine addition to carbonyl compounds. First, the nucleophile can be a base and mono- and diprotonated forms. The monoprotonated and unprotonated forms of hydrazine can act as nucleophiles. In contrast, the diprotonated form lacks a nitrogen atom with a free electron pair, which is required for nucleophilic assault by amines. Second, once the carbonyl compound reacts with one molecule of hydrazine to generate hydrazone, a second molecule of the carbonyl compound may also react to form hydrazone.

Arch]N-N]CHAr 14, a type of azine, is produced due to this reaction (Scheme 3).



The simplest azine, formaldehyde, was created in 1959 by Neureiter5. Aldehyde > dialkyl ketone > alkyl ketone > diaryl ketone is the order in which hydrazine reacts with different carbonyl compounds. Aldazines form more quickly than ketazines when aldehydes and dialkyl ketones are combined with hydrazine in water or an alcoholic media. Aldazine is the typical byproduct because the reaction of aldehyde hydrazones with a second aldehyde molecule proceeds more quickly than with hydrazine. On the other hand, excess ketone plus an acid catalyst, such as acetic or formic acid, are needed to produce ketazines (Scheme 4)



Scheme 4

Azines can aid in isolating, purifying, and characterising carbonyl compounds. They have several benefits as protective agents, including economic benefit due to low cost (only one-half equivalent of protective group is required), ease of product isolation due to symmetrical structure and high melting points, and ease of product identification due to fully conjugated and colourful structures.

The ability of unsymmetrical azines to functionally link two disparate groups in valuable ways makes them particularly intriguing. For instance, they can create derivatives of steroidal opiates that have sustained opioid antagonist action. Because symmetrical azines are often crystalline, recrystallization is a simple way to purify them. This conclusion implies that a novel and generic approach for synthesizing unsymmetrical azines may accelerate the development of other beneficial uses. The simplicity of purification and one-step Synthesis with a quantitative yield of the desired product are two significant benefits of symmetrical azines. However, In optoelectronic devices, azine linkage is used to connect several chromophores. This makes unsymmetrical azines with two separate carbonyl compounds more intriguing because they have a much-reduced tendency to crystallize.

Creation of azines

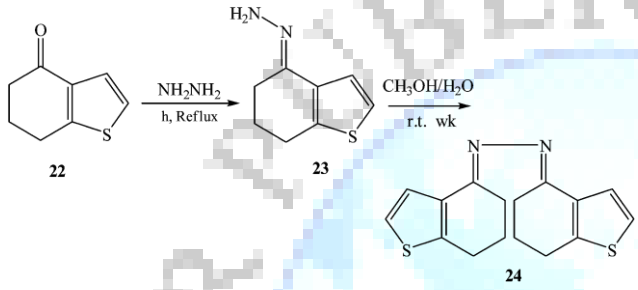
This review describes various methods for synthesizing symmetrical and unsymmetrical azines. The reaction of hydrazine with sufficient aldehyde or ketone efficiently produces symmetrical azines, either directly or indirectly.

However, the production of their unsymmetrical counterparts is more complicated. There have been reports of new and effective procedures for creating mixed azines.

Creating symmetrical azines

from iodoalkylzinc iodide (19), synthetic process. Iodoalkylzinc iodide was utilized by Applequist and Babad in 1962 to create symmetrical azines. By reacting diphenyl diazomethane, 2-diazopropane, or both with ZnI2, compound 19 was created. The diazo compound 17 and the iodoalkylzinc iodide quickly react to produce the azine 20 and the alkene. 4-Oxo-4,5,6,7-tetrahydrothianaphthene (22) and hydrazine are combined throughout the synthetic process. Cook and colleagues created the crystalline azine 24 in 1987 with a 72% yield (Scheme 6). Hydrazone 23 was produced via the interaction of 22 with hydrazine. Then, compound 23 was heated for several hours by reusing ethanolic hydrogen chloride to produce compound.

Phenyldiazomethane and 1diazo-1-phenylethane are combined throughout the synthetic process. Azines are the main byproducts of the thermal decomposition of diazo compounds.19 The reaction of a carbene with a diazo compound and the bimolecular reaction of phenyl diazomethane, 1-diazo-1phenylethane, or both can produce them. Abelt and Pleier investigated the bimolecular dimerization of phenyl diazomethane, 1-diazo-1phenylethane, or both to prepare azi, two diazo substances. The carbon atom of the first diazo compound was found to attack the terminal nitrogen of the second molecule nucleophilically as the reaction's mechanism. The resultant intermediate, which has carbanion and diazonium groups, loses N2 and transforms into azine.



Scheme 6

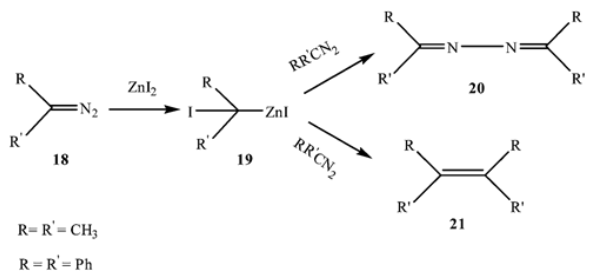
Treatment of a ketone (28) with bis hydrazone (27), leading to a new compound. Azine 29 was synthesized from 28 and 27 in 1995, according to a study by Jenneskens and colleagues (Scheme 8). In this study, oligo(cyclohexylidenes) were prepared using azine precursors.

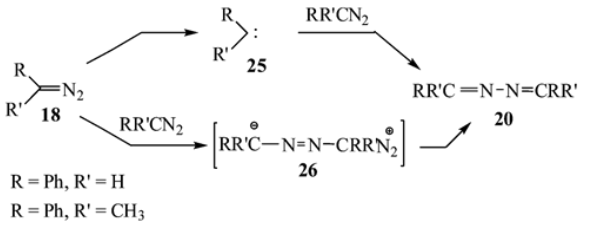
Homoallenylaldehyde (30) and hydrazine monohydrate combine to form the compound. In 1997, Marek created azine 31 from 30 by combining p-TSA in diethyl ether with an equivalent amount of hydrazine monohydrate (Scheme 9). Compound 30 was obtained with a 38% yield after purifying the product using column chromatography on silica gel and CH2Cl2.

Aryl semicarbazones are created through thermolysis (32). In 2000, Shah and Chudgar published a paper on the thermolysis of 32 to azines 35. This reaction occurs through reactive N-substituted isocyanate intermediates 33, which can undergo threefold extrusion (2CO, N2) to produce benzylamine 35 and transform in situ into the unstable isocyanate dimer.

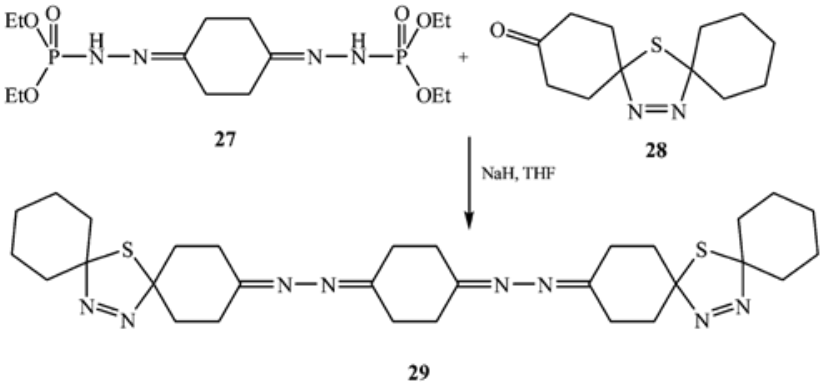
Platinum(0) complexes are used to catalyze the breakdown of diazo compounds. A high yield of di-Loren-9-ylidene-hydrazine was produced by the catalytic breakdown of 9-diazolorene (36) in the presence of the platinum(0) complex [Pt(C2H4)-(PPh3)2] (1% mol) in 2002, according to Michelin et al. (Scheme 11).

1-oxo-1,2,3,4tetrahydrocarbazoles (38) are treated with hydrazine hydrate during the synthetic process. Danish and Prasad reported in 2004 that 38 and hydrazine hydrate reacted in pure ethanol to produce N, N-bis- Derivatives of the carbazolylazine 40. The proposed mechanism makes use of Scheme 5 Scheme 7

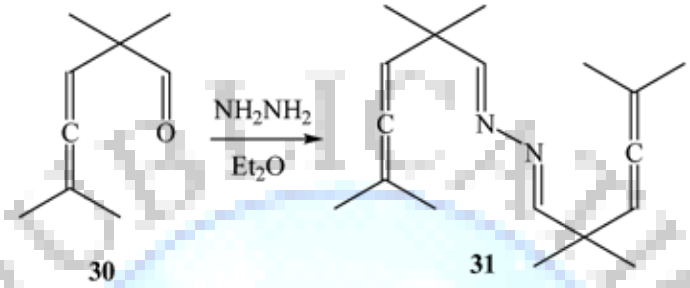




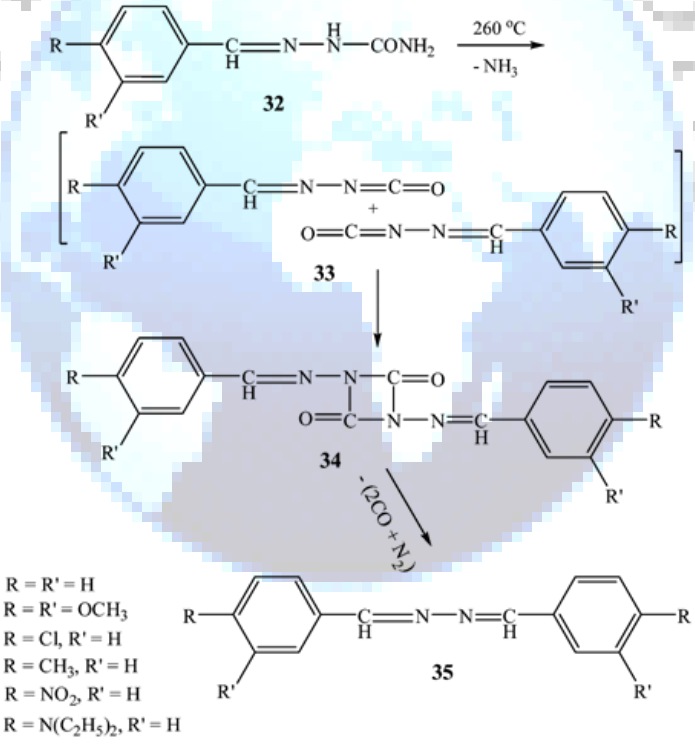
Scheme 5,7



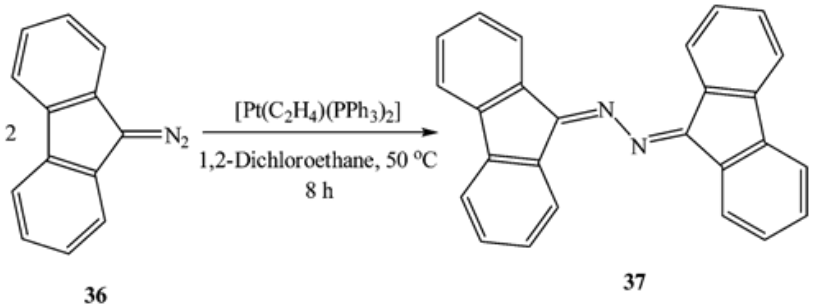
Scheme 8



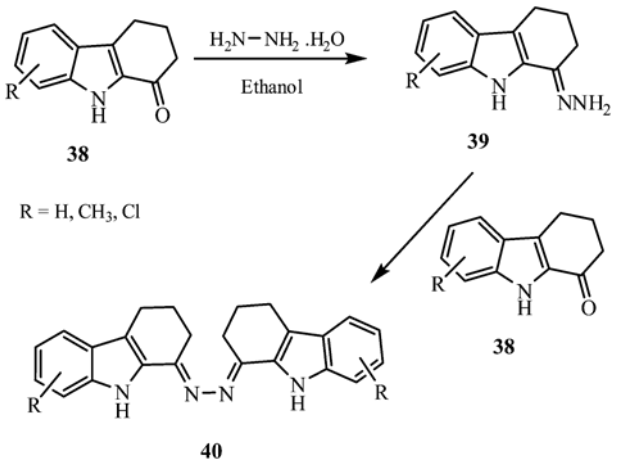
Scheme 9



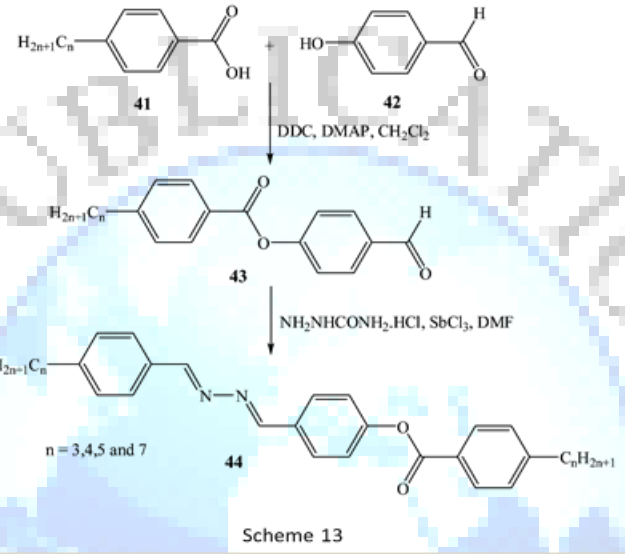
Scheme 10



Scheme 11



Scheme 12



Scheme 13

Scheme 13

Vinyl azides are radical trimethylated during the synthetic process. In order to effectively produce a-tri monomethyl azines 57 (Scheme 16), Chiba et al. devised PhI(OAc)2-mediated radical tri-monomethylation of vinyl azides 55 utilizing Me3SiCF3. Furthermore, simple procedures were developed to transform useful urine-containing chemicals from a-tri monomethyl azines. In their anticipation, the radical tri-

A novel method for synthesizing crucial urine-containing compounds for biological and therapeutic purposes is made possible by the monomethylation of vinyl azides.

Unsymmetrical azines synthesis

Alkylidene group interchange between azines and imines during the synthetic process. In 1982, Barluenga and colleagues published a new technique for making asymmetric azines. According to Scheme 17, it is based on the interchange of the alkylidene group between azines and imines, which is catalyzed by an acid. This procedure offers a quick way to make unsymmetrical azines of type 60.

Erythro-1,2-diaryl-2-(2tosylhydrazino)-ethan-1-ol derivatives (61) and formic acid are treated during the synthetic process. Unsymmetrical azines were created in 1983 by Rosini and colleagues using a different synthesis method (64). This process involves treating 61 with formic acid. A four-membered ring intermediate advances the reaction (Scheme 18).

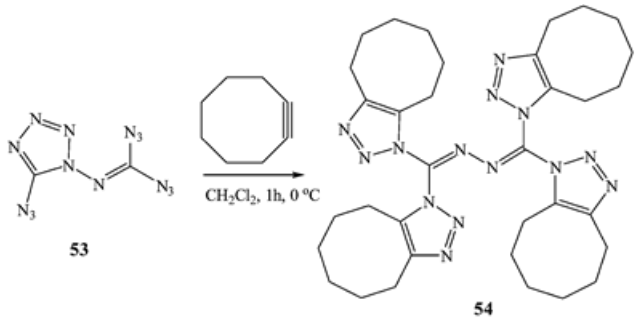
synthesized from S-methylthioacetamidate hydroiodide (71) and acetamidrazone hydrochloride (65). The Synthesis of azines 67 and 68 using 65 and benzaldehyde and the Synthesis via reaction of acetophenone hydrazine with 71 were reported in 1995 by Lee and coworkers. When azines 67 and 68 were combined with isocyanates in dichloromethane at room temperature, triazines 69 and 70 were created (Scheme 19).

Triisopropylsilylhydrazine (72) is synthesized by reacting with aldehydes and ketones. Anhydrous hydrazine and chlorotriisopropylsilane were combined to create 72, which Soderquist and colleagues launched in 2000. Aldehydes and ketones rapidly react with compound 72 to form triisopropylsilyl hydrazones Desilylation

Scheme 14

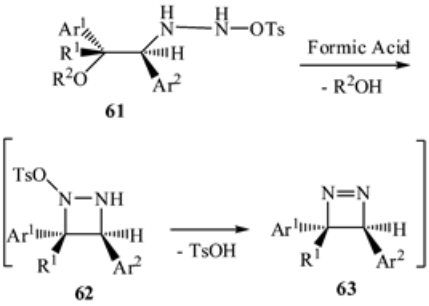
The necessary unsymmetrical azines are produced by combining tetra-n-butylammonium uoride with a second aldehyde or ketone (Scheme 20).

Diazoalkanes and N-heterocyclic carbenes are used in the reaction to synthesize. In 2001, Hopkins and colleagues created a simple and practical method for synthesizing mixed azines. The addition products, azines, are produced when heterocyclic carbenes interact with diazoalkanes (Scheme 21).

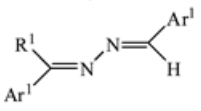


53 54

Scheme 15



61 62 63

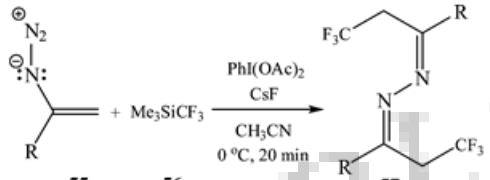


64

$R^1 = R^2 = H$, Alkyl

$Ar^1 = Ar^2 = C_6H_5$, 4-CH_3-C_6H_5, 4-OMe-C_6H_5

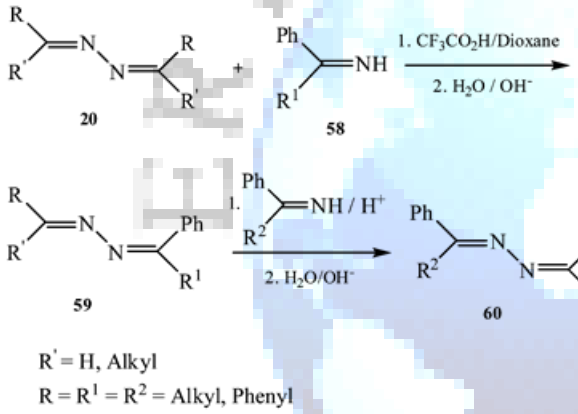
Scheme 18



55 56 57

R = Ph, $PhCH_2CH_2$

Scheme 16

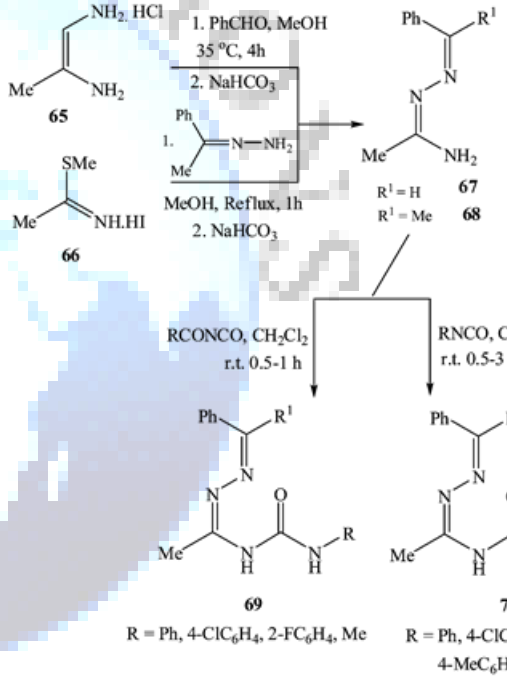


20 58 59 60

R' = H, Alkyl

R = R^1 = R^2 = Alkyl, Phenyl

Scheme 17



65 66 67 68 69 70

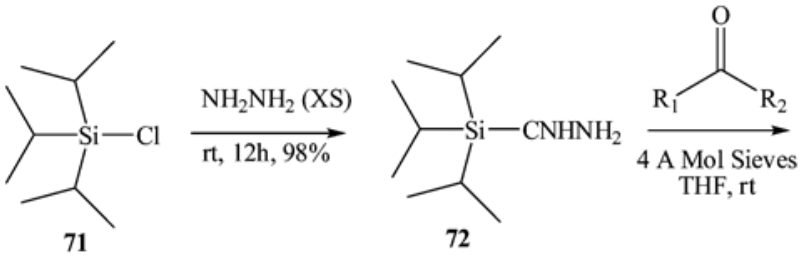
R = Ph, 4-ClC_6H_4, 2-FC_6H_4, Me

R = Ph, 4-ClC_6H_4, 4-$NO_2C_6H_4$ 4-MeC_6H_4, 4-$MeOC_6H_4$

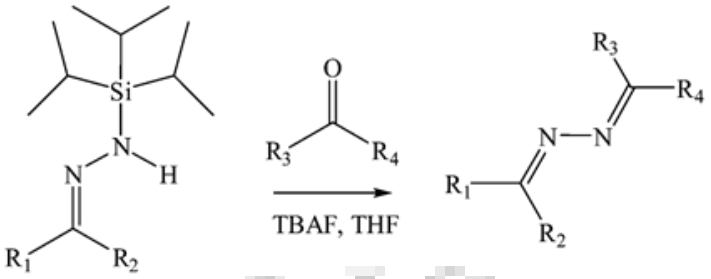
Scheme 19

Nitro-substituted (hetero) aromatic aldehydes and 2-methylthio-1,3-dithiolium salts are used in the Synthesis. The Synthesis and characterization of the first push-pull 1,3-dithiol-2-ylidene derivatives with an azine spacer were reported by Moreno-Manas and colleagues in 2001 (Scheme 22). The nitro-substituted (hetero) aromatic aldehydes were used to react with to create the azines. The electric field-induced second harmonic (EFISH) technique examined their electrochemical and second-order nonlinear optical (NLO) capabilities measurements.

hydrazone is created (84) via Schiff condensation with 4-formyl-benzo-15-crown-5 ether. Using a flexible spacer between the two subunits, Sousa et al. reported synthesizing Schiff base ligands functionalized with crown ethers in 2003. By Schiff condensation of hydrazine with an aldehyde, they created novel unsymmetrical ligands functionalized with NH2 groups (adducts 81, 82, and 83) in the first step. The NH2-functionalized compounds were combined with 84 in the subsequent step. These are the byproducts of the second Schiff condensation



71 72



73 74

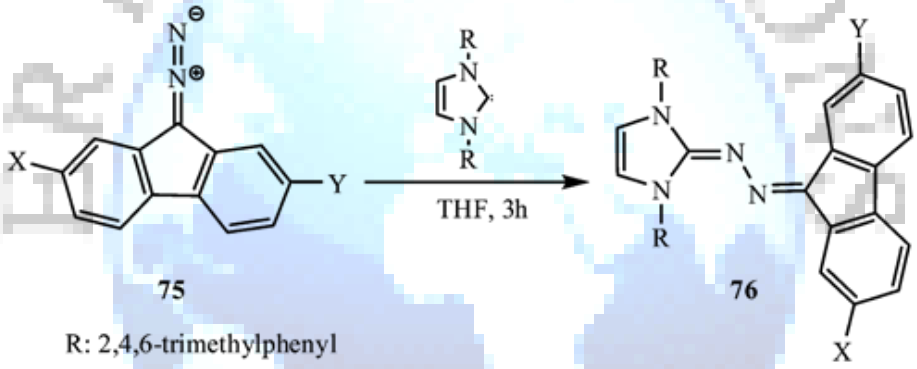
R_1 = H, Me, Et, Cyclopentane, tBu-cyclohexane

R_2 = Et, Ph, Cyclopentane, tBu-cyclohexane

R_3 = H, Ph, Et, Cyclopentane, Furyl

R_4 = H, Et, Ph, Cyclopentane, Furyl

Scheme 20



75 76

R: 2,4,6-trimethylphenyl

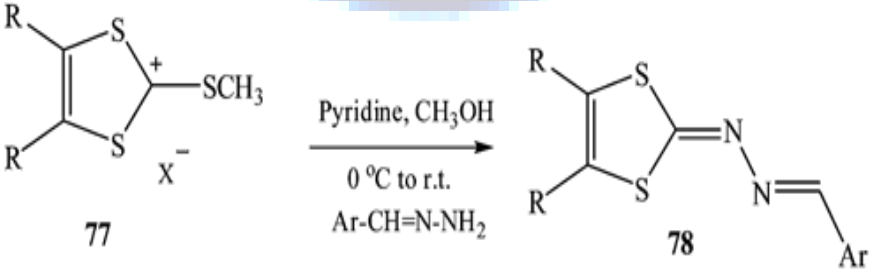
X = Y = H

X = Y = Br

X = Y = Cl

X = F , Y = H

Scheme 21



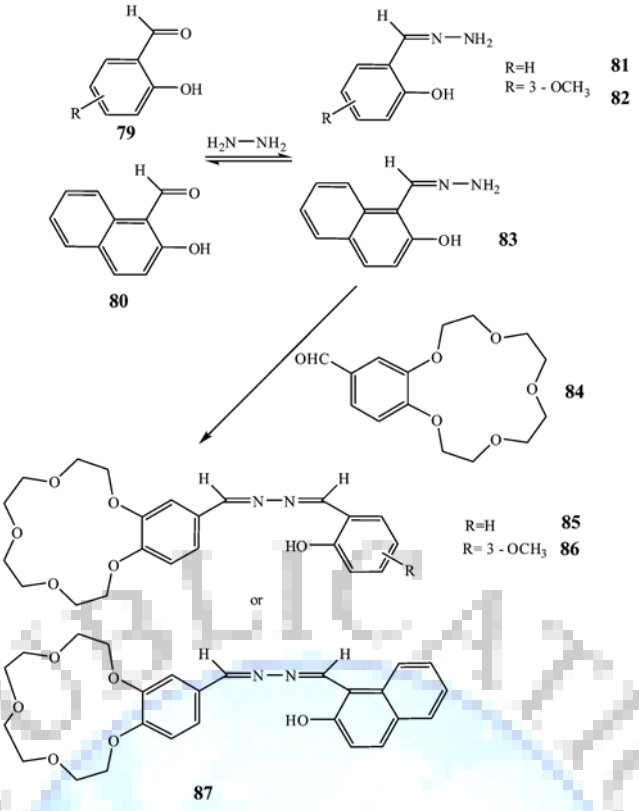
77 78

R = SCH_3, X= BF_4

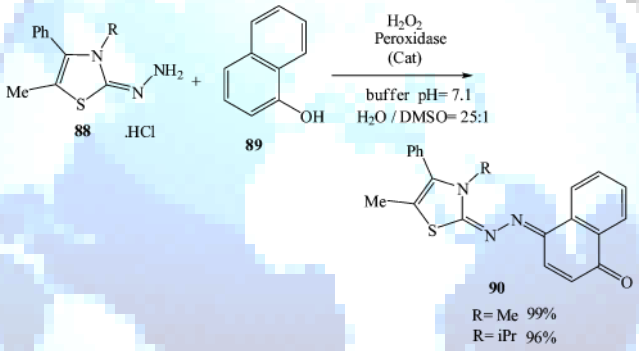
R = H, X= I

Ar = 4-$NO_2C_6H_5$, 2,4-$(NO_2)_2C_6H_4$, 5-NO_2-thiophene

Scheme 22



Scheme 23



Scheme 24

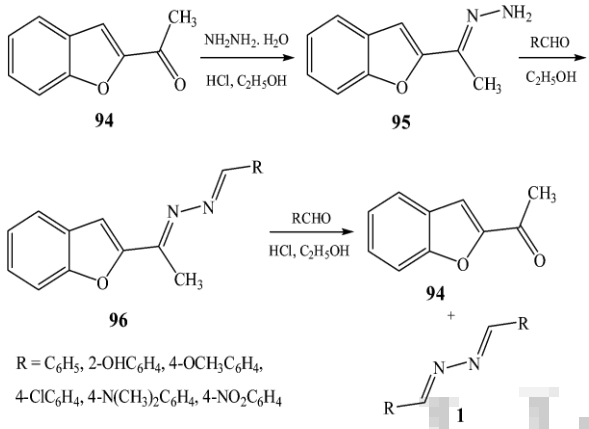
The condensation of 1-pyrene carboxaldehyde with the diethyl phosphorohydrazidate (CH2Cl2) amino group at ambient temperature. Indeed, Zwierzak's approach was used to perform protection. The new dyad was produced by metalizing with butyl lithium in tetrahydrofuran (THF) at 78 C under N2 and then reacting with ferrocene carboxaldehyde, with an overall yield of 60% or recrystallization from (Scheme 25) CH2Cl2-Et2O.

2-Acetylbenzofuranhydrazone and aromatic aldehydes interact. A crucial part of organic chemical transformation is the regeneration of carbonyl compounds from hydrazine, N-substituted hydrazones, and semicarbazones. The hydrolytic cleavage of 95 with aromatic aldehydes in an acidic environment was first documented by Ujjinamatada and Agasimundin in 2007 (Scheme 26). This technique of C]N bond cleavage is a practical strategy to regenerate the ketone 94 from 95 in addition to the Synthesis of Aldzaines.

Synthesis using the hydrazone reaction with another carbonyl molecule and sodium hydride. Galeta et al.'s 2009.37 describes producing a novel, asymmetrical allenyl azines 101 with aliphatic and alicyclic substituents. Zwierzak used the procedure to make asymmetric azines. The first step in this process is to protect one of the nitrogen atoms in the hydrazine molecule by producing diethyl hydrazidophosphate through a reaction with diethyl phosphite. The protected hydrazones 98 or 100 were created by the customary reaction of the intermediate with a carbonyl molecule. The asymmetrical azine 101 (Scheme 27) was produced when another carbonyl compound was treated with hydrazone while sodium hydride was present in dry ether.

From tetrahydropyran (102) is synthesized. Ishmuratov et al. (2009) used [1 + 1] condensation at room temperature to create the potentially valuable 17-membered macrolide-containing azine group 106 from 102. This azine functional group containing macrolides may have intricate characteristics and biological activity. Ketoalcohol 102

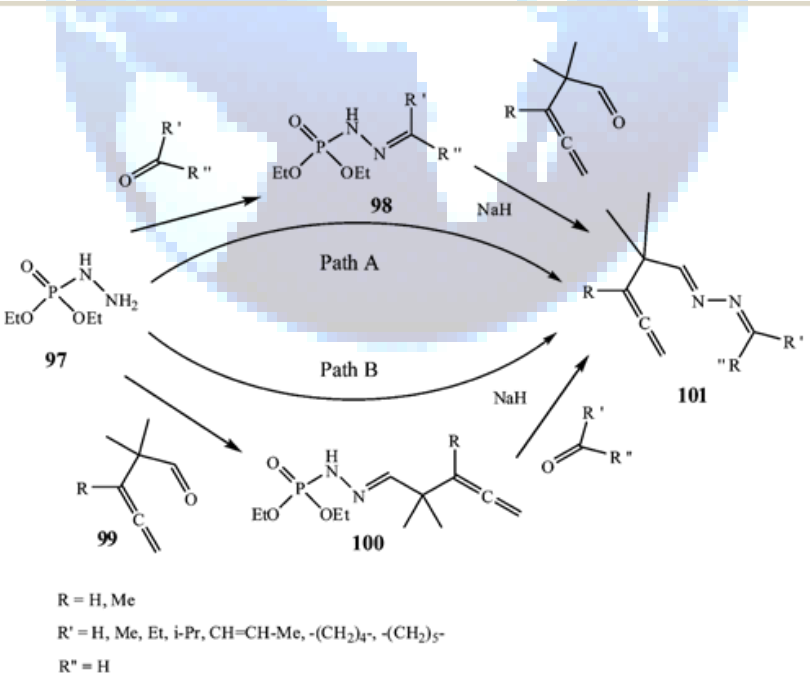
led in three steps to Ketoalcohol 103. Corey oxidized keto alcohol 103 to yield 7-oxo octanal (104), a ketoaldehyde. Using 104 and catalytic amounts of aluminium, the Tishchenko reaction was used to create 7Oxooctyl-7-oxo octanoate (105) triisopropoxide. At high dilution and room temperature, [1 + 1] condensation of 105 in dioxane with hydrazine hydrate yielded macrolides with azine fragment 106 in good yields (40–50%).



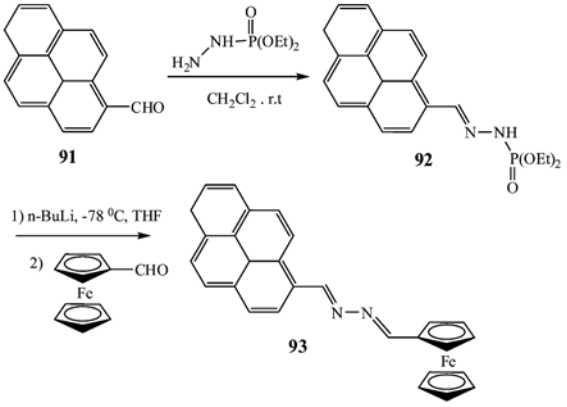
Scheme 26

synthesized from ketones or aldehydes and benzophenone hydrazone (107). In 2011, Swaminathan and colleagues published their work on the easy physical grinding method for the Synthesis of azine derivatives 108 from 107 and ketones or aldehydes in the presence of sulfated anatase titania (TiO2-SO42), a solid acid catalyst (Scheme 29). At room temperature, sulfated titania is a catalyst for synthesizing azine derivatives.

Synthesis using hydrazine and 2-ketomethylquinolines (110). In 2013, Loghmani-Khouzani and colleagues looked into the three-step Synthesis of novel azines. Several compounds were originally synthesized. Numerous researchers have clarified tautomerism in this group of chemicals. In the following stage, 2-ketomethylquinolinehydrazones were produced in good to high yields by reacting with hydrazine in an ethanol solution with a drop of acetic acid (catalyst). In the third stage, various aldehydes and ketones were used to treat 111 and 112 in an ethanol solution, and in the unsymmetrical azines are produced when acetic acid is present as a catalyst (Scheme 30).

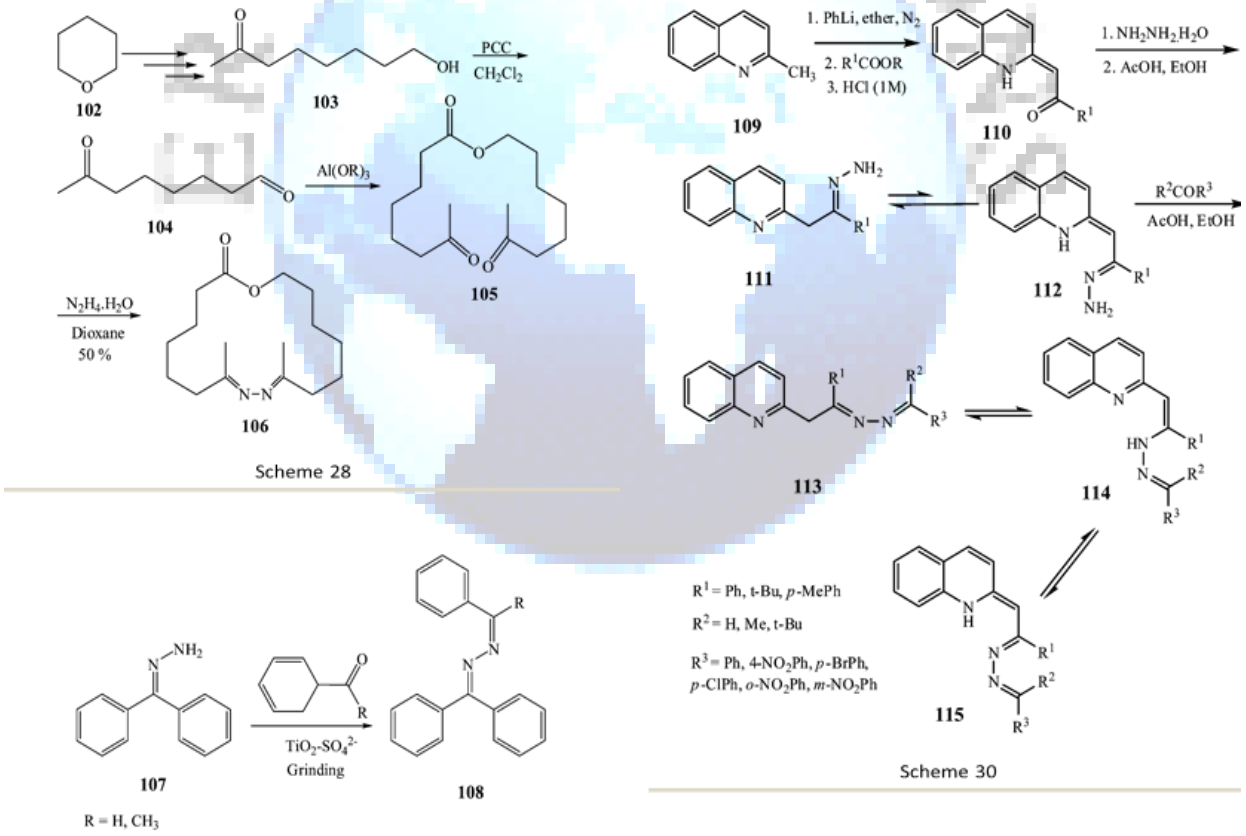


Aldehydes and N-tosylhydrazones from ketone reactions are used in the synthetic process. An effective one-pot technique for synthesizing unsymmetrical azines was created by Wei et al. in 2013. Triphenylphosphine could capture the in-situ produced diazo compounds in the absence of metals. In good yields, the matching unsymmetrical azines were produced (Plot 31) Azines' characteristics.



Delocalization

Delocalization happens in compounds with bonding orbitals dispersed among three or more atoms rather than being coupled to two atoms. As mentioned, numerous research studies have looked at how localized azines are. Planarity is a well-known requirement for maximum conjugation in a system. Glaser looked at the bond lengths to find evidence for conjugation. Some linkages were found by examining potential resonance structures of the symmetric and asymmetric acetophenone azines with considerable conjugation. However, in-depth X-ray investigations of the N-N and Ar-C bonds' conformational characteristics, bond length assessments, and theoretical studies failed to indicate conjugation. Although the C]N-N]C spacer appears to have the requisite structural components to serve as a suitable conjugation bridge, Glaser found the solid state. The lack of conjugative solid contact is consistent with azines' X-ray crystallography findings. Azines in the solid state feature gauche geometries around the >C]N-N]C moiety and more recent data are comparable to Glaser's findings and demonstrate that the bond lengths are inconsistent with any prolonged conjugation (for example, it lacks a significant -N]N- character).

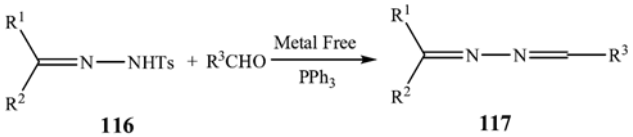


Properties NLO

The features of organic NLO materials, such as their incredibly rapid response times, decreased. Compared to conventional inorganic solids, these have lower electric constants and easier processing. Applications for NLO materials can be found in optical computing, communications, and lasers.

Because of their NLO characteristics, azines have recently generated interest. The two imine bonds that make up the azine moiety can be considered polar acceptor groups oriented in opposite directions. They include an N-N bond, making them suitable candidates for NLO materials. A macroscopic dipole moment established with suitable

donor or acceptor substituents on the azine may make them suitable candidates for NLO materials. They are perfect candidates for NLO materials because of this property of azines linked to two aryl rings with a donor and an acceptor group.



116 117

61-86 %

R^1= Ph, 4-Cl-C_6H_4, 4-MeOC_6H_4, 4-$NO_2C_6H_4$, 4-CNC_6H_4, 4-$MeCO_2C_6H_4$, 4-$MeCONHC_6H_4$, 4-MeC_6H_4, 1-Naphtyl

R^2 = Me, Et, Ph

R^3= Ph, 4-Cl-C_6H_4, 4-MeOC_6H_4, 4-$Me_2NC_6H_4$, 4-$NO_2C_6H_4$, 2-$NO_2C_6H_4$, 2-Thienyl

LC possessions

However, most studies on azines concentrated primarily on analyzing their crystal structures and dipolar properties because these issues are crucial in designing and understanding NLO-active displays. Some azines that are liquid crystal (LC) compounds were also investigated molecules.

Isomerization

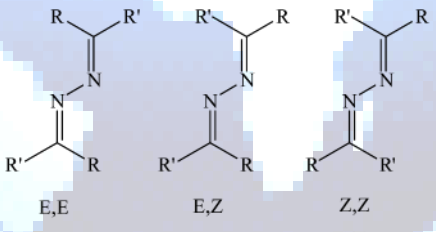
Aldazines and ketazines can exist as the three configurational isomers (E, E), (E, Z), and (Z, Z), respectively (see Fig. 4).3,59 Azines go through photochemical E/Z isomerization of the C]N bonds to produce (E/Z) and (Z/Z) isomers from the thermodynamically most stable (E/E) form.

A chain of four atoms governs the shape of aromatic azines, C]N-N]C. The large groups attached to the C]N bonds are trans to the N-N bond in nearly all studied aromatic azines in the preferred (E, E) configuration. The s1 angle determines the stereochemistry of the azines' N-N bond. S114 180 C for the gauche conformation and S1 180 C for the s-trans conformation. Azine's two halves can conjugate most effectively in the s-trans conformation.

THE USES OF AZINES

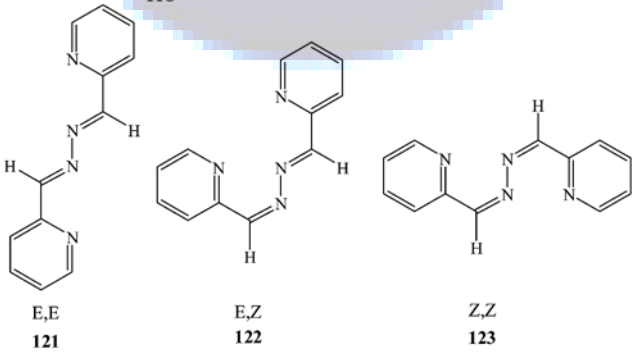
Uses for chemicals

Azines have particular uses in chemistry. Azines are frequently used as starting materials in the Synthesis of organic compounds.



E,E E,Z Z,Z

118 119 120



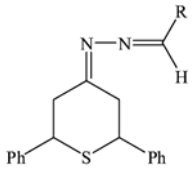
E,E E,Z Z,Z

121 122 123

These readily available compounds have been widely used as substrates in synthesizing substituted hydrazones62 and heterocyclic compounds37, such as pyrazoles, purines, and pyrimidines. As dipolarophils, they can undergo 1,3-cycloadditions and thus provide an efficient route to afford 1,5-diazabicyclo[3.3.0]octanes by crisscross addition. Not only can they be used as good synthons for heterocyclic Synthesis, but they can also be employed in certain useful synthetic transformations. Azines have also been investigated for potential applications in analytical and synthetic chemistry and their potential in bond formation reactions.

Applications in Biology

Azines constitute an important class of stereochemically significant nitrogen donor ligands in organometallic complexes with pharmacological and biological activity.74 The specific role of azine ligands as binding molecules or modulators of biological receptors makes them suitable candidates for drug development.75 The molluscacidal activity displayed by azines of certain p-benzoquinones was largely attributed to their parent quinines.76–78 The biological activity of some novel N(1)-arylidene-N(2)-cis-2,6-diphenyltetrahydrothiopyran-4-one azine derivatives 124 is well-known. Their antibacterial activities against Streptococcus faecalis, Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, and Staphylococcus aureus, as well as their antifungal activities against Candida-6, Candida-51, Aspergillus niger, and Aspergillus favus, were evaluated.

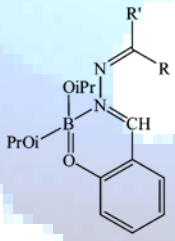


124

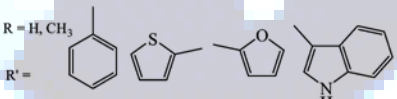
R = 2-NO_2-Ph, 4-OMe-Ph, 2-OH-Ph

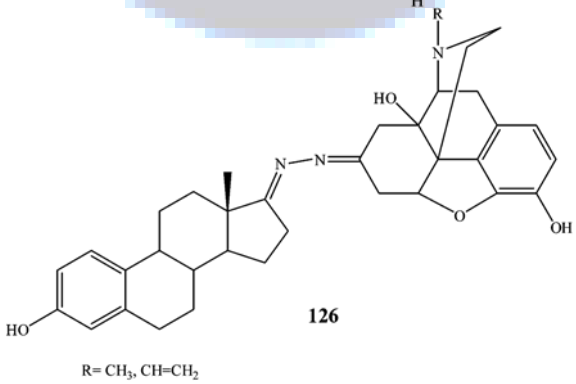
Fig. Azines have four configurational isomers.

Azines were also studied for their use as antimalarial and therapeutic agents.80 Some heterocyclic azines inhibit tumour growth81 in murine models. Mixed azines synthesized from opioid antagonists and steroidal ketones82 show various biological effects, including ultralong opioid antagonist activity.83 Some unsymmetrical azines have antibacterial properties.73 Furthermore, diazines (N–N-linked diimines) have recently attracted attention because of their biological properties as anticonvulsants, antidepressants, anti-inflammatories, antiviral, or antitumor agents.84 Some boron derivatives of mixed azines 125 have been reported to be effective bactericides, fungicides, and trichomonads. There have also been descriptions of organoboranes used as plant growth regulators and insecticides. The inhibition abilities of boron complexes are more potent than those of their free ligands. Based on chelation theory, the increased biological activity and complexation may be explained.



125





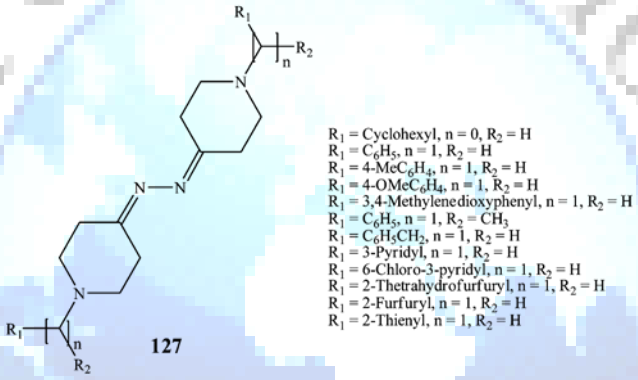
126

R= CH_3, CH=CH_2

Mixed azines 126 formed from estrone and naloxone, novel non-peptide selective opiate antagonists, were also discovered A series of novel symmetrical trans-bis-Schiff bases (azines) 127 were designed and prepared as novel anticancer analogues. The potential analogues showed anti-leukemic activity half maximal inhibitory concentration (IC50¼ 6.35 mg mL1) higher than that of the drug 5-□fluorouracil (IC50 ¼ 8.48 mg mL1)

Physical applications

Asymmetric azines with donor and acceptor groups at the terminal of the p-conjugated backbone were introduced as novel organic NLO materials.86 Azines are used as ion-selective optical sensors,87,88 conducting materials,68 dye lasers, image recording materials,89 and in supramolecular chemistry90,91 and applications of materials.92–95 Conjugated polyazines may be doped with iodine to give conducting materials.96 Azines with aromatic and various heterocyclic substituents are photochromic and undergo thermal isomerization and photochemical E–Z isomerization about the C]N double bond. The photochromic properties of organic substances can be used to fabricate dosimeters for ultraviolet radiation, screens for protecting the eyes, and optical devices against powerful sources of light (for example, nuclear explosions).97 Substituted aromatic azines such as ortho-hydroxyacetophenone azine have gained considerable interest for their lasing properties and valuable applications in colouring and dyeing processes.98 Some unsymmetrical azines are used as organic luminophores, and others are used to synthesize unsymmetrical diarylethylenes.73 In 1959, a series of azine-type LCs were synthesized and were found to exhibit high clearing points.99 A series of salicylaldehyde azine derivatives exhibited exciting characteristics of aggregation-induced emission enhancement.100 In addition, 1,4-disubstituted 2,3-diaza-1,3-butadienes bearing two redox ferrocene groups, a photoactive pyrene group, and a p-methoxyphenyl group were introduced for use in two new sensors exhibiting higher sensitivity and selectivity for Hg2+ in aqueous environments.101 Additionally, 1,4-bis(4-pyridyl)-2,3diaza-1,3-butadiene was introduced as a new ligand for solid phase extraction of mercury. The photoluminescence properties of this complex in the solid state were studied.102 Symmetrical azine-based polymers possessing 1-phenyl-1,2,3,4tetrahydroquinoline moieties were used as materials for optoelectronics. Symmetrical azines tend to crystallize because of numerous aliphatic fragments, good ionization potential, and sufficient charge drive mobility.



127

REACTIONS OF AZINES

Formation of a stilbene derivative with the evolution of nitrogen on heating

In 1953, Clark found that aryl azines are not readily degraded. Thus, heating at 300 C led to the evolution of nitrogen and forming a stilbene derivative Aryl azines with free ortho positions were found to yield phenanthrenes 130 (Scheme 32).

Exchange of the]N–N] group with an azo group

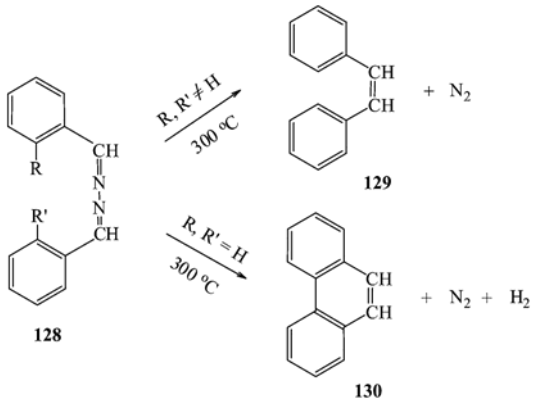
Exchange of the]N–N] group with an azo group (–N]N–) may be performed by reduction of an azine (127) over palladium or platinum catalyst at 50 lb in2 pressure to give the hydrazine compound 128. This compound could be readily oxidized to the required azo hydrocarbon 129 by using cupric salts,104 oxygen, or hydrogen peroxide (Scheme 33).

Action of Grignard reagents on phenanthrenequinone benzophenone azine

Awad et al. investigated 1960 the action of Grignard reagents on phenanthrenequinone benzophenone azine (130). Aryl magnesium halides were preferentially added to the carbonyl group of 130. When excess Grignard reagent was used, a cleavage–condensation reaction occurred with the formation of 9,10diarylphenanthrene. However, excess phenyl or anisyl magnesium bromide afforded 9,10-diphenyl or 9,10-dianisylphenanthrene, respectively, as a final product in moderate yield (Scheme 34).

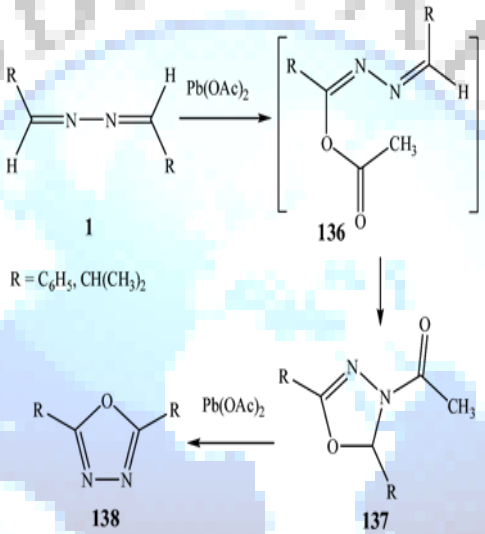
Oxidation of azines by lead tetraacetate

In 1967, Gillis and Lamontagne reported the oxidation of aldazines and ketazines with lead tetraacetate. 1,3,4-Oxadiazolines 137 could be converted to 1,3,4-oxadiazole 138 upon further oxidation with lead tetraacetate (Scheme 35). When ketazines were treated with one equiv. of lead tetraacetate, the a,b-unsaturated azo acetate was isolated (Scheme 36). Aromatic ketazine failed to react with lead tetraacetate.

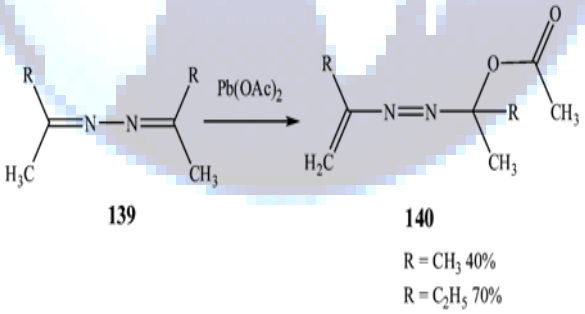


Reaction of acetone azine with p-toluenesulfonyl azide

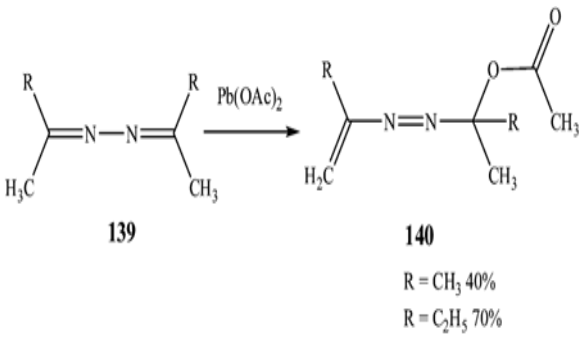
Acetone azine reacts with 143, producing compound 144 aner 1,3-dipolar cycloaddition by diazomethane extrusion. The product was assigned the structure of N-[l-(isopropylidenehydrazino) ethylidene]p-toluenesulfonamide (145; Scheme 37). Hartzler suggested this reaction in 1971. The reaction occurred very slowly under re□ux in tetrahydrofuran solution, producing 145 at 12% yield for seven days. The reaction proceeded approximately at the same rate as deuterium (from D2O) was incorporated into the azine. NMR spectroscopy confirmed the structure of 145, showing the absorption by four different methyl groups. Infrared spectroscopy showed Scheme 32 Scheme 34



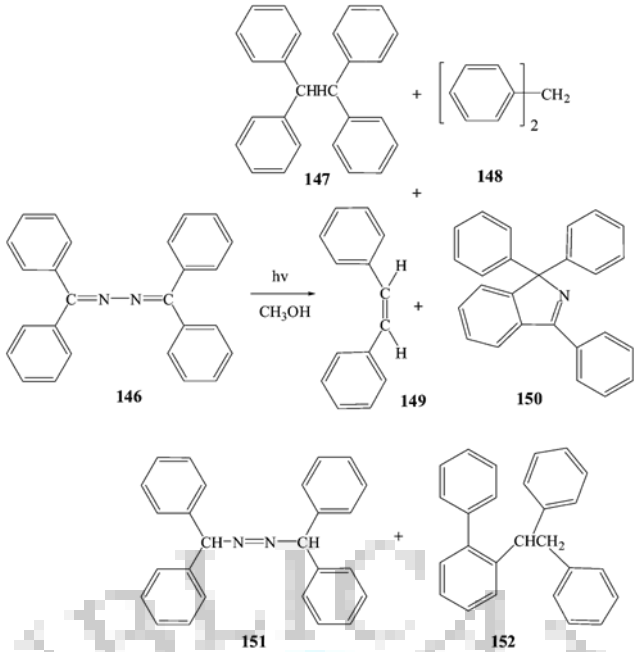
Scheme 35



Scheme 36



Scheme 37



Scheme 38

Different photochemical reactions. The first reaction is molecular rearrangement leading to 1,3,3-triphenylisoindole, and the second is photoreduction forming l,l,l0,l0-tetraphenylazomethane (Scheme 38). Compound 151 is photochemically unstable, yielding l,l-(Z, Z)-tetraphenylethane (147) and diphenylmethane (148). Compound 147 had been previously shown to decompose by photolysis to cis-stilbene (149), 1- (Scheme 39). All of these compounds were isolated from the photolysis of benzophenone azine.

Rearrangement of the azine of salicylaldehyde propargyl ether

In 1917, two papers by Bailey et al. provided the first report on crisscross addition.109 The first article describes the cycloaddition of cyanic acid to benzalazine.109a The second explains the cycloaddition of cyanic acid, isothiocyanic acid, and phenyl isocyanate with aromatic aldazines prepared from benzaldehyde, 3-nitrobenzaldehyde, cinnamaldehyde, and furfuraldehyde.109b In 1975, Suschitsky et al. prepared dihydropyrazolopyrazole (155) by rearrangement of the azine of 154 in reducing diethylaniline (Scheme 40).

CONCLUSIONS

The current review describes a variety of conventional and modified azine synthesis methods. According to the literature, azines' significance in chemistry, physics, and biology is also discussed. Recent development in these essential and practical methods offers a platform for future innovation because of their adaptability, molecular economy, and tremendous potential for synthesizing complex organic molecules. These compounds' biological properties have recently been scrutinized, and several novel actions have been noted. Some of the compounds in this class may soon be used in clinical settings, increasing their commercial value.

This scaffold is being modified with additional synthetic advances to suit biological uses better. These compounds' cycloaddition chemistry can be explored using various substituents or double bonds. We hope this effort will inspire more significant future research.

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