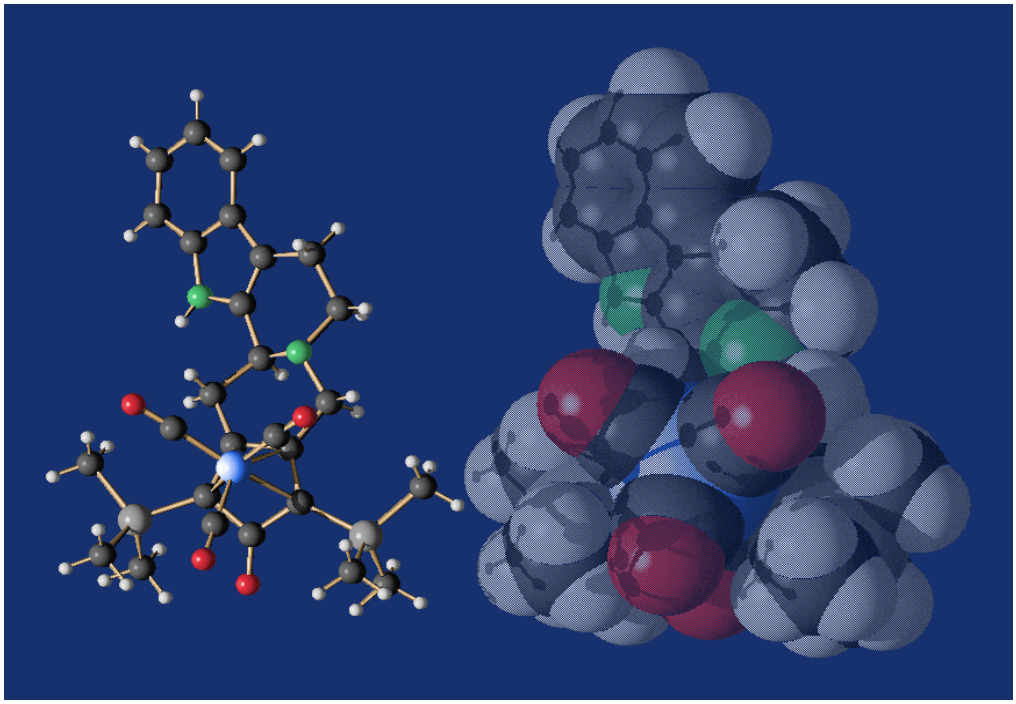
Transition Metal-Mediated Syntheses of Yohimbane and Indolizidine Alkaloids



Sameer Agarwal

Transition Metal-Mediated Syntheses of Yohimbane and Indolizidine Alkaloids

D I S S E R T A T I O N

zur Erlangung des akademischen Grades

Doctor rerum naturalium
(Dr. rer. nat.)

vorgelegt

der Fakultät Mathematik und Naturwissenschaften
der Technischen Universität Dresden

von

M. Tech.
Sameer Agarwal
geboren am 21. Juli 1973 in Dehra Dun, Indien

Gutachter: Prof. Dr. Hans-Joachim Knölker
Prof. Dr. Peter Metz
Prof. Dr. Dieter Schinzer

Eingereicht am: 17.02.2005
Tag der Verteidigung: 02.06.2005

Transition Metal-Mediated Syntheses of Yohimbane and Indolizidine Alkaloids

D I S S E R T A T I O N

for the partial fulfillment of the requirements
for the academic degree of

Doctor rerum naturalium
(Dr. rer. nat.)

submitted to

Faculty of Mathematics and Natural Sciences
Technical University Dresden

by

M. Tech.
Sameer Agarwal
born on 21. July 1973 in Dehra Dun, India

Referees: Prof. Dr. Hans-Joachim Knölker
Prof. Dr. Peter Metz
Prof. Dr. Dieter Schinzer

Submitted on: 17.02.2005
Date of Thesis Defence: 02.06.2005

To my parents

This research work was carried out at *Department of Chemistry, University of Karlsruhe, Germany,* from 01st June 2000 to 30th November 2001 and at *the Institute of Organic Chemistry, Technical University of Dresden, Germany,* from 01st December 2001 to 31st October 2004, under the supervision of *Prof. Dr. Hans-Joachim Knölker.*

Index

Abbreviations

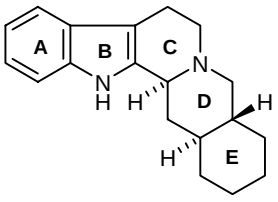
abs.	absolute
Ac	acetyl
Ac_2O	acetic anhydride
Ans	anisole
Boc	*tert*-butyloxycarbonyl
Bn	benzyl
Bu	butyl
B. V. Ox.	Baeyer-Villiger oxidation
Cp	cyclopentadienyl
δ	chemical shift
d	days
DCC	*N*,*N*'-dicyclohexylcarbodiimide
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEPT	Distortionless Enhancement by Polarization Transfer
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMPU	*N*,*N*'-dimethylpropyleneurea
DMS	dimethyl sulphide
DMSO	dimethyl sulfoxide
DNPH	2,4-dinitro phenyl hydrazine
drift	diffuse reflexion
EtOAc	ethyl acetate
eq.	equivalent
h	hour
λ	Wavelength
Hz	Hertz
HMDS	hexa methyl disilazane
IR	Infrared spectra

GC	gas chromatography
GC-MS	gas chromatography- mass spectroscopy
J	Coupling constant
LDA	lithium diisopropylamide
LHMDS	lithium hexamethyldisilazane
mCPBA	3-chloroperoxybenzoic acid
M	molar
Me	methyl
min	minute
MMPP	magnesium mono perpthalate
M.P.	melting point
MS	Mass spectra
n-BuLi	n-butyllithium
NCS	*N*-chlorosuccinimide
NMR	nuclear magnetic resonance
ν	frequency
PCC	pyridinium chlorochromate
Pd/C	palladium on active carbon
PDC	pyridinium dichromate
Ph	phenyl
r.t	room temperature
R, R’	alkyl Rest
Ra-Ni	Raney Nickel
Rf	reflux
R_f	retention factor
S.M.	starting material
T	temperature
t	time
TBAI	*tetra*-n-butylammonium iodide
TBAHS	*tetra*-butylammonium hydrogen sulfate
tert	tertiary

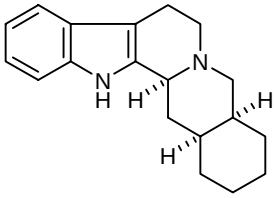
THF	tetrahydrofuran
TLC	Thin layer chromatography
TMS	trimethylsilyl
Tos	tosyl
Ts	4-toluenesulfonyl
UV	Ultraviolet
W	Watt

1 Introduction

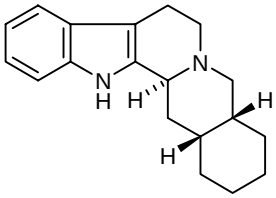
Polycyclic nitrogen containing heterocycles form the basic skeleton of numerous natural products and physiologically active drugs.[1-3] Yohimbane and alloyohimbane are members of the *Rauwolfia* alkaloid family. Representative members of this family include reserpine, ajmalicine, and yohimbine (Figure 1). These alkaloids have a characteristic pentacyclic ring framework with an indole moiety comprising rings A and B. Much of the stereochemical and functional group complexity resides on the E-ring.



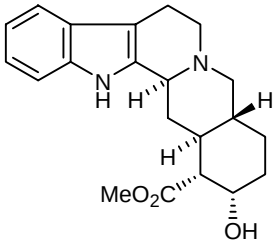
Yohimbane (**1**)



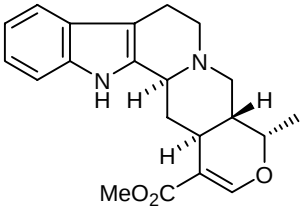
Alloyohimbane (**2**)



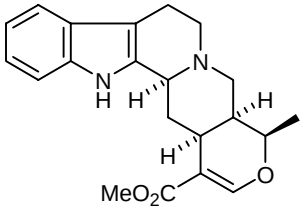
3-Epialloyohimbane (**3**)



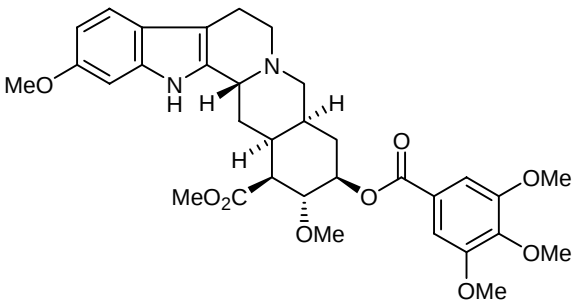
Yohimbine (**4**)



Ajmalicine (**5**)



Rauniticine (**6**)



Reserpine (**7**)

Figure 1

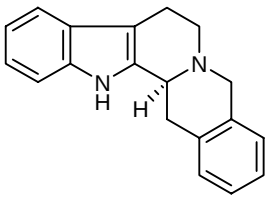
These alkaloids possess a wide range of interesting biological activities, including antihypertensive and antipsychotic properties.[4] Receptor-binding studies have demonstrated that several subtypes exist for α-adrenoceptor types, depending on species and tissue.[5] In addition to genetic coding, pharmacological response to agonists and antagonists determine the classifications depending on their binding potency to the receptors. The most common probes used in these studies are agonists, such as clonidine, and antagonists: yohimbine and yohimbine-like compounds such as rauwolscine or corynanthine. Each of these compounds has various binding affinities for the α-adrenoceptors types. Some, such as yohimbine, exhibit weak binding to α_1-adrenoceptors as well as high affinity for the α_2-adrenoceptors.

Considered a sympatholytic, yohimbine has been used in herbal medicine for centuries. Yohimbine is one example of a large family of indole alkaloids called yohimbanes. Indole alkaloids are naturally-occurring heterocyclic amines derived from botanical sources. Yohimbine is the principal alkaloid found in extracts from the bark of the *Pausinystlia yohimbe* tree which grows in tropical West Africa and the Congo. It is structurally similar to reserpine and can also be isolated from the roots of *Rauwolfia.* Typical of many alkaloids, the yohimbanes have diverse pharmacological properties.

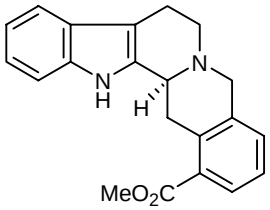
The yohimbine molecular structure contains five asymmetric carbons; yohimbine is one of 32 isomers within this family. The yohimbane alkaloids include antagonists that are selective for the α-adrenoceptor. The selectivity of the various yohimbane alkaloids depends on the stereochemical configuration of the five carbon centres. The shape and position of the various components of the compound determines their interaction with the receptors and potency of their response. Not only do they have differential activity at the α-adrenoceptor types (α_1 versus α_2), but also within the subtypes.[5,6] Recently, yohimbine has been promoted as a dietary supplement to enhance athletic performance and fat loss. Clinically, yohimbine has been administered to induce anxiety in psychiatric patients, orthostatic hypotension and other autonomic failure conditions, adjunct therapy for opiate withdrawal, and male organic impotence.[6,7] It is widely used by veterinarians to reverse

sedation or anaesthesia in animals. Other therapeutic applications currently under research are the use as a glucose-dispersal agent for the treatment of non-insulin dependent diabetes and to treat adverse effects of anti-depressants.

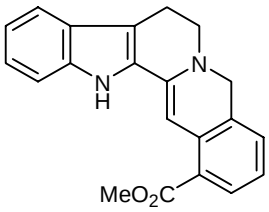
Ajmalicine (also called raubasine and δ-yohimbine), a member of the general family of heteroyohimbane alkaloids, is prescribed widely in the treatment of cardiovascular diseases. It is a potent peripheral vasodilating muscle calibre for short periods.[8] Ajmalicine also reduces platelet aggregation in patients at risk due to complications of atherosclerosis,[9] and has also been prescribed for the treatment of Raynaud's disease.[10] Ajmalicine exhibits few side effects and does not cause acute hypotension even at relatively high doses (2 mg/kg).[8,11] The isolation of ajmalicine from the roots of commercially grown *Catharanthus roseus* has been highly optimised and recent attention directed toward the production of ajmalicine by cell culture techniques.[12,13] Heteroyohimbane alkaloids related to ajmalicine are selective α-adrenoreceptor blocking agents.[14]



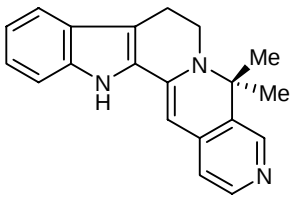
Demethoxycarbonyldihydro-gambirtannine (**8**)



Dihydrogambirtannine (**9**)



Gambirtannine (**10**)



3,14-Didehydro-19-methyl-normalindine (**11**)

Figure 2

Gambirtannine (**10**) and dihydrogambirtannine (**9**) are aromatized yohimbane alkaloids (Figure 2) isolated from extracts of the leaves and stems of the Rubiacea *Uncaria gambier* (*Ourouparia gambir*), a tree growing in Southeast Asia.[15] Demethoxycarbonyl dihydrogambirtannine (**8**) was first isolated from the leaves of *Ochrosia lifuana* and *Ochrosia miana* (Apocynaceae).[16] Subsequently, it was found that **8** represents the main alkaloid of the fruits of *Strychnos usambarensis*, a plant of the family Loganiaceae found in Africa.[17] The consumption of these fruits was reported to cause poisoning. Recently, 3,14-didehydro-19-methylnormalindine (**11**), an indolopyridonaphthyridine alkaloid was isolated from the aerial parts of *Ophiorrhiza rosacea* Ridley (Rubiaceae).[18]

In the light of these interesting biological activities and the difficulty in obtaining large quantities of these alkaloids from their natural sources, they have piqued the interest of synthetic organic chemists for decades. This is both due to their challenging and intricate structures and their prominence as medicinal agents and pharmacological tools.

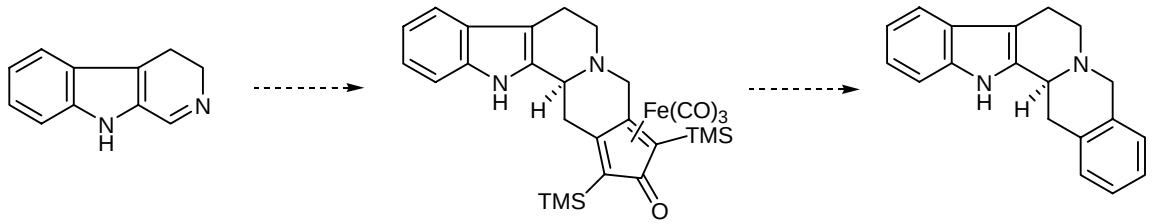
The historic total synthesis of reserpine by Woodward[19,20] in 1956 stands as a milestone because of its tactical elegance and timely achievement and is frequently cited as a model strategy in preparative organic chemistry; the first total synthesis of yohimbine by van Tamelen[21] displays a similar level of accomplishment. Since then, construction of the core indolo[2,3-*a*]quinolizidine skeleton found in yohimbine has presented a formidable challenge to synthetic organic chemistry, and several elegant methods have been developed to achieve this goal.[2-4,22,23] Key synthetic elements in some of these approaches have included Diels-Alder cycloaddition,[24] radical cyclization,[25] Oxy-Cope[26] and amino-Claisen rearrangements,[27] and photocyclization.[28]

The most common synthetic entry to the yohimbane and heteroyohimbane alkaloids is based on a ABDE → ABCDE construction in which the C-ring is formed late in the synthesis. This approach requires the initial preparation of various DE bicycles, followed by their attachment to a suitable tryptophyl synthon, and stereoselective formation of the C ring.

In an unified approach to the yohimbane and other classes of indole alkaloids, Knölker and Cämmerer developed recently a general method that features the synthesis of the pentacyclic nucleus via an ABC → ABCDE approach.[29]

In a key reaction, the iron-mediated [2+2+1] cycloaddition of 1,2-bis(trimethylsilylpropargyl)-1,2,3,4-tetrahydro-β-carboline, generated by *C*-alkylation of 3,4-dihydro-β-carboline (**12**) followed by *N*-alkylation, delivered the iron complex **13** having a pentacyclic nucleus characteristic of yohimbane alkaloids. The iron complex **13** was transformed into racemic demethoxycarbonyldihydrogambirtannine (**8**), completing a highly efficient total synthesis that required only six steps from 3,4-diydro-β-carboline and gave a 49% overall yield (Scheme 1).

Scheme 1



12 **13** **8**

This had demonstrated for the first time that the iron-mediated [2+2+1] cycloaddition of diynes can be applied to the construction of pentacyclic frameworks and the total synthesis of biologically active yohimbane and related indole alkaloids. We were specifically interested in using the iron-mediated [2+2+1] cycloaddition chemistry as a key strategy for the total synthesis of yohimbane, heteroyohimbane and aromatized yohimbane alkaloids.

Transition metals effecting [2+2+1] cycloadditions

The transition metal-mediated [2+2+1] cycloaddition of two alkynes to cyclopentadienones represents a simple and direct method for the synthesis of substituted

cyclopentadienones. A variety of transition metals have been shown to be quite effective in inducing this transformation.

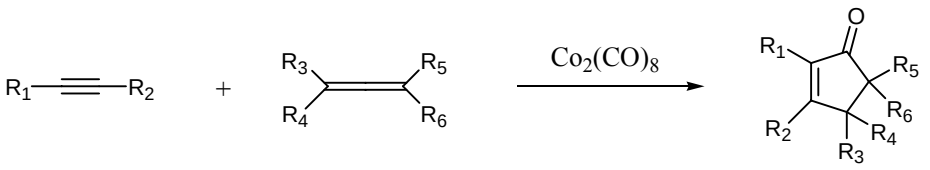
Negishi reported a zirconium-promoted intramolecular [2+2+1] cycloaddition involving a zirconabicyclic intermediate.[30] Carbonylation occurs under an atmosphere of CO to afford the cyclopentenone in good yields. Nickel(0) has been shown to effect the intramolecular cyclization of enynes with isocyanides to form the 1-imino-2-cyclopentenes.[31] This product is subsequently hydrolyzed to afford a cyclopentenone. Later, a carbonylative $Ni(CO)_4$-mediated intermolecular cycloaddition between acetylenes and allylic halides was reported by Moreto that affords the cyclopentenone directly.[32] Molybdenum carbonyl species also effect the intra- and intermolecular [2+2+1] cycloaddition process. Hanaoka has shown that bis(cyclopentadienyl) tetracarbonyldimolybdenum-alkyne complexes also give cyclopentenones.[33] Jeong reported that molybdenum hexacarbonyl effects the cycloaddition in the presence of DMSO.[34] Hoye has demonstrated that tungsten carbonyl species promote the intramolecular [2+2+1] cycloaddition.[35] A THF solution of the hexacarbonyl tungsten is photolyzed to form $W(CO)_5 \cdot THF$ which effects the cyclization of enynes in good yields.

The use of alternative metals has been most effective in the development of a catalytic version of the [2+2+1] cycloaddition. Buchwald has extended his titanocene methodology to a catalytic version for the synthesis of both 1-imino-2-cyclopentenes[36] and cyclopentanones.[37] Buchwald has also reported a nickel(0)-catalyzed synthesis of 1-imino-2-cyclopentenes.[38]

Catalytic versions of the cycloaddition have also been reported using later transition metals. Murai[39] and Mitsudo[40] simultaneously reported that $Ru_3(CO)_{12}$ catalyzes the intramolecular cycloaddition of enynes in good yields. Likewise, the laboratories of Narasaka[41] and Jeong[42] both reported the catalysis of the intramolecular cycloaddition of enynes using rhodium carbonyl metal species. Recently, Wender[43] reported the first example of a rhodium(I)-catalyzed [2+2+1] cycloaddition reaction involving a diene, an alkene, and CO.

Cobalt remains the metal of choice in effecting the formal [2+2+1] cycloaddition process involved in the Pauson-Khand (P-K) reaction. The P-K reaction is a cycloaddition of an alkene, an alkyne and carbon monoxide to generate a cyclopentenone. It was discovered by Khand and Pauson in the early seventies.[44] In general, alkynes react with $Co_2(CO)_8$ to generate the thermally stable, readily characterized complexes. These complexes then react with alkenes to generate cyclopentenones in satisfactory yields (Scheme 2). The P-K reaction usually gives good regio- and stereoselectivity.

Scheme 2



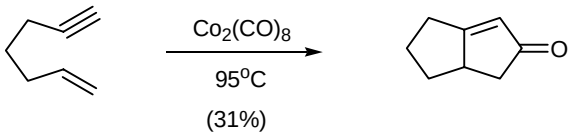
14 **15** **16**

A well accepted mechanistic understanding is based on the observations of regio- and stereochemistry in a large number of examples and the direct evidence that the alkyne cobalt complex is involved at the first stage of the process. The dicobalt octacarbonyl complexes to the alkyne first to form an alkyne cobalt complex, subsequently, the oxidative addition of the alkene π-bond into one of the cobalt-carbon bonds of the alkyne complex occurs, followed by carbon monoxide insertion to the resulting cobalt metallacycle. Reductive elimination followed by decomplexation of the $Co_2(CO)_6$ fragment affords the P-K reaction product, a cyclopentenone.

The most satisfactory results are obtained with acetylene and simple terminal alkynes, while internal alkynes give lower yields of cyclopentenones. Initially, the scope of the reaction with respect to the alkene was somewhat limited. While strained cyclic alkenes are good substrates, usually delivering yields above 50%, sterically hindered alkenes reduce the efficiency of this reaction considerably. The P-K reaction is compatible with a wide range of functionalities, including alcohols, ethers, ketones, ketals, esters, tertiary amines and amides, thioethers, aromatic and heteroaromatic rings.

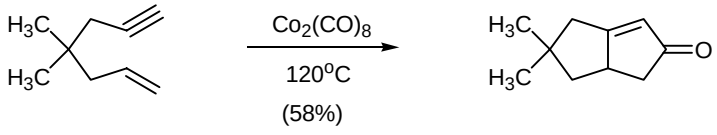
Schore[45] improved the efficiency and reliability of this reaction by tethering the alkene and alkyne moieties together, which also resulted in excellent regio- and stereo control of the products. The intramolecular P-K reaction has been the most extensively studied. The products of the cycloaddition, e.g. bicyclo[3.3.0]oct-1-en-3-ones, are very useful intermediates in the synthesis of cyclopentane-based polycyclic compounds. Intramolecularity permits satisfactory results with terminal, internal, and even trisubstituted alkenes, although reactions of trisubstituted alkenes are limited to terminal alkynes due to steric hindrance. Substitution at C-4 has no stereochemical consequences, but improves the yields and may shorten the reaction time (Schemes 3 and 4).

Scheme 3



17 **18**

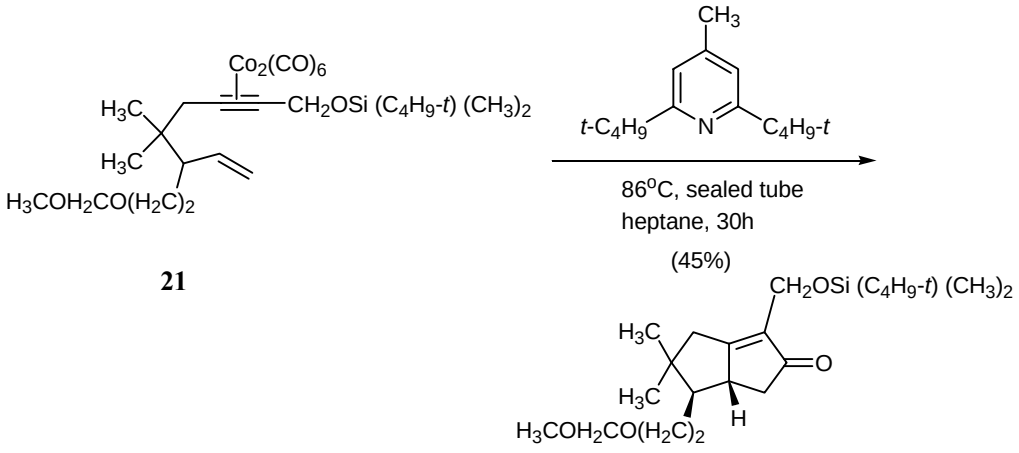
Scheme 4



19 **20**

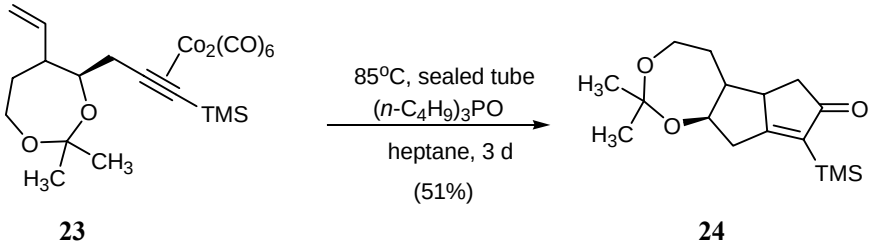
The Pauson-Khand cycloaddition has been successfully used as a key step in many syntheses of natural products, including methylenomycin B, cyclomethylenomycin A, cyclosarkomycin, and Japanese hop ether.[46] The intramolecular Pauson-Khand preparation of bicyclo[3.3.0]oct-1-en-3-ones was first applied to the synthesis of complex natural products by Magnus.[47] He has shown that larger substituents give greater stereoselectivity (Scheme 5).[48] The bicyclo[3.3.0]oct-1-en-3-one shown has been used by Magnus in synthesis of coriolin, hirsutic acid, and quadrone respectively.

Scheme 5



A stereoselective synthesis of optically pure carbocycline analogs has achieved by the intramolecular cycloaddition of enynes derived from D-(+)-ribonolactone (Scheme 6)[49] as well as nonracemic glyceraldehyde derivatives. Bicyclo[3.3.0]oct-1-ene-3-ones have also been used for syntheses of pentalenene and pentalenolactone E methyl ester.[50]

Scheme 6



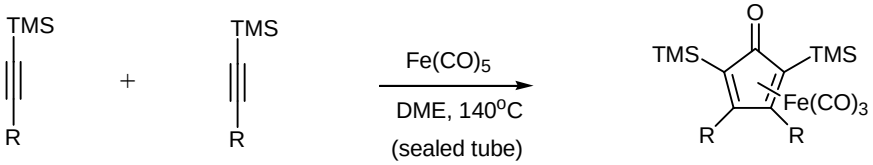
Moreover, Brummond has demonstrated that allenes can be used in place of olefins in the P-K reaction.[51]

Although discovered very early[52] the iron-mediated [2+2+1] cycloaddition has found only few and limited applications and has not been exploited for organic synthesis. The studies of the Knölker group towards the application of tricarbonyliron-diene complexes to organic synthesis, investigated the synthetic utility of [2+2+1] cycloaddition

reactions.[53] The development of this chemistry based on iron, instead of cobalt and other metals, has profound financial benefits.

The reaction of two equivalents of trimethylsilylacetylene with pentacarbonyliron at 140°C, in a sealed tube, exclusively provides the 2,5-bistrimethylsilyl-substituted tricarbonyl(η^4-cyclopentadienone) iron-complex **26** as a single regioisomer in 69% yield (Scheme 7, Table 1).

Scheme 7



25 **26**

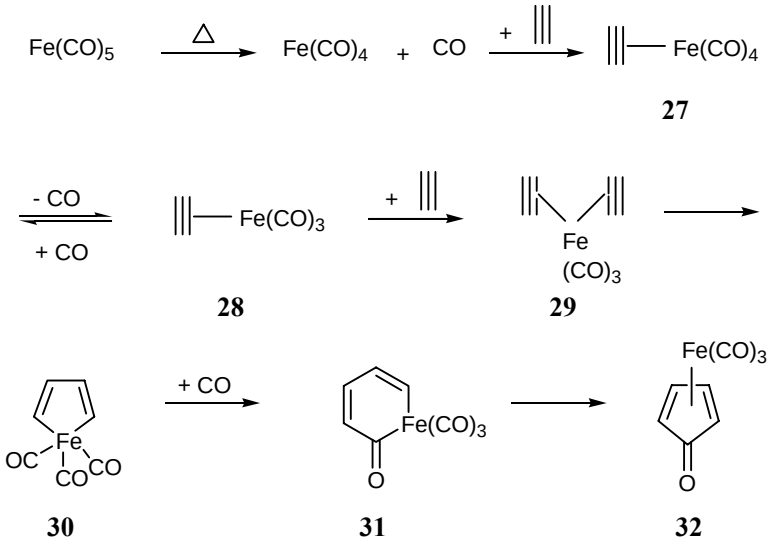
Generality of this transformation was further demonstrated by the cycloaddition of methoxytrimethylsilylacetylene and methyl trimethylsilylpropyonate on reaction with pentacarbonyliron to the corresponding tricarbonyliron-complexed cyclopentadienones (entries 2 and 3).

Table 1

Entry	R	Yield [%]
1	H	69
2	OMe	42
3	COOMe	28

Weissberger[54] has proposed the mechanism by which pentacarbonyliron(0) photolytically or thermally couples olefins to carbon monoxide (Scheme 8).

Scheme 8



The iron mediated [2+2+1] cycloaddition is assumed to be initiated by sequential replacement of two CO ligands by two alkynes which generates the tricarbonyl[bis-(η^2-alkyne)]iron complex **29**. Oxidative coupling of the two alkyne units at the transition metal center provides the intermediate ferracyclopentadiene **30**. Insertion of CO into the metal-carbon bond of **30** and reductive elimination of the ferracyclohexadienone **31** afford the tricarbonyliron-complexed cyclopentadienone **32**.

The reaction of the bistrimethylsilyl-substituted terminal diyne **33** with pentacarbonyliron under standard conditions offers easy access to the bicyclic tricarbonyliron complex **34** in high yield (Scheme 9). By variation of the linkage, a broad range of carbo- and heterobicyclic ring systems are available using this method (Table 2).[55]

Scheme 9

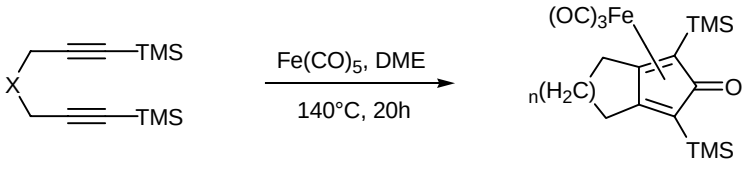
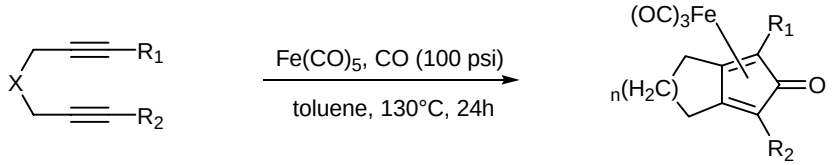


Table 2

Entry	X	Yield [%]
1	CH_2	78
2	$(CH_2)_2$	82
3	$(CH_2)_3$	15
4	$(CH_3OOC)_2C$	84
5	O	85
6	S	76
7	$C_6H_5CH_2N$	86

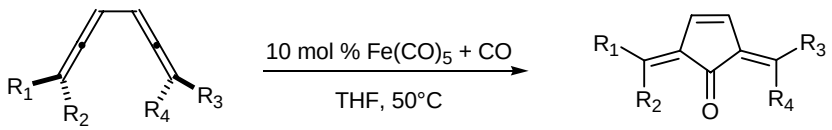
Pearson[56] has also reported a high-yielding procedure for the intramolecular carbonylative coupling of α,ω-diynes to give tricarbonyl(cyclopentadienone)iron complexes (Scheme 10).

Scheme 10



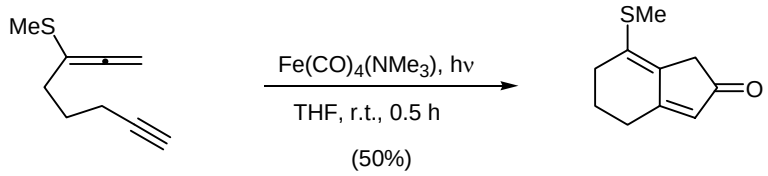
Eaton[57,58] has discovered the catalytic iron-mediated [4+1] cycloaddition of diallenes with carbon monoxide to give 2,5-dialkylidenecyclopentenones (Scheme 11). In addition, this catalytic iron-mediated [4+1] cycloaddition reaction did not require the extremes of thermal and/or photochemical activation that usually accompanies the use of $Fe(CO)_5$.

Scheme 11



In another interesting example, Narasaka[59] has reported a intramolecular allene-alkyne coupling reaction in the presence of $Fe(CO)_4(NMe_3)$ under photoirradiation conditions to provide various bicyclic dienones (Scheme 12).

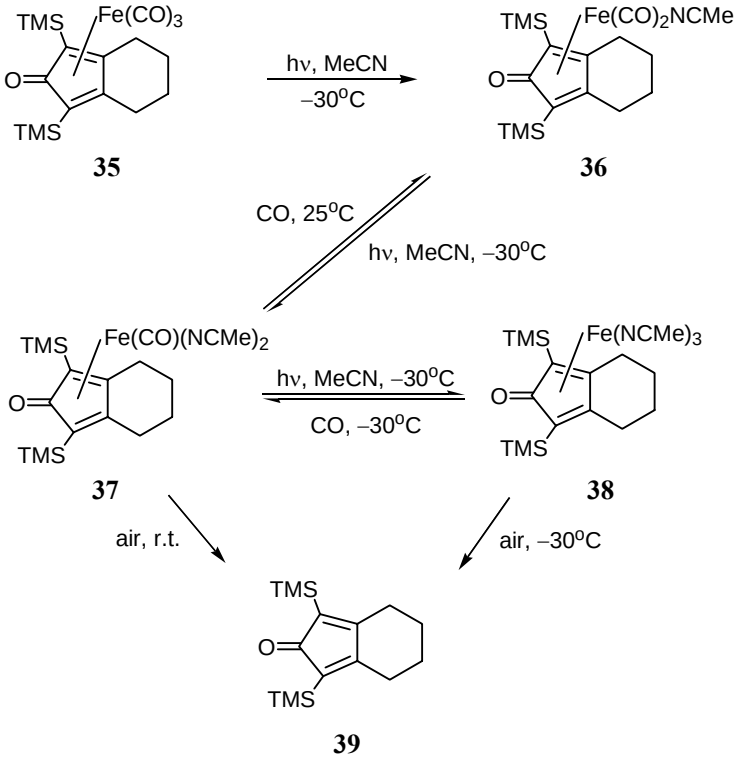
Scheme 12



Demetalation

Tricarbonyl (η^4-1,3-diene)iron complexes are a useful class of organometallic compounds with versatile applications to organic synthesis. The coordination of the conjugated diene to the transition metal fragment leads to a significant alteration of its reactivity. Therefore, the tricarbonyliron fragment has been used for the stabilization of labile hydrocarbons and as a protecting group for dienes. After the desired transformations at the ligand of the tricarbonyl(η^4-1,3-diene)iron complex a demetalation is required to provide the free diene. This decomplexation of tricarbonyliron complexes is usually achieved under strong oxidizing reaction conditions, for example with ferric chloride,[60] ceric ammonium nitrate,[61] trimethylamine *N*-oxide (TMANO),[62] cupric chloride,[63] or hydrogen peroxide / sodium hydroxide. Another possibility is to liberate the ligand by an exchange reaction, in general with a phosphine.[64] Recently, Knölker described a mild and a very efficient procedure for the demetalation of tricarbonyliron-diene complexes using a photolytically induced exchange of the carbonyl ligands by acetonitrile at low temperature and subsequent demetalation on bubbling air through the solution (Scheme 13).[65]

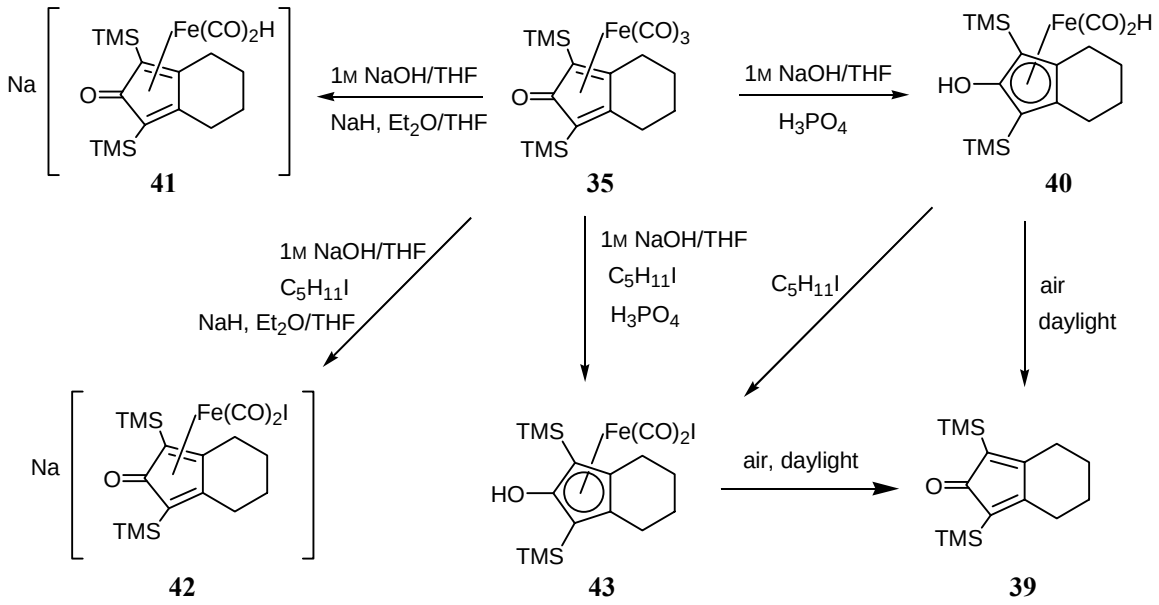
Scheme 13



This procedure involves the photolysis of **35** in acetonitrile at –30°C affording **37** in 76% yield, which on injection of argon into the solution during photolysis provides the triacetonitrile complex **38** (Scheme 13). The addition of the third acetonitrile ligand is reversible even at –30°C. Therefore, the complexes **37** or **38** can be prepared selectively. On injection of air into the solution of **38** in acetonitrile at –30°C the free ligand **39** is obtained in excellent yield and stirring the solution of complex **37** in the air at room temperature also led the formation of the free ligand **39** quantitatively.

Another novel procedure developeded in our group for the demetalation of tricarbonyl(η^4-cyclopentadienone)iron complexes involves ligand exchange initiated by sodium hydroxide.[66]

Scheme 14



Reaction of complex **35** with aqueous NaOH in THF leads to an equilibrium of the corresponding hydrido complexes **40** and **41** in a ratio of about 13:1 (Scheme 14). Addition of H_3PO_4 affords **40** in 94% yield, while reaction with NaH shifts the equilibrium towards the salt **41**. Reaction of the hydrido complex **40** with 1-iodopentane provides the iodo complex **43**. The addition of 1-iodopentane after the reaction of **35** with NaOH affords an equilibrium of the iodo complexes **43** and **42** that can be shifted again by addition of H_3PO_4 or NaH respectively.

Stirring a solution of **40** in diethyl ether for 5 h in the air leads to demetalation and provides the free ligand **39** in 80% yield based on **35**. However, stirring a solution of **43** in the air with exposure to daylight leads to a highly selective demetalation within 3 h and provides the free cyclopentadienone **39** in 95% yield based on complex **35**.

2 Objectives

The first project involves the application of the iron-mediated [2+2+1] cycloaddition for the total synthesis of racemic alloyohimbane and 3-epialloyohimbane. This cycloaddition appears to be useful for the construction of pentacyclic ring systems as found in yohimbane alkaloids. Following the successful total synthesis of alloyohimbane, the iron-mediated [2+2+1] cycloaddition should be applied to the synthesis of rauniticine. It was of interest to study a similar protocol for the generation of aromatized yohimbane alkaloids. The formation of a pyrrole containing polycyclic ring system during our efforts in preparing aromatized yohimbane alkaloids has opened up a new area of research for investigations. The possibility of preparing a range of substituted pyrroles *via* a silver(I)-promoted oxidative cyclization of homopropargylamines was also explored. Based on these results, the next project involves the total synthesis of harmicine. Following the development of this novel methodology, the total synthesis of crispine A and the synthesis of 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*] isoquinoline were studied, in order to demonstrate the applicability of the silver(I)-promoted oxidative cyclization for the synthesis of pyrroles in the total synthesis of biologically active polycyclic compounds.

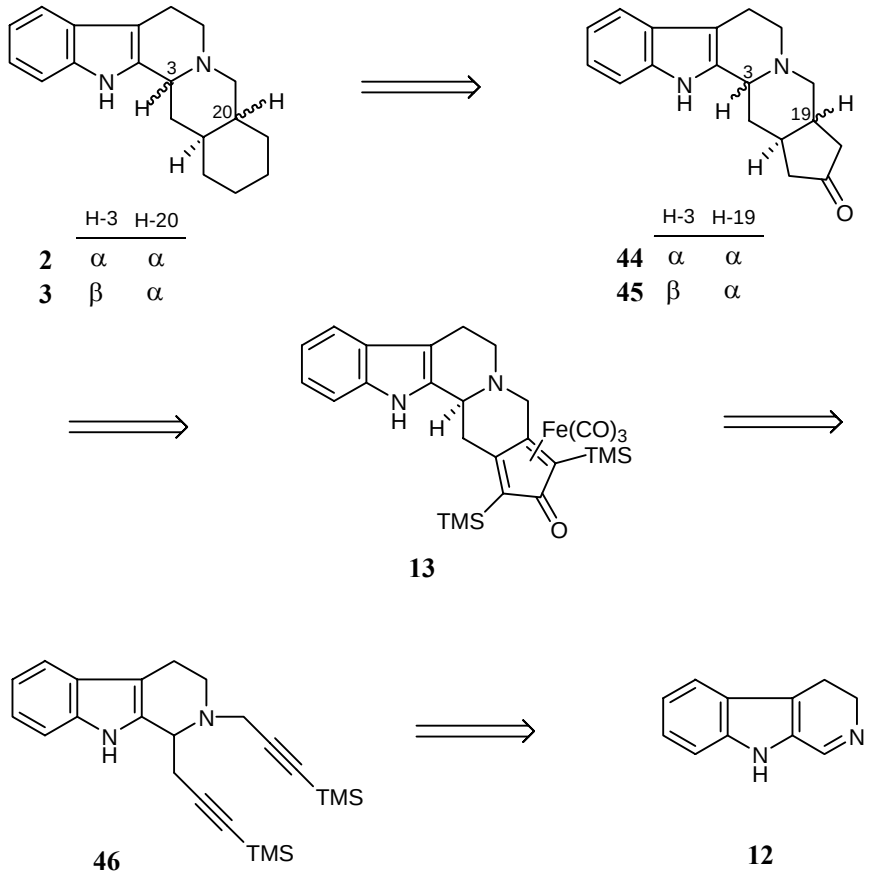
3 Results and Discussions

3.1 Total synthesis of Alloyohimbane and 3-Epialloyohimbane

3.1.1 Retrosynthetic analysis of Alloyohimbane (2) and 3-Epialloyohimbane (3)

The retrosynthetic analysis of alloyohimbane (**2**) and 3-epialloyohimbane (**3**) is based on the iron-mediated [2+2+1] cycloaddition as the key step for the construction of the pentacyclic ring system having an indolo[2,3-*a*]quinolizidine skeleton as found in yohimbane alkaloids (Scheme 15). This strategy has already been applied to the total synthesis of an aromatized yohimbane alkaloid.[29]

Scheme 15



The key intermediate iron-complex **13** can be prepared in high yields by complexation of the bis-TMS-diyne **46** which in turn is conveniently obtained by the *C*-alkylation of 3,4-dihydro-β-carboline (**12**) followed by *N*-alkylation.

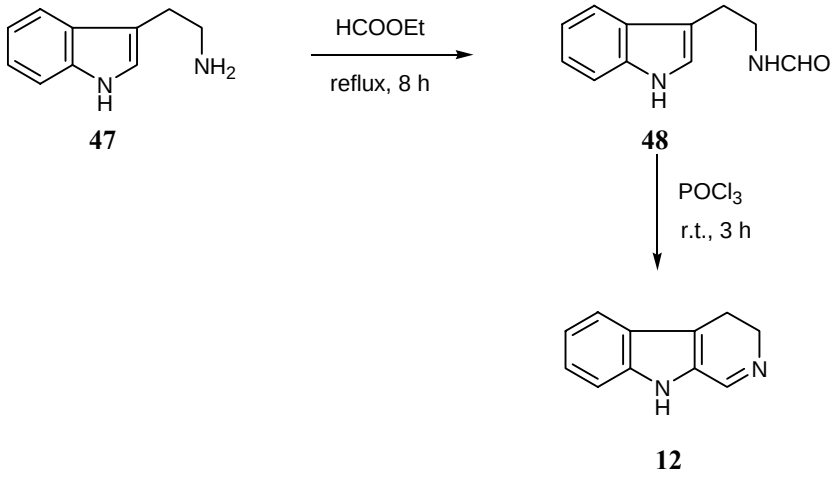
Demetalation of the iron-complex **13** followed by hydrogenation should give the completely saturated cyclopentanone (**44** or **45**) having the stereochemistry *cis* and/or *trans* with respect to C3 as found in alloyohimbane and 3-epialloyohimbane. The relative stereochemistry drawn is assumed and primarily based on the fact that the *cis*-ring junction is lower in energy according to molecular mechanics calculations.[67]

Alloyohimbane (**2**) is accessible by E-ring enlargement of the *cis*-cyclopentanone **44** followed by Wolff-Kishner reduction. Accordingly, 3-Epialloyohimbane (**3**) is accessible by E-ring enlargement of the *trans*-cyclopentanone **45** followed by Wolff-Kishner reduction.

3.1.2 Synthesis of the noryohimbane derivative (53)

The required starting material, 3,4-dihydro-β-carboline (**12**), was easily synthesized from commercially available tryptamine.[68] Tryptamine **47** was first converted to *N*-formyl-tryptamine **48** by refluxing with an excess of ethyl formate. *N*-Formyl-tryptamine **48** was then cyclised under Bischler-Napieralski reaction conditions by reacting with $POCl_3$ (Scheme 16). Thus, 3,4-dihydro-β-carboline (**12**) was available from tryptamine in 94% overall yield in large quantities.

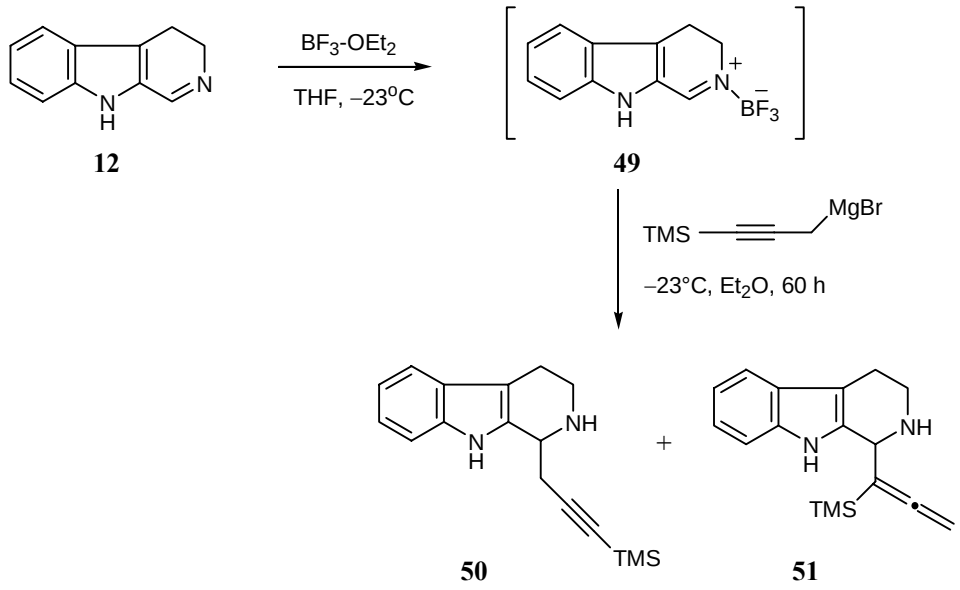
Scheme 16



The alkylation of 3,4-dihydro-β-carboline (**12**) with trimethylsilylpropargylmagnesium bromide was achieved by using the procedure of Nakagawa.[69] Addition of Grignard reagent was carried out in the presence of BF_3-etherate for the activation of the C=N double bond. A solution of 3,4-dihydro-β-carboline (**12**) in dry THF was treated with BF_3-etherate at –23°C to obtain the BF_3-iminium salt **49.** Subsequent addition of trimethylsilylpropargylmagnesium bromide gave 1-(3-trimethylsilylprop-2-ynyl)-2,3,4,9-tetrahydro-1*H*-β-carboline (**50**) in 52% yield along with 1-(1-trimethylsilyl-propa-1,2-dienyl)-2,3,4,9-tetrahydro-1*H*-β-carboline (**51**) in 8% yield (Scheme 17).

The allene **51** was unequivocally identified by its ^{1}H and ^{13}C NMR spectra. In particular the resonance of the central allenic carbon atom at δ = 210.12 ppm is diagnostic. Allenic hydrocarbons and heterocycles are useful precursors for organic synthesis.[70,71]

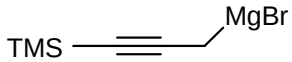
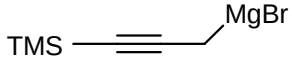
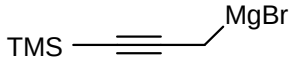
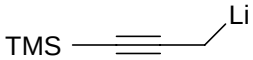
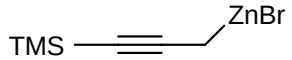
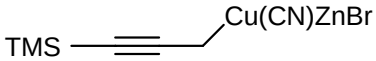
Scheme 17



A number of different organometallic reagents was also tested for this transformation. Thus, the alkylation of 3,4-dihydro-β-carboline (**12**) using organolithium, organocopper and organozinc reagents was investigated and the results are summarized in Table 3.

The use of Grignard reagent at –23°C, gave compound **50** in 52% yield along with allene **51** in 8% yield (entry 1). By lowering or increasing the reaction temperature, no significant change in terms of yield was observed using the same reagent (entries 2 and 3). A similar reaction with the corresponding lithium reagent provided **50** in 42% yield along with **51** in 8% yield (entry 4). We also tested zinc[72] and copper-zinc[73] reagents. However, the use of organozinc reagent afforded **50** in a moderate yield of 14% (entry 5), while the organocopperzinc reagent led to only 8% yield of **50** (entry 6). The formation of 1-(1-trimethylsilylpropa-1,2-dienyl)-2,3,4,9-tetrahydro-1H-β-carboline (**51**) was not observed in either case. Hence, after using various organometallic reagents, it was found that the Grignard reagent was best in terms of yield and experimental convenience.

Table 3

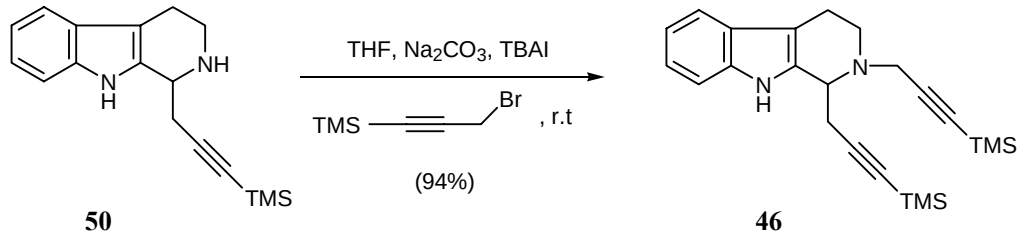
Entry	Reagent	Temp	Yield [%]	
			50	**51**
1		–23°C	52	8
2		–30°C	48	4
3		–10 °C	43	6
4		–23°C	42	8
5		–23°C	14	-
6		–23°C	8	-

Notably, this transformation was very efficient on large scale and thus demonstrating its viability in total synthesis.

The next step in the synthesis involved *N*-alkylation of the compound **50** to afford the bis-TMS-diyne **46**. This transformation has been previously achieved in our laboratory[74] in 99% yield using 3-(trimethylsilyl)propargyl iodide, as alkylating agent, which in turn was synthesized from 3-(trimethylsilyl)propargyl bromide in 80% yield.

We were gratified to discover that this transformation using commercially available 3-(trimethylsilyl)propargyl bromide as alkylating agent in presence of catalytic amounts of tetrabutylammonium iodide under *in situ* Finkelstein reaction conditions afforded 1,2-bis(3-trimethylsilylprop-2-ynyl)-2,3,4,9-tetrahydro-1*H*-β-carboline (**46**) in 94% yield (Scheme 18). Thus, the modified procedure afforded compound **46** in one step with improved overall yields.

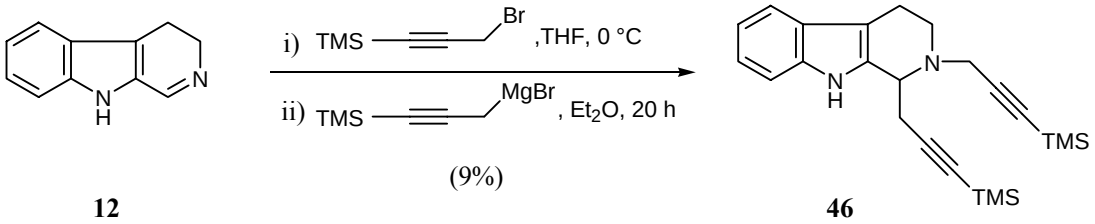
Scheme 18



50 **46**

In another reaction, an attempt was made to synthesize 1,2-bis(3-trimethylsilylprop-2-ynyl)-2,3,4,9-tetrahydro-1*H*-β-carboline (**46**) directly from 3,4-dihydro-β-carboline (**12**) in one step (Scheme 19).

Scheme 19



12 **46**

Thus, a solution of 3,4-dihydro-β-carboline (**12**) in dry THF was treated with trimethylsilylpropargyl bromide, followed by the addition of trimethylsilylpropargylmagnesium bromide. This resulted in formation of the bis-TMS-diyne **46** in moderate yield of 9% along with uncharacterized products.

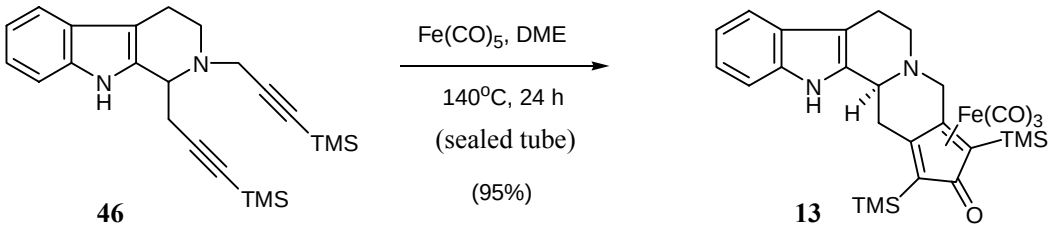
Low yields of the bis-TMS-diyne **46** were observed indicating that both the *C*- and *N*-alkylation could occur in the same reaction pot. Nevertheless, the yield of this double alkylation (9%) was too low for any practical application of this method.

The key-step in our synthetic route is the iron-mediated [2+2+1] cycloaddition of the diyne for the construction of the pentacyclic ring system. The iron-mediated [2+2+1] cycloaddition of trimethylsilylacetylenes and pentacarbonyliron for the synthesis of

cyclopentadienones has already been demonstrated in our laboratory as a novel methodology for organic synthesis.[53,55]

Using optimized reaction conditions, the bis-TMS-diyne **46** was successfully converted to the iron complex **13** (Scheme 20). Thus, heating of diyne **46** with two equivalents of pentacarbonyliron in dry dimethoxyethane at 140°C for 24 h in a sealed tube afforded almost quantitatively the tricarbonyliron-complexed cyclopentadienone **13** as a mixture of two diastereoisomers in a ratio of 2:1, *anti*-**13** as the major and *syn*-**13** as the minor isomer. The major isomer could be separated by recrystallizing in diethyl ether.

Scheme 20



A *trans* conformation of the indolo[2,3-*a*]quinolizidine ring system was confirmed by the presence of Bohlmann bands[75] in the IR spectrum at ν = 2849 cm^{-1} and 2799 cm^{-1}.

The expected structure and stereochemical outcome (preferential approach of the tricarbonyliron group from the less hindered face) was additionally confirmed by an X-ray crystal structure analysis of *syn*-**13** (Figure 3).

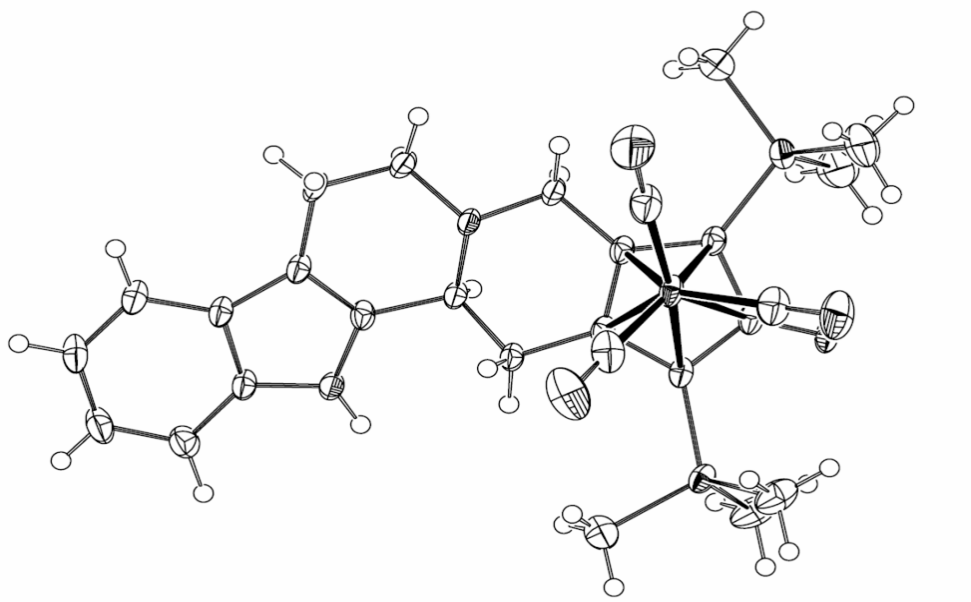
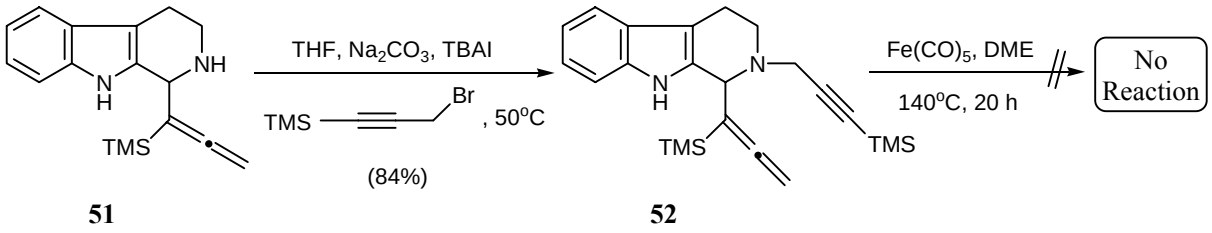


Figure 3 : ORTEP plot of the molecular structure of compound *syn*-**13** in the crystal.

This successful result encouraged us to explore the iron-mediated [2+2+1] cycloaddition of the yne-allene. Therefore, we synthesized the yne-allene **52** in 84% yield from allene **51**, employing standard *N*-alkylation conditions (Scheme 21). Allene **51** was obtained as a by-product during addition of the Grignard reagent to the 3,4-dihydro-β-carboline. Unfortunately, exposure of **52** and pentacarbonyliron to the reaction conditions for [2+2+1] cycloaddition resulted in complete decomposition.

Scheme 21

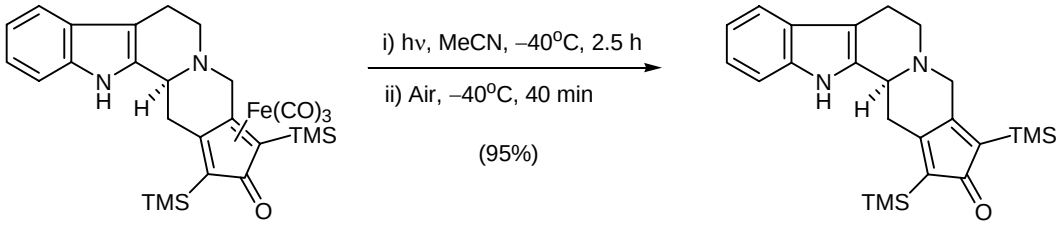


51 **52**

For the application of the iron-mediated [2+2+1] cycloaddition to organic synthesis it is crucial to achieve a selective demetalation of the tricarbonyliron complexes to the corresponding stable cyclopentadienones. A novel procedure recently developed in our

laboratory for the demetalation of tricarbonyl(η^4-cyclopentadienone)iron complexes involves photolytically induced successive exchange of CO ligands by acetonitrile to give the intermediate triacetonitrile(η^4-cyclopentadienone)iron complex and subsequent demetalation in air.[65] Application of this method to the demetalation of the iron complex **13** afforded the free ligand **53** in 95% yield (Scheme 22).

Scheme 22



13 **53**

The transformation was achieved in a typical pyrex glass photo reactor. A three neck 120 mL Pyrex flask equipped with an inner jacket which was cooled continuously by circulating oil with the help of cryostat, was charged with the iron complex and acetonitrile under argon atmosphere. The stirred reaction mixture was irradiated by a 150 W middle pressure Hg lamp at –40°C for 2.5 h with continuous purging of argon. An efficient stirring of the flask contents was essential to avoid deposition of iron complex on the walls of the flask, which would reduce the light intensity. After 2.5 h of irradiation, air was bubbled into the reaction mixture for 40 minutes at –40°C. An increase in time for bubbling air through the reaction mixture from 20 minutes to 40 minutes enhanced the yield to 95% (Table 4).

Table 4

Entry	Air bubbling time	Yield [%]
1	20 min	89
2	40 min	95

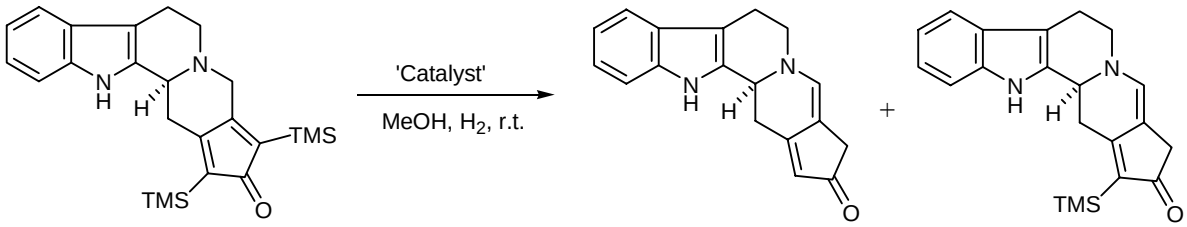
The adaptability of this protocol to a large scale process was also investigated. Complete conversion of the iron complex **13** on a 1.5 g scale was achieved in a pyrex glass photo reactor charged with 750 mL of acetonitrile, by irradiation using a 150 W middle pressure Hg lamp at –40°C for 5 h and afforded the free ligand **53** in 80% yield.

3.1.3 Hydrogenation studies on nor-yohimbane derivatives

In order to assemble a defined stereochemistry as found in target alkaloids, an extensive study of hydrogenation of nor-yohimbane derivatives was carried out in the presence of various catalysts under different reaction conditions.[76]

We initially decided to perform a hydrogenation of the bis-TMS-dienone **53** with ruthenium on carbon as hydrogenation catalyst. In our hands, this catalyst gave very poor results, with the formation of **54** in only 10% yield (Scheme 23, Table 5). Ruthenium on alox was next used as hydrogenation catalyst. The TLC analysis of the reaction mixture showed two spots along with starting material. Careful isolation afforded compounds **54** and **55** in moderate yields of 4% each along with the recovery of starting material (entry 2). While rhodium on alox as hydrogenation catalyst afforded **55** in only 5% yield (entry 3).

Scheme 23



53 **54** **55**

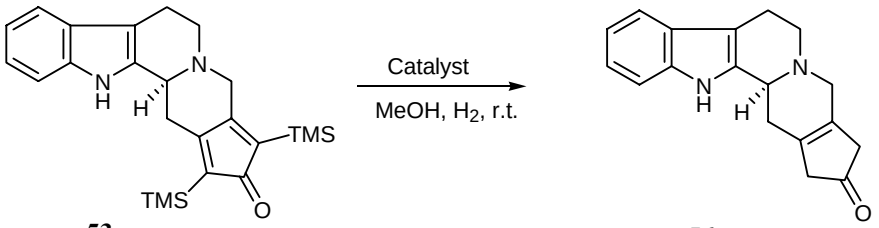
Table 5

Entry	Catalyst	54, Yield [%]	55, Yield [%]	% SM recov.
1	Ru/C	10	-	-
2	Ru/Alox	4	4	74
3	Rh/Alox	-	5	55

The ^{1}H NMR spectrum of compound **54** showed singlets at 5.71 ppm and 6.48 ppm due to olefinic protons in the 16-position and 20-position. Compound **55** showed a singlet at 6.20 ppm due to an olefinic proton in the 20-position.

Due to the poor results obtained, we next decided to examine the effect of palladium as hydrogenation catalyst. Thus, the treatment of **53** with a catalytic amount of 5% palladium on $BaSO_4$ in methanol under hydrogen atmosphere resulted in formation of one major compound. It was isolated in a moderate yield of 28% and identified as compound **56** (Scheme 24, Table 6).

Scheme 24



53 **56**

To our surprise hydrogenation led to 1,4-addition of hydrogen and, under the reaction conditions, the resulting deconjugated cyclopentenone was protodesilylated, leading selectively to compound **56**.

Compound **56** was obtained in 68% yield when 10% palladium on carbon was used as catalyst (entry 2). Finally, to our delight, employing 30% palladium on carbon as catalyst provided compound **56** in almost quantitative yield (entry 3). The purity of the material was confirmed by ^{1}H and ^{13}C NMR and this provided evidence of quantitative conversion.

Table 6

Entry	Catalyst	56, Yield [%]
1	5% $Pd/BaSO_4$	28
2	10% Pd/C	68
3	30% Pd/C	98

The X-ray analysis of single crystals of **56** unequivocally established the 1,4-addition of hydrogen leading to a deconjugated cyclopentenone (Figure 4).

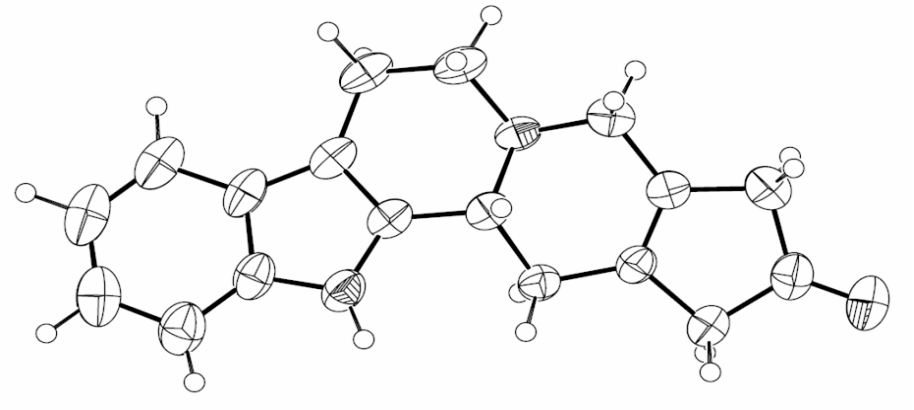
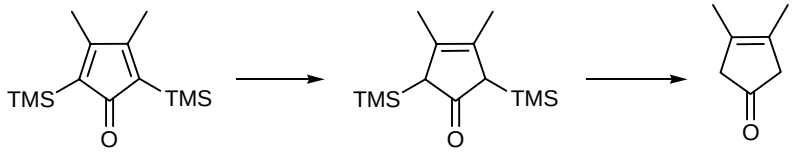


Figure 4 : ORTEP plot of the molecular structure of compound **56** in the crystal.

A plausible reaction mechanism could be that the bis-TMS-cyclopentadienone **57** upon hydrogenation afforded **58** as an intermediate due to addition of hydrogen to the

conjugated diene by 1,4-addition and the resulting allylsilane underwent protodesilylation under the reaction conditions to afford **59** (Scheme 25). Ian Fleming[77] has demonstrated that allylsilanes are prone to protodesilylation.

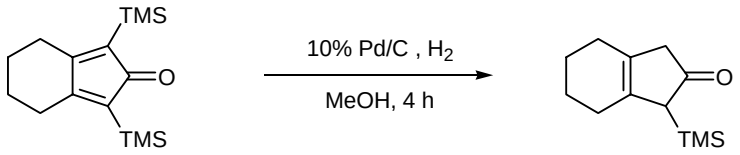
Scheme 25



57 **58** **59**

There is no literature precedence, to our knowledge, for this type of addition of hydrogen to conjugated dienes by 1,4-addition in the presence of a carbonyl functionality and therefore, we wanted to generalize this reaction. We have chosen compound **39** as model compound which was synthesized in our laboratory.[78] The structure of this model compound **39** was confirmed by X-ray crystal structure determination (Appendix).

Scheme 26



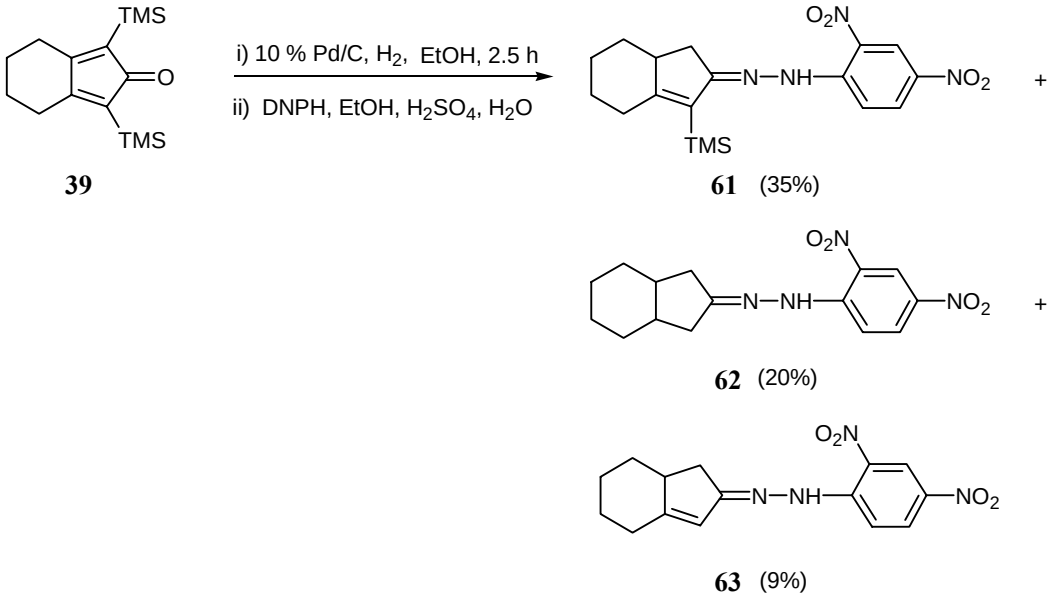
39 **60**

Thus, on subjecting compound **39** to the hydrogenation conditions as described above, a mixture of products was obtained, one of which was found to be compound **60** in 10% yield (Scheme 26). The other products could not be isolated and characterized due to their volatile nature. Since these compounds were expected to be ketones, we tried to isolate them as their corresponding 2,4-dinitrophenylhydrazones.

Therefore, in a further attempt compound **39** was hydrogenated in the presence of palladium on carbon as catalyst under hydrogen atmosphere at room temperature for 2.5

h and the crude product was treated with a solution of 2,4-dinitrophenylhydrazine in conc. sulphuric acid and ethanol. The TLC analysis showed three spots and careful isolation of these products gave compounds **61**, **62**, and **63** in 35%, 20% and 9% yields respectively (Scheme 27).

Scheme 27



39

61 (35%)

62 (20%)

63 (9%)

The structures of all compounds were assigned on the basis of their spectral and analytical data. The structure assignment of compound **61** made earlier based solely on the ^{1}H and ^{13}C NMR spectra, was unequivocally confirmed by X-ray crystal structure determination (Figure 5).

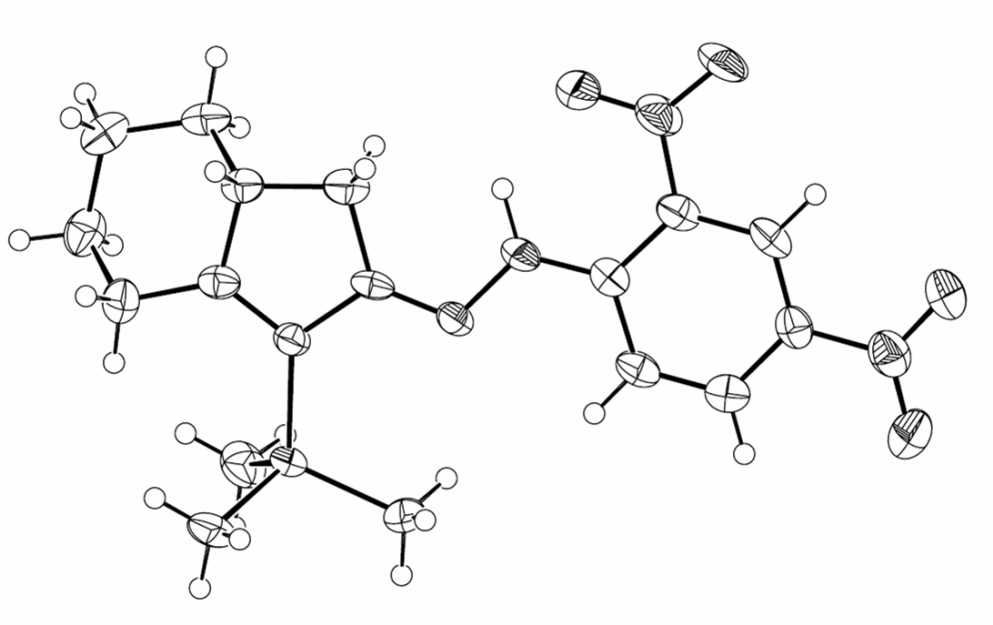


Figure 5 : ORTEP plot of the molecular structure of compound **61** in the crystal.

Although the exact pathway of this transformation is not clear, the plausible scenarios could be suggested on the basis of experimental results. We assume that in this transformation, 1,4-addition of hydrogen takes place during hydrogenation over Pd/C leading to a deconjugated cyclopentenone. Upon acid treatment while formation of 2,4-dinitrophenylhydrazones, the double bond between the two rings isomerizes to form the conjugated cyclopentenone. It is assumed that in this case the isomerization is faster than the protodesilylation and hence led to the formation of the mono-TMS conjugated cyclopentenone **61** as a major product. Protodesilylation led to **63** while hydrogenation afforded **62**.

Hence, it is concluded that during our model studies clean formation of product with 1,4-addition of hydrogen was not observed, as found during the conversion of bis-TMS-dienone **53** to deconjugated cyclopentenone **56**. Further investigations with model compounds were beyond the scope of our studies.

Continuing with our synthesis, in order to generate a fully saturated E-ring, we employed the more reactive Adam's catalyst for hydrogenation of the bis-TMS-dienone **53**, which

gave different products under different reaction conditions (Scheme 28, Table 7). After 3 h of hydrogenation with Adam's catalyst in methanol, the deconjugated cyclopentenone **56** was obtained in 68% yield (entry 1). While, on increasing the reaction time to 6 h, the deconjugated cyclopentenone **56** and the *cis*-cyclopentanone **44** were formed in 37% and 20% yields, respectively, along with a trace amount of the *cis*-carbinol **64** (entry 2). The spectral and analytical data of these compounds are in agreement with the assigned structures.

Scheme 28

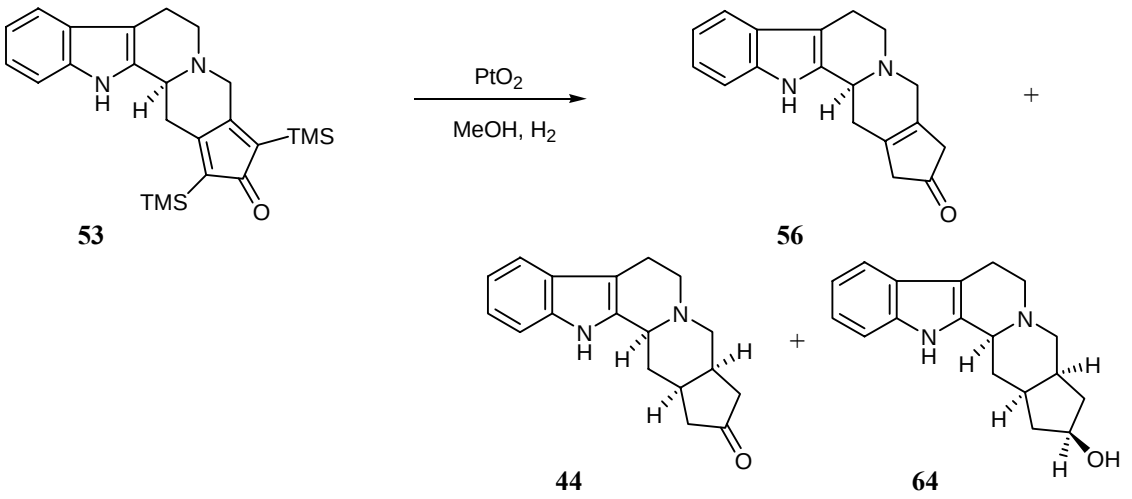


Table 7

Entry	Reaction time	56, Yield [%]	44, Yield [%]	64, Yield [%]
1	3 h	68	-	-
2	6 h	37	20	Trace
3	14 h	-	42	22
4	3 days	-	19	45

Further increase of the hydrogenation time to 14 h gave the *cis*-cyclopentanone **44** in 42% yield and the carbinol **64** in 22% yield (entry 3). Finally, to better understand the stereoselectivity and reaction behaviour, we extended the reaction time to 3 days. This resulted in formation of the *cis*-cyclopentanone **44** and the *cis*-carbinol **64** in 19% and 45% yields, respectively (entry 4). Despite the fact that mixtures of products were obtained, careful chromatography enabled separation of all the products.

The structure assignment and stereochemistry of the *cis*-cyclopentanone **44** is confirmed by an X-ray analysis of a single crystal (Figure 6). The relative stereochemistry of the *cis*-carbinol **64** is assumed as a result of stereoselective hydrogenation.

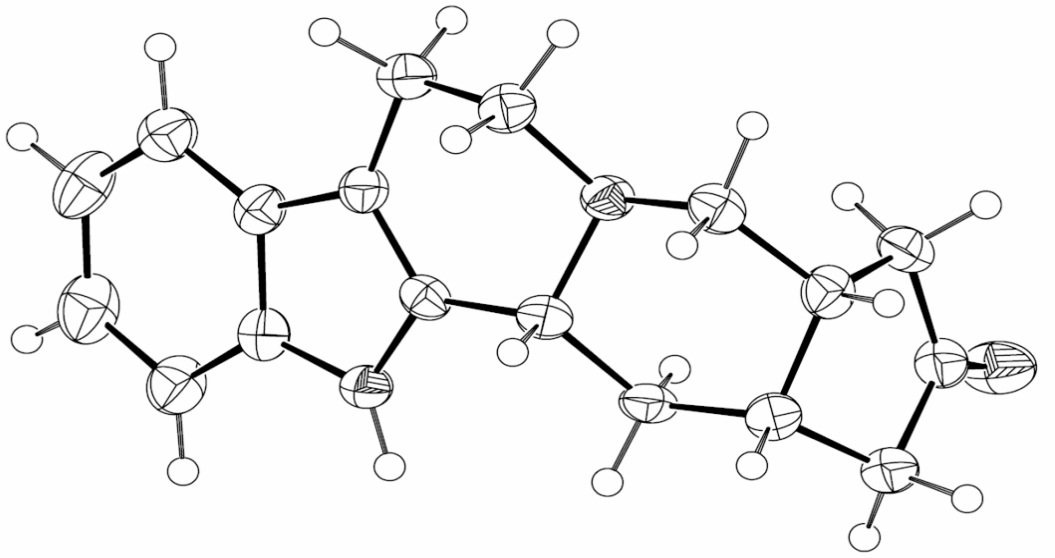
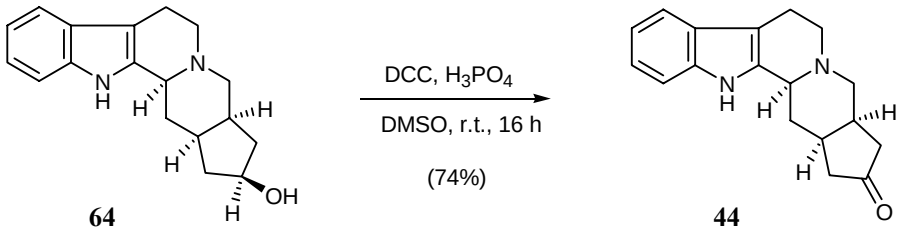


Figure 6 : ORTEP plot of the molecular structure of compound *cis*-**44** in the crystal.

Use of Adam's catalyst resulted in stereoselective hydrogenation, with all hydrogen atoms delivered from the same face, thus giving rise to the observed '*cis*' stereochemistry. The reaction pathway is assumed to proceed *via* the formation of the deconjugated cyclopentenone **56** which is further hydrogenated stereoselectively to give the *cis*-cyclopentanone **44** and the *cis*-carbinol **64**.

It was already noted before that hydrogenation of the bis-TMS-cyclopentadienone **53** with Adam's catalyst proceeded with low chemoselectivity, since formation of the *cis*-cyclopentanone **44** was always accompanied with carbinol **64**. In order to get more material of the required *cis*-cyclopentanone **44**, the carbinol **64** was subjected to oxidation (Scheme 29, Table 8).

Scheme 29



Attempted oxidation of carbinol **64** with TPAP[79] and PCC[80,81] as oxidizing agent under standard reaction conditions led unfortunately to decomposition providing the *cis*-cyclopentanone **44** in low yields, perhaps due to the fact that carbinol **64** is not readily soluble in solvents like CH_2Cl_2 and DMF (entries 1-3).

Table 8

Entry	Reagent	Solvent	44, Yield [%]
1	TPAP	CH_2Cl_2	8
2	PCC	CH_2Cl_2	Trace
3	PCC	DMF	Trace
4	DCC/H_3PO_4	DMSO	74

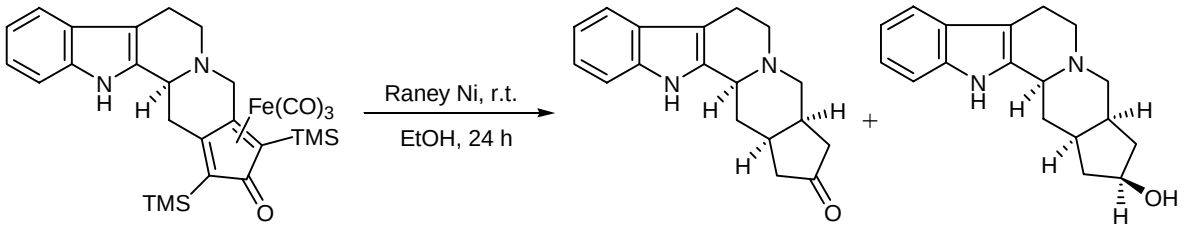
Albright and Goldman[82] have described the Moffatt-Pfitzner[83] oxidation as a mild oxidative condition for the conversion of hydroxyl groups in indole alkaloids to carbonyl derivatives using *N*,*N*'-dicyclohexylcarbodiimide (DCC), crystalline *ortho*-phosphoric

acid, and dimethyl sulfoxide (DMSO). Eventually, it was found that oxidation of carbinol **64** under these conditions gave the *cis*-cyclopentanone **44** in 74% yield (entry 4).

On the basis of this result we propose a *cis*-stereochemical orientation of the carbinol **64**. The oxidation of the *cis*-carbinol **64** back to the *cis*-cyclopentanone **44** had also improved the overall efficiency of our synthetic route.

Raney-nickel has become an enormously valuable reagent for inducing chemical transformations in the research laboratory as well as on commercial scale.[84]
The *cis*-cyclopentanone **44** can also be obtained using a novel method reported by Franck-Neumann,[85] which describes the demetalation of tricarbonyliron-diene complexes by complete hydrogenation with Raney-nickel. Thus, treatment of iron-complex **13** with activated Raney-nickel in ethanol at room temperature afforded the *cis*-cyclopentanone **44** and the *cis*-carbinol **64** in moderate yields of 18% and 5% respectively (Scheme 30). It is assumed that demetalation of the iron-complex takes place upon its treatment with Raney-nickel followed by stereoselective hydrogenation, giving rise to the *cis*-cyclopentanone **44** and the *cis*-carbinol **64**.

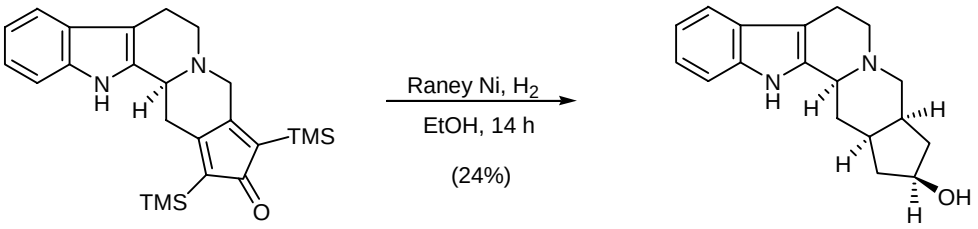
Scheme 30



13 **44** (18%) **64** (5%)

Treatment of the cyclopentadienone **53** with an excess of activated Raney-nickel in ethanol afforded the *cis*-carbinol **64** as the only isolated product in a moderate yield of 24% (Scheme 31). As proven by TLC analysis, a trace amount of *cis*-cyclopentanone **44** was also present in the reaction mixture.

Scheme 31

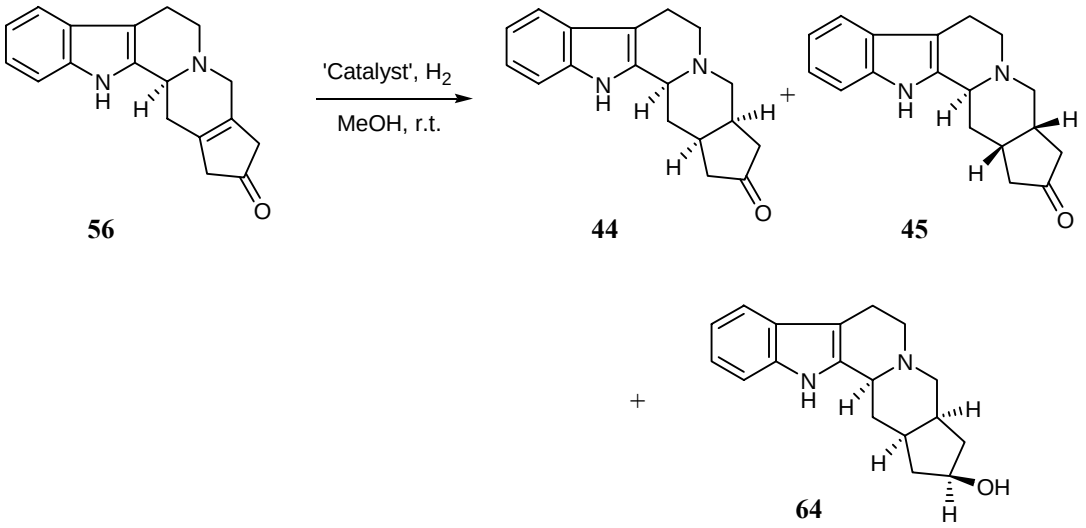


53 **64**

These results led us to the conclusion that, Raney-nickel leads to stereoselective hydrogenation.

Next, we examined the reduction of the double bond of the deconjugated cyclopentenone **56** under various hydrogenation conditions, using different catalysts (Scheme 32, Table 9). It is known that among double bonds the most difficult to hydrogenate are those common to two rings.[86]

Scheme 32



56 **44** **45** **64**

Table 9

Entry	Catalyst	Reaction time	44, Yield [%]	45, Yield [%]	64, Yield [%]	% SM recovered
1	10% Pd/C	7 days	-	-	-	100
2	30% Pd/C	7 days	trace	-	-	98
3	5% Rh/Alox	18 h	-	-	-	100
4	PtO_2	4 h	11	3	trace	39
5	PtO_2	14 h	29	6	38	-

Catalytic hydrogenation of the deconjugated cyclopentenone **56** was attempted using 10% or 30% Pd/C, however, only starting material was recovered (entries 1 and 2). Moreover, no transformation was observed, when 5% Rh/Alox was used as hydrogenation catalyst (entry 3).

In contrast, hydrogenation of deconjugated cyclopentenone **56** with Adam's catalyst yielded different products under different reaction conditions. Thus, hydrogenation of the deconjugated cyclopentenone **56** with PtO_2 for 4 h afforded *cis*-cyclopentanone **44** in 11 % yield, *trans*-cyclopentanone **45** in 3% yield and *cis*-carbinol **64** in trace amount along with recovery of 39% of starting material (entry 4). It is assumed that, probably under the reaction conditions, isomerization of the double bond might have occurred, whose hydrogenation resulted in the *trans*-cyclopentanone **45**. After 14 h of hydrogenation with PtO_2 complete consumption of starting material was observed on analysis by TLC. However, careful isolation of three close products revealed the formation of *cis*-cyclopentanone **44** in 29% yield, *trans*-cyclopentanone **45** in 6% yield and *cis*-carbinol **64** in 38% yield (entry 5).

3.1.4 Synthesis of Alloyohimbane (2)

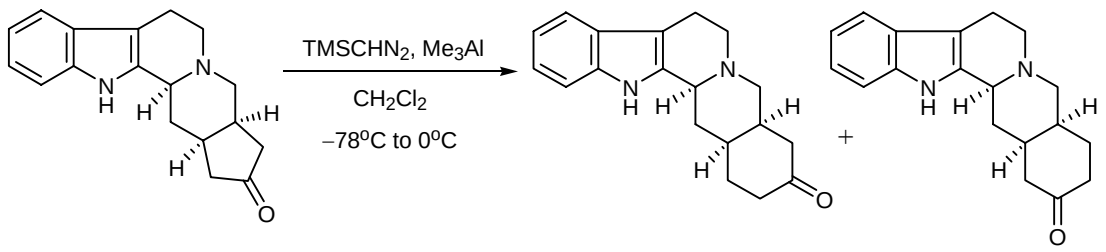
Having considerable amounts of the *cis*-cyclopentanone **44**, the ring expansion of ring E constitutes the final task in our synthesis. The most effective approach is obviously the direct insertion of a methylene unit from diazomethane to carbonyl substrates.[87] However, this reaction has severe experimental limitations. The most serious of which include low reactivity, multiple homologations, and oxirane formation, depending on the nature of the alkyl substituents of carbonyl substrates, apart from the fact that diazomethane is a highly toxic and explosive gas and should be manipulated with great care. The diazomethane ring expansion is generally unsatisfactory with cyclopentanones because the initially formed cyclohexanone is more reactive than the starting material and reacts preferentially with diazomethane. Thus, cyclopentanones and diazomethane mixed in equimolar amounts yield a mixture containing cyclopentanones, cycloheptanones, and very little cyclohexanone.[88]

However, the problem of multiple ring expansion can be minimized if substituted diazomethanes are used in place of diazomethane itself. Shioiri[89,90] and coworkers reported the use of trimethylsilyldiazomethane as a stable and safe diazomethane substitute, for the homologation of ketones. They have found that trimethylsilyldiazomethane easily reacts with various ketones in the presence of boron trifluoride etherate in methylene chloride solution, to give homologated ketones in moderate to good yields.

In 1994 Yamamoto *et al*.[91] demonstrated a new technique for single ring expansion of carbonyl compounds promoted by organoaluminium reagents. He reported that certain bulky, oxygenophilic organoaluminium reagents are useful for single homologation or ring expansion of carbonyl substrates with diazoalkane because of their carbonyl activation ability without affecting the interaction of diazoalkane. He found that the trimethylaluminium-promoted single expansion of cyclopentanone can be affected with trimethylsilyldiazomethane, where the homologated cyclohexanone was successfully trapped as its trimethylsilyl enol ether.

We investigated the scope of the above-mentioned trimethylaluminium-promoted ring expansion of carbonyl compounds using trimethylsilyldiazomethane with the *cis*-cyclopentanone **44**. The expansion of ring E using the reagents and conditions as described by Yamamoto resulted in satisfactory yields (Scheme 33, Table 10). Our attempts to optimize the reaction under various conditions are summarized in Table 10.

Scheme 33



44 **65a** **65b**

Using 1.1 equivalent of trimethylsilyldiazomethane and 1.2 equivalents of trimethylaluminium, the desired regio isomers **65a** and **65b** were formed in a moderate yield of 10% with the recovery of 48% starting material (entry 1). The two regio isomers were formed in a ratio of about 2:1. The data show that the best result was obtained by the use of 8.0 equivalents of trimethylsilyldiazomethane and 1.2 equivalents of trimethylaluminium, which resulted in a combined yield of 31% of the ketones **65a** and **65b** with a recovery of 18% of starting material (entry 6). Apart from the desired product mixture, a small amount of multiple homologated products were also formed. An increase of the reaction time and a slight increase of the amount of trimethylsilyldiazomethane led to no significant difference of the obtained yields (entries 2-4). By using 3.0 equivalents of trimethylsilyldiazomethane and 1.2 equivalents of trimethylaluminium the desired mixture of **65a** and **65b** was isolated in 23% yield with recovery of 28% of starting material (entry 5). Use of 18 equivalents of trimethylsilyldiazomethane afforded **65a** and **65b** in a combined yield of 17% along with multiple ring homologation products. We also investigated the use of BF_3-etherate instead of trimethylaluminium, but this resulted in almost complete decomposition (entry 9).

Table 10

Entry	$TMSCHN_2$	Lewis acid	Temp. (time)	65a + 65b, yield*[%]	% SM recovered
1	1.1 eq	Me_3Al (1.2 eq)	–78°C (1h) to –20°C (1h) to 0°C (1h)	10	48
2	1.1 eq	Me_3Al (1.2 eq)	–78°C (3h) to –20°C (3h) to 0°C (3h)	10	45
3	1.1 eq	Me_3Al (1.2 eq)	–78°C (1h) to –20°C (1.5h) to 0°C (1.5h)	13	36
4	2.0 eq	Me_3Al (1.2 eq)	–78°C (0.5h) to –20°C (2h) to 0°C (1h)	13	23
5	3.0 eq	Me_3Al (1.2 eq)	–78°C (1.5h) to –20°C (1.5h) to 0°C (1.5h)	23	28
6	8.0 eq	Me_3Al (1.2 eq)	–78°C (1h) to –20°C (1.5h) to 0°C (1.5h)	31	18
7	8.0 eq	Me_3Al (2.0 eq)	–78°C (1h) to –20°C (1.5h) to 0°C (1.5h)	28	20
8	18.0 eq	Me_3Al (1.2 eq)	–78°C (1h) to –20°C (1.5h) to 0°C (1.5h)	17	21
9	8.0 eq	$BF_3.Et_2O$ (3.0 eq)	–78°C (1h) to –20°C (1.5h) to 0°C (1.5h)	Trace	-

* Combined yield of **65a** and **65b**

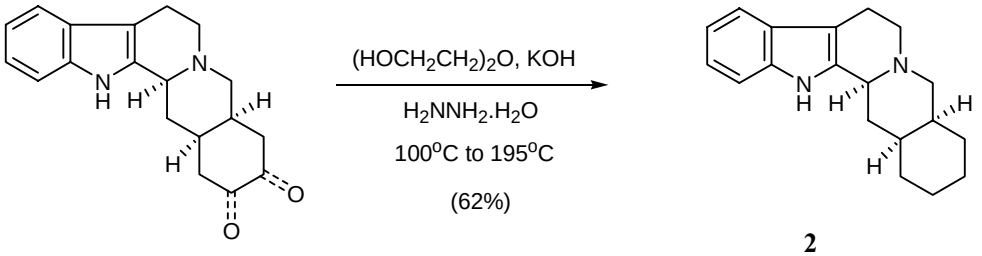
Unfortunately, 18-ketoalloyohimbane **65a** and alloyohimbone **65b** have very similar R_f values, so that a straightforward chromatographic separation was not possible and only a small amount of pure 18-ketoalloyohimbane **65a** could be isolated essentially as a single isomer.

Analysis of HMQC, HMBC, and COSY experiments allowed a full assignment of the proton and carbon resonances for the 18-ketoalloyohimbane **65a**.

Recently, Ogasawara[92] has demonstrated the potential of 18-ketopseudoyohimbane as a precursor for the construction of corynanthe type indole alkaloids, by its transformation to (–)-isocorynantheol, isolated from *Cinchona ledgeriana*.[93] However, further investigations in this direction were beyond the scope of our studies.

The last step of our synthetic route is the reduction of the carbonyl group to a methylene group. Recently, Chandrasekhar *et al.*[94] applied the polymethylhydrosiloxane (PMHS)–tris(pentafluorophenyl)borane combination for direct and rapid conversion of carbonyl groups to methylene groups under very mild conditions. In this reaction tris-(pentafluorophenyl)borane has been used as a non-conventional Lewis acid catalyst to activate PMHS. It was found that both aromatic and aliphatic carbonyl compounds were effectively reduced to give alkanes in good yields. Application of this protocol to our system led to the recovery of 76% of starting material.

Scheme 34



65a + **65b** **2**

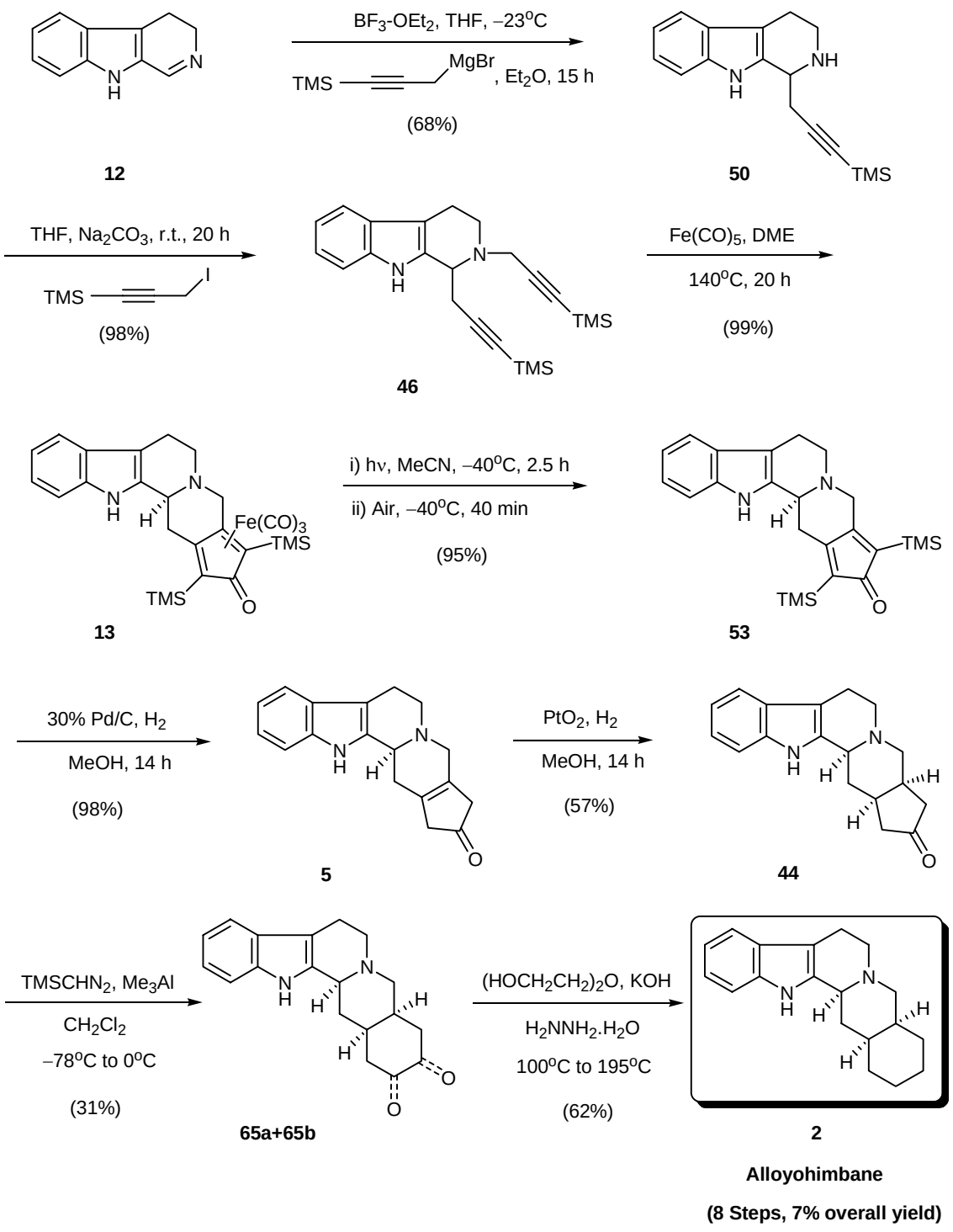
Godleski[95] reported the transformation of alloyohimbone **65b** to alloyohimbane **2** using classical Wolff-Kishner reduction conditions as described by Huang-Minlon.[96] Treatment of the mixture of 18-ketoalloyohimbane **65a** and alloyohimbone **65b** with potassium hydroxide and hydrazine hydrate in diethylene glycol, at 100°C to 195°C gave (±)-alloyohimbane [(±)-**2**] in 62% yield (Scheme 34). The spectral and analytical data of our

product were in complete agreement with those reported in the literature.[97-100] Analysis of HMQC, HMBC, and COSY experiments performed on synthetic [(±)-(**2**)] allowed a full assignment of the proton and carbon resonances.

Thus, the stereoselective synthesis of racemic alloyohimbane (**2**) was accomplished *via* a linear eight-step sequence in 7% overall yield (Scheme 35). It was demonstrated that the iron-mediated [2+2+1] cycloaddition of diynes can be applied to the synthesis of indole alkaloids with pentacyclic frameworks.

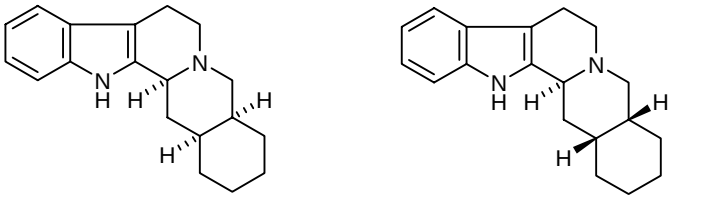
STEREOSELECTIVE TOTAL SYNTHESIS OF (±)-ALLOYOHIMBANE

Scheme 35



3.1.5 Studies towards the total synthesis of (±)-3-Epialloyohimbane

The successful synthesis of alloyohimbane (**2**) by E-ring expansion prompted us to apply this method to the preparation of the alkaloid 3-epialloyohimbane (**3**) (Figure 7).

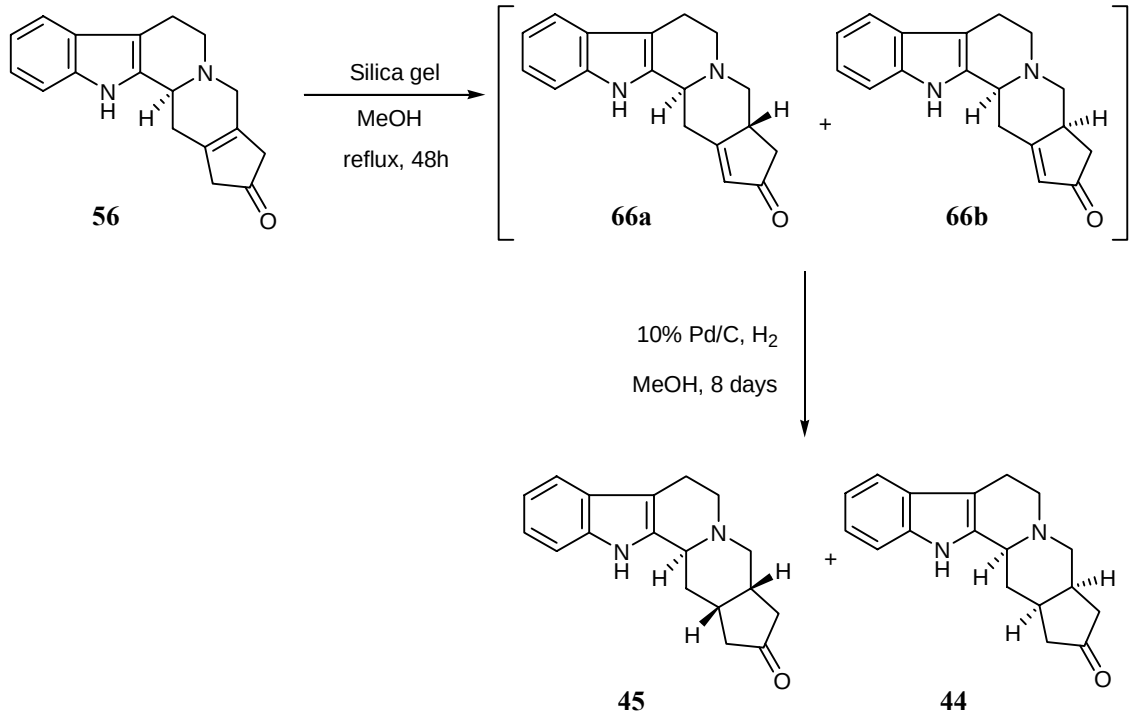


Alloyohimbane (**2**) 3-Epialloyohimbane (**3**)

Figure 7

For this purpose, isomerization of the double bond of **56** was attempted by treatment with rhodium (III) chloride trihydrate in hot ethanol.[101] This led to the formation of a mixture of products. Ninomiya[102] observed the isomerization of a deconjugated enone into the conjugated enone upon treatment with silica gel at the 17-ketoalloyohimbane framework. A similar type of double bond migration was reported by Okamura and Yamada[103] in the presence of pyridine. The double bond migration was found to be effective by heating a mixture of deconjugated cyclopentenone **56** with silica gel in methanol affording a mixture of *trans*-**66a** and *cis*-**66b** in 72% yield (Scheme 36). Its ^{1}H NMR spectrum showed a singlet at 5.83 ppm for the olefinic proton at the 16-position. A separation of the mixture of diastereoisomers was unsuccessful by column chromatography. The ratio of *trans*-**66a** to *cis*-**66b** was found to be 3:4 and was determined by a ^{1}H NMR spectrum of the crude product. A migration of the double bond was also observed at room temperature but the conversion was found to be very slow and after 30 days a mixture of *trans*-**66a** and *cis*-**66b** was formed in 69% isolated yield.

Scheme 36



Since a chromatographic separation of *trans*-**66a** and *cis*-**66b** proved to be very difficult, the crude mixture was hydrogenated to the corresponding mixture of cyclopentanones **45** and **44** (Scheme 36). These products were readily separated by column chromatography. The isolated yields, 35% of **45** and 46% of **44**, were in good agreement with the initial product ratio of *trans*-**66a** and *cis*-**66b**.

Single crystals of *trans*-**66a** were obtained from an ethyl acetate solution of the **66a** and **66b**-mixture. Subsequent X-ray crystallographic studies confirmed the structure and stereochemical assignment (Figure 8).

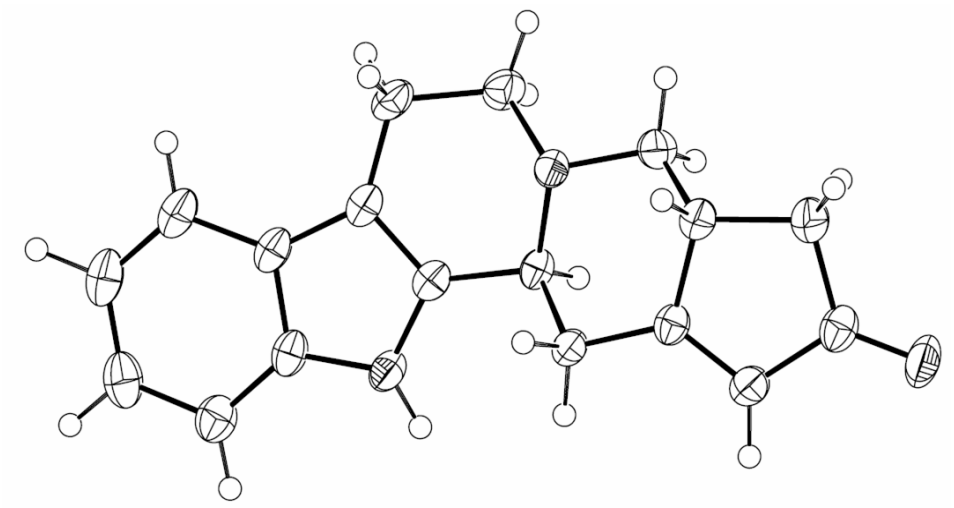
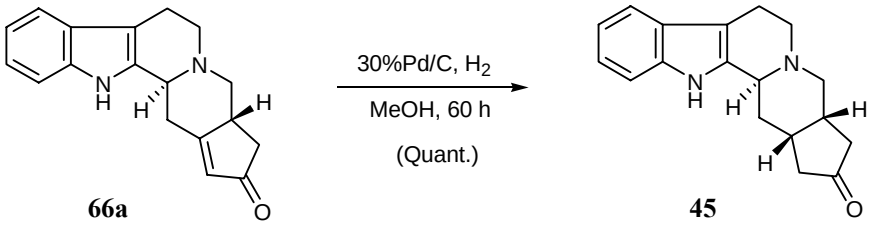


Figure 8 : ORTEP plot of the molecular structure of compound *trans*-**66a** in the crystal.

Catalytic hydrogenation of pure *trans*-**66a** with 30% palladium on charcoal afforded the *trans*-cyclopentanone **45** in quantitative yield (Scheme 37).

Scheme 37



The crystal structure determination of compound **45** allowed us to define unambiguously its relative stereochemistry (Figure 9).

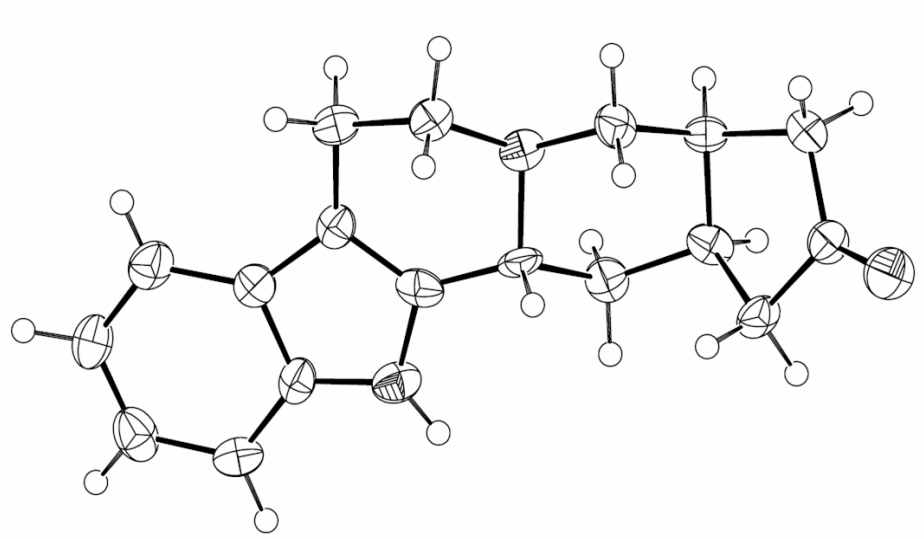
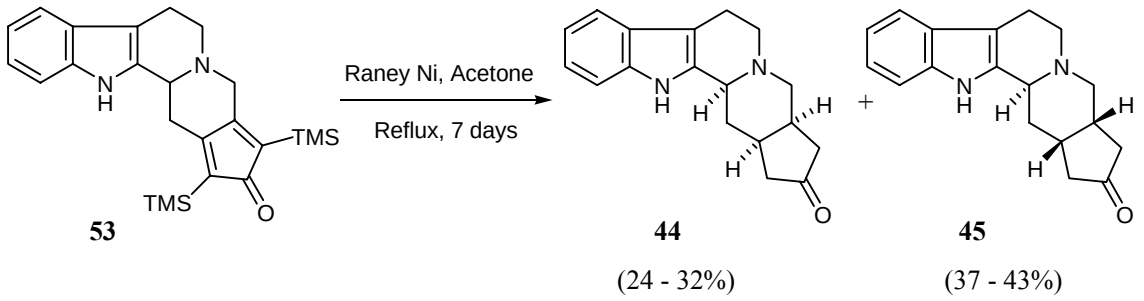


Figure 9 : ORTEP plot of the molecular structure of compound **45** in the crystal.

The structure and stereochemical assignment of *cis*-**66b** was confirmed by its conversion to *cis*-**44**.

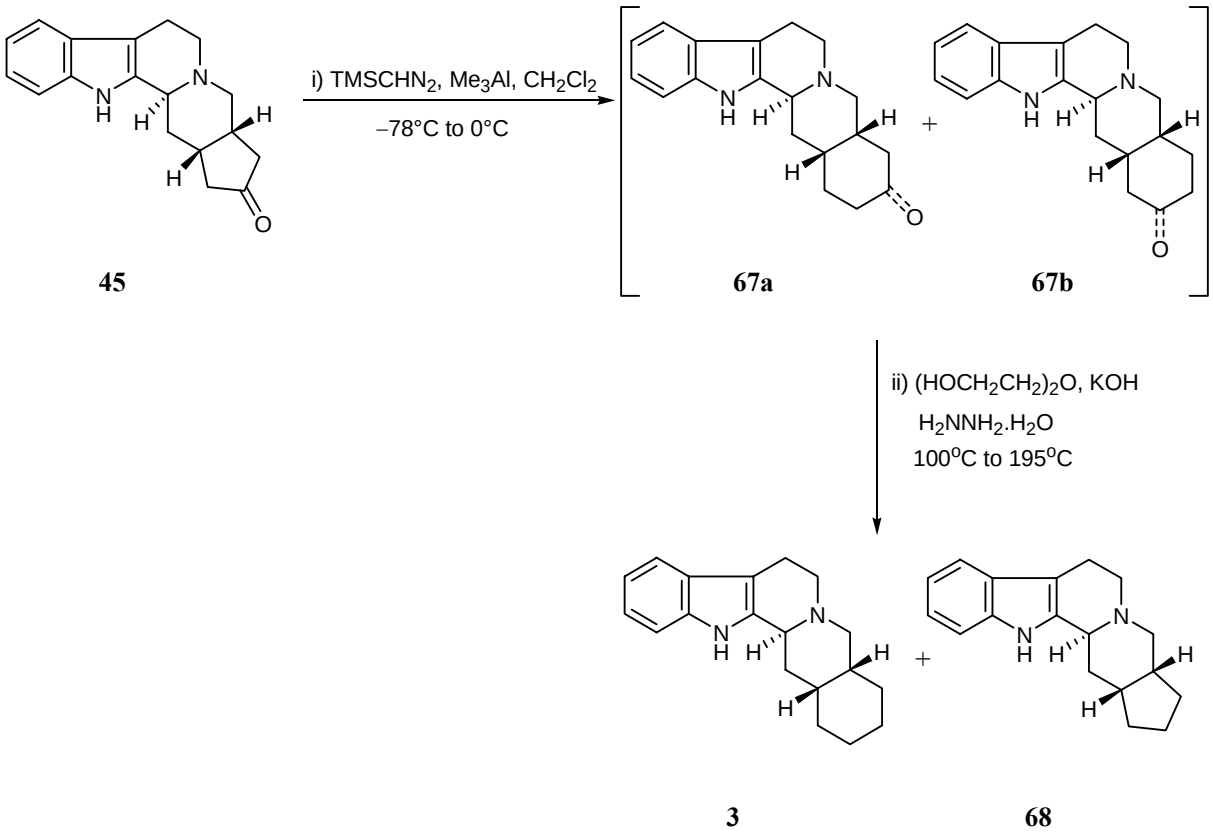
Additionally *trans*-**45** could also be obtained from the bis-TMS-dienone **53**. The treatment of **53** with Raney-nickel in boiling acetone afforded a mixture of diastereoisomers with the *trans*-cyclopentanone **45** as major and the *cis*-cyclopentanone **44** as minor isomer in 37-43% and 24-32% yields, respectively (Scheme 38). It is known that the activity of Raney nickel decreases in acetone. Due to the reduced activity of Raney nickel no carbinol was observed. However, the same reaction in ethanol resulted in formation of carbinol (see scheme 31).

Scheme 38



With compound *trans*-**45** in hand, all that remained to complete the synthesis was an E-ring expansion followed by Wolff-Kishner reduction. The optimized conditions for the E-ring expansion were applied to *trans*-**45** using trimethylsilyldiazomethane (Scheme 39, Table 11).

Scheme 39



45 **67a** **67b** **3** **68**

It was found that the use of 8.0 equivalents of trimethylsilyldiazomethane and 2.0 equivalents of trimethylaluminium, an intermediate mixture of desired two regio isomers **67a** and **67b** was obtained in 36% yield with recovery of 43% of starting material (entry 5). The intermediate reaction mixture was analyzed by GC-MS. No significant difference in terms of yield was observed by little variation in equivalents of trimethylsilyl-diazomethane. We also attempted the reaction using a trimethylsilyldiazomethane

solution in diethyl ether, instead of its solution in hexane, but this resulted only in moderate yield (entry 4). The use of 16 equivalents of trimethylsilyldiazomethane, gave 30% yield with a recovery of 30% of starting material, along with small amounts of cycloheptanone, cyclooctanone and cyclononanone.

Table 11

Entry	$TMSCHN_2$	Me_3Al	Temp. (time)	67a + 67b Yield [%]*	% SM recovered
1	1.5 eq (soln. in hexane)	1.5 eq	–78°C (2h) to –20°C (2h) to 0°C (2h)	16	50
2	8.0 eq (soln. in hexane)	2.0 eq	–78°C (5h) to –20°C (5h) to 0°C (12h)	24	18
3	8.0 eq (soln. in hexane)	2.0 eq	–78°C (2h) to –20°C (2h) to 0°C (2h)	34	38
4	8.0 eq (soln. in Et_2O)	2.0 eq	–78°C (2h) to –20°C (2h) to 0°C (2h)	16	51
5	8.0 eq (soln. in hexane)	2.0 eq	–78°C (2h) to –20°C (3.5h) to 0°C (3.5h)	36	43
6	12.0 eq (soln. in hexane)	2.0 eq	–78°C (2h) to –20°C (3.5h) to 0°C (3.5h)	29	37
7	10.0 eq (soln. in hexane)	2.0 eq	–78°C (2h) to –20°C (3.5h) to 0°C (3.5h)	29	43
8	16.0 eq (soln. in hexane)	2.0 eq	–78°C (5h) to –20°C (5h) to 0°C (12h)	30	30

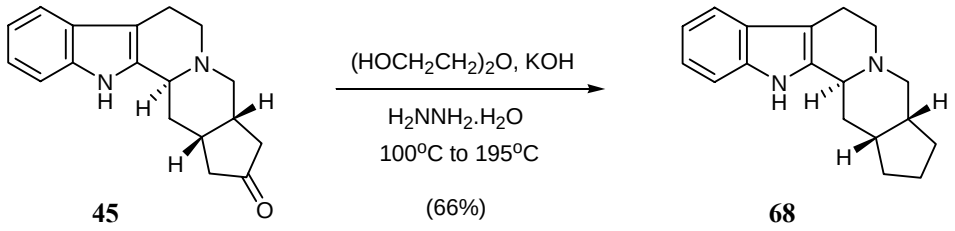
*ratio of yields to SM recovered is calculated as per GC-MS of crude product

All attempts to separate the individual regioisomers and the unreacted starting material were unsuccessful and hence, we decided to subject the crude product to the next transformation since both of these regioisomers should be reduced to afford a single product.

Thus, employing standard Wolff-Kishner conditions, the reaction of crude mixture from above mentioned transformation with potassium hydroxide and hydrazine hydrate in diethylene glycol gave a mixture of 3-epialloyohimbane **3** and nor-3-epialloyohimbane **68** as a chromatographically inseparable mixture (Scheme 39).

Though NMR spectra of the mixture of 3-epialloyohimbane **3** and nor-3-epialloyohimbane **68** contains all the signals for 3-epialloyohimbane **3**, *trans*-**45** was converted to nor-3-epialloyohimbane **68** under standard Wolff-Kishner conditions to assign the signals (Scheme 40).

Scheme 40



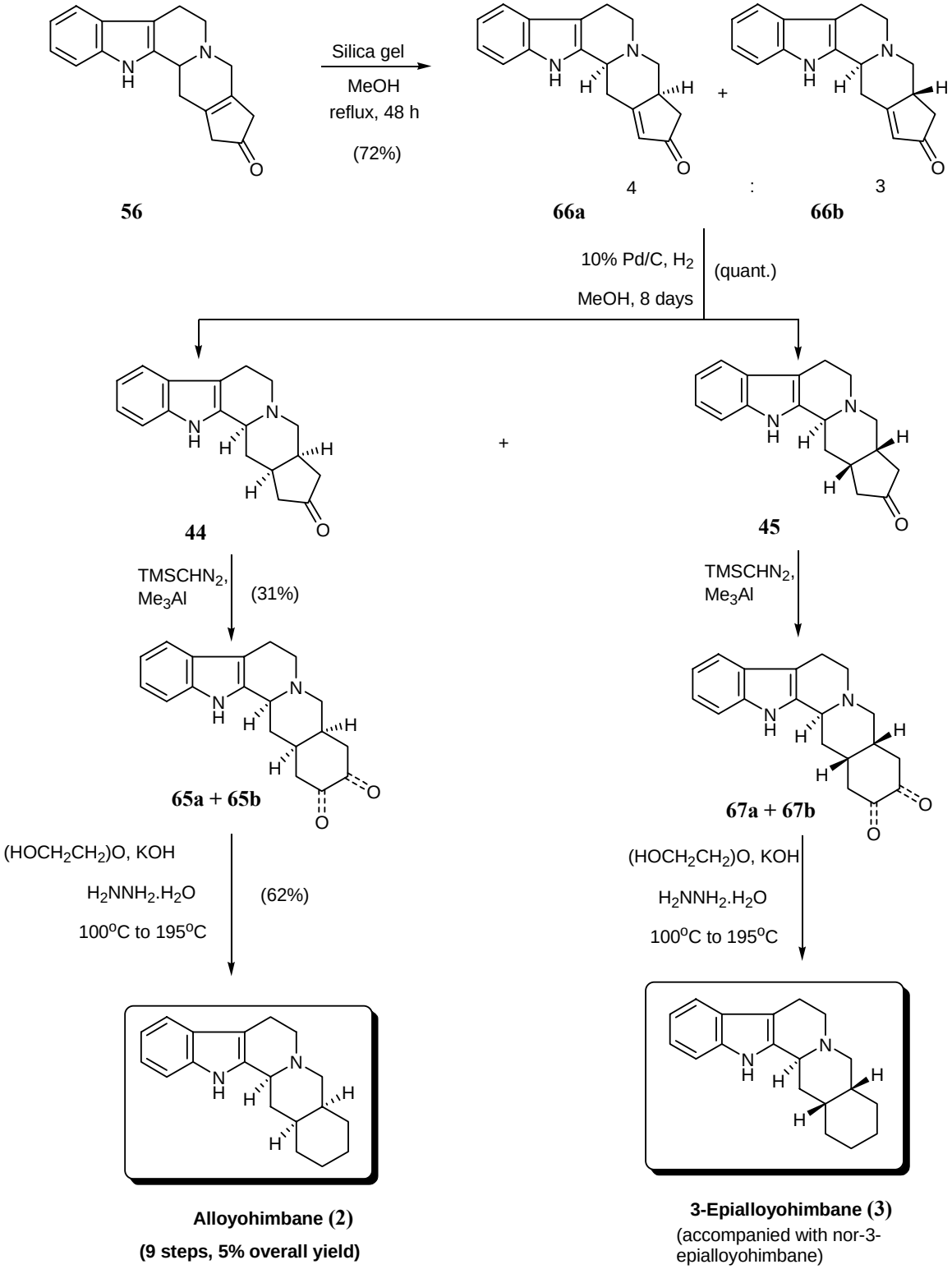
45 **68**

Comparison of the NMR spectra of pure nor-3-epialloyohimbane **68** and of the mixture of 3-epialloyohimbane **3** and nor-3-epialloyohimbane **68** reveals the presence of the signals of 3-epialloyohimbane **3**.[98,100] MS, IR and UVspectra of our synthesized product were in good agreement with those reported.[104]

In conclusion, the utility of the iron-mediated [2+2+1] cycloaddition of diynes for the synthesis of (±)-3-epialloyohimbane has been demonstrated and also an alternative route for the total synthesis of (±)-alloyohimbane has been accomplished in nine-steps with 5% overall yield based on 3,4-dihydro-β-carboline (Scheme 41). The chemistry described demonstrates that the iron-mediated [2+2+1] cycloaddition of diynes can be applied to the total synthesis of complex biologically active natural products.

TOTAL SYNTHESIS OF (±)-ALLOYOHIMBANE (2) AND (±)-3-EPIALLOYOHIMBANE (3)

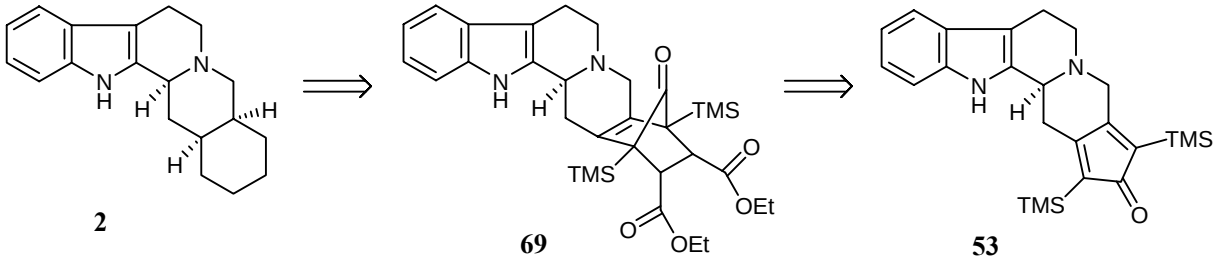
Scheme 41



3.1.6 Attempted alternative approach towards the synthesis of Alloyohimbane

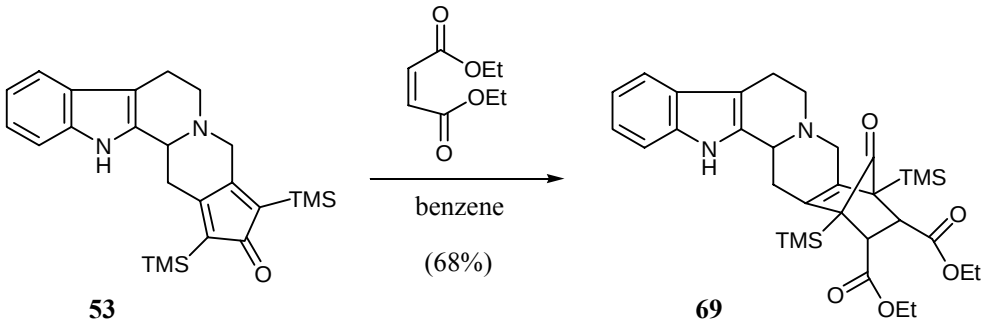
An alternative approach to the synthesis of yohimbane alkaloids is based on the Diels-Alder cycloaddition of the bis-TMS-dienone **53** with appropriate dienophiles, for the construction of the E-ring. We envisioned that the bis-TMS-dienone **53** and dimethyl maleate would readily undergo a Diels-Alder cycloaddition to form the six membered E-ring (Scheme 42). Decarbonylation of the resulting cycloadduct **69** followed by hydrolysis and decarboxylation should provide Alloyohimbane.

Scheme 42



Cyclopentadienones are highly reactive in Diels-Alder cycloadditions. They can function as dienes and dienophiles and dimerize if no bulky substituents are present in the molecule[105]. It has been already demonstrated in our laboratory[106] that annulated 2,5-bis(trimethylsilyl)cyclopentadienones are stable towards dimerization for steric reasons and show no tendency to react as dienophiles. However, they represent useful dienes for Diels-Alder[105] cycloaddition reactions in presence of appropriate dienophiles. Heating equimolar amounts of diethyl maleate and the bis-TMS-dienone **53** in benzene at 80°C resulted in formation of the Diels-Alder product **69** in 68% yield (Scheme 43). This reaction exhibited the typical *endo* selectivity.

Scheme 43



53 **69**

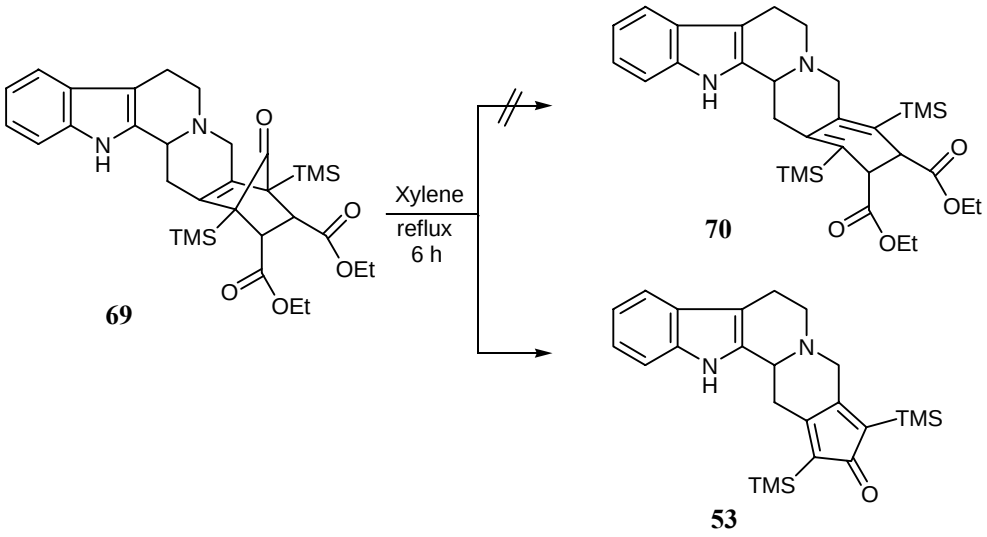
This Diels-Alder reaction has been investigated under different conditions and the results are summarized in Table 12.

Table 12

Entry	Conditions	69, Yield [%]	% SM recovered
1	r.t., benzene, 4 h	-	80
2	reflux, benzene, 14 h	68	-
3	reflux, benzene, 56 h	50	-

In order to achieve the decarbonylation, we heated the Diels-Alder product **69** in xylene at reflux for 6 h (Scheme 44).

Scheme 44



This reaction did not gave any expected decarbonylated product **70.** However, a retro-Diels-Alder reaction gave the bis-TMS-dienone **53** in moderate yield of 18%. This condition proved to be harsh for this transformation and hence, **69** was heated in toluene at reflux for 6 h to afford the bis-TMS-dienone **53** in a trace amount without any formation of the decarbonylated product **70**.

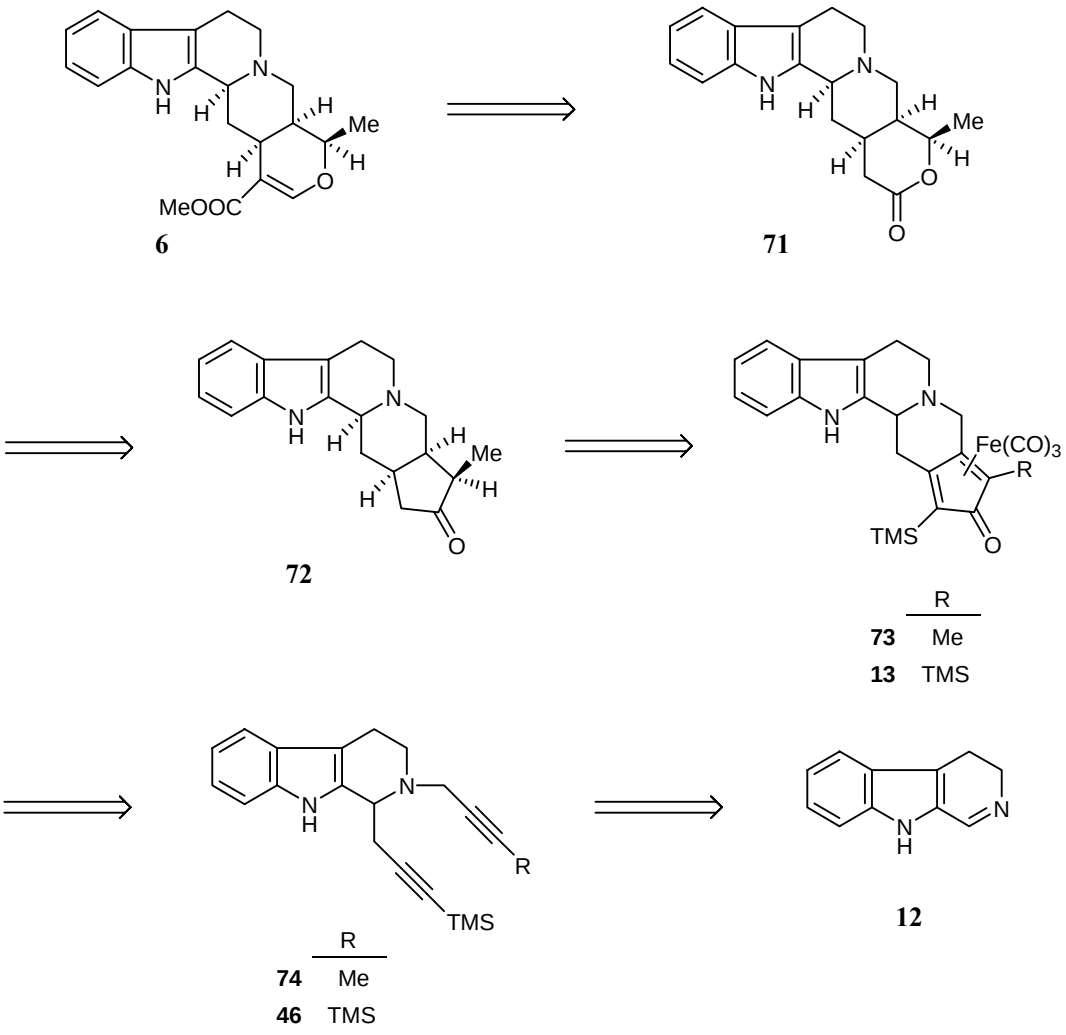
Due to the above observation the synthetic route towards a total synthesis of alloyohimbane by Diels-Alder cycloaddition was abandoned.

3.2 Synthetic approach towards Rauniticine

3.2.1 Retrosynthetic analysis of Rauniticine (6)

We wanted to demonstrate that the iron-mediated [2+2+1] cycloaddition could provide the pentacyclic indolo[2,3-*a*]quinolizidine skeleton found in hetero-yohimbane alkaloids (Scheme 45).

Scheme 45



The retrosynthesis of rauniticine begins with compound **71** which represents a formal total synthesis, since it has been previously converted to compounds like rauniticine, ajmalicine and 19-epi-ajmalicine *via* a known procedure.[107,108]

The key intermediate iron-complexes **73** or **13** can be prepared in high yields by cycloaddition of the diyne **74** or **46** respectively, which in turn is conveniently obtained by the *C*-alkylation of 3,4-dihydro-β-carboline (**12**) followed by *N*-alkylation.

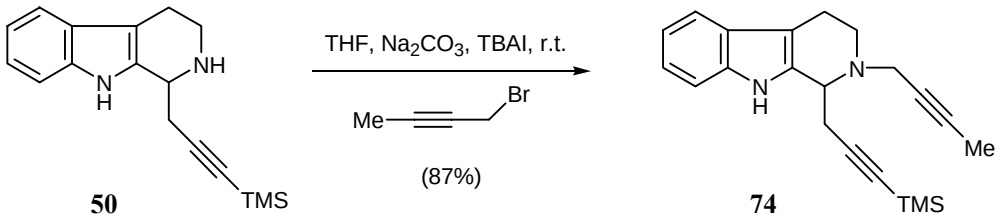
Demetalation of the iron-complex followed by hydrogenation should provide the fully saturated cyclopentanone **72**. We predict a *cis* arrangement of the hydrogen atoms as found in rauniticine based on an addition of all hydrogen atoms from the same side.

The lactone **71** could be accessible by Baeyer-Villiger oxidation of the cyclopentanone **72**. Finally, rauniticine should be obtained from lactone **71** by a known procedure.

3.2.2 Synthesis of iron-complex (73)

The 1-(3-trimethylsilylprop-2-ynyl)-2,3,4,9-tetrahydro-1*H*-β-carboline (**50**) has been previously used as a precursor in our iron-mediated total synthesis of yohimbane alkaloids (Section 3.1). Subsequent *N*-alkylation of **50** led to the 2-but-2-ynyl-1-(3-trimethylsilylprop-2-ynyl)-2,3,4,9-tetrahydro-1*H*-β-carboline (**74**) (Scheme 46).

Scheme 46

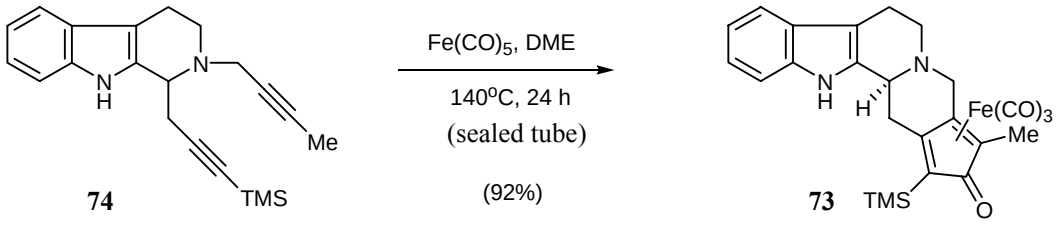


This transformation has been previously achieved in our laboratory[74] in 74% yield using 1-iodo-2-butyne as alkylating agent, which in turn was synthesized from 1-bromo-2-butyne in 50% yield. We performed the *N*-alkylation of **50** directly from commercially available 1-bromo-2-butyne in the presence of a catalytic amount of tetrabutyl-ammonium iodide (TBAI), under *in-situ* Finkelstein reaction conditions to afford diyne **74** in 87% yield. Thus, our modified procedure proved to be highly efficient and diyne **74** is obtained in one step with improved overall yield.

The key-step in our synthetic route is the iron-mediated [2+2+1] cycloaddition for the construction of the pentacyclic ring system. This procedure has already been used for the total synthesis of yohimbane alkaloids.

Thus, under optimized reaction conditions, heating of the mono-TMS-diyne **74** with two equivalents of pentacarbonyliron in dry dimethoxyethane at 140°C for 24 h in a sealed tube afforded almost quantitatively the tricarbonyliron-complexed cyclopentadienone **73** as a mixture of two diastereoisomers in a ratio of 3:1 (Scheme 47).

Scheme 47

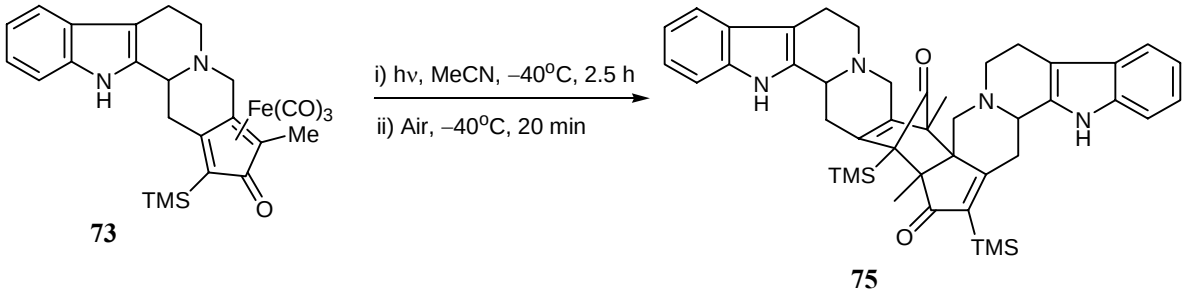


This result emphasized that using our optimized reaction conditions the iron-mediated [2+2+1] cycloaddition of diynes is a very efficient process.

A *trans* conformation of the indolo[2,3-*a*]quinolizidine ring system was confirmed by the presence of Bohlmann's bands[75] in the IR spectrum at $\nu = 2800\ cm^{-1}$ and $2750\ cm^{-1}$.

Cämmerer[74,109] had demonstrated that demetalation of the tricarbonyliron-complexed cyclopentadienone **73** afforded *via* dimerization compound **75** (Scheme 48).

Scheme 48



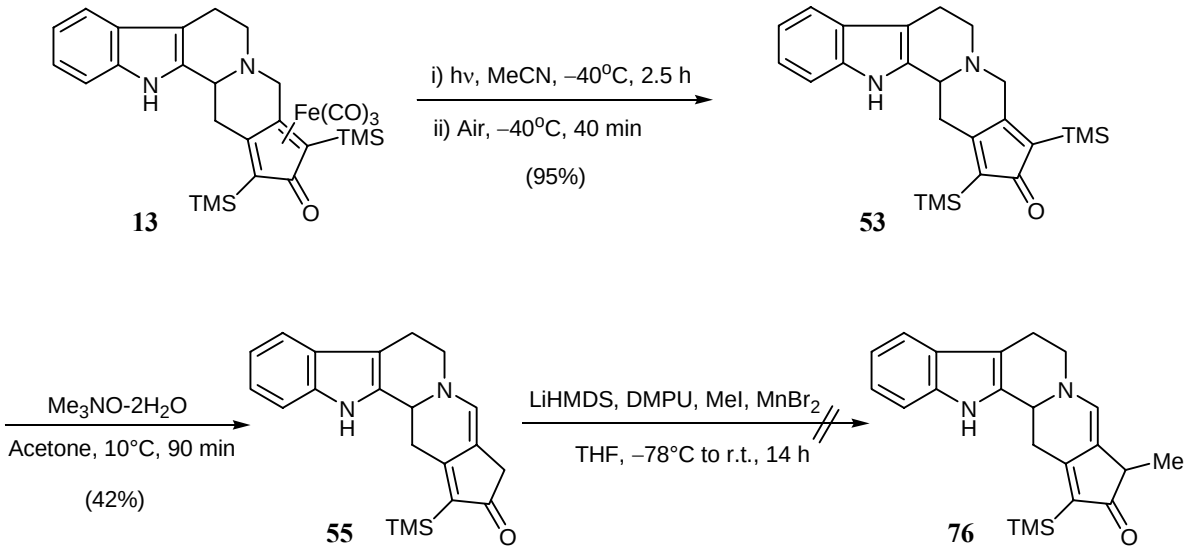
3.2.3 Attempt of introduction of the methyl group

The cyclopentadienone moiety is anti-aromatic, hence quite reactive. In fact, cyclopentadienones have been shown to dimerize upon standing, unless stabilized by bulky substituents.[105] Coordination to a metal also affords temporary stabilization of the

reactive anti-aromatic system.[105,110] To this end, we thought of trimethylsilyl groups as substituents to afford a stable demetalated product.

We then envisioned another possible pathway *via* demetalation of the bis-TMS substituted iron-complex **13** to the corresponding free ligand. As described in section 3.1, the demetalation of iron-complex **13** afforded free ligand **53** in high yield (Scheme 49). The mono protodesilylation of **53** was achieved using trimethylamine *N*-oxide to afford **55** in moderate yield of 42%. A number of different reaction conditions including variation in reaction time and temperature were attempted, but without any significant success in terms of yield.

Scheme 49

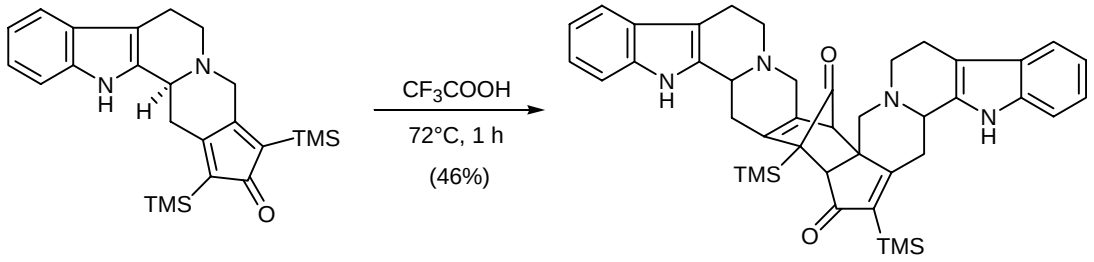


Reetz[111] reported a mild method for the α-methylation of ketones in which manganese enolates react with the equivalent amount of methyl iodide to provide the α-methylated product which is essentially free of undesired polyalkylated by-products. Unfortunately, employing this procedure on compound **55** gave intractable mixtures (Scheme 49).

During the course of related model study, it was found that acid treatment of the free ligand led to the double protodesilylation.[78] Unfortunately, standard methods using

various acids and solvent mixtures (e.g., MeOH/HCl, THF/HCl/H_2O) were ineffective leading to decomposition or mixtures. While on treatment with boiling trifluoroacetic acid, compound **53** underwent dimerization to afford **77** in 46% yield (Scheme 50). It was apparent at this point that another route to rauniticine was needed.

Scheme 50



53 **77**

3.2.4 Demetalation of the Iron-complex followed by hydrogenation

Recently, Franck-Neumann[85] developed a novel method for demetalation of tricarbonyliron diene complexes by hydrogenation with Raney nickel. Application of this strategy in our synthetic route seemed to be attractive because demetalation of iron-complex **73** leads to Diels-Alder dimerization. We subjected the iron-complex **73** to Raney nickel in order to achieve demetalation and hydrogenation. Thus, treatment of iron-complex **73** with excess of activated Raney nickel in ethanol resulted in a series of products (Scheme 51, Table 13).

Reaction of iron-complex **73** with highly activated Raney nickel in ethanol at room temperature for 14 h provided chemo- and stereoselectively the cyclopentanone **72** in 39% yield. Besides the cyclopentanone **72**, the deconjugated cyclopentenone **78** and the carbinol **79** were obtained in 12% and 5% yields, respectively. TLC analysis indicated also the presence of a trace amount of Diels-Alder dimerized product **75**. Despite the fact that mixtures of products were obtained, careful chromatography enabled separation of all the products. On extension of the reaction time to 8 days, the cyclopentanone **72** was obtained in 17% yield along with the deconjugated cyclopentenone **78** in 6% and the

carbinol **79** in 11% yield. In another reaction, this transformation was performed in boiling acetone instead of ethanol. This, to our surprise, resulted in formation of the deconjugated cyclopentenone **78** in 30% yield as major product along with a trace amount of cyclopentanone **72** (entry 3). After 8 days of reflux in acetone, the cyclopentanone **72** was formed in 17% yield along with different diastereoisomers isolation of which was not possible using standard chromatographic techniques (entry 4).

Scheme 51

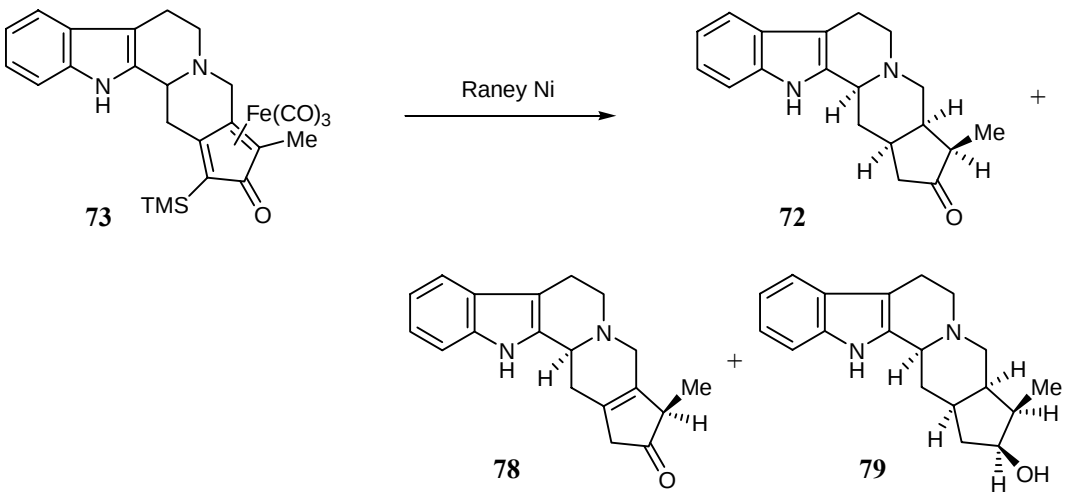
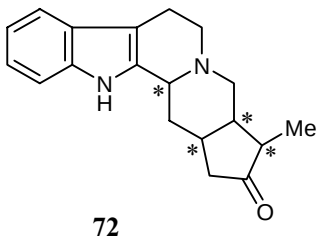


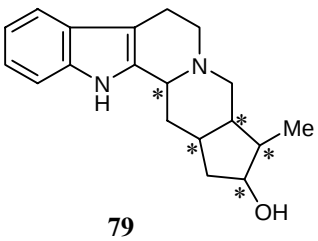
Table 13

Entry	Conditions	72, Yield [%]	78, Yield [%]	79, Yield [%]
1	r.t., ethanol, 14 h	39	12	5
2	r.t., ethanol, 8 days	17	6	11
3	reflux, acetone, 14 h	trace	30	-
4	reflux, acetone, 8 days	17	-	-

It noteworthy that this demetalation followed by hydrogenation constructed the three contiguous stereogenic centers required for the synthesis of rauniticine in one-step. The ^{1}H NMR and ^{13}C NMR spectra revealed that the products **72** and **79** were obtained essentially as single isomers with four and five stereogenic centers respectively (Figure 10).



72



79

Figure 10

In an analogous experiment the tricarbonyliron-complexed bis-TMS-cyclopentadienone **13** was shown previously to afford the *cis*-cyclopentanone **44** on treatment with Raney nickel in ethanol. The relative stereochemistry of the *cis*-cyclopentanone **44** was unambiguously demonstrated by crystallographic studies of single crystals. Based on this observation we propose a *cis* arrangement of all the hydrogen atoms of **72**. This transformation shows that the treatment of the iron-complex **73** with Raney nickel shows a high stereoselectivity.

The present transformation is attractive because it afforded product **72** directly as a single diastereoisomer. The elegance of this one-pot conversion of iron complex **73** to the cyclopentanone **72** is shown by comparison with the original five-step sequence which we envisioned *via* the bis-TMS route (Figure 11).

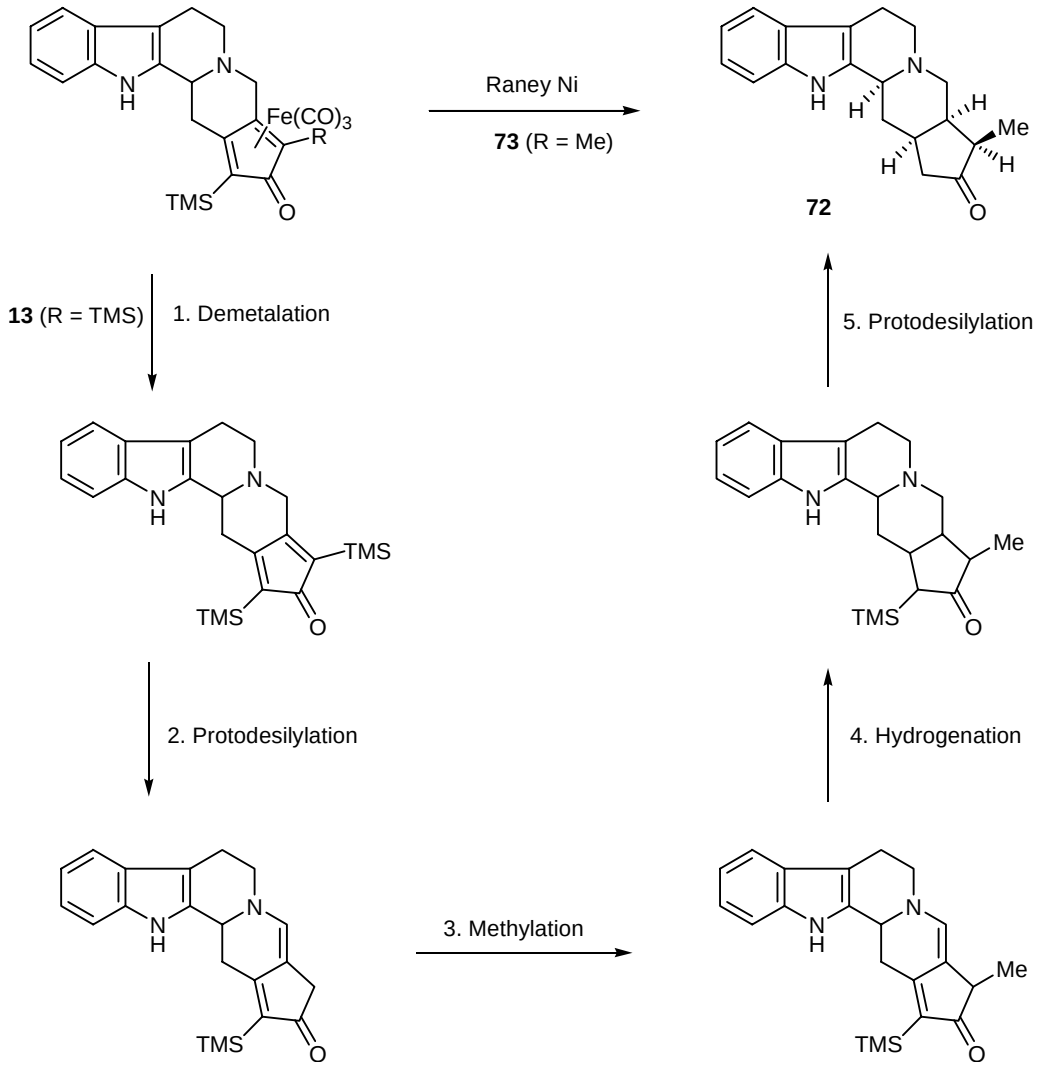


Figure 11

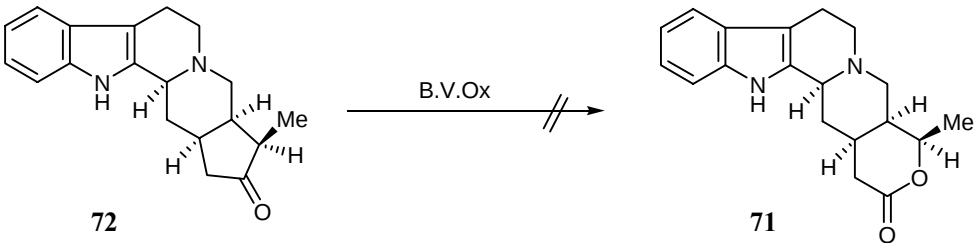
The mechanism by which the heterogeneous hydrogenation proceeds is complex and difficult to study as the reaction takes place on the surface of the catalyst onto which hydrogen is dissociatively adsorbed.[112,113] It is assumed that the olefin is adsorbed onto the surface of the catalyst and the addition of all hydrogen atoms takes place from the same side. This explains the *syn* mode of hydrogen addition.

It has been demonstrated that the demetalation of the iron-complex followed by hydrogenation to the reduced free ligand can be achieved using Raney nickel.

3.2.5 Baeyer-Villiger oxidation

Having prepared enough ketone **72**, the next crucial step for the synthesis of rauniticine was the regioselective transformation of the cyclopentanone **72** to the lactone **71** *via* a Baeyer-Villiger oxidation.[114,115]

Scheme 52



A number of different reagents are available for this purpose.[115] We initially decided to use mCPBA as reagent for the projected Baeyer-Villiger oxidation. Although this transformation appeared fairly straightforward, it proved to be rather difficult. Reaction of cyclopentanone **72** with mCPBA did not provide the desired lactone **71** (Scheme 52, Table 14). Instead only complex mixtures that included solid, intractable material were obtained along with some unreacted **72**. A number of acid- and base-catalyzed Baeyer-Villiger oxidations using mCPBA were also tried without any success. Similar results were obtained even when a large excess of mCPBA was used. Several conditions were tested for Baeyer-Villiger oxidation of **72** using mCPBA, but all attempts led to decomposition.

Efforts to convert the cyclopentanone **72** to the lactone **71** using various reagents including MMPP,[116] trifluoroperacetic acid,[117] and bis(trimethylsilyl)peroxide[118] were also unsuccessful.

Table 14

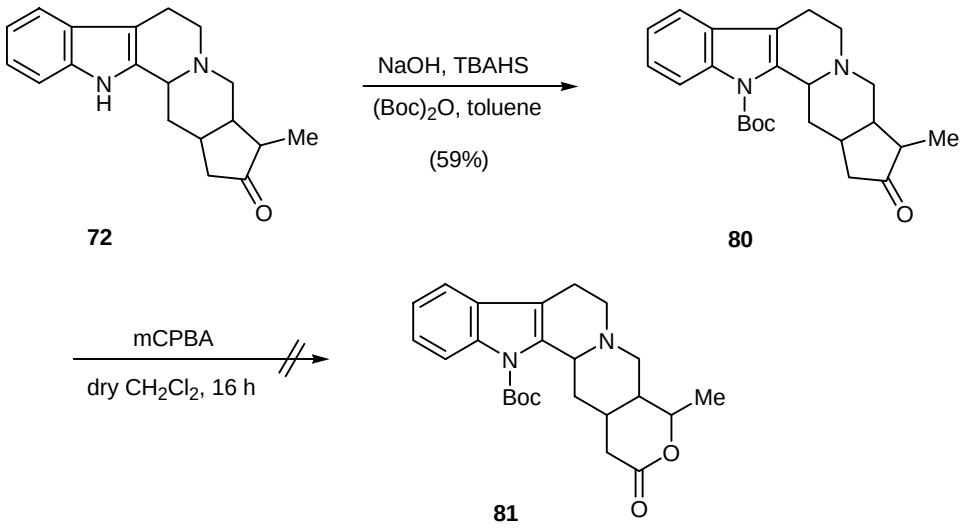
Entry	Conditions	% Yield / remarks
1	1.5 eq mCPBA**,** $NaHCO_3$, r.t., 16 h	45% SM recovered
2	2.0 eq mCPBA**,** $NaHCO_3$, r.t., 60 h	25% SM recovered
3	1.5 eq mCPBA, TsOH, r.t., 60 h	24% SM recovered
4	5.0 eq mCPBA**,** $NaHCO_3$, r.t., 20 h	Decomp.
5	5.0 eq mCPBA**,** r.t., 16 h	Decomp.
6	MMPP/$NaHCO_3$, r.t., 20 h	Decomp.
7	5.0 eq mCPBA**,** 1 eq conc. HCl, r.t., 16 h	Decomp.
8	5.0 eq $(CF_3CO)_2O$, 35% H_2O_2, r.t., 16 h	Decomp.
9	1.2 eq TMS-O-O-TMS, TMSOTf, –40° to –25°C, 20 h	100% SM recovered
10	4 eq TMS-O-O-TMS, TMSOTf, –40° to 0°C, 20 h	76% SM recovered

One possible explanation is that the presence of the basic nitrogen interfers with the Baeyer-Villiger oxidation conditions. Only very few examples of Baeyer-Villiger oxidation in the presence of a basic nitrogen are known.[115]

The introduction and removal of protecting groups are among the most common transformations during the synthesis of polyfunctional molecules.[119] We wanted to investigate if a protecting group at the indole nitrogen would be helpful for the Baeyer-Villiger oxidation.

Thus, compound **72** was protected as the corresponding *tert*-butyl carbamate.[104] Treatment of compound **72** with di-*tert*-butyl carbonate [$(Boc)_2O$], sodium hydroxide and TBAHS in toluene afforded the *N*-Boc derivative **80** in 59% yield (Scheme 53).

Scheme 53

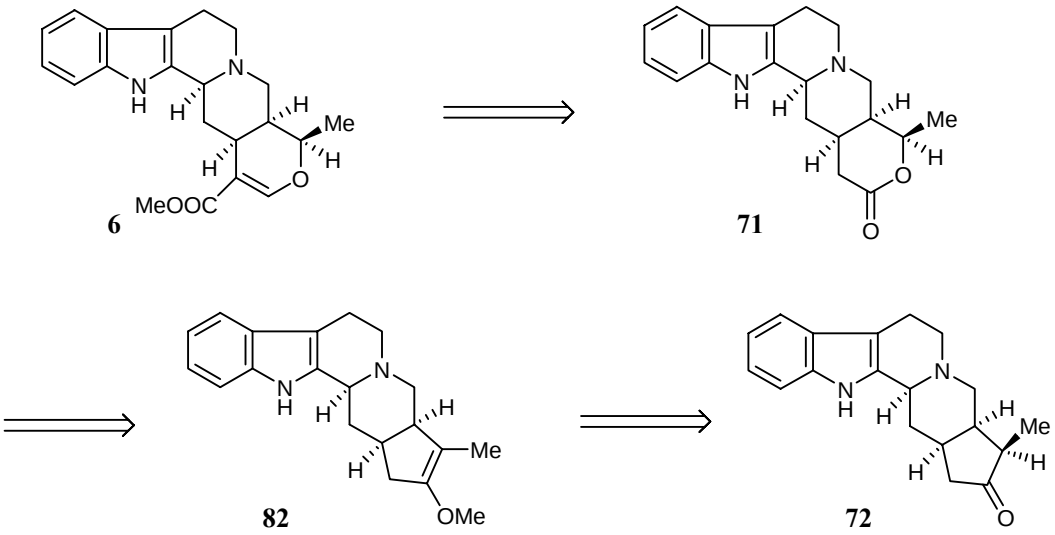


An attempted Baeyer-Villiger oxidation of the *N*-Boc-cyclopentanone **80** using mCPBA was also unsuccessful and led to decomposition.

3.2.6 An alternative approach for construction of the oxygen-containing E-ring

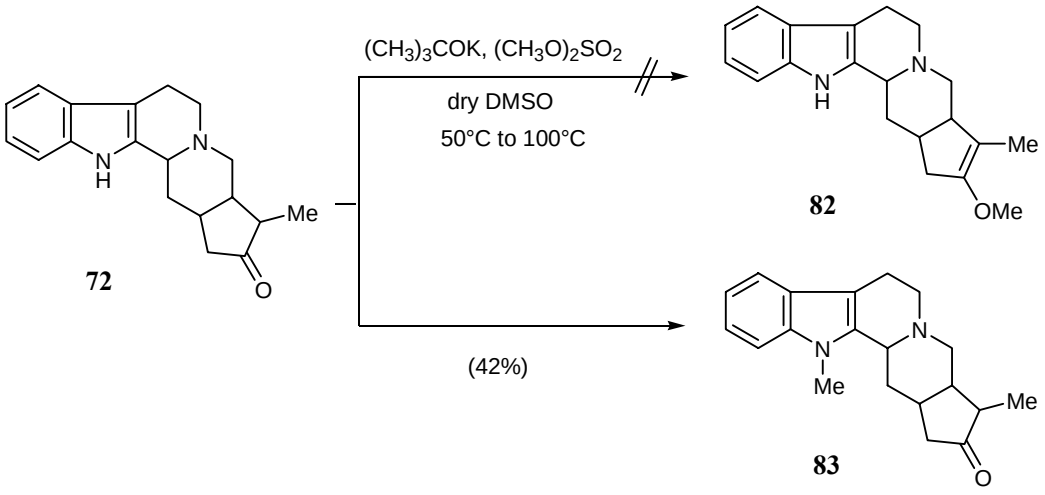
At this stage of our investigations, we decided to study an alternative way to obtain an oxygen-containing E-ring (Scheme 54). Our aim was to perform ozonolysis of **82** followed by reductive workup, which should provide **71**. The enol ether **82** should be easily accessible from **72**.

Scheme 54



It is known in the literature that *O*-alkylation of enolates is achieved using potassium *tert*-butoxide and dimethyl sulfate in DMSO.[120] However, the reaction of cyclopentanone **72** under these conditions was found to undergo *N*-methylation to **83** in 42% yield, instead of the desired methyl enol ether **82** (Scheme 55).

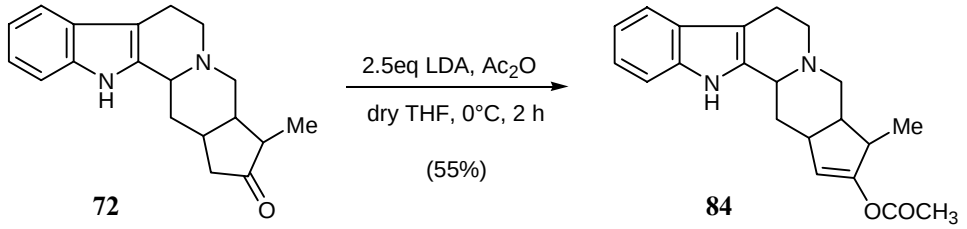
Scheme 55



In light of the above observation, we decided to use an *N*-Boc protection. Treatment of *N*-Boc cyclopentanone **80** under standard conditions for enol formation using potassium *tert*-butoxide and dimethyl sulfate resulted in a complex mixture.

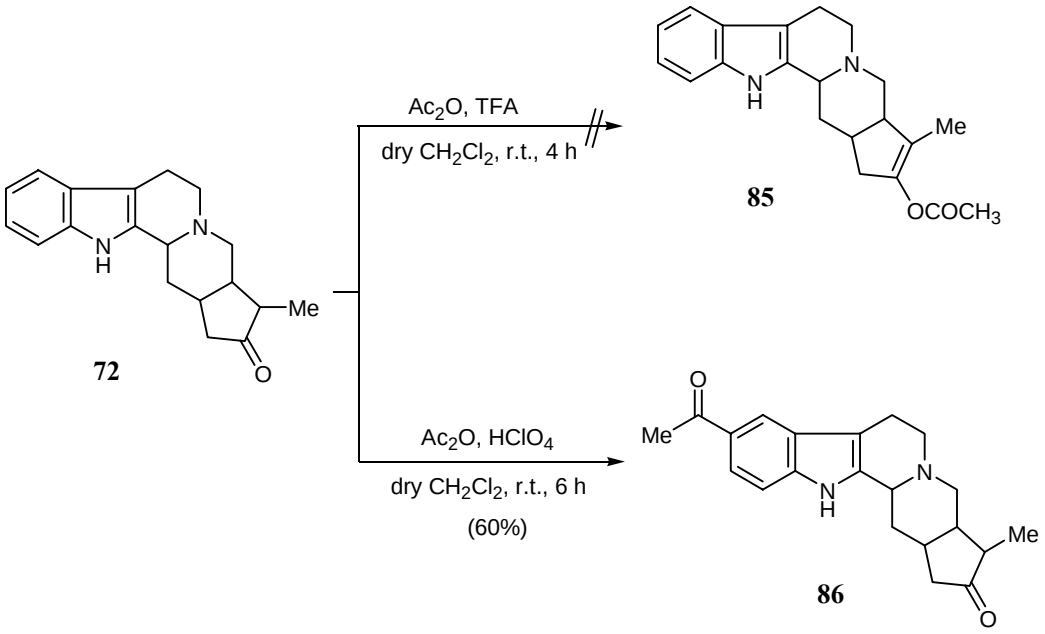
In a further attempt using a procedure described in the literature,[121] the cyclopentanone **72** was treated with trimethyl *ortho*-formate in dry methanol and pyridinium *p*-toluene-sulfonate (PPTS) at room temperature. Unfortunately, no reaction was observed under these conditions. Next, we decided to synthesize the enol acetate **85**. Thus, the enolate formed by proton abstraction with LDA at 0°C was quenched with excess acetic anhydride, but afforded the undesired kinetically controlled enol acetate **84** in 55% yield (Scheme 56).

Scheme 56



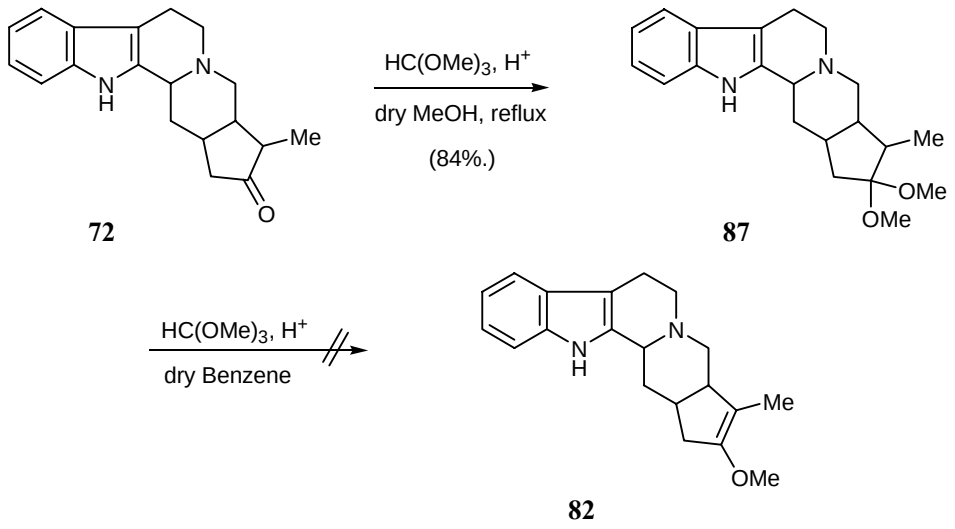
In a further attempt the reaction of cyclopentanone **72** with acetic anhydride in the presence of trifluoroacetic acid led only to recovery of starting material (Scheme 57). The reaction of cyclopentanone **72** with acetic anhydride in the presence of perchloric acid[122] gave the acetyl derivative **86** in 60% yield.

Scheme 57



For the synthesis of the methyl enol ether **82**, it was thought to transform the cyclopentanone **72** to ketal the **87**, which was expected to be easily converted to **82**. Using the protocol described by Winterfeldt,[123] treatment of **72** with trimethyl *ortho*-formate in the presence of *p*-toluenesulfonic acid in boiling methanol, led cleanly to the formation of ketal **87** in 84% yield (Scheme 58).

Scheme 58

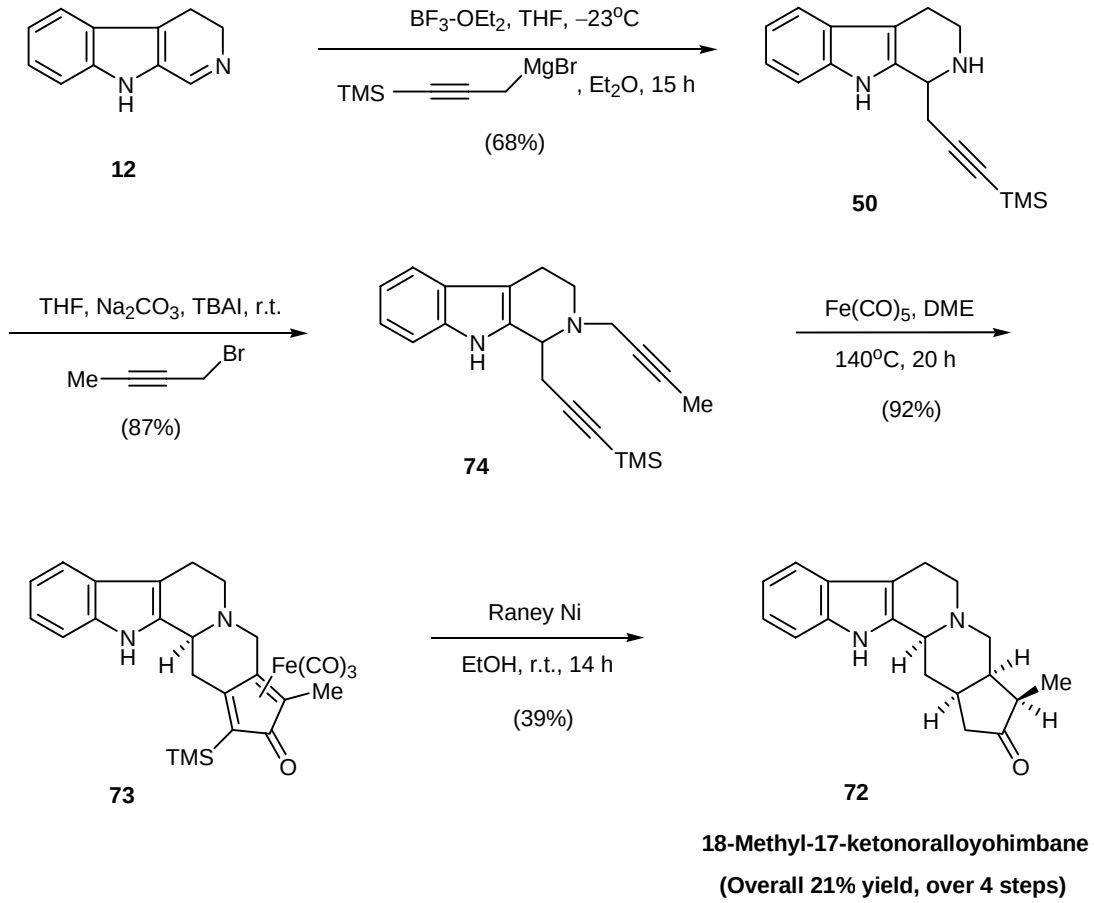


Surprisingly, the formation of methyl enol ether **82** from ketal **87** proved to be difficult. No reaction was observed using trimethyl *ortho*-formate and dry benzene in the presence of *p*-toluene sulfonic acid (Scheme 58).

In conclusion, the synthetic approach towards the total synthesis of rauniticine was stopped.

It is worth mentioning that the 18-methyl-17-ketonoralloyohimbane (**72**) has been synthesized using the iron-mediated [2+2+1] cycloaddition in 4 steps and 21% overall yield based on 3,4-dihydro-β-carboline (Scheme 59).

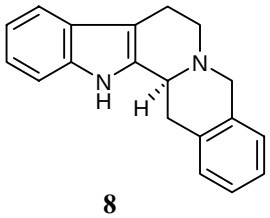
Scheme 59



18-methyl-17-ketonoralloyohimbane could be employed as key synthetic building block for biologically important natural and unnatural products possessing this framework. The biological activity of compound **72** is under investigation.

3.3 Synthetic approach towards aromatized yohimbane alkaloids

3.3.1 Optimized Synthesis of (±)-demethoxycarbonyldihydrogambirtannine [(±)-(**8**)]



8

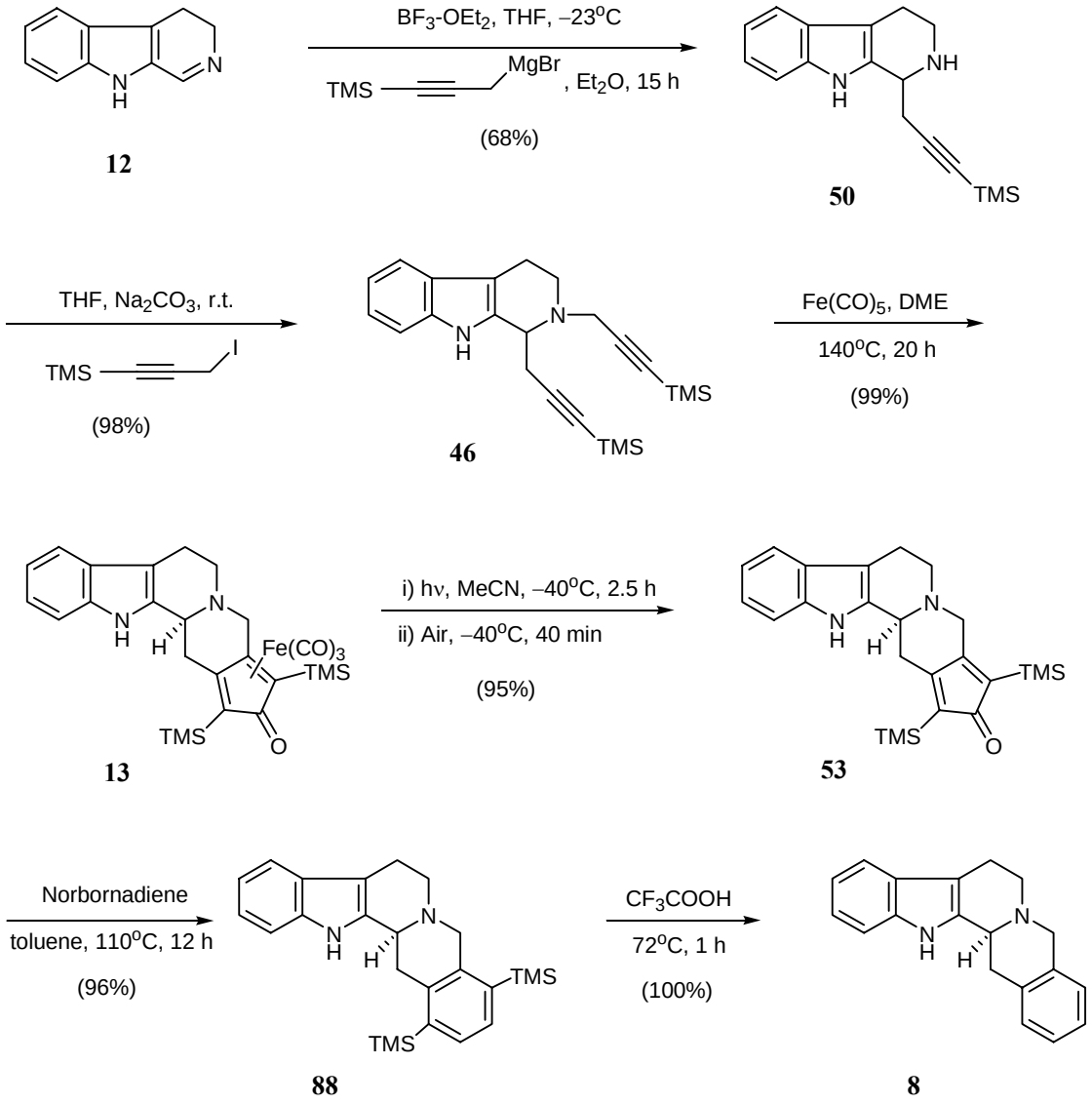
Demethoxycarbonyldihydrogambirtannine (**8**) is an aromatized yohimbane alkaloid first isolated from the leaves of *Ochrosia lifuana* and *Ochrosia miana* (Apocynaceae).[16] Subsequently it was found that **8** represents the main alkaloid of the fruits of *Strychnos usambarensis*, a plant of the family Loganiaceae found in Africa.[17] The consumption of these fruits was reported to cause poisoning.

Our group has a continuous program directed towards the development of novel methodologies for organic synthesis using tricarbonyliron-diene complexes.[124] Knölker and Cämmerer have reported a highly efficient total synthesis of (±)-demethoxycarbonyldihydrogambirtannine [(±)-(**8**)] in six steps and 49% overall yield.[29] In the course of our studies on the iron-mediated [2+2+1] cycloaddition for the synthesis of indole alkaloids, we were able to optimize this synthesis further.

As described earlier, addition of the Grignard reagent to the preformed BF_3–iminium salt of 3,4-dihydro-β-carboline (**12**) afforded 1-(3-trimethylsilylpropargyl)-1,2,3,4-tetrahydro-β-carboline (**50**) (Scheme 60). Subsequent *N*-alkylation of **50** led to the 1,2-bis(3-trimethylsilylprop-2-ynyl)-2,3,4,9-tetrahydro-β-carboline (**46)** (67% yield over both steps). Heating the bis-TMS-diyne **46** with two equivalents of pentacarbonyliron in dimethoxyethane at 140°C for 20 h in a sealed tube afforded quantitatively the

tricarbonyliron-complexed cyclopentadienone **13** as a mixture of two diastereoisomers in a ratio of 2:1 (*syn* : *anti*). The expected structure and stereochemical outcome was additionally confirmed by X-ray crystallographic studies of *syn*-**13**.

Scheme 60



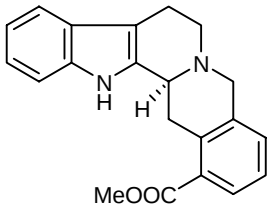
The conversion of complex **13** to the free ligand **53** was achieved by a photolytically induced ligand exchange reaction to the intermediate triacetonitrile(η^4-cyclopentadienone)iron complex and subsequent demetalation in the air.[65] Cämmerer has reported a 89% yield for this transformation. Extension of the time for bubbling of air

from 20 minutes to 40 minutes led to complete conversion to the product **53** in 95% yield.

The Diels-Alder cycloaddition of the cyclopentadienone **53** and norbornadiene in toluene at reflux with concomitant extrusion of carbon monoxide and cyclopentadiene afforded 16,19-bis(trimethylsilyl)-15,16,17,18,19,20-hexadehydroyohimbane (**88**) in 96% yield. This reaction was highly reproducible. Finally, double protodesilylation of **88** using trifluoroacetic acid at reflux provided (±)-demethoxycarbonyldihydrogambirtannine [(±)-(**8**)] quantitatively, although Cämmerer has reported 89% yield for this transformation. The spectral data of compound **8** are in good agreement with those reported in the literature.[16,17,29]

In conclusion, the iron-mediated [2+2+1] cycloaddition of diynes has been efficiently applied to the synthesis of (±)-demethoxycarbonyldihydrogambirtannine. Optimized reaction conditions for the demetalation and double protodesilylation afforded the title compound in six steps and 60% overall yield based on 3,4-dihydro-β-carboline.

3.3.2 Synthetic approach towards the total synthesis of (±)-Dihydrogambirtannine [(±)-9]

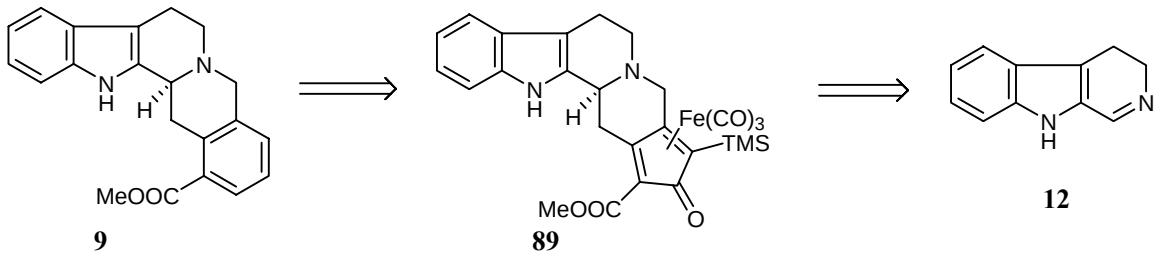


9

Dihydrogambirtannine is one of several yohimboid constituents of the tanning material gambir, isolated from *Uncaria gambier* Roxb.,[15] and coincidentally the enantiomer of a degradation product of the natural base deserpideine.[125] This alkaloid has been the target of various synthetic approaches.[2]

In continuation of our studies on the synthesis of indole alkaloids by the iron-mediated [2+2+1] cycloaddition a synthesis of dihydrogambirtannine (**9**) was projected.

Scheme 61



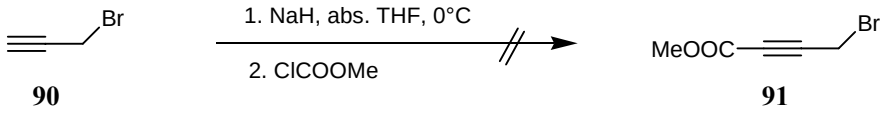
9 **89**

The retrosynthetic analysis of dihydrogambirtannine (**9**) has been outlined in Scheme 61. It is based on the iron-mediated [2+2+1] cycloaddition to provide the pentacyclic ring system of the core indolo[2,3-*a*]quinolizidine skeleton as found in aromatized yohimbane alkaloids.

We were interested to introduce the ester functionality of dihydrogambirtannine from the beginning of the synthesis. We therefore envisioned to prepare 4-bromo-2-butynoate **91** from commercial 3-bromopropyne (**90**). The ester **91** should be added to the C=N functionality of 3,4-dihydro-β-carboline (**12**).

We attempted the synthesis of 4-bromo-2-butynoate **91** (Scheme 62). However, reaction of 3-bromo-propyne with methylchloroformate and sodium hydride afforded a mixture of products.

Scheme 62

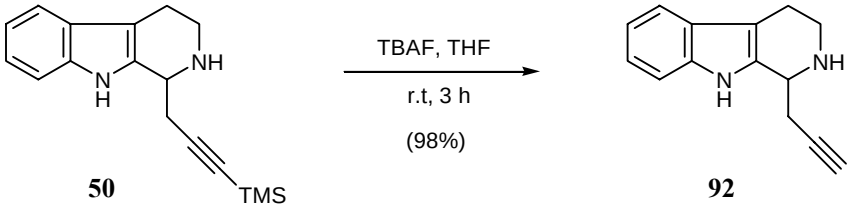


90 **91**

Earl and Townsend[126] had similar trouble with this transformation and addressed the problem to isolate the product to its tendency to undergo rearrangement to allenic compounds or to react further with bases present in the reaction mixture.

We decided to introduce the ester functionality in a stepwise manner. Thus, compound **50** was protodesilylated using TBAF to provide 1-propargyl-1,2,3,4-tetrahydro-β-carboline (**92**) in 98% yield (Scheme 63).

Scheme 63

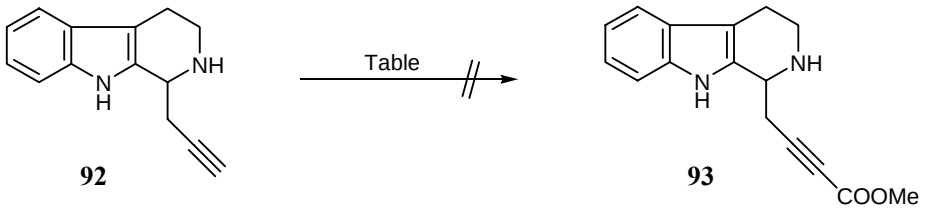


50 **92**

The introduction of the ester functionality was attempted under different reaction conditions (Scheme 64, Table 15). Treatment of compound **92** with LDA at −78°C followed by addition of methylchloroformate resulted in formation of a complex mixture

(entry 1). Next, we examined this transformation with methyllithium and dry ice followed by esterification with methanol and sulfuric acid. Again a mixture of products was formed (entry 2). Use of a large excess of methyllithium also failed (entry 3).

Scheme 64



92 **93**

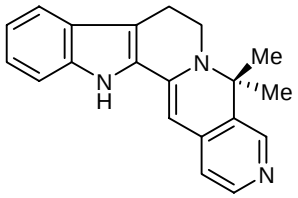
Table 15

Entry	Conditions	Yield [%]/ Remarks
1	i) LDA (1eq), –78°C, dry THF ii) ClCOOMe, –78°C to r.t.	Mix. of products
2	i) MeLi (1eq), 0°C to r.t., dry THF ii) Dry Ice iii) MeOH/H_2SO_4, 14 h	Mix. of products + 34% SM
3	i) MeLi (3eq), 0°C to r.t., dry THF ii) Dry Ice iii) MeOH/H_2SO_4, 14 h	Mix. of products

Winterfeldt and coworkers[127] have reported a synthesis of **93,** but they have isolated and characterized this compound as the corresponding *N*-acetyl derivative in moderate yield.

The synthetic approach towards the total synthesis of (±)-dihydrogambirtannine [(±)-**9**] was stopped due to the problems to obtain a methoxycarbonyl-containing precursor.

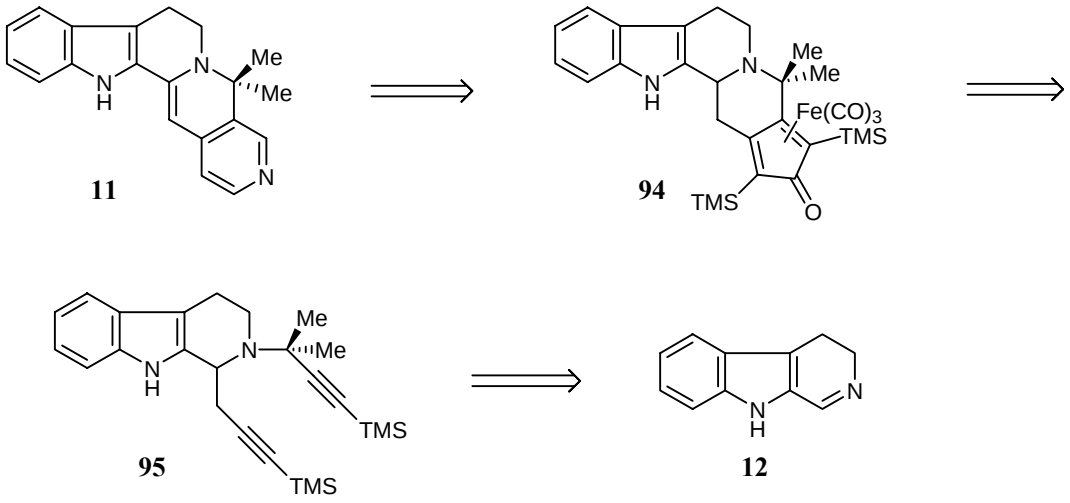
3.3.3 Synthetic approach towards the total synthesis of (±)-3,14-didehydro-19-methylnormalindine [(±)-11]



11

3,14-Didehydro-19-methylnormalindine (**11**) has been recently extracted from the aerial parts of *Ophiorrhiza rosacea* Ridley (Rubiaceae).[18] *Ophiorrhiza rosacea* is a small herbaceous shrub growing in Indonesia and exhibits a characteristic red colour on maceration with methanol. No traditional medicinal value has been reported for this plant.

Scheme 65



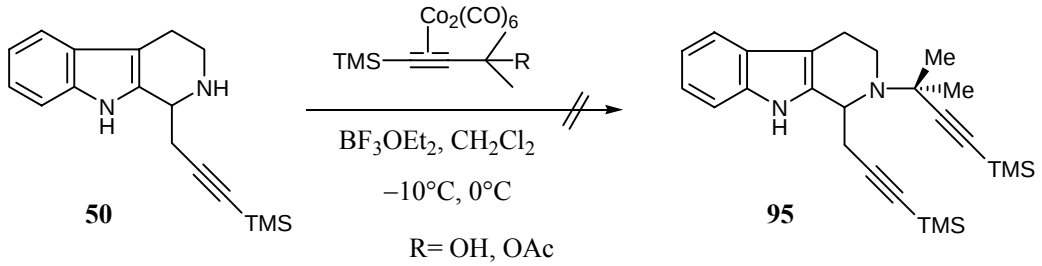
The retrosynthetic analysis of (±)-3,14-didehydro-19-methylnormalindine (**11**) based on the iron-mediated [2+2+1] cycloaddition as the key step is shown in Scheme 65.

The iron complex can be prepared by cycloaddition of the diyne **95** which should derive from the *C*-alkylation of 3,4-dihydro-β-carboline (**12**) followed by *N*-alkylation with the alkyl chain. The alkaloid **11** could be accessible *via* Beckmann rearrangement of the free ligand followed by further transformation.

3,14-Didehydro-19-methylnormalindine has a gem-dimethyl group at the 19-position of the pentacyclic ring system. The reaction of cobalt-complexed propargylic alcohols with HBF_4 or BF_3-etherate developed by Nicholas[128,129] appeared attractive since a cobalt-stabilized carbocation can react with a variety of nucleophiles to provide alkylated products.

Reaction of **50** with propargylic alcohol dicobalt hexacarbonyl in the presence of BF_3-etherate resulted in decomposition to complex mixtures (Scheme 66). A number of different reaction conditions including variation in reaction time and temperature were attempted, but without any success.

Scheme 66



Several conditions were tested for *N*-alkylation using various reagents and conditions, but all attempts failed (Scheme 67, Table 16). It is assumed that steric hindrance due to the gem-dimethyl group on the alkyl chain hinders the *N*-alkylation.

Scheme 67

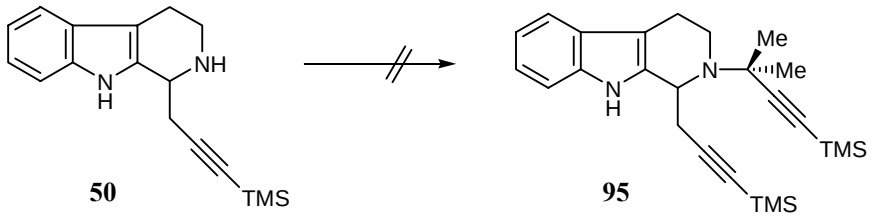
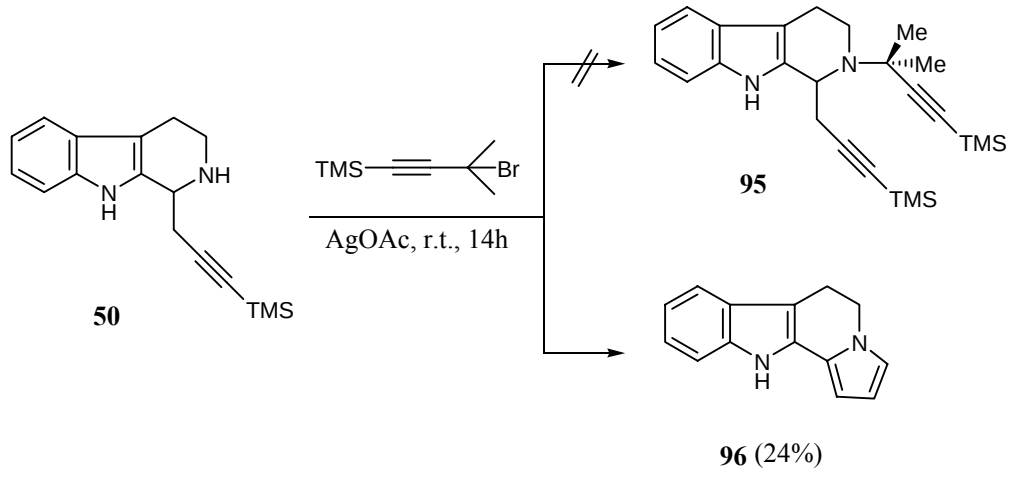


Table 16

Entry	Reagent / Conditions		Yield [%]/ Remarks
1	TMS—≡—Cl	Na_2CO_3, TBAI, DMF, reflux, 40h	Decomp. + SM
2	TMS—≡—OH	TFA, –25°C to 0°C	Decomp.
3	TMS—≡—Cl	CuCl, Et_2O, r.t	Decomp. + SM
4	TMS—≡—Br	CuBr(cat.), MeCN, r.t. to reflux	Decomp.

In the presence of silver acetate compound **50** was treated with 3,3-dimethyl-trimethylsilylpropargyl bromide (Scheme 68).

Scheme 68



The reaction was monitored by TLC and only one spot was observed. On careful isolation, to our surprise, the product from this reaction was found to be the dihydroindolizino[8,7-*b*]indole **96** (Scheme 68).

The dihydroindolizino[8,7-*b*]indole **96** could be employed as a useful precursor for biologically important natural and unnatural products. In addition, represents a novel pyrrole synthesis.

The synthetic approach towards 3,14-didehydro-19-methylnormalindine was given up.

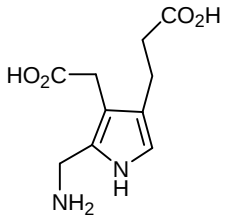
3.4 A novel pyrrole synthesis

The formation of the dihydropyrrolo[2,1-*a*]isoquinoline **96** provides an example of a novel pyrrole annulation at 3,4-dihydro-β-carboline. We were interested to extend this methodology to the synthesis of a variety of substituted pyrroles.

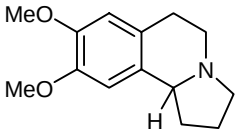
3.4.1 General introduction to pyrroles

The pyrrole ring is probably the most important of the five-membered heteroaromatic ring systems. It was discovered by Runge in 1834. Pyrrole moieties and their derivatives are found in a range of biologically active natural and unnatural compounds.[130] Pyrroles also form the backbone of several important pharmaceuticals including the blockbuster drug Atorvastatin Calcium,[131] as well as important antiinflammatants,[132] antitumor agents,[133] and immunosuppressants.[134] Similarly, polypyrroles are of growing relevance in the material science as conjugated polymers.[135]

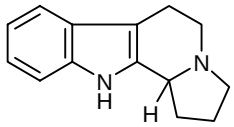
The pyrrole ring system is incorporated as a basic structural unit in prophyrins: porphin (haem) and chlorine (chlorophyll) and corrins (vitamin B_{12}).[136] Apart from these, the pyrrole ring is also a structural unit in many other natural products of plant and marine origin such as ningalins,[137] polycitone, storniamides, lukianols[138] and lamellarins[139] (Figure 12). Porphobilinogen (PBG) is a trisubstituted pyrrole which contains only alkyl substituents. PBG is used in the biosynthesis of tetrapyrrolic pigments. The tetrapyrrolic pigments such as heme, chlorophyll and vitamine B_{12} play an important role for central processes of life. They are universally distributed and therefore, have been named “pigments of life”.



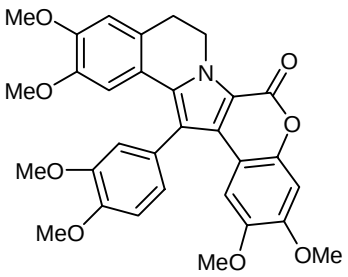
Porphobilinogen



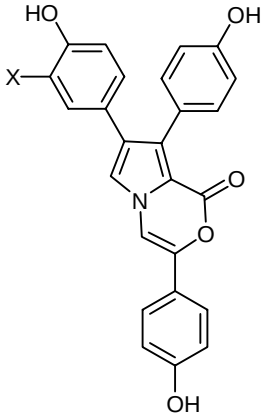
Crispine A



Harmicine



Lamellarin G



Lukianol A X = H
Lukianol B X = I

Figure 12

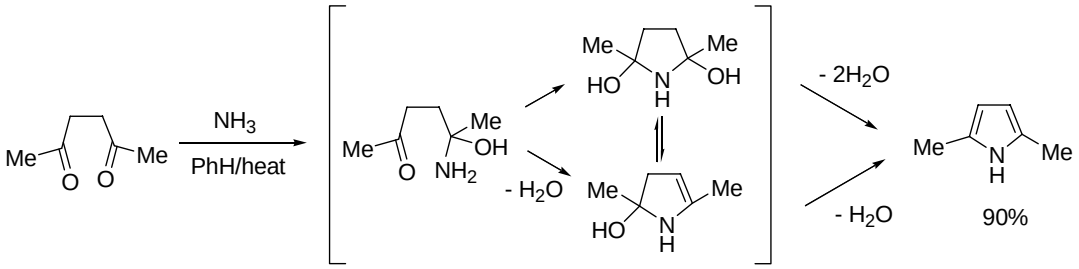
Crispine A[140] and Harmicine[141] are biologically important recently isolated natural products containing a tricyclic and tetracyclic ring system respectively. These natural products have a fused aromatic heterocyclic system containing a saturated pyrrole ring.

The lamellarins are a rapidly growing class of marine natural products. More than thirty lamellarins have been identified since their first isolation[139] from the prosobranch mollusk *Lamellaria* species in 1985. The lamellarins are polyaromatic pyrrole alkaloids isolated from diverse marine organisms, mainly but not exclusively ascidians and sponges. Inhibition of HIV-1 integrase by lamellarin α20-sulfate and human topoisomerase I by lamellarin D and Molluscum contagiosum virus topoisomerase by lamellarin H, along with other effects on nuclear proteins, provide an experimental basis indicating that DNA manipulating enzymes are important targets for the lamellarins.

Some of these marine compounds exhibit cytotoxic activities against tumor cells *in vitro* and are insensitive to Pgp-mediated drug efflux.[142]

The synthesis and functionalization of pyrrole and its derivatives has been the subject of research for over hundred years. Therefore, it is not surprising that the wide array of classical established and practical pyrrole syntheses such as *Hantzsch*, *Knorr* and *Paal-Knorr* is continuously supplemented by novel methods to prepare substituted and functionalized pyrroles, in particular those that are not readily available by classical approaches. Pyrroles are synthesized using the classical *Paal-Knorr*[143,144] reaction from ammonia or a primary amine and a 1,4-dicarbonyl compound (Scheme 69).

Scheme 69



The methods reported for the synthesis of substituted and functionalized pyrroles are too many to be included in a brief introduction and therefore, attention is drawn to reviews on a comprehensive coverage of this class of compounds.[136,145-147] Novel recent pyrrole syntheses include the reductive ring contraction of pyridazines,[148] the Cu(I)-assisted 1,5-cyclization of alkynyl imines,[149] the palladium-catalyzed cyclization of α-propargyl-β-iminophosphanoxides,[150] cyclization of 4-aminobut-2-en-1-ones,[151] 4-amino-3-hydroxy-ketones,[152] and of δ-enaminoesters with *N*-bromosuccinimide.[153]

Transition-metal compounds such as Pd(0 or II),[154] Hg(II),[155] and organo-lanthanides[156] have been reported to be effective for cyclization reactions. The first reaction belonging to silver(I)-mediated cyclization category was developed by Claesson[157] in 1979. The silver(I)-catalyzed/mediated reaction includes cyclization of 4-allenylazetinones to Δ^1-

carbapenems,[158] 1,2,3,4-tetrahydroisoquinoline to pyrrole-dihydroisoquinoline,[159] and very recently Dovey[160,161] has reported a silver-mediated reaction for the synthesis of functionalized pyrroles.

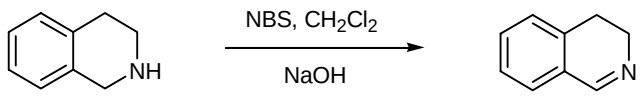
We investigated whether homopropargylamines can be cyclized to substituted pyrroles using a transition-metal based system. Homopropargylamines are readily available by addition of a propargyl Grignard reagent to *Schiff* bases. Thus, a new general method for the synthesis of pyrroles was developed. The scope and limitations of this methodology is described in the present section.

We have chosen 3,4-dihydroisoquinoline (**98**) as substrate for our studies. The tetrahydroisoquinoline skeleton is widely represented in many plant families and provides a challenging target for synthesis.[162,163]

3.4.2 Oxidative annelation of a pyrrole ring at 3,4-dihydroisoquinoline

The required model compound for our studies, 3,4-dihydroisoquinoline (**98**) was easily synthesized from commercially available 1,2,3,4-tetrahydroisoquinoline (**97**).[164] 1,2,3,4-Tetrahydroisoquinoline (**97**) was oxidized with *N*-bromosuccinimide followed by treatment with sodium hydroxide to afford 3,4-dihydroisoquinoline (**98**) as a colourless oil, which turns into white crystals on cooling (Scheme 70). Thus, 3,4-dihydroisoquinoline was available in 94% yield in large quantities.

Scheme 70

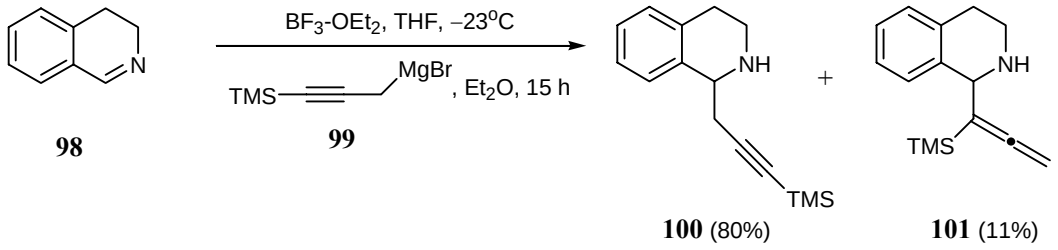


97 **98**

The addition of 3-trimethylsilylpropargylmagnesium bromide (**99**) to 3,4-dihydroisoquinoline (**98**) using Nakagawa's procedure (formation of a BF_3–imine

complex prior to Grignard addition) afforded 1-(3-trimethylsilylpropargyl)-1,2,3,4-tetrahydroisoquinoline (**100**) in 80% yield along with 1-(1-trimethylsilylpropa-1,2-dienyl)-1,2,3,4-tetrahydroisoquinoline (**101**) in 11% yield (Scheme 71).

Scheme 71

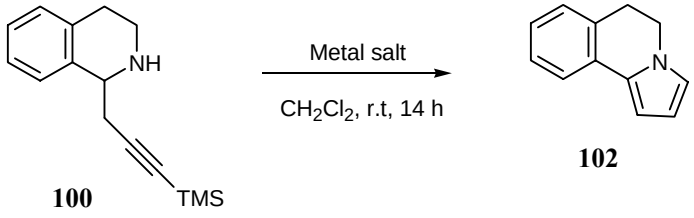


98 **99** **100** (80%) **101** (11%)

Silver(I) salts are known to provide stable π-complexes with terminal acetylenes.[165] Therefore, we expected that the observed activation of the acetylene may be utilized for cyclization reactions by intramolecular nucleophilic attack onto the acetylene. Silver(I) salts have been reported to be effective catalysts for cyclization reactions.[154,157,159,161,166]

Compound **100** was treated with silver acetate in dichloromethane solution at room temperature. After 14 h the TLC analysis indicated that the dihydropyrrolo[2,1-*a*]isoquinoline **102** was the sole product (Scheme 72).[167] During the reaction the deposition of metallic silver is observed. Although, dichloromethane was found to be the most effective solvent, acetone could also be employed as an alternative.

Scheme 72



100 **102**

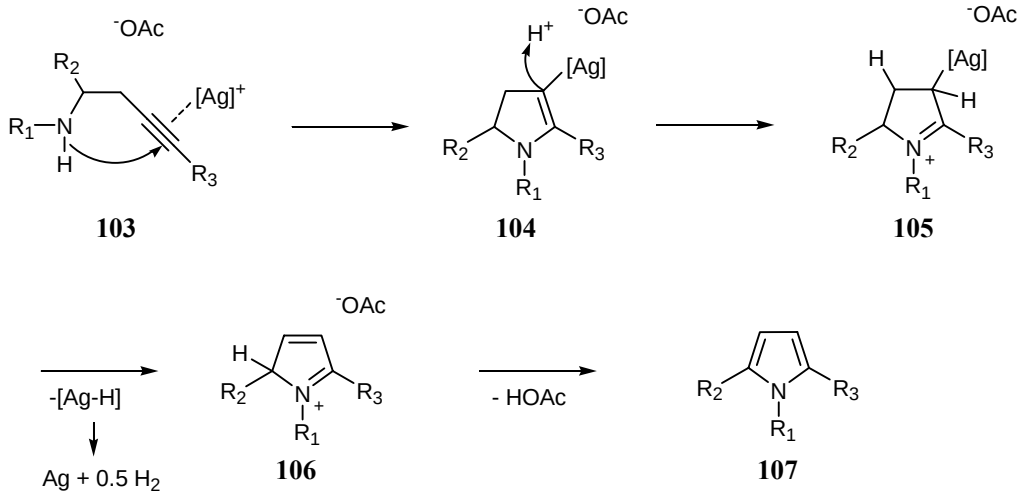
An extensive variation of the metal salt and its stoichiometry has been investigated (Table 17).[167] It was found that the reaction works best using 1.1 equivalents of silver acetate (entry 1). Application of a larger excess of the silver(I) salt does not improve the yield (entry 2) and since the reaction represents an oxidative cyclization, it is not catalytic in silver and resulted in only 5% yield on loading 0.1 equivalents of silver acetate (entry 3). The results presented in Table 17 indicate the important role of the oxidation potential of the metal ion. Remarkably, cuprous acetate afforded a 56% yield of **102**, in contrast to cupric acetate which led only to recovery of starting material (entries 4 and 5). Palladium(II) acetate gave a moderate yield of 18% of the anellated pyrrole **102** (entry 6). Salts of noble metals, like $PtCl_2$, resulted in complete decomposition, while AuCl gave only a trace amount of **102** (entries 7 and 8). Another salt of gold, Ph_3PAuCl, led to the complete recovery of starting material (entry 9).

Table 17

Entry	Metal salt	Equivalents	102, Yield [%]
1	AgOAc	1.1 eq	72
2	AgOAc	2.1 eq	66
3	AgOAc	0.1 eq	5
4	CuOAc	1.1 eq	56
5	$Cu(OAc)_2$	1.1 eq	-
6	$Pd(OAc)_2$	1.1 eq	18
7	$PtCl_2$	1.1 eq	-
8	AuCl	1.1 eq	trace
9	Ph_3PAuCl	1.1 eq	-

A tentative plausible mechanism for the formation of pyrroles by the silver(I)-promoted oxidative cyclization of homopropargylamines is depicted in Scheme 73. The coordination of the alkyne to the silver cation **103** initiates a nucleophilic attack of the amine at the alkyne leading to intermediate **104**. Protonation of **104** affords the iminium ion **105**, which on subsequent β-hydride elimination generates the pyrrylium ion **106** and metallic silver. Finally, proton loss of **106** provides the pyrrole **107**. For trimethylsilyl-substituted homopropargylamines **103** (R_3 = TMS), the 1,2,5-trisubstituted pyrrole **107** (R_3 = TMS) formed initially is protodesilylated by acetic acid to a 1,2-disubstituted pyrrole **107** (R_3 = H).

Scheme 73

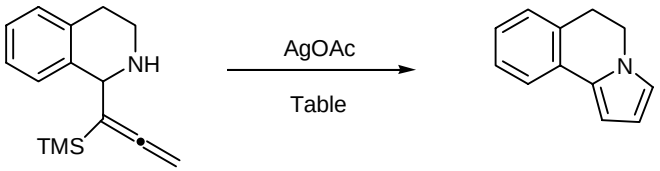


The formation of the dihydropyrrolo[2,1-*a*]isoquinoline **102** provides an example of a novel pyrrole synthesis involving a silver(I)-promoted oxidative cyclization of a homopropargylamine. In addition, this cyclization to pyrroles could be utilized as key-step for the construction of structurally diverse heterocyclic compounds and for the framework of several classes of alkaloids.

Allenes serve as extremely useful precursors in organic synthesis.[70] The ability of allenes to undergo either inter- or intramolecular cyclization reactions with a variety of reagents is known for decades.[168] Substituted allenes are known to undergo cyclization to 2,5-dihydropyrroles in the presence of silver(I) salts.[169]

The allene **101,** obtained as a by-product during the addition of the propargyl Grignard reagent to the 3,4-dihydro-isoquinoline, also underwent smooth silver(I)-promoted oxidative cyclization to the dihydropyrrolo[2,1-*a*]isoquinoline **102** in 56% yield (Scheme 74).

Scheme 74



101 **102**

Table 18

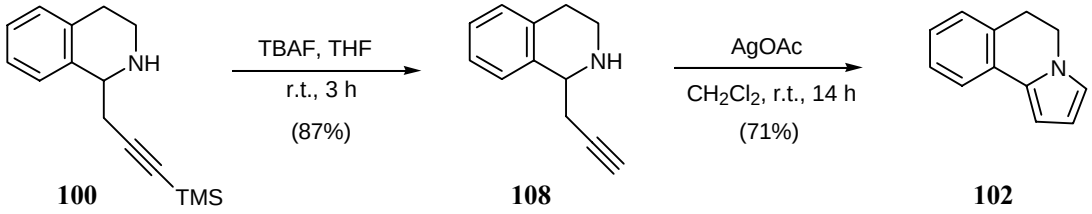
Entry	Conditions	102, Yield [%] / Remarks
1	CH_2Cl_2, r.t., 14 h	90% SM recov.
2	Acetone, reflux, 14 h	56

Although, the overnight treatment of **101** with silver acetate in dichloromethane at room temperature led only to recovered starting material (Table 18, entry 1), the reaction in boiling acetone was found to be effective for the transformation (entry 2). Thus, the silver(I)-promoted oxidative cyclization reaction is also effective for allenes as substrates.

We also explored the oxidative cyclization of homopropargylamines to pyrroles for terminally unprotected alkynes. We synthesized the unprotected alkyne **108** by protodesilylation of compound **100**. Treatment of compound **100** with TBAF in THF at

room temperature led to 1-propargyl-1,2,3,4-tetrahydroisoquinoline (**108**) in 87% yield. Subsequent treatment with silver acetate using our optimized conditions gave the dihydropyrrolo[2,1-*a*]isoquinoline **102** in 71% yield (Scheme 75).

Scheme 75



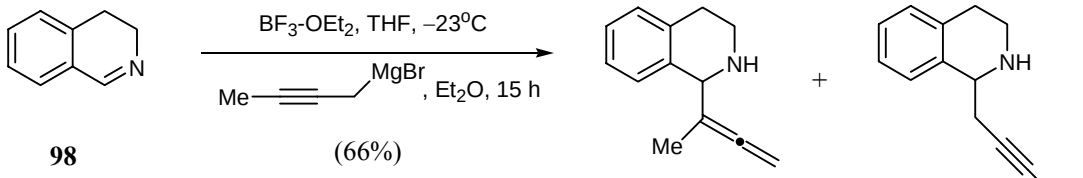
100 **108** **102**

Thus, it was demonstrated that the oxidative cyclization of homopropargylamines to pyrroles works even for terminal alkynes.

To broaden the utility of this reaction, we decided to synthesize 1,2,3- or 1,2,5-trisubstituted pyrroles and to investigate the regioselectivity of systems with alkyl or aryl substituents at the alkyne.

It was therefore decided to prepare methyl- and phenyl-substituted internal alkynes. The addition of 3-methylpropargylmagnesium bromide to 3,4-dihydroisoquinoline in the presence of BF_3-etherate gave a mixture of 1-(1-methylpropa-1,2-dienyl)-1,2,3,4-tetrahydroisoquinoline (**109**) and 1-but-2-ynyl-1,2,3,4-tetrahydroisoquinoline (**110**) in 66% yield (Scheme 76). The ratio of **109** and **110** was found to be 10:1.

Scheme 76

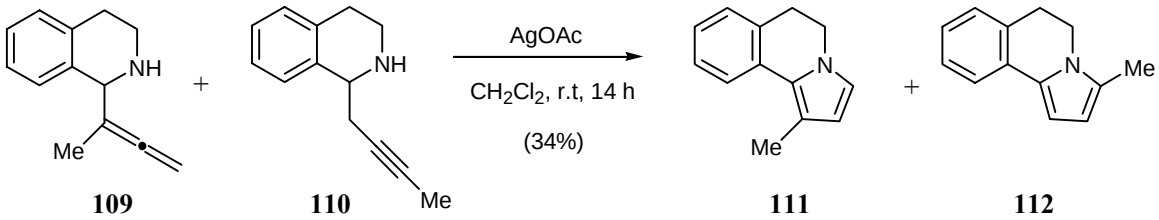


98 (66%) **109** : **110**

10 : 1

On reaction with silver acetate a mixture of **109** and **110** underwent smooth cyclization to the corresponding mixture of **111** and **112** in 34% yield (Scheme 77). The regio isomeric ratio of the starting material was maintained during the transformation.

Scheme 77

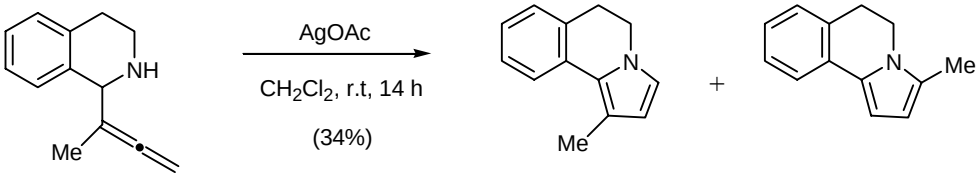


109 **110** **111** **112**

10 : 1 10 : 1

A very careful column chromatography enabled us to isolate compound **109** in pure form. Silver(I)-promoted oxidative cyclization of compound **109** resulted in formation of the pyrroles **111** and **112** as a 10:1 mixture in 34% yield (Scheme 78).

Scheme 78

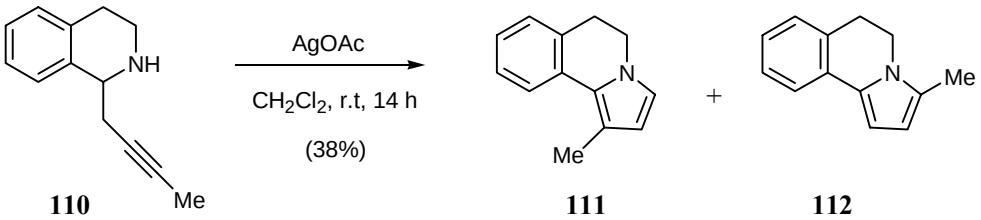


109 **111** **112**

10 : 1

The careful column chromatography enabled us to get also compound **110** in pure form. Treatment of **110** with silver acetate afforded the pyrroles **111** and **112** as a 1:10 mixture in 38% yield (Scheme 79).

Scheme 79



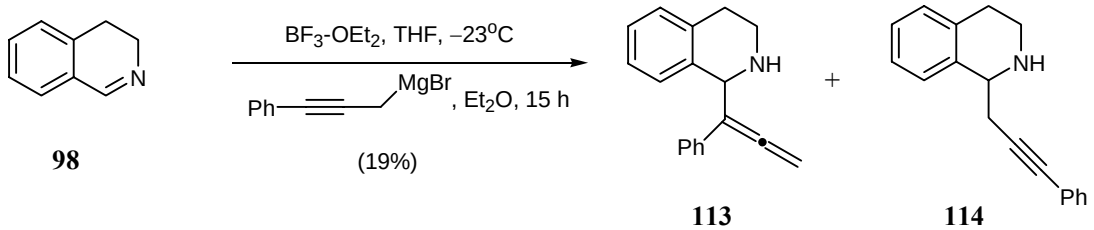
110 **111** **112**

1 : 10

The above studies indicated that the silver(I)-promoted oxidative cyclization of the homopropargylamine **110** favors the formation of the 5-substituted pyrrole **112**, while the allene **109** favors the formation of the 3-substituted pyrrole **111.** However, a complete regio selectivity was not observed during this transformation.

The addition of 3-phenylpropargylmagnesium bromide to 3,4-dihydroisoquinoline in the presence of BF_3-etherare afforded a mixture of 1-(1-phenylpropa-1,2-dienyl)-1,2,3,4-tetrahydroisoquinoline (**113**) and 1-(3-phenylprop-2-ynyl-1,2,3,4-tetrahydroisoquinoline (**114**) in 19% yield (Scheme 80). The ratio of **113** and **114** was found to be 1.5:1.

Scheme 80

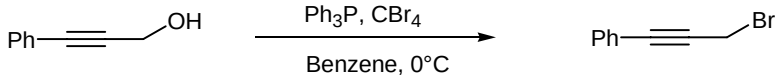


98 **113** **114**

1.5 : 1

The propargyl bromide **116** was obtained from the commercially available alcohol **115** by reaction with CBr_4 and Ph_3P in nearly quantitative yield (Scheme 81).[170]

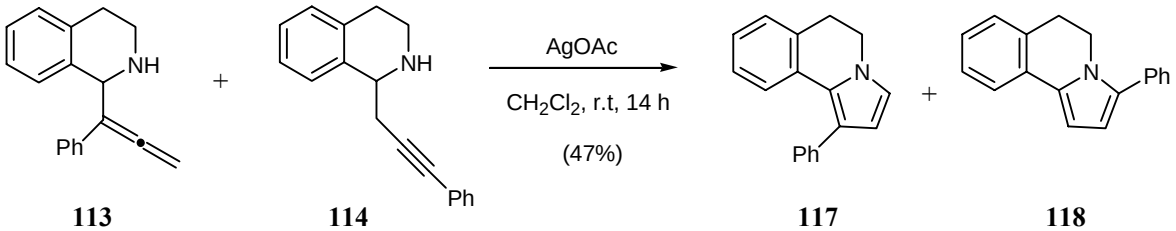
Scheme 81



115 **116**

The separation of the two products **113** and **114** by chromatographic procedures proved to be very difficult. Thus, the mixture of **113** and **114** was converted to the corresponding substituted pyrroles **117** and **118** in 47% yield by treatment with silver acetate in dichloromethane at room temperature (Scheme 82). The regio isomeric ratio of the starting material was also found in product.

Scheme 82

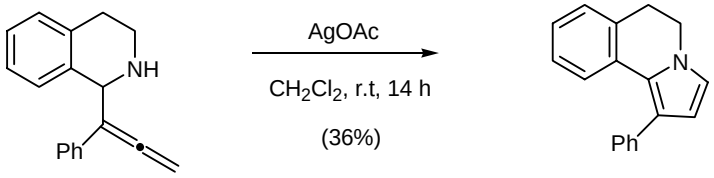


113 **114** **117** **118**

1.5 : 1 1.5 : 1

By column chromatography we were able to isolate compound **113** in pure form. Silver(I)-promoted oxidative cyclization of compound **113** resulted in formation of the pyrrole **117** in 36% yield (Scheme 83).

Scheme 83



113 **117**

The structure of **117** was unambiguously assigned by extensive 2D-NMR investigations. A closer inspection revealed that the regio isomer **118** was also formed in trace quantities.

These studies demonstrate that silver acetate mediates the cyclization process for the synthesis of 1,2-disubstituted and 1,2,3- or 1,2,5-trisubstituted pyrroles.

The ^{13}C NMR spectra provide an excellent tool for the structural analysis of allenes. In general the central sp-hybridized carbon of allenes is found at extremely low field, in the range of 201 - 220 ppm.

3.4.3 Synthesis of monocyclic pyrroles

These successful results encouraged us to examine the applicability of our method to monocyclic pyrroles. Schiff bases, generated from simple arylaldehydes, were reacted with trimethylsilylpropargylmagnesium bromide (**99**) in the presence of BF_3-etherate to give the corresponding homopropargylamines **120a - 120e** in 68 - 88% yields (Scheme 84, Table 19).

Scheme 84

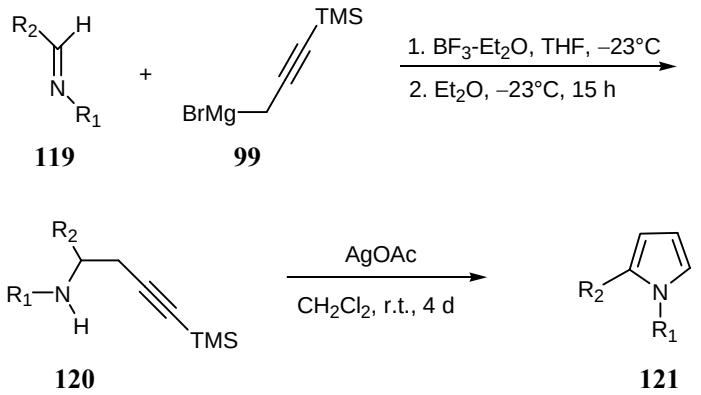


Table 19

Entry	R_1	R_2	120, Yield (%)	Conditions (from 120 to 121)	121, Yield (%)
1(**a**)	4-$MeOC_6H_4$	C_6H_5	78	CH_2Cl_2, r.t, 14 h	35
2				$C_2H_4Cl_2$, reflux, 2 d	59
3				CH_2Cl_2, r.t, 4 d	99
4(**b**)	4-MeC_6H_4	4-$MeOC_6H_4$	80	CH_2Cl_2, r.t, 4 d	85
5				CH_2Cl_2, r.t, 6 d	72
6(**c**)	$C_6H_5CH_2$	C_6H_5	68	CH_2Cl_2, r.t, 14 h	25
7				CH_2Cl_2, r.t, 3.5 d, 2 h reflux	20
8(**d**)	4-$MeOC_6H_4CH_2$	4-$MeOC_6H_4$	68	CH_2Cl_2, r.t, 14 h	20
9				CH_2Cl_2, r.t, 4 d, 1 d reflux	20
10(**e**)	4-$MeOC_6H_4$	C_6H_5CH=CH	88	CH_2Cl_2, r.t, 14 h	42
11				CH_2Cl_2, r.t, 4 d	78

In the course of a detailed investigation of the silver(I)-promoted oxidative cyclization of the homopropargylamine **120a** we found that treatment with silver acetate in dichloromethane at room temperature overnight resulted in formation of **121a** in moderate yield of 35% (entry 1). On heating the reaction mixture in dichloroethane a slight increase in the yield of **121a** was observed (entry 2). An almost quantitative yield of **121a** was obtained by extending the reaction time to 4 days in dichloromethane at room temperature (entry 3).[167] The *N*-Anisyl group constitutes a pyrrole protecting group which could be easily removed to afford the free pyrrole for broader application in organic synthesis.[171]

Treatment of compound **120b** with silver acetate in dichloromethane solution at room temperature for 4 days resulted in formation of pyrrole **121b** in 85% yield along with a little starting material (Table 22, entry 4).[167] On extending the reaction time to 6 days, pyrrole **121b** was obtained in 72% (entry 5).

In order to have an easily removable group on nitrogen, we decided to synthesize *N*-benzyl substituted pyrroles. Treatment of the homopropargylamine **120c** with silver acetate in dichloromethane at room temperature for 14 h afforded the pyrrole **121c** in low yield (25%) along with formation of an uncharacterized by-product (entry 6). Extension of the reaction time at elevated temperature gave similar results (entry 7).

The homopropargylamine **120d** gave the pyrrole **121d** on treatment with silver acetate in a yield of 20% along with the formation of an uncharacterized by-product (entry 8). Extension of the reaction time and increasing the temperature led to similar results (entry 9).

These results indicate that one limitation of our method is the low yield of *N*-benzylpyrroles.

An attempt to obtain a homopropargylamine from an imine prepared from *p*-anisaldehyde and *N*,*N*-dimethylhydrazine failed. Variation of reaction temperature or stoichiometry of BF_3-etherate was ineffective and unreacted starting material was recovered.

As a further demonstration of the functional group tolerance of this new pyrrole synthesis the homopropargylamine **120e** was successfully converted to the corresponding pyrrole **121e**. The imine **119e**, easily prepared from cinnamaldehyde and *p*-anisidine,[172] was transformed to the corresponding homopropargylamine **120e** in 88% yield (entry 10).[167] Subsequent treatment of **120e** with silver acetate in dichloromethane at room temperature for 4 days resulted in smooth formation to **121e** in 78% yield (entry 11). It is noteworthy that conjugated double bonds of α,β-unsaturated imines are tolerated in this reaction.

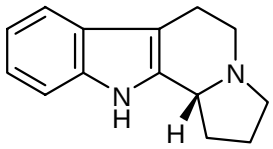
Isolation and characterization of these pyrroles was difficult due to their instability. The electron-rich pyrroles undergo cycloaddition with molecular oxygen (air) and other oxidative processes leading to decomposition.

The structures of the pyrroles were assigned on the basis of their ^1H and ^{13}C NMR, Mass, IR and UV spectroscopic data. The pyrrole protons appeared as doublets or singlets between $\delta = 5.9 - 6.5$ ppm in the ^1H NMR spectrum.

In conclusion, we have developed a novel two-step procedure for the synthesis of pyrroles by addition of a propargyl Grignard reagent to a *Schiff* base and subsequent silver(I)-promoted oxidative cyclization of the resulting homopropargylamine. This reaction proved to be general in scope with the exception of *N*-benzyl-substituted pyrroles, which gave poor yields.

The versatility of this methodology should allow application to the synthesis of biologically important and naturally occurring pyrrole derivatives. This cyclization could be utilized as a key-step for the construction of structurally diverse heterocyclic compounds.

3.5 Total synthesis of (±)-Harmicine [(±)-(**122**)]



122

Nineteen different alkaloids have been isolated from the ethanol extract of the leaves of the Malaysian plant *Kopsia griffithii*.[141] The strong anti-leishmania activity found on preliminary screening was ascribed to the basic fraction of the leaf extract, which draws the attention to the alkaloids. One of the novel alkaloid obtained from *Kopsia griffithii* was harmicine (**122**), an optically active natural product. Harmicine (**122**) has an indolizidino[8,7-*b*]indole framework.

The only total synthesis of harmicine was reported recently by Ohsawa.[173,174] He has synthesized *ent*-harmicine and assigned the absolute configuration of the natural product as *R*. The total synthesis used an asymmetric synthesis of 1-allyl-1,2,3,4-tetrahydro-β-carboline and was accomplished *via* a seven-step sequence from β-carboline.

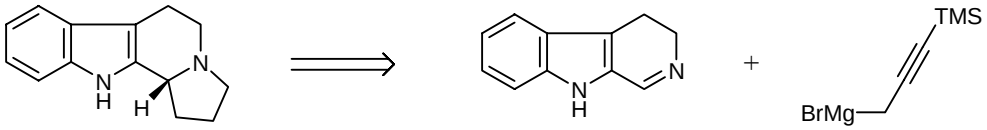
Before the isolation from nature by Kam and Sim in 1998, racemic 2,3,5,6,11,11b-hexahydro-1*H*-indolizino[8,7-*b*]indole [(±)-**122**] was already prepared by synthesis[175-179] and used as a precursor en route to indole alkaloids like (±)-tubifoline, (±)-condyfoline, (±)-geissoschizoline, (±)-fluorocurarine, and others[180-184].

We envisaged a short and direct total synthesis of harmicine (**122**) by using a novel pyrrole synthesis recently developed by us.[167]

3.5.1 Retrosynthetic analysis of Harmicine

We envisioned that harmicine could be obtained using a silver(I)-promoted oxidative cyclization[167] as a key step from the readily available 3,4-dihydro-β-carboline (**12**) and 3-trimethylsilylpropargylmagnesium bromide (**99**) (Scheme 85).

Scheme 85



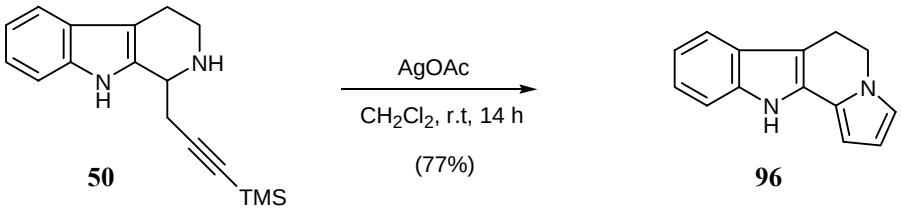
122 **12** **99**

3.5.2 Silver(I)-promoted oxidative cyclization

Compound **50** served already as precursor in our iron-mediated synthesis of yohimbane alkaloids (Sections 3.1, 3.2 and 3.3). Having all the carbon atoms present required for a total synthesis of harmicine (**122**), we thought about a method for cyclization of **50** generating a pyrrole ring. Silver(I) salts are known to provide stable π-complexes with terminal acetylenes.[165] We anticipated that the observed activation of the acetylene may be exploited for a nucleophilic attack onto the acetylene. In case of an intramolecular nucleophile being present, as for compound **50**, the interaction of the silver(I) ion with the acetylene should lead to a silver(I)-promoted cyclization reaction.

Silver(I)-promoted cyclization of substituted allenes to heterocyclic ring systems including 2,5-dihydropyrroles were reported previously.[157,158,169]

Scheme 86



50 **96**

Treatment of **50** with silver acetate in dichloromethane solution at room temperature overnight resulted in complete consumption of the starting material (Scheme 86).[167,185] The only product from this reaction was the dihydroindolizino[8,7-*b*]indole **96** in 77% yield. Although dichloromethane was found to be the most effective solvent, acetone could also be employed as an alternative.

The pyrrole **96** showed evidence of decomposition during flash chromatography, even when silica gel was pre treated with triethylamine. Isolation and characterization of these pyrroles was difficult due to their instability. The electron-rich pyrroles undergo cycloaddition with molecular oxygen (air) and other oxidative processes leading to decomposition.

The successful formation of the dihydroindolizino[8,7-*b*]indole **96** is unambiguously supported by ^{1}H NMR, ^{13}C NMR, IR and MS spectroscopy and additionally, it is corroborated by 2D NOESY experiments.

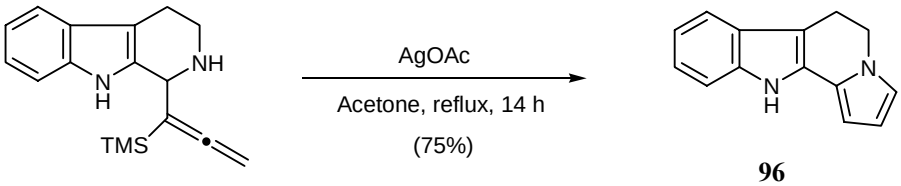
At this stage of our investigations we decided to study the influence of different metals on the oxidative cyclization to the pyrroles. In particular, we were interested to know whether metals like copper and palladium would also affect the cyclization. Therefore, we subjected compound **96** to these metal salts. An optimization of reaction conditions has not been carried out for each case. However, the following results demonstrate that **50** underwent an oxidative cyclization analogous to that with silver (Table 20).

Table 20

Entry	Metal salt	96, Yield [%]
1	$Pd(OAc)_2$	10
2	CuOAc	13

The ability of allenes to undergo either inter- or intramolecular cyclization reactions with a variety of reagents is known for decades.[168] The allene **51**, obtained as a side product during the addition of the propargyl Grignard reagent to the 3,4-dihydro-β-carboline, also underwent smooth silver(I)-promoted oxidative cyclization to the dihydroindolizino[8,7-*b*]indole **96** in 75% yield (Scheme 87).

Scheme 87



51 **96**

Although, the treatment of **51** with silver acetate in dichloromethane solution overnight at room temperature led only to the starting material (Table 21, entry 1), the reaction in boiling acetone was found to be effective for this transformation (entry 2).

Table 21

Entry	Conditions	96, Yield [%] / Remarks
1	CH_2Cl_2, r.t., 14 h	100% SM recov.
2	Acetone, reflux, 14 h	75

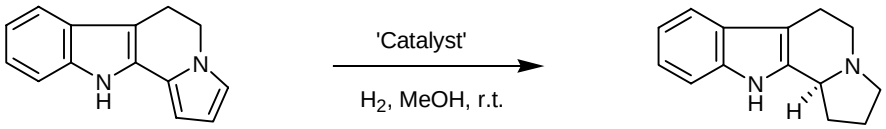
This result demonstrates that the silver(I)-promoted oxidative cyclization reaction can also be performed with allenes as substrates.

It is noteworthy mentioning that both products (**50** and **51**) obtained as a result of addition of trimethylsilylpropargylmagnesium bromide to 3,4-dihydro-β-carboline underwent smooth oxidative cyclization with silver acetate to afford the dihydroindolizino[8,7-*b*]indole **96** in high yields. The formation of compound **96** provides another example of the novel pyrrole synthesis by silver(I)-promoted oxidative cyclization.

3.5.3 Hydrogenation of dihydroindolizino[8,7-*b*]indole

The final step of the total synthesis of harmicine is the hydrogenation of the pyrrole ring (Scheme 88, Table 22). Pyrroles can be chemoselectively hydrogenated at atmospheric pressure in the presence of other aromatic ring systems.[186,187]

Scheme 88



96 **122**

A number of standard catalysts for the hydrogenation of **96** including PtO_2 and Rh/Alox were attempted without any success (entries 1 and 2). Hydrogenation of the pyrrole ring in the case of cephalotaxine alkaloids has been successfully carried out using Rhodium on charcoal.[186] Thus, we decided to examine Rh/C as hydrogenation catalyst in methanol. Recovery of starting material was observed even after 8 days of heating (entry 4).

Table 22

Entry	Catalyst / Conditions	122, Yield [%]/ Remarks
1	PtO_2, MeOH, 8 days, r.t.	SM recov.
2	Rh/Alox, MeOH, 17 days, r.t.	-
3	Rh/C, MeOH, 8 days, r.t.	Trace + SM
4	Rh/C, MeOH, 8 days, reflux	SM recov.
5	Rh/C, MeOH + CH_3COOH, 18 h, r.t.	SM recov.
6	Rh/C, MeOH + CH_3COOH, 8 days, r.t.	88

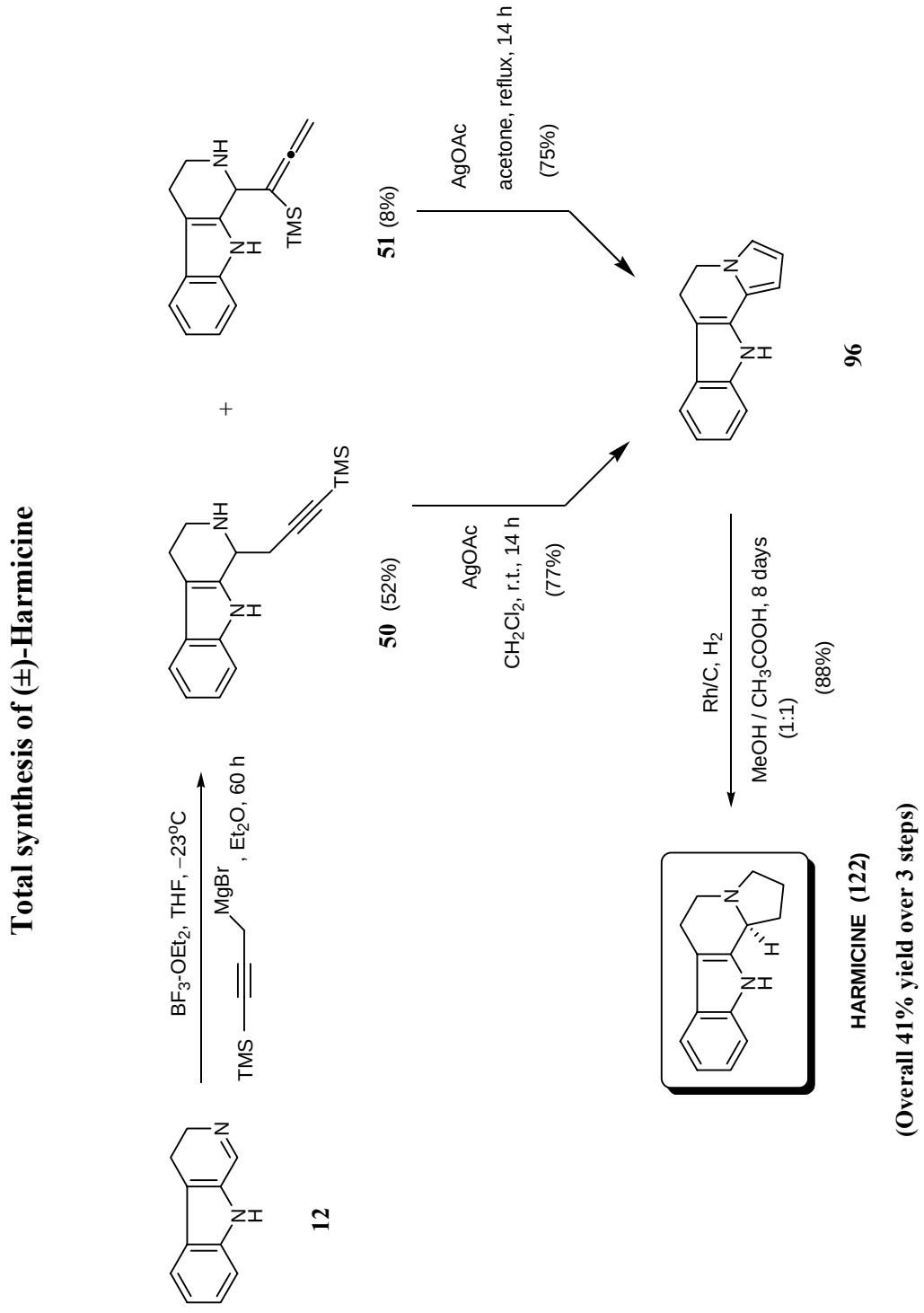
Finally, a chemoselective hydrogenation of the pyrrole ring of **96** using 5% rhodium on activated charcoal as catalyst in methanol/acetic acid (1:1) at room temperature provided directly (±)-harmicine [(±)-**122**], without any further purification, in excellent yield of 88% (entry 6).[185]

The spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR, MS) of our synthetic harmicine are in full agreement with those reported for the natural product. The observation of Bohlmann's bands in the IR spectrum (2780 and 2835 cm^{-1}) suggests that the C/D ring junction is *trans*.

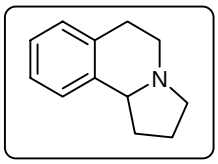
In conclusion, we developed a straightforward synthesis providing (±)-harmicine [(±)-**122**] in three steps and 41% overall yield from 3,4-dihydro-β-carboline (**12**) (Scheme 89).[185] The efficiency and the economy of steps of this sequence are noteworthy.

The application of the silver(I)-promoted cyclization to the total synthesis of (±)-harmicine has shown the value of this reaction for organic chemistry.

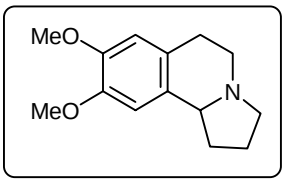
Scheme 89


Total synthesis of (±)-Harmicine
12
BF3-OEt2, THF, –23°C
MgBr
TMS
, Et2O, 60 h
+
50 (52%)
51 (8%)
AgOAc
CH2Cl2, r.t., 14 h
(77%)
AgOAc
acetone, reflux, 14 h
(75%)
96
Rh/C, H2
MeOH / CH3COOH, 8 days
(1:1)
(88%)
HARMICINE (122)
(Overall 41% yield over 3 steps)

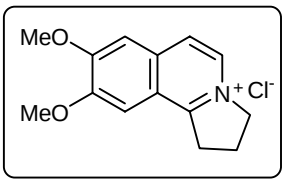
3.6 Synthesis of 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (123) and total synthesis of crispine A (124)



123



124



125

Pyrrolidinoisoquinoline alkaloids and their derivatives are found in a variety of natural products and other pharmacologically important compounds. 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (**123**) is an unnatural bioactive compound. The pyrrolidinoisoquinoline **123** was first obtained by the degradative reduction of the alkaloid norsecurinone during its structural elucidation.[188] Derivatives of this compound are known to show antidepressant activities.[189] Recently, it has been discovered that the pyrrolidinoisoquinoline **123** shows a strong affinity towards α_2-adrenoceptors.[190] α_2-Adrenoceptors are potentially useful in the treatment of disease states such as depression, age-dependent memory impairment, impotence and sexual dysfunction, and a variety of vascular disorders. Due to these important and interesting biological activities the pyrrolidinoisoquinoline **123** has been a target of various synthetic approaches.[191-194]

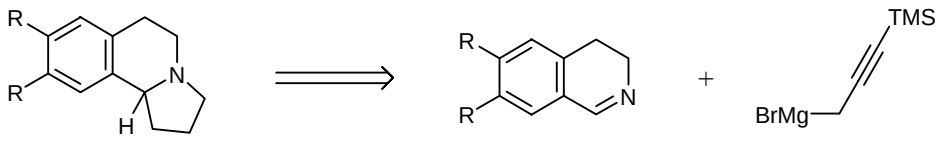
Crispine A (**124**) and B (**125**) are among the four novel isoquinoline alkaloids isolated from the extracts of *Carduus crispus*.[140] *Carduus crispus L.* has been used in Chinese folk medicine for the treatment of cold, stomach ache and rheumatism. Moreover, a screening test revealed that the extracts *in vitro* inhibit the growth of some human cancer lines and exhibit a significant cytotoxic activity. Before the isolation from nature in 2002, racemic 8,9-dimethoxy-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (±)-**124** was already prepared by synthesis.[195,196]

Recently we developed a novel, general and efficient method for the construction of the pyrrole ring and fused aromatic pyrroloheterocycles *via* silver(I)-promoted oxidative cyclization of homopropargylamines.[167] The synthetic utility of this novel method was demonstrated by the shortest synthesis of (±)-harmicine (three steps and 42% overall yield).[185] Our interest in the above mentioned isoquinoline alkaloids was prompted by the desire to explore the silver(I)-promoted oxidative cyclization as a key strategy for the assembly of these compounds.

3.6.1 Retrosynthetic analysis of 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline and crispine A

The retrosynthetic analysis of 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (**123**) and crispine A (**124**) based on the silver(I)-promoted oxidative cyclization for the construction of the pyrrolo[2,1-*a*]isoquinoline framework leads to 3,4-dihydroisoquinoline (**98**), 6,7-dimethoxy-3,4-dihydroisoquinoline (**125**), and 3-trimethylsilylpropargylmagnesium bromide (**99**) (Scheme 90).

Scheme 90



123 R = H
124 R = OMe

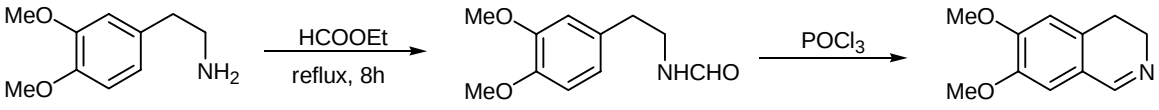
98 R = H
125 R = OMe

99

3.6.2 Silver(I)-promoted oxidative cyclization

6,7-Dimethoxy-3,4-dihydroisoquinoline (**125**) was readily prepared by Bischler-Napieralski cyclization of the *N*-formylphenylethylamine (**127**), which in turn is obtained from the commercially available amine **126** (Scheme 91).[197]

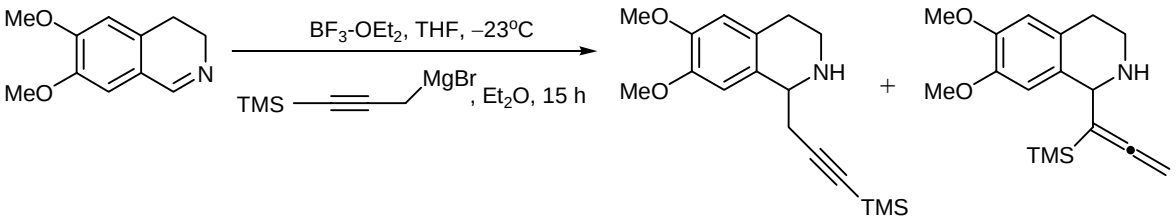
Scheme 91



126 **127** **125**

The alkylation of 6,7-dimethoxy-3,4-dihydroisoquinoline (**125**) with 3-trimethylsilylpropargylmagnesium bromide in the presence of BF_3-etherate provided 6,7-dimethoxy-1-(3-trimethylsilylpropargyl)-1,2,3,4-tetrahydroisoquinoline (**128**) in 61% yield along with 6,7-dimethoxy-1-(3-trimethylsilylpropa-1,2-dienyl)-1,2,3,4-tetrahydro-isoquinoline (**129**) in 2% yield (Scheme 92).[198]

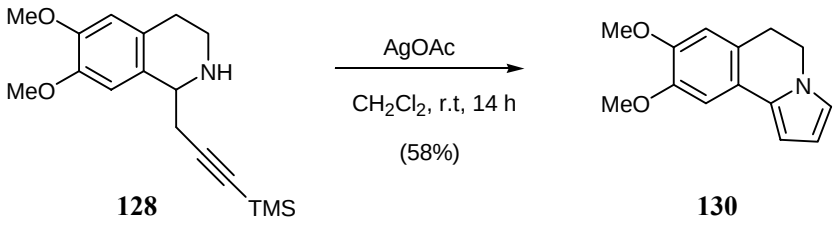
Scheme 92



125 **128** (61%) **129** (2%)

Compound **128** was successfully transformed to the dihydropyrrolo[2,1-*a*]isoquinoline **130** in 58% yield upon its treatment with silver acetate in dry dichloromethane (Scheme 93).[198]

Scheme 93

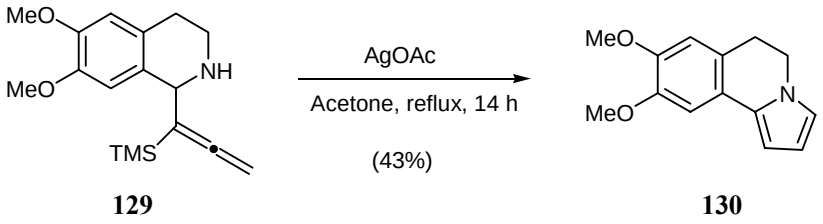


128 **130**

The above results clearly demonstrate that our silver(I)-promoted oxidative cyclization is a simple, straightforward and highly efficient process for the synthesis of pyrroles.

Our model studies already revealed that allenes also undergo a silver(I)-promoted oxidative cyclization to afford the corresponding pyrroles. The treatment of allene **129** with silver acetate in boiling acetone for 14 h resulted in smooth oxidative cyclization forming the dihydropyrrolo[2,1-*a*]isoquinoline **130** in 43% yield (Scheme 94).

Scheme 94

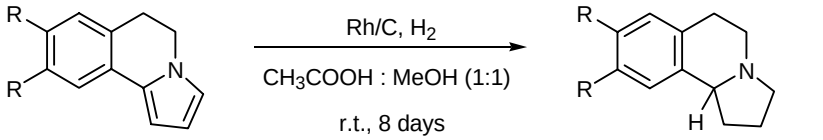


129 **130**

3.6.3 Hydrogenation of the dihydropyrrolo[2,1-*a*]isoquinoline

The final step to achieve the total syntheses of 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (**123**) and crispine A (**124**) is the chemoselective hydrogenation of the pyrrole ring. It is already known that pyrroles can be chemoselectively hydrogenated at atmospheric pressure in the presence of benzene rings.[186,187]

Scheme 95



102 R = H
130 R = OMe

123 R = H (91%)
124 R = OMe (66%)

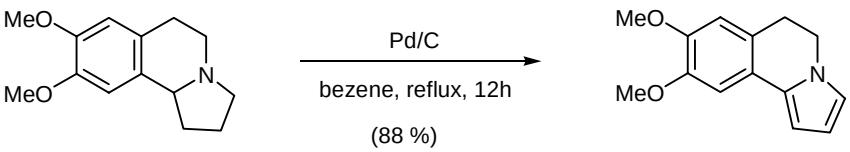
The synthesis of the dihydropyrrolo[2,1-*a*]isoquinoline **102** has been described during our model studies in Section 3.4. A chemoselective hydrogenation of the pyrrole ring of **102** using 5% rhodium on activated charcoal as a catalyst in methanol/acetic acid (1:1) at room temperature provided directly (±)1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline [(±)-**123**] in an excellent yield of 91% (Scheme 95). Under the same conditions the catalytic hydrogenation of **130** afforded (±)-crispine A [(±)-**124**] in 66% yield.[198]

The spectroscopic data (IR, ^{1}H NMR, ^{13}C NMR, and MS) of our synthetic crispine A are in full agreement with those reported for the natural product.[140]

For the transformation of crispine A to crispine B several conditions were tested [(a) I_2, KOAc, EtOH, reflux, 15 min; (b) DDQ, reflux, 12 h; (c) MnO_2, benzene, reflux)], but all attempts led to decomposition of the starting material.

In another attempt crispine A was heated in benzene in the presence of a catalytic amount of palladium on charcoal. This experiment afforded the dihydropyrrolo[2,1-*a*]isoquinoline **130** in 88% yield (Scheme 96).[198]

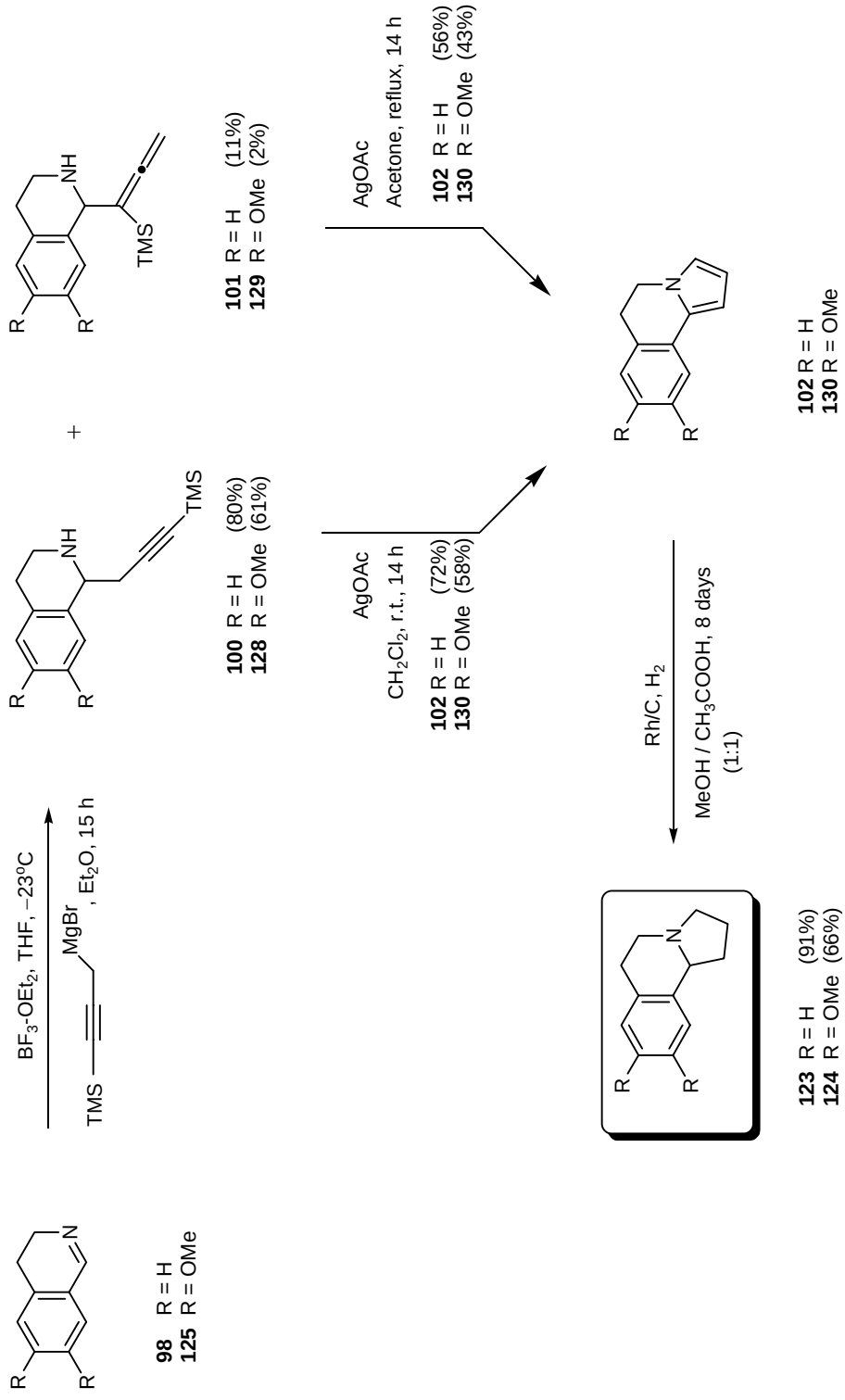
Scheme 96



124 **130**

In conclusion, a highly efficient synthesis of the biologically active 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (**123**) and the total synthesis of the antitumor active alkaloid (±)-crispine A (**124**) have been achieved in a three-step sequence with 58% and 24% overall yields using the silver(I)-promoted oxidative cyclization as the key strategy (Scheme 97).[198] This strategy represents a conceptually novel and highly expeditious route towards certain polycyclic alkaloid skeletons. Moreover, our approach can be easily applied to the synthesis of a wide range of synthetic analogues for structure-activity studies.

Synthesis of 1,2 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*] isoquinoline (123) and total synthesis of crispine A (124)



Scheme 97

4 Conclusion

A general strategy for the concise syntheses of various members of the yohimbane alkaloid family has been developed. The key strategic element for the formation of the pentacyclic ring system is the highly efficient iron-mediated [2+2+1] cycloaddition of a diyne. The iron-complex **13** has been prepared in high yield by cycloaddition of the bis-TMS-diyne **46** which in turn is conveniently obtained by the *C*-alkylation of 3,4-dihydro-β-carboline (**12**) followed by *N*-alkylation. Demetalation of the iron-complex **13** followed by hydrogenation of the free ligand **53** with 30% Pd/C as hydrogenation catalyst provided **56**. There is no literature precedence, to our knowledge, for this type of 1,4-addition of hydrogen to a conjugated diene in the presence of a carbonyl functionality. Stereoselective hydrogenation of **56** with Adams's catalyst provided the *cis*-cyclopentanone **44**. E-Ring expansion of **44** with trimethylsilyldiazomethane followed by Wolff-Kishner reduction afforded (±)-alloyohimbane [(±)-**2**]. The total synthesis of the biologically active alkaloid alloyohimbane **2** has been achieved by a convergent and highly modular approach in eight steps and 7% overall yield based on 3,4-dihydro-β-carboline. Isomerization of the deconjugated enone **56** on treatment with silica gel afforded a mixture of the conjugated enones **66a** and **66b**. Hydrogenation of **66a** afforded the *trans*-cyclopentanone **45**. E-Ring expansion of **45** and Wolff-Kishner reduction provided 3-epialloyohimbane **3** and nor-3-epialloyohimbane **68**. This method can serve as a short and efficient approach towards polycyclic alkaloids. In an attempt of a total synthesis of rauniticine the diyne **74** was successfully transformed to the iron-complex **73**. The iron-mediated cycloaddition proved to be a powerful synthetic method. Demetalation of the iron-complex **73** followed by hydrogenation provided the ketone **72** as a single isomer with all hydrogen atoms at stereogenic centers on the same face. All attempts of Baeyer-Villiger oxidation of **72** failed. A novel procedure for pyrrole annulations by silver(I)-promoted oxidative cyclization of homopropargylamines has been developed. It was shown that a broad variety of substituted monocyclic pyrroles can be prepared by this novel methodology. The formation of the dihydropyrrolo[2,1-

a]isoquinoline **96** *via* the silver(I)-promoted cyclization of the homopropargylamine **50** has been used for a synthesis of (±)-harmicine [(±)-**122**]. The total synthesis of harmicine has been achieved in three-steps and 41% overall yield. The silver(I)-promoted oxidative cyclization has been successfully applied to the total synthesis of the antitumor active pyrrole[2,1-*a*]isoquinoline alkaloid (±)-crispine A [(±)-**124**] (three steps and 24% overall yield) and for the biologically active 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (**123**) (three steps and 58% overall yield).

5 Experimental section

5.1 General Methods

All reactions were carried out under Argon in flame-dried glassware using standard Schlenck-line and glove box techniques unless otherwise indicated.

Tetrahydrofuran (THF) and diethyl ether were freshly distilled from sodium/ benzophenone under argon. Other solvents used for reactions were purified according to standard procedures.

Thin layer chromatography (TLC) was performed on Merck precoated silica gel F254 aluminium foil. Visualization was accomplished with UV light and / or phosphomolybdic acid solution followed by heating. Flash chromatography was performed using Merck flash silica gel 60 (40μm).

Melting points were measured with an apparatus Heiztischmikroskop H600 and are uncorrected.

UV spectra were obtained on a Perkin Elmer Lambda UV/Vis spectrometer. The wavelengths are reported in nm.

IR spectra were obtained on an Avatar 360 FT-IR spectrometer and were measured by ATR method. The wavelengths are reported in cm^{-1}.

NMR spectra were obtained on a Bruker advance DRX 500. ^{1}H NMR shifts were obtained in $CDCl_3$ and reported in ppm relative to the solvent shift of residual chloroform of $\delta = 7.26$. Chemical shift values δ (ppm) are based on the signal of residual deuterated solvent. ^{13}C NMR shifts were obtained in $CDCl_3$ and reported in ppm relative to $CDCl_3$

77.0. Chemical shift values δ (ppm) are based on the signal of residual deuterated solvent.

Mass spectra and HRMS measurements were performed on a TGA 100 from Leybold AG; ionization potential: 70 eV.
GC-MS spectra were obtained at an ionization potential of 70 eV on HP 5890/5891 series GC/MSD

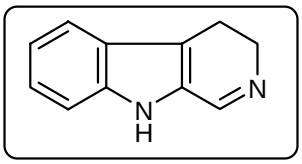
Elemental analysis was obtained on a Euro Vector CHNS-O elemental analyzer.

X-ray analyses: The data were collected on a STOE STADI-4 diffractometer using Mo-Kα radiation. The program SCHAKAL-92 was used for the graphical representation of the crystal structures. All ORTEP diagrams were produced with the Ortep3 software package.

5.2 Experimental procedure and spectral data

5.2.1 Referring to Section 3.1

3,4-Dihydro-β-carboline (12)



A solution of tryptamine **47** (10 g, 62.5 mmol) in ethyl formate (200 mL) was refluxed for 8 h and then the solvent was removed under reduced pressure to afford *N*-formyl-tryptamine. The crude *N*-formyl-tryptamine thus obtained was treated with phosphoryl chloride (50 mL) and stirred for 3 h at room temperature. The reaction mixture was poured onto crushed Ice. The aqueous solution was filtered and neutralized with NaOH solution and further basified with ammonia solution (200 mL). The precipitated 3,4-dihydro-β-carboline **12** was filtered, washed with water and dried.

Yield: 10 g (94%); pale yellow crystals

M.P.: 124 - 126°C

UV (MeOH): λ = 206, 318 nm.

IR (drift): ν = 3394, 3058, 2918, 2834, 2731, 1623, 1570, 1548, 1450, 1375, 1323, 1303, 1224, 1163, 1114, 1041, 1009, 983, 949, 869, 738, 659, 620, 593, 574, 555 cm^{-1}.

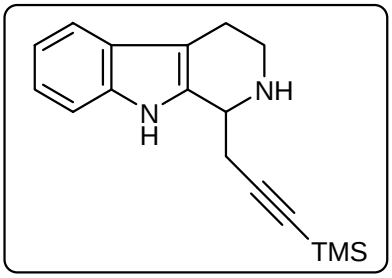
^{1}H-NMR (500 MHz, MeOD): δ = 2.95 (t, *J* = 8.49 Hz, 4H), 3.88 - 3.92 (m, 1H), 7.12 - 7.15 (m, 1H), 7.28 - 7.31 (m, 1H), 7.44 (d, *J* = 8.3 Hz, 1H), 7.62 (d, *J* = 8.06 Hz, 1H), 8.38 (m, 1H).

^{13}C-NMR and DEPT (125 MHz, MeOD): δ = 19.98 (CH_2), 48.90 (CH_2), 113.32 (CH), 117.22 (C), 120.88 (CH), 121.07 (CH), 125.71 (CH), 126.27 (C), 129.36 (C), 139.17 (C), 154.13 (CH).

MS (150°C): *m/z* (%) = 170 (78, M^+), 169 (100), 142 (14), 115 (10), 18 (11).

HRMS: $C_{11}H_{10}N_2$ **C**alculated: 170.0844 found: 170.0853.

1-(3-Trimethylsilylprop-2-ynyl)-2,3,4,9-tetrahydro-1H-β-carboline (50) and 1-(1-Trimethylsilylpropa-1,2-dienyl)-2,3,4,9-tetrahydro-1H-β-carboline (51)



To a solution of 3,4-dihydro-β-carboline **12** (2.1 g, 12.35 mmol) in dry THF (50 mL) was added drop wise $BF_3{\cdot}OEt_2$ (1.6 mL, 12.35 mmol) at –23°C. After stirring for 0.5 h, a solution of trimethylsilylpropargyl magnesium bromide (37.05 mmol) in dry diethyl ether (20 mL) was added drop wise to this suspension. After stirring for 60 h at –23°C, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl (100 mL) and extracted with EtOAc (4 × 100 mL). The combined organic layers were washed with H_2O (50 mL) and dried with Na_2SO_4. Evaporation of the solvent in *vacuo* and flash chromatography of the residue on silica gel (Hexane/EtOAc 1:1) afforded in the sequence of increasing polarity the compounds **51** as yellow crystals, yield: 274 mg (8%), **50** as light yellow crystals, yield: 1.8 g (52%).

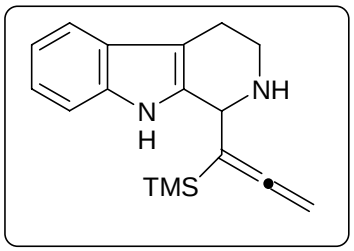
Spectroscopic data for compound **50**

M.P.: 111 - 114°C

Elemental Analysis:	Calculated:	C: 72.29	H: 7.85	N: 9.92
	Found:	C: 72.24	H: 8.15	N: 9.75.

For further spectroscopic data see reference[109]

1-(1-Trimethylsilylpropa-1,2-dienyl)-2,3,4,9-tetrahydro-1H-β-carboline (51)



M.P.: 86°C

UV (MeOH): λ = 193, 226, 283, 290 nm.

IR (drift): ν = 3411, 3345, 3138, 3053, 2928, 2840, 2755, 1924, 1879, 1756, 1642, 1622, 1587, 1505, 1470, 1445, 1345, 1324, 1308, 1297, 1244, 1225, 1195, 1155, 1144, 1092, 1052, 1008, 973, 849, 783, 735, 716, 696, 639, 614 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.12 (s, 9H), 1.69 (s, 1H), 2.69 - 2.74 (m, 1H), 2.76 - 2.82 (m, 1H), 3.02 (hept., *J* = 4.3 Hz, 1H), 3.32 - 3.36 (m, 1H), 4.46 - 4.50 (m, 2H), 4.78 (t, *J* = 1.65 Hz, 1H), 7.08 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.14 (dt, *J* = 7.5, 1.2 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.8 Hz, 1H), 7.73 (br s, 1H).

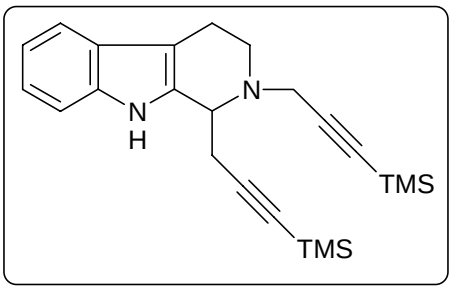
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = –0.67 ($3CH_3$), 22.54 (CH_2), 42.85 (CH_2), 55.53 (CH), 70.47 (CH_2), 97.93 (C), 109.21 (C), 110.72 (CH), 118.13 (CH), 119.20 (CH), 121.37 (CH), 127.57 (C), 135.21 (C), 135.51 (C), 210.13 (C).

MS (80°C): *m*/*z* (%) = 282 (1, M^+), 172 (11), 171 (100), 170 (2), 169 (5), 156 (1), 144 (4), 73 (4).

HRMS: $C_{17}H_{22}N_2Si$ **C**alculated: 282.1552 found: 282.1546.

Elemental Analysis:	Calculated:	C: 72.34	H: 7.80	N: 9.92
	Found:	C: 71.97	H: 7.72	N: 9.88.

1,2-Bis-(3-Trimethylsilyl-prop-2-ynyl)-2,3,4,9-tetrahydro-1H-β-carboline (46)



A solution of 3-(trimethylsilyl)-propargyl bromide (407 mg, 2.12 mmol) in dry THF (10 mL) was added to a mixture of compound **50** (500 mg, 1.77 mmol), Na_2CO_3 (940 mg, 8.85 mmol), TBAI (50 mg) and dry THF (40 mL) and stirred at r.t for 60 h under argon atmosphere. The reaction mixture was poured into saturated aqueous solution of NH_4Cl (50 mL), extracted with EtOAc (4 × 100 mL) and dried over anhydrous Na_2SO_4 and subsequently concentrated in *vacuo.* The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 15:1) to afford the product **46** as yellow solid.

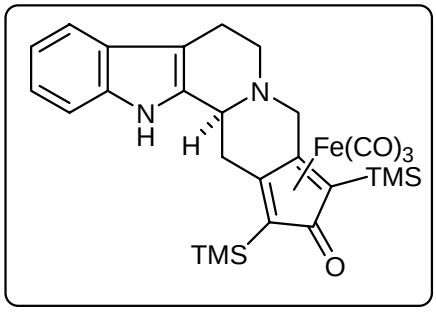
Yield: 653 mg (94%); yellow solid.

M.P.: 64 - 67°C

Elemental Analysis:	**C**alculated	C: 70.41%	H: 8.16%	N: 7.14%
	Found	C: 71.16%	H: 7.91%	N: 7.65%

For further spectroscopic data see reference[74]

Tricarbonyl [η^4-16,18-bis(trimethylsilyl)-15,18-diene-17-keto-nor-yohimbane]iron (13)



A solution of compound **46** (1.15 g, 2.93 mmol) and pentacarbonyliron (1.15 g, 5.88 mmol) in 1,2-dimethoxyethane (40 mL) was prepared in a glass ampoule inside the glove box. Ampoule was sealed and heated at 140^{o}C for 24 h. Then the solvent was

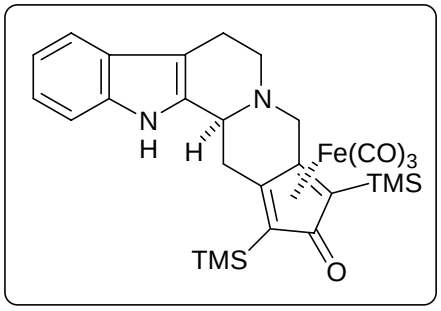
removed in *vacuo* and flash chromatography of the residue on silica gel (Hexane/EtOAc 3:1) provided the tricarbonyl[η^4-cyclopentadienone]iron complex **13**.

Yield: 1.56 g (95%); Yellowish Orange Crystal.

M.P.: 198°C

For further spectroscopic data see reference[74]

Spectroscopic data for *anti*-13



M.P.: 206°C

UV (MeOH): λ = 196, 224, 290 nm.

IR (KBr): ν = 3302, 3049, 2951, 2903, 2849, 2799, 2071, 2018, 1999, 1591, 1494, 1457, 1457, 1408, 1363, 1332, 1322, 1278, 1254, 1159, 1137, 1102, 1070, 1049, 1006, 988, 969, 845, 803, 768, 744, 695, 616 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.30 (s, 9H), 0.32 (s, 9H), 2.78 - 2.87 (m, 3H), 2.95 - 3.03 (m, 2H), 3.21 (dd, *J* = 10.78, 4.9 Hz, 1H), 3.64 (d, *J* = 15.35 Hz, 1H), 3.78 (d, *J* = 10.9 Hz, 1H), 3.96 (d, *J* = 15.36 Hz, 1H), 7.13 - 7.16 (m, 1H), 7.19 - 7.22 (m, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.52 (d, *J* = 7.73 Hz, 1H), 7.75 (br s, 1H).

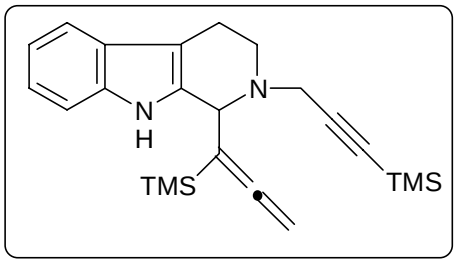
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = –0.43 (CH_3), –0.33 (CH_3), 21.42 (CH_2), 32.72 (CH_2), 52.07 (CH_2), 53.31 (CH_2), 55.16 (CH), 70.91 (C), 71.33 (C), 108.42 (C), 109.27 (C), 109.44 (C), 110.96 (CH), 118.42 (CH), 119.89 (CH), 122.23 (CH), 126.88 (C), 132.39 (C), 136.48 (C), 180.72 (CO), 208.77 (CO).

MS (210°C): *m/z* (%) = 560 (1, M^+), 545 (2), 532 (22), 506 (8), 505 (27), 504 (61), 478 (11), 477 (32), 476 (100), 460 (11), 403 (9), 387 (6), 238 (9), 170 (9), 73 (15), 58 (19), 57 (12), 43 (51).

HRMS: $C_{27}H_{32}FeN_2Si_2O_4$ **C**alculated: 560.1250 found: 560.1245.

Elemental Analysis:	**C**alculated	C: 57.85%	H: 5.75%	N: 5.00%
	Found	C: 57.43%	H: 5.82%	N: 4.88%

1-(1-Trimethylsilylpropa-1,2-dienyl)-2-(3-trimethylsilanyl-prop-2-ynyl)-2,3,4,9-tetrahydro-1H-β-carboline (52)



A solution of 3-(trimethylsilyl)-propargyl bromide (194 mg, 1.02 mmol) in dry THF (10 mL) was added to a mixture of compound **51** (220 mg, 0.78 mmol), Na_2CO_3 (414 mg, 3.91 mmol), TBAI (30 mg) and dry THF (40 mL) and heated at 50°C for 48 h under argon atmosphere. The reaction mixture was quenched with saturated aqueous solution of NH_4Cl (25 mL), extracted with EtOAc (4 × 50 mL) and dried over anhydrous Na_2SO_4 and subsequently concentrated in *vacuo.* The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 15:1) to afford the product **52**.

Yield: 256 mg (84%); light yellow solid.

M.P.: 120°C

UV (MeOH): λ = 198, 226, 284, 292 nm.

IR (KBr): ν = 3459, 2952, 2899, 2847, 2822, 2784, 2160, 1928, 1458, 1452, 1441, 1373, 1357, 1320, 1303, 1267, 1243, 1201, 1161, 1113, 1095, 1069, 1042, 1009, 974, 941, 914, 838, 759, 749, 697, 679, 628, 603, 577 cm^{-1}.

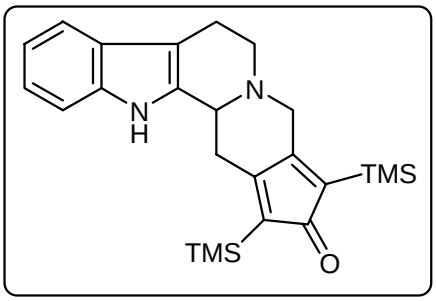
^{1}H-NMR (500 MHz, $CDCl_3$): δ = – 0.05 (s, 9H), 0.17 (s, 9H), 2.76 - 2.90 (m, 3H), 3.15 - 3.17 (m, 1H), 3.53 (d, *J* = 17 Hz, 1H), 3.65 (d, *J* = 17 Hz, 1H), 4.55 (m, 3H), 7.08 - 7.16 (m, 4H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.68 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = –0.80 ($3CH_3$), 0.08 ($3CH_3$), 21.29 (CH_2), 44.74 (CH_2), 49.40 (CH_2), 61.33 (CH), 69.44 (CH_2), 90.10 (C), 96.59 (C), 101.19 (C), 108.52 (C), 110.68 (CH), 118.13 (CH), 119.24 (CH), 121.31 (CH), 127.26 (C), 134.36 (C), 135.88 (C), 211.49 (C).

MS (75°C): *m*/*z* (%) = 392 (1, M^+), 377 (4), 283 (11), 282 (47), 281 (100), 169 (23), 73 (7).

HRMS: $C_{23}H_{32}N_2Si_2$	**C**alculated: 392.2104		found: 392.2105.	
Elemental Analysis:	**C**alculated	C: 70.35%	H: 8.21%	N: 7.13%
	Found	C: 69.53%	H: 8.28%	N: 6.67%

16,18-bis(trimethylsilyl)-15,18-diene-17-keto-nor-yohimbane (53)



A three neck 120 mL Pyrex flask equipped with an inner jacket which is cooled continuously by circulating oil with the help of cryostat, is flushed with argon and charged with iron-complex **13** (500 mg, 0.89 mmol) and acetonitrile (120 mL). The stirred reaction mixture is irradiated by a 150 W middle pressure Hg lamp at –40°C for 2.5 h with continuous purging of argon. A suitable lamp

circuit, constructed to avoid contact of the circulating oil with the lamp, is made with quartz tube. Efficient stirring of the flask contents is essential to avoid deposition of Iron complex on the walls of the flask, which will reduce light intensity. After 2.5 h of irradiation, air is bubbled into the reaction mixture for 40 minutes and finally filtered over a bed of celite-577 and rinsed thoroughly with EtOAc, the solvent was evaporated, and the residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 10:1) to afford the product **53**.

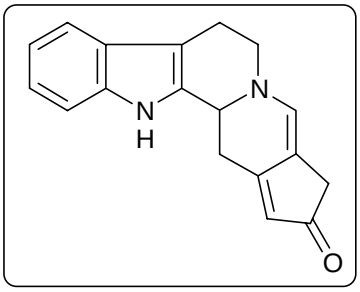
Yield: 355 mg (95%); bright orange crystals

M.P.: 158 - 162°C.

Elemental Analysis:	**C**alculated	C: 68.52%	H: 7.67%	N: 6.66%
	Found	C: 68.76%	H: 7.81%	N: 6.56%

For further spectroscopic data see reference[74]

15,19-diene-17-keto-nor-yohimbane (54)



A solution of **53** (158 mg, 0.376 mmol) in methanol (20 mL) was vigorously stirred in presence of Ruthenium on carbon (10% by wt., 16 mg) in the hydrogen atmosphere at room temperature for 20 h. The catalyst was filtered off over a bed of celite, which was subsequently rinsed with methanol and the filtrate was concentrated. The residue was subjected to flash chromatography on silica gel (EtOAc) to provide the compound **54**.

Yield: 10 mg (10%); light yellow crystals.

M.P. 136 - 138°C

UV (MeOH): λ = 196, 223, 272, 397 nm.

IR (drift): ν = 3270, 2916, 2848, 1744, 1617, 1540, 1452, 1376, 1322, 1301, 1268, 1246, 1178, 1146, 1089, 1054, 1008, 990, 933, 846, 743, 689 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.80 (m, 2H), 2.96 (m, 3H), 3.33 (m, 2H), 3.58 (m, 1H), 4.46 (m, 1H), 5.71 (s, 1H), 6.48 (s, 1H), 7.12 (m, 2H), 7.36 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 8.23 (br s, 1H).

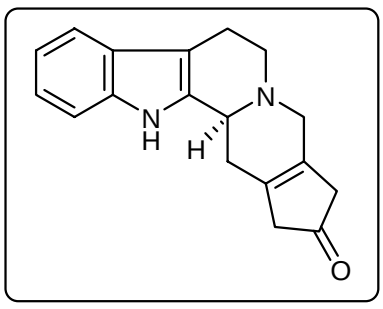
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 22.48 (CH_2), 32.53 (CH_2), 38.80 (CH_2), 51.44 (CH_2), 53.77 (CH), 109.48 (C), 111.20 (C), 111.55 (CH), 118.70 (CH), 120.33 (CH), 120.42 (CH), 122.69 (CH), 127.12 (C), 132.34 (C), 136.71 (C), 136.82 (CH), 168.24 (C), 206.52 (CO).

MS (120°C): *m*/*z* (%) = 276 (100, M^+), 275 (49), 247 (16), 169 (13), 58 (13), 43 (36).

HRMS: $C_{18}H_{16}N_2O$ Calculated: 276.1262 found: 276.1257

15,19-Dehydro-17-keto-nor-yohimbane (56)

A solution of **53** (96 mg, 0.229 mmol) in methanol (10 mL) was vigorously stirred in presence of 30% Pd/C (15% by wt., 15 mg) in the hydrogen atmosphere at room temperature for 14 h at 20°C. The catalyst was filtered off over a bed of celite, which was subsequently rinsed with methanol and the filtrate was concentrated. The residue



was subjected to flash chromatography on silica gel (EtOAc) to provide the compound **56**.

Yield: 62 mg (98%); colourless crystals

M.P. 203°C

UV (MeOH): λ = 224, 281 nm.

IR (drift): ν = 3365, 3053, 2893, 2848, 2788, 2757, 1750, 1690, 1625, 1593, 1494, 1473, 1453, 1426, 1388, 1360, 1342, 1325, 1311, 1273, 1262, 1237, 1221, 1209, 1186, 1168, 1154, 1144, 1125, 1096, 1060, 1043, 1007, 965, 945, 917, 878, 840, 811, 797, 759, 737, 683, 674, 626 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.37 (dt, *J* = 12.5, 2.0 Hz, 1H), 2.55 (br d, *J* = 16.52 Hz, 1H), 2.72 - 2.81 (m, 2H), 2.89 - 2.93 (m, 3H), 2.98 - 3.06 (m, 2H), 3.17 - 3.25 (m, 2H), 3.49 (br d, *J* = 15.43 Hz, 1H), 3.70 (dd, *J* = 9.6, 1.8 Hz, 1H), 7.09 - 7.18 (m, 2H), 7.31 (d, *J* = 7.95 Hz, 1H), 7.50 (d, *J* = 7.69 Hz, 1H), 7.77 (br s, 1H).

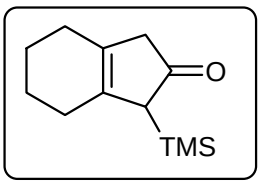
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.53 (CH_2), 31.93 (CH_2), 44.49 (CH_2), 45.64 (CH_2), 52.23 (CH_2), 54.44 (CH_2), 55.76 (CH), 108.74 (C), 110.71 (CH), 118.22 (CH), 119.53 (CH), 121.66 (CH), 127.02 (C), 130.34 (C), 131.71 (C), 134.01 (C), 136.20 (C), 214.56 (CO).

MS (130°C): *m*/*z* (%) = 278 (90, M^+), 277 (23), 185 (21), 170 (100), 169 (92), 158 (60), 86 (19), 84 (42), 73 (25).

HRMS: $C_{18}H_{18}N_2O$ Calculated: 278.1419 found: 278.1402

Elemental Analysis:	Calculated:	C: 77.67	H: 6.52	N: 10.06
	Found:	C: 77.10	H: 6.60	N: 10.13

3-Trimethylsilyl-1,4,5,6,7,7a-hexahydro-inden-2-one (60)



A solution of compound **39** (235 mg, 0.845 mmol) in methanol (20 mL) was vigorously stirred in the presence of 10% Palladium on carbon (15% by wt., 35 mg) in the hydrogen atmosphere at room temperature for 4 h. The catalyst was filtered off over a bed of celite, which was subsequently rinsed with methanol and the filtrate was concentrated. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 25:1) to provide the product **60** as colourless oil.

Yield: 17 mg (10%); colourless oil.

IR (ATR): ν = 2930, 2855, 1686, 1589, 1445, 1408, 1344, 1311, 1264, 1245, 1163, 1125, 1092, 940, 935, 908, 887, 837, 759, 695, 633, 573 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.19 (s, 9H), 1.05 (dq, *J* = 12.78, 3.6 Hz, 1H), 1.32 - 1.38 (m, 1H), 1.45 - 1.51 (m, 1H), 1.78 - 1.82 (m, 1H), 1.87 (dd, *J* = 18.37, 2.01 Hz, 1H), 1.97 - 2.01 (m, 1H), 2.12 - 2.19 (m, 2H), 2.45 (dd, *J* = 18.38, 6.90 Hz, 1H), 2.53 - 2.58 (m, 1H), 2.96 - 3.00 (m, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = –0.35 ($3CH_3$), 25.41 (CH_2), 27.49 (CH_2), 31.64 (CH_2), 35.55 (CH_2), 42.82 (CH_2), 43.56 (CH), 136.11 (C), 191.80 (C), 213.03 (C).

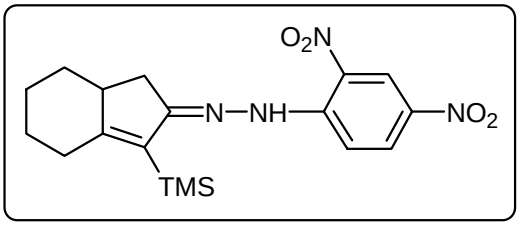
MS (150°C): *m*/*z* (%) = 208 (19, M^+), 207 (26), 193 (27), 192 (100), 191 (32), 190 (10), 180 (10), 74 (42), 73 (19).

HRMS: $C_{12}H_{20}OSi$ Calculated: 208.1283 found: 208.1279

_N_-(2,4-Dinitro-phenyl)-_N´_-(3-trimethylsiyl-1,4,5,6,7,7a-hexahydro-inden-2-ylidene) – hydrazine (61)

A solution of compound **39** (105 mg, 0.378 mmol) in ethanol (10 mL) was vigorously stirred in the presence of Palladium on carbon (15% by wt., 15 mg) in the hydrogen atmosphere at room temperature for 2.5 h. The catalyst was filtered off over a bed of celite, which was subsequently rinsed with ethanol (80 mL). To this, a solution of 2,4-dinitrophenylhydrazine (225 mg, 1.136 mmol) in conc. sulphuric acid (2 mL) / water (3 mL) was added and stirred for 0.5 h. The reaction mixture was poured into saturated aqueous solution of $NaHCO_3$ (25 mL), the organic layers are extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4. Evaporation of the solvent in *vacuo* and flash chromatography of the residue on silica gel (Hexane/EtOAc 15:1) afforded the compounds **61, 62** and **63.**

Spectroscopic data for **_N_-(2,4-Dinitro-phenyl)-_N´_-(3-trimethylsianyl-1,4,5,6,7,7a-hexahydro-inden-2-ylidene)-hydrazine** (**61**)



Yield: 51 mg (35%); red crystals.

M.P.: 196 - 197°C

UV (MeOH): λ = 217, 258, 290, 389 nm.

IR (ATR): ν = 3287, 3112, 2936, 2860, 1615, 1586, 1564, 1537, 1513, 1433, 1410, 1368, 1326, 1294, 1244, 1215, 1126, 1087, 1072, 1049, 959, 918, 887, 831, 758, 740, 693, 664, 597 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.32 (s, 9H), 1.08 (dq, *J* = 12.6, 3.5 Hz, 1H), 1.27 (tq, *J* = 13.0, 3.8 Hz, 1H), 1.46 (tq, *J* = 13.0, 3.4 Hz, 1H), 1.82 (br d, *J* = 13.38 Hz, 1H), 1.97 (dd, *J* = 7.5, 2.5 Hz, 1H), 2.11 (dd, *J* = 13.5, 5.0 Hz, 1H), 2.15 - 2.21 (m, 2H), 2.70 - 2.75

(m, 1H), 2.85 (dd, *J* = 17.3, 7.4 Hz, 1H), 2.95 (br d, *J* = 13.73 Hz, 1H), 7.82 (d, *J* = 9.63 Hz, 1H), 8.26 (dd, *J* = 9.67, 2.5 Hz, 1H), 9.11 (d, *J* = 2.55 Hz, 1H), 10.85 (br s,1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 0.41 ($3CH_3$), 25.45 (CH_2), 27.57 (CH_2), 30.82 (CH_2), 33.48 (CH_2), 35.75 (CH_2), 46.41 (CH), 116.21 (CH), 123.77 (CH), 128.54 (C), 129.98 (CH), 131.88 (C), 137.04 (C), 144.92 (C), 172.38 (C), 177.99 (C).

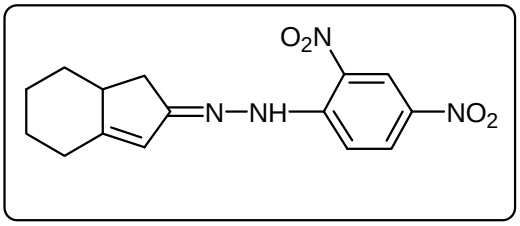
MS (25°C): *m*/*z* (%) = 388 (100, M^+), 373 (8), 337 (12), 240 (6), 206 (5), 193 (9), 75 (7), 73 (23).

HRMS: $C_{18}H_{24}N_4O_4Si$ Calculated: 388.1567 found: 388.1572

Elemental Analysis:	**C**alculated	C: 55.65%	H: 6.23%	N: 14.42%
	Found	C: 55.80%	H: 6.11%	N: 13.82%

Spectroscopic data for ***N*-(2,4-Dinitro-phenyl)-*N´*-(1,4,5,6,7,7a-hexahydro-inden-2-ylidene)-hydrazine** (**63**)

Yield: 11 mg (9%); red crystals.



M.P.: 190 - 191°C

UV (MeOH): λ = 212, 255, 289, 385 nm.

IR (ATR): ν = 3287, 3108, 3056, 2925, 2866, 2846, 1613, 1588, 1531, 1511, 1495, 1423, 1374, 1352, 1327, 1307, 1264, 1219, 1188, 1133, 1071, 977, 946, 917, 875, 860, 827, 775,761, 740, 699, 684, 594, 535 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.07 (dq, *J* = 12.5, 3.3 Hz, 1H), 1.28 (tq, *J* = 13.1, 3.8 Hz, 1H), 1.43 (tq, *J* = 13.3, 3.3 Hz, 1H), 1.83 (dd, *J* = 13.56, 1.2 Hz, 1H), 1.96 - 2.00 (m,

1 H), 2.16 - 2.23 (m, 2H), 2.26 (d, *J* = 2.4 Hz, 1H), 2.72 - 2.78 (m, 2H), 2.90 (dd, *J* = 17.0, 7.0 Hz, 1H), 6.02 (s, 1H), 7.88 (d, *J* = 9.6 Hz, 1H), 8.24 (dd, *J* = 9.6, 2.5 Hz, 1H), 9.10 (d, *J* = 2.56 Hz, 1H), 10.82 (br s, 1H).

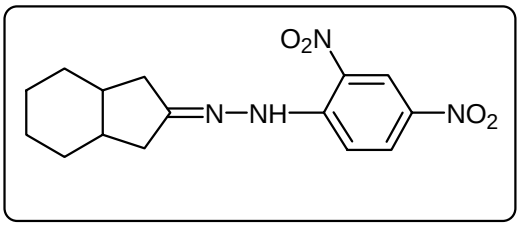
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 25.33 (CH_2), 27.14 (CH_2), 30.26 (CH_2), 33.36 (CH_2), 35.25 (CH_2), 44.09 (CH), 116.23 (CH), 122.29 (CH), 123.71 (CH), 129.86 (CH), 129.95 (C), 137.24 (C), 144.80 (C), 167.45 (C), 169.37 (C).

MS (150°C): *m*/*z* (%) = 316 (100, M^+), 282 (15), 281 (18), 252 (11), 137 (26), 91 (12), 79 (10).

HRMS: $C_{15}H_{16}N_{24}O_4$ **C**alculated: 316.1171 found: 316.1168.

Elemental Analysis:	**C**alculated	C: 55.96%	H: 5.10%	N: 17.17%
	Found	C: 56.28%	H: 5.12%	N: 17.54%

Spectroscopic data for ***N*-(2,4-Dinitro-phenyl)-*N´*-(octahydro-inden-2-ylidene)-hydrazine (62)**



Yield: 24 mg (20%); red crystals.

M.P.: 129 - 131°C

UV (MeOH): λ = 229, 362 nm.

IR (ATR): ν = 3305, 3110, 2923, 2853, 1612, 1585, 1534, 1502, 1446, 1409, 1361, 1331, 1306, 1261, 1216, 1125, 1065, 916, 864, 831, 761, 740, 697, 643, 567 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.23 - 1.41 (m, 2H), 1.42 - 1.67 (m, 6H), 2.17 - 2.24 (m, 1H), 2.31 (dd, *J* = 7.3, 2.0 Hz, 1H), 2.34 - 2.40 (m, 1H), 2.46 (dd, *J* = 17.0, 5.0 Hz,

2H), 2.57 (dd, *J* = 17.4, 7.0 Hz, 1H), 7.89 (br d, *J* = 9.6 Hz, 1H), 8.25 (dd, *J* = 9.65, 2.5 Hz, 1H), 9.10 (d, *J* = 2.56 Hz, 1H), 10.80 (br s, 1H).

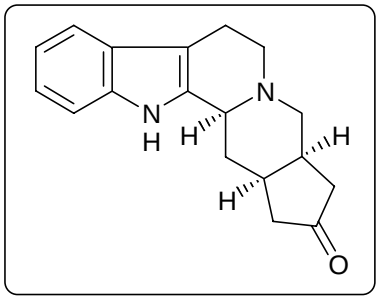
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 22.01 (CH_2), 22.82 (CH_2), 26.93 (CH_2), 27.12 (CH_2), 32.22 (CH_2), 36.76(CH), 36.88 (CH), 38.22 (CH_2), 116.22 (CH), 123.58 (CH), 128.72 (C), 129.93 (CH), 137.49 (C), 144.93 (C), 167.80 (C).

MS (150°C): *m*/*z* (%) = 318 (100, M^+), 281 (45), 193 (12), 152 (13), 139 (18), 121 (13), 95 (19), 79 (13), 67 (12).

HRMS: $C_{15}H_{18}N_4O_4$ **C**alculated: 318.1328 found: 318.1343.

Elemental Analysis:	**C**alculated	C: 56.60%	H: 5.70%	N: 17.60%
	Found	C: 56.23%	H: 5.73%	N: 17.29%

17-Keto-nor-alloyohimbane (44)



A solution of compound **53** (150 mg, 0.357 mmol) in methanol (15 mL) was vigorously stirred in presence of PtO_2 (15% by wt., 23 mg) under hydrogen atmosphere at room temperature for 14 h. The catalyst was filtered off over a bed of celite, which was subsequently rinsed with methanol and the filtrate was concentrated. The residue was subjected to flash chromatography on silica gel with EtOAc as eluent to provide the product **44** and **64**.

Spectroscopic data for compound 44.

Yield: 42 mg (42%); light yellow crystals.

M.P. 189 - 190°C

UV (MeOH): λ = 195, 225, 281, 289, 426 nm.

IR (drift): ν = 3346, 3059, 2952, 2925, 2916, 2850, 2818, 2783, 2754, 1727, 1624, 1570, 1491, 1472, 1457, 1436, 1400, 1387, 1375, 1358, 1339, 1321, 1302, 1277, 1266, 1251, 1211, 1193, 1167, 1143, 1129, 1102, 1070, 1042, 1007, 961, 932, 904, 870, 842, 816, 766, 743, 696, 668, 626 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.35 (q, *J* = 11.94 Hz, 1H), 2.02 - 2.05 (m, 1H), 2.09 (d, *J* = 18.0 Hz, 1H), 2.21 (dd, *J* = 18.7, 7.8 Hz, 1H), 2.40 (d, *J* = 7 Hz, 1H), 2.42 - 2.51 (m, 2H), 2.60 - 2.77 (m, 4H), 2.91 - 3.05 (m, 3H), 3.26 (dd, *J* = 11.56, 1.54 Hz, 1H), 7.06 - 7.14 (m, 2H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.73 (br s, 1H).

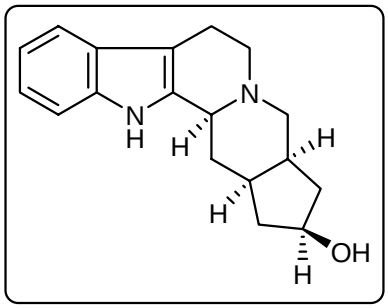
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.64 (CH_2), 32.90 (CH_2), 34.36 (CH), 36.01 (CH), 39.38 (CH_2), 46.76 (CH_2), 53.09 (CH_2), 56.24 (CH_2), 58.50 (CH), 108.65 (C), 110.73 (CH), 118.13 (CH), 119.49 (CH), 121.49 (CH), 127.22 (C), 134.25 (C), 136.02 (C), 219.21 (CO).

MS (120°C): *m*/*z* (%) = 280 (100, M^+), 279 (86), 266 (34), 265 (42), 211 (44), 170 (18), 169 (33), 156 (9), 43 (26).

HRMS: $C_{18}H_{20}N_2O$ Calculated: 280.1575 found: 280.1570

Spectroscopic data for 17-Hydroxy-nor-alloyohimbane (64)

Yield: 22 mg (22%); white solid.



M.P.: 255 - 256°C

UV ($CHCl_3$): λ = 229, 280 nm.

IR (drift): ν = 3439, 3198, 3052, 2947, 2931, 2913, 2885, 2833, 2764, 1624, 1499, 1475, 1455, 1437, 1392, 1376, 1358, 1340, 1323, 1297, 1273, 1232, 1211, 1172, 1141, 1096, 1072, 1040, 1008, 994, 969, 959, 932, 901, 886, 822, 804, 770, 741, 658 cm^{-1}.

^{1}H-NMR (500 MHz, DMSO): δ = 1.30 (dd, *J* = 13.0, 1.75 Hz, 1H), 1.61 (q, *J* = 12.0 Hz, 1H), 1.87 - 2.05 (m, 5H), 2.12 (dd, *J* = 12.9, 2.7 Hz, 1H), 2.40 (dt, *J* = 11.4, 4.0 Hz, 1H), 2.59 (br d, *J* = 13.46 Hz, 1H), 2.75 - 2.78 (m, 1H), 2.88 (br d, *J* = 11.56 Hz, 2H), 2.92 (dd, *J* = 11.1, 5.3 Hz, 1H), 3.03 (br d, *J* = 11.2 Hz, 1H), 4.20 (d, *J* = 6.0 Hz, 1H), 4.49 (br s, 1H), 6.91 (t, *J* = 7.4 Hz, 1H), 6.98 (t, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 7.97 Hz, 1H), 7.34 (d, *J* = 7.70 Hz, 1H), 10.69 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, DMSO): δ = 22.05 (CH_2), 33.44 (CH_2), 36.82 (CH), 37.92 (CH_2), 39.09 (CH), 42.51 (CH_2), 53.39 (CH_2), 56.58 (CH_2), 59.92 (CH), 71.58 (CH), 106.64 (C), 111.35 (CH), 117.83 (CH), 118.68 (CH), 120.68 (CH), 127.10 (C), 136.43 (C), 136.47 (C).

MS (120°C): *m*/*z* (%) = 282 (6, M^+), 281 (7), 221 (2), 177 (7), 133 (24), 89 (51), 87 (19), 73 (8), 45 (100), 43 (11).

HRMS: $C_{18}H_{22}N_2O$ **C**alculated: 282.1732 found: 282.1740.

17-Keto-nor-alloyohimbane (44)

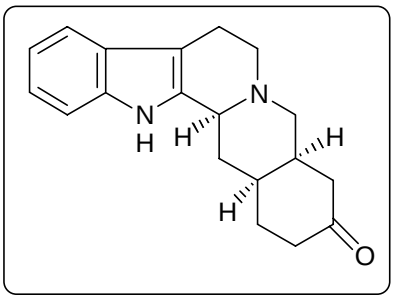
To a solution of compound **64** (65 mg, 0.23 mmol) and DCC (143 mg, 0.693 mmol) in dry DMSO (8 mL) was added crystalline orthophosphoric acid (34 mg, 0.347 mmol). This mixture was allowed to stir for 17 h at r.t and poured into 10 mL of methanol-water (3:2). After standing at r.t for 30 min. the solid was removed by filtration and washed with aqueous methanol and aqueous acetic acid. The filtrate was made basic with

aqueous Na_2CO_3 solution. The basic filtrate was extracted with CH_2Cl_2 (4 × 50 mL); the extracts were washed with water and concentrated in *vacuo*. The residue was subjected to flash chromatography on silica gel with EtOAc to afford the product **44** as colourless crystals.

Yield: 48 mg (74%, correcting for residual *N*,*N*'-dicyclohexylurea by NMR).

Spectroscopic data for compound **44** see above

18-Keto Alloyohimbane (65a)



To a solution of trimethylaluminium (2M soln. in Heptane) (0.17 mL, 0.343 mmol) in dry CH_2Cl_2 (8 mL) was added solution of compound **44** (80 mg, 0.286 mmol) in dry CH_2Cl_2 (7 mL) at –78°C, followed by addition of trimethylsilyldiazomethane (2M soln. in Hexane) (1.14 mL, 2.286 mmol). The reaction mixture was stirred at –78°C for 1 h, at –20°C for 1.5 h and then 0°C for 1.5 h and quenched with 1N HCl (15 mL) and neutralized with a saturated solution of Na_2CO_3. The aqueous layer was extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 1:1) to afford the product mixture **65a** and **65b**.

Yield: 26 mg (31%); light yellow crystals.

Spectroscopic data for **65a**

M.P. 121 - 123^{o}C

UV (MeOH): λ = 224, 282, 290, 358 nm.

IR (ATR): ν = 3371, 3332, 3051, 2919, 2850, 2799, 2757, 1700, 1646, 1491, 1450, 1374, 1360, 1341, 1319, 1277, 1258, 1235, 1214, 1176, 1156, 1140, 1106, 1068, 1050, 1009, 955, 924, 890, 840, 773, 737, 678, 643, 614, 584, 568, 547, 531 cm^{-1}.

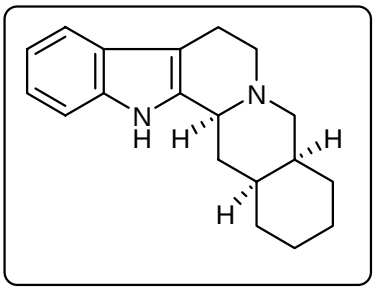
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.85 (td, *J* = 12.26, 3.58 Hz, 1H), 1.91 - 2.00 (m, 1H), 2.03-2.06 (m, 1H), 2.08 - 2.12 (m, 2H), 2.17 - 2.22 (m, 3H), 2.27 - 2.34 (m, 1H), 2.57 - 2.72 (m, 4H), 2.89 - 2.97 (m, 2H), 3.03 (t, *J* = 15.39 Hz, 1H), 3.33 (dd, *J* = 11.0, 2.05 Hz, 1H), 7.05 (dt, *J* = 7.86, 1.18 Hz, 1H), 7.09 (dt, *J* = 8.13, 1.31 Hz, 1H), 7.27 (d, *J* = 7.93 Hz, 1H), 7.44 (d, *J* = 7.69 Hz, 1H), 7.73 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.75 (CH_2), 30.00 (CH_2), 30.93 (CH_2), 33.32 (CH), 36.57 (CH_2), 38.02 (CH), 42.68 (CH_2), 52.98 (CH_2), 59.67(CH), 59.94 (CH_2), 108.61 (C), 110.73 (CH), 118.20 (CH), 119.57 (CH), 121.54 (CH), 127.30 (C), 134.60 (C), 136.02 (C), 212.81 (CO).

MS (150°C): *m*/*z* (%) = 294 (40, M^+), 293 (52), 281 (11), 266 (13), 265 (20), 211 (8), 170 (10), 169 (12), 73 (11), 72 (44), 69 (12), 60 (10), 59 (100), 57 (19), 557 (12).

HRMS: $C_{19}H_{22}N_2O$ **C**alculated: 294.1732 found: 294.1748.

Alloyohimbane (2)



A mixture of regio isomers **65a** and **65b** (40 mg, 0.136 mmol), diethylene glycol (5 mL), potassium hydroxide (26 mg, 0.476 mmol), and 85% hydrazine hydrate (680 mg, 13.6 mmol) was heated to 100°C for 1 h and the condenser was then removed to allow the aqueous liquor to evaporate and the temperature of reaction mixture to rise to 195°C. After heating at this temperature for 1.25 h, the reaction mixture was cooled, and added a

drop of conc.HCl to neutralize. The reaction mixture was quenched with NH_4Cl solution (25 mL), the organic layers are extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4 and subsequently concentrated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 1:1) (1% Et_3N) to afford the product **2** as colourless crystals.

Yield: 23.5 mg (62%); colourless crystals.

M.P. 160°C

UV (MeOH): λ = 226, 282, 290 nm.

IR (ATR): ν = 3416, 3255, 3054, 2921, 2854, 2797, 2751, 1450, 1376, 1341, 1320, 1259, 1200, 1160, 1145, 1123, 1060, 1009, 795, 736, 574 cm^{-1}.

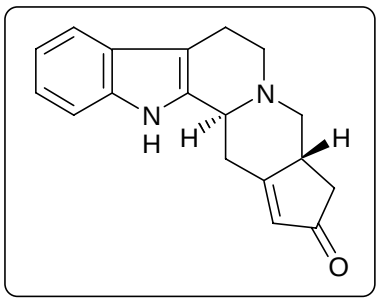
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.22 - 1.97 (series of m, 12H), 2.47 - 2.54 (m, 2H), 2.66 (dd, *J* = 12, 4 Hz, 1H), 2.76 (dd, *J* = 11.2, 1 Hz, 1H), 2.93 – 2.99 (m, 2H), 3.19 (br s, 1H), 7.05 (t, *J* = 7 Hz, 1H), 7.09 (t, *J* = 7 Hz, 1H), 7.28 (d, *J* = 8 Hz, 1H), 7.45 (d, *J* = 8 Hz, 1H), 7.71 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 20.84 (CH_2), 21.73 (CH_2), 26.49 (CH_2), 26.49 (CH_2), 30.50 (CH_2), 31.58 (CH_2), 34.76 (CH), 36.64 (CH), 53.41 (CH_2), 60.49 (CH), 62.00 (CH_2), 108.15 (C), 110.66 (CH), 118.06 (CH), 119.33 (CH), 121.17 (CH), 127.49 (C), 135.49 (C), 135.91 (C).

MS (200°C): *m*/*z* (%) = 280 (69, M^+), 279 (100), 277 (11), 169 (11).

HRMS: $C_{19}H_{24}N_2$ Calculated: 280.1939 found: 280.1941

15-ene-17-keto-nor-yohimbane (66a)



A mixture of compound **56** (45 mg, 0.162 mmol) and silica gel (*ca.* 1.5) and methanol (10 mL) was heated at reflux for 48 h. The solvent was removed from reaction mixture under reduced pressure and the residue was subjected to flash chromatography (EtOAc) on silica gel column to afford the product mixture **66a** and **66b** as light yellow crystals.

Yield: 32 mg (72%); light yellow crystals.

Spectroscopic data for **66a**

M.P.: 266°C

UV (MeOH): λ = 228, 229, 274, 289 nm.

IR (ATR): ν = 3347, 3044, 2938, 2900, 2849, 2787, 2761, 1700, 1738, 1674, 1617, 1467, 1427, 1379, 1346, 1321, 1298, 1280,1262, 1213, 1198, 1156, 1128, 1059, 1035, 1006, 971, 947, 895, 882, 844, 807, 786, 759, 739, 680, 659, 610, 585, 555 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.02 (dd, *J* = 18.6, 2.4 Hz, 1H), 2.25 (t, *J* = 11.05 Hz, 1H), 2.56 - 2.64 (m, 2H), 2.70 (dd, *J* = 11.1, 4.2 Hz, 1H), 2.75 - 2.80 (m, 1H), 2.99 - 3.05 (m, 1H), 3.12 - 3.18 (m, 2H), 3.20 (dd, *J* = 13.0, 3.0 Hz, 1H), 3.41 - 3.44 (m, 2H), 6.02 (s, 1H), 7.10 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.15 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.49 (d, *J* = 7.74 Hz, 1H), 7.76 (br s, 1H).

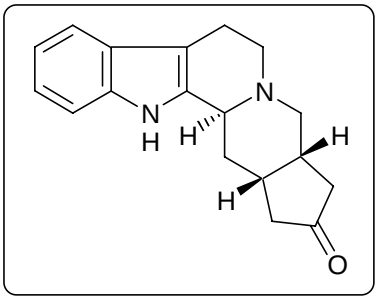
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.82 (CH_2), 35.32 (CH_2), 39.17 (CH_2), 40.89 (CH), 52.41 (CH_2), 59.47 (CH), 62.13 (CH_2), 109.04 (C), 110.86 (CH), 118.35

(CH), 119.76 (CH), 121.95 (CH), 127.04 (C), 128.04 (CH), 133.20 (C), 136.16 (C), 179.57 (C), 207.90 (CO).

MS (150°C): *m*/*z* (%) = 278 (69, M^+), 277 (100), 183 (15), 182 (26), 170 (8), 169 (23), 71 (10), 57 (11).

HRMS: $C_{18}H_{18}N_2O$ Calculated: 278.1419 found: 278.1390

17-Keto-nor-3-Epialloyohimbane (45)



10% Palladium on carbon (25% by wt., 4 mg) was added to a solution of the **66a** (15 mg, 0.054 mmol) in methanol (15 mL) and vigorously stirred under H_2 atmosphere (800-900 Torr) until no further H_2 uptake was detected. The reaction mixture was filtered over a short path of celite (which was subsequently washed with methanol) and the solvent was evaporated. The residue was subjected to flash chromatography (EtOAc) on silica gel column to afford the product **45**.

Yield: 15 mg (99%); light yellow crystals

M.P. 170°C

UV (MeOH): λ = 201, 225, 282 nm.

IR (ATR): ν = 3323, 2930, 2914, 2856, 2821, 2766, 2737, 1719, 1622, 1590, 1492, 1452, 1384, 1357, 1339, 1323, 1292, 1271, 1256, 1231, 1192, 1170, 1149, 1130, 1171, 1050, 1008, 988, 924, 879, 829, 788, 741, 671, 620, 602, 580, 555, 542 cm^{-1}.

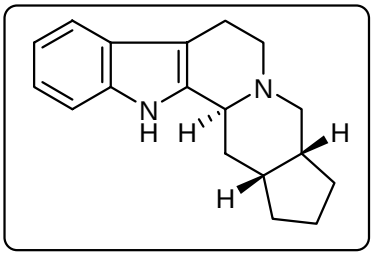
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.94 (td, *J* = 13.2, 5.0 Hz, 1H), 2.04 (d, *J* = 18.5 Hz, 1H), 2.16 - 2.23 (m, 2H), 2.28 (dd, *J* = 18.8, 8.7 Hz, 1H), 2.38 - 2.44 (m, 2H), 2.62 (td, *J* = 11.0, 4.3 Hz, 1H), 2.68 - 2.76 (m, 3H), 2.91 (dd, *J* = 11.9, 5.6 Hz, 1H), 2.97 - 3.04 (m, 1H), 3.06 (dd, *J* = 11.19, 5.9 Hz, 1H), 3.44 (d, *J* = 11.7 Hz, 1H), 7.08 - 7.16 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.75 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.51 (CH_2), 31.13 (CH_2), 33.38 (CH), 34.96 (CH), 38.98 (CH2), 44.10 (CH_2), 53.34 (CH_2), 53.69 (CH), 56.41 (CH_2), 108.83 (C), 110.72 (CH), 118.12 (CH), 119.50 (CH), 121.52 (CH), 127.29 (C), 133.99 (C), 136.06 (C), 218.38 (CO).

MS (150°C): *m*/*z* (%) = 280 (97, M^+), 279 (100), 211 (50), 178 (13), 170 (13), 169 (20), 149 (13), 125 (14), 123 (13), 111 (23), 109 (15), 99 (11), 97 (32), 95 (20), 85 (30), 83 (30), 81 (20), 71 (42), 70 (13), 69 (21), 67 (11), 59 (18), 57 (60), 56 (14), 55 (32).

HRMS: $C_{18}H_{20}N_2O$ Calculated: 280.1576 found: 280.1557

Nor-3-Epi-Alloyohimbane (68)



A mixture of compound **45** (40 mg, 0.136 mmol), diethylene glycol (5 mL), potassium hydroxide (26 mg, 0.476 mmol), and 85% hydrazine hydrate (680 mg, 13.6 mmol) was heated to 100°C for 1 h and the condenser was then removed to allow the aqueous liquor to evaporate and the temperature of reaction mixture to rise to 195°C. After heating at this temperature for 1.25 h, the reaction mixture was cooled, and added a drop of conc.HCl to neutralize. The reaction mixture is poured in saturated aqueous solution of NH_4Cl (25 mL), the organic layers are extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4 and subsequently concentrated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 1:1) (1% Et_3N) to afford the product **68.**

Yield: 25 mg (66%); white solid

M.P. 132°C - 134.5°C

UV (MeOH): λ = 225, 279, 287.

IR (ATR): ν = 3409, 3226, 3053, 2944, 2870, 2810, 2762, 2448, 1709, 1622, 1592, 1468, 1451, 1355, 1323, 1291, 1272, 1224, 1177, 1157, 1119, 1100, 1076,1054, 1008, 981, 908, 787, 737, 646, 614, 587 cm^{-1}.

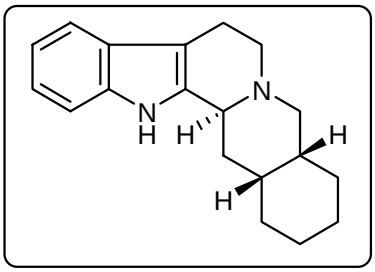
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.23 - 1.26 (m, 1H), 1.34 - 1.40 (m, 1H), 1.61 - 1.78 (m, 4H), 1.87 - 1.93 (m, 1H), 2.08 - 2.21 (m, 3H), 2.32 - 2.38 (m, 1H), 2.56 - 2.61 (m, 1H), 2.69 - 2.77 (m, 2H), 2.97 - 3.07 (m, 2H), 3.36 (d, *J* = 11.17 Hz, 1H), 7.06 (dt, *J* = 7.5, 1.0 Hz, 1H), 7.10 (dt, *J* = 7.5, 1.2 Hz, 1H), 7.27 (d, *J* = 7.87 Hz, 1H), 7.45 (d, *J* = 7.65 Hz, 1H), 7.69 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.56 (CH_2), 22.52 (CH_2), 27.13 (CH_2), 29.30 (CH_2), 31.27 (CH_2), 37.54 (CH), 38.06 (CH), 53.55 (CH_2), 54.66 (CH), 57.41 (CH_2), 108.43 (C), 110.65 (CH), 118.03 (CH), 119.32 (CH), 121.23 (CH), 127.44 (C), 135.22 (C), 136.02 (C).

MS (120°C): *m*/*z* (%) = 266 (64, M^+), 265 (100), 170 (17), 169 (27).

HRMS: $C_{18}H_{22}N_2$ Calculated: 266.1783 found: 266.1777

3-Epialloyohimbane (3)



To a solution of trimethylaluminium (2M soln. in Heptane) (0.43 mL, 0.786 mmol) in dry CH_2Cl_2 (8 mL) was added solution of compound **45** (110 mg, 0.393 mmol) in dry CH_2Cl_2 (7 mL) at –78°C, followed by addition of trimethylsilyldiazomethane (2M soln. in Hexane) (1.57 mL, 3.14 mmol). The reaction mixture was stirred at –78°C for 2 h, at –20°C for 3.5 h and then 0°C for 3.5 h and quenched with 1N HCl (15 mL) and neutralized with a saturated solution of Na_2CO_3. The aqueous layer was extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo*.

The crude product mixture, diethylene glycol (5 mL), potassium hydroxide (53 mg, 0.946 mmol), and 85% hydrazine hydrate (1.36 g, 27.2 mmol) was heated to 100°C for 1 h and further for 1.25 h at 195°C. The reaction mixture was cooled to r.t. and added a drop of conc.HCl and quenched with saturated aqueous solution of NH_4Cl (25 mL), the organic layers are extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4 and subsequently concentrated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 1:1) (1%Et_3N) to afford the mixture of compounds **3** and **68**.

Yield: 18 mg (18%); white solid.

Spectroscopic data for **3**

M.P. 174 - 177 ^oC

UV (MeOH): λ = 229, 280, 287 nm.

IR (ATR): ν = 3327, 3049, 2921, 2857, 2820, 2773, 1466, 1450, 1363, 1319, 1292, 1261, 1239, 1183, 1156, 1097, 1078, 1045, 1008, 982, 966, 920, 794, 759, 735, 682, 627, 613, 581, 555 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.24 - 2.04 (series of m, 11H), 2.11 (m, 1H), 2.57 - 2.787 (m, 4H), 2.98 – 3.10 (m, 2H), 3.50 (br s, 1H), 7.08 (t, *J* = 8 Hz, 1H), 7.10 (t, *J* = 8 Hz, 1H), 7.28 (d, *J* = 8 Hz, 1H), 7.45 (d, *J* = 7.3 Hz, 1H), 7.70 (br s, 1H).

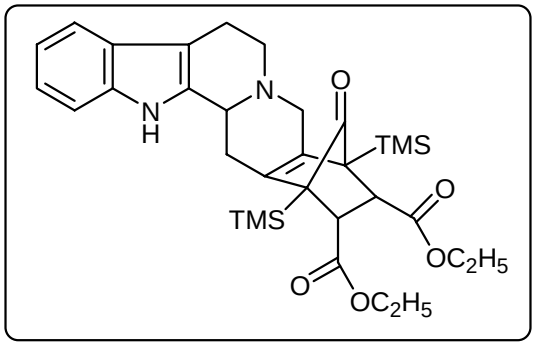
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 21.51 (CH_2), 22.53 (CH_2), 27.15 (CH_2), 27.15 (CH_2), 29.64 (CH_2), 31.21 (CH_2), 33.80 (CH), 34.66 (CH), 53.36 (CH_2), 54.45 (CH), 57.31 (CH_2), 108.32 (C), 110.66 (CH), 118.05 (CH), 119.34 (CH), 121.24 (CH), 127.51 (C), 135.12 (C), 135.94 (C).

MS (150°C): *m*/*z* (%) = 280 (82, M^+), 279 (100), 266 (54), 265 (63), 170(15), 169 (20), 18 (5).

HRMS: $C_{19}H_{24}N_2$ Calculated: 280.1939 found: 280.1926

Compound 69

A mixture of compound **53** (100 mg, 0.238 mmol) and diethyl maleate (41 mg, 0.238 mmol) in dry benzene (15 mL) was refluxed for 14 h. The solvent was evaporated and the residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 15:1) to provide the product **69**.



Yield: 96 mg (68%); orange crystalline solid.

M.P.: 134 - 135°C

UV (MeOH): λ = 279, 289, 234 nm.

IR (ATR): ν = 3595, 3466, 3392, 2977, 2955, 2902, 2847, 2804, 1739, 1627, 1452, 1371, 1323, 1248, 1189, 1138, 1099, 1044, 1008, 977, 904, 834, 794, 736, 693, 624, 547, 530 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.16 (s, 9H), 0.18 (s, 9H), 1.21 - 1.30 (m, 6H), 2.43 - 2.49 (m, 1H), 2.70 - 2.75 (m, 2H), 2.99 - 3.07 (m, 2H), 3.18 - 3.21 (m, 1H), 3.48 - 3.52 (m, 3H), 3.57 (dd, *J* = 15.6, 1.6 Hz, 1H), 3.74 (d, *J* = 9.93 Hz, 1H), 3.98 - 4.13 (m, 4H), 7.06 - 7.14 (m, 2H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.94 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = –1.83 ($3CH_3$), –1.74 ($3CH_3$), 21.40 (CH_2), 32.88 (CH_2), 48.24 (CH), 48.53 (CH), 51.79 (C), 52.15 (CH_2), 52.25 (C), 55.29 (CH), 55.76 (CH_2), 60.73 (CH_2), 60.86 (CH_2), 108.35 (C), 110.66 (CH), 118.09 (CH), 119.24 (CH), 121.31 (CH), 127.17 (C), 134.58 (C), 136.20 (C), 136.75 (C), 136.87 (C), 171.14 (CO), 171.24 (CO), 198.93 (CO).

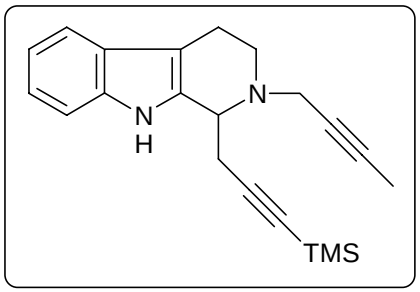
MS (150°C): *m*/*z* (%) = 592 (18, M^+), 491 (13), 422 (24), 420 (62), 170 (38), 169 (22), 149 (25), 148 (26), 147 (100), 131 (15), 127 (32), 99 (88), 97 (14), 86 (21), 85 (18), 84 (35), 83 (17).

HRMS: $C_{32}H_{44}Si_2N_2O_5$ Calculated: 592.2789 found: 592.2796

Elemental Analysis:	**C**alculated	C: 64.83%	H: 7.48%	N: 4.73%
	Found	C: 62.23%	H: 7.56%	N: 4.22%

5.2.2 Referring to Section 3.2

2-But-2-ynyl-1-(3-trimethylsilylprop-2-ynyl)-2,3,4,9-tertahydro-1*H*-β-carboline (74)

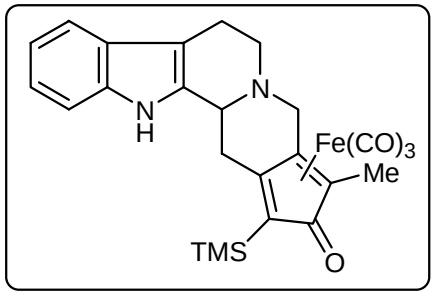


A solution of 1-bromo-2-butyne (613 mg, 4.61 mmol) in dry THF (10 mL) was added to a mixture of compound **50** (970 mg, 3.447 mmol), Na_2CO_3 (1.79 g, 16.92 mmol), TBAI (82 mg) and dry THF (40 mL) and stirred at r.t for 60 h under argon atmosphere. The reaction mixture was quenched with saturated aqueous solution of NH_4Cl (50 mL), extracted with EtOAc (4 × 100 mL) and dried over anhydrous Na_2SO_4 and subsequently concentrated in *vacuo.* The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 10:1) to afford the product **74**.

Yield: 1.0 g (87%); colourless oil.

For further spectroscopic data see reference[109]

Tricarbonyl[η^4-16-trimethylsilyl-18-methyl-15,18-diene-17-keto-nor-yohimbane] Iron (73)

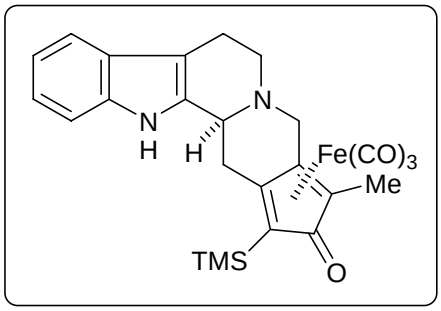


To a solution of diyne **74** (500 mg, 1.5 mmol) in dry 1,2-dimethoxyethane (25 mL) was added pentacarbonyliron (587 mg, 3.0 mmol) under argon atmosphere in glove box. The reaction mixture was then heated in a sealed tube for 24 h at 140°C. After this time the solvent was removed in *vacuo*. Flash chromatography of the residue on silica gel (Hexane/EtOAc/MeOH 3:1:0.1) provided the tricarbonyl[η^4-cyclopentadienone]iron complex **73**.

Yield: 691 mg (92%); orange crystals.

For further spectroscopic data see reference[109]

Spectroscopic data for *anti*-73



M.P. 186 - 188°C

UV (MeOH): λ = 196, 223, 272, 397 nm.

IR (ATR): ν = 3367, 2942, 2908, 2799, 2737, 2059, 2015, 1993, 1601, 1495, 1454, 1409, 1391, 1369, 1341, 1324, 1271, 1248, 1208, 1162, 1138, 1082, 1024, 1004, 975, 957, 921,839, 814, 760, 739, 722, 694, 637, 611, 590, 572 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.30 (s, 9H), 1.74 (s, 3H), 2.72 (dd, *J* = 16.0, 10.7 Hz, 1H), 2.79 - 2.86 (m, 2H), 2.91 (dd, *J* = 16.0, 3.1 Hz, 1H), 2.98 - 3.05 (m, 1H), 3.22 - 3.25 (m, 1H), 3.60 (d, *J* = 15.29 Hz, 1H), 3.80 (d, *J* = 10.47 Hz, 1H), 3.91 (d, *J* = 15.53 Hz, 1H), 7.12 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.18 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.36 (d, *J* = 8.01 Hz, 1H), 7.51 (d, *J* = 7.74 Hz, 1H), 7.84 (br s, 1H).

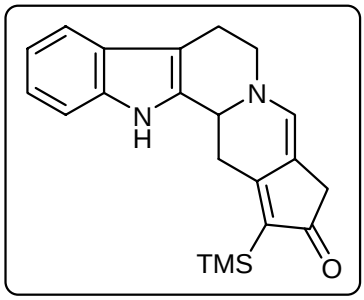
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = –0.32 (CH_3), 8.62 (CH_3), 21.45 (CH_2), 32.18 (CH_2), 50.84 (CH_2), 52.08 (CH_2), 55.29 (CH), 67.51 (C), 80.50 (C), 103.91 (C), 104.03 (C), 109.23 (C), 110.97 (CH), 118.41 (CH), 119.87 (CH), 122.21 (CH), 126.85 (C), 132.34 (C), 136.48 (C), 175.75 (CO), 208.91 (CO).

MS (150°C): *m*/*z* (%) = 502 (1, M^+), 474 (27), 446 (61), 418 (100), 402 (20), 362 (54), 344 (13), 170 (13), 169 (24), 73 (12).

HRMS: $C_{25}H_{26}N_2SiO_4Fe$ Calculated: 502.1011 found: 502.1024

Elemental Analysis:	**C**alculated	C: 59.77%	H: 5.22%	N: 5.58%
	Found	C: 59.41%	H: 5.26%	N: 5.04%

16-trimethylsilyl-15,19-diene-17-keto-nor-yohimbane (55)

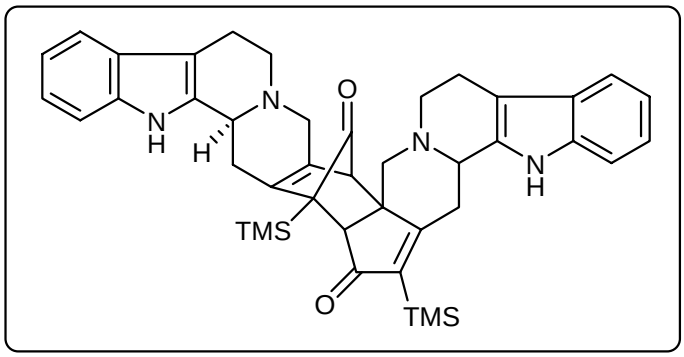


A solution of compound **53** (100 mg, 0.238 mmol) in acetone (10 mL) was added to a suspension of $Me_3NO{\cdot}2H_2O$ (53 mg, 0.476 mmol) in acetone (10 mL) at 10°C. After stirring for 1.5 h, the reaction mixture is filtered over silica gel and the solvent was evaporated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 1:1) to provide the product **55**.

Yield: 35 mg (42%); orange crystals.

For further spectroscopic data see reference[74]

Compound 77



A mixture of compound **53** (95 mg, 0.226 mmol) and trifluoroacetic acid (15 mL) was refluxed with stirring for 1 h and than cooled to room temperature. The mixture was quenched with ice and neutralized with a saturated solution of Na_2CO_3. The aqueous layer was extracted with CH_2Cl_2 (4 × 50 mL)

and dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 5:1) to afford the product **77**.

Yield: 36 mg (46%); colourless crystals.

M.P. 199 ^{o}C

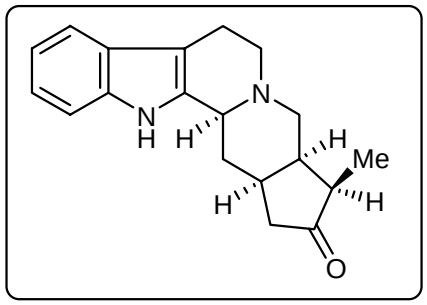
IR (ATR): ν = 3377, 3053, 2950, 2903, 2844, 2803, 2741, 1759, 1691, 1593, 1455, 1375, 1312, 1250, 1161, 1125, 1101, 1041, 1007, 953, 907, 843, 792, 741, 630, 587, 580, 551 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.25 (s, 9H), 0.28 (s, 9H), 1.96 (t, *J* = 12.30 Hz, 2H), 2.25 (dd, *J* = 2.112, 10.99 Hz, 2H), 2.45 - 2.51 (m, 1H), 2.63 - 2.69 (m, 1H), 2.72 - 2.89 (m, 3H), 2.94 - 3.10 (m, 3H), 3.16 - 3.21 (m, 2H), 3.33 - 3.37 (m, 3H), 3.52 (d, *J* = 16.46 Hz, 1H), 3.93 (d, *J* = 11.55 Hz, 1H), 4.09 - 4.11 (m, 1H), 7.10 - 7.11 (m, 2H), 7.14 - 7.17 (m, 2H), 7.30 - 7.32 (m, 2H), 7.47 - 7.49 (m, 2H), 7.60 (br s, 1H), 7.96 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = –1.77 (CH_3), 0.18 (CH_3), 21.38 (CH_2), 21.80 (CH_2) 31.26 (CH_2), 37.53 (CH_2), 51.64 (CH_2), 52.34 (C), 52.41 (CH_2), 52.94 (C), 54.64 (CH_2), 55.51 (CH), 56.18 (CH_2), 56.25 (CH), 56.52 (CH), 57.23 (CH), 60.39 (C), 108.53 (C), 109.12 (C), 110.71 (CH), 110.99 (CH), 118.14 (CH), 118.38 (CH), 119.60 (CH), 119.70 (CH), 121.83 (CH), 126.97 (C), 127.06 (C), 131.63 (C), 132.79 (C), 133.37 (C), 136.14 (C), 136.26 (C), 137.77 (C), 145.21 (C), 179.52 (C), 199.76 (CO), 208.54 (CO).

For further spectroscopic data see reference[74]

18-methyl-17-keto-nor-yohimbane (72)



A mixture of Raney nickel (*ca.* 5 g), iron-complex **73** (100 mg, 0.199 mmol) and ethanol (30 mL) was stirred at room temperature for 14 h. The mixture was filtered through celite and the filter cake washed thoroughly with methanol. Concentration of the filtrate in *vacuo* and flash chromatography (Hexane/EtOAc 1:1) on silica gel column afforded the products **72**, **78** and **79**.

Spectroscopic data for **72**

Yield: 23 mg (39%); light yellow crystals

M.P. 100°C

UV (MeOH): λ = 219, 229, 281, 438 nm

IR (ATR): ν = 3365, 3051, 2923, 2852, 2804, 2754, 1727, 1557, 1453, 1374, 1343, 1319, 1271, 1206, 1180, 1167, 1123, 1098, 1072, 1025, 1009, 893, 871, 850, 775, 734, 666, 562 cm^{-1}.

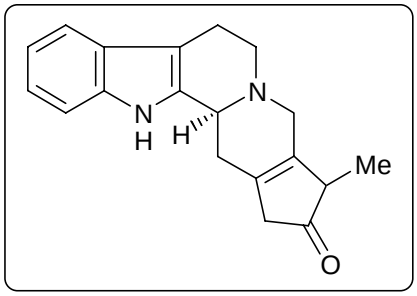
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.09 (d, *J* = 6.95 Hz, 3H), 1.39 (q, *J* = 12.3 Hz, 1H), 1.92 - 1.94 (m, 1H), 2.06 - 2.10 (m, 1H), 2.13 (br d, *J* = 19.3 Hz, 1H), 2.38 (dd, *J* = 18.39, 7.7 Hz, 1H), 2.45 - 2.50 (m, 1H), 2.61 - 2.73 (m, 4H), 2.92 - 2.98 (m, 1H), 3.0 (dd, *J* = 11.0, 5.6 Hz, 1H), 3.07 (br d, *J* = 12.0 Hz, 1H), 3.28 (dd, *J* = 11.58, 1.67 Hz, 1H), 7.06 (dt, *J* = 7.8, 1.1 Hz, 1H), 7.11 (dt, *J* = 7.2, 1.1 Hz, 1H), 7.28 (d, *J* = 7.95 Hz, 1H), 7.45 (d, *J* = 7.66 Hz, 1H), 7.67 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.71 (CH_3), 21.61 (CH_2), 32.53 (CH), 33.68 (CH_2), 43.03 (CH), 43.92 (CH), 44.98 (CH_2), 53.23 (CH_2), 55.25 (CH_2), 58.80 (CH), 108.63 (C), 110.73 (CH), 118.14 (CH), 119.51 (CH), 121.52 (CH), 127.26 (C), 136.04 (C), 220.80 (CO).

MS (150°C): *m/z* (%) = 294 (93, M^+), 293 (100), 225 (26), 169 (13), 43 (11).

HRMS: $C_{19}H_{22}N_2O$ Calculated: 294.1732 found: 294.1702

15,19-Dehydro-18-methyl-17-keto-nor-yohimbane (78)



Yield: 7 mg (12%); light yellow crystals

M.P. 157°C

UV (MeOH): λ = 205, 226, 283, 290, 312, 358 nm.

IR (ATR): ν = 3331, 3051, 2918, 2850, 2749, 1692, 1654, 1553, 1494, 1453, 1372, 1319, 1270, 1227, 1176, 1160, 1069, 1046, 1003, 969, 942, 910, 835, 779, 739, 673, 587, 564 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.25 (d, *J* = 5.6 Hz, 3H), 1.41 (q, *J* = 11.94 Hz, 1H), 2.04 (s, 1H), 2.17 (d, *J* = 6.2 Hz, 1H), 2.50 (ddd, *J* = 12.4, 5.6, 2.0 Hz, 1H), 2.62 (d, *J* = 3.43 Hz, 1H), 2.76 - 2.84 (m, 2H), 2.97 - 3.04 (m, 1H), 3.19 - 3.23 (m, 2H), 3.62 (br d, *J* = 10.67 Hz, 1H), 4.02 - 4.07 (m, 1H), 7.07 (dt, *J* = 7.4, 0.7 Hz, 1H), 7.12 (dt, *J* = 8.0, 0.8 Hz, 1H), 7.29 (d, *J* = 7.98 Hz, 1H), 7.46 (d, *J* = 7.71 Hz, 1H), 7.73 (br s, 1H).

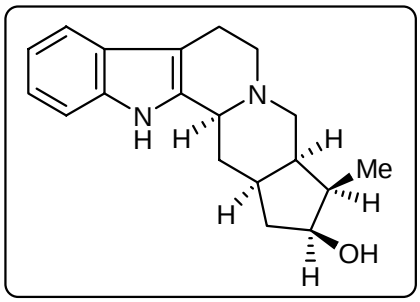
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 7.90 (CH_3), 21.59 (CH_2), 37.25 (CH_2), 38.42 (CH), 40.47 (CH_2), 53.06 (CH2), 54.52 (CH_2), 58.88 (CH), 108.39 (C), 110.82 (CH), 118.21 (CH), 119.54 (CH), 121.69 (CH), 127.11 (C), 133.30 (C), 134.74 (C), 136.10 (C), 167.26 (C), 208.38 (CO).

MS (150°C): *m*/*z* (%) = 292 (94, M^+), 291 (91), 170 (10), 169 (29), 156 (26), 101 (15), 83 (23), 60 (15), 59 (100), 58 (11), 43 (55), 41 (11).

HRMS: $C_{19}H_{20}N_2O$ Calculated: 292.1576 measured: 292.1561

Spectroscopic data for **79**

18-methyl-17-hydroxy-nor-yohimbane (79)



Yield: 3 mg (5%); white solid.

M.P.: 250°C

UV (MeOH): λ = 219, 223, 227, 281, 289, 353.

IR (ATR): ν = 3226, 3094, 2941, 2913, 2866, 2823, 2760, 1455, 1373, 1342, 1319, 1296, 1066, 784, 737, 567, 528 cm^{-1}.

^{1}H-NMR (500 MHz, DMSO): δ = 0.97 (d, *J* = 6.62 Hz, 3H), 1.15 - 1.23 (m, 1H), 1.40 - 1.56 (m, 2H), 1.97 - 2.05 (m, 2H), 2.11 - 2.21 (m, 2H), 2.39 - 2.63 (m, 1H), 2.74 - 2.80 (m, 1H), 2.89 - 2.96 (m, 2H), 3.03 (d, *J* = 10.79 Hz, 1H), 3.30 - 3.38 (m, 1H), 3.58 - 3.63 (m, 1H), 4.53 (d, *J* = 5.26 Hz, 1H), 6.91 - 6.94 (m, 1H), 6.98 - 7.01 (m, 1H), 7.26 (d, *J* = 8.0 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 10.68 (br s, 1H).

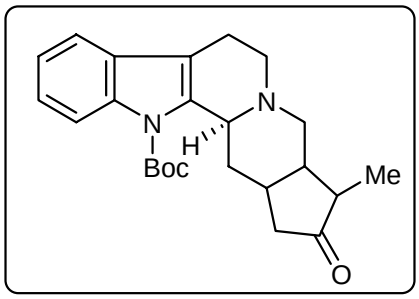
^{13}C-NMR and DEPT (125 MHz, DMSO): δ = 16.52 (CH_3), 21.53 (CH_2), 34.62 (CH_2), 35.73 (CH), 40.16 (CH_2), 41.62 (CH), 45.16 (CH), 53.01 (CH_2), 54.61 (CH_2), 59.50 (CH), 78.98 (CH), 106.16 (C), 110.90 (CH), 117.38 (CH), 118.21 (CH), 120.22 (CH), 126.62 (C), 135.93 (C), 135.98 (C).

MS (150°C) : *m*/*z* (%) = 296 (89, M^+), 295 (100), 294 (18), 293(18), 225 (18), 223 (10), 184 (9), 170 (17), 169 (22), 166 (9), 156 (10), 144 (10), 97 (8), 85 (10), 83 (9), 71 (15), 69 (11), 57 (20), 55 (12).

HRMS: $C_{19}H_{24}N_2O$ Calculated: 296.1889 found: 296.1887

Elemental Analysis:	Calculated:	C: 76.99	H: 8.16	N: 9.45
	Found:	C: 76.03	H: 8.00	N: 9.20.

1-N-Boc-18-methyl-17-keto-nor-yohimbane (80)



50% NaOH (5 mL) was added to the solution of compound **72** (85 mg, 0.289 mmol) in toluene (15 mL), and then tetrabutylammonium hydrogen sulphate (30 mg, 0.088 mmol). The two phase system was stirred under argon atmosphere for 30 minutes. Di-*t*-butyl dicarbonate [$(Boc)_2O$] (127 mg, 0.578 mmol) in toluene (2 mL) was added during 10 min and stirring was continued for further 1 h. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (4 × 50 mL), dried over anhydrous Na_2SO_4 and subsequently concentrated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 1:1) (1% Et_3N) to yield pure compound **80**.

Yield: 67 mg (59%); light yellow crystals

M.P. 169°C

UV (MeOH): λ = 228, 267 nm.

IR (ATR): ν = 2973, 2917, 2800, 2761, 1726, 1477, 1455, 1407, 1392, 1367, 1357, 1328, 1313, 1271, 1256, 1218, 1157, 1145, 1127, 1116, 1063, 1027, 1013, 979, 941, 920, 860, 845, 787, 763, 745, 702, 665, 578 cm^{-1}.

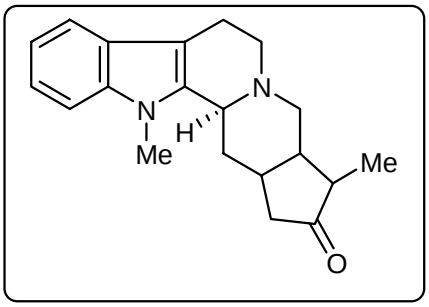
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.08 (d, *J* = 6.97 Hz, 3H), 1.17 - 1.26 (m, 1H), 1.66 (s, 9H), 1.79 - 1.90 (m, 1H), 2.03 - 2.07 (m, 1H), 2.22 - 2.26 (m, 1H), 2.34 - 2.41 (m, 1H), 2.49 - 2.55 (m, 1H), 2.58 - 2.65 (m, 2H), 2.70 - 2.75 (m, 1H), 2.81 - 2.92 (m, 3H), 3.03 (d, *J* = 12 Hz, 1H), 3.69 (dd, *J* = 1.66, 1.63 Hz, 1H), 7.14 - 7.26 (m, 2H), 7.38 (m, 1H), 7.99 (d, *J* = 8 Hz, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.67 (CH_3), 22.58 (CH_2), 28.24 (CH_3), 33.25 (CH), 35.01(CH_2), 43.22 (CH), 43.87 (CH), 44.98 (CH_2), 51.24 (CH_2), 55.54(CH_2), 60.41 (CH), 83.65 (C), 115.30 (CH), 117.32 (C), 117.94 (CH), 122.64(CH), 123.91 (CH), 129.13 (C), 136.48 (C), 136.95 (C), 150.47 (CO), 220.79 (CO).

MS (150°C): *m*/*z* (%) = 394(1, M^+), 338 (17), 337 (39), 295 (11), 294 (53), 293 (61), 281 (38), 225 (18), 208 (22), 180 (18), 169 (14), 131 (17), 114 (12), 85 (15), 83 (12), 70 (10), 59 (48), 57 (100), 56 (23), 55 (15), 44 (26), 43 (25), 41 (33), 32 (11), 29 (12).

HRMS: $C_{24}H_{30}N_2O_3$ Calculated: 394.2256 found: 394.2279

1-*N*-Methyl-18-methyl-17-keto-nor-yohimbane (83)



A solution of ketone **72** (100 mg, 0.34 mmol) and potassium *tert*-butoxide (154 mg, 1.37 mmol) in dry DMSO (15 mL) was heated at 50°C under argon atmosphere for 30 minutes. Then, dimethyl sulphate (88 mg, 0.70 mmol) was then added to the reaction mixture and further heated at 100°C for 1.5 h. The cooled reaction mixture was poured in water (50 mL), extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4 and

subsequently concentrated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 5:1) to afford the product **83**.

Yield: 44 mg (42%); colourless oil

UV (MeOH): λ = 277, 283, 291 nm.

IR (ATR): ν = 3052, 2922, 2800, 2744, 1735, 1468, 1375, 1340, 1307, 1272, 1205, 1182, 1143, 1063, 1039, 1012, 911, 835, 767, 739, 570, 555 cm^{-1}.

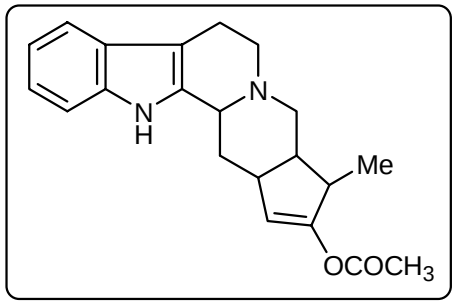
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.10 (d, *J* = 6.97 Hz, 3H), 1.23 - 1.26 (m, 1H), 1.36 - 1.92 (m, 1H), 2.28 - 2.32 (m, 1H), 2.49 - 2.54 (m, 1H), 2.63 - 2.70 (m, 3H), 2.86 - 2.95 (m, 3H), 3.07 (dd, *J* = 11.18, 1 Hz, 1H), 3.42 (d, *J* = 11.10 Hz, 1H), 3.67 (s, 3H), 7.06 - 7.09 (m, 1H), 7.15 - 7.18 (m, 1H), 7.23 (d, *J* = 8.12 Hz, 1H), 7.46 (d, *J* = 7.79 Hz, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.67 (CH_3), 22.37 (CH_2), 31.49 (CH), 33.22 (CH), 34.65 (CH_2), 43.27 (CH), 43.78 (CH_3), 44.99 (CH_2), 52.60 (CH_2), 55.65 (CH_2), 58.94 (CH), 108.75 (CH), 109.15 (C), 118.04 (CH), 119.03 (CH), 121.14 (CH), 126.51 (C), 136.02 (C), 138.04 (C), 220.97 (CO).

MS (150°C): *m*/*z* (%) = 308 (100, M^+), 307 (71), 239 (44), 198 (18), 184 (16), 183 (11), 168 (12), 86 (14), 84 (21).

HRMS: $C_{20}H_{24}N_2O$ Calculated: 308.1888 found: 308.1896

16,17-Dehydro-17-Acetoxy-18-methyl-nor-yohimbane (84)



Lithium diisopropyl amide (LDA) was prepared by drop wise addition of BuLi (22 mg, 0.340 mmol) to a solution of diisopropyl amine (41 mg, 0.408 mmol) in dry THF (5 mL) at 0°C. After 1 h, a solution of compound **72** (40 mg, 0.136 mmol) in dry THF (5 mL) was added *via* cannula. The bath temperature was maintained at 0°C and stirring was continued for 2 h. Then, acetic anhydride (31 mg, 0.286 mmol) was added to the reaction mixture and stirred for another 2 h at the same temperature. Then the solution was concentrated at reduced pressure and the residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 5:1) to afford the product **84**.

Yield: 25 mg (55%); light yellow oil

UV (MeOH): λ = 224, 287 nm.

IR (ATR): ν = 3357, 2918, 2798, 2758, 2359, 2344, 1766, 1735, 1703, 1653, 1624, 1458, 1368, 1347, 1319, 1207, 1178, 1114, 1098, 1048, 1008, 907, 834, 773, 742, 581 cm^{-1}.

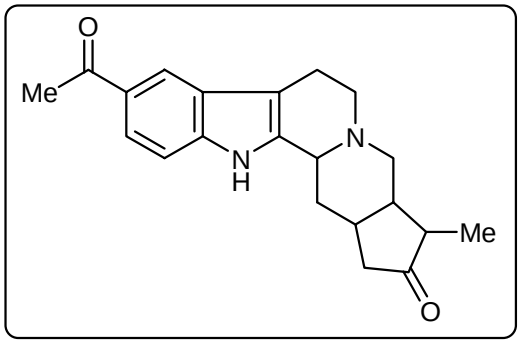
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 6.78 Hz, 3H), 1.34 (q, *J* = 12.50 Hz, 1H), 1.84 - 1.89 (m, 1H), 2.10 - 2.21 (m, 4H), 2.29 - 2.36 (m, 1H), 2.51 - 2.74 (m, 4H), 2.71 - 3.11 (m, 4H), 5.63 (t, *J* = 2.40 Hz, 1H), 7.04 - 7.12 (m, 2H), 7.26 - 7.28 (m, 1H), 7.44 (d, *J* = 7.60 Hz, 1H), 7.68 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.67 (CH_3), 22.37 (CH_2), 31.49 (CH), 33.22 (CH), 34.65(CH_2), 43.27 (CH), 43.78 (CH_3), 44.99 (CH_2), 52.60 (CH_2), 55.65 (CH_2), 58.94 (CH), 108.75 (CH), 109.15 (C), 118.04 (CH), 119.03(CH), 121.14 (CH), 126.51 (C), 136.02 (C), 138.04 (C), 220.97 (CO).

MS (150°C): *m*/*z* (%) = 336 (68, M^+), 335 (51), 294 (19), 293 (84), 277 (15), 184 (17), 169 (13), 156 (17), 44 (10), 43 (100).

HRMS: $C_{21}H_{24}N_2O_2$ Calculated: 336.1837 found: 336.1829

10-Acetyl-18-methyl-17-keto-nor-yohimbane (86)



To a solution of ketone **72** (50 mg, 0.17 mmol) in dry CH_2Cl_2 (10 mL) was added acetic anhydride (82 mg, 0.773 mmol) and $HClO_4$ (70%, 99 mg, 0.69 mmol) and stirred at room temperature for 6 h. The reaction mixture was poured in Ice (50 mL), and neutralized with saturated solution of sodium carbonate (25 mL), extracted with CH_2Cl_2 (4 × 50 mL), dried over anhydrous Na_2SO_4 and subsequently concentrated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 4:1) to afford the product **86**.

Yield: 34 mg (60%); light yellow crystals.

M.P. 101°C

UV (MeOH): λ = 255, 287 nm.

IR (ATR): ν = 3330, 2929, 2912, 2800, 2752, 1734, 1656, 1620, 1587, 1567, 1479, 1457, 1392, 1359, 1307, 1324, 1276, 1248, 1207, 1180, 1166, 1120, 1099, 1034, 949, 893, 811, 775, 731, 641 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.09 (d, *J* = 6.96 Hz, 3H), 1.38 (q, *J* = 12.39 Hz, 1H), 1.92 - 1.96 (m, 1H), 2.05 - 2.10 (m, 1H), 2.12 (d, *J* = 18.27 Hz, 1H), 2.38 - 2.50 (m, 2H),

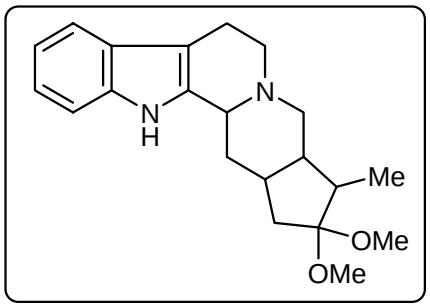
2.60 - 2.76 (m, 7H), 2.92 - 3.09 (m, 3H), 3.27 (dd, *J* = 9.71, 1.96 Hz, 1H), 7.28 (d, *J* = 8.52 Hz, 1H), 7.78 - 7.98 (m, 1H), 8.13 (br s, 1H), 8.14 (s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 12.73 (CH_3), 21.55 (CH_2), 26.69 (CH), 32.50 (CH), 33.55 (CH_2), 42.99 (CH), 43.86 (CH_3), 44.99 (CH_2), 53.00 (CH_2), 55.20 (CH_2), 58.59 (CH), 110.49 (CH), 120.14 (CH), 122.19 (CH), 126.96 (C), 129.65 (C), 135.95 (C), 138.79 (C), 198.39 (CO), 220.97 (CO).

MS (150°C): *m*/*z* (%) = 336 (100, M^+), 335 (94), 294 (15), 293 (19), 292 (13), 291 (11), 267 (50), 265 (11), 226 (11), 211 (14), 43 (100).

HRMS: $C_{21}H_{24}N_2O_2$ Calculated: 336.1824 found: 336.1838

17-Dimethoxy-18-methyl-nor-yohimbane (87)



To a solution of ketone **72** (60 mg, 0.204 mmol) in dry methanol (10 mL) was added methyl *ortho*-formate (217 mg, 2.04 mmol) and a catalytic amount of *p*-toluenesulfonic acid. After 6 h at reflux the reaction mixture was cooled and quenched with sodium bicarbonate solution (25 mL). The aqueous layers were extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 2:1) to afford the product **87**.

Yield: 58 mg (84%); light yellow crystals

M.P. 70 - 72°C

UV (MeOH): λ = 225, 281, 286 nm.

IR (ATR): ν = 3311, 2934, 2910, 2832, 2793, 2756, 1452, 1434, 1381, 1342, 1320, 1293, 1263, 1236, 1204, 1137, 1107, 1073, 1027, 1008, 1001, 975, 932, 896, 866, 842, 824, 777, 734, 701, 681, 638, 589, 567 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.02 (d, *J* = 6.90 Hz, 3H), 1.25 (m, 1H), 1.70 - 1.77 (m, 2H), 1.82 - 1.85 (m, 1H), 2.05 - 2.11 (m, 2H), 2.47 - 2.57 (m, 3H), 2.67 - 2.71 (m, 1H), 2.94 - 3.01 (m, 3H), 3.10 (s, 3H), 3.21 (s, 3H), 7.06 - 7.13 (m, 2H), 7.26 (d, *J* = 7.73 Hz, 1H), 7.46 (d, *J* = 7.53 Hz, 1H), 7.78 (br s, 1H).

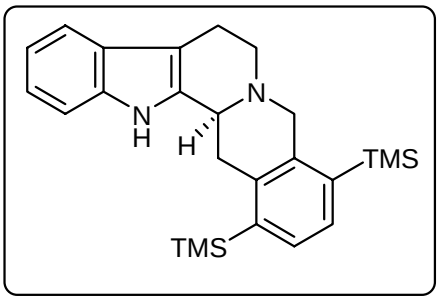
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 14.30 (CH_3), 21.65 (CH_2), 32.47 (CH_2), 35.43 (CH), 40.23 (CH), 42.97 (CH_2), 46.90 (CH_3), 48.52 (CH), 48.67 (CH_3), 53.44 (CH_2), 55.13 (CH_2), 59.31 (CH), 108.13 (C), 110.46 (C), 110.71 (CH), 117.99 (CH), 119.29 (CH), 121.18 (CH), 127.32 (C), 135.25 (C), 135.93 (C).

MS (150°C): *m*/*z* (%) = 340 (1, M^+), 309 (12), 308 (30), 307 (21), 294 (20), 293 (85), 223 (10), 87 (10), 86 (62), 83 (100), 47 (12), 43 (10).

HRMS: $C_{21}H_{28}N_2O_2$ Calculated: 340.2151 found: 340.2138

5.2.3 Referring to Section 3.3

15,18-Bis(trimethylsilyl)yohimban-15,17,19-triene (88)



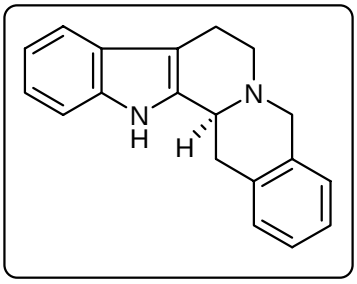
A mixture of compound **53** (100 mg, 0.238 mmol) and norbonadiene (1500 mg, 16 mmol) in toluene (10 mL) was refluxed with stirring for 12 h. The solvent was evaporated and the residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 15:1) to provide the product **88**.

Yield: 99 mg (100%); white crystals.

M.P. : 179 - 180 °C

For further spectroscopic data see literature[74]

Demethoxycarbonyldihydrogambirtannine (8)



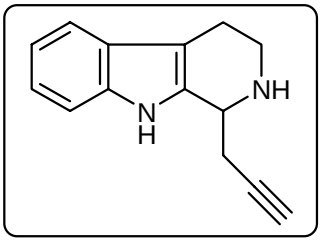
A mixture of compound **88** (100 mg, 0.239 mmol) and trifluoroacetic acid (15 mL) was refluxed with stirring for 1 h and then cooled to room temperature. The mixture was quenched with ice and neutralized with a saturated solution of Na_2CO_3. The aqueous layer was extracted with EtOAc (4 × 50 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 5:1) to afford the product **8**.

Yield: 65 mg (100%); white crystals

M.P. : 196 - 197 °C

For further spectroscopic data see literature[16,17,74]

1-Prop-2-ynl-2,3,4,9-tetrahydro-1H-β-carboline (92)



To a solution of the compound **50** (250 mg, 0.89 mmol) in THF (12 mL) was added drop wise TBAF (1M soln. in THF) (1.0 mL, 0.98 mmol) and stirred for 3 h at room temperature. The reaction was quenched with brine solution (25 mL). The aqueous layers were extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 1:2) to afford the product **92**.

Yield: 182 mg (98%); light yellow crystals.

M.P.: 123 - 125°C

UV (MeOH): λ = 223, 282, 290 nm.

IR (ATR): ν = 3402, 3283, 3193, 3054, 2925, 2849, 2740, 1715, 1656, 1619, 1550, 1451, 1317, 1302, 1287, 1246, 1156, 1111, 1043, 1009, 989, 908, 838, 742, 643, 586, 569, 554 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.82 (br s, 1H), 2.22 (t, *J* = 2.66 Hz, 1 H), 2.58 (ddd, *J* = 16.5, 8.35, 2.67 Hz, 1H), 2.66 (dd, *J* = 5.56, 2.73 Hz, 1H), 2.69 - 2.81 (m, 2H), 3.05 - 3.10 (m, 1H), 3.28 - 3.33 (m, 1H), 4.27 - 4.29 (m, 1H), 7.08 (dt, *J* = 7.5, 1 Hz, 1H), 7.14

(dt, *J* = 8.04, 1.2 Hz, 1H), 7.32 (br d, *J* = 8 Hz, 1H), 7.48 (br d, *J* = 7.8 Hz, 1H),8.31 (br s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 22.49 (CH_2), 25.46 (CH_2), 42.40 (CH_2), 51.73(CH), 71.31 (CH), 81.94 (C), 109.49 (C), 110.89 (CH), 118.19 (CH), 119.40 (CH), 121.84 (CH), 126.99 (C), 134.85 (C), 135.59 (C).

MS (150°C): *m*/*z* (%) = 210 (13, M^+), 209 (6), 180 (5), 172 (11), 171 (100), 170 (8), 169 (11), 154 (7), 144 (7), 143 (3), 142 (3), 86 (4), 85 (8), 59 (5), 43 (9), 18 (66), 17 (13).

HRMS: $C_{14}H_{14}N_2$ **C**alculated: 210.1157 found: 210.1169.

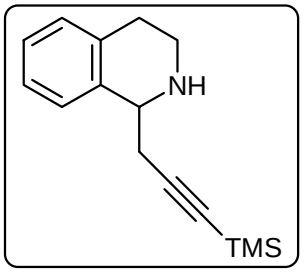
Elemental Analysis:	Calculated:	C: 79.97	H: 6.71	N: 13.32
	Found:	C: 79.96	H: 6.60	N: 13.06.

5.2.4 Referring to Section 3.4

General procedure for the addition of propargyl Grignard to the 3,4-dihydro-isoquinoline

To a solution of 3,4-dihydro-isoquinoline **98** (1.0 eq.) in dry THF (50 mL) was added drop wise $BF_3 \cdot OEt_2$ (1.0 eq.) at –23°C. After stirring for 0.5 h, a solution of trimethylsilylpropargyl magnesium bromide (3.0 eq.) dry in diethyl ether (20 mL) was added drop wise to this suspension. After stirring for 15 h at –23°C, the reaction mixture was poured into a saturated aqueous solution of NH_4Cl (100 mL) and extracted with EtOAc. The combined organic layers were washed with H_2O and dried with Na_2SO_4. Evaporation of the solvent in *vacuo* and flash chromatography of the residue on silica gel (Hexane/EtOAc 1:1) afforded the homopropargylamines **100, 110** or **114** and allene **101**, **109** or **113**.

1-(3-trimethylsilylprop-2-ynyl)-1,2,3,4-tetrahydroisoquinoline (100)



Yield: 80% light yellow oil

UV (MeOH): λ = 265, 272, 349 nm.

IR (ATR): ν = 3063, 3020, 2957, 2925, 2808, 2171, 1493, 1454, 1426, 1377, 1315, 1249, 1125, 1038, 1007, 959, 838, 758, 738, 718, 699, 649, 629, 600, 566 cm^{-1}.

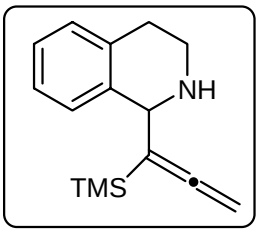
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.15 (s, 9H), 2.26 (br s, 1H), 2.61 (dd, *J* = 16.87, 9.37 Hz, 1 H), 2.74 (dd, *J* =16.92, 4.0 Hz, 1H), 2.80 - 2.83 (m, 1H), 2.99 (quint., *J* = 6.1 Hz, 1H), 3.20 (quint., *J* = 5.49 Hz, 1H), 4.14 (dd, *J* = 9.2, 3.9 Hz, 1H), 7.08 - 7.15 (m, 4H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 0.05 ($3CH_3$), 27.94 (CH_2), 29.86 (CH_2), 40.36 (CH_2), 54.68 (CH), 87.05 (C), 104.50 (C), 125.74 (CH), 126.21 (CH), 126.35 (CH), 129.20 (CH), 135.30 (C), 137.39 (C).

MS (25°C): *m*/*z* (%) = 244 (3, $[M+1]^+$), 228 (6), 133 (30), 132 (100), 131 (4), 130 (13), 117 (15), 105 (10), 103 (3), 97 (2), 96 (3), 83 (2), 77 (4), 73 (5).

HRMS: $C_{15}H_{22}NSi$ $[M+1]^+$ **C**alculated: 244.1522 found: 244.1498

1-(1-Trmethylsilyl-propa-1,2-dienyl)-1,2,3,4-tetrahydroisoquinoline (101)



Yield: 11% light yellow oil

UV (MeOH): λ = 196 nm.

IR (ATR): ν = 3069, 3020, 2952, 2896, 2794, 1927, 1603, 1533, 1491, 1453, 1428, 1367, 1317, 1292, 1244, 1194, 1125, 1076, 1041, 1007, 991, 941, 836, 808, 771, 741, 719, 691, 666, 640, 619, 590, 555 cm^{-1}.

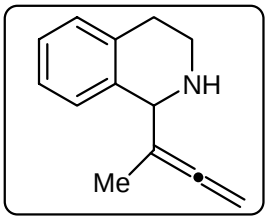
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.11 (s, 9H), 2.08 (br s, 1H), 2.71 (td, *J* = 16.2, 5.0 Hz, 1H), 2.87 - 2.93 (m, 1H), 3.0 - 3.05 (m, 1H), 3.25 - 3.30 (m, 1H), 4.39 (t, *J* = 1.57 Hz, 2H), 4.75 (br s, 1H), 7.07 - 7.15 (m, 4H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 0.65 ($3CH_3$), 29.49 (CH_2), 41.45 (CH_2), 59.37 (CH), 69.42 (CH_2), 99.40 (C), 125.13 (CH), 125.90 (CH), 127.44 (CH), 128.70 (CH), 134.86 (C), 138.10 (C), 211.02 (C).

MS (80°C): *m*/*z* (%) = 244 (6, $[M+1]^+$), 228 (9), 133 (36), 132 (100), 130 (11), 117 (15), 115 (7), 105 (10), 73 (10).

HRMS: $C_{15}H_{21}NSi$ **C**alculated: 243.1443 found: 243.1412.

1-(1-Methylpropa-1,2-dienyl)-1,2,3,4-tetrahydroisoquinoline (109)



Yield: 66% light yellow oil (as mixture of **109** and **110**)

UV (MeOH): λ = 198, 203, 264, 273 nm.

IR (ATR): ν = 3057, 3019, 2922, 2830, 1957, 1492, 1453, 1428, 1366, 1292, 1209, 1124, 1057, 1037, 990, 940, 846, 796, 742, 642, 579, 565 cm^{-1}.

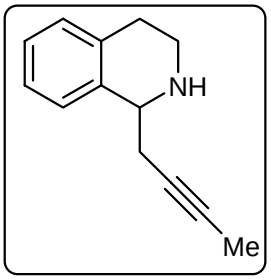
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.66 (t, *J* = 3.09 Hz, 3H), 2.42 (br s, 1H), 2.70 (dt, *J* = 16.2, 4.6 Hz, 1H), 2.87 - 2.93 (m, 1H), 3.01 - 3.06 (m, 1H), 3.25 - 3.29 (m, 1H), 4.60 (s, 1H), 4.63 - 4.66 (m, 2H), 7.07 - 7.10 (m, 1H), 7.12 - 7.16 (m, 3H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 14.59 (CH_3), 29.40 (CH_2), 41.80 (CH_2), 60.72 (CH), 74.31 (CH_2), 100.64 (C), 125.51 (CH), 126.30 (CH), 127.08 (CH), 128.88 (CH), 135.43 (C), 136.29 (C), 208.15 (C).

MS (25°C): *m*/*z* (%) = 185 (8, M^+), 170 (12), 169 (17), 141 (12), 133 (80), 132 (100), 131 (16), 130 (48), 117 (58), 115 (23), 105 (34), 103 (14), 77 (14).

HRMS: $C_{13}H_{15}N$ **C**alculated: 185.1204 found: 185.1198.

1-But-2-ynyl-1,2,3,4-tetrahydroisoquinoline (110)



UV (MeOH): λ= 283, 361, 403 nm.

IR (ATR): ν = 3057, 3019, 2917, 2832, 2732, 1626, 1578, 1492, 1454,

1428, 1377, 1316, 1210, 1125, 1033, 961, 878, 819, 792, 741, 712, 693, 625, 591, 557 cm^{-1}.

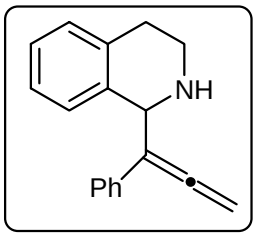
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.80 (t, *J* = 2.5 Hz, 3H), 2.05 (br s, 1H), 2.52 - 2.58 (m, 1H), 2.66 - 2.84 (m, 3H), 2.99 - 3.04 (m, 1H), 3.20 (quint., *J* = 6.0 Hz, 1 H), 4.07 (dd, *J* = 9.5, 3.7 Hz, 1H), 7.07 - 7.16 (m, 4H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 3.62 (CH_3), 26.61 (CH_2), 29.85 (CH_2), 40.46 (CH_2), 54.99 (CH), 76.46 (C), 77.87 (C), 125.78 (CH), 126.11 (CH), 126.31 (CH), 129.23 (CH), 135.29 (C), 137.68 (C).

MS (25°C): *m*/*z* (%) = 185 (1, M^+), 184 (3), 133 (12), 132 (100), 131 (7), 130 (12), 117 (10), 105 (8), 103 (4), 77 (4).

HRMS: $C_{13}H_{15}N$ **C**alculated: 185.1204 found: 185.1201.

1-(1-Phenylpropa-1,2-dienyl)-1,2,3,4-tetrahydroisoquinoline (113)



Yield: 19% light yellow oil (as mixture of **113** and **114**)

UV (MeOH): λ = 201, 249 nm.

IR (ATR): ν = 3055, 3021, 2916, 2832, 1936, 1596, 1492, 1449, 1426, 1290, 1180, 1156, 1113, 1060, 1032, 912, 847, 738, 692, 669, 612, 592, 565 cm^{-1}.

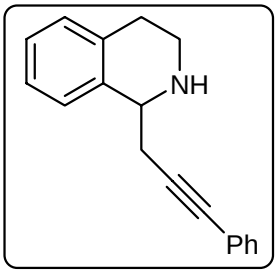
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.5 (br s, 1H), 2.87 - 2.89 (m, 2H), 3.05 (quint, *J* = 5.8 Hz, 1H), 3.27 (quint, *J* = 5.8 Hz, 1H), 4.92 (dd, *J* = 8.0, 1.2 Hz, 2H), 5.22 (s, 1H), 7.10 (t, *J* = 2.7, 3H), 7.13 - 7.17 (m, 1H), 7.20 (t, *J* = 7.3 Hz, 1H), 7.3 (t, *J* = 7.9 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 28.95 (CH_2), 40.65 (CH_2), 57.29 (CH), 79.07 (CH_2), 108.06 (C), 125.67 (CH), 126.55 (CH), 126.91 (2CH), 127.07 (CH), 127.76 (CH), 128.65 (2CH), 128.93 (CH), 134.70 (C), 134.85 (C), 136.2 (C), 210.24 (C).

MS (25°C): *m*/*z* (%) = 247 (8, M^+), 246 (14), 133 (9), 132 (100), 130 (6), 117 (7), 115 (6).

HRMS: $C_{18}H_{17}N$ **C**alculated: 247.1361 found: 247.1364.

1-(3-Phenylprop-2-ynyl)-1,2,3,4-tetrahydroisoquinoline (114)



UV (MeOH): λ= 240, 250 nm.

IR (ATR): ν = 3060, 3020, 2929, 2226, 1628, 1598, 1490, 1452, 1426, 1315, 1210, 1156, 1121, 1070, 1031, 908, 848, 727, 691, 641, 590, 556 cm^{-1}.

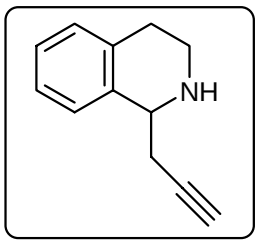
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.73 (t, *J* = 7.8, 2H), 2.84 - 2.89 (m, 2H), 2.97 (d, *J* = 4.1, 1H), 3.74 (dt, *J* = 8.0, 2.2 Hz, 1H), 4.27 (dd, *J* = 8.9, 4.1 Hz, 1H), 7.07 - 7.49 (series of m, 9H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 29.25 (CH_2), 29.50 (CH_2), 40.43 (CH_2), 54.75 (CH), 82.80 (C), 87.07 (C), 125.45 (CH), 126.17 (CH), 126.30 (2CH), 127.00 (CH), 127.71 (CH), 128.16 (2CH), 128.88 (CH), 136.75 (C), 136.94 (C).

MS (25°C): *m*/*z* (%) = 247 (3, M^+), 204 (13), 133 (10), 132 (100), 130 (9), 117 (7), 115 (7).

HRMS: $C_{18}H_{17}N$ **C**alculated: 247.1361 found: 247.1357.

1-Prop-2-ynyl-1,2,3,4-tertahydro-isoquinoline (108)



To a solution of the compound **100** (547 mg, 2.25 mmol) in THF (15 mL) was added drop wise TBAF (1M soln. in THF) (2.25 mL, 2.25 mmol) and stirred for 3 h at room temperature. The reaction was quenched with brine solution (25 mL). The aqueous layer was extracted with CH_2Cl_2 (4 × 50 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated in *vacuo*. The residue was subjected to flash chromatography on silica gel (Hexane/EtOAc 1:2) to afford the product **108**.

Yield: 333 mg (87%); light orange oil

IR (ATR): ν = 3402, 3283, 3193, 3054, 2925, 2849, 2740, 1715, 1656, 1619, 1550, 1451, 1317, 1302, 1287, 1246, 1156, 1111, 1043, 1009, 989, 908, 838, 742, 643, 586, 569, 554 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.05 (t, *J* = 2.67 Hz, 1 H), 2.21 (br s, 1H), 2.58 (ddd, *J* = 16.8, 9.2, 2.65 Hz, 1H), 2.69 - 2.70 (m, 1H), 2.72 - 2.86 (m, 2H), 2.98 - 3.03 (m, 1H), 3.18 - 3.23 (m, 1H), 4.12 (dd, *J* = 9.1, 3.8, 1H), 7.05 - 7.18 (m, 4H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 26.01 (CH_2), 29.49 (CH_2), 40.20 (CH_2), 54.32 (CH), 70.21 (CH), 81.66 (C), 125.51 (CH), 125.72 (CH), 126.12 (CH), 128.99 (CH), 135.01 (C), 137.07 (C).

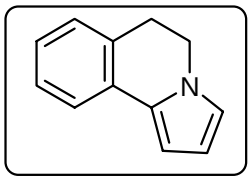
MS (25°C): *m*/*z* (%) = 171 (2, M^+), 133 (23), 132(100), 130 (16), 117 (20), 115 (10), 105 (14), 103 (7), 77 (7).

HRMS: $C_{12}H_{13}N$ **C**alculated: 171.1048 found: 171.1037.

General procedure for the silver(I)-promoted oxidative cyclization of homopropargylamine derivatives of isoquinoline

Silver(I) acetate (1.1 eq.) was added to a solution of the homopropargylamine **100**, **101**, **108**, **109**, **110**, **113** or **114** (1.0 eq.) in anhydrous CH_2Cl_2 or acetone. In the absence of light, the solution was stirred at room temperature under an argon atmosphere for 14 h (compounds **100**, **108**, **109**, **110**, **113** and **114**) or acetone reflux for 14 h (compound **101**). Filtration over a short path of neutral alumina (Hexane/EtOAc 1:1) and removal of the solvent provided the pyrroles **102**, **111**, **112**, **117** or **118**.

5,6-Dihydro-pyrrolo[2,l-*a*]isoquinoline (102)



Yield: 72% light yellow oil

UV (MeOH): λ = 293, 303 (sh) nm.

IR (ATR): ν = 2927, 2879, 1689, 1606, 1577, 1550, 1494, 1460, 1427, 1413, 1334, 1316, 1245, 1230, 1200, 1167, 1102, 1070, 1045, 751, 706, 689, 673, 605 cm^{-1}.

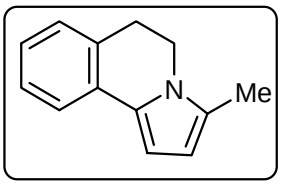
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 3.08 (t, *J* = 6.6 Hz, 2H), 4.09 (t, *J* = 6.6 Hz, 2H), 6.24 (dd, *J* = 3.5, 2.7 Hz, 1H), 6.53 (dd, *J* = 3.5, 1.5 Hz, 1H), 6.69 (m, 1H), 7.11 (dt, *J* = 1.1, 7.4 Hz, 1H), 7.18 (dd, *J* = 7.4, 0.4 Hz, 1H), 7.24 (m, 1H), 7.54 (dd, *J* = 7.4, 0.4 Hz, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 29.45 (CH_2), 44.08 (CH_2), 103.59 (CH), 108.53 (CH), 120.79 (CH), 122.36 (CH), 125.49 (CH), 127.07 (CH), 127.90 (CH), 129.56 (C), 129.79 (C), 130.27 (C).

MS (25°C): *m*/*z* (%) = 169 (100, M^+), 168 (67), 167 (25), 166 (4), 154 (5), 141 (5), 84 (9).

HRMS: $C_{12}H_{11}N$ **C**alculated: 169.0891 found: 169.0888.

3-Methyl-5,6-dihydropyrrolo[2,1-*a*]isoquinoline (112)



Yield: 34% orange crystals (as mixture of **112** and **113**)

M.P. : 67°C

UV (MeOH): λ = 305 nm.

IR (ATR): ν = 2924, 2887, 2854, 1656, 1603, 1578, 1511, 1476, 1453, 1407, 1338, 1318, 1255, 1195, 1181, 1071, 1048, 1023, 952, 899, 869, 837, 785, 749, 683, 659, 617, 587, 563 cm^{-1}.

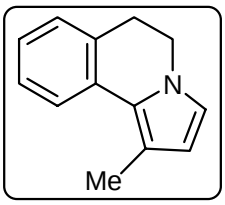
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.27 (s, 3H), 3.03 (t, *J* = 6.0 Hz, 2H), 3.93 (t, *J* = 6.6 Hz, 2H), 5.95 (d, *J* = 3.44 Hz, 1H), 6.44 (d, *J* = 3.58 Hz, 1H), 7.04 (dt, *J* = 1.1, 7.4 Hz, 1H), 7.15 (dd, *J* = 7.3, 0.4 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.48 (dd, *J* = 7.7, 0.4 Hz, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 11.89 (CH_3), 29.28 (CH_2), 40.55 (CH_2), 102.80 (CH), 107.20 (CH), 122.03 (CH), 125.03 (CH), 127.02 (CH), 127.75 (CH), 128.76 (C), 129.10 (C), 129.64 (C), 129.97 (C).

MS (25°C): *m*/*z* (%) = 183 (100, M^+), 182 (97), 181 (13), 180 (29), 167 (55).

HRMS: $C_{13}H_{13}N$ **C**alculated: 183.1048 found: 183.1043.

1-Methyl-5,6-dihydropyrrolo[2,1-*a*]isoquinoline (111)



UV (MeOH): λ = 197, 298 nm.

IR (ATR): ν = 2939, 2866, 1684, 1603, 1577, 1555, 1494, 1478, 1454, 1429, 1381, 1327, 1264, 1220, 1192, 1159, 1118, 1052, 1030, 1008, 969, 938, 909, 867, 782, 759, 732, 713, 671, 617, 600, 557 cm^{-1}.

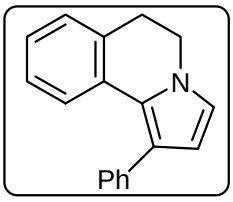
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.43 (s, 3H), 3.03 (t, *J* = 6.0 Hz, 2H), 4.04 (t, *J* = 6.0 Hz, 2H), 6.07 (d, *J* = 2.5 Hz, 1H), 6.60 (d, *J* = 2.5 Hz, 1H), 7.09 (dt, *J* = 1.1, 7.4 Hz, 1H), 7.20 (dd, *J* = 7.0, 0.6 Hz, 1H), 7.27 (m, 1H), 7.61 (dd, *J* = 7.8, 0.4 Hz, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 13.98 (CH_3), 30.36 (CH_2), 44.41 (CH_2), 110.70 (CH), 116.08 (C), 119.16 (CH), 123.10 (CH), 124.71 (CH), 125.16 (C), 126.92 (CH), 127.95 (CH), 130.70 (C), 131.37 (C).

MS (25°C): *m*/*z* (%) = 183 (100, M^+), 182 (82), 180 (12), 167 (20), 147 (22), 146 (13), 118 (16).

HRMS: $C_{13}H_{13}N$ **C**alculated: 183.1048 found: 183.1045.

1-Phenyl-5,6-dihydropyrrolo[2,1-*a*]isoquinoline (117)



Yield: 46% orange oil (as mixture of **117** and **118**)

UV (MeOH): λ = 241, 256, 309 nm.

IR (ATR): ν = 3029, 3053, 2952, 2879, 1736, 1697, 1603, 1498, 1471, 1458, 1445, 1397, 1329, 1263, 1213, 1188, 1072, 1015, 942, 911, 761, 730, 699, 650, 623, 580, 552 cm^{-1}.

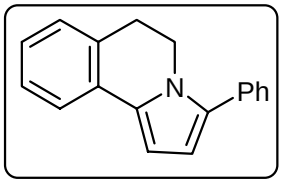
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 3.08 (t, *J* = 6.4 Hz, 2H), 4.05 (t, *J* = 6.4 Hz, 2H), 6.23 (d, *J* = 2.6 Hz, 1H), 6.72 (d, *J* = 2.6 Hz, 1H), 6.97 (dt, *J* = 1.2, 7.5 Hz, 1H), 7.03 (dt, *J* = 1.3, 7.4 Hz, 1H), 7.17 (d, *J* = 7.3 Hz, 1H), 7.26 (dt, *J* = 1.5, 7.4 Hz, 1H), 7.32 - 7.37 (m, 3H), 7.48 - 7.50 (m, 2H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 30.22 (CH_2), 44.67 (CH_2), 110.47 (CH), 120.26 (CH), 122.48 (C), 123.98 (CH), 124.81 (C), 125.56 (CH), 126.08 (CH), 126.59 (CH), 127.92 (CH), 128.38 (2CH), 128.98 (2CH), 129.70 (C), 131.88 (C), 137.66 (C).

MS (25°C): *m*/*z* (%) = 245 (100, M^+), 244 (81), 243 (34), 242 (20), 241 (18), 194 (12).

HRMS: $C_{18}H_{15}N$ **C**alculated: 245.1204 found: 245.1209.

3-Phenyl-5,6-dihydropyrrolo[2,1-*a*]isoquinoline (118)



UV (MeOH): λ = 314 nm.

IR (ATR): ν = 3058, 2924, 1699, 1652, 1602, 1577, 1556, 1493, 1481, 1455, 1406, 1329, 1263, 1186, 1157, 1119, 1072, 1029, 1015, 979, 910, 754, 730, 699, 649, 621, 573, 555 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 3.01 (t, *J* = 6.4 Hz, 2H), 4.14 (t, *J* = 6.4 Hz, 2H), 6.32 (d, *J* = 3.7 Hz, 1H), 6.60 (d, *J* = 3.7 Hz, 1H), 6.98 - 7.69 (series of m, 9H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 29.65 (CH_2), 42.09 (CH_2), 104.22 (CH), 109.38 (CH), 122.47 (C), 122.61 (CH), 125.60 (CH), 127.19 (C), 127.73 (CH), 128.44 (2CH), 128.57 (2CH), 129.89 (C), 132.05 (C), 132.13 (C).

MS (25°C): *m*/*z* (%) = 245 (100, M^+), 244 (54), 243 (19).

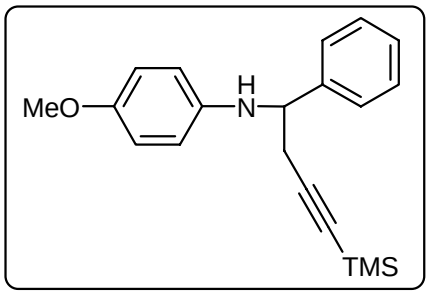
HRMS: $C_{18}H_{15}N$ cal.: 245.1204, found: 245.1233.

General procedure for the synthesis of homopropargylamines

To a solution of *Schiff* base **119a-e** (1.0 eq.) in dry THF was added drop wise $BF_3 \cdot OEt_2$ (1.0 eq.) at –23°C. After stirring for 0.5 h, a solution of trimethylsilylpropargyl magnesium bromide **99** (3.0 eq.) in dry diethyl ether was added drop wise to this suspension. After stirring for 15 h at –23°C (compounds **119a-d**) or 0°C (compound **119e**), the reaction mixture was poured into a saturated aqueous solution of NH_4Cl (100 ml) and extracted with EtOAc. The combined organic layers were washed with H_2O and dried with Na_2SO_4. Evaporation of the solvent in *vacuo* and flash chromatography of the residue on silica gel (Hexane/EtOAc 5:1) afforded the homopropargylamines **120a-e**.

(4-Methoxy-phenyl)-(1-phenyl-4-trimethylsilyl-but-3ynyl)amine (120a)

Yield: 78% light yellow oil



IR (ATR): ν = 3393, 3063, 3029, 2956, 2899, 2831, 2174, 1927, 1620, 1509, 1453, 1408, 1354, 1295, 1237, 1179, 1121, 1038, 839, 818, 757, 699, 641, 575 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.30 (s, 9H), 2.72 (dd, *J* = 16.9, 7.3 Hz, 1H), 2.81 (dd, *J* = 16.9, 5.4 Hz, 1H), 3.76 (s, 3H), 4.36 (br s, 1H), 4.52 (t, *J* = 6.1 Hz, 1H), 6.6 - 6.68 (m, 2H), 6.79 - 6.83 (m, 2H), 7.33 - 7.36 (m, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.49 (d, *J* = 7.79 Hz, 2H).

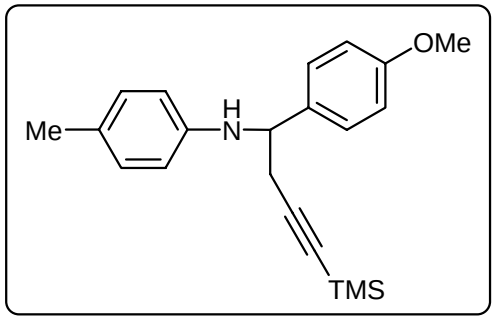
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = – 0.12 ($3CH_3$), 29.56 (CH_2), 55.36 (CH_3), 57.42 (CH), 87.95 (C), 102.95 (C), 114.54 (CH), 114.95 (CH), 126.29 (CH), 127.17 (CH), 128.34 (CH), 141.30 (C), 142.46 (C), 152.11 (C).

MS (25°C) : *m*/*z* (%) = 323 (5, M^+), 213 (14), 212 (100), 180 (10), 179 (46), 179 (5), 128 (17), 112 (11), 107 (79), 97 (5), 79 (20), 77 (10), 75 (22), 73 (43), 43 (6), 29 (6).

HRMS: $C_{20}H_{25}NOSi$ **C**alculated: 323.1705 found: 323.1695.

[1-(4-Methoxyphenyl)-4-trimethylsilyl-but-3-ynyl]-*p*-totyl-amine (120b)

Yield: 80% pale yellow solid



M.P. : 69 - 70°C

UV (MeOH): λ = 227, 247 nm.

IR (ATR): ν = 3408, 3002, 2961, 2903, 2862, 2171, 1613, 1584, 1509, 1458, 1441, 1420, 1403, 1317, 1301, 1245, 1212, 1168,1128, 1113, 1096, 1055, 1033, 1010, 834, 808, 761, 726, 703, 645, 602, 573 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.16 (s, 9H), 2.20 (s, 1H), 2.60 (dd, *J* = 16.9, 7.24 Hz, 1H), 2.70 (dd, *J* = 16.97, 5.37 Hz, 1H), 3.79 (s, 3H), 4.32 (br s, 1H), 4.41 (t, *J* = 5.9 Hz, 1H), 6.46 (d, *J* = 8.3 Hz, 1H), 6.85 (d, *J* = 8.6 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 7.30 (d, *J* = 8.6 Hz, 1H).

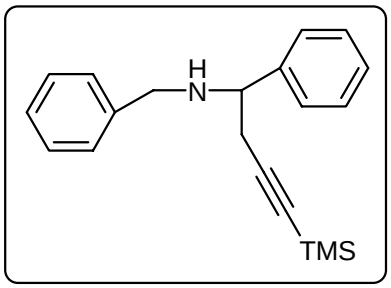
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = – 0.12 ($3CH_3$), 20.34 (CH), 29.85 (CH_2), 55.20 (CH), 56.38 (CH), 88.10 (C), 103.02 (C), 113.86 (2CH), 113.92 (2CH), 126.85 (C), 127.41 (2CH), 129.55 (2CH), 134.62 (C), 145.05 (C), 158.77 (C).

MS (25°C) : *m*/*z* (%) = 337 (20, M^+), 322 (5), 228 (8), 227 (77), 226 (100), 225 (5), 224 (7), 211 (4), 182 (8),164 (5), 118 (18), 91 (20), 73 (23).

HRMS: $C_{21}H_{27}NOSi$ **C**alculated: 337.1862 found: 337.1845.

Elemental Analysis:	Calculated:	C: 74.73	H: 8.06	N: 4.15
	Found:	C: 73.82	H: 8.50	N: 4.09

Benzyl-(1-phenyl-4-trimethylsilyl-but-3-ynyl)-amine (120c)



Yield: 68% colourless oil

UV (MeOH): λ = 252, 258, 264 nm.

IR (ATR): ν = 3062, 3027, 2958, 2900, 2838, 2173, 1602, 1494, 1453, 1421, 1354, 1328, 1249, 1201, 1117, 1074, 1028, 1012, 911, 837, 757, 732, 696, 649, 627, 598 cm^{-1}.

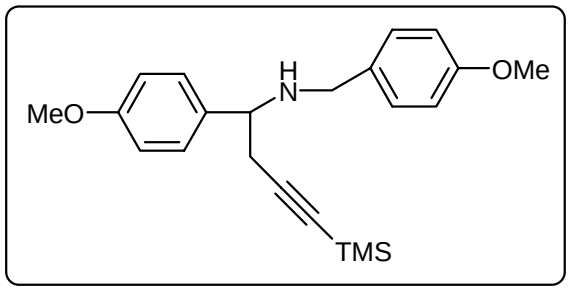
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.26 (s, 9H), 2.28 (br s, 1H), 2.62 (d, *J* = 6.77 Hz, 2H), 3.63 (d, *J* = 13.5 Hz, 1H), 3.82 (d, *J* = 13.5 Hz, 1H), 3.92 (t, *J* = 6.8 Hz, 1H), 7.31 - 7.44 (m, 8H), 7.46 (d, *J* = 7.5 Hz, 2 H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = – 0.03 ($3CH_3$), 29.73 (CH_2), 51.19 (CH_2), 60.52 (CH), 86.99 (C), 104.21 (C), 126.78 (CH), 127.10 (CH), 127.36 (CH), 127.95 (CH), 128.28 (CH), 128.33 (CH), 140.28 (C), 142.52 (C).

MS (25°C) : *m*/*z* (%) = 308 (25, $[M+1]^{+1}$), 307 (1, M^+), 197 (7), 196 (51), 92 (6), 91 (100), 73 (21).

HRMS: $C_{20}H_{25}NSi$ **C**alculated: 307.1756 found: 307.1770.

(4-Methoxybenzyl)-[1-(4-methoxy-phenyl)-4-trimethylsilyl-but-3-ynyl]-amine (120d)



Yield: 68% yellow oil

UV (MeOH): λ = 225, 275, 282 nm.

IR (ATR): ν = 2999, 2956, 2834, 2173, 1698, 1610, 1579, 1509, 1463, 1442, 1421, 1301, 1243, 1171, 1160, 1107, 1033, 830, 781, 758, 698, 641, 596 cm^{-1}.

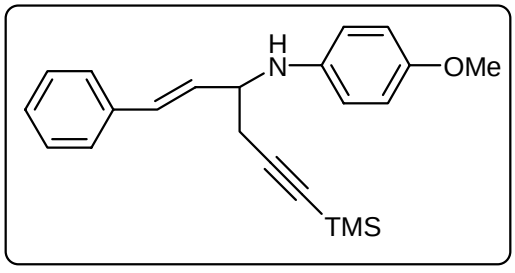
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.14 (s, 9H), 2.12 (br s, 1H), 2.49 (d, *J* = 6.6 Hz, 2H), 3.45 (d, *J* = 13.22 Hz, 1H), 3.64 (d, *J* = 13.22 Hz, 1H), 3.79 (s, 3H), 3.80 (s, 3H), 3.88 (s, 1H), 6.83 - 6.89 (m, 4H), 7.17 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 0.00 ($3CH_3$), 29.84 (CH_2), 50.54 (CH_2), 55.20 ($2CH_3$), 59.80 (CH), 86.96 (C), 104.42 (C), 113.73 (4CH), 128.19 (2CH), 129.18 (2CH), 132.49 (C), 134.62 (C), 158.51 (C), 158.87 (C).

MS (25°C): *m*/*z* (%) = 368 (1, $[M+1]^+$), 257 (12), 256 (79), 137 (51), 135 (12), 121 (100).

HRMS: $C_{22}H_{30}NO_2Si$ $[M+1]^+$ **C**alculated: 368.2046 found: 368.2037.

(4-Methoxyphenyl)-(1-styryl-4-trimethylsilyl-but-3-ynyl)-amine (120e)



Yield: 88% light yellow oil

UV (MeOH): λ = 250, 285, 292 nm.

IR (ATR): ν = 3028, 2957, 2899, 2831, 2173, 1509, 1464, 1448, 1408, 1294, 1238, 1179, 1123, 1072, 1037, 965, 838, 817, 747, 693, 639, 565 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.17 (s, 9H), 2.62 (d, *J* = 5.8 Hz, 1H), 3.74 (s, 3H), 3.83 (br s, 1H), 4.08 - 4.15 (m, 1H), 6.24 (ddd, *J* = 15.2, 6.3, 1.4 Hz, 1H), 6.64 - 6.68 (m, 3H), 6.76 (d, *J* = 1.5 Hz, 1H), 7.21 - 7.26 (m, 1H), 7.29 (t, *J* = 7.8 Hz, 2H), 7.36 (d, *J* = 7.9 Hz, 2H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 0.06 ($3CH_3$), 27.13 (CH_2), 55.25 (CH), 55.71 (CH_3), 88.04 (C), 102.92 (C), 114.80 (2CH), 115.61 (2CH), 126.41 (2CH), 127.50 (CH), 128.50 (2CH), 130.57 (CH), 131.00 (CH), 136.77 (C), 141.20 (C), 152.53 (C).

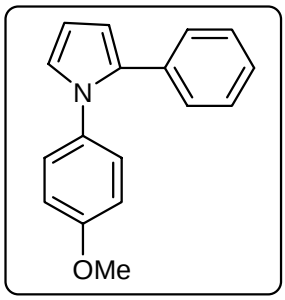
MS (25°C) : *m*/z (%) = 349 (1, M^+), 153 (8), 134 (10), 133 (100), 115 (17), 105 (6), 103 (6), 77 (9), 75 (14), 73 (16).

HRMS: $C_{22}H_{27}NOSi$ **C**alculated: 323.1862 found: 349.1883.

General procedure for the silver(I)-promoted oxidative cyclization of homopropargylamines

Silver(I) acetate (1.1 eq.) was added to a solution of the homopropargylamine **120a-e** (1.0 eq.) in dry CH_2Cl_2. In the absence of light, the solution was stirred at room temperature under an argon atmosphere for 4 d. Filtration over a short path of neutral alumina (Hexane/EtOAc 1:1) and removal of the solvent provided the pyrroles, **121a–e**.

1-(4-Methoxyphenyl)-2-phenyl-1*H*-pyrrole (121a)



Yield: 99% light yellow oil

UV (MeOH): λ = 225, 277 nm.

IR (ATR): ν = 1603, 1511, 1493, 1464, 1442, 1299, 1245, 1180, 1169, 1105, 1073, 1060, 1039, 946, 907, 884, 833, 798, 757, 725, 696, 664, 646, 617, 607 cm^{-1}

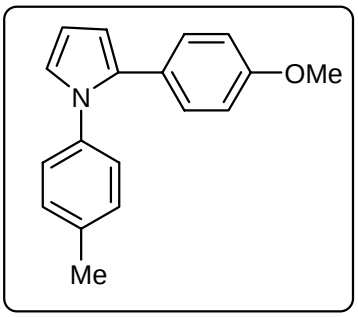
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 3.82 (s, 3H), 6.38 (m, 1H), 6.47 (dd, *J* = 3.5, 1.8 Hz, 1H), 6.87 (d, *J* = 8.9 Hz, 2H), 6.92 (m, 1H), 7.13 (d, *J* = 8.9 Hz, 2H), 7.16 - 7.19 (m, 3H), 7.22 - 7.25 (m, 2H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 55.34 (CH_3), 108.81 (CH), 110.05 (CH), 114.06 (2 CH), 124.47 (CH), 126.08 (CH), 126.87 (2CH), 127.97 (2CH), 128.15 (2CH), 132.98 (C), 133.66 (C), 133.82 (C), 158.13 (C).

MS (25°C): *m*/*z* (%) = 249 (100, M^+), 234 (47), 206 (5), 204 (5), 179 (6)

HRMS: $C_{17}H_{15}NO$ **C**alculated: 249.1154 found: 249.1182.

2-(4-Methoxyphenyl)-1-*p*-tolyl-1*H*-pyrrole (121b)



Yield: 85% light yellow oil

UV (MeOH): λ = 226 (sh), 270 nm.

IR (ATR): ν = 2924, 1675, 1598, 1510, 1460, 1420, 1366, 1304, 1246, 1168, 1109, 1024, 965, 902, 814, 714, 693, 632, 604 cm^{-1}.

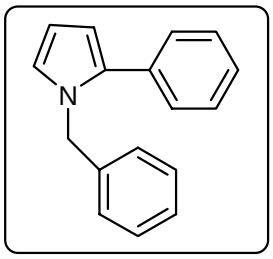
^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.35 (s, 3H), 3.77 (s, 3H), 6.33 (m, 1H), 6.34 (dd, *J* = 3.5, 1.9 Hz, 1H), 6.76 (d, *J* = 8.8 Hz, 2H), 6.88 (dd, *J* = 2.6, 1.9 Hz, 1H), 7.03 - 7.08 (m, 4H), 7.11 (d, *J* = 8.4 Hz, 2H).

^{13}C NMR and DEPT (125 MHz, $CDCl_3$): δ = 20.99 (CH_3), 55.15 (CH_3), 108.79 (CH), 109.52 (CH), 113.48 (2CH), 123.72 (CH), 125.52 (2 CH), 125.78 (C), 129.52 (2CH), 129.56 (2CH), 133.60 (C), 136.24 (C), 138.10 (C), 158.13 (C).

MS (25°C): *m*/*z* (%) = 263 (100, M^+), 248 (57), 220 (5), 189 (8), 135 (12).

HRMS: $C_{18}H_{17}NO$ **C**alculated: 263.1310 found: 263.1313.

1-Benzyl-2-phenyl-1*H*-pyrrole (121c)



Yield: 25% colourless oil

UV (MeOH): λ = 277 nm.

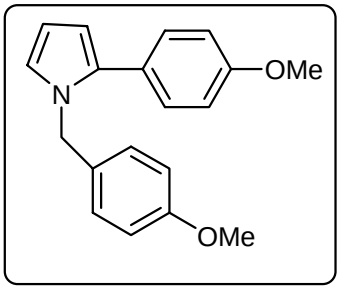
IR (ATR): ν = 3060, 3027, 2939, 2798, 1602, 1493, 1472, 1452, 1417, 1356, 1310, 1275, 1177, 1138, 1073, 1028, 989, 913, 804, 755, 719, 695, 675, 645, 622, 581, 554 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 5.23 (s, 2H), 6.38 (dd, *J* = 2.6, 1.6 Hz, 1H), 6.53 (d, *J* = 1.9 Hz, 1H), 6.84 (dd, *J* = 2.0, 1.1 Hz, 1H), 7.10 - 7.16 (m, 3H), 7.24 - 7.50 (m, 6H), 7.58 (m, 1H).

MS (25°C): *m*/*z* (%) = 233 (100, M^+), 232 (5), 142 (7), 115 (6), 92 (6), 91 (98), 65 (5).

HRMS: $C_{17}H_{15}N$ **C**alculated: 233.1204 found: 233.1207.

1-(4-Methoxybenzyl)-2-(4-methoxy-phenyl)-1*H*-pyrrole (121d)



Yield: 20% light yellow oil

UV (MeOH): λ = 225, 274 nm.

IR (ATR): ν = 2953, 1610, 1585, 1509, 1463, 1440, 1356, 1289, 1242, 1173, 1138, 1106, 1033, 909, 886, 832, 761, 727, 633, 605, 576 cm^{-1}.

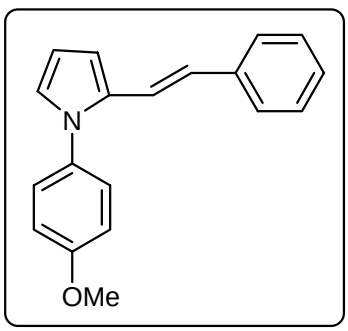
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 3.82 (s, 3H), 3.82 (s, 3H), 5.04 (s, 2H), 6.19 (dd, *J* = 3.5, 1.8 Hz, 1H), 6.24 (d, *J* = 3.0 Hz, 1H), 6.30 (d, *J* = 1.8 Hz, 1H), 6.70 - 6.73 (m, 2H), 6.81 - 6.98 (m, 3H), 7.24 - 7.30 (m, 2H), 7.38 - 7.40 (m, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 51.50 (CH_2), 55.22 ($2CH_3$), 108.11 (CH), 108.23 (CH), 112.75 (2CH), 113.61 (2CH), 120.45 (CH), 126.19 (C), 128.57 (2CH), 129.99 (2CH), 134.61 (C), 137.19 (C), 158.04 (C), 158.31 (C).

MS (25°C): *m*/*z* (%) = 293 (75, M^+), 210 (17), 209 (99), 121 (100), 73 (25).

HRMS: $C_{19}H_{19}NO_2$ **C**alculated: 293.1416 found: 293.1433.

1-(4-Methoxyphenyl)-2-styryl-1*H*-pyrrole (121e)



Yield: 78% orange oil

UV (MeOH): λ = 228, 334 nm.

IR (ATR): ν = 1629, 1598, 1512, 1459, 1418, 1298, 1248,

1180, 1147, 1106, 1040, 956, 893, 835, 801, 784, 747, 714, 692, 634, 613 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 3.88 (s, 3H), 6.32 (m, 1H), 6.64 (dd, *J* = 3.5, 1.6 Hz, 1H), 6.78 (d, *J* = 16.3 Hz, 1H), 6.84 (dd, *J* = 2.7, 1.6 Hz, 1H), 6.86 (d, *J* = 16.3 Hz, 1H), 6.99 (d, *J* = 8.9 Hz, 2H), 7.17 (tt, *J* = 7.2, 1.2 Hz, 1H), 7.25 - 7.29 (m, 2H), 7.28 (d, *J* = 8.9 Hz, 2H), 7.33 (m, 2H).

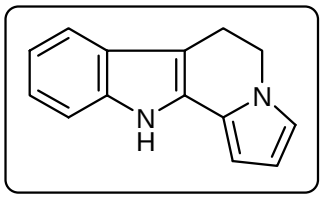
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 55.54 (CH_3), 106.91 (CH), 109.29 (CH), 114.29 (2 CH), 118.04 (CH), 123.68 (CH), 125.94 (3 CH), 126.88 (CH), 127.49 (2 CH), 128.53 (2 CH), 132.47 (C), 132.66 (C), 137.78 (C), 158.75 (C).

MS (25°C): *m*/*z* (%) = 275 (76, M^+), 274 (26), 260 (14), 201 (49), 167 (13), 158 (12), 108 (56), 106 (85), 105 (89), 78 (27), 77 (100).

HRMS: $C_{19}H_{17}NO$ **C**alculated: 275.1310 found: 275.1310.

5.2.5 Referring to Section 3.5

6,11-Dihydro-5*H*-indolizino[8,7-*b*] indole (96)



a) To a solution of compound **50** (100 mg, 0.35 mmol) in dry CH_2Cl_2 (20 mL), AgOAc (65 mg, 0.39 mmol) was added under argon atmosphere. The solution was then stirred at room temperature for 14 h, during which time the flask was prevented from light. The crude mixture was filtered over short path of neutral alumina (Hexane/EtOAc 1:1) to provide the product **96** as light green powder, yield: 52 mg (71%).

b) To a solution of compound **51** (100 mg, 0.35 mmol) in dry Acetone (20 mL), AgOAc (65 mg, 0.39 mmol) was added under argon atmosphere. The solution was then heated at reflux for 14 h, during which time the flask was prevented from light. The crude mixture was filtered over short path of neutral alumina (Hexane/EtOAc 1:1) to provide the product **96** as light green powder, yield: 55 mg (75%).

M.P.: 161 - 163°C

UV (MeOH): λ = 194, 224, 281 nm.

IR (drift): ν = 3425, 3383, 3101, 3053, 2963, 1921, 1624, 1603, 1575, 1479, 1438, 1369, 1352, 1331, 1320, 1307, 1272, 1244, 1234, 1188, 1137, 1110, 1069, 1008, 996, 925, 844, 746, 711, 693, 684, 628, 603 cm^{-1}.

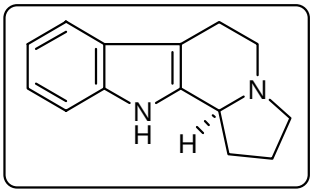
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 3.18 (t, *J* = 7.0 Hz, 2H), 4.22 (t, *J* = 7.0 Hz, 2H), 6.26 (dd, *J* = 3.4, 2.7 Hz, 1H), 6.33 (dd, *J* = 3.4, 1.4 Hz, 1H), 6.80 (dd, *J* = 2.7, 1.4 Hz, 1H), 7.18 (m, 2H), 7.39 (m, 1H), 7.54 (m, 1H), 8.10 (br s, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 21.25 (CH_2), 45.35 (CH_2), 101.87 (CH), 105.16 (C), 108.14 (CH), 110.92 (CH), 117.80 (CH), 119.93 (CH), 121.43 (CH), 121.76 (CH), 124.62 (C), 127.12 (C), 128.95 (C), 136.37 (C).

MS (65°C): *m*/*z* (%) = 208 (100, M^+), 207 (67), 206 (17), 205 (3), 115 (4), 104 (2), 71 (2), 43 (2).

HRMS: $C_{14}H_{12}N_2$ **C**alculated: 208.1000 found: 208.0994.

Harmicine (2,3,5,6,11,11b-Hexahydro-1*H*-indolizino[8,7-b] indole) (122)



To a solution of **96** (40 mg, 0.189 mmol) in methanol (5 mL) and glacial acetic acid (5 mL) was added 5% Rhodium on carbon (22 mg). The mixture was then vigorously stirred under a hydrogen atmosphere (800-900 Torr) at room temperature until no further hydrogen uptake was detected (8 days). The reaction mixture was filtered over a short path of celite (which was subsequently washed with methanol) and the solvent was evaporated. The residue was neutralized with saturated solution of sodium carbonate, extracted with CH_2Cl_2 (4 × 50 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to afford the product **122** as light yellow powder.

Yield: 36 mg (88%); light yellow powder

M.P.: 106-108 °C

IR (ATR): ν = 3185, 3059, 2925, 2853, 1610, 1558, 1519, 1450, 1384, 1302, 1233, 1147, 1059, 1008, 923, 738 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.77 - 1.87 (m, 1H), 1.88 - 1.97 (m, 2H), 2.28 - 2.36 (m, 1H), 2.69 - 2.74 (m, 1H), 2.89 - 2.97 (m, 2H), 2.99 - 3.03 (m, 1H), 3.10 - 3.16 (m, 1H), 3.31 (ddd, *J* = 12.9, 5.0, 2.3 Hz, 1H), 4.41 (m, 1H), 7.07 (dt, *J* = 1.0, 7.5 Hz, 1H), 7.12 (dt, *J* = 1.2, 7.5 Hz, 1H), 7.31 (br d, *J* = 7.5 Hz, 1H), 7.45 (br d, *J* = 7.5 Hz, 1H), 8.73 (br s, 1H).

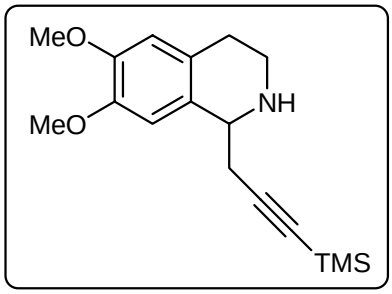
^{13}C-NMR (125 MHz, $CDCl_3$): δ = 17.38 (CH_2), 23.14 (CH_2), 29.50 (CH_2), 45.63 (CH_2), 49.06 (CH_2), 56.98 (CH), 107.03 (C), 110.95 (CH), 117.98 (CH), 119.30 (CH), 121.50 (CH), 126.90 (C), 133.96 (C), 136.20 (C).

MS (150°C): *m*/*z* (%) = 212 (62, M^+), 211 (100), 184 (21), 183 (9), 170 (7), 169 (6), 168 (7), 156 (12), 106 (6), 105 (5), 97 (4), 91 (4), 84 (11), 71 (6), 69 (5), 60 (5), 57 (8), 45 (8), 43 (16).

HRMS: $C_{14}H_{16}N_2$ **C**alculated: 212.1313 found: 212.1332.

5.2.6 Referring to Section 3.6

6,7-Dimethoxy-1-(3-trimethylsilyl-prop-2-ynyl)-1,2,3,4-tetrahydroisoquinoline (128) and 6,7-Dimethoxy-1-(1-trimethylsilyl-prop-2-dienyl)-1,2,3,4-tetrahydro-isoquinoline (129)



To a solution of 3,4-dihydro-6,7-dimethoxyisoquinoline **125** (1.5 g, 7.85 mmol) in dry THF (40 mL) was added drop wise $BF_3 \cdot OEt_2$ (1.0 mL, 7.85 mmol) at –23°C. After stirring for 0.5 h, a solution of trimethylsilylpropargyl magnesium bromide (5.06 g, 23.54 mmol) in dry diethyl ether (20 mL) was added drop wise to this suspension. After stirring for 15 h at –23°C, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl (100 mL) and extracted with EtOAc (4 × 100 mL). The combined organic layers were washed with H_2O (50 mL) and dried with Na_2SO_4. Evaporation of the solvent in *vacuo* and flash chromatography of the residue on silica gel (Hexane/EtOAc 1:1) afforded in the sequence of increasing polarity the compounds **129** as yellow oil, yield: 55 mg (2%) and **128** as light yellow crystals, yield: 1.44 g (61%).

Spectroscopic data for compound **128**

M.P.: 59 - 69°C

UV (MeOH): λ = 206, 232, 285 nm.

IR (ATR): ν = 2998, 2955, 2905, 2832, 2170, 1610, 1515, 1464, 1376, 1354, 1326, 1301, 1250, 1224, 1113, 1036, 982, 841, 760, 700, 643, 571 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.15 (s, 9H), 1.78 (br s, 1H), 2.60 (dd, *J* = 17.0, 8.8 Hz, 1H), 2.70 (d, *J* = 4.3 Hz, 1H), 2.72 (t, *J* = 5.0 Hz, 2H), 2.97 (quint., *J* = 6.0 Hz, 1H),

3.17 (quint., J = 6.0 Hz, 1H), 3.83 (s, 3H), 3.84 (s, 3H), 4.08 - 4.10 (m, 1H), 6.57 (s, 1H), 6.65 (s, 1H).

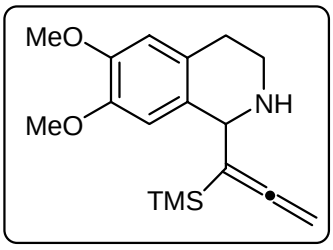
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 0.11 ($3CH_3$), 28.18 (CH_2), 29.40 (CH_2), 40.42 (CH_2), 54.54 (CH), 55.83 (CH_3), 55.96 (CH_3), 87.03 (C), 104.64 (C), 109.26 (CH), 111.65 (CH), 127.37 (C), 129.39 (C), 147.16 (C), 147.61(C).

MS (25°C) : *m*/*z* (%) = 304 (5, $[M+1]^+$), 288 (7), 193 (68), 192 (100), 190 (6), 177 (14), 176 (39), 148 (18), 147 (10), 131 (9), 118 (6), 73 (7).

HRMS: $C_{17}H_{25}NO_2Si$ **C**alculated: 303.1655 found: 303.1653

Elemental Analysis:	Calculated	C: 67.28	H: 8.30	N: 4.62
	Found	C: 67.07	H: 8.31	N: 4.79.

Spectroscopic data for compound 129



UV (MeOH): λ = 209, 227, 282, 328 nm.

IR (ATR): ν = 2999, 2951, 2905, 2831, 1927, 1609, 1558, 1514, 1464, 1355, 1325, 1249, 1222, 1119, 1031, 840, 761, 698, 643, 615, 566 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 0.06 (s, 9H), 1.59 (br s, 1H), 2.59 (td, J = 16.0, 4.6 Hz, 1H), 2.74 - 2.80 (m, 1H), 2.93 - 2.98 (m, 1H), 3.18 - 3.22 (m, 1H), 3.81 (s, 3H), 3.84 (s, 3H), 4.35 (d, J = 1.1 Hz, 2H), 4.62 (br s, 1H), 6.54 (s, 1H), 6.57 (s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = –0.57 ($3CH_3$), 29.20 (CH_2), 41.72 (CH_2), 55.71 (CH_3), 55.86 (CH_3), 59.15 (CH), 69.56 (CH_2), 99.64 (C), 110.59 (CH), 111.23 (CH), 127.12 (CH), 130.25 (CH), 146.62 (C), 147.27 (C), 210.90 (C).

MS (25°C): *m*/*z* (%) = 304 (7, $[M+1]^+$), 288 (9), 194 (8), 193 (69), 192 (100), 191 (6), 190 (7), 177 (17), 176 (41), 148 (21), 147 (12), 131 (10), 118 (6), 73 (8).

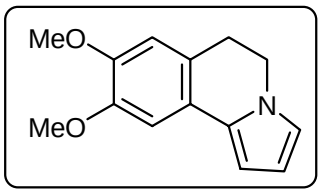
HRMS: $C_{17}H_{26}NO_2Si$ $[M+1]^+$ **C**alculated: 304.1733 found: 304.1724

8,9-Dimethoxy-5,6-dihydro-pyrrolo[2,1-*a*]isoquinoline (130)

a) To a solution of compound **128** (140 mg, 0.46 mmol) in dry CH_2Cl_2 (12 mL), AgOAc (85 mg, 0.51 mmol) was added under argon atmosphere. The solution was then stirred at room temperature for 14 h, during which time the flask was prevented from light. The crude mixture was filtered over short path of neutral alumina (Hexane/EtOAc 1:1) to provide the product **130** as light yellow crystals, yield: 61 mg (58%).

b) To a solution of compound **129** (40 mg, 0.132 mmol) in dry Acetone (12 mL), AgOAc (25 mg, 0.15 mmol) was added under argon atmosphere. The solution was then heated at reflux for 6 h, during which time the flask was prevented from light. The crude mixture was filtered over short path of neutral alumina (Hexane/EtOAc 1:1) to provide the product **130** as light yellow crystals, yield: 13 mg (43%).

M.P.: 110 - 112 °C



UV (MeOH): λ = 293, 308 (sh), 314 nm.

IR (ATR): ν = 2935, 1611, 1553, 1506, 1464, 1441, 1333, 1266, 1226, 1210, 1166, 1131, 1070, 1050, 1015, 859, 791, 711 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 2.99 (t, *J* = 6.6 Hz, 2H), 3.88 (s, 3H), 3.91 (s, 3H), 4.05 (t, *J* = 6.6 Hz, 2H), 6.19 (br s, 1H), 6.38 (br d, *J* = 2.3 Hz, 1H), 6.64 (br s, 1H), 6.69 (s, 1H), 7.01 (s, 1H).

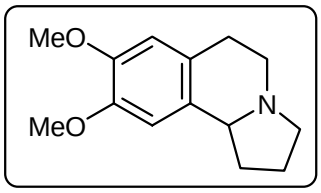
^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 29.05 (CH_2), 44.25 (CH_2), 56.00 (CH_3), 56.01 (CH_3), 102.22 (CH), 105.91 (CH), 108.30 (CH), 111.29 (CH), 120.36 (CH), 122.57 (C), 122.75 (C), 129.91 (C), 147.20 (C), 148.22 (C).

MS (25°C): *m*/*z* (%) = 229 (100, M^+), 214 (46), 186 (19), 185 (6), 171 (7).

HRMS: $C_{14}H_{15}NO_2$ **C**alculated: 229.1103, found: 229.1105.

Elemental Analysis:	Calculated	C: 73.34	H: 6.59	N: 6.11
	Found	C: 73.37	H 6.88	N: 6.05.

Crispine A (124)



To a solution of **130** (90 mg, 0.393 mmol) in methanol (5 mL) and glacial acetic acid (5 mL) was added 5% Rhodium on carbon (25% by wt., 23 mg). The mixture was then vigorously stirred under a hydrogen atmosphere (800-900 Torr) at room temperature until no further hydrogen uptake was detected (8 days). The reaction mixture was filtered over a short path of celite (which was subsequently washed with methanol) and the solvent was evaporated. The residue was neutralized with 2 N sodium hydroxide solution, extracted with CH_2Cl_2 (4 × 50 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo.* to afford the product **124**.

Yield: 60 mg (66%); colourless crystals

M.P.: 76 - 78 °C

IR (ATR): ν = 2921, 2801, 1607, 1517, 1466, 1409, 1376, 1359, 1323, 1312, 1250, 1228, 1211, 1198, 1159, 1135, 1111, 1086, 1012, 850, 811, 762, 721 cm^{-1}.

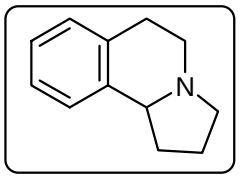
^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.71 (m, 1H), 1.86 (m, 1H), 1.92 (m, 1H), 2.31 (m, 1H), 2.55 (br q, *J* = 8.5 Hz, 1H), 2.63 (dt, *J* = 10.8, 4.6 Hz, 1H), 2.72 (br dt, *J* = 16.4, 3.5 Hz, 1H), 3.01 (m, 1H), 3.07 (dt, *J* = 8.7, 3.7 Hz, 1H), 3.17 (ddd, *J* = 11.3, 6.2, 2.9 Hz, 1H), 3.41 (br t, *J* = 8.0 Hz, 1H), 3.83 (s, 3H), 3.84 (s, 3H), 6.56 (s, 1H), 6.60 (s, 1H).

^{13}C-NMR and DEPT (125 MHz, $CDCl_3$): δ = 22.21 (CH_2), 28.03 (CH_2), 30.47 (CH_2), 48.35 (CH_2), 53.14 (CH_2), 55.87 (CH_3), 55.98 (CH_3), 62.94 (CH), 108.81 (CH), 111.30 (CH), 126.20 (C), 130.94 (C), 147.19 (C), 147.31 (C).

MS (25°C): *m*/*z* (%) = 233 (63, M^+), 232 (100), 218 (6), 216 (7), 205 (49), 190 (28), 177 (5).

HRMS: $C_{14}H_{19}NO_2$ **C**alculated: 233.1416, found: 233.1391.

1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (123)



To a solution of **102** (86 mg, 0.51 mmol) in methanol (5 mL) and glacial acetic acid (5 mL) was added 5% Rhodium on carbon (25% by wt., 22 mg). The mixture was then vigorously stirred under a hydrogen atmosphere (800-900 Torr) at room temperature until no further hydrogen uptake was detected (8 days). The reaction mixture was filtered over a short path of celite (which was subsequently washed with methanol) and the solvent was evaporated. The residue was neutralised with 2 N sodium hydroxide solution, extracted with CH_2Cl_2 (4 × 50 mL), dried over anhydrous Na_2SO_4 and concentrated in *vacuo* to afford the product **123**.

Yield: 80 mg (91%); light yellow oil.

IR (ATR): ν = 2922, 2872, 2783, 1578, 1493, 1452, 1377, 1351, 1325, 1285, 1255, 1218, 1182, 1162, 1136, 1116, 1082, 1040, 1013, 932, 913, 740 cm^{-1}.

^{1}H-NMR (500 MHz, $CDCl_3$): δ = 1.71 - 1.78 (m, 1H), 1.82 - 1.98 (m, 2H), 2.37 (m, 1 H), 2.62 (q, *J* = 8.1 Hz, 1H), 2.70 (ddd, *J* = 14.8, 10.1, 4.7 Hz, 1H), 2.84 (dt, *J* = 16.6, 4.0 Hz, 1H), 3.14 - 3.12 (m, 2H), 3.14 - 3.20 (m, 1H), 3.53 (t, *J* = 8.3 Hz, 1H), 7.06 - 7.16 (m, 4H).

^{13}C-NMR (125 MHz, $CDCl_3$): δ = 17.38 (CH_2), 23.14 (CH_2), 29.50 (CH_2), 45.63 (CH_2), 49.06 (CH_2), 56.98 (CH), 107.03 (C), 110.95 (CH), 117.98 (CH), 119.30 (CH), 121.50 (CH), 126.90 (C), 133.96 (C), 136.20 (C).

MS (25°C): *m*/*z* (%) = 173 (46, M^+), 172 (100), 170 (11), 145 (36), 117 (18).

HRMS: $C_{12}H_{15}N$ **C**alculated: 173.1204, found: 173.1206.

6 Appendix

6.1 X-Ray crystallographic data

Table 1. Crystal data and structure refinement for compound 56

Empirical formula	$C_{18}H_{18}N_2O$	
Formula weight	278.34	
Temperature	198(2) K	
Wavelength	0.71073 Å	
Crystal system	Rhombohedral	
Space group	R-3	
Unit cell dimensions	a = 31.474(3) Å	α= 90°.
	b = 31.474(3) Å	β= 90°.
	c = 7.6323(10) Å	γ = 120°.
Volume	6547.7(12) $Å^3$	
Z	18	
Density (calculated)	1.271 Mg/m^3	
Absorption coefficient	0.080 mm^{-1}	
F(000)	2664	
Crystal size	0.3 x 0.2 x 0.2 mm^3	
Diffractometer type	Nonius-CCD	
Theta range for data collection	4.95 to 22.00°.	
Index ranges	-33<=h<=33, -27<=k<=33, -8<=l<=7	
Reflections collected	3865	
Independent reflections	1721 [R(int) = 0.0495]	
Completeness to theta = 22.00°	96.7 %	
Absorption correction	None	
Structure solution	direct method	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1721 / 0 / 209	
Goodness-of-fit on F^2	1.168	

Final R indices [I>2sigma(I)]	R1 = 0.0440, wR2 = 0.0902
R indices (all data)	R1 = 0.0708, wR2 = 0.1067
Extinction coefficient	0.0011(4)
Largest diff. peak and hole	0.133 and -0.200 e.Å^{-3}
Treatment of H-atoms	H-atom were found in peak list and were refined in 'riding positions' with free iso. U's in the last cycles.
Used programs	Collect (Nonius BV, 1997-2000), DirAx (A.J.K. Duisenberg), SHELXS-97 (Sheldrick, 1990), SHELXL-97 (Sheldrick, 1997), Schakal-99 (E.Keller 1999)

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **56**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	10006(1)	5371(1)	2150(3)	82(1)
C(1)	9590(1)	5290(1)	1912(4)	53(1)
C(2)	9439(1)	5671(1)	1850(4)	49(1)
C(3)	8906(1)	5381(1)	1426(3)	39(1)
C(4)	8749(1)	4906(1)	1297(3)	39(1)
C(5)	9150(1)	4793(1)	1604(4)	50(1)
C(6)	8580(1)	5589(1)	1170(3)	42(1)
C(7)	8101(1)	5209(1)	314(3)	39(1)
N(8)	7904(1)	4734(1)	1213(2)	39(1)
C(9)	8231(1)	4534(1)	927(3)	44(1)
C(10)	7723(1)	5359(1)	352(3)	41(1)
C(11)	7241(1)	5067(1)	720(3)	43(1)
C(12)	7035(1)	4536(1)	1107(3)	49(1)
C(13)	7407(1)	4385(1)	589(3)	48(1)
N(14)	7821(1)	5829(1)	-18(3)	48(1)
C(15)	7389(1)	5840(1)	107(3)	47(1)
C(16)	7301(1)	6222(1)	-176(4)	64(1)

C(17)	6825(1)	6123(2)	-19(4)	70(1)
C(18)	6449(1)	5660(2)	436(4)	70(1)
C(19)	6538(1)	5282(1)	752(4)	58(1)
C(20)	7016(1)	5365(1)	575(3)	47(1)

Table 3. Bond lengths [Å] and angles [°] for **56**.

O(1)-C(1)	1.215(3)	O(1)-C(1)-C(2)	125.2(3)
C(1)-C(2)	1.498(4)	O(1)-C(1)-C(5)	125.3(3)
C(1)-C(5)	1.502(4)	C(2)-C(1)-C(5)	109.5(2)
C(2)-C(3)	1.489(4)	C(3)-C(2)-C(1)	103.1(2)
C(3)-C(4)	1.325(3)	C(4)-C(3)-C(6)	122.6(2)
C(3)-C(6)	1.480(4)	C(4)-C(3)-C(2)	112.3(2)
C(4)-C(9)	1.483(4)	C(6)-C(3)-C(2)	125.1(2)
C(4)-C(5)	1.490(4)	C(3)-C(4)-C(9)	123.1(2)
C(6)-C(7)	1.524(3)	C(3)-C(4)-C(5)	112.1(2)
C(7)-N(8)	1.472(3)	C(9)-C(4)-C(5)	124.7(2)
C(7)-C(10)	1.485(4)	C(4)-C(5)-C(1)	103.0(2)
N(8)-C(9)	1.466(3)	C(3)-C(6)-C(7)	110.1(2)
N(8)-C(13)	1.469(3)	N(8)-C(7)-C(10)	108.4(2)
C(10)-C(11)	1.354(3)	N(8)-C(7)-C(6)	110.3(2)
C(10)-N(14)	1.380(3)	C(10)-C(7)-C(6)	112.2(2)
C(11)-C(20)	1.435(4)	C(9)-N(8)-C(13)	110.2(2)
C(11)-C(12)	1.489(4)	C(9)-N(8)-C(7)	109.67(19)
C(12)-C(13)	1.520(4)	C(13)-N(8)-C(7)	111.0(2)
N(14)-C(15)	1.378(3)	N(8)-C(9)-C(4)	111.4(2)
C(15)-C(16)	1.378(4)	C(11)-C(10)-N(14)	110.1(2)
C(15)-C(20)	1.409(4)	C(11)-C(10)-C(7)	126.4(2)
C(16)-C(17)	1.375(4)	N(14)-C(10)-C(7)	123.5(2)
C(17)-C(18)	1.387(5)	C(10)-C(11)-C(20)	106.9(2)
C(18)-C(19)	1.373(5)	C(10)-C(11)-C(12)	120.9(3)
C(19)-C(20)	1.400(4)	C(20)-C(11)-C(12)	132.1(2)

C(11)-C(12)-C(13)	109.2(2)	C(16)-C(17)-C(18)	121.3(3)
N(8)-C(13)-C(12)	112.4(2)	C(19)-C(18)-C(17)	121.2(3)
C(15)-N(14)-C(10)	108.5(2)	C(18)-C(19)-C(20)	119.1(3)
C(16)-C(15)-N(14)	129.9(3)	C(19)-C(20)-C(15)	118.2(3)
C(16)-C(15)-C(20)	122.6(3)	C(19)-C(20)-C(11)	134.9(3)
N(14)-C(15)-C(20)	107.5(2)	C(15)-C(20)-C(11)	106.9(2)
C(17)-C(16)-C(15)	117.5(3)		

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for **56**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	53(2)	86(2)	116(2)	4(1)	-14(1)	41(1)
C(1)	47(2)	64(2)	53(2)	5(2)	0(1)	31(2)
C(2)	38(2)	49(2)	56(2)	-1(2)	-3(1)	20(2)
C(3)	34(2)	42(2)	38(2)	2(1)	3(1)	17(1)
C(4)	41(2)	42(2)	32(1)	2(1)	4(1)	19(1)
C(5)	59(2)	50(2)	48(2)	3(1)	5(1)	31(2)
C(6)	36(2)	39(2)	46(2)	7(1)	4(1)	15(1)
C(7)	37(2)	44(2)	31(2)	2(1)	2(1)	15(1)
N(8)	35(1)	36(1)	34(1)	2(1)	3(1)	10(1)
C(9)	51(2)	42(2)	37(2)	-2(1)	5(1)	21(2)
C(10)	36(2)	48(2)	30(1)	3(1)	1(1)	15(1)
C(11)	34(2)	56(2)	28(1)	-4(1)	-1(1)	14(2)
C(12)	35(2)	55(2)	35(2)	-8(1)	1(1)	7(1)
C(13)	42(2)	45(2)	39(2)	-6(1)	0(1)	8(1)
N(14)	36(2)	55(2)	49(1)	11(1)	3(1)	18(1)
C(15)	40(2)	66(2)	37(2)	3(1)	-2(1)	27(2)
C(16)	56(2)	82(3)	57(2)	10(2)	-1(2)	38(2)
C(17)	69(3)	100(3)	61(2)	-2(2)	-7(2)	58(2)
C(18)	53(2)	111(3)	56(2)	-18(2)	-7(2)	49(2)
C(19)	41(2)	85(3)	41(2)	-15(2)	-2(1)	27(2)
C(20)	34(2)	73(2)	29(1)	-8(1)	-4(1)	24(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **56**.

	x	y	z	U(eq)
H(21)	9508	5846	2959	71(10)
H(22)	9647	5932	1004	66(9)
H(51)	9200	4637	597	62(9)
H(52)	9096	4596	2676	55(8)
H(61)	8732	5884	473	45(7)
H(62)	8512	5682	2310	50(8)
H(7)	8173	5164	-984	41(7)
H(91)	8206	4422	-326	43(7)
H(92)	8132	4241	1732	38(6)
H(121)	6938	4460	2355	55(8)
H(122)	6730	4324	410	49(7)
H(131)	7403	4350	-719	38(6)
H(132)	7329	4063	1082	49(8)
H(14)	8102	6092	-257	64(10)
H(16)	7570	6522	-463	64(9)
H(17)	6758	6393	-253	81(11)
H(18)	6102	5596	535	93(11)
H(19)	6294	4954	1131	73(10)

Table 6. Torsion angles [°] for **56**.

O(1)-C(1)-C(2)-C(3)	176.8(3)	C(7)-C(10)-C(11)-C(20)	-179.1(2)
C(5)-C(1)-C(2)-C(3)	-2.3(3)	N(14)-C(10)-C(11)-C(12)	178.0(2)
C(1)-C(2)-C(3)-C(4)	1.6(3)	C(7)-C(10)-C(11)-C(12)	-1.2(4)
C(1)-C(2)-C(3)-C(6)	-178.4(2)	C(10)-C(11)-C(12)-C(13)	-13.4(3)
C(6)-C(3)-C(4)-C(9)	-1.5(4)	C(20)-C(11)-C(12)-C(13)	163.8(3)
C(2)-C(3)-C(4)-C(9)	178.5(2)	C(9)-N(8)-C(13)-C(12)	171.0(2)
C(6)-C(3)-C(4)-C(5)	179.7(2)	C(7)-N(8)-C(13)-C(12)	-67.2(3)
C(2)-C(3)-C(4)-C(5)	-0.3(3)	C(11)-C(12)-C(13)-N(8)	46.4(3)
C(3)-C(4)-C(5)-C(1)	-1.2(3)	C(11)-C(10)-N(14)-C(15)	-0.2(3)
C(9)-C(4)-C(5)-C(1)	-179.9(2)	C(7)-C(10)-N(14)-C(15)	179.0(2)
O(1)-C(1)-C(5)-C(4)	-177.0(3)	C(10)-N(14)-C(15)-C(16)	-178.7(3)
C(2)-C(1)-C(5)-C(4)	2.1(3)	C(10)-N(14)-C(15)-C(20)	0.3(3)
C(4)-C(3)-C(6)-C(7)	-14.3(3)	N(14)-C(15)-C(16)-C(17)	177.5(3)
C(2)-C(3)-C(6)-C(7)	165.7(2)	C(20)-C(15)-C(16)-C(17)	-1.2(4)
C(3)-C(6)-C(7)-N(8)	47.5(3)	C(15)-C(16)-C(17)-C(18)	1.1(5)
C(3)-C(6)-C(7)-C(10)	168.5(2)	C(16)-C(17)-C(18)-C(19)	0.2(5)
C(10)-C(7)-N(8)-C(9)	169.97(19)	C(17)-C(18)-C(19)-C(20)	-1.3(4)
C(6)-C(7)-N(8)-C(9)	-66.8(2)	C(18)-C(19)-C(20)-C(15)	1.2(4)
C(10)-C(7)-N(8)-C(13)	48.0(3)	C(18)-C(19)-C(20)-C(11)	-177.1(3)
C(6)-C(7)-N(8)-C(13)	171.2(2)	C(16)-C(15)-C(20)-C(19)	0.1(4)
C(13)-N(8)-C(9)-C(4)	171.6(2)	N(14)-C(15)-C(20)-C(19)	-178.9(2)
C(7)-N(8)-C(9)-C(4)	49.0(3)	C(16)-C(15)-C(20)-C(11)	178.8(2)
C(3)-C(4)-C(9)-N(8)	-15.9(3)	N(14)-C(15)-C(20)-C(11)	-0.2(3)
C(5)-C(4)-C(9)-N(8)	162.7(2)	C(10)-C(11)-C(20)-C(19)	178.5(3)
N(8)-C(7)-C(10)-C(11)	-15.8(3)	C(12)-C(11)-C(20)-C(19)	0.9(5)
C(6)-C(7)-C(10)-C(11)	-137.8(3)	C(10)-C(11)-C(20)-C(15)	0.1(3)
N(8)-C(7)-C(10)-N(14)	165.1(2)	C(12)-C(11)-C(20)-C(15)	-177.4(2)
C(6)-C(7)-C(10)-N(14)	43.1(3)		
N(14)-C(10)-C(11)-C(20)	0.1(3)		

Table 1. Crystal data and structure refinement for compound *syn*-13

Empirical formula	$C_{27}H_{34}FeN_2O_5Si_2$	
Formula weight	578.59	
Temperature	198(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.970(1) Å	α= 64.564(5)°.
	b = 12.243(1) Å	β= 76.539(6)°.
	c = 12.792(2) Å	γ = 66.796(4)°.
Volume	1421.8(3) $Å^3$	
Z	2	
Density (calculated)	1.352 Mg/m^3	
Absorption coefficient	0.653 mm^{-1}	
F(000)	608	
Crystal size	0.4 x 0.2 x 0.2 mm^3	
Diffractometer type	Nonius-CCD	
Theta range for data collection	4.82 to 27.50°.	
Index ranges	-14<=h<=14, -15<=k<=15, -15<=l<=14	
Reflections collected	16978	
Independent reflections	5892 [R(int) = 0.0523]	
Completeness to theta = 27.50°	90.2 %	
Absorption correction	None	
Structure solution	direct method	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5892 / 0 / 341	
Goodness-of-fit on F^2	1.049	
Final R indices [I>2sigma(I)]	R1 = 0.0392, wR2 = 0.0946	
R indices (all data)	R1 = 0.0512, wR2 = 0.1041	
Largest diff. peak and hole	0.513 and -0.637 $e.Å^{-3}$	
Treatment of H-atoms	H-atom were found in peak list and were refined in 'riding positions' with free iso. U's in the last cycles.	

Used programs	Collect (Nonius BV, 1997-2000), DirAx (A.J.K. Duisenberg), SHELXS-97 (Sheldrick, 1990), SHELXL-97 (Sheldrick, 1997), Schakal-99 (E.Keller 1999)

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for ***syn*-13**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Fe(1)	-6587(1)	-5638(1)	-2754(1)	23(1)
Si(1)	-4445(1)	-7893(1)	-467(1)	22(1)
O(1)	-7655(2)	-7092(1)	-40(1)	28(1)
C(1)	-7180(2)	-7111(2)	-1016(2)	21(1)
Si(2)	-9794(1)	-6083(1)	-1906(1)	30(1)
O(2)	-1746(2)	-1194(2)	-2121(2)	47(1)
C(2)	-5761(2)	-7435(2)	-1438(2)	20(1)
C(3)	-5677(2)	-7568(2)	-2517(2)	19(1)
C(4)	-6979(2)	-7103(2)	-2883(2)	20(1)
C(5)	-7926(2)	-6681(2)	-2028(2)	22(1)
C(6)	-4498(2)	-8196(2)	-3181(2)	21(1)
C(7)	-4949(1)	-8555(1)	-3991(1)	20(1)
N(8)	-5991(1)	-7449(1)	-4683(1)	21(1)
C(9)	-7215(1)	-7209(1)	-3935(1)	25(1)
C(10)	-3831(2)	-8998(2)	-4797(2)	22(1)
C(11)	-3851(2)	-8603(2)	-5960(2)	22(1)
C(12)	-5079(2)	-7691(2)	-6569(2)	26(1)
C(13)	-6256(2)	-7640(2)	-5659(2)	26(1)
N(14)	-2615(2)	-9880(2)	-4427(2)	24(1)
C(15)	-1828(2)	-10069(2)	-5385(2)	24(1)
C(16)	-532(2)	-10883(2)	-5455(2)	31(1)
C(17)	29(2)	-10887(2)	-6538(2)	35(1)
C(18)	-677(2)	-10098(2)	-7532(2)	34(1)
C(19)	-1957(2)	-9285(2)	-7462(2)	29(1)

C(20)	-2566(2)	-9272(2)	-6373(2)	23(1)
O(21)	-3997(2)	-5308(2)	-3623(2)	55(1)
C(21)	-5025(3)	-5388(2)	-3321(2)	35(1)
C(22)	-7453(3)	-4465(2)	-4005(2)	38(1)
O(22)	-8053(2)	-3721(2)	-4769(2)	64(1)
C(23)	-7168(3)	-4614(2)	-1928(2)	33(1)
O(23)	-7537(2)	-3980(2)	-1410(2)	51(1)
C(111)	-4652(3)	-6501(2)	-121(3)	41(1)
C(112)	-2759(3)	-8445(3)	-1155(3)	48(1)
C(113)	-4665(3)	-9225(2)	901(2)	40(1)
C(211)	-10313(3)	-7326(3)	-624(3)	52(1)
C(212)	-10423(3)	-4540(3)	-1693(3)	55(1)
C(213)	-10461(3)	-5836(3)	-3232(3)	46(1)

Table 3. Bond lengths [Å] and angles [°] for ***syn*-13**.

Fe(1)-C(22)	1.784(3)	C(1)-C(2)	1.476(3)
Fe(1)-C(21)	1.788(3)	C(1)-C(5)	1.480(3)
Fe(1)-C(23)	1.814(2)	Si(2)-C(211)	1.852(3)
Fe(1)-C(4)	2.080(2)	Si(2)-C(212)	1.856(3)
Fe(1)-C(3)	2.0834(18)	Si(2)-C(213)	1.862(3)
Fe(1)-C(2)	2.1107(19)	Si(2)-C(5)	1.877(2)
Fe(1)-C(5)	2.116(2)	C(2)-C(3)	1.435(3)
Fe(1)-C(1)	2.330(2)	C(3)-C(4)	1.423(3)
Si(1)-C(112)	1.850(3)	C(3)-C(6)	1.500(3)
Si(1)-C(113)	1.855(2)	C(4)-C(5)	1.441(3)
Si(1)-C(111)	1.857(2)	C(4)-C(9)	1.494(2)
Si(1)-C(2)	1.882(2)	C(6)-C(7)	1.522(2)
O(1)-C(1)	1.243(3)	C(7)-N(8)	1.4644

C(7)-C(10)	1.492(2)	C(21)-Fe(1)-C(5)	156.95(9)
N(8)-C(9)	1.4630	C(23)-Fe(1)-C(5)	100.01(10)
N(8)-C(13)	1.473(2)	C(4)-Fe(1)-C(5)	40.16(8)
C(10)-C(11)	1.355(3)	C(3)-Fe(1)-C(5)	67.27(8)
C(10)-N(14)	1.374(3)	C(2)-Fe(1)-C(5)	67.88(8)
C(11)-C(20)	1.433(3)	C(22)-Fe(1)-C(1)	133.47(11)
C(11)-C(12)	1.491(3)	C(21)-Fe(1)-C(1)	130.82(10)
C(12)-C(13)	1.524(3)	C(23)-Fe(1)-C(1)	82.89(9)
N(14)-C(15)	1.376(3)	C(4)-Fe(1)-C(1)	63.89(8)
C(15)-C(16)	1.387(3)	C(3)-Fe(1)-C(1)	63.51(7)
C(15)-C(20)	1.414(3)	C(2)-Fe(1)-C(1)	38.42(7)
C(16)-C(17)	1.3800	C(5)-Fe(1)-C(1)	38.52(8)
C(17)-C(18)	1.401(3)	C(112)-Si(1)-C(113)	108.65(15)
C(18)-C(19)	1.373(3)	C(112)-Si(1)-C(111)	110.36(14)
C(19)-C(20)	1.402(3)	C(113)-Si(1)-C(111)	108.85(13)
O(21)-C(21)	1.132(3)	C(112)-Si(1)-C(2)	111.08(12)
C(22)-O(22)	1.132(3)	C(113)-Si(1)-C(2)	108.24(11)
C(23)-O(23)	1.128(3)	C(111)-Si(1)-C(2)	109.60(10)
		O(1)-C(1)-C(2)	126.8(2)
C(22)-Fe(1)-C(21)	95.59(12)	O(1)-C(1)-C(5)	126.95(19)
C(22)-Fe(1)-C(23)	95.71(11)	C(2)-C(1)-C(5)	105.96(17)
C(21)-Fe(1)-C(23)	97.56(12)	O(1)-C(1)-Fe(1)	134.61(14)
C(22)-Fe(1)-C(4)	92.27(11)	C(2)-C(1)-Fe(1)	62.72(10)
C(21)-Fe(1)-C(4)	120.45(9)	C(5)-C(1)-Fe(1)	62.91(11)
C(23)-Fe(1)-C(4)	140.15(10)	C(211)-Si(2)-C(212)	110.31(16)
C(22)-Fe(1)-C(3)	122.66(10)	C(211)-Si(2)-C(213)	110.12(15)
C(21)-Fe(1)-C(3)	89.69(9)	C(212)-Si(2)-C(213)	109.00(15)
C(23)-Fe(1)-C(3)	140.12(10)	C(211)-Si(2)-C(5)	106.43(12)
C(4)-Fe(1)-C(3)	39.98(8)	C(212)-Si(2)-C(5)	109.68(13)
C(22)-Fe(1)-C(2)	159.91(11)	C(213)-Si(2)-C(5)	111.28(11)
C(21)-Fe(1)-C(2)	94.45(10)	C(3)-C(2)-C(1)	106.48(18)
C(23)-Fe(1)-C(2)	100.16(10)	C(3)-C(2)-Si(1)	131.61(15)
C(4)-Fe(1)-C(2)	67.65(8)	C(1)-C(2)-Si(1)	120.66(15)
C(3)-Fe(1)-C(2)	40.02(8)	C(3)-C(2)-Fe(1)	68.97(11)
C(22)-Fe(1)-C(5)	97.36(11)	C(1)-C(2)-Fe(1)	78.86(11)

Si(1)-C(2)-Fe(1)	127.70(10)	C(7)-N(8)-C(13)	112.50(9)
C(4)-C(3)-C(2)	109.40(17)	N(8)-C(9)-C(4)	111.44(9)
C(4)-C(3)-C(6)	120.22(19)	C(11)-C(10)-N(14)	111.00(18)
C(2)-C(3)-C(6)	130.12(19)	C(11)-C(10)-C(7)	126.21(18)
C(4)-C(3)-Fe(1)	69.89(11)	N(14)-C(10)-C(7)	122.78(17)
C(2)-C(3)-Fe(1)	71.01(10)	C(10)-C(11)-C(20)	106.89(19)
C(6)-C(3)-Fe(1)	129.75(14)	C(10)-C(11)-C(12)	121.55(18)
C(3)-C(4)-C(5)	108.61(19)	C(20)-C(11)-C(12)	131.5(2)
C(3)-C(4)-C(9)	121.65(16)	C(11)-C(12)-C(13)	108.12(18)
C(5)-C(4)-C(9)	129.45(18)	N(8)-C(13)-C(12)	111.82(18)
C(3)-C(4)-Fe(1)	70.13(12)	C(10)-N(14)-C(15)	107.49(18)
C(5)-C(4)-Fe(1)	71.26(12)	N(14)-C(15)-C(16)	129.3(2)
C(9)-C(4)-Fe(1)	129.14(12)	N(14)-C(15)-C(20)	108.56(18)
C(4)-C(5)-C(1)	106.64(17)	C(16)-C(15)-C(20)	122.15(18)
C(4)-C(5)-Si(2)	131.18(17)	C(17)-C(16)-C(15)	117.44(12)
C(1)-C(5)-Si(2)	120.58(15)	C(16)-C(17)-C(18)	121.52(11)
C(4)-C(5)-Fe(1)	68.57(12)	C(19)-C(18)-C(17)	121.0(2)
C(1)-C(5)-Fe(1)	78.58(12)	C(18)-C(19)-C(20)	119.0(2)
Si(2)-C(5)-Fe(1)	129.69(10)	C(19)-C(20)-C(15)	118.9(2)
C(3)-C(6)-C(7)	110.35(16)	C(19)-C(20)-C(11)	135.1(2)
N(8)-C(7)-C(10)	108.59(9)	C(15)-C(20)-C(11)	106.05(18)
N(8)-C(7)-C(6)	110.02(8)	O(21)-C(21)-Fe(1)	175.3(2)
C(10)-C(7)-C(6)	112.04(14)	O(22)-C(22)-Fe(1)	177.0(3)
C(9)-N(8)-C(7)	109.2	O(23)-C(23)-Fe(1)	179.5(3)
C(9)-N(8)-C(13)	109.28(10)		

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3)for ***syn*-13**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Fe(1)	33(1)	14(1)	15(1)	-6(1)	1(1)	-4(1)
Si(1)	30(1)	19(1)	18(1)	-9(1)	-2(1)	-8(1)
O(1)	35(1)	29(1)	16(1)	-10(1)	5(1)	-9(1)
C(1)	30(1)	14(1)	18(1)	-7(1)	2(1)	-7(1)
Si(2)	25(1)	34(1)	26(1)	-17(1)	0(1)	-1(1)
O(2)	60(1)	43(1)	28(1)	6(1)	-12(1)	-23(1)
C(2)	28(1)	13(1)	15(1)	-5(1)	2(1)	-6(1)
C(3)	27(1)	12(1)	14(1)	-6(1)	-2(1)	-4(1)
C(4)	27(1)	15(1)	16(1)	-7(1)	-2(1)	-3(1)
C(5)	27(1)	18(1)	18(1)	-9(1)	0(1)	-4(1)
C(6)	24(1)	18(1)	17(1)	-9(1)	0(1)	-3(1)
C(7)	26(1)	18(1)	14(1)	-7(1)	-1(1)	-3(1)
N(8)	26(1)	19(1)	14(1)	-9(1)	-3(1)	-1(1)
C(9)	27(1)	28(1)	17(1)	-13(1)	-3(1)	-1(1)
C(10)	26(1)	16(1)	19(1)	-9(1)	0(1)	-2(1)
C(11)	30(1)	19(1)	16(1)	-9(1)	0(1)	-5(1)
C(12)	34(1)	27(1)	13(1)	-11(1)	-4(1)	-2(1)
C(13)	30(1)	28(1)	18(1)	-13(1)	-5(1)	-3(1)
N(14)	27(1)	22(1)	16(1)	-9(1)	-3(1)	0(1)
C(15)	29(1)	23(1)	19(1)	-12(1)	1(1)	-6(1)
C(16)	29(1)	28(1)	29(1)	-12(1)	0(1)	-2(1)
C(17)	29(1)	34(1)	35(1)	-19(1)	7(1)	-2(1)
C(18)	37(1)	35(1)	26(1)	-17(1)	11(1)	-10(1)
C(19)	37(1)	30(1)	19(1)	-13(1)	3(1)	-10(1)
C(20)	29(1)	21(1)	18(1)	-11(1)	2(1)	-7(1)
O(21)	51(1)	38(1)	68(2)	-18(1)	22(1)	-24(1)
C(21)	47(2)	17(1)	32(1)	-8(1)	7(1)	-10(1)
C(22)	49(2)	24(1)	26(1)	-8(1)	0(1)	0(1)
O(22)	76(2)	42(1)	33(1)	-2(1)	-16(1)	14(1)
C(23)	45(1)	21(1)	30(1)	-10(1)	2(1)	-10(1)

O(23)	70(1)	39(1)	52(1)	-35(1)	6(1)	-13(1)
C(111)	61(2)	28(1)	42(2)	-17(1)	-18(1)	-11(1)
C(112)	30(1)	72(2)	51(2)	-40(2)	1(1)	-10(1)
C(113)	59(2)	33(1)	27(1)	2(1)	-18(1)	-20(1)
C(211)	40(2)	73(2)	40(2)	-17(1)	6(1)	-27(2)
C(212)	45(2)	53(2)	67(2)	-43(2)	1(2)	4(1)
C(213)	31(1)	61(2)	41(2)	-27(1)	-7(1)	0(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for ***syn*-13**.

	x	y	z	U(eq)
H(21)	-1919	-1729	-1526	53(10)
H(22)	-1067	-1166	-2170	91(18)
H(61)	-4009	-7708	-3633	26(6)
H(62)	-3890	-8966	-2643	28(7)
H(7)	-5306	-9200	-3542	27(6)
H(91)	-7642	-7911	-3631	34(7)
H(92)	-7849	-6507	-4408	39(8)
H(122)	-5010	-6846	-6988	34(7)
H(121)	-5217	-7989	-7090	34(7)
H(131)	-6496	-8430	-5370	39(8)
H(132)	-7000	-6907	-6041	30(7)
H(14)	-2386	-10297	-3710	26(6)
H(16)	-40	-11458	-4721	34(7)
H(17)	851	-11397	-6598	45(8)
H(18)	-278	-10040	-8278	34(7)
H(19)	-2422	-8776	-8156	34(7)
H(111)	-5547	-6222	246	61
H(112)	-4528	-5795	-837	61
H(113)	-3990	-6752	412	61
H(114)	-2641	-7760	-1894	72

H(115)	-2649	-9205	-1298	72
H(116)	-2093	-8663	-639	72
H(117)	-5554	-8943	1277	60
H(118)	-3991	-9474	1422	60
H(119)	-4566	-9962	727	60
H(211)	-9961	-7445	69	78
H(212)	-9966	-8137	-744	78
H(213)	-11286	-7052	-520	78
H(214)	-10235	-3867	-2411	83
H(215)	-9981	-4632	-1063	83
H(216)	-11385	-4307	-1494	83
H(217)	-10195	-5166	-3901	69
H(218)	-11434	-5573	-3125	69
H(219)	-10105	-6639	-3366	69

Table 6. Torsion angles [°] for ***syn*-13**.

C(22)-Fe(1)-C(1)-O(1)	-91.5(3)	C(23)-Fe(1)-C(1)-C(5)	115.99(14)
C(21)-Fe(1)-C(1)-O(1)	93.5(2)	C(4)-Fe(1)-C(1)-C(5)	-41.33(11)
C(23)-Fe(1)-C(1)-O(1)	-0.4(2)	C(3)-Fe(1)-C(1)-C(5)	-86.16(12)
C(4)-Fe(1)-C(1)-O(1)	-157.7(3)	C(2)-Fe(1)-C(1)-C(5)	-127.68(16)
C(3)-Fe(1)-C(1)-O(1)	157.5(3)	O(1)-C(1)-C(2)-C(3)	169.14(19)
C(2)-Fe(1)-C(1)-O(1)	116.0(3)	C(5)-C(1)-C(2)-C(3)	-16.8(2)
C(5)-Fe(1)-C(1)-O(1)	-116.3(3)	Fe(1)-C(1)-C(2)-C(3)	-63.92(12)
C(22)-Fe(1)-C(1)-C(2)	152.53(15)	O(1)-C(1)-C(2)-Si(1)	0.5(3)
C(21)-Fe(1)-C(1)-C(2)	-22.46(17)	C(5)-C(1)-C(2)-Si(1)	174.56(13)
C(23)-Fe(1)-C(1)-C(2)	-116.33(14)	Fe(1)-C(1)-C(2)-Si(1)	127.44(14)
C(4)-Fe(1)-C(1)-C(2)	86.35(13)	O(1)-C(1)-C(2)-Fe(1)	-126.9(2)
C(3)-Fe(1)-C(1)-C(2)	41.53(12)	C(5)-C(1)-C(2)-Fe(1)	47.12(13)
C(5)-Fe(1)-C(1)-C(2)	127.68(16)	C(112)-Si(1)-C(2)-C(3)	7.4(2)
C(22)-Fe(1)-C(1)-C(5)	24.85(17)	C(113)-Si(1)-C(2)-C(3)	-111.8(2)
C(21)-Fe(1)-C(1)-C(5)	-150.14(14)	C(111)-Si(1)-C(2)-C(3)	129.6(2)

C(112)-Si(1)-C(2)-C(1)	172.77(17)	C(23)-Fe(1)-C(3)-C(4)	115.85(18)
C(113)-Si(1)-C(2)-C(1)	53.57(18)	C(2)-Fe(1)-C(3)-C(4)	120.00(17)
C(111)-Si(1)-C(2)-C(1)	-65.01(19)	C(5)-Fe(1)-C(3)-C(4)	37.81(12)
C(112)-Si(1)-C(2)-Fe(1)	-87.18(16)	C(1)-Fe(1)-C(3)-C(4)	80.16(13)
C(113)-Si(1)-C(2)-Fe(1)	153.61(14)	C(22)-Fe(1)-C(3)-C(2)	-166.25(14)
C(111)-Si(1)-C(2)-Fe(1)	35.04(17)	C(21)-Fe(1)-C(3)-C(2)	97.31(14)
C(22)-Fe(1)-C(2)-C(3)	35.6(3)	C(23)-Fe(1)-C(3)-C(2)	-4.1(2)
C(21)-Fe(1)-C(2)-C(3)	-84.19(14)	C(4)-Fe(1)-C(3)-C(2)	-120.00(17)
C(23)-Fe(1)-C(2)-C(3)	177.30(14)	C(5)-Fe(1)-C(3)-C(2)	-82.19(13)
C(4)-Fe(1)-C(2)-C(3)	36.98(12)	C(1)-Fe(1)-C(3)-C(2)	-39.84(12)
C(5)-Fe(1)-C(2)-C(3)	80.53(13)	C(22)-Fe(1)-C(3)-C(6)	66.9(2)
C(1)-Fe(1)-C(2)-C(3)	112.67(17)	C(21)-Fe(1)-C(3)-C(6)	-29.6(2)
C(22)-Fe(1)-C(2)-C(1)	-77.0(3)	C(23)-Fe(1)-C(3)-C(6)	-131.0(2)
C(21)-Fe(1)-C(2)-C(1)	163.14(14)	C(4)-Fe(1)-C(3)-C(6)	113.1(2)
C(23)-Fe(1)-C(2)-C(1)	64.63(14)	C(2)-Fe(1)-C(3)-C(6)	-126.9(3)
C(4)-Fe(1)-C(2)-C(1)	-75.69(12)	C(5)-Fe(1)-C(3)-C(6)	150.9(2)
C(3)-Fe(1)-C(2)-C(1)	-112.67(17)	C(1)-Fe(1)-C(3)-C(6)	-166.7(2)
C(5)-Fe(1)-C(2)-C(1)	-32.14(11)	C(2)-C(3)-C(4)-C(5)	-0.9(2)
C(22)-Fe(1)-C(2)-Si(1)	162.6(2)	C(6)-C(3)-C(4)-C(5)	173.74(17)
C(21)-Fe(1)-C(2)-Si(1)	42.83(15)	Fe(1)-C(3)-C(4)-C(5)	-61.18(14)
C(23)-Fe(1)-C(2)-Si(1)	-55.69(15)	C(2)-C(3)-C(4)-C(9)	-175.30(15)
C(4)-Fe(1)-C(2)-Si(1)	164.00(15)	C(6)-C(3)-C(4)-C(9)	-0.6(3)
C(3)-Fe(1)-C(2)-Si(1)	127.01(19)	Fe(1)-C(3)-C(4)-C(9)	124.45(17)
C(5)-Fe(1)-C(2)-Si(1)	-152.46(15)	C(2)-C(3)-C(4)-Fe(1)	60.25(13)
C(1)-Fe(1)-C(2)-Si(1)	-120.32(18)	C(6)-C(3)-C(4)-Fe(1)	-125.08(18)
C(1)-C(2)-C(3)-C(4)	11.2(2)	C(22)-Fe(1)-C(4)-C(3)	142.52(14)
Si(1)-C(2)-C(3)-C(4)	178.11(15)	C(21)-Fe(1)-C(4)-C(3)	44.68(16)
Fe(1)-C(2)-C(3)-C(4)	-59.56(13)	C(23)-Fe(1)-C(4)-C(3)	-115.79(17)
C(1)-C(2)-C(3)-C(6)	-162.78(19)	C(2)-Fe(1)-C(4)-C(3)	-37.02(12)
Si(1)-C(2)-C(3)-C(6)	4.1(3)	C(5)-Fe(1)-C(4)-C(3)	-118.74(17)
Fe(1)-C(2)-C(3)-C(6)	126.5(2)	C(1)-Fe(1)-C(4)-C(3)	-79.13(12)
C(1)-C(2)-C(3)-Fe(1)	70.76(13)	C(22)-Fe(1)-C(4)-C(5)	-98.74(14)
Si(1)-C(2)-C(3)-Fe(1)	-122.33(17)	C(21)-Fe(1)-C(4)-C(5)	163.43(14)
C(22)-Fe(1)-C(3)-C(4)	-46.25(17)	C(23)-Fe(1)-C(4)-C(5)	3.0(2)
C(21)-Fe(1)-C(3)-C(4)	-142.69(14)	C(3)-Fe(1)-C(4)-C(5)	118.74(17)

C(2)-Fe(1)-C(4)-C(5)	81.72(12)	C(21)-Fe(1)-C(5)-C(4)	-38.9(3)
C(1)-Fe(1)-C(4)-C(5)	39.62(11)	C(23)-Fe(1)-C(5)-C(4)	-178.08(13)
C(22)-Fe(1)-C(4)-C(9)	27.35(18)	C(3)-Fe(1)-C(5)-C(4)	-37.64(12)
C(21)-Fe(1)-C(4)-C(9)	-70.48(19)	C(2)-Fe(1)-C(5)-C(4)	-81.09(12)
C(23)-Fe(1)-C(4)-C(9)	129.05(18)	C(1)-Fe(1)-C(5)-C(4)	-113.15(16)
C(3)-Fe(1)-C(4)-C(9)	-115.2(2)	C(22)-Fe(1)-C(5)-C(1)	-162.09(12)
C(2)-Fe(1)-C(4)-C(9)	-152.19(18)	C(21)-Fe(1)-C(5)-C(1)	74.2(3)
C(5)-Fe(1)-C(4)-C(9)	126.1(2)	C(23)-Fe(1)-C(5)-C(1)	-64.93(13)
C(1)-Fe(1)-C(4)-C(9)	165.71(19)	C(4)-Fe(1)-C(5)-C(1)	113.15(16)
C(3)-C(4)-C(5)-C(1)	-9.7(2)	C(3)-Fe(1)-C(5)-C(1)	75.51(12)
C(9)-C(4)-C(5)-C(1)	164.09(17)	C(2)-Fe(1)-C(5)-C(1)	32.06(11)
Fe(1)-C(4)-C(5)-C(1)	-70.17(14)	C(22)-Fe(1)-C(5)-Si(2)	-41.64(16)
C(3)-C(4)-C(5)-Si(2)	-174.91(15)	C(21)-Fe(1)-C(5)-Si(2)	-165.3(2)
C(9)-C(4)-C(5)-Si(2)	-1.1(3)	C(23)-Fe(1)-C(5)-Si(2)	55.52(16)
Fe(1)-C(4)-C(5)-Si(2)	124.63(18)	C(4)-Fe(1)-C(5)-Si(2)	-126.4(2)
C(3)-C(4)-C(5)-Fe(1)	60.47(14)	C(3)-Fe(1)-C(5)-Si(2)	-164.04(17)
C(9)-C(4)-C(5)-Fe(1)	-125.74(19)	C(2)-Fe(1)-C(5)-Si(2)	152.51(16)
O(1)-C(1)-C(5)-C(4)	-169.67(19)	C(1)-Fe(1)-C(5)-Si(2)	120.45(19)
C(2)-C(1)-C(5)-C(4)	16.3(2)	C(4)-C(3)-C(6)-C(7)	-15.4(2)
Fe(1)-C(1)-C(5)-C(4)	63.30(13)	C(2)-C(3)-C(6)-C(7)	158.04(18)
O(1)-C(1)-C(5)-Si(2)	-2.6(3)	Fe(1)-C(3)-C(6)-C(7)	-103.49(19)
C(2)-C(1)-C(5)-Si(2)	-176.62(13)	C(3)-C(6)-C(7)-N(8)	50.40(15)
Fe(1)-C(1)-C(5)-Si(2)	-129.60(15)	C(3)-C(6)-C(7)-C(10)	171.30(14)
O(1)-C(1)-C(5)-Fe(1)	127.0(2)	C(10)-C(7)-N(8)-C(9)	165.65(10)
C(2)-C(1)-C(5)-Fe(1)	-47.02(13)	C(6)-C(7)-N(8)-C(9)	-71.39(9)
C(211)-Si(2)-C(5)-C(4)	111.8(2)	C(10)-C(7)-N(8)-C(13)	44.16(14)
C(212)-Si(2)-C(5)-C(4)	-128.9(2)	C(6)-C(7)-N(8)-C(13)	167.11(16)
C(213)-Si(2)-C(5)-C(4)	-8.2(2)	C(7)-N(8)-C(9)-C(4)	52.44(9)
C(211)-Si(2)-C(5)-C(1)	-51.7(2)	C(13)-N(8)-C(9)-C(4)	175.87(15)
C(212)-Si(2)-C(5)-C(1)	67.6(2)	C(3)-C(4)-C(9)-N(8)	-17.59(19)
C(213)-Si(2)-C(5)-C(1)	-171.68(17)	C(5)-C(4)-C(9)-N(8)	169.33(17)
C(211)-Si(2)-C(5)-Fe(1)	-152.73(17)	Fe(1)-C(4)-C(9)-N(8)	71.66(15)
C(212)-Si(2)-C(5)-Fe(1)	-33.4(2)	N(8)-C(7)-C(10)-C(11)	-10.5(2)
C(213)-Si(2)-C(5)-Fe(1)	87.28(18)	C(6)-C(7)-C(10)-C(11)	-132.2(2)
C(22)-Fe(1)-C(5)-C(4)	84.76(14)	N(8)-C(7)-C(10)-N(14)	169.05(16)

C(6)-C(7)-C(10)-N(14) 47.3(2)
N(14)-C(10)-C(11)-C(20) 0.0(3)
C(7)-C(10)-C(11)-C(20)179.57(18)
N(14)-C(10)-C(11)-C(12)177.08(19)
C(7)-C(10)-C(11)-C(12) -3.4(3)
C(10)-C(11)-C(12)-C(13)-15.5(3)
C(20)-C(11)-C(12)-C(13)160.8(2)
C(9)-N(8)-C(13)-C(12) 171.30(13)
C(7)-N(8)-C(13)-C(12) -67.27(17)
C(11)-C(12)-C(13)-N(8) 48.8(2)
C(11)-C(10)-N(14)-C(15) -0.5(3)
C(7)-C(10)-N(14)-C(15)179.87(18)
C(10)-N(14)-C(15)-C(16)-178.7(2)
C(10)-N(14)-C(15)-C(20) 0.9(2)
N(14)-C(15)-C(16)-C(17)179.80(18)
C(20)-C(15)-C(16)-C(17) 0.3(2)
C(15)-C(16)-C(17)-C(18)0.30(16)
C(16)-C(17)-C(18)-C(19) 0.2(3)
C(17)-C(18)-C(19)-C(20) -1.3(4)
C(18)-C(19)-C(20)-C(15) 1.8(3)
C(18)-C(19)-C(20)-C(11)-178.3(2)
N(14)-C(15)-C(20)-C(19)179.0(2)
C(16)-C(15)-C(20)-C(19) -1.4(3)
N(14)-C(15)-C(20)-C(11) -0.9(2)
C(16)-C(15)-C(20)-C(11)178.72(19)
C(10)-C(11)-C(20)-C(19)-179.4(2)
C(12)-C(11)-C(20)-C(19) 4.0(4)
C(10)-C(11)-C(20)-C(15) 0.5(2)
C(12)-C(11)-C(20)-C(15)-176.2(2)
C(22)-Fe(1)-C(21)-O(21) -162(3)
C(23)-Fe(1)-C(21)-O(21) 102(3)
C(4)-Fe(1)-C(21)-O(21) -66(3)
C(3)-Fe(1)-C(21)-O(21) -39(3)
C(2)-Fe(1)-C(21)-O(21) 1(3)
C(5)-Fe(1)-C(21)-O(21) -38(3)
C(1)-Fe(1)-C(21)-O(21) 14(3)
C(21)-Fe(1)-C(22)-O(22) -161(6)
C(23)-Fe(1)-C(22)-O(22) -63(6)
C(4)-Fe(1)-C(22)-O(22) 78(6)
C(3)-Fe(1)-C(22)-O(22) 105(5)
C(2)-Fe(1)-C(22)-O(22) 79(6)
C(5)-Fe(1)-C(22)-O(22) 38(6)
C(1)-Fe(1)-C(22)-O(22) 22(6)
C(22)-Fe(1)-C(23)-O(23) 93(31)
C(21)-Fe(1)-C(23)-O(23)-171(100)
C(4)-Fe(1)-C(23)-O(23) -8(31)
C(3)-Fe(1)-C(23)-O(23) -72(31)
C(2)-Fe(1)-C(23)-O(23) -75(31)
C(5)-Fe(1)-C(23)-O(23) -6(31)
C(1)-Fe(1)-C(23)-O(23) -41(31)

Table 1. Crystal data and structure refinement for compound 66a

Empirical formula	$C_{18}H_{18}N_2O$	
Formula weight	278.34	
Temperature	198(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.109(1) Å	α=83.48(1)°.
	b = 9.231(1) Å	β= 63.36(1)°.
	c = 9.777(1) Å	γ = 70.93(1)°.
Volume	693.97(13) $Å^3$	
Z	2	
Density (calculated)	1.332 Mg/m^3	
Absorption coefficient	0.084 mm^{-1}	
F(000)	296	
Crystal size	0.61 x 0.20 x 0.10 mm^3	
Diffractometer type	Nonius-CCD	
Theta range for data collection	5.14 to 24.99°.	
Index ranges	-10<=h<=10, -10<=k<=10, -11<=l<=11	
Reflections collected	8909	
Independent reflections	2416 [R(int) = 0.0702]	
Completeness to theta = 24.99°	99.0 %	
Absorption correction	None	
Structure solution	direct method	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2416 / 0 / 209	
Goodness-of-fit on F^2	1.063	
Final R indices [I>2sigma(I)]	R1 = 0.0500, wR2 = 0.0952	
R indices (all data)	R1 = 0.0885, wR2 = 0.1097	
Extinction coefficient	0.018(7)	
Largest diff. peak and hole	0.257 and -0.187 $e.Å^{-3}$	

Treatment of H-atoms	were found in peak list and refined in riding positions in last cycles with isotropic temperature factors.
Used programs	Collect (Nonius BV, 1997-2000), DirAx (A.J.K. Duisenberg), SHELXS-97 (Sheldrick, 1990), SHELXL-97 (Sheldrick, 1997), Schakal-99 (E.Keller 1999)

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **66a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3869(2)	1369(2)	2188(2)	44(1)
C(1)	4357(3)	46(2)	2533(2)	33(1)
C(2)	4059(3)	-493(2)	4064(2)	33(1)
C(3)	4925(2)	-1986(2)	4000(2)	27(1)
C(4)	5753(3)	-2678(2)	2428(2)	34(1)
C(5)	5462(3)	-1318(2)	1428(3)	41(1)
C(6)	5205(2)	-2962(2)	5232(2)	27(1)
C(7)	7135(3)	-3896(2)	4626(2)	27(1)
N(8)	7678(2)	-4723(2)	3198(2)	27(1)
C(9)	7626(3)	-3631(2)	2000(2)	33(1)
C(10)	7489(2)	-5023(2)	5737(2)	27(1)
C(11)	8450(2)	-6525(2)	5401(2)	28(1)
C(12)	9302(3)	-7182(2)	3817(2)	34(1)
C(13)	9385(3)	-5889(2)	2701(2)	35(1)
N(14)	6847(2)	-4692(2)	7279(2)	30(1)
C(15)	7438(3)	-6005(2)	7955(2)	30(1)
C(16)	7175(3)	-6248(3)	9461(3)	36(1)
C(17)	7924(3)	-7706(3)	9821(3)	43(1)
C(18)	8908(3)	-8891(3)	8696(3)	44(1)
C(19)	9166(3)	-8643(2)	7213(3)	39(1)
C(20)	8432(2)	-7177(2)	6806(2)	30(1)

Table 3. Bond lengths [Å] and angles [°] for **66a**.

O(1)-C(1)	1.221(2)	C(2)-C(3)-C(4)	112.08(18)
C(1)-C(2)	1.454(3)	C(6)-C(3)-C(4)	118.60(17)
C(1)-C(5)	1.507(3)	C(3)-C(4)-C(9)	110.32(18)
C(2)-C(3)	1.338(3)	C(3)-C(4)-C(5)	104.54(17)
C(3)-C(6)	1.486(3)	C(9)-C(4)-C(5)	116.29(18)
C(3)-C(4)	1.485(3)	C(1)-C(5)-C(4)	104.95(18)
C(4)-C(9)	1.524(3)	C(3)-C(6)-C(7)	109.03(16)
C(4)-C(5)	1.529(3)	N(8)-C(7)-C(10)	108.78(16)
C(6)-C(7)	1.541(3)	N(8)-C(7)-C(6)	108.89(16)
C(7)-N(8)	1.468(3)	C(10)-C(7)-C(6)	112.21(16)
C(7)-C(10)	1.485(3)	C(9)-N(8)-C(7)	109.80(15)
N(8)-C(9)	1.462(2)	C(9)-N(8)-C(13)	111.27(15)
N(8)-C(13)	1.470(2)	C(7)-N(8)-C(13)	112.85(16)
C(10)-C(11)	1.360(3)	N(8)-C(9)-C(4)	108.82(16)
C(10)-N(14)	1.380(3)	C(11)-C(10)-N(14)	110.19(18)
C(11)-C(20)	1.430(3)	C(11)-C(10)-C(7)	125.49(19)
C(11)-C(12)	1.483(3)	N(14)-C(10)-C(7)	124.31(17)
C(12)-C(13)	1.519(3)	C(10)-C(11)-C(20)	106.54(18)
N(14)-C(15)	1.380(3)	C(10)-C(11)-C(12)	121.31(19)
C(15)-C(16)	1.386(3)	C(20)-C(11)-C(12)	132.15(18)
C(15)-C(20)	1.406(3)	C(11)-C(12)-C(13)	109.32(17)
C(16)-C(17)	1.381(3)	N(8)-C(13)-C(12)	110.12(16)
C(17)-C(18)	1.399(3)	C(15)-N(14)-C(10)	108.46(17)
C(18)-C(19)	1.365(3)	N(14)-C(15)-C(16)	130.3(2)
C(19)-C(20)	1.401(3)	N(14)-C(15)-C(20)	107.32(18)
O(1)-C(1)-C(2)	126.6(2)	C(16)-C(15)-C(20)	122.41(19)
O(1)-C(1)-C(5)	125.7(2)	C(17)-C(16)-C(15)	117.7(2)
C(2)-C(1)-C(5)	107.60(18)	C(16)-C(17)-C(18)	120.8(2)
C(3)-C(2)-C(1)	110.38(19)	C(19)-C(18)-C(17)	121.2(2)
C(2)-C(3)-C(6)	129.25(19)	C(18)-C(19)-C(20)	119.6(2)

C(19)-C(20)-C(15)	118.3(2)	C(15)-C(20)-C(11)	107.49(17)
C(19)-C(20)-C(11)	134.2(2)		

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3)for **66a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	65(1)	24(1)	51(1)	9(1)	-36(1)	-9(1)
C(1)	37(1)	27(1)	42(1)	4(1)	-25(1)	-10(1)
C(2)	37(1)	27(1)	33(1)	-1(1)	-17(1)	-4(1)
C(3)	29(1)	23(1)	32(1)	3(1)	-17(1)	-10(1)
C(4)	41(1)	26(1)	33(1)	3(1)	-17(1)	-5(1)
C(5)	54(2)	32(1)	35(1)	5(1)	-23(1)	-7(1)
C(6)	29(1)	21(1)	29(1)	1(1)	-14(1)	-5(1)
C(7)	30(1)	20(1)	33(1)	3(1)	-15(1)	-9(1)
N(8)	28(1)	23(1)	28(1)	3(1)	-11(1)	-6(1)
C(9)	36(1)	29(1)	30(1)	1(1)	-10(1)	-12(1)
C(10)	24(1)	23(1)	35(1)	1(1)	-14(1)	-8(1)
C(11)	25(1)	22(1)	39(1)	3(1)	-16(1)	-7(1)
C(12)	25(1)	24(1)	43(1)	-2(1)	-12(1)	-1(1)
C(13)	24(1)	31(1)	38(1)	0(1)	-7(1)	-4(1)
N(14)	36(1)	21(1)	36(1)	0(1)	-20(1)	-6(1)
C(15)	29(1)	25(1)	41(1)	7(1)	-21(1)	-9(1)
C(16)	37(1)	34(1)	43(1)	4(1)	-23(1)	-9(1)
C(17)	45(1)	47(2)	46(2)	17(1)	-30(1)	-16(1)
C(18)	47(1)	33(1)	58(2)	16(1)	-32(1)	-11(1)
C(19)	36(1)	26(1)	53(2)	6(1)	-23(1)	-5(1)
C(20)	26(1)	22(1)	44(1)	4(1)	-18(1)	-7(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **66a**.

	x	y	z	U(eq)
H(2)	3454	175	4957	33(6)
H(4)	5111	-3448	2441	58(7)
H(51)	6551	-1185	709	47(7)
H(52)	4953	-1458	754	58(8)
H(61)	4873	-2346	6150	23(5)
H(62)	4511	-3720	5519	36(6)
H(7)	7789	-3172	4427	33(6)
H(91)	8302	-2913	1880	39(6)
H(92)	8154	-4216	1021	31(5)
H(121)	10501	-7817	3536	37(6)
H(122)	8684	-7841	3667	41(6)
H(131)	10257	-5400	2633	41(6)
H(132)	9710	-6287	1618	32(5)
H(14)	6415	-3740	7707	36(6)
H(16)	6502	-5423	10215	30(6)
H(17)	7730	-7906	10877	50(7)
H(18)	9450	-9957	8967	61(7)
H(19)	9839	-9445	6425	48(7)

Table 6. Torsion angles [°] for **66a**.

O(1)-C(1)-C(2)-C(3)	-173.8(2)	C(1)-C(2)-C(3)-C(4)	-6.6(2)
C(5)-C(1)-C(2)-C(3)	3.5(2)	C(2)-C(3)-C(4)-C(9)	132.57(19)
C(1)-C(2)-C(3)-C(6)	170.49(19)	C(6)-C(3)-C(4)-C(9)	-44.9(2)

C(2)-C(3)-C(4)-C(5)	6.8(2)	C(7)-C(10)-C(11)-C(12)	1.7(3)
C(6)-C(3)-C(4)-C(5)	-170.58(18)	C(10)-C(11)-C(12)-C(13)	17.2(3)
O(1)-C(1)-C(5)-C(4)	178.1(2)	C(20)-C(11)-C(12)-C(13)	-161.4(2)
C(2)-C(1)-C(5)-C(4)	0.8(2)	C(9)-N(8)-C(13)-C(12)	-168.51(17)
C(3)-C(4)-C(5)-C(1)	-4.3(2)	C(7)-N(8)-C(13)-C(12)	67.5(2)
C(9)-C(4)-C(5)-C(1)	-126.2(2)	C(11)-C(12)-C(13)-N(8)	-49.6(2)
C(2)-C(3)-C(6)-C(7)	-132.1(2)	C(11)-C(10)-N(14)-C(15)	1.4(2)
C(4)-C(3)-C(6)-C(7)	44.9(2)	C(7)-C(10)-N(14)-C(15)	-179.93(17)
C(3)-C(6)-C(7)-N(8)	-53.5(2)	C(10)-N(14)-C(15)-C(16)	178.8(2)
C(3)-C(6)-C(7)-C(10)	-173.93(16)	C(10)-N(14)-C(15)-C(20)	-1.5(2)
C(10)-C(7)-N(8)-C(9)	-170.16(15)	N(14)-C(15)-C(16)-C(17)	179.4(2)
C(6)-C(7)-N(8)-C(9)	67.27(19)	C(20)-C(15)-C(16)-C(17)	-0.2(3)
C(10)-C(7)-N(8)-C(13)	-45.4(2)	C(15)-C(16)-C(17)-C(18)	-0.2(3)
C(6)-C(7)-N(8)-C(13)	-167.96(15)	C(16)-C(17)-C(18)-C(19)	0.4(3)
C(7)-N(8)-C(9)-C(4)	-66.6(2)	C(17)-C(18)-C(19)-C(20)	-0.2(3)
C(13)-N(8)-C(9)-C(4)	167.71(17)	C(18)-C(19)-C(20)-C(15)	-0.3(3)
C(3)-C(4)-C(9)-N(8)	52.8(2)	C(18)-C(19)-C(20)-C(11)	179.3(2)
C(5)-C(4)-C(9)-N(8)	171.57(18)	N(14)-C(15)-C(20)-C(19)	-179.24(17)
N(8)-C(7)-C(10)-C(11)	11.6(3)	C(16)-C(15)-C(20)-C(19)	0.5(3)
C(6)-C(7)-C(10)-C(11)	132.1(2)	N(14)-C(15)-C(20)-C(11)	1.1(2)
N(8)-C(7)-C(10)-N(14)	-166.91(17)	C(16)-C(15)-C(20)-C(11)	-179.21(18)
C(6)-C(7)-C(10)-N(14)	-46.4(3)	C(10)-C(11)-C(20)-C(19)	-179.9(2)
N(14)-C(10)-C(11)-C(20)	-0.7(2)	C(12)-C(11)-C(20)-C(19)	-1.1(4)
C(7)-C(10)-C(11)-C(20)	-179.35(18)	C(10)-C(11)-C(20)-C(15)	-0.3(2)
N(14)-C(10)-C(11)-C(12)	-179.64(18)	C(12)-C(11)-C(20)-C(15)	178.5(2)

Table 1. Crystal data and structure refinement for compound 44

Empirical formula	$C_{18}H_{20}N_2O$	
Formula weight	280.36	
Temperature	198(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 11.615(3) Å	α= 90°.
	b = 10.570(2) Å	β= 103.94(1)°.
	c = 12.157(2) Å	γ = 90°.
Volume	1448.6(5) $Å^3$	
Z	4	
Density (calculated)	1.286 Mg/m^3	
Absorption coefficient	0.080 mm^{-1}	
F(000)	600	
Crystal size	0.30 x 0.20 x 0.20 mm^3	
Diffractometer type	Nonius-CCD	
Theta range for data collection	5.18 to 23.00°.	
Index ranges	-12<=h<=12, -11<=k<=11, -13<=l<=13	
Reflections collected	9304	
Independent reflections	1997 [R(int) = 0.0804]	
Completeness to theta = 23.00°	98.9 %	
Structure solution	direct method	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1997 / 0 / 211	
Goodness-of-fit on F^2	1.094	
Final R indices [I>2sigma(I)]	R1 = 0.0460, wR2 = 0.0812	
R indices (all data)	R1 = 0.0806, wR2 = 0.0955	
Extinction coefficient	0.0021(12)	
Largest diff. peak and hole	0.145 and -0.183 $e.Å^{-3}$	
Treatment of H-atoms	were found in peak list and refined in riding positions in last cycles with isotropic temperature factors.	

Used programs	Collect (Nonius BV, 1997-2000), DirAx (A.J.K. Duisenberg), SHELXS-97 (Sheldrick, 1990), SHELXL-97 (Sheldrick, 1997), Schakal-99 (E.Keller 1999)

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **44**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	2346(2)	-599(2)	5507(1)	46(1)
C(1)	2814(2)	336(3)	6015(2)	32(1)
C(2)	3263(2)	1454(2)	5482(2)	33(1)
C(3)	4256(2)	1958(2)	6448(2)	30(1)
C(4)	3747(2)	1789(2)	7493(2)	32(1)
C(5)	3092(2)	523(3)	7281(2)	36(1)
C(7)	6261(2)	1352(2)	7698(2)	28(1)
C(6)	5378(2)	1170(2)	6561(2)	30(1)
N(8)	5682(2)	1034(2)	8618(2)	28(1)
C(9)	4698(2)	1898(2)	8591(2)	32(1)
C(10)	7329(2)	517(2)	7843(2)	26(1)
C(11)	7861(2)	-102(2)	8810(2)	27(1)
C(12)	7446(2)	28(2)	9878(2)	32(1)
N(14)	7883(2)	226(2)	6988(2)	29(1)
C(14)	6538(2)	1093(2)	9737(2)	32(1)
C(15)	8795(2)	-615(2)	7417(2)	30(1)
C(16)	9597(2)	-1195(3)	6894(2)	40(1)
C(17)	10376(2)	-2048(3)	7521(2)	48(1)
C(18)	10386(2)	-2305(3)	8653(2)	47(1)
C(19)	9622(2)	-1707(2)	9186(2)	37(1)
C(20)	8802(2)	-845(2)	8566(2)	29(1)

Table 3. Bond lengths [Å] and angles [°] for **44**.

O(1)-C(1)	1.221(3)	C(9)-C(4)-C(5)	116.2(2)
C(1)-C(2)	1.500(3)	C(9)-C(4)-C(3)	112.01(19)
C(1)-C(5)	1.507(3)	C(5)-C(4)-C(3)	103.74(18)
C(2)-C(3)	1.530(3)	C(1)-C(5)-C(4)	105.17(19)
C(3)-C(6)	1.525(3)	N(8)-C(7)-C(10)	106.95(18)
C(3)-C(4)	1.535(3)	N(8)-C(7)-C(6)	109.28(18)
C(4)-C(9)	1.519(3)	C(10)-C(7)-C(6)	112.98(19)
C(4)-C(5)	1.531(3)	C(7)-C(6)-C(3)	112.76(19)
C(7)-N(8)	1.476(3)	C(9)-N(8)-C(7)	109.76(18)
C(7)-C(10)	1.498(3)	C(9)-N(8)-C(14)	110.13(18)
C(7)-C(6)	1.522(3)	C(7)-N(8)-C(14)	111.10(17)
N(8)-C(9)	1.457(3)	N(8)-C(9)-C(4)	111.93(19)
N(8)-C(14)	1.480(3)	C(11)-C(10)-N(14)	110.2(2)
C(10)-C(11)	1.357(3)	C(11)-C(10)-C(7)	125.3(2)
C(10)-N(14)	1.384(3)	N(14)-C(10)-C(7)	124.4(2)
C(11)-C(20)	1.433(3)	C(10)-C(11)-C(20)	107.23(19)
C(11)-C(12)	1.496(3)	C(10)-C(11)-C(12)	122.2(2)
C(12)-C(14)	1.524(3)	C(20)-C(11)-C(12)	130.6(2)
N(14)-C(15)	1.385(3)	C(11)-C(12)-C(14)	109.24(19)
C(15)-C(16)	1.390(3)	C(10)-N(14)-C(15)	108.17(18)
C(15)-C(20)	1.416(3)	N(8)-C(14)-C(12)	111.44(19)
C(16)-C(17)	1.372(4)	N(14)-C(15)-C(16)	130.3(2)
C(17)-C(18)	1.400(4)	N(14)-C(15)-C(20)	107.69(19)
C(18)-C(19)	1.372(3)	C(16)-C(15)-C(20)	122.0(2)
C(19)-C(20)	1.401(3)	C(17)-C(16)-C(15)	117.5(2)
O(1)-C(1)-C(2)	125.3(2)	C(16)-C(17)-C(18)	121.4(2)
O(1)-C(1)-C(5)	125.6(2)	C(19)-C(18)-C(17)	121.5(3)
C(2)-C(1)-C(5)	109.1(2)	C(18)-C(19)-C(20)	118.6(2)
C(1)-C(2)-C(3)	102.67(19)	C(19)-C(20)-C(15)	119.0(2)
C(6)-C(3)-C(2)	110.4(2)	C(19)-C(20)-C(11)	134.3(2)
C(6)-C(3)-C(4)	110.70(19)	C(15)-C(20)-C(11)	106.7(2)
C(2)-C(3)-C(4)	102.98(18)		

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for **44**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	62(1)	40(1)	36(1)	0(1)	9(1)	-14(1)
C(1)	30(1)	33(2)	33(2)	2(1)	8(1)	1(1)
C(2)	35(2)	33(2)	30(1)	5(1)	8(1)	1(1)
C(3)	33(1)	22(2)	34(1)	4(1)	8(1)	2(1)
C(4)	30(1)	33(2)	35(1)	-3(1)	9(1)	7(1)
C(5)	34(2)	45(2)	30(1)	2(1)	13(1)	-6(1)
C(7)	33(1)	25(2)	28(1)	2(1)	10(1)	-1(1)
C(6)	36(1)	29(2)	26(1)	7(1)	12(1)	1(1)
N(8)	30(1)	31(1)	25(1)	0(1)	9(1)	4(1)
C(9)	34(2)	31(2)	33(1)	-3(1)	14(1)	3(1)
C(10)	28(1)	25(1)	27(1)	-2(1)	10(1)	-4(1)
C(11)	26(1)	28(2)	27(1)	-1(1)	4(1)	-3(1)
C(12)	37(1)	31(2)	27(1)	1(1)	7(1)	-4(1)
N(14)	29(1)	35(1)	25(1)	3(1)	8(1)	3(1)
C(14)	35(1)	34(2)	26(1)	-5(1)	6(1)	-1(1)
C(15)	28(1)	27(2)	34(1)	-3(1)	6(1)	0(1)
C(16)	37(2)	47(2)	37(2)	-6(1)	8(1)	8(1)
C(17)	39(2)	52(2)	54(2)	-10(2)	10(2)	14(2)
C(18)	40(2)	44(2)	50(2)	-1(1)	-2(2)	16(2)
C(19)	37(2)	34(2)	36(2)	0(1)	5(1)	-3(1)
C(20)	28(1)	25(2)	31(1)	-1(1)	3(1)	-2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **44**.

	x	y	z	U(eq)
H(21)	3513	1231	4798	35(7)
H(22)	2571	2088	5271	47(7)
H(3)	4433	2817	6328	27(6)
H(4)	3196	2474	7503	26(6)
H(51)	2375	496	7534	34(6)
H(52)	3610	-213	7656	48(8)
H(7)	6522	2264	7757	30(6)
H(61)	5164	243	6499	29(6)
H(62)	5754	1385	5952	30(6)
H(91)	4366	1699	9259	31(6)
H(92)	4983	2833	8649	45(7)
H(122)	8149	231	10566	34(6)
H(121)	7059	-776	10038	37(7)
H(14)	7693	480	6245	37(7)
H(141)	6972	1941	9851	31(6)
H(142)	6030	1030	10327	34(6)
H(16)	9557	-1006	6101	35(7)
H(17)	10940	-2468	7201	52(8)
H(18)	10938	-2906	9040	62(9)
H(19)	9665	-1864	10004	37(7)

Table 6. Torsion angles [°] for **44**.

O(1)-C(1)-C(2)-C(3)	-152.3(2)	C(7)-C(10)-C(11)-C(20)	176.8(2)
C(5)-C(1)-C(2)-C(3)	24.8(2)	N(14)-C(10)-C(11)-C(12)	-179.7(2)
C(1)-C(2)-C(3)-C(6)	79.5(2)	C(7)-C(10)-C(11)-C(12)	-2.3(4)
C(1)-C(2)-C(3)-C(4)	-38.7(2)	C(10)-C(11)-C(12)-C(14)	-9.8(3)
C(6)-C(3)-C(4)-C(9)	46.6(3)	C(20)-C(11)-C(12)-C(14)	171.3(2)
C(2)-C(3)-C(4)-C(9)	164.7(2)	C(11)-C(10)-N(14)-C(15)	0.5(3)
C(6)-C(3)-C(4)-C(5)	-79.4(2)	C(7)-C(10)-N(14)-C(15)	-177.0(2)
C(2)-C(3)-C(4)-C(5)	38.6(2)	C(9)-N(8)-C(14)-C(12)	168.93(19)
O(1)-C(1)-C(5)-C(4)	176.1(2)	C(7)-N(8)-C(14)-C(12)	-69.2(2)
C(2)-C(1)-C(5)-C(4)	-1.0(3)	C(11)-C(12)-C(14)-N(8)	43.6(3)
C(9)-C(4)-C(5)-C(1)	-146.6(2)	C(10)-N(14)-C(15)-C(16)	179.2(3)
C(3)-C(4)-C(5)-C(1)	-23.2(2)	C(10)-N(14)-C(15)-C(20)	-0.1(3)
N(8)-C(7)-C(6)-C(3)	57.3(3)	N(14)-C(15)-C(16)-C(17)	-176.6(3)
C(10)-C(7)-C(6)-C(3)	176.21(19)	C(20)-C(15)-C(16)-C(17)	2.6(4)
C(2)-C(3)-C(6)-C(7)	-162.54(19)	C(15)-C(16)-C(17)-C(18)	-1.5(4)
C(4)-C(3)-C(6)-C(7)	-49.2(3)	C(16)-C(17)-C(18)-C(19)	-0.5(4)
C(10)-C(7)-N(8)-C(9)	174.61(18)	C(17)-C(18)-C(19)-C(20)	1.5(4)
C(6)-C(7)-N(8)-C(9)	-62.8(2)	C(18)-C(19)-C(20)-C(15)	-0.4(4)
C(10)-C(7)-N(8)-C(14)	52.6(2)	C(18)-C(19)-C(20)-C(11)	177.0(3)
C(6)-C(7)-N(8)-C(14)	175.18(19)	N(14)-C(15)-C(20)-C(19)	177.7(2)
C(7)-N(8)-C(9)-C(4)	62.1(2)	C(16)-C(15)-C(20)-C(19)	-1.7(4)
C(14)-N(8)-C(9)-C(4)	-175.24(19)	N(14)-C(15)-C(20)-C(11)	-0.3(3)
C(5)-C(4)-C(9)-N(8)	64.9(3)	C(16)-C(15)-C(20)-C(11)	-179.7(2)
C(3)-C(4)-C(9)-N(8)	-54.1(3)	C(10)-C(11)-C(20)-C(19)	-177.0(3)
N(8)-C(7)-C(10)-C(11)	-18.7(3)	C(12)-C(11)-C(20)-C(19)	2.0(5)
C(6)-C(7)-C(10)-C(11)	-139.0(2)	C(10)-C(11)-C(20)-C(15)	0.6(3)
N(8)-C(7)-C(10)-N(14)	158.4(2)	C(12)-C(11)-C(20)-C(15)	179.6(2)
C(6)-C(7)-C(10)-N(14)	38.1(3)		
N(14)-C(10)-C(11)-C(20)	-0.7(3)		

Table 1. Crystal data and structure refinement for compound 39

Empirical formula	$C_{15}H_{26}OSi_2$	
Formula weight	278.54	
Temperature	198(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$Pna2_{(1)}$	
Unit cell dimensions	a = 10.534(1) Å	α= 90°.
	b = 11.647(1) Å	β= 90°.
	c = 13.797(1) Å	γ = 90°.
Volume	1692.7(2) $Å^3$	
Z	4	
Density (calculated)	1.093 Mg/m^3	
Absorption coefficient	0.199 mm^{-1}	
F(000)	608	
Crystal size	0.52 x 0.23 x 0.20 mm^3	
Diffractometer type	Nonius-CCD	
Theta range for data collection	4.87 to 25.00°.	
Index ranges	-12<=h<=10, -13<=k<=12, -13<=l<=16	
Reflections collected	6646	
Independent reflections	2573 [R(int) = 0.0467]	
Completeness to theta = 25.00°	98.5 %	
Absorption correction	None	
Max. and min. transmission	0.9604 and 0.9032	
Structure solution	direct method	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2573 / 1 / 170	
Goodness-of-fit on F^2	1.109	
Final R indices [I>2sigma(I)]	R1 = 0.0439, wR2 = 0.0849	
R indices (all data)	R1 = 0.0622, wR2 = 0.0936	
Absolute structure parameter	0.01(18)	
Largest diff. peak and hole	0.214 and -0.230 e.$Å^{-3}$	

Treatment of H-atoms	were found in peak list and refined in riding positions in last cycles with isotropic temperature factors.
Used programs	Collect (Nonius BV, 1997-2000), DirAx (A.J.K. Duisenberg), SHELXS-97 (Sheldrick, 1990), SHELXL-97 (Sheldrick, 1997), Schakal-99 (E.Keller 1999)

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **39**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Si(1)	5435(1)	3920(1)	2748(1)	33(1)
C(1)	4112(3)	1379(3)	822(2)	26(1)
Si(2)	4979(1)	-920(1)	1460(1)	30(1)
C(2)	3334(4)	1107(3)	-51(3)	39(1)
C(5)	3544(4)	3546(3)	652(3)	42(1)
C(6)	4233(3)	2606(3)	1172(2)	26(1)
C(7)	4965(3)	2665(3)	1971(2)	28(1)
O(8)	5948(2)	1107(2)	2875(2)	44(1)
C(8)	5331(3)	1436(3)	2182(3)	28(1)
C(9)	4764(3)	671(2)	1412(3)	27(1)
C(11)	4204(4)	4148(4)	3693(3)	58(1)
C(12)	7012(4)	3648(3)	3313(3)	45(1)
C(13)	5576(4)	5241(3)	1998(3)	55(1)
C(21)	6712(4)	-1250(3)	1506(4)	62(1)
C(22)	4223(5)	-1649(3)	408(3)	58(1)
C(23)	4240(3)	-1438(3)	2585(3)	44(1)
C(31)	2379(11)	2030(11)	-304(8)	48(2)
C(41)	3074(12)	3181(13)	-356(9)	47(2)
C(32)	2973(10)	2151(9)	-646(7)	48(2)
C(42)	2557(11)	3171(11)	-18(8)	47(2)

Table 3. Bond lengths [Å] and angles [°] for **39**.

Si(1)-C(11)	1.858(4)	C(2)-C(1)-C(6)	120.3(3)
Si(1)-C(13)	1.861(4)	C(23)-Si(2)-C(22)	109.08(18)
Si(1)-C(12)	1.862(4)	C(23)-Si(2)-C(21)	108.6(2)
Si(1)-C(7)	1.879(3)	C(22)-Si(2)-C(21)	110.6(2)
C(1)-C(9)	1.346(5)	C(23)-Si(2)-C(9)	107.73(17)
C(1)-C(2)	1.491(5)	C(22)-Si(2)-C(9)	111.89(18)
C(1)-C(6)	1.514(4)	C(21)-Si(2)-C(9)	108.94(15)
Si(2)-C(23)	1.839(4)	C(1)-C(2)-C(31)	113.6(5)
Si(2)-C(22)	1.860(4)	C(1)-C(2)-C(32)	113.9(5)
Si(2)-C(21)	1.866(4)	C(31)-C(2)-C(32)	30.5(4)
Si(2)-C(9)	1.868(3)	C(42)-C(5)-C(6)	115.5(6)
C(2)-C(31)	1.513(12)	C(42)-C(5)-C(41)	27.5(5)
C(2)-C(32)	1.516(10)	C(6)-C(5)-C(41)	112.8(6)
C(5)-C(42)	1.459(13)	C(7)-C(6)-C(5)	129.2(3)
C(5)-C(6)	1.497(5)	C(7)-C(6)-C(1)	110.9(3)
C(5)-C(41)	1.537(14)	C(5)-C(6)-C(1)	119.8(3)
C(6)-C(7)	1.346(4)	C(6)-C(7)-C(8)	104.8(3)
C(7)-C(8)	1.510(5)	C(6)-C(7)-Si(1)	131.1(3)
O(8)-C(8)	1.219(4)	C(8)-C(7)-Si(1)	124.0(3)
C(8)-C(9)	1.510(5)	O(8)-C(8)-C(7)	125.9(3)
C(31)-C(41)	1.53(2)	O(8)-C(8)-C(9)	125.3(3)
C(32)-C(42)	1.534(15)	C(7)-C(8)-C(9)	108.8(3)
C(11)-Si(1)-C(13)	109.1(2)	C(1)-C(9)-C(8)	105.4(3)
C(11)-Si(1)-C(12)	110.67(19)	C(1)-C(9)-Si(2)	133.7(3)
C(13)-Si(1)-C(12)	107.59(19)	C(8)-C(9)-Si(2)	120.8(2)
C(11)-Si(1)-C(7)	109.13(17)	C(2)-C(31)-C(41)	108.4(9)
C(13)-Si(1)-C(7)	110.32(18)	C(31)-C(41)-C(5)	110.8(9)
C(12)-Si(1)-C(7)	110.00(17)	C(2)-C(32)-C(42)	112.7(7)
C(9)-C(1)-C(2)	129.7(3)	C(5)-C(42)-C(32)	112.7(8)
C(9)-C(1)-C(6)	110.0(3)		

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3) for **39**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1)	31(1)	25(1)	43(1)	-7(1)	-1(1)	0(1)
C(1)	31(2)	22(2)	26(2)	-1(2)	5(2)	-4(1)
Si(2)	37(1)	20(1)	34(1)	0(1)	3(1)	-1(1)
C(2)	48(2)	39(2)	30(2)	1(2)	-4(2)	-3(2)
C(5)	57(2)	27(2)	44(2)	2(2)	-3(2)	9(2)
C(6)	28(2)	24(2)	28(2)	3(1)	4(2)	3(1)
C(7)	29(2)	22(2)	34(2)	-1(2)	4(2)	4(1)
O(8)	55(2)	31(1)	44(2)	2(1)	-20(2)	8(1)
C(8)	29(2)	23(2)	33(2)	-1(2)	2(2)	4(1)
C(9)	28(2)	23(2)	29(2)	-3(2)	1(2)	-1(1)
C(11)	39(2)	68(3)	66(3)	-33(3)	4(2)	-5(2)
C(12)	40(2)	39(2)	57(3)	-9(2)	-4(2)	-6(2)
C(13)	63(3)	26(2)	77(3)	2(2)	-11(2)	-9(2)
C(21)	48(2)	30(2)	108(4)	7(3)	23(3)	8(2)
C(22)	104(4)	29(2)	40(2)	-5(2)	-2(3)	-14(2)
C(23)	44(2)	41(2)	48(3)	8(2)	2(2)	-4(2)
C(31)	57(6)	56(4)	30(6)	-1(4)	-7(3)	18(5)
C(41)	65(8)	48(3)	28(7)	4(5)	-5(4)	19(6)
C(32)	57(6)	56(4)	30(6)	-1(4)	-7(3)	18(5)
C(42)	65(8)	48(3)	28(7)	4(5)	-5(4)	19(6)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **39**.

	x	y	z	U(eq)
H(22)	2875	407	59	47

H(21)	3870	797	-549	47
H(51)	4142	4155	549	51
H(52)	3087	3926	1162	51
H(111)	3381	4321	3434	87
H(112)	4576	4744	4081	87
H(113)	4186	3411	4006	87
H(121)	7185	4277	3743	68
H(122)	6758	2911	3558	68
H(123)	7605	3362	2843	68
H(131)	4754	5463	1764	83
H(132)	5922	5885	2343	83
H(133)	6196	5086	1505	83
H(211)	7059	-1097	876	93
H(212)	6716	-2068	1418	93
H(213)	7118	-800	1999	93
H(221)	3318	-1574	465	86
H(222)	4718	-1417	-142	86
H(223)	4322	-2433	611	86
H(231)	4327	-2237	2742	66
H(232)	3563	-1331	2670	66
H(233)	4485	-1010	3149	66
H(311)	1706	2062	196	57
H(312)	1977	1857	-936	57
H(411)	2493	3774	-616	57
H(412)	3806	3114	-802	57
H(321)	2273	1943	-1091	57
H(322)	3710	2385	-1046	57
H(421)	2322	3820	-445	57
H(422)	1793	2950	356	57

Table 6. Torsion angles [°] for **39**.

C(9)-C(1)-C(2)-C(31)	158.8(6)	C(2)-C(1)-C(9)-C(8)	-178.5(3)
C(6)-C(1)-C(2)-C(31)	-20.0(7)	C(6)-C(1)-C(9)-C(8)	0.4(4)
C(9)-C(1)-C(2)-C(32)	-167.8(5)	C(2)-C(1)-C(9)-Si(2)	-2.0(6)
C(6)-C(1)-C(2)-C(32)	13.4(6)	C(6)-C(1)-C(9)-Si(2)	176.9(3)
C(42)-C(5)-C(6)-C(7)	-163.4(5)	O(8)-C(8)-C(9)-C(1)	176.8(4)
C(41)-C(5)-C(6)-C(7)	166.5(6)	C(7)-C(8)-C(9)-C(1)	-1.1(4)
C(42)-C(5)-C(6)-C(1)	14.3(6)	O(8)-C(8)-C(9)-Si(2)	-0.2(5)
C(41)-C(5)-C(6)-C(1)	-15.8(6)	C(7)-C(8)-C(9)-Si(2)	-178.1(2)
C(9)-C(1)-C(6)-C(7)	0.5(4)	C(23)-Si(2)-C(9)-C(1)	-114.4(4)
C(2)-C(1)-C(6)-C(7)	179.5(3)	C(22)-Si(2)-C(9)-C(1)	5.5(4)
C(9)-C(1)-C(6)-C(5)	-177.6(3)	C(21)-Si(2)-C(9)-C(1)	128.0(4)
C(2)-C(1)-C(6)-C(5)	1.5(5)	C(23)-Si(2)-C(9)-C(8)	61.6(3)
C(5)-C(6)-C(7)-C(8)	176.7(3)	C(22)-Si(2)-C(9)-C(8)	-178.5(3)
C(1)-C(6)-C(7)-C(8)	-1.1(4)	C(21)-Si(2)-C(9)-C(8)	-55.9(3)
C(5)-C(6)-C(7)-Si(1)	-0.7(6)	C(1)-C(2)-C(31)-C(41)	51.8(9)
C(1)-C(6)-C(7)-Si(1)	-178.5(3)	C(32)-C(2)-C(31)-C(41)	-45.6(12)
C(11)-Si(1)-C(7)-C(6)	87.3(4)	C(2)-C(31)-C(41)-C(5)	-67.6(10)
C(13)-Si(1)-C(7)-C(6)	-32.5(4)	C(42)-C(5)-C(41)-C(31)	-53.0(17)
C(12)-Si(1)-C(7)-C(6)	-151.1(3)	C(6)-C(5)-C(41)-C(31)	48.7(10)
C(11)-Si(1)-C(7)-C(8)	-89.6(3)	C(1)-C(2)-C(32)-C(42)	-42.7(9)
C(13)-Si(1)-C(7)-C(8)	150.5(3)	C(31)-C(2)-C(32)-C(42)	53.7(12)
C(12)-Si(1)-C(7)-C(8)	32.0(3)	C(6)-C(5)-C(42)-C(32)	-43.8(9)
C(6)-C(7)-C(8)-O(8)	-176.5(4)	C(41)-C(5)-C(42)-C(32)	47.0(16)
Si(1)-C(7)-C(8)-O(8)	1.1(5)	C(2)-C(32)-C(42)-C(5)	59.5(11)
C(6)-C(7)-C(8)-C(9)	1.4(4)		
Si(1)-C(7)-C(8)-C(9)	179.0(2)		

Table 1. Crystal data and structure refinement for compound 45

Empirical formula	$C_{18}H_{20}N_2O$	
Formula weight	280.36	
Temperature	198(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 9.936(2) Å	α= 86.60(2)°.
	b = 10.721(3) Å	β= 88.93(2)°.
	c = 13.607(4) Å	γ = 84.08(2)°.
Volume	1439.1(6) $Å^3$	
Z	2	
Density (calculated)	1.294 Mg/m^3	
Absorption coefficient	0.081 mm^{-1}	
F(000)	600	
Crystal size	0.39 x 0.28 x 0.13 mm^3	
Diffractometer type	Nonius-CCD	
Theta range for data collection	4.83 to 23.00°.	
Index ranges	-10<=h<=10, -11<=k<=11, -14<=l<=14	
Reflections collected	15847	
Independent reflections	3945 [R(int) = 0.2083]	
Completeness to theta = 23.00°	98.8 %	
Structure solution	direct method	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3945 / 0 / 379	
Goodness-of-fit on F^2	1.126	
Final R indices [I>2sigma(I)]	R1 = 0.1372, wR2 = 0.3182	
R indices (all data)	R1 = 0.2044, wR2 = 0.3731	
Largest diff. peak and hole	0.828 and -0.412 e.$Å^{-3}$	
Treatment of H-atoms	were found in peak list and refined in riding positions in last cycles with isotropic temperature factors.	

Used programs	Collect (Nonius BV, 1997-2000), DirAx (A.J.K. Duisenberg), SHELXS-97 (Sheldrick, 1990), SHELXL-97 (Sheldrick, 1997), Schakal-99 (E.Keller 1999)

Table 1. Crystal data and structure refinement for compound 61

Empirical formula	$C_{18}H_{24}N_4O_4Si$	
Formula weight	388.50	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/(c)$	
Unit cell dimensions	a = 15.993(1) Å	α= 90°.
	b = 7.936(2) Å	β= 107.57(5)°.
	c = 16.301(7) Å	γ = 90°.
Volume	1972.4(18) $Å^3$	
Z	4	
Density (calculated)	1.308 Mg/m^3	
Absorption coefficient	0.150 mm^{-1}	
F(000)	824	
Crystal size	0.49 x 39 x 16 mm^3	
Diffractometer type	Nonius-CCD	
Theta range for data collection	4.82 to 25.01°.	
Index ranges	-18<=h<=19, -9<=k<=9, -16<=l<=19	
Reflections collected	5731	
Independent reflections	1378 [R(int) = 0.0804]	
Completeness to theta = 25.01°	39.5 %	
Structure solution	direct method	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	1378 / 0 / 245	
Goodness-of-fit on F^2	1.211	
Final R indices [I>2sigma(I)]	R1 = 0.0583, wR2 = 0.1102	
R indices (all data)	R1 = 0.0856, wR2 = 0.1219	
Extinction coefficient	0.0015(10)	
Largest diff. peak and hole	0.137 and -0.146 $e.Å^{-3}$	

Treatment of H-atoms	were found in peak list and refined in riding positions in last cycles with isotropic temperature factors.
Used programs	Collect (Nonius BV, 1997-2000), DirAx (A.J.K. Duisenberg), SHELXS-97 (Sheldrick, 1990), SHELXL-97 (Sheldrick, 1997), Schakal-99 (E.Keller 1999)

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^2 x 10^3) for **61**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Si(1)	2988(1)	591(3)	4613(1)	32(1)
N(1)	1279(3)	1360(5)	5348(3)	31(1)
O(1)	-49(3)	1936(7)	6982(3)	67(2)
C(1)	2739(4)	139(8)	5651(4)	29(2)
O(2)	-1239(3)	3363(8)	6819(3)	72(2)
N(2)	620(3)	1734(6)	5715(3)	36(1)
C(2)	1959(4)	639(7)	5884(3)	29(1)
O(3)	-3017(4)	5288(8)	4123(4)	59(2)
C(3)	2065(4)	203(8)	6815(4)	37(2)
N(3)	-672(4)	2778(8)	6538(4)	49(2)
O(4)	-2499(4)	5410(7)	3022(3)	60(2)
C(4)	2955(4)	-671(8)	7126(4)	32(1)
N(4)	-2437(4)	5012(8)	3775(5)	45(2)
C(5)	3611(4)	171(8)	7900(3)	41(2)
C(6)	4524(4)	-572(8)	8073(4)	46(2)
C(7)	4831(4)	-483(8)	7277(4)	45(2)
C(8)	4187(4)	-1308(8)	6487(4)	43(2)
C(9)	3289(4)	-615(7)	6359(3)	32(1)
C(10)	-110(5)	2546(8)	5258(4)	30(2)
C(11)	-761(4)	3040(9)	5627(4)	36(2)

C(12)	-1525(4)	3858(7)	5135(4)	37(1)
C(13)	-1639(4)	4193(7)	4286(4)	33(1)
C(14)	-998(4)	3732(7)	3901(4)	36(1)
C(15)	-261(5)	2925(8)	4375(4)	36(2)
C(16)	3243(5)	-1408(8)	4139(4)	51(2)
C(17)	3965(4)	1988(8)	4840(4)	48(2)
C(18)	2037(4)	1624(9)	3803(4)	47(2)

Table 3. Bond lengths [Å] and angles [°] for **61**.

Si(1)-C(17)	1.860(7)	C(6)-C(7)	1.522(8)
Si(1)-C(16)	1.863(6)	C(7)-C(8)	1.532(8)
Si(1)-C(18)	1.875(6)	C(8)-C(9)	1.492(8)
Si(1)-C(1)	1.886(7)	C(10)-C(11)	1.407(8)
N(1)-C(2)	1.304(7)	C(10)-C(15)	1.419(7)
N(1)-N(2)	1.390(6)	C(11)-C(12)	1.402(9)
O(1)-N(3)	1.236(7)	C(12)-C(13)	1.367(8)
C(1)-C(9)	1.360(8)	C(13)-C(14)	1.403(8)
C(1)-C(2)	1.464(8)	C(14)-C(15)	1.359(9)
O(2)-N(3)	1.224(7)	C(17)-Si(1)-C(16)	108.3(3)
N(2)-C(10)	1.345(8)	C(17)-Si(1)-C(18)	109.5(3)
C(2)-C(3)	1.515(8)	C(16)-Si(1)-C(18)	108.2(3)
O(3)-N(4)	1.243(7)	C(17)-Si(1)-C(1)	109.1(3)
C(3)-C(4)	1.526(8)	C(16)-Si(1)-C(1)	110.0(3)
N(3)-C(11)	1.463(7)	C(18)-Si(1)-C(1)	111.6(3)
O(4)-N(4)	1.243(7)	C(2)-N(1)-N(2)	113.1(4)
C(4)-C(9)	1.500(7)	C(9)-C(1)-C(2)	106.4(5)
C(4)-C(5)	1.530(8)	C(9)-C(1)-Si(1)	126.0(5)
N(4)-C(13)	1.450(8)	C(2)-C(1)-Si(1)	127.5(5)
C(5)-C(6)	1.520(8)	C(10)-N(2)-N(1)	120.6(5)

N(1)-C(2)-C(1)	123.3(5)
N(1)-C(2)-C(3)	126.1(5)
C(1)-C(2)-C(3)	110.6(6)
C(2)-C(3)-C(4)	104.3(5)
O(2)-N(3)-O(1)	123.0(6)
O(2)-N(3)-C(11)	118.0(6)
O(1)-N(3)-C(11)	119.0(5)
C(9)-C(4)-C(3)	103.9(5)
C(9)-C(4)-C(5)	110.3(5)
C(3)-C(4)-C(5)	114.4(5)
O(3)-N(4)-O(4)	123.9(7)
O(3)-N(4)-C(13)	117.8(7)
O(4)-N(4)-C(13)	118.3(6)
C(6)-C(5)-C(4)	111.3(5)
C(5)-C(6)-C(7)	111.3(5)
C(6)-C(7)-C(8)	112.9(5)
C(9)-C(8)-C(7)	109.5(5)
C(1)-C(9)-C(8)	129.0(5)
C(1)-C(9)-C(4)	114.8(5)
C(8)-C(9)-C(4)	116.2(5)
N(2)-C(10)-C(11)	121.9(6)
N(2)-C(10)-C(15)	121.1(6)
C(11)-C(10)-C(15)	117.0(6)
C(12)-C(11)-C(10)	120.9(6)
C(12)-C(11)-N(3)	116.6(5)
C(10)-C(11)-N(3)	122.4(6)
C(13)-C(12)-C(11)	119.8(5)
C(12)-C(13)-C(14)	120.6(6)
C(12)-C(13)-N(4)	119.6(5)
C(14)-C(13)-N(4)	119.7(5)
C(15)-C(14)-C(13)	119.7(6)
C(14)-C(15)-C(10)	122.0(6)

Table 4. Anisotropic displacement parameters ($Å^2$ x 10^3)for **61**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1)	35(1)	40(1)	25(1)	0(1)	15(1)	7(1)
N(1)	34(3)	34(3)	30(3)	-1(2)	16(2)	4(2)
O(1)	49(3)	118(5)	39(3)	13(3)	21(3)	28(3)
C(1)	30(4)	32(4)	27(4)	-1(3)	13(3)	1(3)
O(2)	50(3)	128(5)	47(3)	-11(3)	31(3)	21(3)
N(2)	33(3)	49(3)	31(3)	0(2)	18(2)	3(2)
C(2)	41(4)	24(3)	25(3)	-7(2)	17(3)	-6(3)
O(3)	43(3)	77(4)	61(4)	3(3)	23(3)	18(3)
C(3)	37(4)	45(4)	31(4)	-6(3)	13(3)	-10(3)
N(3)	35(3)	71(5)	46(4)	-7(3)	22(3)	-4(3)
O(4)	55(4)	70(4)	50(3)	16(3)	9(3)	16(3)
C(4)	46(4)	24(3)	28(3)	0(3)	13(3)	-1(3)
N(4)	44(4)	40(4)	52(4)	-8(3)	16(4)	3(3)
C(5)	55(4)	44(4)	24(3)	-5(3)	13(3)	-5(3)
C(6)	49(4)	50(4)	33(3)	6(3)	2(3)	-5(3)
C(7)	39(4)	43(4)	48(4)	10(3)	9(3)	0(3)
C(8)	40(4)	44(4)	44(4)	8(3)	12(3)	11(3)
C(9)	41(3)	28(3)	27(3)	-4(2)	13(3)	-3(3)
C(10)	32(4)	24(4)	37(4)	-3(3)	15(3)	-5(3)
C(11)	30(4)	44(4)	34(4)	-12(3)	13(3)	-9(3)
C(12)	33(3)	38(4)	45(4)	-11(3)	22(3)	-3(3)
C(13)	33(3)	24(3)	42(3)	-8(3)	11(3)	0(3)
C(14)	42(4)	32(3)	34(3)	-4(3)	15(3)	-7(3)
C(15)	36(4)	41(5)	38(4)	-4(3)	22(3)	-6(3)
C(16)	66(5)	57(5)	35(4)	-10(3)	25(3)	13(4)
C(17)	46(4)	50(4)	56(4)	6(3)	27(3)	2(3)
C(18)	47(4)	71(5)	29(3)	15(3)	17(3)	15(4)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^2 x 10^3) for **61**.

	x	y	z	U(eq)
H(2)	757	1617	6351	43
H(3A)	1601	-543	6859	44
H(3B)	2058	1213	7149	44
H(4A)	2872	-1847	7266	38
H(5A)	3631	1370	7793	49
H(5B)	3417	23	8405	49
H(6A)	4519	-1738	8250	55
H(6B)	4931	41	8540	55
H(7A)	5395	-1038	7398	53
H(7B)	4909	688	7148	53
H(8A)	4369	-1087	5981	52
H(8B)	4182	-2519	6569	52
H(12A)	-1952	4173	5386	44
H(14A)	-1077	3978	3325	43
H(15A)	157	2613	4112	43
H(16A)	2714	-2051	3914	76
H(16B)	3659	-2049	4575	76
H(16C)	3486	-1153	3682	76
H(17A)	4134	2122	4326	72
H(17B)	4440	1495	5283	72
H(17C)	3825	3070	5027	72
H(18A)	1866	2611	4053	71
H(18B)	1554	851	3636	71
H(18C)	2205	1938	3307	71

Table 6. Torsion angles [°] for **61**.

C(17)-Si(1)-C(1)-C(9)	-59.5(6)
C(16)-Si(1)-C(1)-C(9)	59.2(6)
C(18)-Si(1)-C(1)-C(9)	179.4(5)
C(17)-Si(1)-C(1)-C(2)	115.1(6)
C(16)-Si(1)-C(1)-C(2)	-126.2(6)
C(18)-Si(1)-C(1)-C(2)	-6.1(7)
C(2)-N(1)-N(2)-C(10)	177.2(6)
N(2)-N(1)-C(2)-C(1)	-179.4(5)
N(2)-N(1)-C(2)-C(3)	0.4(8)
C(9)-C(1)-C(2)-N(1)	-178.0(5)
Si(1)-C(1)-C(2)-N(1)	6.6(9)
C(9)-C(1)-C(2)-C(3)	2.1(7)
Si(1)-C(1)-C(2)-C(3)	-173.3(4)
N(1)-C(2)-C(3)-C(4)	177.8(6)
C(1)-C(2)-C(3)-C(4)	-2.3(7)
C(2)-C(3)-C(4)-C(9)	1.6(6)
C(2)-C(3)-C(4)-C(5)	121.9(6)
C(9)-C(4)-C(5)-C(6)	-53.2(7)
C(3)-C(4)-C(5)-C(6)	-169.9(5)
C(4)-C(5)-C(6)-C(7)	54.9(7)
C(5)-C(6)-C(7)-C(8)	-54.7(7)
C(6)-C(7)-C(8)-C(9)	51.7(7)
C(2)-C(1)-C(9)-C(8)	-177.8(6)
Si(1)-C(1)-C(9)-C(8)	-2.3(10)
C(2)-C(1)-C(9)-C(4)	-1.1(7)
Si(1)-C(1)-C(9)-C(4)	174.4(4)
C(7)-C(8)-C(9)-C(1)	124.4(7)
C(7)-C(8)-C(9)-C(4)	-52.3(7)
C(3)-C(4)-C(9)-C(1)	-0.3(7)
C(5)-C(4)-C(9)-C(1)	-123.5(6)
C(3)-C(4)-C(9)-C(8)	176.8(5)
C(5)-C(4)-C(9)-C(8)	53.7(7)

N(1)-N(2)-C(10)-C(11)	-175.8(5)
N(1)-N(2)-C(10)-C(15)	4.9(9)
N(2)-C(10)-C(11)-C(12)	-178.9(6)
C(15)-C(10)-C(11)-C(12)	0.5(10)
N(2)-C(10)-C(11)-N(3)	2.9(10)
C(15)-C(10)-C(11)-N(3)	-177.8(6)
O(2)-N(3)-C(11)-C(12)	-3.9(8)
O(1)-N(3)-C(11)-C(12)	173.9(7)
O(2)-N(3)-C(11)-C(10)	174.4(7)
O(1)-N(3)-C(11)-C(10)	-7.8(9)
C(10)-C(11)-C(12)-C(13)	-0.4(9)
N(3)-C(11)-C(12)-C(13)	178.0(5)
C(11)-C(12)-C(13)-C(14)	-0.3(9)
C(11)-C(12)-C(13)-N(4)	178.8(6)
O(3)-N(4)-C(13)-C(12)	-4.3(9)
O(4)-N(4)-C(13)-C(12)	174.9(6)
O(3)-N(4)-C(13)-C(14)	174.8(6)
O(4)-N(4)-C(13)-C(14)	-5.9(9)
C(12)-C(13)-C(14)-C(15)	0.9(9)
N(4)-C(13)-C(14)-C(15)	-178.3(6)
C(13)-C(14)-C(15)-C(10)	-0.8(9)
N(2)-C(10)-C(15)-C(14)	179.5(6)
C(11)-C(10)-C(15)-C(14)	0.1(10)

7 Bibliography

(1) Cordell, G. A. *Heterocyclic Compounds: The Monoterpenoid Indole Alkaloids*; Saxton, J. E., Ed.; Wiley: New York, 1983; Vol. 25, p 539.

(2) Szantay, C.; Blesko, G.; Hongy, K.; Dörnyei, G. *The Alkaloids*; Orlando, 1986; Vol. 27, p 131.

(3) Szantay, C. *Pure Appl. Chem.* **1990**, *62*, 1299.

(4) Baxter, E. W.; Marino, P. S. *Alkaloids: Chemical and Biological Perspectives*; Pelletier, S. W., Ed.; Springer-Verlag: New York, 1992; Vol. 8, p 197.

(5) Heible, J. P.; Ruffolo, R. R.; Starke, K. *Identification, characterization and subclassification of a 2-adrenoceptors: an overview. In: "a 2-Adrenergic Receptors: Structure, Function and Therapeutic Implications".* Harwood Academic Press, 1997.

(6) Ruffolo, R. R.; Bondinell, W.; Hieble, J. P. *J. Med. Chem.* **1995**, *38*, 3415.

(7) Berlan, M.; Galitzky, J.; Riviere, D. *Int. J. Obesity* **1991**, *15*, 305.

(8) Anand, N. In *In Comprehensive Medicinal Chemistry*; Hansch, C., Ed.; Pergamon Press: Oxford, 1990; Vol. 1, p 126.

(9) Neuman, J.; de Engel, A. M. F.; Neumann, M. P. *Arzneim.-Forsch* **1986**, *36*, 1394.

(10) Lewis, T.; Pickering, G. W. *Clin. Sci.* **1934**, *1*, 327.

(11) von Poster, G.; Andrade, H. H. R.; da Silva, K. V. C. L.; Henriques, J. A. P. *Mutation Res.* **1990**, *232*, 37.

(12) Schlatmann, J. E.; Vinke, J. L.; Tenhoopen, H. J. G.; Heijnen, J. J. *Biotechnol. Bioeng.* **1995**, *45*, 435.

(13) Asada, M.; Shuler, M. L. *Appl. Microbiol. Biotechnol.* **1989**, *30*, 475.

(14) Baggiolini, E. G.; Pizzolato, G.; Uskokovic, M. R. *Tetrahedron* **1988**, *44*, 3203.

(15) Merlini, L.; Mondelli, R.; Nasini, G.; Hesse, M. *Tetrahedron* **1967**, *23*, 3129.

(16) Peube-Locou, N.; Plat, M.; Koch, M. *Phytochemistry* **1973**, *12*, 199.

(17) Angenot, L.; Coune, C.; Tits, M. *J. Pharm. Belg.* **1978**, *33*, 284.

(18) Dachriyanus.; Arbain, D.; Putra, D. P.; Sargent, M. V.; Susila, R.; Wahyumi, F. S. *Aust. J. Chem.* **2000**, 221.

(19) Woodward, R. B.; Bader, F. E.; Bickel, H.; Frey, A. J.; Kierstead, R. W. *J. Am. Chem. Soc.* **1956**, *78*, 2023.

(20) Woodward, R. B.; Bader, F. E.; Bickel, H.; Frey, A. J.; Kierstead, R. W. *Tetrahedron* **1958**, *2*, 1.

(21) van Tamelen, E. E.; Shamma, M.; Brugstahler, A. W.; Wolinsky, J.; Tamm, R.; Aldrich, P. E. *J. Am. Chem. Soc.* **1958**, *80*, 5006.

(22) Aube, J.; Ghosh, S. *Advances in Heterocyclic Natural Product Synthesis*; Pearson, W. H., Ed.; JAI Press, Inc.: Greenwich, CT, 1996; Vol. 3, p 99.

(23) Winterfeldt, E. *Fortschr. Chem. Org. Naturst.* **1974**, *30*, 469.

(24) Martin, S. F.; Grzejszozak, S.; Ruger, H.; Williamson, S. A. *J. Am. Chem. Soc.* **1985**, *107*, 4072.

(25) Stork, G. *Pure Appl. Chem.* **1989**, *51*, 439.

(26) Wender, P. A.; Schaus, J. M.; White, A. W. *J. Am. Chem. Soc.* **1980**, *102*, 6157.

(27) Baxter, E. W.; Labaree, D.; Ammon, H. L.; Mariano, P. S. *J. Am. Chem. Soc.* **1990**, *112*, 7682.

(28) Pearlman, B. A. *J. Am. Chem. Soc.* **1979**, *101*, 6398, 6404.

(29) Knölker, H.-J.; Cämmerer, S. *Tetrahedron Lett.* **2000**, *41*, 5035.

(30) Negishi, E.; Holmes, S. J.; Tour, J. M.; Miller, J. A. *J. Am. Chem. Soc.* **1985**, *107*, 2568.

(31) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 1286.

(32) Pages, L.; Llebaria, A.; Camps, F.; Molins, E.; Miravitlles, C.; Moreto, J. M. *J. Am. Chem. Soc.* **1992**, *114*, 10449.

(33) Mukai, C.; Uchiyama, M.; Hanaoka, M. *J. Chem. Soc., Chem. Commun.* **1992**, 1014.

(34) Jeong, N.; Lee, S. J.; Lee, B. Y.; Chung, Y. K. *Tetrahedron Lett.* **1993**, *34*, 4027.

(35) Hoye, T. R.; Suriano, J. A. *Organometallics* **1992**, *11*, 2044.

(36) Berk, S. C.; Grossman, R. B.; Buchwald, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 4912.

(37) Hicks, F. A.; Kablaoui, N. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 9450.

(38) Zhang, M.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 4498.

(39) Morimoto, T.; Chatani, N.; Fukumoto, Y.; Murai, S. *J.Org. Chem.* **1997**, *62*, 3762.

(40) Kondo, T.; Suzuki, N.; Okada, T.; Mitsudo, T. *J. Am. Chem. Soc.* **1997**, *119*, 6187.

(41) Koga, Y.; Kobayashi, T.; Narasaka, K. *Chem. Lett.* **1998**, 249.

(42) Jeong, N.; Lee, S.; Sung, B. K. *Organometallics* **1998**, *17*, 3642.

(43) Wender, P. A.; Croatt, M. P.; Deschamps, N. M. *J. Am. Chem. Soc.* **2004**, *126*, 5948.

(44) Khand, I. U.; Knox, G. R.; Pauson, P. L. *J. Chem. Soc., Chem.Comm.* **1971**, 36.

(45) Schore, N. E.; Croudace, M. C. *J. Org. Chem.* **1981**, *46*, 5436.

(46) Schore, N. E. *In Comprehensive Organic Synthesis*; Pergamon: Oxford, 1991; Vol. 5.

(47) Magnus, P.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5861.

(48) Exon, C.; Magnus, P. *J. Am. Chem. Soc.* **1983**, *105*, 2477.

(49) Magnus, P.; Becker, D. P. *J. Am. Chem. Soc.* **1987**, *109*, 7495.

(50) Hua, D. H. *J. Am. Chem. Soc.* **1968**, *108*, 3835.

(51) Brummond, K. M. In *An allenic [2+2+1] Cycloaddition; In Advances in Cycloaddition Chemistry*; Harmata, M., Ed.; Jai Press Inc : Stamford: Connecticut, 1999; Vol. 6, p 211-237.

(52) Reppe, W.; Vetter, H. *Liebigs Ann. Chem.* **1953**, *582*, 133.

(53) Knölker, H.-J.; Heber, J.; Mahler, C. H. *Synlett* **1992**, 1002.

(54) Mantzaris, J.; Weissberger, E. *J. Am. Chem. Soc.* **1974**, *96*, 1880.

(55) Knölker, H.-J.; Heber, J. *Synlett* **1993**, 924.

(56) Pearson, A. J.; Shively, R. J.; Dubbert, R. A. *Organometallics* **1992**, *11*, 4096.

(57) Eaton, B. E.; Rollman, B.; Kaduk, J. A. *J. Am. Chem. Soc.* **1992**, *114*, 6245.

(58) Sigman, M. S.; Eaton, B. E. *J. Am. Chem. Soc.* **1996**, *118*, 11783.

(59) Shibata, T.; Koga, Y.; Narasaka, K. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 911.

(60) Emerson, G. F.; Mahler, J. E.; Kochhar, R.; Pettit, R. *J. Org. Chem.* **1964**, *29*, 3620.

(61) Holmes, J. D.; Pettit, R. *J. Am. Chem. Soc.* **1963**, *85*, 2531.

(62) Knölker, H.-J. *J. Prakt. Chem.* **1996**, *338*, 190.

(63) Thompson, D. J. *J. Organomet. Chem.* **1976**, *108*, 381.

(64) Manuel, T. A.; Stone, F. G. A. *J. Am. Chem. Soc.* **1960**, *82*, 366.

(65) Knölker, H.-J.; Goesmann, H.; Klauss, R. *Angew. Chem., Int. Ed.* **1999**, *38*, 702.

(66) Knölker, H.-J.; Baum, E.; Goesmann, H.; Klauss, R. *Angew. Chem., Int. Ed.* **1999**, *38*, 2064.

(67) Padwa, A.; Beall, L. S.; Heidelbaugh, T. M.; Liu, B.; Sheehan, S. M. *J. Org. Chem.* **2000**, *65*, 2684.

(68) Whittaker *J. Chem. Soc. C* **1969**, 85.

(69) Kawate, T.; Nakagawa, M.; Yamazaki, H.; Hirayama, M.; Hino, T. *Chem. Pharm. Bull.* **1993**, *41*, 287.

(70) Hoffmann-Roeder, A.; Krause, N. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196.

(71) Zimmer, R.; Dinesh, C. U.; Nandanan, E.; Khan, F. A. *Chem. Rev.* **2000**, *100*, 3067.

(72) Knochel, P.; P, J. *Organozinc Reagents. A Practical Approach*; Oxford University Press, 1999.

(73) Knochel, P.; Perea, J. J.; Jones, P. *Tetrahedron* **1998**, *54*, 8275.

(74) Cämmerer, S., Dissertation, University of Karlsruhe, 2000.

(75) Bohlmann, F. *Chem. Ber.* **1958**, *91*, 2157.

(76) Rylander, P. N. *Hydrogenation Methods*; Academic Press: N.Y., 1985.

(77) Fleming, I. *Chem. Soc. Rev.* **1981**, *10*, 83.

(78) Heber, J., Dissertation, University of Karlsruhe, 1996.

(79) Ley, S. V.; Norman, J.; Griffith, W. P.; Marsden, S. P. *Synthesis* **1994**, 639.

(80) Piancatelli, G.; Scettri, A.; D'Auria, M. *Synthesis* **1982**, 245.

(81) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, *15*, 2647.

(82) Albright, J. D.; Goldmann, L. *J. Org. Chem.* **1965**, *30*, 1107.

(83) Pfitzner, K. E.; Moffatt, J. G. *J. Am. Chem. Soc.* **1965**, 5661.

(84) Keefer, L. K.; Lunn, G. *Chem. Rev.* **1989**, *89*, 459.

(85) Frank-Neumann, M.; Geoffory, P.; Bissinger, P.; Adelaide, S. *Tetrahedron Lett.* **2001**, *42*, 6401.

(86) March, J. *Advanced Organic Chemistry*; 4th ed.; John Wiley & Sons: New York, 1992.

(87) Gutsche, C. D.; Redmore, D. *Carbocyclic Ring Expansion Reactions*; Academic Press: New York, 1968.

(88) Giraitis, A. P.; Bullock, J. L. *J. Am. Chem. Soc.* **1937**, 951.

(89) Hashimoto, N.; Aoyama, T.; Shioiri, T. *Tetrahedron Lett.* **1980**, *21*, 4619.

(90) Hashimoto, N.; Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull.* **1982**, *30*, 119.

(91) Maruoka, K.; Concepcion, A. B.; Yamamoto, H. *Synthesis* **1994**, 1283.

(92) Miyazawa, N.; Ogasawara, K. *Tetrahedron Lett.* **2002**, *43*, 4773.

(93) Keene, A. T.; Phillipson, J. D.; Warhurst, D. C.; Koch, M.; Seguin, E. *Planta Med.* **1987**, 201.

(94) Chandrasekhar, S.; Reddy, C. R.; Babu, B. N. *J.Org. Chem.* **2002**, 9080.

(95) Godleski, S. A.; Villhauer, E. B. *J. Org. Chem.* **1986**, *51*, 486.

(96) Huang-Minlon *J. Am. Chem. Soc.* **1946**, *68*, 2487.

(97) Aube, J.; Wang, Y.; Hammond, M.; Tanol, M.; Takuusagawa, F.; Vander Velde, D. *J. Am. Chem. Soc.* **1990**, *112*, 4879.

(98) Wenkert, E.; Chang, C.-J.; Chawala, H. P. S.; Cochran, D. W.; Hagaman, E. W.; King, J. C.; Orito, K. *J. Am. Chem. Soc.* **1976**, *98*, 3645.

(99) Bergmeier, S. C.; Seth, P. P. *J. Org. Chem.* **1999**, *64*, 3237.

(100) Hua, D. H.; Bharathi, S. N.; Panangadan, J. A. K.; Tsujimoto, A. *J. Org. Chem.* **1991**, *56*, 6998.

(101) Grieco, P. A.; Hishizawa, M.; Marinovic, N. *J. Am. Chem. Soc.* **1976**, *98*, 7102.

(102) Naito, T.; Tada, Y.; Nishiguchi, Y.; Ninomiya, I. *Heterocycles* **1982**, *18*.

(103) Okamura, K.; Yamada, S.-I. *Chem. Pharm. Bull.* **1978**, *26*, 2305.

(104) Lounasmaa, M.; Jokela, R. *Tetrahedron* **1990**, *46*, 615.

(105) Ogliaruso, M. A.; Romanelli, M. G.; Becker, E. I. *Chem. Rev.* **1965**, *65*, 261.

(106) Knölker, H.-J.; Baum, E.; Heber, J. *Tetrahedron Lett.* **1995**, *36*, 7647.

(107) Korte, F.; Büchel, K. H. *Angew. Chem.* **1959**, *71*, 709.

(108) van Tamelen, E. E.; Placeway, C.; Schiemenz, G. P.; Wright, I. G. *J. Am. Chem. Soc.* **1969**, *91*, 7359.

(109) Cämmerer, S., Diplomarbeit, University of Karlsruhe, 1996.

(110) Gesing, E. R. F.; Tane, J. P.; Vollhardt, K. P. C. *Angew. Chem., Int. Ed.* **1980**, *12*, 1023.

(111) Reetz, M. T.; Haning, H. *Tetrahedron Lett.* **1993**, *34*, 7395.

(112) Clarke; Rooney *Adv. Catal.* **1976**, *25*, 125.

(113) Burwell; Schrage *J. Am. Chem. Soc* **1965**, *87*, 5234.

(114) Krow, G. R. *Tetrahedron* **1981**, *37*, 2697.

(115) Krow, G. R. *Org. React.* **1993**, *43*, 251.

(116) Mino, T.; Msauda, S.; Masayuki, N.; Yamashita, M. *J. Org. Chem.* **1997**, *62*, 2633.

(117) Dieter, K. R.; Pounds, S. *J. Org. Chem.* **1982**, *47*, 3172.

(118) Suzuki, M.; Takada, R.; Noyori, R. *J. Org. Chem.* **1982**, *47*, 902.

(119) Kocienski, P. J. *Protecting Groups*; 3rd ed.; Georg Thieme: Stuttgart-New York, 2004.

(120) Edwards, B.; Sparks, A.; Voyta, J. C.; Strong, R.; Murphy, O.; Bronstein, I. *J.Org. Chem.* **1990**, *55*, 6225.

(121) Chi, S.; Heathcock, C. H. *Org. Lett.* **1999**, *1*, 3.

(122) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361.

(123) Hölscher, P.; Knölker, H.-J.; Winterfeldt, E. *Isr. J. Chem.* **1991**, *31*, 187.

(124) Knölker, H.-J. *Chem. Soc. Rev.* **1999**, *28*, 151.

(125) Smith, E.; Jaret, R. S.; Shine, R. J.; Shamma, M. *J. Am. Chem. Soc.* **1967**, *89*, 2469.

(126) Earl, R. A.; Townsend, L. B. *Can. J. Chem.* **1980**, *58*, 2550.

(127) Winterfeldt, E.; Franzischka, W. *Chem. Ber.* **1967**, *100*, 3801.

(128) Nicholas, K. M.; Pettit, R. *J. Organomet. Chem.* **1972**, *44*, C12.

(129) Nicholas, K. M. *Acc. Chem. Res.* **1987**, *20*, 207.

(130) Jones, R. A. *Pyrroles, Part II*; Wiley: New York, 1992.

(131) Thompson, R. B. *FASEB J* **2001**, *15*, 1671.

(132) Muchowski, J. M. *Adv. Med. Chem.* **1992**, *1*, 109.

(133) Cozzi, P.; Mongelli, N. *Curr. Pharm. Des.* **1998**, *4*, 181.

(134) Fürstner, A.; Szillat, H.; Gabor, B.; Mynott, R. *J. Am. Chem. Soc.* **1998**, *120*, 8305.

(135) Skotheim, T. A.; Elsenbaumer, R. L.; Reynolds, J. R. *Handbook of Conducting Polymers* 2nd ed.; Marcel Dekker: New York, 1998.

(136) Bean, G. P. *Pyrroles*; ed. Jones, R. A., Wiley: New york, 1990; Vol. -, p.105.

(137) Kang, H.; Fenical, W. *J. Org. Chem* **1997**, *62*, 3254.

(138) Yoshida, W. Y.; Lee, K. K.; Carroll, A. R.; Scheuer, P. J. *Helv. Chim. Acta* **1992**, *75*, 1721.

(139) Anderson, R. J.; Faulkner, D. J.; Cun-Heng, H.; Van Duyne, G. D.; Clardy, J. *J. Am. Chem. Soc.* **1985**, *107*, 5492.

(140) Zhang, Q.; Tu, G.; Zhao, Y.; Cheng, T. *Tetrahedron* **2002**, *58*, 6795.

(141) Kam, T.-S.; Sim, K.-M. *Phytochemistry* **1998**, *47*, 145.

(142) Bailly, C. *Current Medicinal Chemistry - Anti-Cancer Agents* **2004**, *4*, 363.

(143) Knorr, L. *Ber. Dtsch. Chem. Ges.* **1884**, *17*, 1635.

(144) Paal, C. *Ber. Dtsch. Chem. Ges.* **1885**, *18*, 367.

(145) Sundberg, R. J. *Comprehensive Heterocyclic Chemistry*; ed. Katritzky, A. R. and Rees C. W., Pergamon Press: Oxford, 1984; Vol. 4, p. 313.

(146) Sundberg, R. J. *Comprehensive Heterocyclic Chemistry II*; ed. Katritzky, A. R., Rees, C. W. and Scriven, E. F. V., Elsevier: Oxford, 1996; Vol. 2, p. 119.

(147) Gribble, G. W. *Comprehensive Heterocyclic Chemistry II*; ed. Katritzky, A. R., Rees, C. W. and Scriven, E. F. V., Elsevier: Oxford, 1996; Vol. 2, p. 207.

(148) Boger, D. L.; Bozce, C. W.; Labroli, M. A.; Sehon, C. A.; Jin, Q. *J. Am. Chem. Soc.* **1998**, *120*, 12147.

(149) Kel'in, A. V.; Sromek, A. W.; Gevorgyan, V. *J. Am. Chem. Soc.* **2001**, *123*, 2074.

(150) Palacios, F.; Aparicio, D.; Garcia, J.; Vicario, J.; Ezpeleta, J. M. *Eur. J. Org. Chem.* **2001**, 3357.

(151) Dieter, R. K.; Yu, H. *Org. Lett.* **2000**, *2*, 2283.

(152) Lagu, B.; Pan, M.; Wachter, M. P. *Tetrahedron Lett.* **2001**, *42*, 6027.

(153) Agami, C.; Dechoux, L.; Hebbe, S. *Synthesis* **2001**, 1440.

(154) Kimura, M.; Tanaka, S.; Tamaru, Y. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 1689.

(155) Fox, D. N. A.; Lathbury, D.; Mahon, M. F.; Molloy, K. C.; Gallagher, T. *J. Chem. Soc., Chem. Commun.* **1989**, 1073.

(156) Arredondo, V. M.; McDonald, F. E.; Marks, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 4871.

(157) Claesson, A.; Sahlberg, C.; Luthman, K. *Acta Chem. Scand. B* **1979**, *33*, 309.

(158) Prasad, J. S.; Liebeskind, L. S. *Tetrahedron Lett.* **1988**, *29*, 4257.

(159) Grigg, R.; Meyers, P.; Somasunderam, A.; Sridharan, V. *Tetrahedron* **1992**, *48*, 9735.

(160) Gravestock, D.; Dovey, M. C. *Synthesis* **2003**, 523.

(161) Robinson, R. S.; Dovey, M. C.; Gravestock, D. *Tetrahedron Lett.* **2004**, *45*, 6787.

(162) Shamma, M. *The Isoquinoline Alkaloids*; Academic Press: New York, 1978.

(163) Lundstrom, J. *The Alkaloids*; Brossi, A., Ed.; Academic Press: New York, 1983; Vol. 21, p 255.

(164) Pelletier, J. C.; Cava, M. P. *J. Org. Chem.* **1987**, *52*, 616.

(165) Ginnebaugh, J. P.; Maki, J. W.; Lewandos, G. S. *J. Organomet. Chem.* **1980**, *190*, 403.

(166) Prasad, J. S.; Liebeskind, L. S. *Tetrahedron Lett.* **1988**, *29*, 4253.

(167) Agarwal, S.; Knölker, H.-J. *Org. Biomol. Chem.* **2004**, *2*, 3060.

(168) Schuster, H. E.; Coppola, G. M. *Allenes in Organic Chemistry*; John Wiley & Sons: New York, 1984.

(169) Amombo, M. O.; Hausherr, A.; Reissig, H.-U. *Synlett* **1999**, 1871.

(170) Cao, X.; Yang, Y.; Wang, X. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2485.

(171) Milburn, R. R.; Snieckus, V. *Angew. Chem., Int. Ed.* **2004**, *43*, 892.

(172) Knölker, H.-J.; Baum, G.; Foitzik, N.; Goesmann, H.; Gonser, P.; Jones, P. G.; Röttele, H. *Eur. J. Inorg. Chem.* **1998**, 993.

(173) Itoh, T.; Miyazaki, M.; Nagata, K.; Yokoya, M.; Nakamura, S.; Ohsawa, A. *Heterocycles* **2002**, *58*, 115.

(174) Itoh, T.; Miyazaki, M.; Nagata, K.; Nakagawa, M.; Ohsawa, A. *Heterocycles* **2004**, *63*, 655.

(175) Corsano, S.; Algieri, S. *Ann. Chim. (Italy)* **1960**, *50*, 75.

(176) Ashcroft, W. R.; Martinez, S. J. *Tetrahedron* **1981**, *37*, 3005.

(177) Meyers, A. I.; Loewe, M. F. *Tetrahedron Lett.* **1984**, *25*, 2641.

(178) Mandal, S. B.; Giri, V. S.; Sabeena, M. S.; Pakrashi, S. C. *J. Org. Chem.* **1988**, *53*, 4236.

(179) Bernotas, R. C.; Cube, R. V. *Tetrahedron Lett.* **1991**, *32*, 161.

(180) Dadson, B. A.; Harley-Mason, J.; Foster, G. H. *Chem. Commun.* **1968**, 1233.

(181) Harley-Mason, J.; Taylor, C. G. *Chem. Commun.* **1970**, 812.

(182) Crawley, G. C.; Harley-Mason, J. *Chem. Commun.* **1971**, 685.

(183) Calverley, M. J. *J. Chem. Soc., Chem. Commun.* **1981**, 1209.

(184) Schill, G.; Löwer, H.; Priester, C. U.; Windhövel, U. F.; Fritz, H. *Tetrahedron* **1987**, *43*, 3729.

(185) Knölker, H.-J.; Agarwal, S. *Synlett* **2004**, 1767.

(186) Weinstein, B.; Craig, A. R. *J. Org. Chem.* **1976**, *41*, 875.

(187) Kaiser, H.-P.; Muchowski, J. M. *J. Org. Chem.* **1984**, *49*, 4203.

(188) Saito, S.; Tanaka, T.; Kotera, K.; Nakai, H.; Sugimoto, N.; Horii, Z.; Ikeda, M.; Tamura, Y. *Chem. Pharm. Bull.* **1965**, *13*, 786.

(189) Maryanoff, B. E.; McComsey, D. F.; Gardocki, J. F.; Shank, R. P.; Costanzo, M. J.; Nortey, S. O.; Schneider, C. R.; Setler, P. E. *J. Med. Chem.* **1987**, *30*, 1433.

(190) Chung, S.-H.; Yook, J.; Min, B. J.; Lee, J. Y.; Lee, Y. S.; Jin, C. *Arch. Pharm. Res.* **2000**, *23*, 353.

(191) Lee, Y. S.; Kang, D. W.; Lee, S. J.; Park, H. *J. Org. Chem.* **1995**, *60*, 7149.

(192) Pearson, W. H.; Fang, W. *J. Org. Chem.* **2000**, *65*, 7158.

(193) Okamoto, S.; Teng, X.; Fujii, S.; Takayama, Y.; Sato, F. *J. Am. Chem. Soc.* **2001**, *123*, 3462.

(194) Itoh, T.; Nagata, K.; Yokoya, M.; Miyazaki, M.; Kameoka, K.; Nakamura, S.; Ohsawa, A. *Chem. Pharm. Bull.* **2003**, *51*, 951.

(195) Schell, F. M.; Smith, A. M. *Tetrahedron Lett.* **1983**, *24*, 1883.

(196) Orito, K.; Matsuzaki, T.; Suginome, H.; Rodrigo, R. *Heterocycles* **1988**, *27*, 2403.

(197) Jahangir; MacLean, D. B.; Holland, H. L. *Can. J. Chem.* **1986**, *64*, 1031.

(198) Knölker, H.-J.; Agarwal, S. *Tetrahedron Lett.* **2005**, *46*, 1173.

Acknowledgements

This thesis would not have been possible without the help of many people I sincerely acknowledge them.

First, I would like to express my deep gratitude to my Ph.D supervisor, Prof. Dr. Hans-Joachim Knölker for providing excellent working ambience and state-of-art research facilities. His encouragement and guidance were the driving forces of my success. I delighted my scientific freedom under his tutelage. His trust and concern on me fueled my interests. He is an inspiring person who influenced me with his dedication, devotion and determination towards research work.

Certainly I must thank all scientific and technical staff members who have helped me in so many ways while this research was conducted. While it is impossible to name every individual who provided assistance I will attempt to acknowledge those who were an integral part of the research. I would like to thank Dr. Joghee Raju Suresh for his support, encouragement and scientific suggestions during my graduate research. I would also like to thank Dipl.Chem. Simon Dürr for his help during our shift from Karlsruhe to Dresden.

I gratefully acknowledge the assistance of the following people: Dr. M. Gruner, Ms. Rudolph and Ms. Böhler for NMR measurements; Dr. Korschwitz and Ms. Rößler for IR and GC-MS measurements; Ms. Peritz for elemental analysis; Ms. L. Shapoval for MS and HRMS measurements and Ms. S. Goutal for X-ray measurements. I am also thankful to Dr. Tobias Braxmeier for proof reading my thesis.

I remember the warmth of Dr. R. R. Kethiri, Dr. Simon Cämmerer, Dr. Anil Gajare, Dr. M. Chandrashekharam, Dr. Glenn Whitener, Micha Krahl, Arndt Schimdt and all my

fellow Ph.D at Karlsruhe and Dresden during scientific and non-scientific encounters. I would also like to acknowledge the contribution of all of the OC-II students who worked with me over the years. Besides the professional skills, I am grateful to all of the students for the fun filled time in which they introduce me with the fascinating nature and culture of German folks. Although this was a wondrous and lengthy journey but, will be fondly remembered in years to come.

Last but foremost appreciation to my wife Gunjan and son Shubh for their constant love, support, patience and encouragement during this research work. Finally, I am able to achieve the goal with guidance, blessings and a strong believes of my parents.

Sameer Agarwal Dresden, February, 2005

Versicherung

Hiermit versichere ich, dass ich die vorliegende Arbeit ohne unzulässige Hilfe Dritter und ohne Benutzung anderer als der angegebenen Hilfsmittel angefertigt habe; die aus fremden Quellen direkt oder indirekt übernommenen Gedanken sind als solche kenntlich gemacht. Die Arbeit wurde bisher weder im Inland noch im Ausland in gleicher oder ähnlicher Form einer anderen Prüfungsbehörde vorgelegt.

Sameer Agarwal

Erklärung

Die vorliegende Arbeit wurde unter der wissenschaftlichen Betreuung von Prof. Dr. Hans-Joachim Knölker in der Zeit von Dezember 2001 bis Oktober 2004 im Institut für Organische Chemie der Technischen Universität Dresden angefertigt. Es haben keine frühen erfolglosen Promotionsverfahren stattgefunden.

Ich erkenne die Promotionsordnung der Fakultät Mathematik und Naturwissenschaften der Technischen Universität Dresden vom 16. 04. 2003 in vollem Umfang an.

Dresden, den 15. Februar 2005

Sameer Agarwal

Curriculum Vitae

PERSONAL DETAILS

Name	**Sameer Agarwal**
Date of Birth	21st July 1973, Dehra Dun, INDIA
Marital Status	Married, one son born on 06.04.2003
Nationality	Indian

EDUCATION

1979 - 1989	Higher secondary school, CBSE Board, Dehra Dun, India.
1989 - 1991	Senior secondary school, CBSE Board, Dehra Dun, India.
1991 - 1994	Bachelor of Science, Chemistry, H.N.B.Garhwal University, Dehra Dun, India.
1994 - 1996	Master of Science, Organic Chemistry, H.N.B.Garhwal University, (University Gold Medal), Dehra Dun, India.
1998 - 2000	Master of Technology, Chemistry, Indian Institute of Technology (IIT), Delhi, India.
05.99 - 02.00	DAAD Scholarship in Institute of Biological Engineering and Biotechnology of Wastewater, (Prof. Dr. J. Winter), Karlsruhe University, Germany.
06.00 - 11.01	Ph.D research work under supervision of Prof. Dr. H.-J. Knölker, and Research Assistant at Institute of Organic Chemistry, Karlsruhe University, Germany.
12.01 - 10.04	Ph.D research work under supervision of Prof. Dr. H.-J. Knölker, and Research Assistant at Institute of Organic Chemistry, Technical University, Dresden, Germany.

PROFESSIONAL EXPERIENCE

11.04 - till date	Research Scientist, Jado Technologies, Dresden, Germany.

PUBLICATIONS

1. H.-J. Knölker and Sameer Agarwal, *Synlett* **2004**, 1767
2. Sameer Agarwal and H.-J. Knölker, *Org. Biomol. Chem.* **2004**, *2*, 3060
3. H.-J. Knölker and Sameer Agarwal, *Tetrahedron Lett.***2005**, *46*, 1173