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A comprehensive review on the silane-acid reduction of alkenes in organic synthesis†

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Target and diversity-oriented synthesis represents a versatile and efficient strategy for constructing structurally complex and privileged scaffolds from readily or commercially accessible starting materials. The combination of reagents indeed plays a pivotal role in organic synthesis, acting as chemical "tools" that enable specific reactions to occur and driving the creation of new molecules. Reagents facilitate organic transformations, including the controlling of reaction pathways and influencing the complex efficiency and selectivity of the synthesis process. This review highlights the combined use of triethylsilane and trifluoroacetic acid as a powerful system for the chemoselective and regioselective ionic hydrogenation of diverse alkenes. The transformation proceeds through protonation, followed by hydride transfer, affording valuable products with high selectivity. Furthermore, this review covers the reduction of heterocyclic skeletons to saturated compounds *via* the ionic hydrogenation method.

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† Dedicated to Late Dr Braja G. Hazra on the occasion of his death anniversary.

Bapurao B. Shingate

Bapurao B. Shingate, born in 1975 at Salagara (Divati), Dharashiv District of Maharashtra State, is a Full Professor of Organic Chemistry at the Department of Chemistry, Dr Babasaheb Ambedkar Marathwada University (Dr BAMU), Chhatrapati Sambhajinagar, India. He earned his MSc degree from Dr Bamu (1999) and then joined for doctoral research at CSIR-National Chemical Laboratory, Pune, under the guidance of Dr Braja G. Hazra and earned a PhD degree in 2010 from Savitribai Phule Pune University, Pune. His PhD work focused on the stereoselective syntheses of steroidal unnatural C(20R) aldehydes by ionic hydrogenation and their elaboration to naturally occurring 20-epi cholanic acid derivatives, in addition to stereoselective syntheses and ionic hydrogenation of steroidal C-20 tertiary alcohols with aliphatic, vinylic, aromatic, 5- and 6-membered heterocyclic side chains. In 2008, he joined as an Assistant Professor at the Department of Chemistry, Dr Babasaheb Ambedkar Marathwada University, Chhatrapati Sambhajinagar. His current research interests include the design and synthesis of bioactive compounds and drug analogues, development of new synthetic methodologies, multi-component reactions, heterocyclic synthesis and green chemistry. With more than 23 years of research and 17 years of teaching experience, Dr Shingate has supervised eight PhD scholars (Five of whom are currently working) and more than 200 MSc dissertations. Dr Shingate has contributed significantly to more than 135 peer-reviewed publications (Citations: 5003, h-index: 40, i10 index: 108), in addition to 4 patents and 05 invited book chapters of high repute. Recently, he has edited a book on "Five Membered Bioactive N and O-Heterocycles" for IGI Global. His teaching expertise in various aspects of synthetic organic chemistry and research on bioactive compounds and drug analogues has been well recognized with a number of prestigious honors and awards from different academic & scientific bodies such as ICC-Dr S. M. L. Gupta Award (2014), ISCB Academic Scientist Award (2023), BENTHAM AMBASSADOR (2018–2025), GTEA-Best Chemistry Professor of the Year (2020), ISCB-Best Teacher Award (2018), Dr BAMU Research Professor Award (2017), Dr BAMU-Ideal Teacher Award (2014) and IUSSTF-Indo-US Research Fellowship Award (2013). Furthermore, he is a Fellow of the Maharashtra Academy of Sciences (2023) and the Indian Society of Chemists and Biologists (2024). Dr Shingate is highly enthusiastic about teaching synthetic organic chemistry and has delivered more than 100 lectures to post-graduate students in Maharashtra and India. He has also delivered more than 75 invited lectures at national and international conferences.

1. Introduction

Organic synthesis has enormously contributed to improving the living standards and life expectancy of society by providing value-added materials like pharmaceuticals, polymers, textiles, dyes, agrochemicals and smart materials required for electronic device applications. Organic synthesis is considered a constructive science and has played a pivotal role in developing countless number of non-natural molecules. Organic synthesis includes the development of carbon–carbon bond(s) and carbon–heteroatom bond(s) and cleavage of these bonds.[1–5]

The construction and cleavage of bonds using various strategies represent the central idea in organic chemistry, playing an excellent role in assembling the complex carbon frameworks. Thus, the development of different approaches has remained the main focus of synthetic organic chemistry research. The development of carbon–carbon bond is the most essential reaction due to its unique role in the formation of various classes of carbon frameworks.[6–8] There are several significant carbon–carbon bond-forming reactions/rearrangements, and organometallic reagents have been developed and studied in detail for their applications during the current and last centuries. Furthermore, organic functional group transformations, such as oxidation and reduction, are the key steps in the synthesis of natural products, drugs and complex molecules.[9–11]

Hydrogenation has become a significant process in synthetic organic chemistry.[12,13] The successful synthesis of many new compounds often relies on the ability to achieve the selective reduction of a single unsaturated group within a molecule while leaving other functionalities unaffected. The selection of an appropriate hydrogenating system for targeted hydrogenation requires an understanding of the mechanism by which this system operates, and this selection relies on the behavior of the unsaturated group that interacts with the hydrogenating system.

In organic synthesis, reagents play a vital role in facilitating chemical transformations and enabling the conversion of starting materials into the desired products. They can be classified according to their functions, such as oxidizing agents, reducing agents, or those employed in specific named reactions.[14–17] Trifluoroacetic acid (TFA) is widely used in organic synthesis as a catalyst, reagent and solvent. Several synthetic organic transformations, including rearrangements, condensations, oxidations, reductions, hydroarylations, trifluoromethylations, and functional group deprotections, have been performed using trifluoroacetic acid.[18,19]

Organosilanes interact with various unsaturated carbon–carbon and carbon–heteroatom bonds through the addition reaction of hydrogen and silicon atoms, most probably in hydrosilylation, and they have been employed in organic synthesis.[20] The Si–H bond exhibits lower ionic character and shows stability in the presence of water; therefore, hydrosilylation reactions are conducted using transition metal catalysts.[21] These compounds are comparatively less toxic, making their use potentially environmentally benign.

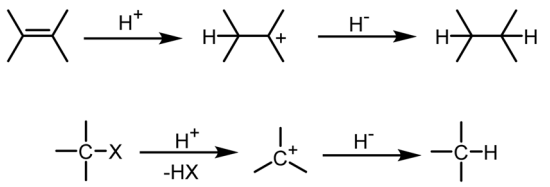
Recent developments have highlighted the use of sustainable and bench-stable reductants, particularly polymethylhydrosiloxane (PMHS), which offers practical and environmentally benign alternatives to conventional hydrosilanes. PMHS has been extensively utilized as a mild and efficient reducing agent in a wide range of functional group transformations, highlighting its importance in modern synthetic chemistry.[22–24]

The scope of silane reductions has further expanded through enantioselective hydrosilylation, where chiral metal complexes enable asymmetric reductions of carbonyl and imine substrates to yield optically active alcohols and amines.[25] Furthermore, several reports have demonstrated the versatility of silanes in the reduction of diverse functional groups.[26–28] Over the past decades, a wide range of transition metal catalysts, based on platinum, rhodium, cobalt, iron, nickel, and copper, have been developed to mediate hydrosilylation and related silane reduction reactions of olefins with high activity and selectivity.[29,30]

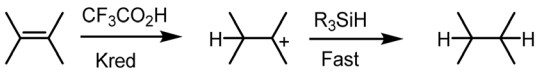
Triethylsilane (TES) is a versatile reducing agent with broad applications across diverse substrates. Its unique properties highlight its significance in modern synthetic chemistry, particularly in chemo- and stereo-selective synthesis of complex molecular frameworks.[31–33]

Ionic hydrogenation relies on the ability of an unsaturated compound to undergo protonation, generating a reactive carbocation intermediate.[34–38] The subsequent hydride transfer from a donor species to this carbocation affords the hydrogenated product. This strategy is applicable to the reduction of a wide range of functionalities, including carbon–carbon, carbon–oxygen, and carbon–nitrogen multiple bonds, as well as certain single bonds such as carbon–halogen and carbon–oxygen linkages. The basic principle of ionic hydrogenation involves the formation of a carbocation, either by protonation of a double bond or through heterolysis of a C–X bond, followed by its reduction *via* hydride donation to form the hydrogenation product (Scheme 1).

In ionic hydrogenation, the hydrogenating pair includes a proton donor and a hydride donor that must fulfill specific criteria: (a) the proton source should be sufficiently acidic to protonate the carbon–carbon double bond, forming a carbocation, but it should not be strongly acidic to protonate the hydride source and generate hydrogen. (b) The carbocation needs to be sufficiently electrophilic to capture a hydride from the hydride source and must not react with other nucleophiles present in the reaction system, such as the conjugate base of the proton source. The typical reduction system used for ionic hydrogenation of double bonds involves trifluoroacetic acid



Scheme 1 Mechanism of ionic hydrogenation.



Scheme 2 Rate-determining step.

paired with an organosilane. Hydrosilanes have been utilized as mild reducing agents in fine organic synthesis.[39,40]

The alkene substrate, however, must be susceptible to protonation by trifluoroacetic acid, which restricts the scope of this method primarily to the reduction of tri- and tetra-substituted alkenes as well as aryl-substituted alkenes (Scheme 2).

In ionic hydrogenation, the rate-determining step involves protonation of the double bond, followed by hydride transfer to the resulting carbocation. The efficiency of this process depends strongly on the nature and number of alkyl or aryl substituents attached to the silicon atom. The hydride-donating ability of silanes generally follows[41,42] the order:

$$Et_3SiH > (n\text{-}C_8H_{19})_3SiH > Et_2SiH_2 > (C_6H_5)_2SiH_2 > (C_6H_5)_3SiH > C_6H_5SiH_3$$

The combination of triethylsilane and trifluoroacetic acid or Lewis acids is used for reduction reactions, such as carbonyls to alcohols,[43,44] carbonyls to alkanes,[45,46] allylic/benzylic/tertiary/propargylic alcohols to alkanes,[47–51] hemiaminals to hydrocarbons,[52] lactols/hemiacetals[53,54] to hydrocarbons and many more.[55–62] Furthermore, triethylsilane and trifluoroacetic acid or Lewis acids are employed for the reductive cleavage of spiroketals,[63] benzylidene acetals,[64] oxazolidinones,[65] bicyclic lactams[66] and the reduction of imines[67] and aromatic nitro[68] functionalities.

The potential of ionic hydrogenation reaction, its unique characteristics, and a comprehensive review of the application of silane-acid reductions to different types of alkenes have not been thoroughly covered in previous literature. This review presents the combination of trifluoroacetic acid and triethylsilane for the reduction of acyclic alkenes, ketene dithioacetal, exocyclic double bonds, cyclic double bonds with and without heteroatoms and aromatic heterocycles.

2. Silane-acid reduction of alkenes

Alkenes amenable to ionic hydrogenation are those capable of generating stabilized carbocations, such as branched alkenes, alkylcyclopropenes, and substituted styrenes. In contrast, unbranched alkenes or those branched at positions other than the alkenic carbon generally do not undergo reduction. This method, therefore, enables the selective hydrogenation of highly substituted double bonds even in the presence of an unsubstituted one. This regioselectivity is opposite to that typically observed in catalytic hydrogenation.

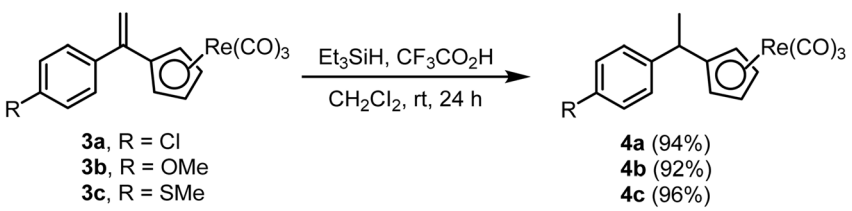
2.1 Reduction of acyclic alkenes

Olefinic compounds bearing bromo- or iodo-substituents are often susceptible to dehalogenation under catalytic hydrogenation conditions. In contrast, ionic hydrogenation does not typically affect such functionalities. Kramer and Waldvogel demonstrated[69] the selective ionic hydrogenation of an iodo-substituted substrate **1** with triethylsilane (Et_3SiH) and trifluoroacetic acid (CF_3CO_2H) in dichloromethane and obtained the saturated compound **2** in quantitative yield (Scheme 3).

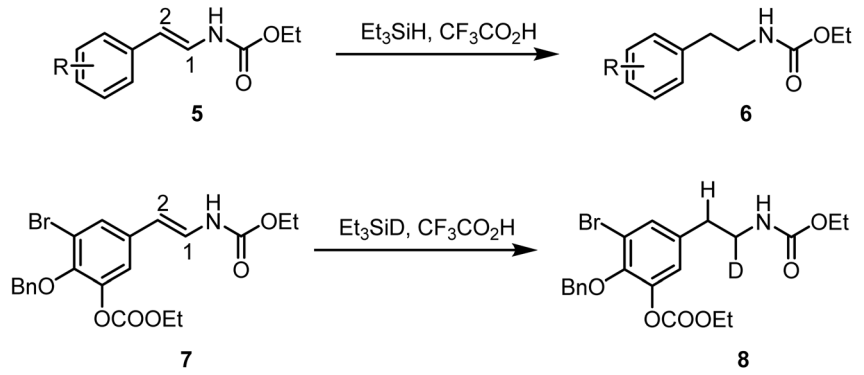
The ionic hydrogenation method is also used for the reduction of double bonds in organometallic compounds. A series of compounds **4** was synthesized[70] from **3** using Et_3SiH and CF_3CO_2H in nearly quantitative yields (Scheme 4).

Masuno and Molinski have reported[71] the selective reduction of 2-aryl-1-*N*-carboalkoxyenamines **5** to the corresponding 2-arylethylamine carbamates **6** by using Et_3SiH in the presence of CF_3CO_2H in excellent yields. The reaction proceeds *via* hydride addition at the C-1 position, with the rate-determining step involving proton transfer from CF_3CO_2H. The mechanism was further investigated by comparing the reaction rates with

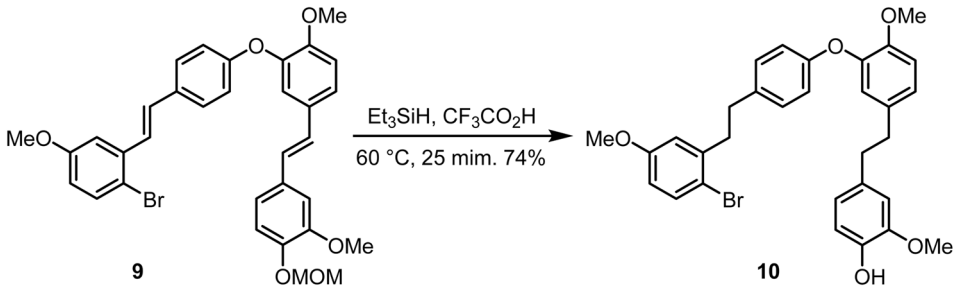
Scheme 3 Ionic hydrogenation of alkenes.



Scheme 4 Reduction of the double bond in an organometallic compound.



Scheme 5 Reduction of *N*-carboalkoxyenamines using ionic hydrogenation.



Scheme 6 Reduction of double bonds and cleavage of the MOM group.

deuterated *versus* non-deuterated reagents. When Et_3SiD was employed instead of Et_3SiH for the reduction of compound **7**, efficient conversion to deuterium-labeled arylethylamine **8** was observed within a similar reaction time (Scheme 5).

Hioki and co-workers reported the reduction[72] of double bonds in compound **9** using triethylsilane in trifluoroacetic acid at 60 °C to compound **10**, in which reductive cleavage of the MOM group also occurs (Scheme 6).

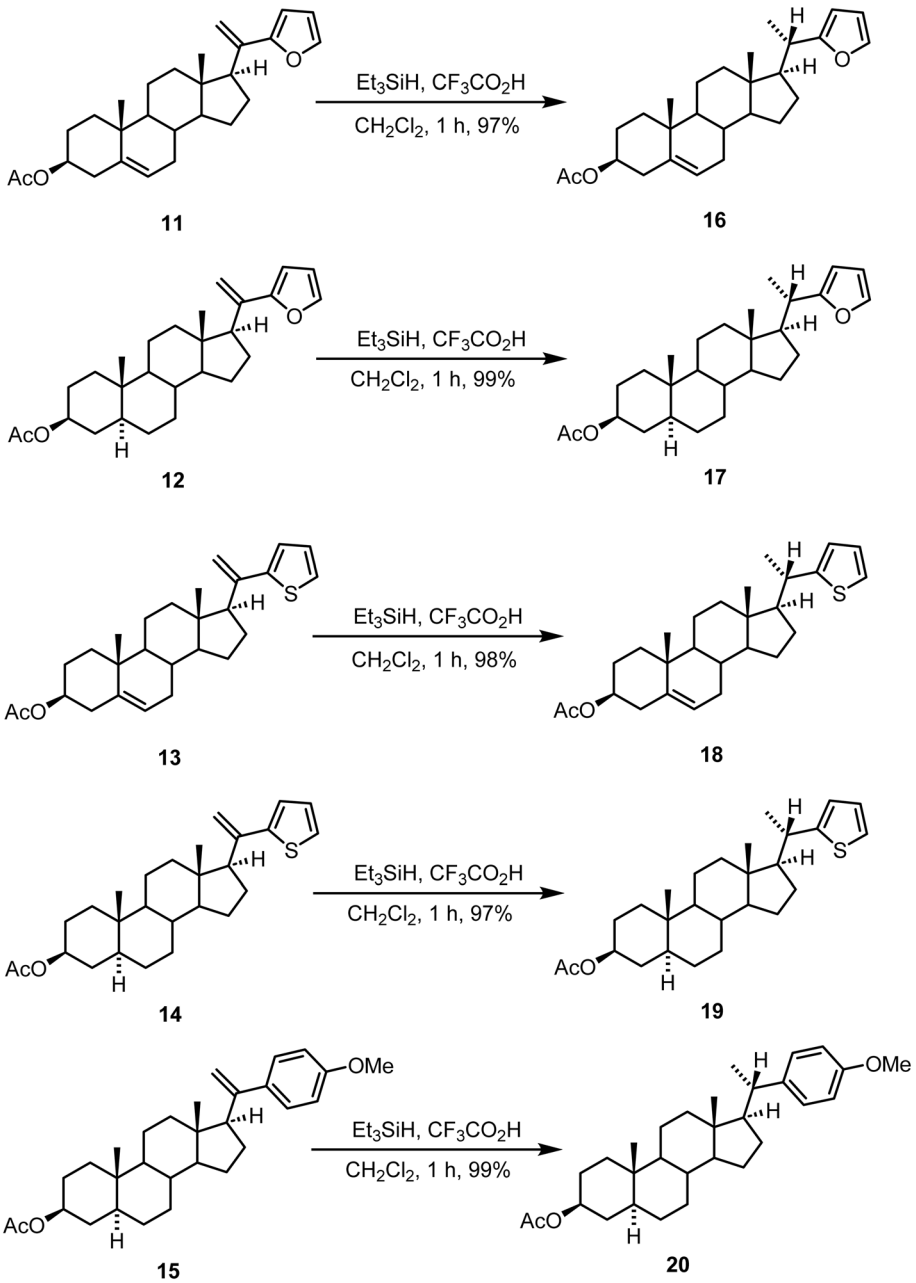
The stereoselective ionic hydrogenation of steroidal C-20(21)-olefinic double bond was achieved in excellent yields.[73] Ionic hydrogenation of the steroidal C-20(21)-olefinic double bond in compounds **11–15** with Et_3SiH and CF_3CO_2H in CH_2Cl_2 at 30 °C resulted in the corresponding **16–20** in almost quantitative yields (Scheme 7). Ionic hydrogenation of compounds **11** and **13** is chemoselective as the 5,6-double bond is unaffected.

Selective reduction of the chalcone double bond (α,β-unsaturated) in compound **21** was achieved[74] by ionic hydrogenation using trifluoroacetic acid as the proton donor and triethylsilane as the hydride donor. The side-chain double bond, being poorly polarized, remained unreactive under these conditions. Furthermore, employing equimolar concentrations of silane and chalcone prevented the reduction of the carbonyl group. The reaction afforded saturated ketone **22** in high yields, which was readily isolated from the mixture (Scheme 8).

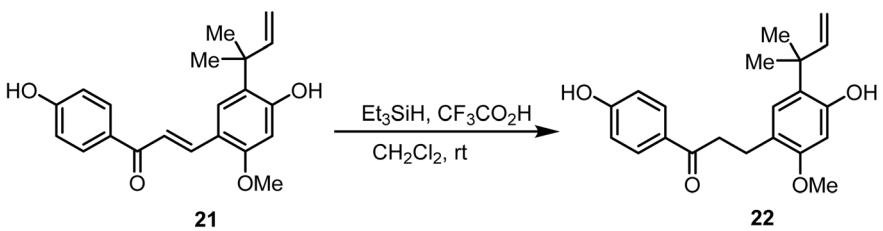
2.1.1 Reduction of ketene dithioacetals. Several ketene thioacetals were reduced[75] to thioacetals *via* a protonation-hydride transfer sequence using Et_3SiH and CF_3CO_2H in dichloromethane, demonstrating the utility of this reaction for converting $R^1R^2C{=}C{=}O$ into R^1R^2CHCHO. Evidence indicated that stabilization of the adjacent carbocation through electron donation from sulfur played a significant role in the process. Ketene thioacetals were generated by the metalation of 2-trimethylsilyl-1,3-dithiane with n-butyllithium in THF, followed by the reaction with aldehydes and ketones. Benzophenone was converted into diphenylacetaldehyde by the reduction of **23a** ($R^1{=}R^2{=}$Ph) to **24**, followed by oxidative hydrolysis of **24** to Ph_2CHCHO. The reduction step, performed with Et_3SiH and CF_3CO_2H in dichloromethane, proceeded in 87% yield (Scheme 9).

Compound **23f** was prepared from cyclohexanone and reduced to 2-cyclohexyl-1,3-dithiane in 63% yield, and on hydrolysis, furnished cyclohexanecarboxaldehyde in 93% yield.[75] The diphenyl and dicyclopropyl ketene thioacetals (**23a** and **23b**) were particularly useful in probing the site of protonation in ketene thioacetals. For the ferrocene-derived ketene thioacetal **23k**, evidence indicated that protonation occurs at the carbon atom adjacent to the ferrocene moiety, generating the sulfur-stabilized carbocation **25**, rather than at the dithiane ring to form the ferrocenylmethyl cation **26**. This observation highlights the strong stabilizing effect of sulfur, most likely through electron donation from its lone pairs to the adjacent carbocation. This is notable because ferrocenylmethyl cations are themselves recognized as highly stable ions (Scheme 10).

Mlynarski and Banaszek reported[76] the reduction of the double bond of ketene dithioacetal **27** with Et_3SiH and CF_3CO_2H in dichloromethane at room temperature, affording the saturated compound **28** in 73% yield (Scheme 11). The primary silyl ether group of **21** is also selectively cleaved under these conditions.

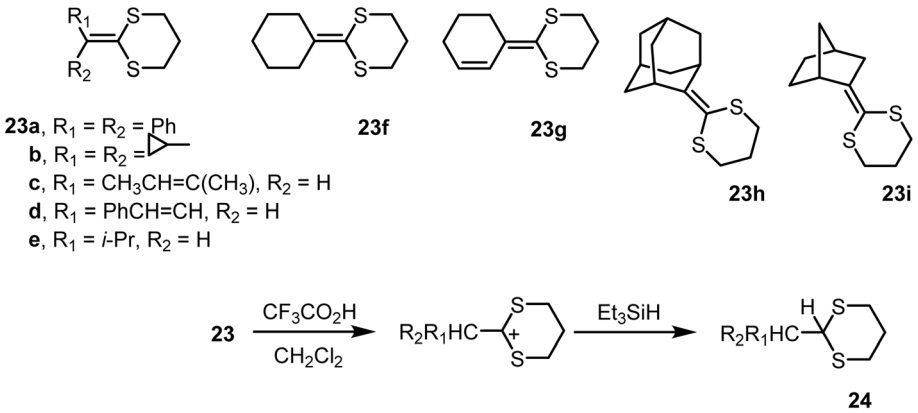


Scheme 7 Stereoselective ionic hydrogenation of steroidal C-20(21)-olefinic double bonds.

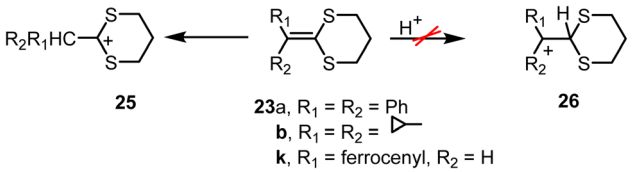


Scheme 8 Reduction of the chalcone double bond.

Ionic hydrogenation of the steroidal C-20,22-ketene dithioacetal **29**, prepared from commercially available[77] 16-dehydropregnenolone acetate with triethylsilane and trifluoroacetic acid in dichloromethane at 25 °C for 18 h afforded[78,79] the C(20R) saturated compound **30** in 89% yield (Scheme 12).



Scheme 9 Ionic hydrogenation of ketene thioacetals.

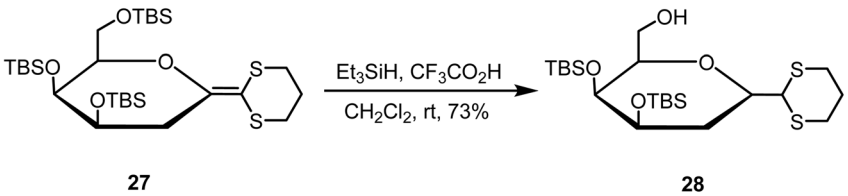


Scheme 10 Protonation of ketene dithioacetals.

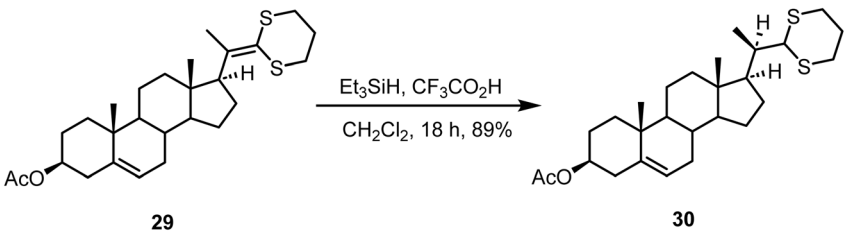
2.1.2 Reduction of exocyclic double bonds. Ho and co-workers reported[80] the reduction of double bonds from the mixture of unsaturated esters **31** and **32** using Et_3SiH and CF_3CO_2H in CH_2Cl_2 at room temperature, which afforded the saturated ester **33** in 82% yield (Scheme 13). Notably, the ester functionality remained unaffected under these conditions.

Vacher and co-workers reported[81] the chemoselective reduction of an *exo*-olefin in ester **34** with triethylsilane and trifluoroacetic acid, affording ester **35** in good yields (Scheme 14). Interestingly, the cyclopropane ring remained unaffected under these conditions.

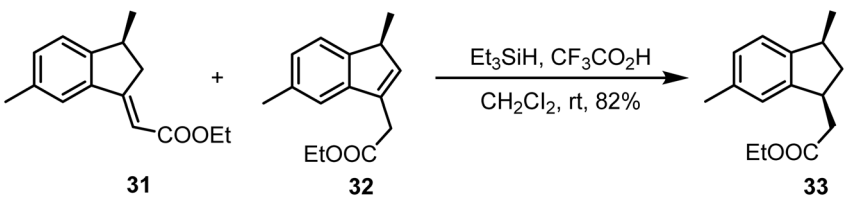
Anzini and co-workers reported[82] the chemoselective reduction of double bonds in unsaturated esters **36**, **37a** and **37b** with triethylsilane in trifluoroacetic acid, providing the



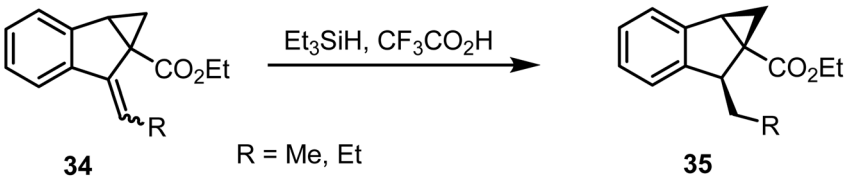
Scheme 11 Reduction of ketene dithioacetal.



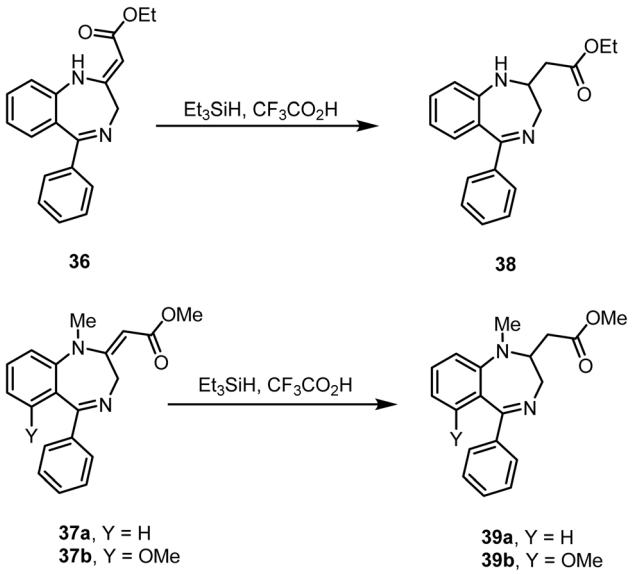
Scheme 12 Ionic hydrogenation of the steroidal C-20,22-ketene dithioacetal.



Scheme 13 Reduction of unsaturated ester.



Scheme 14 Reduction of exocyclic olefins.



Scheme 15 Reduction of an exocyclic unsaturated ester.

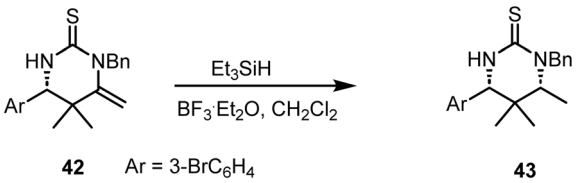
corresponding saturated esters **38, 39a** and **39b,** respectively, in good yields (Scheme 15).

Huang and co-workers reported[83] the selective reduction of a double bond in compound **40** using triethylsilane and trifluoroacetic acid in dichloromethane, affording compound **41** in 92% yield (Scheme 16).

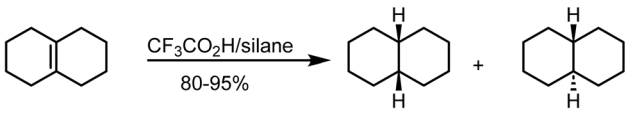
Li and co-workers reported[84] the diastereoselective reduction of dihydropyrimidine thione **42** with triethylsilane and BF_3-$\cdot Et_2O$ in dichloromethane to chiral thiourea **43** in 81% yield (Scheme 17).

2.2 Reduction of cyclic double bonds

2.2.1 Reduction of cyclic double bonds without a heteroatom in the ring. The stereoselectivity of double-bond reduction in ionic hydrogenation is governed by steric accessibility and is highly sensitive to both the substrate structure and the choice of hydride donor.[85] The ionic hydrogenation of olefin **44** (Scheme 18) illustrates that the steric size of the hydride source plays a decisive role. The ionic hydrogenation of $\Delta^{9(10)}$-octalin with CF_3CO_2H and various silanes demonstrated pronounced stereoselectivity. When $BuSiH_3$ was employed as the hydride

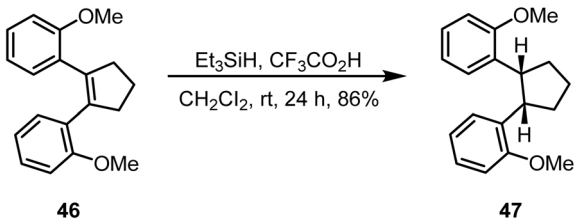


Scheme 17 Reduction of an exocyclic double bond.

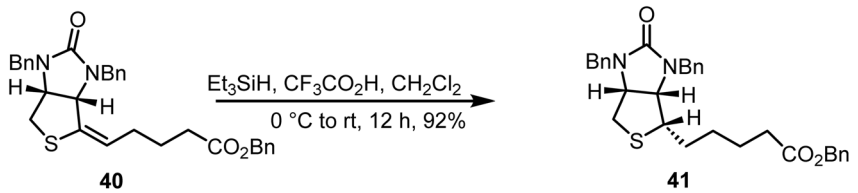


Silane	d.r. (cis/trans)
$BuSiH_3$	22;78
Et_3SiH	42;58
$(s\text{-Bu})_3SiH$	72:28
$(t\text{-Bu})_3SiH$	93:7

Scheme 18 Ionic hydrogenation of $\Delta^{9(10)}$-octalin.



Scheme 19 Ionic hydrogenation of *tetra*-substituted cyclopentene.



Scheme 16 Ionic hydrogenation of an exocyclic double bond.

donor, the reaction furnished *cis*- and *trans*-decalin **45** in a 22 : 78 ratio. In contrast, the use of bulky $^{t}Bu_3SiH$ predominantly afforded the opposite stereoisomer, yielding 93% of the *cis*-decahydronaphthalene product.

The effect of substituents on olefins is important in the reduction reaction. Whiteseil and Apodaca reported[86] a *tetra*-substituted cyclopentene derivative **46** on ionic hydrogenation with Et_3SiH and CF_3CO_2H in dichloromethane to *cis*-cyclopentane **47** in 86% yield (Scheme 19).

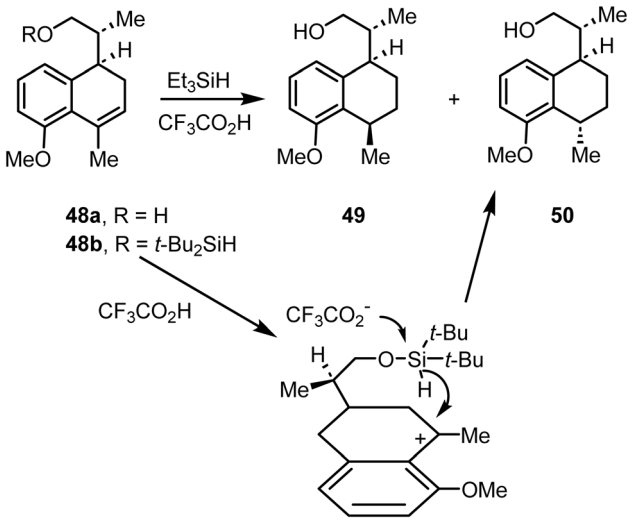
McCombie and co-workers reported[87] the ionic hydrogenation of compound **48** with Et_3SiH and CF_3CO_2H to a 2 : 3 mixture of **49** and **50** (Scheme 20). Furthermore, the intramolecular variant of this methodology was shown to effectively control the stereochemical outcome. The silyl ether **48b** on reaction with trifluoroacetic acid in dichloromethane yielded compound **50** with >95% enantiomeric purity (Scheme 20).

Ravindranathan and co-workers reported[88] the ionic hydrogenation of compound **51** with Et_3SiH and CF_3CO_2H at 0 °C, which afforded the isomeric mixture of trifluoroacetates **52a** and **52b** (44%, 2 : 1), along with alcohols **52c** and **52d** (28%, 2 : 1) (Scheme 21).

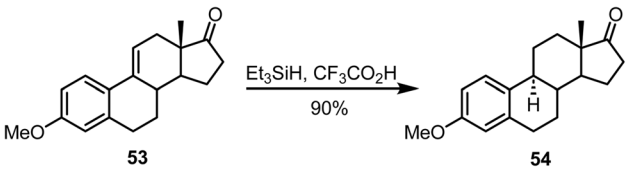
Posner and Switzer reported[89] the synthesis of estrone methyl ether with exceptionally high enantiomeric purity by ionic hydrogenation of $\Delta^{9(11)}$-estrone derivative **53** using Et_3SiH and CF_3CO_2H, which afforded compound **54** in 90% yield (Scheme 22).

The mixture of compound **55** was first treated with HF/MeCN to remove the hydroxyl protecting group, and the resultant alcohols were subsequently subjected[90] to Et_3SiH and CF_3CO_2H in benzene, which provided the desired *trans*-fused tetracycle **56** in 45% yield (Scheme 23).

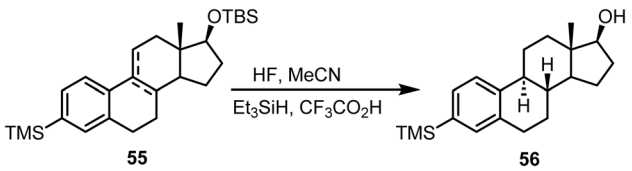
Sugahara and Ogasawara reported[91] the ionic hydrogenation of $\Delta^{8(9)}$-estrone derivative **57** with triethylsilane and trifluoroacetic acid, which afforded compound **54** in 65% yield (Scheme 24).



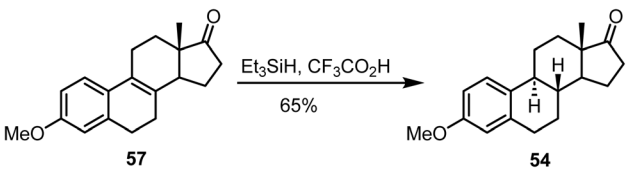
Scheme 20 Ionic hydrogenation of compound **48**.



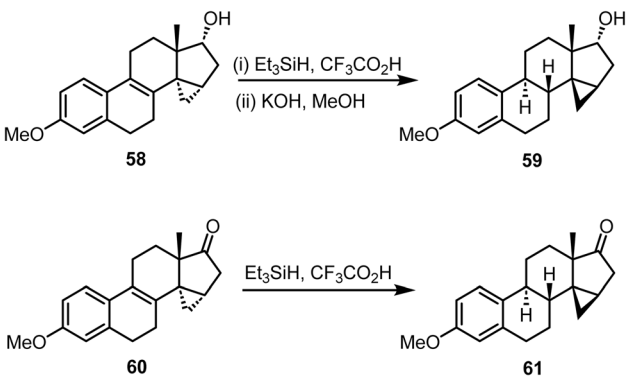
Scheme 22 Ionic hydrogenation of $\Delta^{9(11)}$-estrone derivative.



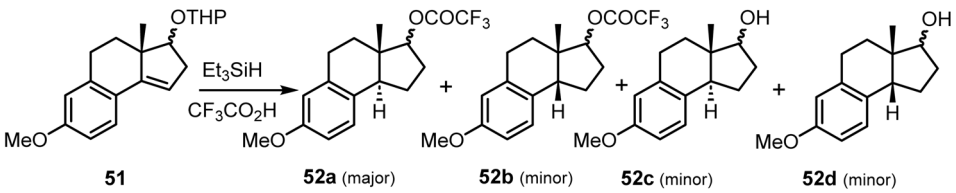
Scheme 23 Ionic hydrogenation of compound **55**.



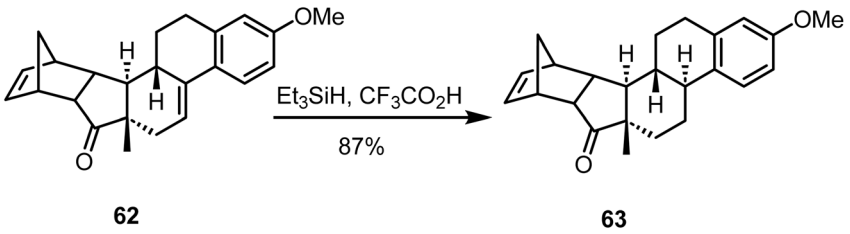
Scheme 24 Ionic hydrogenation of $\Delta^{8(9)}$-estrone.



Scheme 25 Ionic hydrogenation of $\Delta^{8(9)}$-estrone derivatives.



Scheme 21 Ionic hydrogenation of compound **51**.



62 63

Scheme 26 Chemoselective ionic hydrogenation of 62.

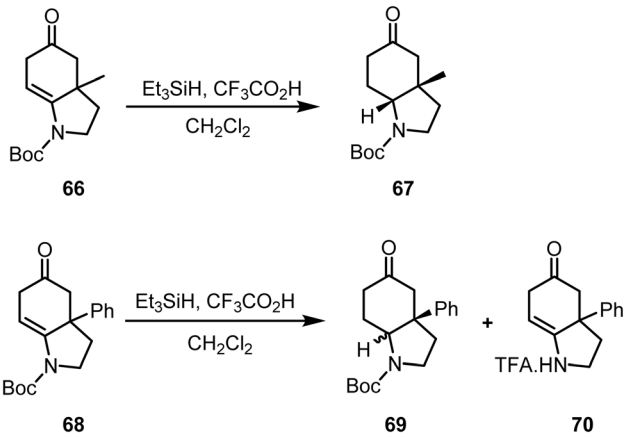
Schwarz and coworkers reported[92] the ionic hydrogenation of 3-methoxy-14α,15α-methylenestra-1,3,5(10),8-tetraen-17α-ol **58** with triethylsilane and trifluoroacetic acid, resulting in 3-methoxy-14β,15β-methylenestra-1,3,5(l0)-trien-17α-ol **59**, rather than the 14α,15α-methylene-9β product. Furthermore, ionic hydrogenation of the 8-double bond in compound **60** predominantly yielded an 8β,9α-dihydro product. However, this ionic hydrogenation process was accompanied by an additional inversion of the 14α,15α-methylene bridge to compound **61** (Scheme 25).

Takano and co-workers reported[93] the chemoselective ionic hydrogenation of **62** using triethylsilane and trifluoroacetic acid, which afforded the *trans*-B/C fused product **63** in 87% yield (Scheme 26). This intermediate **63** was converted to (+) estrone *via* a multistep synthesis.

Cannon and co-workers reported[94] the reduction of a fused carbocyclic ring system containing a carbon–carbon double bond shared by two rings. The ionic hydrogenation with trifluoroacetic acid and triethylsilane in dichloromethane at room temperature yielded the *trans*-fused ring fusion. In this study, application of this hydrogenation method to a series of tetrahydroquinolines **64** provided the corresponding *trans*-fused lactams **65** in 33–95% yield (Scheme 27).

Under ionic reduction conditions (triethylsilane/trifluoroacetic acid), the enamine group of methyl-*N*-Boc-hexahydro-1*H*-indolin-5(6*H*)-one **66** was reduced[95] to afford exclusively a *cis*-fused product **67**. In contrast, the reduction of phenyl-*N*-Boc-hexahydro-1*H*-indolin-5(6*H*)-one **68** furnished a distereomeric mixture **69**, along with a minor amount of the Boc-deprotected compound **70** (Scheme 28).

Saito *et al.* reported[96] the ionic hydrogenation of compound **71** with triethylsilane and trifluoroacetic acid, which furnished

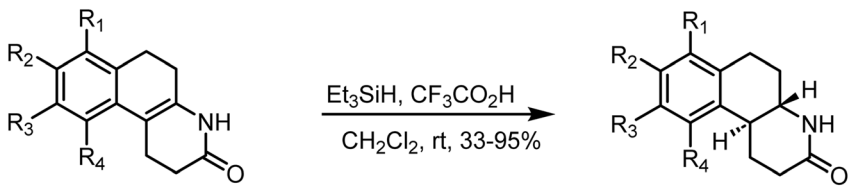


66 67 68 69 70

Scheme 28 Reduction of enamines by ionic hydrogenation.

the *cis*-fused aryloctahydroindol-2-one **72** as the sole product (Scheme 28). Similarly, reduction of the distereomeric mixture of hexahydroindol-3-ones **73** under similar conditions afforded octahydroindol-2-one **74a** as the major product and its isomer **74b** as a minor product (Scheme 29).

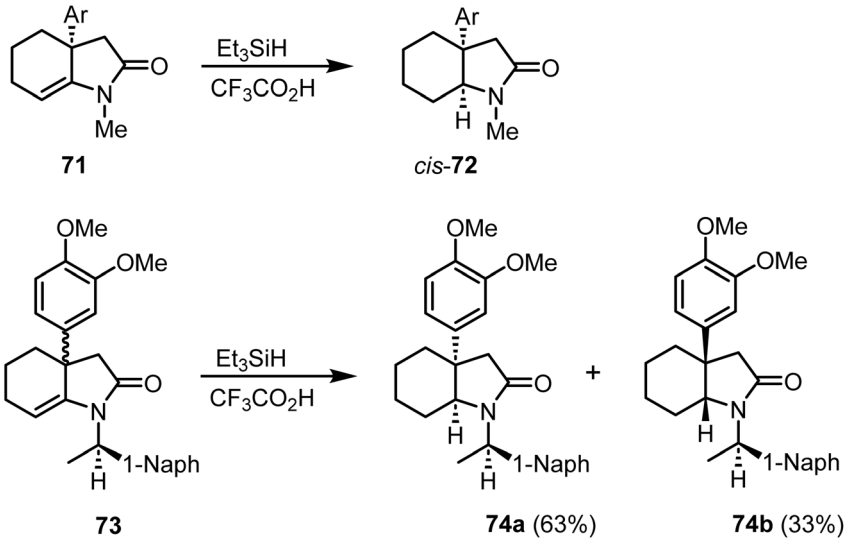
2.2.2 Reduction of cyclic double bonds with a heteroatom in the ring. The reduction[97,98] of naphthopyrandione **75b** with triethylsilane and trifluoroacetic acid afforded eleutherin **76b** and isoeleutherin **77** (Scheme 30). Eleutherin **76b** and isoeleutherin **77** are antibiotics found in *Eleutherine bulbosa*. Similarly, the reduction of compound **75a** under identical reaction conditions at room temperature afforded *cis*-1,3-dimethyl-3,4-dihydro-1*H*-naphtho[2,3-*c*]pyran-5,10-dione **76a** in excellent yield. Furthermore, compound **75b** under similar



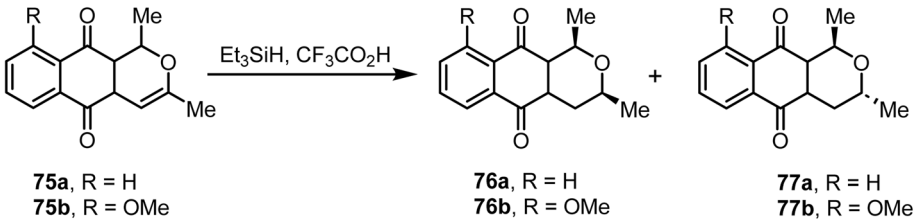
64 65

a, R_1 = OMe, R_2 = H, R_3 = H, R_4 = H
b, R_1 = OMe, R_2 = OMe, R_3 = H, R_4 = H
c, R_1 = H, R_2 = OCH_2Ph, R_3 = OMe, R_4 = H
d, R_1 = OMe, R_2 = H, R_3 = H, R_4 = OMe

Scheme 27 Reduction of a fused double bond.



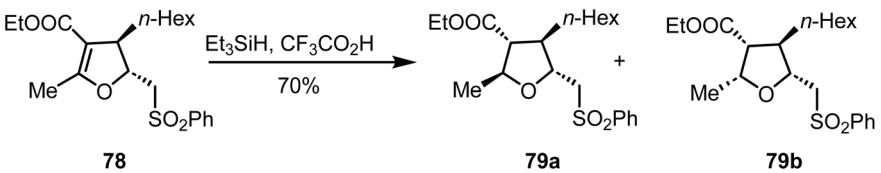
Scheme 29 Reduction of a fused double bond by ionic hydrogenation.



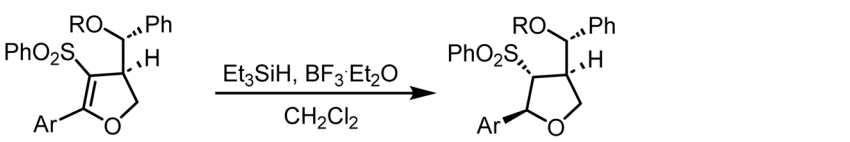
Scheme 30 Ionic hydrogenation of a double bond.

reaction conditions resulted in a 1 : 5 mixture of **76b** and its diastereoisomer (±)-isoeleutherin **77** in moderate yields (Scheme 30). In these transformations, the hydride source from triethylsilane determines the stereochemical outcome of the products.

The highly substituted dihydrofuran derivative **78** on ionic hydrogenation[99] with Et_3SiH in CF_3CO_2H at 60 °C afforded an 86 : 14 mixture of enantiomerically pure tetrahydrofurans **79a** and **79b** in 70% yield (Scheme 31).



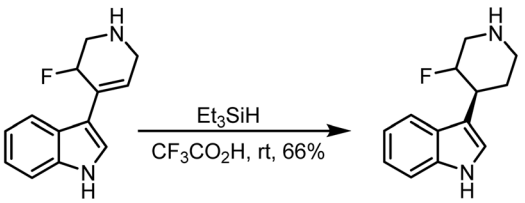
Scheme 31 . Reduction of dihydrofuran derivative **78**.



Scheme 32 Reduction of dihydrofuran derivatives.

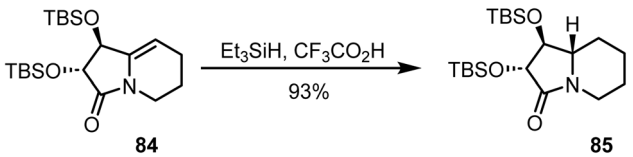
The stereoselective reduction[100] of compounds **80** using ionic hydrogenation with Et_3SiH and $BF_3 \cdot Et_2O$ resulted in the corresponding tetrahydrofuran derivatives (Scheme 32). Reduction of the double bond in **80b** was readily achieved by treating with Et_3SiH and $BF_3 \cdot Et_2O$ in dichloromethane, obtaining the alcohol **81a** in 83% yield. Similarly, the tetrahydrofurans **81b** and **81c** were synthesized in 75% and 85% yields, respectively, from **80a** and **80c** (Scheme 32).

The substitution at the C-3 position of the indole nucleus with certain double-bonded compounds can be selectively reduced by ionic hydrogenation.[101] The tri-substituted double bond in tetrahydropyridine **82** on ionic reduction with trifluoroacetic acid and triethylsilane afforded *trans*-fluoropiperidine **83** in 66% yield (Scheme 33).



82 **83**

Scheme 33 Reduction of a tetrahydropyridine by ionic hydrogenation.



84 **85**

Scheme 34 Stereoselective reduction of unsaturated lactam.

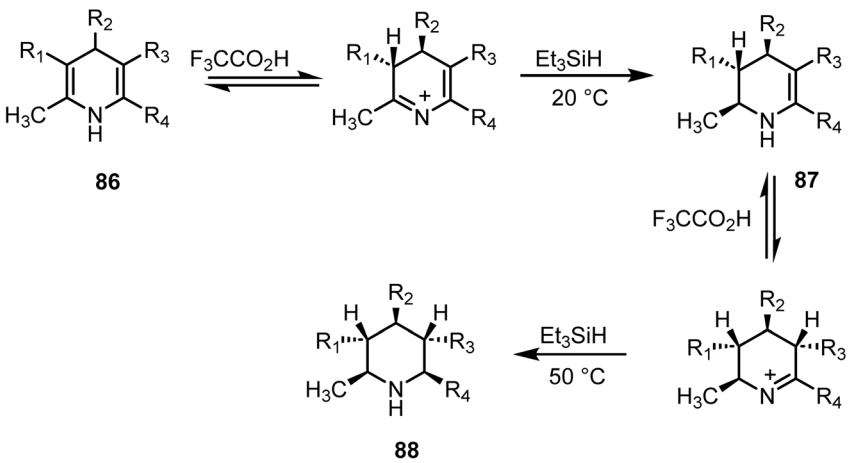
Ha and co-workers reported[102] the stereoselective reduction of unsaturated lactam **84** with Et_3SiH and CF_3CO_2H, which provided the saturated lactam **85** in 93% yield, serving as an intermediate in the synthesis of alkaloid (+)-lentiginosine (Scheme 34).

Rosentreter reported[103] the ionic hydrogenation of substituted 1,4-dihydropyridine **86** using triethylsilane and trifluoroacetic acid. With 1 equivalent of triethylsilane at room temperature, the partially reduced pyridine **87** was obtained selectively. Furthermore, the use of 3 equiv. of triethylsilane at 50 °C produced the corresponding piperidine derivatives **88** (Scheme 35).

Baldwin and co-workers demonstrated[104,105] the synthesis of acromelic acid analogues *via* ionic hydrogenation of substituted dihydropyrrole derivatives **89** using triethylsilane in trifluoroacetic acid at 60 °C. This reaction resulted in epimers of the protected acromelic acid analogues **90a** and **90b** (1 : 1 ratio) in satisfactory yields (Scheme 36).

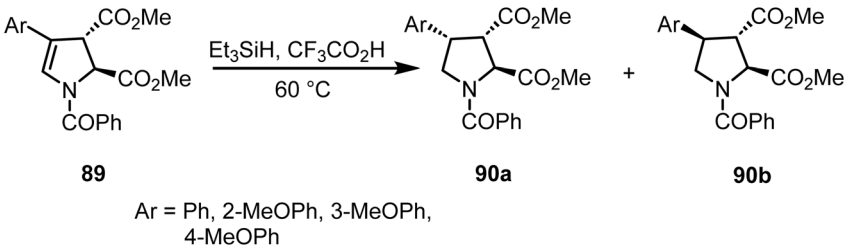
Magnus and co-workers reported[106] a synthetic strategy for the formation of 1,3-*cis*-substituted tetrahydroisoquinolines from *ortho*-iodo imines *via* Larock isoquinoline synthesis, organolithium addition to unactivated isoquinolines, and ionic hydrogenation. Compound **91**, on reaction with CF_3CO_2H and triethylsilane in CH_2Cl_2 at −10 °C to 25 °C, afforded compound **92** in 97% yield (Scheme 36). Furthermore, reduction of the enecarbamate moiety in **93** using Et_3SiH and CF_3CO_2H in CH_2Cl_2 led to the competitive formation of **94b** in 61% yield and the expected product **94** in 31% yield (Scheme 37). Moreover, performing the same reaction in the presence of benzyl alcohol (15 equiv.) enhanced the yield of **94** to 71%, while **94b** was obtained in 22% yield.

Roach and co-workers reported[107] the ionic hydrogenation of dihydroquinoline **95** with triethylsilane and trifluoroacetic acid



a, $R_1 = CO_2Me$, $R_2 = Ph$, $R_3 = CO_2Me$, $R_4 = Me$
b, $R_1 = CO_2Me$, $R_2 = 2\text{-}NO_2\text{-}Ph$, $R_3 = CO_2Me$, $R_4 = Me$
c, $R_1 = CO_2Me$, $R_2 = 2\text{-}CF_3\text{-}Ph$, $R_3 = CO_2Me$, $R_4 = Me$
d, $R_1 = COMe$, $R_2 = 3\text{-}NO_2\text{-}Ph$, $R_3 = COMe$, $R_4 = Me$
e, $R_1 = CO_2Me$, $R_2 = 3\text{-}NO_2\text{-}Ph$, $R_3 = CN$, $R_4 = Me$
f, $R_1 = CO_2Et$, $R_2 = 3\text{-}NO_2\text{-}Ph$, $R_3 = CO_2Et$, $R_4 = CO_2Et$

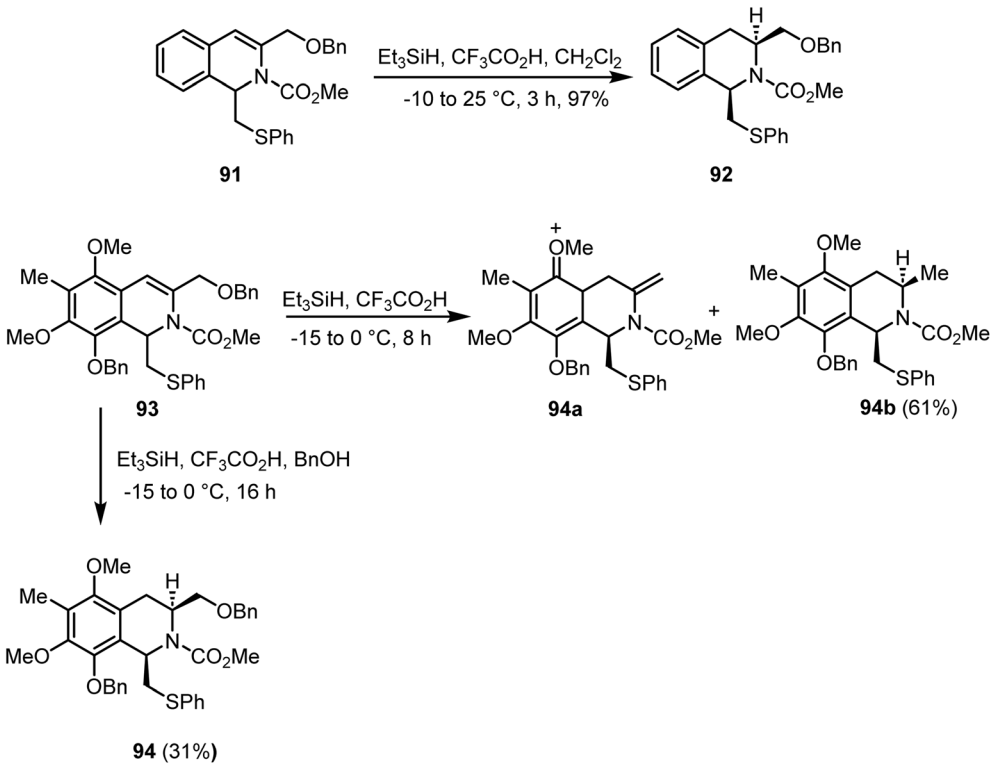
Scheme 35 Ionic hydrogenation of 1,4-dihydropyridine derivatives.



89 90a 90b

Ar = Ph, 2-MeOPh, 3-MeOPh, 4-MeOPh

Scheme 36 Ionic hydrogenation of dihydropyrrole derivatives.

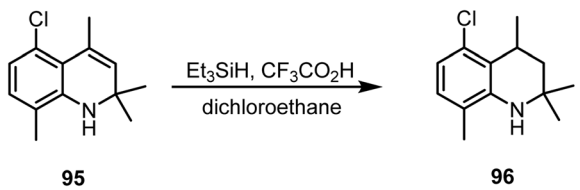


91 92

93 94a 94b (61%)

94 (31%)

Scheme 37 Ionic hydrogenation of double bonds in compounds **91** and **93**.

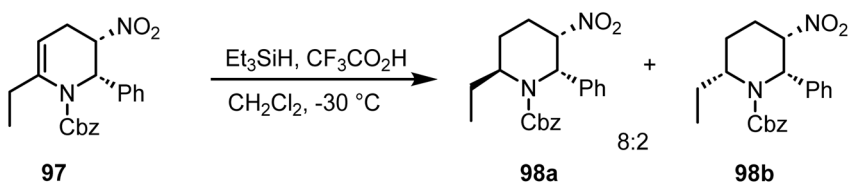


95 96

Scheme 38 Ionic hydrogenation of dihydroquinoline.

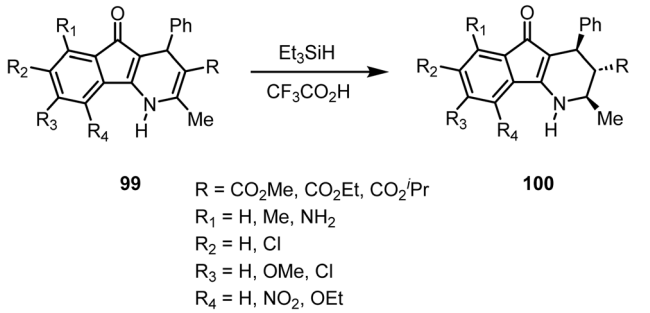
in dichloroethane at 80 °C, yielding compound **96**, as shown in Scheme 38.

Humphrey and co-workers reported[108] the regioselective reduction of the double bond in **95** with triethylsilane and trifluoroacetic acid in dichloromethane at −30 °C, which resulted in an 8 : 2 *trans*/*cis* ratio of **98a** and **98b** (Scheme 39). Compound **98a** was obtained in 72% yield after crystallization. Moreover, the reaction conditions do not affect the reducible functionalities, NO_2 and Cbz, present in compound **97**.



97 98a 98b

Scheme 39 Regioselective reduction of tetrahydropyridine derivatives.



Scheme 40 Regio- and chemo-selective reduction of dihydropyridine derivatives.

Stupnikova and co-workers reported[109] the reduction of 5-oxo-4-phenyl-1*H*-4,5-dihydroindeno[1,2-*b*]pyridines **99** with triethylsilane in trifluoroacetic acid, which afforded the corresponding 1,2,3,4-tetrahydroindeno[1,2-*b*]pyridines **100** with a *trans*-configuration, as shown in Scheme 40.

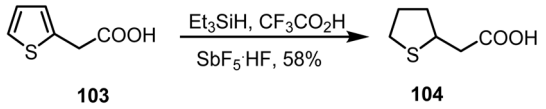
Ibrahim-Quali reported[110] the reduction of the $\Delta^{9,11}$ double bond in compound **101** using 10 equiv. of triethylsilane and 50 equiv. of trifluoroacetic acid, and after hydrolysis of the 17-trifluoroacetate group, the desired steroid analogue **102** was obtained in 73% yield (Scheme 41).

2.3 Reduction of cyclic double bonds in aromatic heterocycles

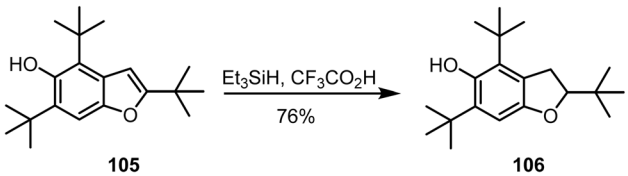
The salient feature of ionic hydrogenation is that sulfur-containing compounds can be reduced, which typically poison catalysts in conventional hydrogenation methods. Using the silane-trifluoroacetic acid system, substrates such as thiophenes, benzothiophenes and octahydrothioxanthenes were successfully converted to their dihydro- and tetra-hydro derivatives. Thiophene-2-acetic acid **103** on ionic hydrogenation[111] with Et_3SiH in CF_3CO_2H containing a trace amount of superacid ($HSbF_6$) afforded tetrahydro-thiophene-2-acetic acid **104** in 58% yield (Scheme 42).

The highly substituted benzofuran derivative **105** on ionic hydrogenation[112] with triethylsilane and trifluoroacetic acid from 0 °C to room temperature afforded the racemic dihydro-derivative **106** in 76% yield (Scheme 43).

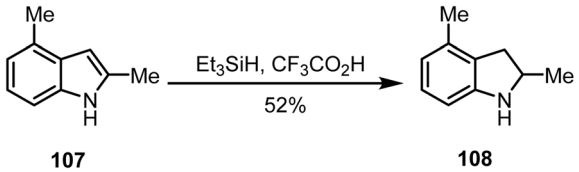
Electron-deficient aromatic heterocycles, such as pyridines and related compounds, are unreactive under ionic hydrogenation conditions. Therefore, this method is most suitable for the more reactive five-membered ring heteroaromatics.



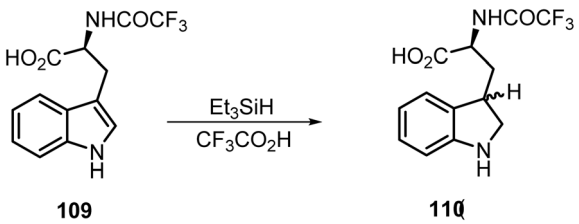
Scheme 42 Ionic hydrogenation of thiophene.



Scheme 43 Ionic hydrogenation of a benzofuran derivative.



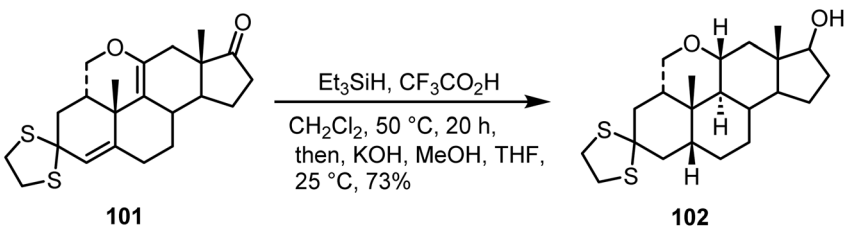
Scheme 44 Reduction of indole derivative **107**.



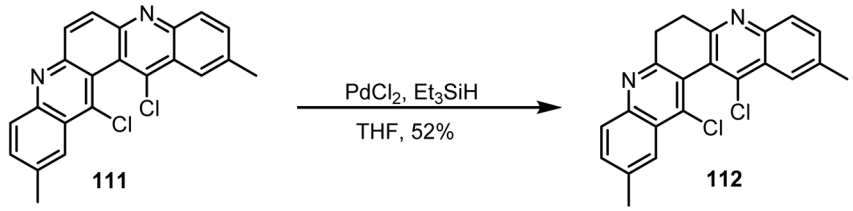
Scheme 45 Reduction of indole derivative **109**.

Moreover, indoles and pyrroles can be effectively reduced *via* ionic hydrogenation. Stachel and co-workers reported the ionic hydrogenation[113] of 2,4-dimethyl indole **107** with triethylsilane in trifluoroacetic acid, which yielded 2,4-dimethyl-dihydroindole **108** in 52% yield (Scheme 44).

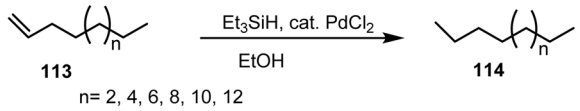
Carr and co-workers reported[114] the ionic hydrogenation of the trifluoroacetyl derivative of L-tryptophan **109** at the C-2 double bond using CF_3CO_2H and Et_3SiH. This led to a diastereomeric mixture of indolines **110** (45 : 55) in good yield (Scheme 45).



Scheme 41 Reduction of double bonds and keto functionality.



Scheme 46 Selective reduction of the 6,7-double bond in compound **111**.



Scheme 47 Reduction of 1-alkenes by triethylsilane and $PdCl_2$.

2.4 Miscellaneous

Lartia and coworkers reported[115] the selective reduction of the 5,7-double bond in compound **111** using triethylsilane and palladium chloride, which afforded the 6,7-dihydrogenated product **112** in 52% yield (Scheme 46).

Mirza-Aghayan and co-workers reported[116] the reduction of 1-alkenes **113** using triethylsilane and palladium(II) chloride in ethanol at room temperature, which afforded the corresponding alkanes **114** in excellent yields (Scheme 47).

Olah and co-workers reported[117] the reduction of alkenes using triethylsilane, trifluoroacetic acid and ammonium fluoride in dichloromethane, which afforded the corresponding alkanes in good yields.

3. Summary

This review compiles a diverse and valuable collection of methodologies for the synthesis of fine chemicals, intermediates of complex molecules, natural products, and bioactive compounds. A wide range of alkene-containing substrates has been successfully reduced *via* ionic hydrogenation using triethylsilane and trifluoroacetic acid/Lewis acid, and related information is collected from the literature and described here. As demonstrated over the past four to five decades, continued advancement in this field holds promise for broader applications of ionic hydrogenation in synthetic organic chemistry. Future innovations will depend on a deeper mechanistic understanding and strategic application of the principles outlined in this review. We dedicate this work to the researchers who have contributed to the field of ionic hydrogenation and hope it serves to inspire the next generation of chemists to further expand its scope and utility.

Conflicts of interest

The author declares that there is no financial or personal conflict of interest that could influence the integrity or outcomes of this study.

Abbreviations

Ac	acetyl
Ar	aryl
aq.	aqueous
Bn	benzyl
Boc	*tert*-butyloxycarbonyl
°C	degree Celsius
cat.	catalytic
Cbz	benzyloxycarbonyl
dr	distereomeric ratio
equiv.	equivalent
Et	ethyl
h	hour (s)
MOM	methoxy methyl
Nap	naphthyl
Ph	phenyl
PMHS	polymethylhydrosiloxane
rt	room temperature
TBS	tertiary butyl dimethylsilyl
TES	triethylsilane
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	tetrahydropyranyl
TMS	trimethylsilyl

Data availability

The information and data referenced in this review are derived from publicly accessible scientific publications, such as peer-reviewed journal articles. Proper attribution has been provided for all cited sources within the manuscript.

Acknowledgements

I sincerely acknowledge various research colleagues for the reprints or preprints and also for their valuable suggestions and discussions. I would like to thank Professor R. A. Mane, Professor M. S. Shingare and Professor B. R. Sathe for their timely help and co-operation during the preparation of this review.

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