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New advances in the catalysis of organic reactions by iron compounds

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The review summarizes and systematizes the literature data on a new promising application area of iron compounds, that is, catalysis of organic reactions. The considered reactions include halogenation, formation of C – C bonds with the participation of various substrates, new methods for the synthesis of ethers and aromatic and heteroaromatic carboxylic acid esters, *N*-alkylation of aliphatic and aromatic amines and amidation of olefins and cyclopropane-containing hydrocarbons. The advances in the synthesis of quinolines and unusual cyclization reactions catalyzed by iron complexes are described.
The bibliography includes 144 references.

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1. Introduction

Iron compounds (including complexes) are widely used in organic chemistry. They serve as efficient catalysts for numerous organic reactions[1–4] such as linear and cyclic oligomerization of alkenes and dienes,[1] positional isomerization of the double bond,[5] oxidation,[2,3] reduction,[1,3,5] cross-coupling,[3,6] alkylation,[7,8] hydrofunctionalization of alkenes and alkynes,[2,9] hydrosilylation,[10,11] amination,[12] cycloaddition[13] and many other. Iron complexes are among the best catalysts for C – H bond activation in alkenes, aromatics and alkynes.[10,13–15] A fundamental review published in 2015,[4] which covers the literature up to 2014, illustrates the extensive potential of iron-containing catalysts in organic synthesis. The most recent reviews address narrow subjects, considering hydrogenation and hydrometallation reactions[16] and reactions involving iron pentacarbonyl.[17]

As indicated by the analysis of the literature, the number of reactions catalyzed by iron compounds and complexes increases every year. This stimulated us to summarize the new data on the application of these derivatives.

The following abbreviations and designations are used in the review:

acac — acetylacetonate,
Ad — adamantyl,
BIAN — 1,2-[bis(2,6-diisopropylphenyl)imino]acenaphthene,
Bmim — 1-n-butyl-3-methylimidazolium,
Boc — *tert*-butoxycarbonyl,
Cbz — benzyloxycarbonyl,
CPME — cyclopentyl methyl ether,
Cy — cyclohexyl,
DCE — dichloroethane,
dimb — di(isobutyryl)methane,
DMEDA — 1,2-dimethylethylenediamine,

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DMI — 1,3-dimethylimidazolidin-2-one,
DMC — dimethyl carbonate,
DTBP — di-*tert*-butyl peroxide,
FeHYmmm — iron-containing micro-, meso- and macroporous HY zeolite,
Fu — furyl,
MS — molecular sieves,
Ms — methanesulfonyl (mesyl),
Naph — naphthyl,
NIS — *N*-iodosuccinimide,
NMP — *N*-methyl-2-pyrrolidone,
PMHS — polymethylhydrosiloxane,
Py — pyridyl,
TBPB — *tert*-butyl peroxybenzoate,
TBS — *tert*-butyldimethylsilyl,
Tf — trifluoromethanesulfonyl (triflyl),
Th — thienyl,
TMEDA — *N*,*N*,*N*′,*N*′-tetramethylethylenediamine,
TMS — trimethylsilyl,
TON — catalyst turnover number (the number of moles of the converted substrate per mole of the catalyst),
TPP — *meso*-tetraphenylporphyrin,
TsOH — *p*-toluenesulfonic acid.

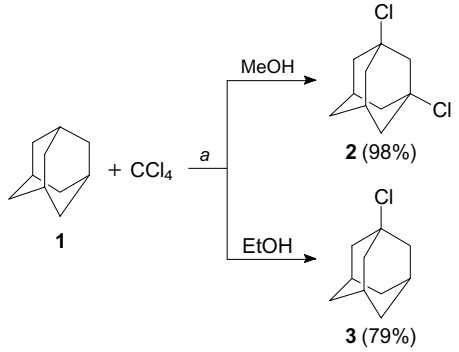
2. Halogenation

Iron compounds and complexes are successfully used for halogenation of organic compounds of various classes. A distinctive feature of these reactions is that, instead of chlorine (bromine) or hydrogen chloride (bromide), reagents such as CCl_4, CBr_4, Bu^tOCl, dichlorodiphenylmethane and *N*-chlorosuccinimide serve as halogen sources.

Iron-containing catalysts activated by alcohols, water and nitrile ligands promote the chlorination of alkanes, cycloalkanes and adamantane with carbon tetrachloride. The optimal ratios of the catalyst and reactants and reaction conditions for the selective synthesis of chlorinated hydrocarbons were found.[18] According to the published data,[19] $FeCl_3$ was one of the first catalysts to be used for adamantane chlorination with CCl_4.

The best results were obtained when iron catalysts were promoted with alcohols, methanol and ethanol, which considerably affected the yield of products and selectivity of the reaction. For example, in the presence of $Fe(acac)_3$ (acac is acetylacetonate) as the catalyst and MeOH as the solvent (in 1 : 30 ratio), the reaction of adamantane (**1**) with CCl_4 carried out at 160 °C for 6 h gives 1,3-dichloroadamantane (**2**) as the only product. The replacement of methanol by ethanol results in the selective formation of 1-chloroadamantane (**3**), the yield of which was 79% in the presence of $Fe(acac)_3$ – EtOH and 93% with ferrocene – EtOH (Scheme 1).

Scheme 1

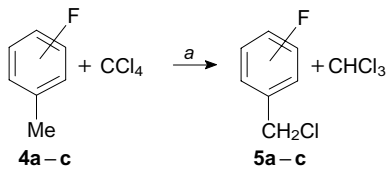


(*a*) $Fe(acac)_3$, 160 °C, 6 h [$Fe(acac)_3$: **1** : CCl_4 : ROH = 0.03 : 1 : 2 : 1]; R = Me, Et

The experiments on the chlorination of adamantane with carbon tetrachloride were carried out at elevated temperature (160 – 170 °C) for 1 – 6 h. Apart from chloroadamantanes **2** and **3**, GLC and GC/MS analysis of the reaction mixture revealed the presence of chloroform (major product) and dichloromethane; this indicates that chlorination mainly occurs as displacement of an adamantane hydrogen atom, predominantly in the bridgehead position.

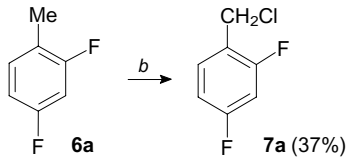
The reactions of 2-fluoro-, 3-fluoro- and 4-fluorotoluenes **4a** – **c** with CCl_4 in methanol catalyzed by iron compounds [$FeCl_3$, $FeBr_2$, $FeCl_2 \cdot 4H_2O$, $Fe_2(CO)_9$ and $Fe(\eta\text{-}C_5H_5)_2$] resulted in the synthesis of monofluorobenzyl chlorides **5a** – **c** (Scheme 2).[20,21] Under similar conditions, 2,4-difluoro-, 2,5-difluoro- and 2,6-difluorotoluenes **6a** – **c** are converted to difluorobenzyl chlorides **7a** – **c**, with degrees of conversion being 45%, 24% and 42%, respectively. The maximum yields of mono- (**5a** – **c**) and difluorobenzyl chlorides (**7a** – **c**) were attained when the reaction was catalyzed by $FeCl_2 \cdot 4H_2O$ and $FeBr_2$ with addition of amides, among which formamide was the most efficient. At a temperature of 180 °C and reaction time of 6 h, the highest yields were 67% for fluorobenzyl chlorides and 37% for difluorobenzyl chlorides. In the absence of the catalyst and alcohol, no reaction was observed.

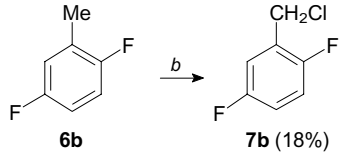
Scheme 2

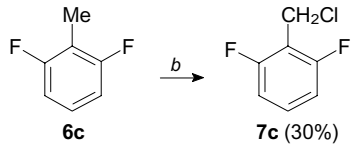


(*a*) [Fe], $HC(O)NH_2$, MeOH, 180 °C, 6 h; F position: 2 (**a**), 3 (**b**), 4 (**c**)

[Fe]	Yield of **5a** (%)	Yield of **5b** (%)	Yield of **5c** (%)
$FeCl_2 \cdot 4H_2O$	30	35	67
$FeBr_2$	15	11	58







(*b*) CCl_4, $FeBr_2$, $HC(O)NH_2$, MeOH, 180 °C, 6 h
[$FeBr_2$: $HC(O)NH_2$: **6** : CCl_4 : MeOH = 1 : 50 : 100 : 200 : 50]

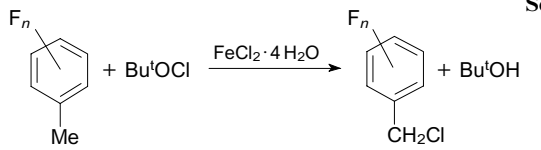
In the authors' opinion, the role of methanol is to generate methyl hypochlorite, which can act as the chlorinating agent or initiate the radical chlorination with CCl_4, as evidenced by iodometric titration data. The concentration of 'active' chlorine during the experiment is 1.1–1.5 mg mL^{-1}. Methyl hypochlorite is relatively unstable; it readily decomposes to give CH_2O and HCl; therefore, for the reaction to proceed smoothly, an excess of methanol is needed. According to the results of titration, ammonium ions were detected in the reaction mixture (Scheme 3); the concentration of NH_4^+ in various experiments was 17.8–25.79 mg mL^{-1}. Evidently, ammonia needed to bind HCl results from decomposition of formamide, which is facilitated by elevated temperature (180 °C). Thus, formamide acts as the acceptor of HCl released upon decomposition of MeOCl.

Scheme 3

$$MeOH + CCl_4 \xrightarrow{[Fe]} MeOCl + CHCl_3$$
$$MeOCl \longrightarrow CH_2O + HCl$$
$$HC(O)NH_2 \longrightarrow NH_3 + CO$$
$$NH_3 + HCl \longrightarrow NH_4Cl$$

In order to confirm the assumption that methyl hypochlorite, which is generated from CCl_4 and methanol in the presence of the catalyst, participates in the chlorination of fluorotoluenes **4a–c**, **6a–c**, the authors attempted to chlorinate 4-fluorotoluene (**4c**) with stable *tert*-butyl hypochlorite (Scheme 4).[20,21] The reaction of compound **4c** with Bu^tOCl carried out at 20 °C for 3 h in the presence of 1 mol.% $FeCl_2 \cdot 4H_2O$ resulted in the formation of 4-fluorobenzyl chloride (**5c**) in 65% yield. In the absence of a catalyst, the substrate conversion did not exceed 8%. The second reaction product was Bu^tOH formed in a stoichiometric amount.

Scheme 4



4a–c, **6a–c** **5a–c**, **7a–c**

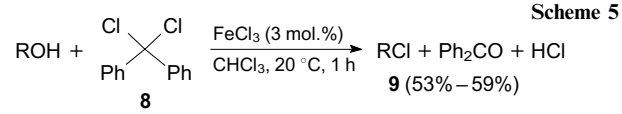
n = 1, 2

2-Fluoro- and 3-fluorotoluenes **4a**,**b** and 2,4-difluoro-, 2,5-difluoro- and 2,6-difluorotoluenes **6a–c** can also be chlorinated on treatment with Bu^tOCl in the presence of iron catalysts. The yields of mono- and difluorobenzyl chlorides **5a**,**b** and **7a–c** are 24%–36%. The function of the iron catalyst is apparently to cleave Bu^tOCl and generate $Bu^tO^{\bullet}$ and $Cl^{\bullet}$ radicals; subsequently, the latter reacts with fluorotoluenes **4a–c** and **6a–c** at the methyl group.

An interesting method has been developed for the chlorination of alcohols using α,α-dichlorodiphenylmethane (**8**) as a chlorinating agent and $FeCl_3$ as a catalyst, which gave alkyl chlorides **9** (Scheme 5). The same method can also be used to convert carboxylic acids to acyl chlorides **10** in high yields under mild conditions.[22]

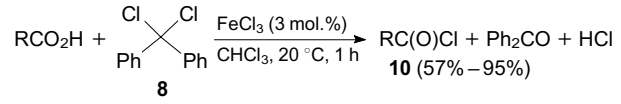
A probable mechanism of the reaction is presented in Scheme 6 as applied to the reaction of (*R*)-PhCH(OH)Me (**11**) with α,α-dichlorodiphenylmethane (**8**). Complex **12**, resulting from elimination of Cl^- from reagent **8** under the action of $FeCl_3$, is the key intermediate. The chlorination of aliphatic alcohols and carboxylic acids proceeds by a similar mechanism.

Scheme 5



8

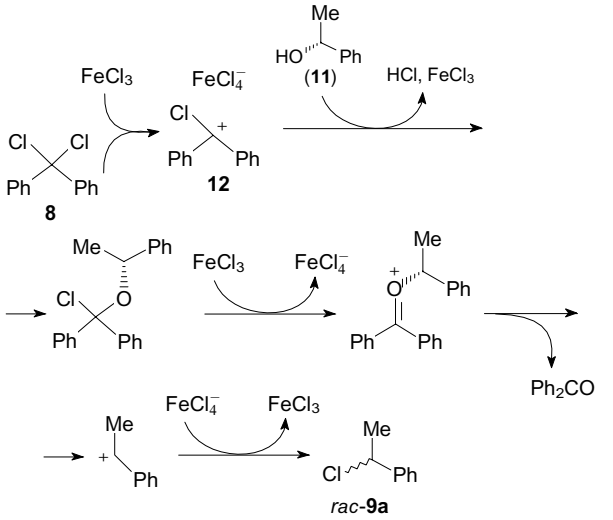
R = n-C_8H_{17}, $Ac(CH_2)_3$, Bn, 4-$MeC_6H_4CH_2$, 4-$F_3CC_6H_4CH_2$, 4-$ClC_6H_4CH_2$, $Ph(CH_2)_2$, $PhCH_2CHMe$, $PhCH_2CMe_2$, 2-$FuCH_2$, 2-$ThCH_2$; Fu is furyl, Th is thienyl



8

R = Ph, 4-$MeC_6H_4CH_2$, 4-$F_3CC_6H_4CH_2$, 4-$FC_6H_4CH_2$

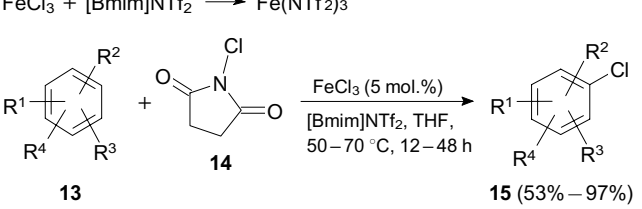
Scheme 6



In the presence of the ionic liquid [Bmim]NTf_2 [Bmim is 1-n-butyl-3-methylimidazolium, Tf is trifluoromethanesulfonyl (triflyl)], the iron salt $FeCl_3$ catalyzes the chlorination of benzene derivatives **13** with *N*-chlorosuccinimide (**14**) to give chlorides **15** (Scheme 7).[23]

Khusnutdinov *et al.*[24] performed bromination of adamantane (**1**) and its derivatives with carbon tetrabromide in the presence of iron catalysts: $Fe_2(CO)_9$, $Fe_3(CO)_{12}$, $Fe(acac)_2$, $Fe(acac)_3$, $Fe(OAc)_2 \cdot 4H_2O$, $FeCl_3 \cdot 6H_2O$ and $Fe[O_2CH(Et)Bu^n]_3$; the best results were obtained for $Fe(acac)_3$. The bromination occurred exclusively at the

Scheme 7

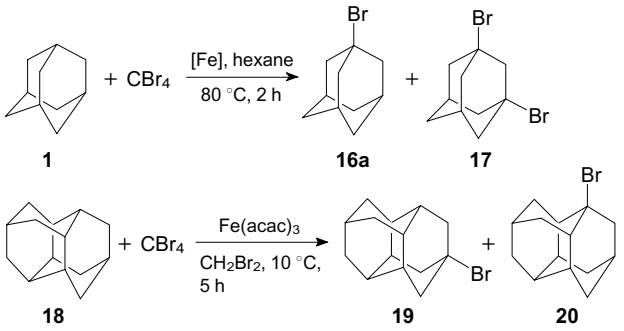


13 **14** **15** (53%–97%)

R^1, R^2, R^3, R^4 = H, CHO, OMe, CO_2H, OH, NO_2, Ac, HNAc, Cl, CN, NH_2, CF_3

bridgehead carbon atom of compound **1** and resulted in a mixture of 1-bromo- (**16a**) and 1,3-dibromoadamantanes (**17**). Diamantane (**18**) was also brominated only at the C(1) and C(4) bridgehead atoms and was thus converted to a mixture of 1-bromo- (**19**) and 4-bromodiamantanes (**20**) in 2 : 1 ratio (Scheme 8).

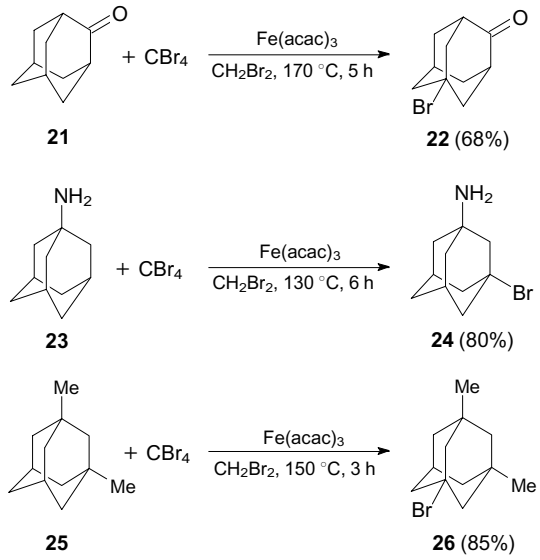
Scheme 8



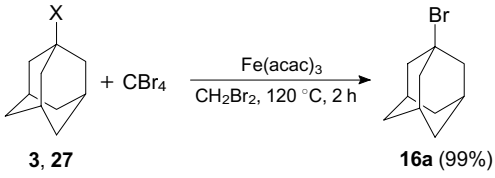
[Fe]	Yield of **16a** (%)	Yield of **17** (%)
$Fe(acac)_2$	27	3
$Fe(OAc)_2 \cdot 4H_2O$	27	6
$Fe_2(CO)_9$	34	5
$FeCl_3 \cdot 6H_2O$	38	6
$Fe_3(CO)_{12}$	42	12
$Fe(acac)_3$	54	12

The pathway of the iron-catalyzed reaction between adamantane derivatives and CBr_4 depends on the natures of the substituent and the solvent (Scheme 9). For example, bromination of adamantan-2-one (**21**) on treatment with CBr_4 in the presence of $Fe(acac)_3$ in CH_2Br_2 affords 1-bromoadamantan-4-one (**22**). 1-Aminoadamantane (**23**) also reacts very actively with CBr_4, being converted to 1-amino-3-bromoadamantane (**24**) in high yield within 6 h at 130 °C. The bromination of 1,3-dimethyladamantane (**25**) with the same reagent in the presence of $Fe(acac)_3$ carried out at 150 °C for 3 h occurs exclusively into the cage giving rise to product **26**.

Scheme 9



Scheme 10

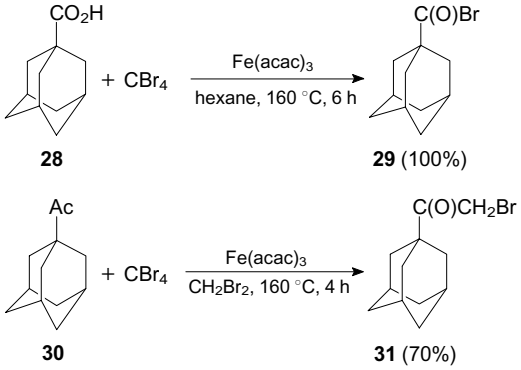


X = Cl (**3**), OH (**27**)

Under similar conditions, 1-adamantanol (**27**) or 1-chloroadamantane (**3**) are converted to substitutive bromination product **16a** in a quantitative yield (Scheme 10).

Adamantane-1-carboxylic acid (**28**) reacts with CBr_4 in hexane to give adamantanecarboxylic acid bromide **29**. The bromination of 1-acetyladamantane (**30**) with carbon tetrabromide in CH_2Br_2 affords adamantyl bromomethyl ketone **31** (Scheme 11).

Scheme 11

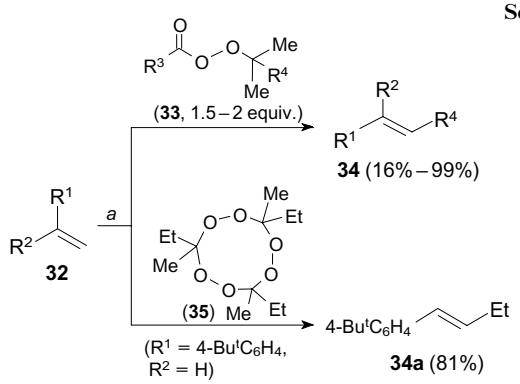


3. Design of the C – C bond

3.1. Formation of C – C bonds in reactions of alkenes

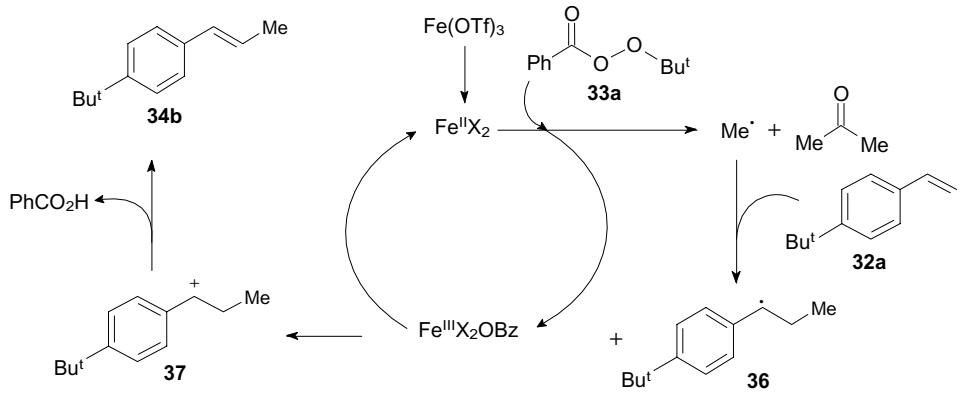
In a series of studies, iron compounds were used to construct the C – C bonds *via* reactions of alkenes with various substrates. For example, an unusual method has been developed for alkylation of alkenes **32** with monoperoxycarbonates **33** in the presence of $Fe(OTf)_3$. The reaction affords di- and trisubstituted alkenes **34**, the yields of which reach 99% (Scheme 12).[25] Similarly, 4-*tert*-butylstyrene

Scheme 12



(*a*) $Fe(OTf)_3$ (2.5 mol.% – 5 mol.%), dioxane, 80 °C, 12 h;
R^1 = H, Me, 4-$Bu^tC_6H_4$; R^2 = H, Ar, 2-Naph, EtC≡C;
R^3 = Alk, Ar, OAlk-cyclo, OAlk; R^4 = Me, Et, Pr^n; Napth is naphthyl

Scheme 13



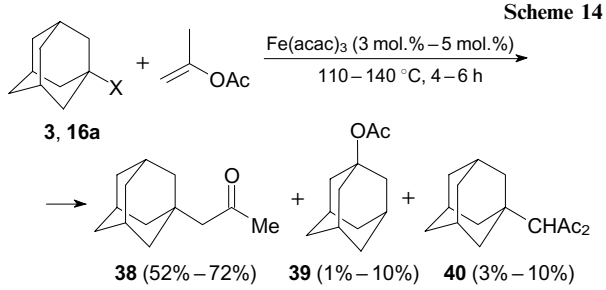
X = OTf, OBz

(**32a**) is converted to alkene **34a** on treatment with peroxyether **35**.

This unusual transformation resembles the Heck reaction, but proceeds by a radical mechanism (Scheme 13). Radical **36** is generated upon decomposition of peroxyesters and peroxycarbonates (*e.g.*, compound **33a**) under the action of $Fe(OTf)_3$ and is then converted to cation **37** and further to product **34b**.

Khusnutdinov *et al.*[26] reported an efficient method for the synthesis of 1-(2-oxopropyl)adamantane (**38**) by the reaction of 1-bromo(chloro)adamantane **3** or **16a** with isopropylidene acetate [1 : (3 – 5) ratio] in the presence of $Fe(acac)_3$. Under the indicated conditions, the yield of the major product reaches 72%, while the yields of by-products (compounds **39** and **40**) do not exceed 10% (Scheme 14).

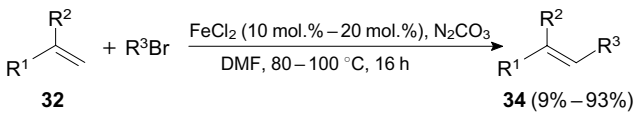
Scheme 14



X = Cl (**3**), Br (**16a**)

Iron(II) chloride catalyzes the Heck reaction of styrenes **32** with functionalized secondary and tertiary alkyl bromides. The yields of cross-coupling reaction products **34** depend on the nature of reactants and reach 93%. It should be noted that functionalized tertiary alkyl halides participate with difficulty in the classical palladium-catalyzed Heck reaction because of the competing β-hydride elimination reaction (Scheme 15).[27]

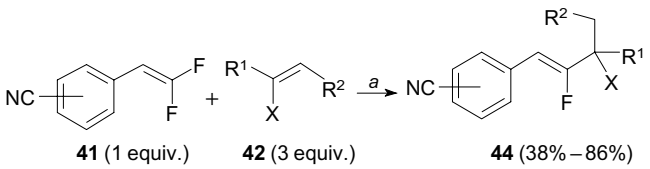
Scheme 15



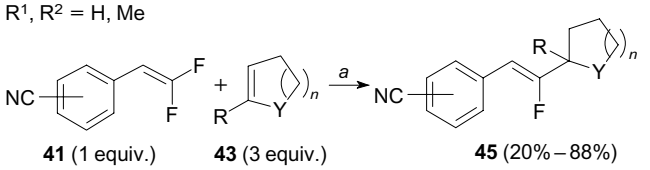
R^1 = H, 4-$MeOC_6H_4$, 2-$MeOC_6H_4$, 3,4-$(MeO)_2C_6H_3$, 4-MeC_6H_4, 2,4-$Me_2C_6H_3$, 4-$Bu^tC_6H_4$, 4-PhC_6H_4, 4-$Me_2NC_6H_4$, 4-$TMSC_6H_4$, 4-FC_6H_4, 4-ClC_6H_4; R^2 = H, Ph;
R^3 = $Me_2C(CN)$, $Me_2C(CO_2C_6H_4Me\text{-}4)$, $MeCH(CO_2Me)$, 4-$ClC_6H_4CH_2$, $PhCH{=}CHCH_2$, $PhCH(CO_2Et)$, PhCH(Me);
TMS is trimethylsilyl

Yang *et al.*[28] accomplished reductive cross-coupling of *gem*-difluoroalkenes **41** (CN group in different positions) with various unactivated (**42**) and heteroatom-substituted alkenes (**43**) *via* Fe-catalyzed transfer of hydrogen atom from phenylsilane $PhSiH_3$ (Scheme 16). The resulting monofluoroalkenes **44** and **45** have *Z*-configuration.

Scheme 16



X = Et, Bu^n, Bn, OPh, OTMS, NCbz, SPh, $(CH_2)_2OH$, CH_2OH;
R^1, R^2 = H, Me



Y = O, NCbz, NBoc; *n* = 1, 2; R = OTMS, CH_2OMe, OMe;
(*a*) $Fe(dimb)_3$ (10 mol.%), $PhSiH_3$ (6 equiv.%), EtOH, O_2, N_2, 60 °C, 18 h;
Cbz is benzyloxycarbonyl, Boc is *tert*-butoxycarbonyl,
dimb is di(isobutyryl)methane

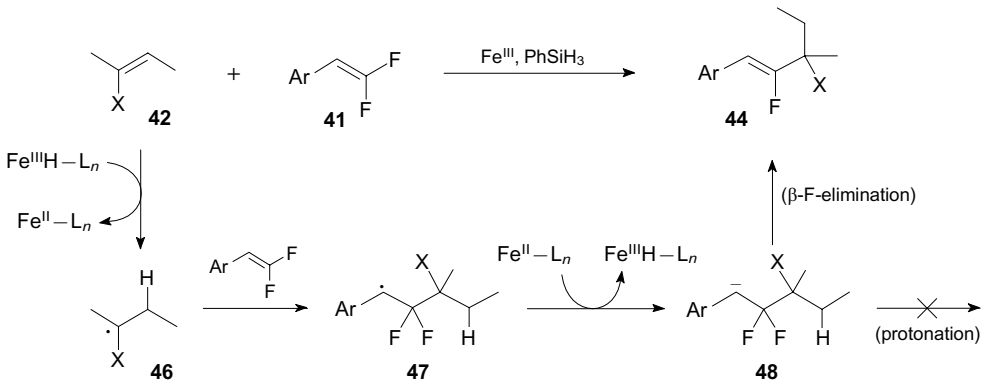
The reaction is accompanied by removal of one fluorine atom and formation of the $C(sp_2)-C(sp_3)$ bond *via* intermediates **46** – **48** (Scheme 17).

Zhang *et al.*[29] reported a rare example of direct bisalkylation of thiophenes **49** with vinyl acetates catalyzed by iron compounds (Scheme 18). This strategy makes it possible to convert simple thiophenes to symmetric dithienylethane derivatives **50**, **51** under mild conditions.

In the authors' opinion, the key step of the reaction is the protonation of the vinyl acetate multiple bond with *p*-toluenesulfonic acid to give carbonium ion **52**, which is converted to the target product **50a** *via* intermediate cations **53** – **55** (Scheme 19).[29]

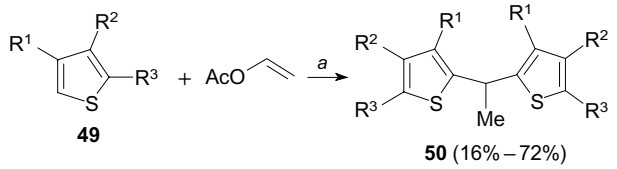
Iron(III) triflate, which behaves as a soft Lewis acid, catalyzes the Friedel – Crafts-type alkylation of arenes **56** on treatment with alkenes **57** bearing polar substituents, cinnamic acid esters or aromatic ketones, resulting in the

Scheme 17

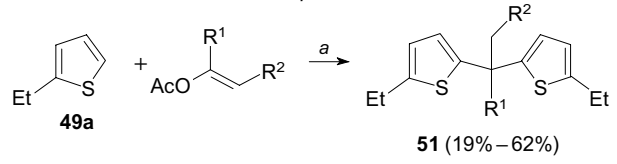


L$_n$ are ligands

Scheme 18



(*a*) $FeCl_3$ (5 mol.%), TsOH (5 mol.%), CH_2Cl_2, 20 °C, 48 h;
$R^1 = R^2 = H$: R^3 = Me, Et, Cl, n-C_5H_{11}, CH_2CN, 2-Th;
$R^1 = R^3 = H$, R^2 = Cl; R^1 = Br, $R^2 = H$, R^3 = Me;
R^1 = Me, $R^2 – R^3$ is benzo; TsOH is *p*-toluenesulfonic acid



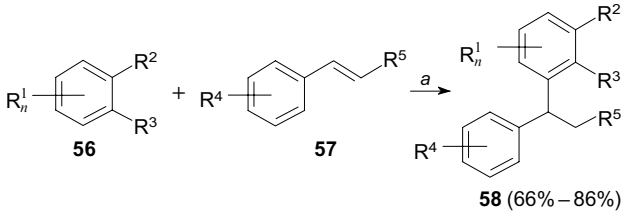
R^1 = Me: R^2 = H, CH_2CO_2H; $R^1 – R^2 = (CH_2)_4$

formation of diarylalkanes **58**. The salts $FeCl_3$ and $FeBr_3$ showed a moderate activity in this reaction, while Fe_2O_3, $Fe_2(SO_4)_3$ and $Fe(NO_3)_2 \cdot 6H_2O$ proved to be completely inert. This transformation also proceeds rather smoothly with indoles **59** to give products **60** (Scheme 20).[30]

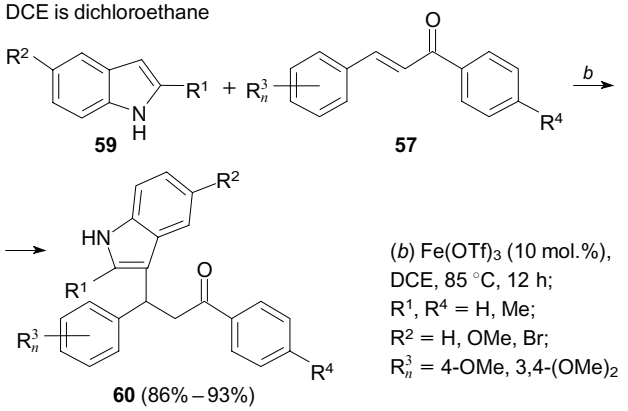
3.2. Formation of C – C bonds in reactions of Mg and Li organic derivatives

The cross-coupling of aryl (**61**) and hetaryl chlorides **62**, **63** with 1.20 – 3.00 equiv. of Grignard reagents is catalyzed by $Fe(acac)_3$ with high efficiency [TON = 2440 – 3600, where TON is the catalyst turnover number (the number of moles of the converted substrate per mole of the catalyst)] (Scheme 21). A remarkable feature of this method is that 1,3-dimethylimidazolidin-2-one (DMI) is used as the ligand; the yields of products **64** – **66** are relatively high.[31]

Scheme 20



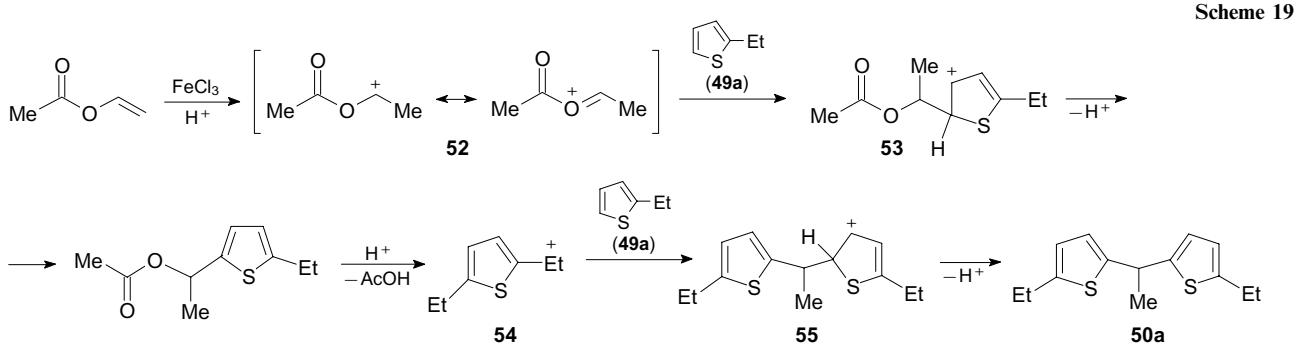
(*a*) $Fe(OTf)_3$ (10 mol.%), DCE, 85 °C, 24 h;
$R^2 = R^3 = H$: R^1_n = 1,2-$(OMe)_2$, 1,2,3-$(OMe)_3$, 1,3,5-$(OMe)_3$, OMe and OH (in different positions); $R^2 – R^3$ is benzo;
R^4 = H, 3,4-$(OMe)_2$, 4-OMe;
R^5 = CO_2Me, C(O)Ar (Ar = Ph, 4-MeC_6H_4, 4-MeOC_6H_4);
DCE is dichloroethane



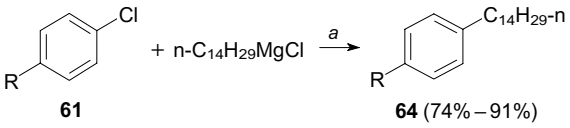
(*b*) $Fe(OTf)_3$ (10 mol.%), DCE, 85 °C, 12 h;
R^1, R^4 = H, Me;
R^2 = H, OMe, Br;
R^3_n = 4-OMe, 3,4-$(OMe)_2$

The cross-coupling of chlorobenzenesulfonamides **67** with Grignard reagents (1.20 – 3.00 equiv. per 0.5 mmol of the substrate) catalyzed by $Fe(acac)_3$ in *N*-methylpyrrolidone (NMP) is used to synthesize benzenesulfonamides **68** alkylated on the aromatic ring (Scheme 22).[32]

Scheme 19

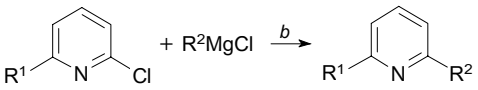


Scheme 21



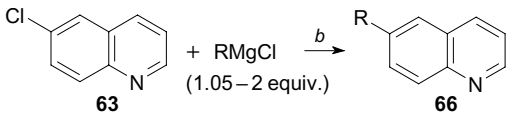
61 **64** (74% – 91%)

(*a*) $Fe(acac)_3$ (0.1 mol.% – 0.5 mol.%), DMI (200 mol.% – 600 mol.%), THF, 85 °C, 10 min – 18 h;
R = CF_3, CN, CO_2Me, $SO_2NPr^i_2$, Cl, $C(O)NMe_2$ (90%; TON = 3600), $C(O)NPr^i_2$ (89%; TON = 3560), $C(O)N(CH_2CH_2)_2O$-cyclo (86%; TON = 2440)



62 **65** (50% – 99%)

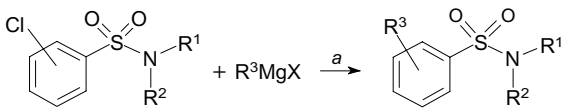
R^1 = H, OMe; R^2 = n-$C_{14}H_{29}$, Pr^i, Cy, $Ph(CH_2)_2$; Cy is cyclohexyl



63 **66**

(*b*) $Fe(acac)_3$ (0.05 mol.% – 0.5 mol.%), DMI (200 mol.% – 600 mol.%), THF, 0 °C, 18 h; R = n-$C_{14}H_{29}$, Pr^i, Cy, $Ph(CH_2)_2$

Scheme 22

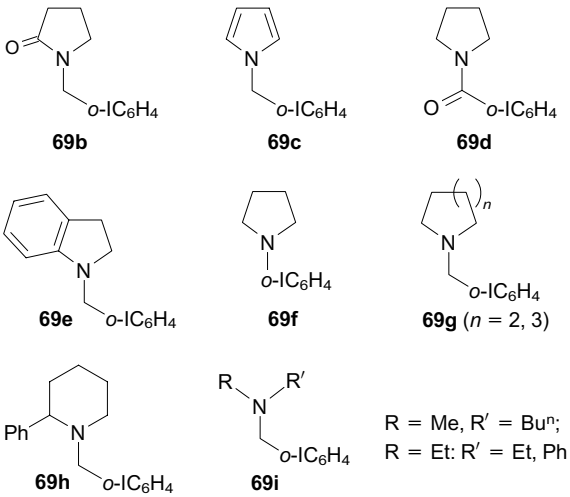


67 **68** (50% – 98%)

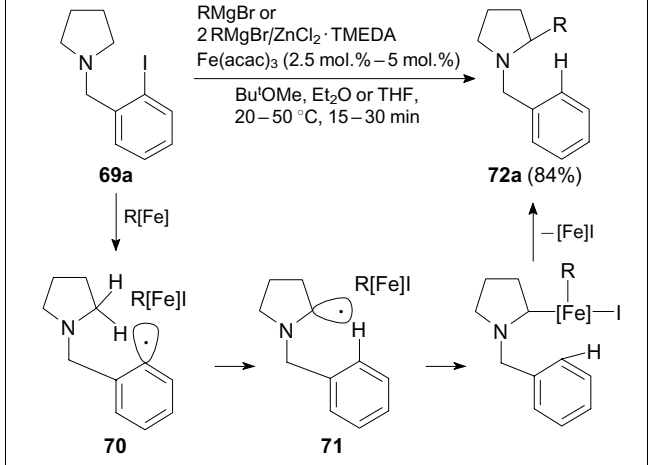
(*a*) $Fe(acac)_3$ (5 mol.%), NMP, THF, 0 – 23 °C, 10 min – 15 h;
4-Cl isomer: R^1 = R^2 = Me, Pr^i; $R^1 – R^2$ = $(CH_2)_4$;
R^1 = Me: R^2 = Ph, Bn; 2-Cl isomer: R^1 = R^2 = Me;
3-Cl isomer: R^1 = R^2 = Me; R^3 = Et, Pr^i, Cy, $Ph(CH_2)_2$, 1,3-dioxan-2-ylmethyl

The $Fe(acac)_3$-catalyzed reactions of Grignard reagents (RMgBr) or Ph_2Zn with iodoarenes **69** containing nitrogen heterocycles or amines as *ortho*-substituents occurs as cross-coupling at the $C(sp^3) – H$ bond located in the α-position relative to the heterocyclic nitrogen atom rather than at the I – Ar bond (Scheme 23; shown for compound **69a**). In the authors' opinion, the reaction follows a radical mechanism and starts with elimination of the iodine atom under the action of $Fe(acac)_3$, which affords radical **70**. This is followed by 1,5-transfer of hydrogen from the α-CH_2 group to the aromatic ring (intermediate **71**). At the final step, a bond is formed between the pyrrolidine radical and

Structures 69

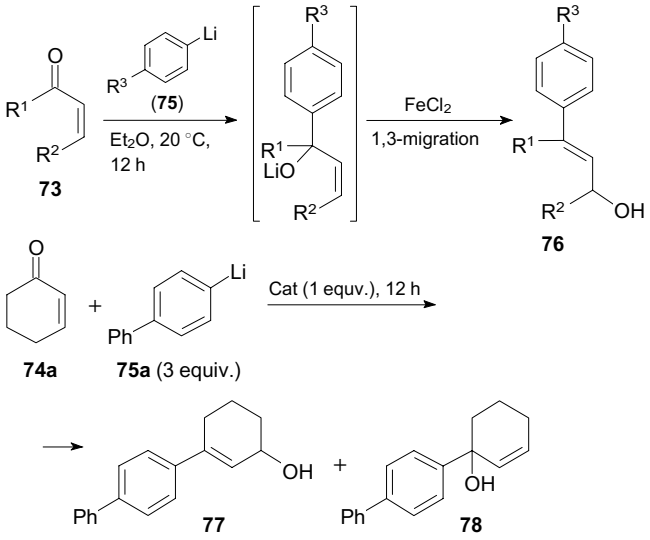


Scheme 23



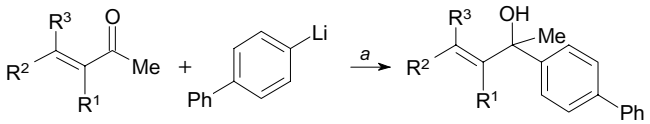
R = Ph, 4-ClC_6H_4, 4-FC_6H_4, 4-$MeOC_6H_4$, 2-MeC_6H_4, 2-Py, 1-Naph, $CH_2{=}C(Me)$, $Me_2C{=}CH$, n-C_6H_{13};
Py is pyridyl, Naph is naphthyl,
TMEDA is *N*,*N*,*N*′,*N*′-tetramethylethylenediamine

Scheme 24



Cat	Conditions	Yield of **77** (%)	Yield of **78** (%)
$FeCl_2$	Et_2O, 25 °C	87	17
$Fe(OAc)_2$	Et_2O, 25 °C	35	27
FeF_3	Et_2O, 25 °C	25	40
$Fe(acac)_2$	Et_2O, 25 °C	41	44
$Fe(acac)_3$	Et_2O, 25 °C	30	29
$FeCl_2$	Et_2O, –78 °C	0	90
$FeCl_2$	20 °C	71	0

Scheme 25



73 **75a** (3 equiv.) **76** (32% – 77%)

(*a*) $FeCl_2$ (1 equiv.), Et_2O, $-78 \rightarrow 20$ °C, 12 h (1,2-addition);
R^1, R^3 = H, Me; R^2 = Me, Ph

substituent R present in the complex R[Fe]I. This reaction was carried out for a broad range of iodoarenes **69** and Grignard reagents, with the yields of products **72** being 40% – 91%.[33]

The condensation of linear (**73**) and cyclic (**74**) α,β-unsaturated enones with aromatic lithium derivatives **75** was accomplished in the presence of $FeCl_2$,[34] which promoted 1,3-migration of the tertiary hydroxyl group to give 3-substituted allylic alcohols **76** – **79** (Schemes 24 – 26).

A probable mechanism of these reactions, considered in relation to the reaction of cyclohexenone **74b** with phenyllithium (**75b**), includes the formation of iron complexes **80** and **81** (see Scheme 26).

3.3. Alkylation of ketones and diketones

Seck *et al.*[35] described the synthesis of peculiar bifunctional iron complexes **82** and **83** containing a cyclopentadienone ligand, which can undergo reversible hydrogenation and dehydrogenation during the catalytic process (Scheme 27). These complexes showed high activity towards the alkylation of ketones with alcohols. The reaction is general, being possible for both aliphatic and aromatic ketones **84**. The yields of alkylated products **85** range from 62% to 100%.

Mono- and dimethylation of ketones **84** with methanol was accomplished in the presence of cyclopentadienone iron tricarbonyl complexes **82** and **86**. In most experiments, the yields of products **87** varied in the range of 70% – 80% (Scheme 28).[36]

Scheme 29 depicts a putative reaction mechanism. The first step is dehydrogenation of methanol with transfer of one hydrogen atom to the cyclopentadienone ligand and transfer of the other hydrogen atom to the iron ion. The dehydrogenation gives formaldehyde, which attacks the CH_2 group of ketone **84a** in the presence of a base. This affords alcohol **88**, which is dehydrated giving rise to alkene **89**. The final step is the formal hydrogenation of the double bond (with complex **90** serving as the hydrogen atom donor) to give methylated ketone **87a**. It should be specially mentioned that this is a unique example of the direct involvement in the reaction of one of the ligands present in the catalytically active complex.

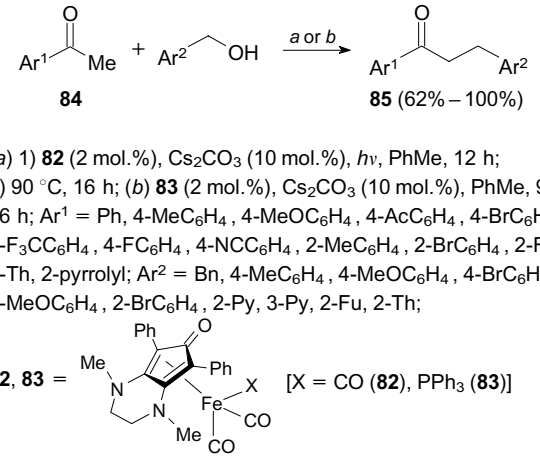
Alkylation of diketones **91** at the active methylene group with benzylic and allylic alcohols under mild conditions has been reported (Scheme 30). The reaction is carried out in the presence of catalytic amounts of anhydrous $FeCl_3$ in dichloromethane and affords products **92** in moderate to high yields.[37]

Unlike $FeCl_3$, iron(III) triflate catalyzes the retro-Claisen rearrangement of 1,3-diketones **91** with alcohols. The reaction occurs without a solvent; it is accompanied by C – C bond cleavage and furnishes ketones **93** and esters **94** in a total yield of 48% – 98% (30 examples are described) (Scheme 31).[38]

Apparently, the reaction proceeds *via* the formation of iron-containing intermediates **95** – **99** (Scheme 32).

A highly efficient method for the synthesis of propargyl-substituted 1,3-dicarbonyl compounds **100** consists in alkylation of diketones **91** with propargyl alcohols **101** in the presence of $FeCl_3$ (Scheme 33). The reaction takes place at room temperature.[39]

Scheme 27

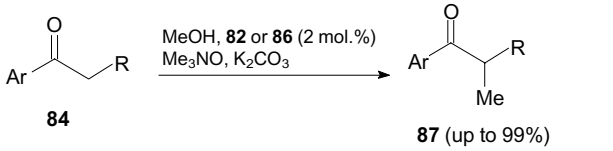


84 **85** (62% – 100%)

(*a*) 1) **82** (2 mol.%), Cs_2CO_3 (10 mol.%), *hν*, PhMe, 12 h;
2) 90 °C, 16 h; (*b*) **83** (2 mol.%), Cs_2CO_3 (10 mol.%), PhMe, 90 °C, 16 h; Ar^1 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-AcC_6H_4, 4-BrC_6H_4, 4-$F_3CC_6H_4$, 4-FC_6H_4, 4-NCC_6H_4, 2-MeC_6H_4, 2-BrC_6H_4, 2-Fu, 2-Th, 2-pyrrolyl; Ar^2 = Bn, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-BrC_6H_4, 2-$MeOC_6H_4$, 2-BrC_6H_4, 2-Py, 3-Py, 2-Fu, 2-Th;

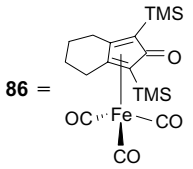
82, **83** = [X = CO (**82**), PPh_3 (**83**)]

Scheme 28

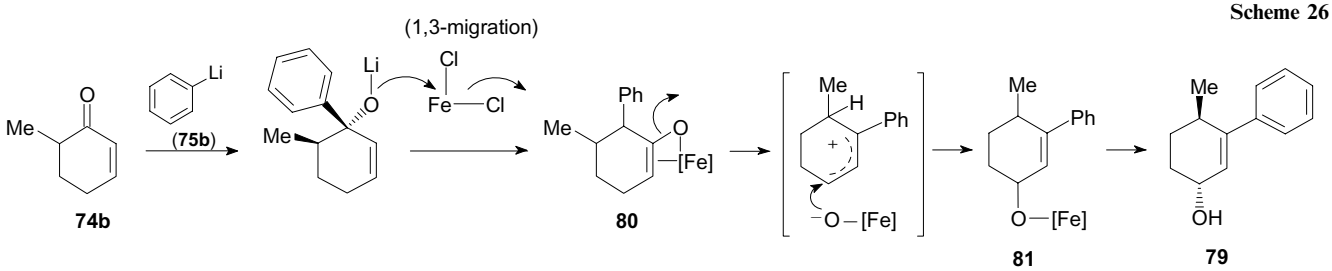


84 **87** (up to 99%)

Ar = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-ClC_6H_4, 4-BnC_6H_4, 4-$F_3CC_6H_4$, 2-$F_3CC_6H_4$, 2-Py, 3-Py, 2-Fu, 2-Th, 2-Naph;
R = Me, Et, Pr^n, Bu^n, Bn, NHPh, OPh;

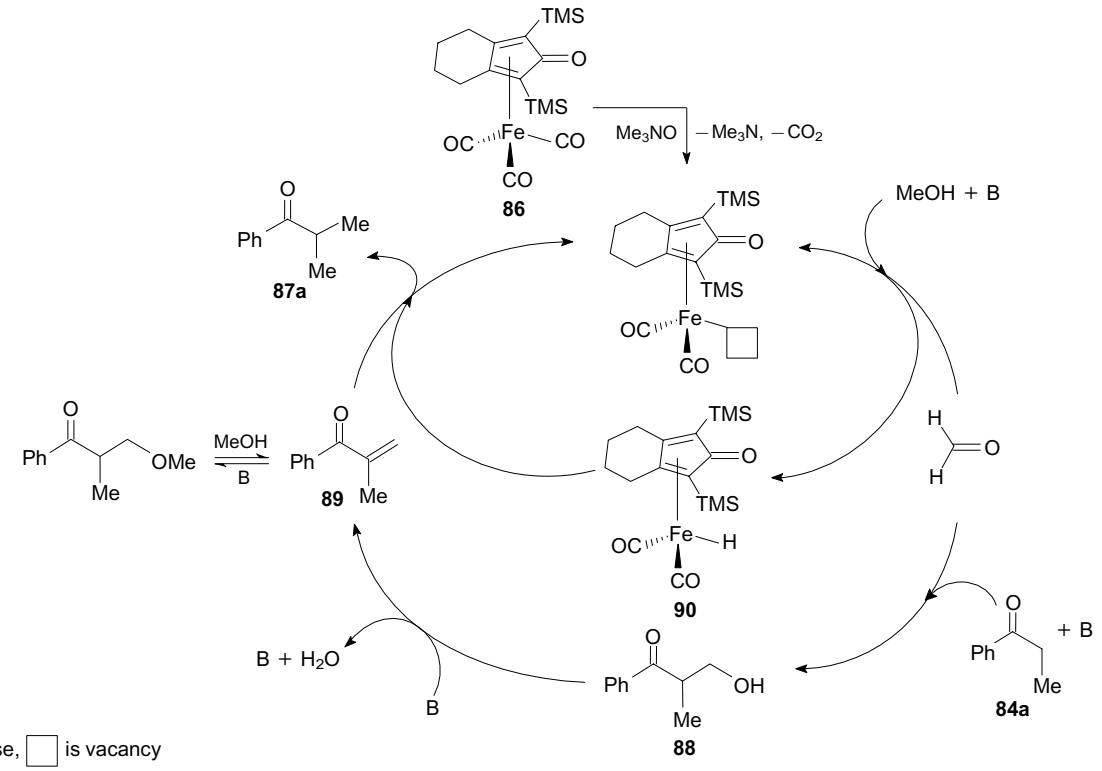
86 = 

Scheme 26

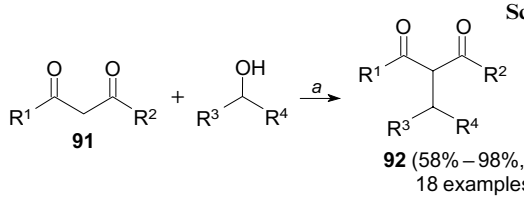


74b **80** **81** **79**

Scheme 29

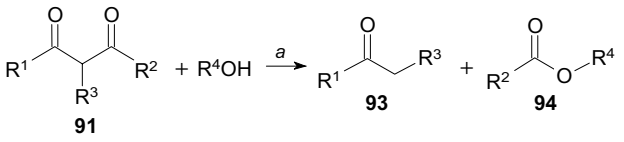


Scheme 30



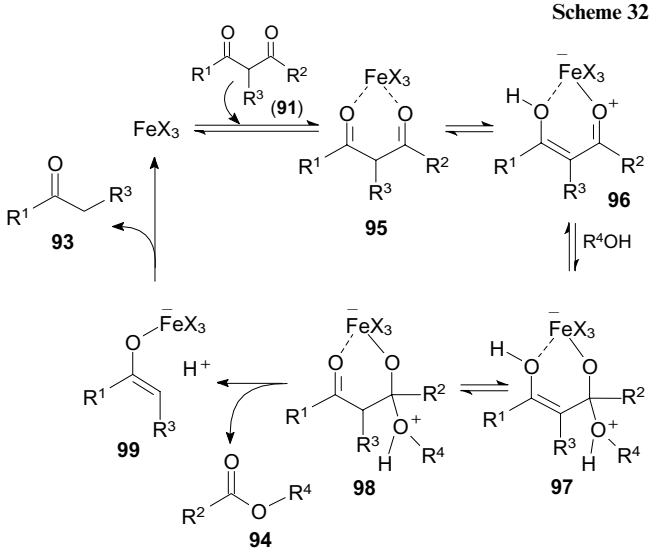
(*a*) $FeCl_3$ (10 mol.%), CH_2Cl_2, Δ, 3 – 12 h;
R^1, R^2 = Me, OEt; R^3 = H, Ph, 4-$MeOC_6H_4$, 4-ClC_6H_4;
R^4 = Me, Et, Ph, PhCH=CH

Scheme 31



(*a*) $Fe(OTf)_3$ (5 mol.% – 10 mol.%), 80 – 120 °C; R^1 – R^4 = Alk

Scheme 32



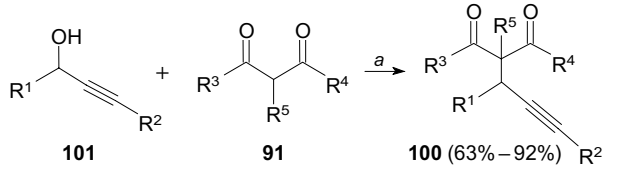
The $Fe(acac)_3$ complex catalyzes the reactions of 1-bromoadamantane (**16a**) with dicarbonyl compounds **91a**,**b**, which produce substituted adamantanes **102** and **103** (Scheme 34).[40]

According to Khusnutdinov *et al.*,[41] 1-chloro- (**3**), 1-bromo- (**16a**) and 1-hydroxyadamantanes (**27**) may act as adamantylation agents with respect to acetylacetone (**91c**) in the presence of $Fe(acac)_3$ (Scheme 35).

3.4. Alkylation and acylation of heterocycles

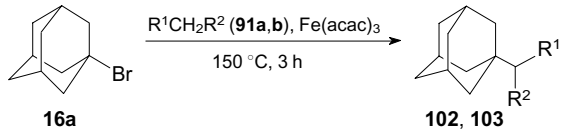
It is known that iron compounds and complexes are not inferior to $AlCl_3$ in the activity towards alkylation of aromatic compounds with simple haloalkanes, but are superior to $AlCl_3$ in the functional group tolerance. Therefore, they can be successfully used to alkylate a broad range of substrates. Yamane *et al.*[42] reported $FeCl_2$-catalyzed

Scheme 33



(*a*) $FeCl_3$ (5 mol.%), CH_2Cl_2, 20 °C, 8 – 10 h;
R^1 = Pr^n, Ph, 4-$MeOC_6H_4$, 4-ClC_6H_4, 4-$O_2NC_6H_4$, 2-Th;
R^2 = Bu^n, Ph; R^3 = Me, Ph; R^4 = Me, Ph, OMe, OEt; R^5 = H, Me

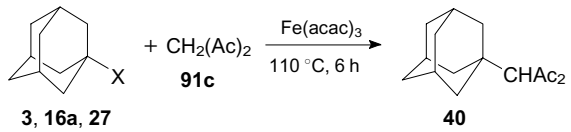
Scheme 34



16a **102**, **103**

$R^1 = R^2 = Bz$ (**91a**; **102**, 79%);
$R^1 = Ac$, $R^2 = CO_2Et$ (**91b**; **103**, 76%)

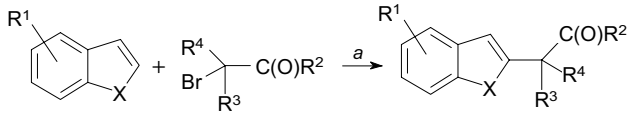
Scheme 35



3, **16a**, **27** **40**

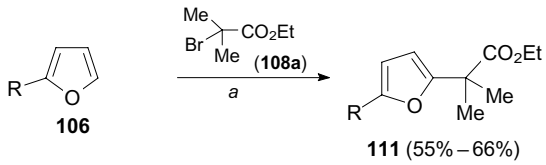
X = Cl (**3**, 75%), Br (**16a**, 93%), OH (**27**, 71%)

Scheme 36



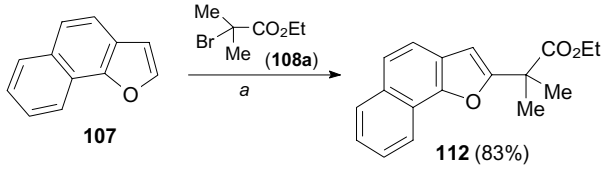
104, **105** **108** **109**, **110** (26% – 78%)

X = O (**104**, **109**), S (**105**, **110**); R^1 = H, Me, Br (in different positions);
R^2 = OMe, OEt, OBu^t, OBn, OPh, O(CH$_2$)$_3$Br, NHPh, NHCy;
R^3 = H, Me, Pr^n, Bu^n, CO_2Et; R^4 = H, Et, Pr^n, cyclo-C_4H_7, Cy



106 **111** (55% – 66%)

R = Et, CHO, Ac, Br



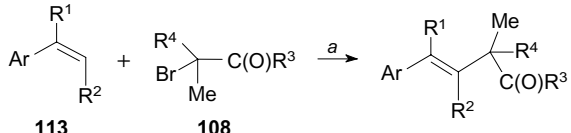
107 **112** (83%)

(*a*) $FeCl_2$ (5 mol.%), Pr^i_2NEt (2 equiv.), 1,4-dioxane, 110 °C, 24 h

selective alkylation of heteroaromatic compounds **104** – **107** with α-bromo-substituted esters and amides **108** to give products **109** – **112** (Scheme 36).

Other reactions that follow a similar route are the alkylation of alkenes **113** with α-bromo-substituted reagents **108**, giving rise to products **114** (Scheme 37), and trans-

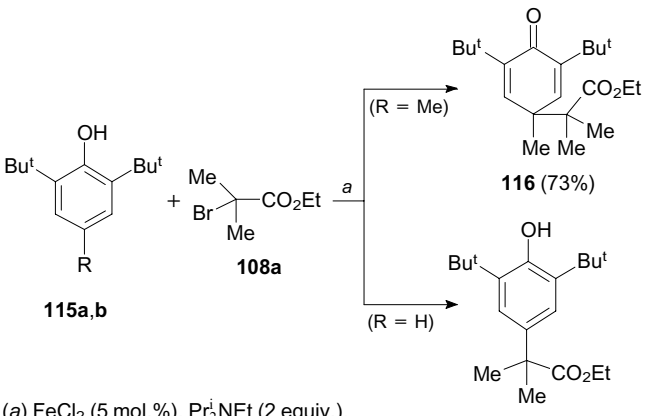
Scheme 37



113 **108** **114** (53% – 86%)

(*a*) $FeCl_2$ (5 mol.%), Pr^i_2NEt (2 equiv.), 1,4-dioxane, 110 °C, 24 h;
Ar = Ph, 4-MeOC$_6$H$_4$; R^1, R^2 = H, Me; R^3 = Me, OEt, NHPh;
R^4 = Me, CO_2Et

Scheme 38

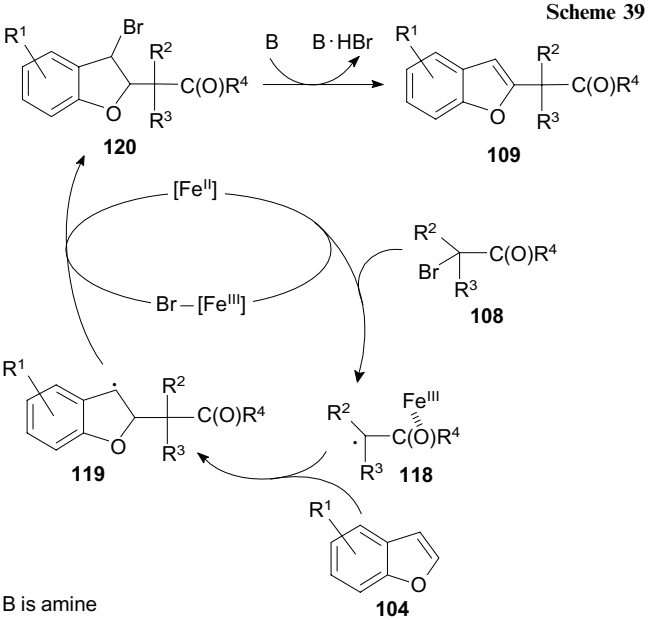


(*a*) $FeCl_2$ (5 mol.%), Pr^i_2NEt (2 equiv.), 1,4-dioxane, 110 °C, 24 h;
R = H (**a**), Me (**b**)

formation of aromatic compounds **115a**,**b** to ketone **116** and phenol **117** (Scheme 38).[42]

Scheme 39 depicts a probable reaction mechanism as applied to substrate **104**. According to Yamane *et al.*,[42] $FeCl_2$ acts as a single-electron source and increases the reactivity of tertiary alkyl radical **118**, generated from a β-bromocarbonyl compound, towards the conversion to radical **119** and then to 3-bromo derivative **120**.

Scheme 39



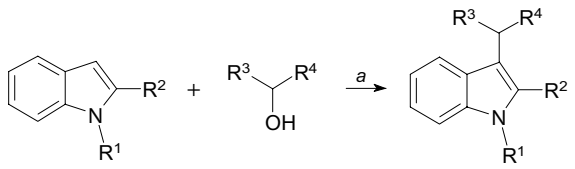
B is amine

According to Jana *et al.*,[43] $FeCl_3$ catalyzes the selective Friedel – Crafts C(3) alkylation of indoles **59** on treatment with not only benzylic, but also allylic and propargylic alcohols (Scheme 40). The reaction was carried out in nitromethane under mild conditions to give 3-substituted indoles **121** in moderate to high yields. This method can be used for the alkylation of pyrrole.

3-Benzyl-substituted indoles **121** were synthesized by the reaction of indoles **59** with primary and secondary benzylic alcohols in the presence of iron(II) phthalocyanine complex **122** (Scheme 41).[44]

The authors proposed a probable reaction mechanism, according to which the function of Fe(II) complex **122** is to

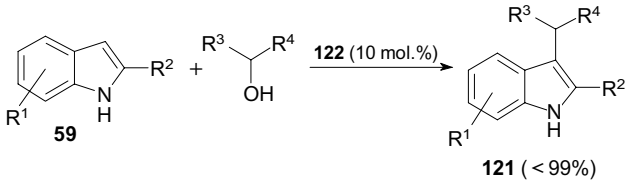
Scheme 40



59 **121** (40% – 98%)

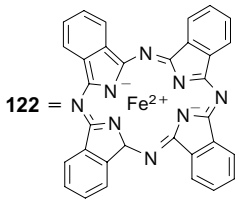
(*a*) $FeCl_3$ (10 mol.%), $MeNO_2$, 25 – 60 °C, 1 – 4 h; R^1 = H, Me, Ts; R^2 = H, Me; R^3 = Me, Ph; R^4 = Ph, 2-Th, 4-$MeOC_6H_4CH{=}CH$, 4-$ClC_6H_4CH{=}CH$, $PhC{\equiv}C$

Scheme 41

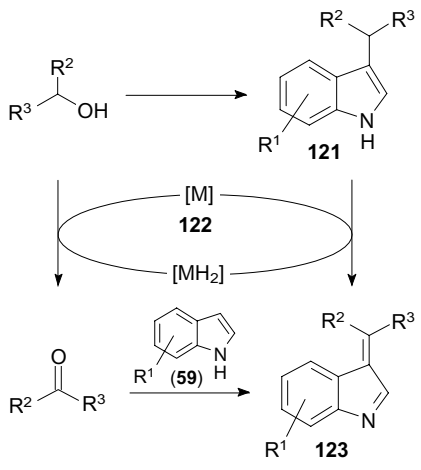


59 **121** (< 99%)

R^1 = H, 4-OMe, 5-F, 6-Me, 6-Cl; R^2 = H, Ph;
R^3 = XC_6H_4 (X = 2-Me, 3-Me, 4-Me, 3-Ph, 4-OMe, 2-NH_2, 2-OH, 2-Cl, 4-F, 4-CF_3, 4-CN), 3,5-$Cl_2C_6H_3$, 3,4,5-$(MeO)_3C_6H_2$, 1-Naph, 2-Fu, 2-Th; R^4 = H, Me, Ph, CH_2NHAc;



Scheme 42

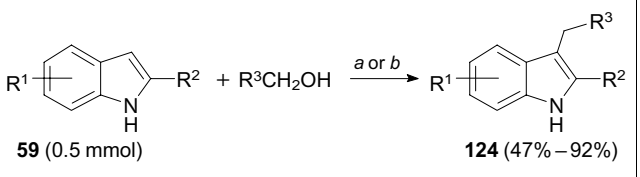


dehydrogenate of the starting alcohol and to hydrogenate of intermediate **123** (Scheme 42).

The alkylation of indole and its derivatives with aliphatic and benzylic alcohols taken in a threefold excess is efficiently catalyzed by bifunctional cyclopentadienone iron carbonyl complexes **82** and **83** (Scheme 43). The reaction follows an unusual mechanism, including hydrogen atom transfer with the participation of the ligand under mild conditions, and affords products **124**.[45]

Isoquinoline (**125**) reacts with CCl_4 and methanol in the presence of $Fe(\eta\text{-}C_5H_5)_2$ to give 1-dichloromethylisoquinoline **126** (substrate conversion of 54% – 60%; selectivity of

Scheme 43

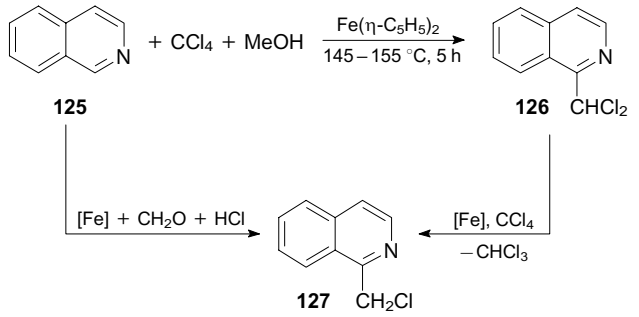


59 (0.5 mmol) **124** (47% – 92%)

(*a*) 1) **82** (2 mol.%), K_2O_4, *hv*, 2 h; 2) 110 °C, 16 h;
(*b*) **83** (2 mol.%), K_3PO_4, 110 – 140 °C, 16 h;
R^1 = H, 5-Br, 5-Me, 6-OMe, 6-Cl, 6-Me; R^2 = H, Me;
R^3 = H, Me, Pr^n, XC_6H_4 (X = H, 4-MeO, 2-Br, 4-I), 2-Py, 2-Fu, 2-Th

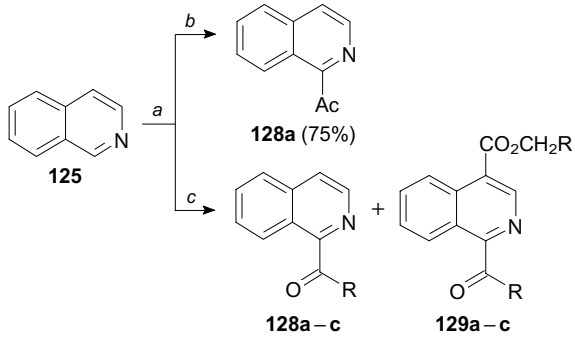
95% – 98%). The same product can be obtained in two steps *via* preliminary formation of 1-chloromethyl derivative **127** (Scheme 44).[46,47] Compound **126** is of interest for the synthesis of highly efficient pharmaceutical drugs, *e.g.*, papaverine, which is a well-known vasodilator.

Scheme 44



When methanol is replaced by ethanol, n-propanol and n-butanol, the reaction pathway changes towards the formation of 1-acetyl-, 1-propionyl- and 1-butyrolylisoquinolines **128a – c**, which are widely used in pharmaceutical chemistry.[48,49] When the reaction time increases to 10 – 14 h, 1-acetylisoquinoline (**128a**) that formed initially

Scheme 45



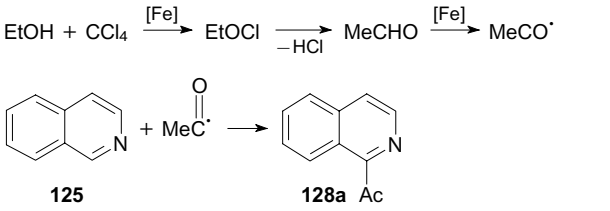
(*a*) $Fe(\eta\text{-}C_5H_5)_2$, 150 °C; (*b*) CCl_4, EtOH, 5 h;
(*c*) CCl_4, RCH_2OH, 5 – 14 h

Compound **128**, **129**	R	Yield of **128** (%)	Yield of **129** (%)
a	Me	82	18
b	Et	46	4
c	Pr^n	38	2

reacts with CCl_4 and ethanol to give ethyl 1-acetylisoquinoline-4-carboxylate (**129a**). Similarly, the use of n-propanol and n-butanol resulted in the formation of by-products, the corresponding esters of 1-propionyl- (**129b**) and 1-butyroylisoquinoline-4-carboxylates (**129c**) (Scheme 45).

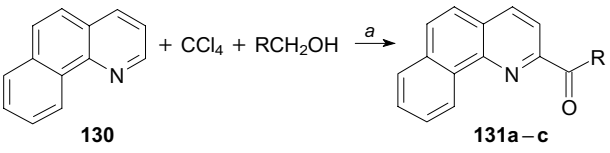
Regarding the mechanism of this reaction, the authors assume that the key role in the formation of 1-acetylisoquinoline **128a** is played by acetaldehyde, which is generated from ethanol (Scheme 46). Subsequently, acetaldehyde can be converted to the acetyl radical under the action of the catalyst or the oxidant, ethyl hypochlorite (EtOCl); the acetyl radical attacks isoquinoline **125** at position 1 to give product **128a**.[50]

Scheme 46



7,8-Benzoquinoline **130** can participate in a similar reaction with CCl_4 and ethanol, n-propanol or n-butanol in the presence of $Fe(\eta\text{-}C_5H_5)_2$ to give 2-acetyl-, 2-propionyl- and 2-butyroyl-7,8-benzoquinolines **131a – c** in 42%, 44% and 30% yields, respectively (Scheme 47).[51]

Scheme 47



(*a*) $Fe(\eta\text{-}C_5H_5)_2$, 170 °C, 6 h
($Fe(\eta\text{-}C_5H_5)_2$: **130** : CCl_4 : RCH_2OH = 1 : 100 : 1000 : 1000);
R = Me (**a**), Et (**b**), Pr^n (**c**)

Iron compounds catalyze the unusual acylation reaction of pyrazine (**132**) and quinoxalines **133** with α-keto acids to give products **134** and **135** (Scheme 48).[52] A similar reaction also takes place in the presence of the $(NH_4)_2S_2O_8$ oxidant and is accompanied by decarboxylation of α-keto acids.[53 – 56]

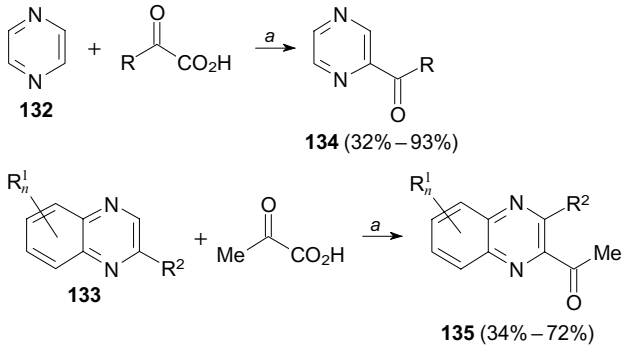
Using this approach, a broad range of derivatives **136 – 144** containing an acetyl group in the α-position to nitrogen was prepared from pyruvic acid and various azaheterocycles (cinnoline, isoquinoline, 4-acetyl-6-methoxy- and 4-methylquinolines, 1,3-benzothiazole, caffeine, 2-cyanopyrazine and 2-cyano-5-methoxypyrazine).[53 – 56]

Scheme 49 depicts a probable reaction mechanism as applied to pyrazine (**132**). In the authors' opinion, $(NH_4)_2S_2O_8$ performs two functions: oxidation of Fe^{2+} to Fe^{3+} and dehydrogenation of intermediate **145**.

4. Iron compounds in the synthesis of aromatic and heteroaromatic carboxylic acids

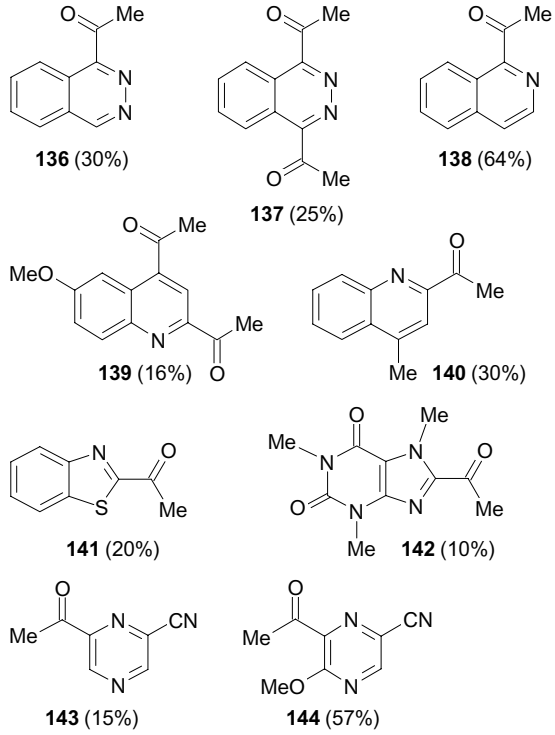
In a series of studies,[57 – 76] metallic iron Fe^0(met.) and iron compounds and complexes were used to prepare esters of

Scheme 48



(*a*) $FeSO_4 \cdot 7H_2O$ (8 mol.%), HCOOH (1 mmol),
$(NH_4)_2S_2O_8$ (3 mmol), DMSO, H_2O, CH_2Cl_2, 40 °C;
R = H, Pr^n, Pr^i, Bu^i, $Ph(CH_2)_2$, XC_6H_4 (X = H, 4-Me, 4-Bu^i, 4-OMe, 4-Br, 4-Cl, 4-F, 3-F, 2-F), 3,4-$(MeO)_2C_6H_3$, 2,4,6-$Me_3C_6H_2$, 2-Th;
R^1_n = H, 7-Me, 7-OMe, 7-Cl, 8-Cl, 6,7-F_2, 6,7-Me_2,
6,7-Cl_2 (substituent positions are indicated for the substrate);
R^2 = H, Me

Structures 136 – 144

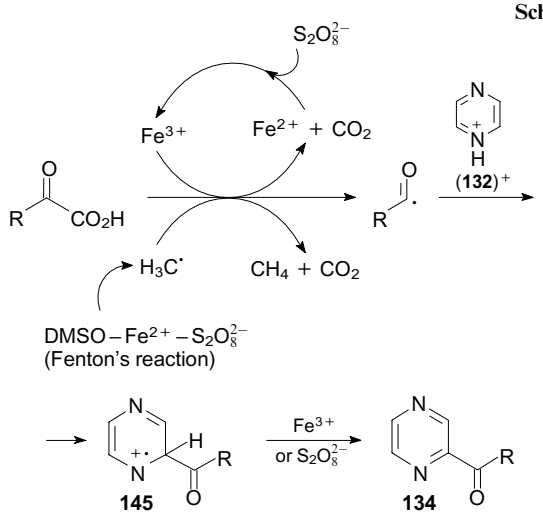


aromatic and heteroaromatic carboxylic acids by a multicomponent reaction of arenes and heteroarenes with CCl_4 and alcohols.

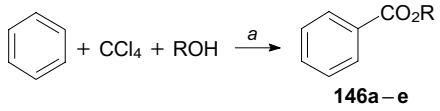
For example, benzene reacts with carbon tetrachloride and an aliphatic alcohol (MeOH, EtOH, Pr^nOH, Bu^nOH or n-$C_5H_{11}OH$) in the presence of metallic iron and acetylacetone (acacH) as a chelating ligand to afford benzoic acid esters **146a – e**. Their yields depend on the nature of the alcohol, reactant to catalyst ratio and the reaction conditions (Scheme 50).[57]

Naphthalene can also react with CCl_4 and alcohols in the presence of the Fe^0(met.) – acetylacetone system. Under typical conditions (130 °C, 6 h), the yields of the alkyl 1-naphthalenecarboxylates **147a – c** formed as the major products are 36% – 70%, depending on the nature of the

Scheme 49



Scheme 50

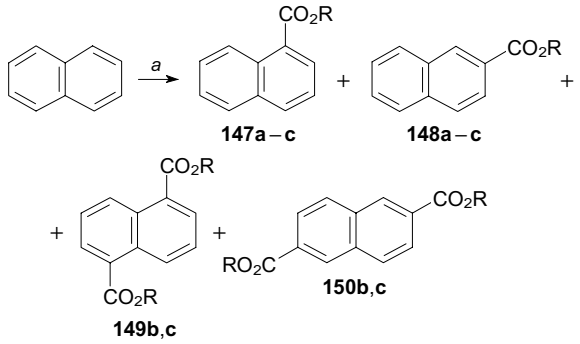


(*a*) Fe^0 (met.), acacH, 130 °C, 6 h
(Fe^0 : acacH : substrate : CCl_4 : ROH = 10 : 1 : 20 : 200 : 200);
R = Me (**a**, 4%), Et (**b**, 42%), Pr^n (**c**, 50%), Bu^n (**d**, 32%),
n-C_5H_{11} (**e**, 30%)

alcohol; mono- (**148**) and diesters (**149**, **150**) were isolated as by-products (Scheme 51, Table 1).[58, 59]

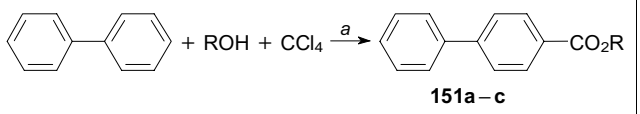
For carboxyalkylation of biphenyl with carbon tetrachloride and alcohols (MeOH, EtOH, Pr^nOH), $Fe_2(CO)_9$ proved to be the catalyst of choice; with this catalyst, the reaction gave alkyl biphenyl-4-carboxylates **151a–c** (Scheme 52).[60, 61]

Scheme 51



(*a*) CCl_4, ROH, Fe^0 (met.), acacH, 130 °C, 6 h
(Fe^0 : acacH : substrate : CCl_4 : ROH = 50 : 5 : 100 : 1000 : 1000)

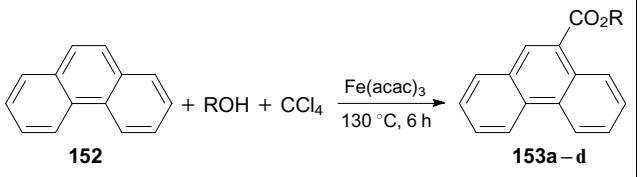
Scheme 52



(*a*) $Fe_2(CO)_9$, 130 °C, 8 h
[$Fe_2(CO)_9$: substrate : CCl_4 : ROH = 1 : 10 : 100 : 100];
R = Me (**a**, 45%), Et (**b**, 14%), Pr^n (**c**, 90%)

A similar iron-catalyzed reaction with CCl_4 and alcohols can readily be carried out for phenanthrene (**152**). The reaction yields alkyl phenanthrene-9-carboxylates **153a–d** (Scheme 53).[62, 63] Among the tested catalysts [$FeBr_2$, $FeCl_3 \cdot 6H_2O$, $Fe(acac)_3$], the highest activity was found for iron(III) acetylacetonate, which provided the formation of esters **153** in up to 96% yield.

Scheme 53



R = Me (**a**, 74%), Et (**b**, 80%), Pr^n (**c**, 96%), Bu^n (**d**, 85%)

Khusnutdinov *et al.*[62] proposed the following possible reaction pathway: the reaction starts with $Fe(acac)_3$-catalyzed Friedel–Crafts alkylation of phenanthrene (**152**) with CCl_4. The next step is alcoholysis of intermediate 9-trichloromethylphenanthrene (**154**) to give phenanthrene-9-carboxylic acid ester **153** (Scheme 54).

The iron-containing catalysts $FeBr_3$, $FeCl_3 \cdot 6H_2O$, $Fe_2(CO)_9$, $FeCl_2$, $FeCl_3$, $Fe(acac)_3$ and $FeCl_2 \cdot 4H_2O$ showed a noticeable activity towards the reaction with CCl_4 and alcohols to introduce the ester group into phenol (**155a**), anisole (**155b**) and phenetole (**155c**) molecules. The reaction products are alkyl hydroxy-, methoxy-, ethoxybenzoates and hydroxytoluates **156**, **157**.[64–66] The reaction

Scheme 54

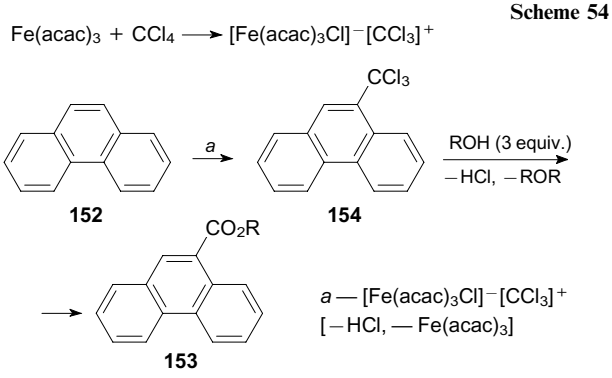
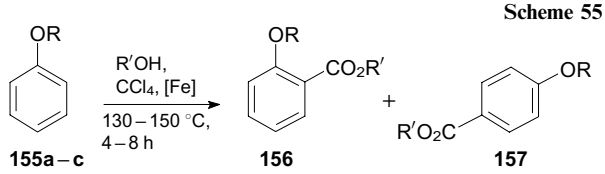


Table 1. Products of the reaction of naphthalene with carbon tetrachloride and alcohols in the presence of iron (see Scheme 51).[58, 59]

Compound **147–150**	R	Substrate conversion	Yield of **147** (%)	Yield of **148** (%)	Yield of **149** (%)	Yield of **150** (%)
a	Me	50	36	14	0	0
b	Et	90	65	6	14	5
c	Pr^n	100	70	0	22	8

involves complete conversion of phenol and phenol ethers and leads to the predominant formation of *para*-isomers [the **156** : **157** ratio is 1 : (2 – 3)] (Scheme 55).

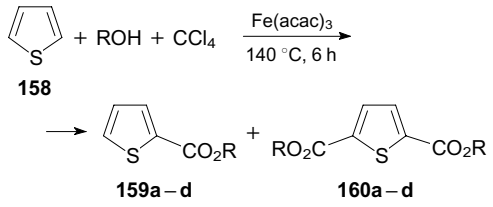
Scheme 55



R = H, Me, Et; R′ = Me, Et, Pr^n, Bu^n

Heterocyclic compounds such as thiophene, furan, pyrrole and their derivatives are alkoxycarbonylated rather intensely with the systems CX_4 – ROH – iron catalyst system. For example, thiophene (**158**) reacts with CCl_4 and alcohols in the presence of $Fe(acac)_3$, giving rise to alkyl thiophene-2-carboxylates (**159a – d**) and thiophene-2,5-dicarboxylates (**160a – d**) (Scheme 56).[51, 67 – 71]

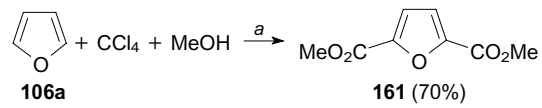
Scheme 56



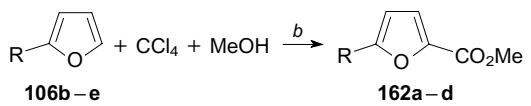
Compound **159**, **160**	R	Yield of **159** (%)	Yield of **160** (%)
a	Me	44	9
b	Et	78	22
c	Pr^n	60	3
d	Pr^i	92	5

In the case of furan (**106a**), double alkoxycarbonylation takes place under these conditions to give dimethyl furan-2,5-dicarboxylate **161** (Scheme 57), a practically valuable compound used to obtain pharmaceutical drugs, heat-resistant polymers, fibers and membranes with osmotic activity.[51] Similar reactions were carried out for silvan (**106b**), 2-acetyl- (**106c**) and 2-chlorofurans (**106d**) and furoic acid (**106e**) (see Scheme 57), with furoic acid esters **162a – d** being isolated as the major products.

Scheme 57



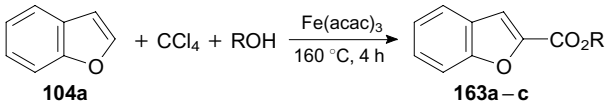
(*a*) $Fe(acac)_3$, 150 °C, 6 h
[$Fe(acac)_3$: substrate : CCl_4 : ROH = 1 : 100 : 750 : 6500]



(*b*) $Fe(acac)_3$, 90 – 120 °C, 6 – 9 h; R = Me (**106b**; **162a**, 42%), Ac (**106c**; **162b**, 95%), Cl (**106d**; **162c**, 65%), CO_2H (**106e**; **162d**, 98%)

High regioselectivity is also typical of the reaction of benzofuran (**104a**) with CCl_4 and alcohols in the presence of $Fe(acac)_3$, which affords alkyl benzofuran-2-carboxylates **163a – c** in a quantitative yield (Scheme 58).[72 – 74]

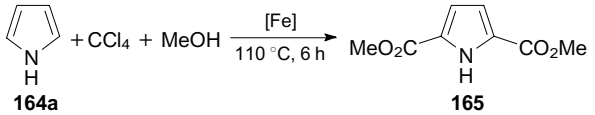
Scheme 58



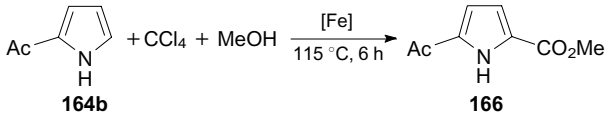
163: R = Me (**a**, 99%), Et (**b**, 92%), Pr^n (**c**, 95%)

The alkoxycarbonylation of pyrrole and its derivatives on treatment with CCl_4 and ROH in the presence of $Fe(acac)_3$, $Fe(OAc)_2$ or $FeBr_2$ takes place under milder conditions (110 °C, 6 h) (Scheme 59).[75, 76] The composition of products depends on the position and the nature of substituent in the pyrrole molecule. Pyrrole (**164a**) is converted to 2,5-dimethoxycarbonyl derivative **165**, while 2-acetylpyrrole (**164b**) is quantitatively converted to methyl 2-acetylpyrrole-5-carboxylate **166**.

Scheme 59



[Fe] = $Fe(acac)_3$ (99%), $Fe(OAc)_2$ (97%), $FeBr_2$ (95%)



[Fe] = $Fe(\eta\text{-}C_5H_5)_2$ (98%), $Fe(acac)_3$ (95%), $Fe(OAc)_2$ (90%), $FeBr_2$ (87%)

In the case of N-substituted pyrrole **164c**, the reaction pathway is ambiguous and, depending on the catalyst and substituent nature and duration of the experiment, the reaction gives alkyl pyrrole-2-carboxylates (**167**) and/or -2,5-dicarboxylates **168** (Scheme 60). Under similar conditions, 1-phenyl- and 1-(chlorophenyl)-1*H*-pyrroles **164d,e** are converted to a mixture of methyl 2-monocarboxylates (**169a,b**) and methyl 2,5-dicarboxylates **170a,b**.

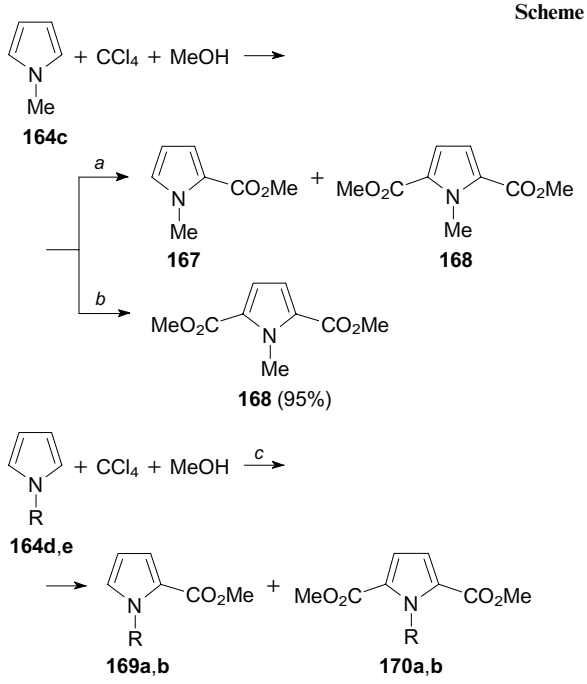
Other examples of successful use of iron-containing catalysts for the synthesis of carboxylic acid esters are also known.

It was found[77] that methyl esters of aliphatic and aromatic carboxylic acids **156a** (R = 2-OH), **157a** (R = 4-OH), **159a**, **171**, **172** and **173** can be prepared in high yields by the reaction of the appropriate carboxylic acid with a green chemistry reagent, dimethyl carbonate, in the presence of $Fe_2(CO)_9$ (Scheme 61).

The $Fe_2(CO)_9 - Et_3N$ catalytic system exhibited high activity in a similar transformation of diacid **174** to diester **175** (Scheme 62).

The synthesis of levulinic acid esters **176a – d** based on the reaction of furfuryl alcohol (**106f**) with aliphatic alcohols in the presence of $Fe(acac)_3$ (Scheme 63) was

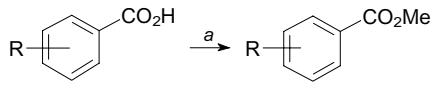
Scheme 60



(*a*) Fe(η-C_5H_5)$_2$, 110 °C, 3 h (100% conversion, **167** : **168** = 10 : 1);
(*b*) $FeBr_2$, 110 °C, 8 h (100% conversion);
(*c*) Fe(η-C_5H_5)$_2$, 105 °C, 6 – 9 h

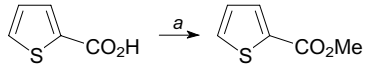
Substrate	Product	R	Yield (%)
164d	**169a**	Ph	66
	170a	Ph	34
164e	**169b**	4-ClC_6H_4	87
	170b	4-ClC_6H_4	13

Scheme 61

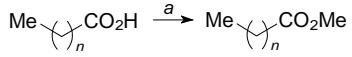


156a, **157a**, **171**

R = 2-OH (**156a**), 4-OH (**157a**), 3-OH, 2,4-(OH)$_2$, Me, OMe, Br, Cl (in different positions) (**171**)

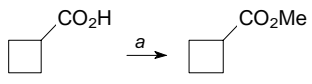


159a (95%)



172 (95% – 98%)

n = 0 – 4, 10, 20



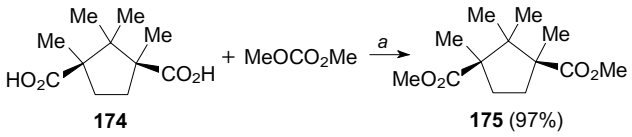
173 (98%)

(*a*) $MeOCO_2Me$, $Fe_2(CO)_9$, (1 mol.%), 180 °C, 1 h (– MeOH, – CO_2)

reported.[78,79] The reaction proceeds in CCl_4 at elevated temperature for 4 h.

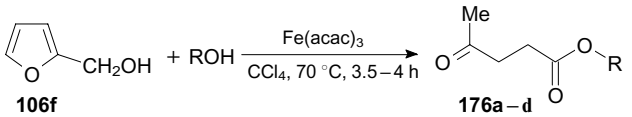
The synthesis of levulinic acid esters from furfuryl alcohol prepared from biomass is also catalyzed by α-Fe_2O_3 (reaction conditions: 250 °C, 60 min).[80]

Scheme 62



(*a*) $Fe_2(CO)_9$ (1 mol.%) – Et_3N (10 : 1), 150 °C, 5 h (– MeOH, – CO_2)

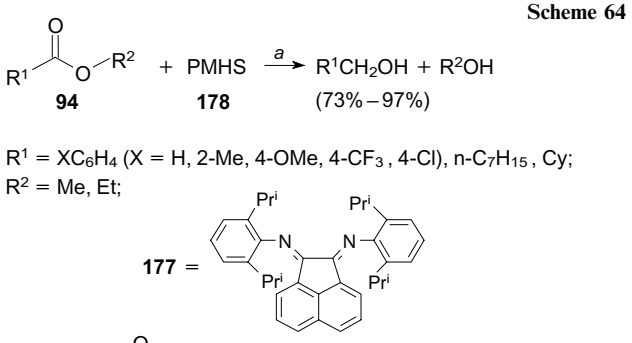
Scheme 63



176: R = Me (**a**, 98%), Et (**b**, 95%), Pr^n (**c**, 85%), Pr^i (**d**, 80%)

It is noteworthy that iron compounds catalyze not only the formation of esters, but also their reductive cleavage to alcohols.[81] For example, (BIAN)$FeCl_2$, where BIAN is 1,2-[bis(2,6-diisopropylphenyl)imino]acenaphthene (**177**), together with polymethylhydroxysiloxane (PMHS, **178**), was used for the reductive cleavage of aliphatic and aromatic esters to give the corresponding alcohols (Scheme 64). Under similar conditions, heterocyclic esters also give alcohols: for example, nicotinic acid derivatives **179** are converted to 3-hydroxymethylpyridines **180** (see Scheme 64).

Scheme 64



R^1 = XC_6H_4 (X = H, 2-Me, 4-OMe, 4-CF_3, 4-Cl), n-C_7H_{15}, Cy;
R^2 = Me, Et;

(*a*) $FeCl_2$ — **177** (1 mol.%), Bu^nLi (3 mol.%), PhMe, 100 °C, 20 h (substrate : **178** = 1 : 3)

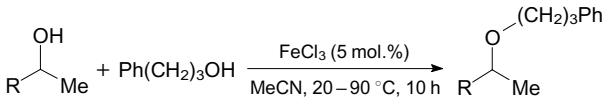
5. Iron compounds in the synthesis of ethers

Iron compounds are efficient catalysts for the synthesis of ethers by intermolecular dehydration of alcohols.

In particular, $FeCl_3$ showed a noticeable activity in the synthesis of ethers **181a**,**b** by the reaction of alcohols **101a** and **182** with 3-phenylpropanol (Scheme 65).[82]

Iron(III) chloride catalyzes the formation of ethers **183** by the reaction of benzoin derivatives **184** with alcohols taken in a 30-fold molar excess (Scheme 66). The reaction is

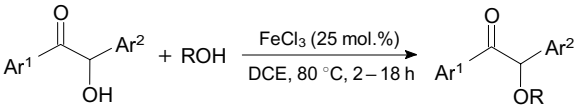
Scheme 65



101a, **182** **181a**,**b**

R = PhC≡C (**101a**; **181a**, 54%), Bu^t (**182**; **181b**, 23%)

Scheme 66



184 **183** (20% – 85%)

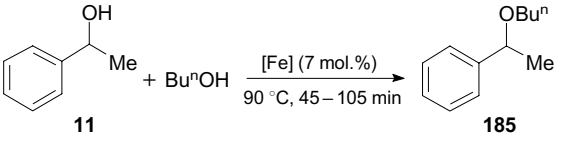
Ar^1 = Ph, 4-$MeOC_6H_4$, 4-FC_6H_4; Ar^2 = Ph, 4-$MeOC_6H_4$, 4-FC_6H_4, 3-Fu; R = Pr^n, Bu^n, Bu^t, PhCHMe

carried out at 80 °C in dichloroethane, with the product yields being up to 85%.[83]

The iron compounds $FeCl_3$ and $Fe(NO_3)_3 \cdot 9H_2O$ have been successfully used for intermolecular dehydration of diphenylmethanol with diols and phenols affording the corresponding ethers.[84, 85]

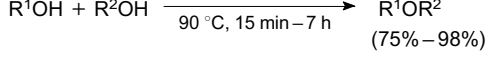
Moghadam *et al.*[86] studied the reaction of benzylic alcohols with aliphatic alcohols in the presence of the following iron salts and complexes: $FeCl_3 \cdot 6H_2O$, $Fe(NO_3)_3 \cdot 9H_2O$ and $Fe(HSO_4)_3$ (Scheme 67). In the case of $FeCl_3 \cdot 6H_2O$ or $Fe(NO_3)_3 \cdot 9H_2O$, the yield of ether **185** was 45%. The best results were obtained in the $Fe(HSO_4)_3$-catalyzed reaction: the yield of compound **185** was 95%, while the yields of the other ethers, which are depicted in Scheme 67, reached 98%.

Scheme 67



11 **185**

[Fe] = $FeCl_3 \cdot 6H_2O$ (45%), $Fe(NO_3)_2 \cdot 9H_2O$ (45%), $Fe(HSO_4)_3$ (95%)

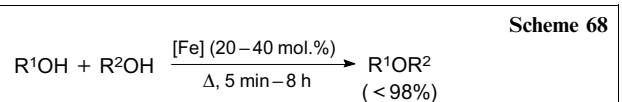


R^1 = PhCHMe, PhCHPh, Bn, 4-$MeOC_6H_4CH_2$, 4-$ClC_6H_4CH_2$, Ph_3C; R^2 = Et, Bu^n, Bn, $Ph(CH_2)_3$, Bu^iCH_2, EtCHMe, Bu^{n}CHMe, n-C_6H_{13}CHMe, Cy

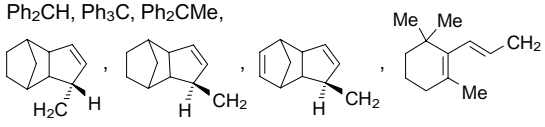
According to the results of Salehi *et al.*,[87] the intermolecular dehydration involving unsaturated alcohols to give unsymmetrical ethers is efficiently catalyzed by $FeCl_3$ and $Fe(ClO_4)_3$ (Scheme 68).

Ether **186**, formed in the reaction of chiral alcohol **187** {$[\alpha]_D^{23} = +50°$ ($CHCl_3$)} with methanol in the presence of $FeCl_3$, proved to be racemic, indicating the intermediate formation of carbocation **188**, which then attacks methanol (Scheme 69).[87]

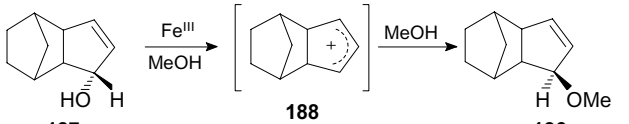
Scheme 68



[Fe] = $FeCl_3$, $Fe(ClO_4)_3$; R^2 = Me, Pr^n, Pr^i, Bu^t; R^1 = PhCH=CHCH$_2$, PhCH=CHCH(Me), PhCH=CHCH(Ph), Ph_2CH, Ph_3C, Ph_2CMe,



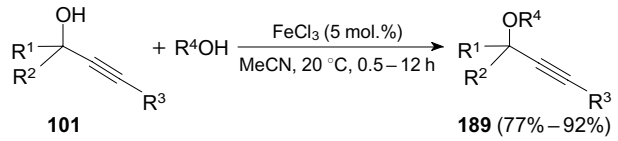
Scheme 69



187 **188** ***rac*-186**

Under mild conditions (20 °C), iron(III) chloride provides the formation of ethers **189** in the reaction of propargyl (**101**) and aliphatic alcohols taken in 1 : 3 ratio (Scheme 70).[88]

Scheme 70

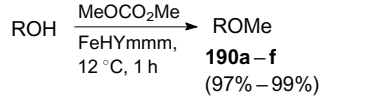


101 **189** (77% – 92%)

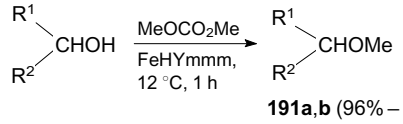
R^1 = Me, Ph; R^2 = H, Me; R^3 = H, Bu^n, Ph, TMS; R^4 = Et, Pr^i, Bn, $Cl(CH_2)_3$, $AllCH_2$

Iron-containing catalysts were utilized in the synthesis of ethers **190** – **192** by the reaction of alcohols with dimethyl carbonate (DMC). It was found[89] that the iron-containing micro-, meso- and macroporous zeolite (FeHYmmm) is an efficient catalyst for methylation of the appropriate alcohols on treatment with DMC (Scheme 71). The reaction proceeds on heating, with the yields of methyl ethers of primary, secondary and tertiary alcohols reaching 99%.

Scheme 71

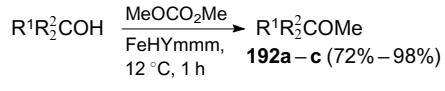


R = Et (**a**), Pr^n (**b**), Bu^n (**c**), n-C_5H_{11} (**d**), n-C_6H_{13} (**e**), n-C_8H_{17} (**f**)



191a,**b** (96% – 99%)

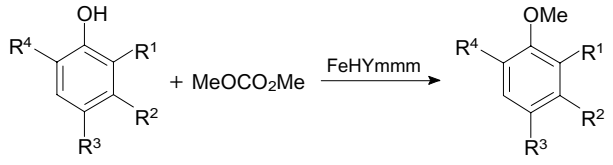
R^1 = Et, R^2 = n-C_7H_{15} (**a**); R^1 = R^2 = Cy (**b**)



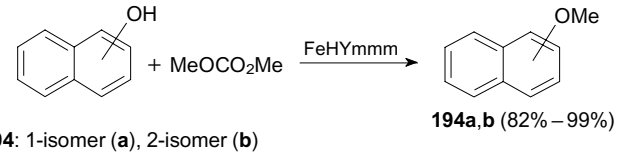
R^1 = R^2 = Me (**a**), 1-Ad (**b**); R^1 = Me, R^2 = cyclo-C_3H_5 (**c**); Ad is adamantyl

The catalyst FeHYmmm was highly active in the *ortho*-methylation of phenol and its derivatives and 1- and 2-naphthols with dimethyl carbonate; products **193** and **194a**,**b** were formed in up to quantitative yields (Scheme 72).[90]

Scheme 72



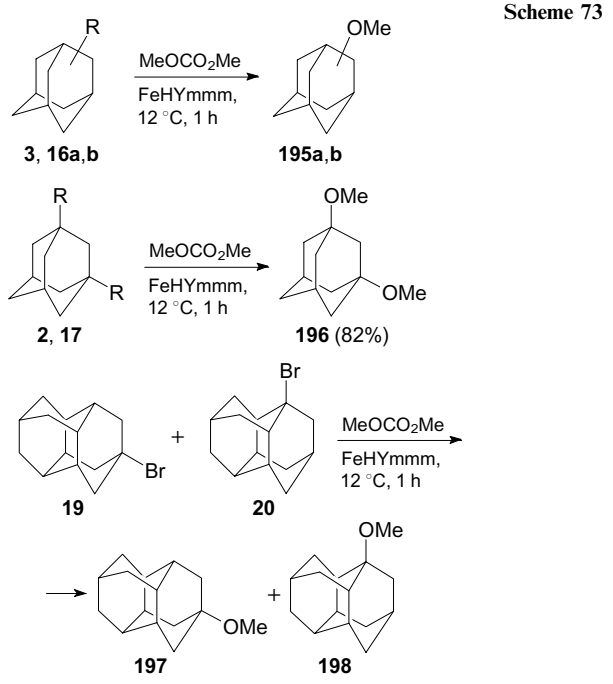
R^1 = H, Me, Cl; R^2, R^3, R^4 = H, Me



194: 1-isomer (**a**), 2-isomer (**b**)

Khusnutdinov *et al.*[91] accomplished the synthesis of adamantyl-substituted mono- (**195a**,**b**) and dimethyl ethers (**196**) by the reaction of haloadamantanes **2**, **3**, **16a**,**b** and **17** with DMC in the presence of FeHYmmm (Scheme 73). Under similar conditions, a mixture of bromodiamantanes **19** and **20** (9 : 1 ratio) was converted to a mixture of diamantyl methyl ethers **197** and **198** in a total yield of 75% and with the same ratio of regioisomers.

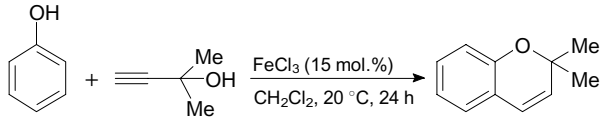
Scheme 73



R = Cl (**2**, **3**), Br (**16**, **17**); isomers: 1 (**3** and **16a**; **195a**, 78% and 80%); 2 (**16b**; **195b**, 76%)

The salt $FeCl_3$ catalyzes the cyclocondensation of phenol (**155a**) with 1,1-dimethylpropargyl alcohol (**101b**) taken in a threefold excess to give 2,2-dimethyl-2*H*-chromene **199** (Scheme 74).[92]

Scheme 74



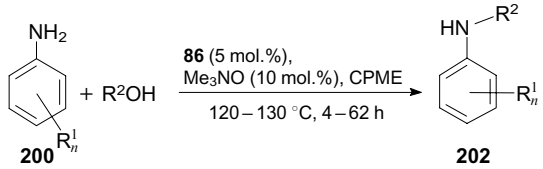
6. *N*-Alkylation of aliphatic and aromatic amines

A series of studies[93 – 100] describes one more reaction catalyzed by iron compounds. An example is direct *N*-alkylation of amines such as anilines (**200**), benzylamines (**201**), furfurylamine (**106g**), piperidine and n-pentylamine with alcohols and diols, resulting in the formation of compounds **202** – **206** (Schemes 75 – 77).[93] Note that anilines **200** with electron-withdrawing *para*-substituents (R^1_n = 4-CO_2Me, 4-NO_2, 4-CN) do not react with pentyl alcohol under these conditions.

As indicated by the mechanism proposed for this reaction by the authors (Scheme 78), the hydrogen atom transfer from the alcohol to the intermediate imine occurs with the participation of the cyclopentadienyl ligand (complex **207**).

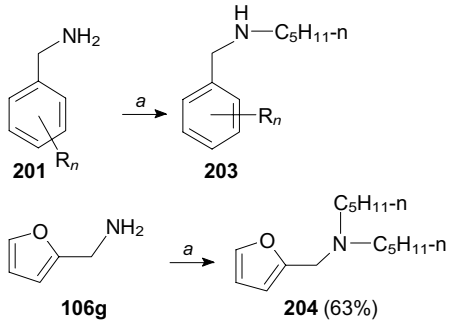
Aminov and co-workers[94,95] studied the reaction of aniline with methanol in the presence of $FeCl_3 \cdot 6H_2O$ in CCl_4 (Scheme 79). By varying reaction conditions, it is possible to direct the reaction towards *N*-alkylation to give a mixture of *N*-methyl- (**202a**) and *N*,*N*-dimethylanilines (**208**) or a mixture of *N*,*N*-dimethylaniline (**208**) and bis(4-dimethylaminophenyl)methane (**209**). The composition and the yields of products considerably depend on the

Scheme 75



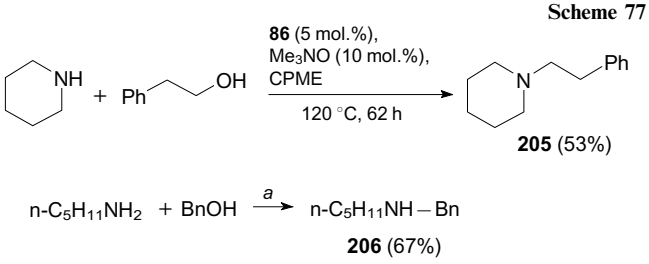
R^2 = n-C_5H_{11}: R^1_n = H (90%), 2-OMe (42%), 4-OMe (91%), 2-Me (49%), 3-Me (84%), 4-Me (91%), 2-F (13%), 4-Cl (76%), 4-I (8%), 2-NH_2 (52%), 3-Me-4-Br (58%), 3-NH_2-4-Me (58%);
R^1_n = 4-OMe: R^2 = Et (85%), Pr^i (12%), n-C_8H_{17} (69%), Cy (14%), Bn (12%), $BnCH_2$ (75%), $HO(CH_2)_2$ (74%), $HO(CH_2)_6$ (43%);
CPME is cyclopentyl methyl ether

Scheme 76



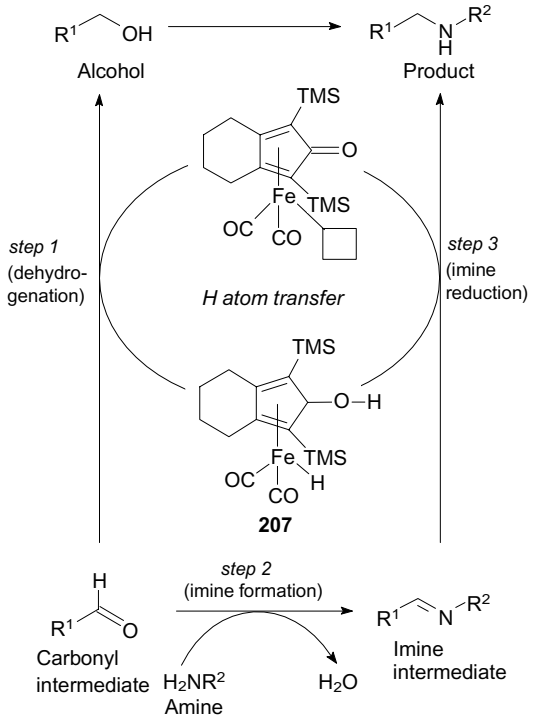
(*a*) n-$C_5H_{11}OH$, **86** (5 mol.%), Me_3NO (10 mol.%), CPME, 120 – 130 °C, 4 – 63 h; R_n = H (62%), 4-Me (30%), 3-Cl (80%), 3-F (87%), 3-CF_3 (95%), 3-CF_3-5-F (95%), 3-Cl-4-F (43%)

Scheme 77



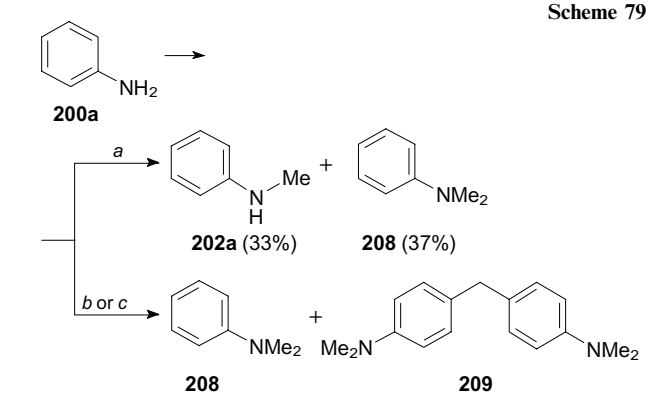
(*a*) **86** (5 mol.%), Me_3NO (10 mol.%), CPME, 130 °C, 62 h

Scheme 78



reaction time and reactant concentrations. When the CCl_4 : MeOH ratio is 1 : 2 and the temperature is 140 °C, the reaction carried out for 4 h gives equimolar amounts of *N*-methylated anilines **202a** and **208**; the major product formed within 8 h is *N*,*N*-dimethylaniline (**208**) (92% yield). Apart from this compound, the reaction mixture also contains bis-product **209** (6%). When the amount of methanol is increased twofold and heating is continued for 16 h, the yield of the bis-product increases to 45% and the yield of *N*,*N*-dimethylaniline decreases to 47%.

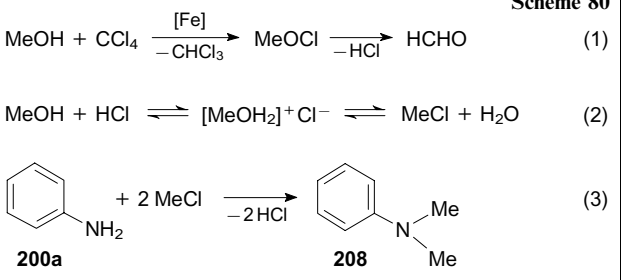
Scheme 79



(*a*) MeOH – CCl_4 (2 : 1), $FeCl_3 \cdot 6H_2O$, 140 °C, 4 h;
(*b*) MeOH – CCl_4 (2 : 1), $FeCl_3 \cdot 6H_2O$, 140 °C, 8 h;
(*c*) MeOH – CCl_4 (4 : 1), $FeCl_3 \cdot 6H_2O$, 140 °C, 16 h

It was found experimentally that *N*-alkylation of aniline with methanol in the presence of $FeCl_3 \cdot 6H_2O$ does not proceed without CCl_4. To disclose the role of CCl_4 in this reaction, the reaction mixture was analyzed by gas chromatography – mass spectrometry, which detected the presence of chloroform, methyl formate (*m*/*z* 60) and (in the gas phase) methyl chloride (*m*/*z* 50). This composition of by-products suggests the reaction mechanism that starts with the oxidation of methanol with CCl_4 in the presence of an iron catalyst to give formaldehyde *via* the formation of methyl hypochlorite [Scheme 80, reaction (1)]. Unstable MeOCl decomposes to give CH_2O and HCl.[68,96] Then the released hydrogen chloride reacts with methanol yielding methyl chloride [reaction (2)], which methylates aniline (**200a**) [reaction (3)].[97]

Scheme 80



It is noteworthy that known methods for the synthesis of bis(4-dimethylaminophenyl)methane (**209**) are based on condensation of *N*,*N*-dimethylaniline (**208**) with formaldehyde in the presence of HCl, H_2SO_4, $FeCl_3$ and $FeCl_3 \cdot 6H_2O$.[98,99] It is likely that formaldehyde, which is generated *in situ* from methyl hypochlorite, is responsible also for the formation of this product.[68]

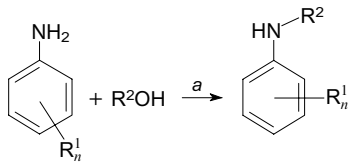
Lator *et al.*[100] reported that iron complex **82** containing a cyclopentadienone ligand in the coordination sphere catalyzes *N*-methylation and *N*-ethylation of aromatic (**200**, **210**) and heteroaromatic amines (**211**, **212**) with methanol or ethanol in the presence of CsOH (Scheme 81). The reaction was performed with 0.5 mmol of the starting amine, 2 mL of CPME and an alcohol as a 0.5 M solution. As a result, secondary amines **202**, **213a**,**b**, **214** and **215** were obtained in high yields.

According to density functional theory (DFT) calculations, in the alkylation of amines with alcohols under a hydrogen atmosphere, hydrogen acts not only as a reducing agent, but also as a reactant for shifting the thermodynamic equilibrium (Scheme 82).[100]

Secondary amines **202b**, **203a**, **216** and **217** were also alkylated under these conditions (Scheme 83).

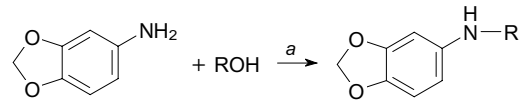
Li and Cai[101] reported an iron-catalyzed oxidative *N*-alkylation of amines **200a**,**b** and amides **218** and **219** with cycloalkanes **220** (Scheme 84). The experiments were carried out in the presence of oxidants, di-*tert*-butyl peroxide (DTBP) or *tert*-butyl peroxybenzoate. These reactions proceed smoothly for a broad range of substrates and give *N*-cycloalkyl derivatives **221** – **223**. Compounds **218** and **219** are also alkylated with toluene to give products **224** and **225** in 76% and 69% yields.

Scheme 81



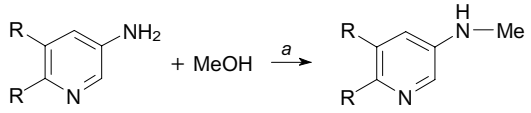
200 **202**

R^2 = Et: R^1 = 4-OMe (97%), 4-CN (73%), 4-I (96%), 3,5-$(CF_3)_2$ (95%);
R^2 = Me: R^1 = H (99%), 4-Me (94%), 4-OMe (97%), 4-Br (97%), 4-I (83%), 3-Br (99%), 3,5-$(CF_3)_2$ (87%), 4-CN (87%), 4-Ac (77%), 4-CH=CH_2 (89%), 4-Bz (96%)



210 **213a**,**b**

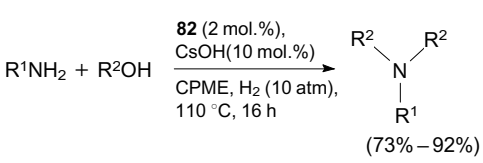
R = Et (**a**, 99%), Me (**b**, 97%)



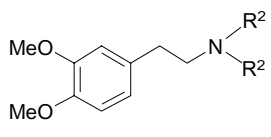
211, **212** **214**, **215** (94% – 99%)

R = H (**211**, **214**), R – R is benzo (**212**, **215**);
(*a*) **82** (2 mol.%), CsOH (10 mol.%), CPME, 110 °C, 16 h

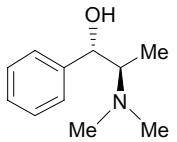
Scheme 82



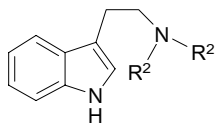
Examples of products



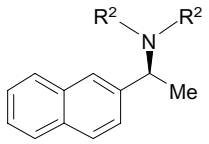
R^2 = Me (92%), Et (89%)



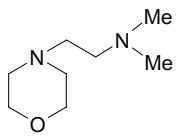
(87%)



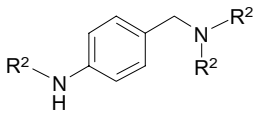
R^2 = Me (83%), Et (91%)



R^2 = Me (85%), Et (73%)



(92%)

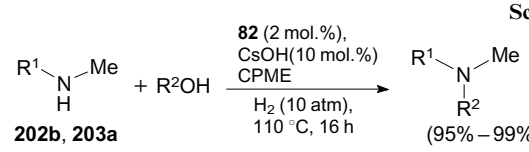


R^2 = Me (87%), Et (82%)

Under similar conditions, arenesulfonamides **226** are *N*-(trans)alkylated when treated with cycloalkanes **220,** or with toluene or β-picoline; this results in the synthesis of sulfonamides **227** – **229** (Scheme 85).[101]

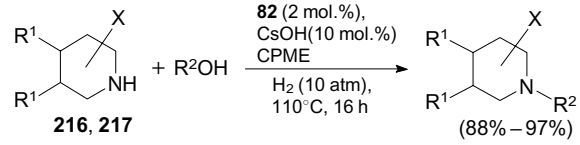
The authors proposed a probable mechanism of this reaction, as applied to the reaction of benzenesulfonamide (**226a**) with cyclohexane (**220a**), based on the single-electron transfer (SET) and the Fe^{II}/Fe^{III} cycle (Scheme 86). The reaction starts with the thermal decomposition of di-*tert*-butyl peroxide giving the *tert*-butoxyl radical, which attacks

Scheme 83



202b, **203a** (95% – 99%)

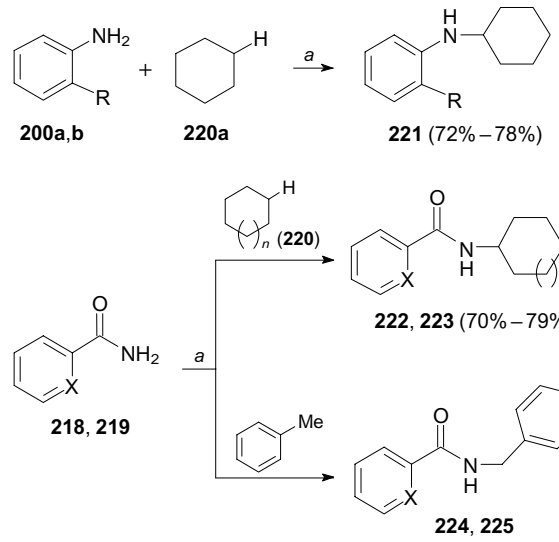
R^1 = 4-$MeOC_6H_4$ (**202b**), Bn (**203a**); R^2 = Me, Et



216, **217** (88% – 97%)

X = H, CH_2OH; R^1 = H (**216**), R^1 – R^1 is benzo (**217**); R^2 = Me, Et

Scheme 84



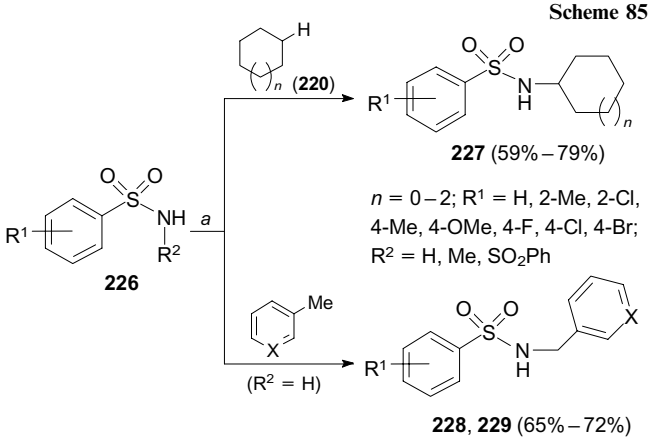
200a,**b** **220a** **221** (72% – 78%)

222, **223** (70% – 79%)

218, **219** **224**, **225**

(*a*) $Fe(acac)_3$ (15 mol.%), DTBP (2 equiv.), PPh_3 (15 mol.%), 100 °C, 18 h; X = CH (**218**, **222**, **224**), N (**219**, **223**, **225**);
200: R = H (**a**), Cl (**b**); *n* = 0 – 2

Scheme 85



226 **227** (59% – 79%)

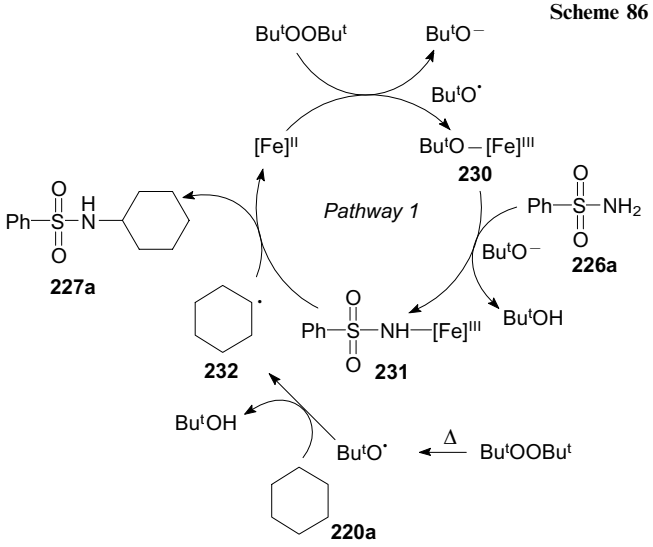
n = 0 – 2; R^1 = H, 2-Me, 2-Cl, 4-Me, 4-OMe, 4-F, 4-Cl, 4-Br;
R^2 = H, Me, SO_2Ph

228, **229** (65% – 72%)

(*a*) $Fe(acac)_3$ (15 mol.%), DTBP (2 equiv.), 100 °C, 18 h

X = CH (**228**), N (**229**);
R^1 = H, 4-Me, 4-Cl

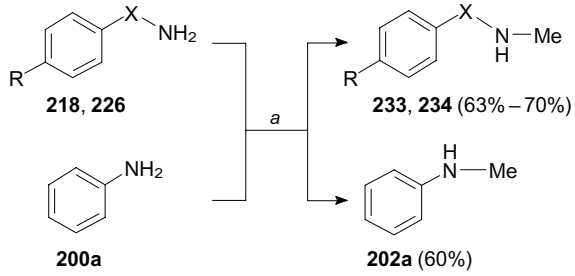
Scheme 86



cyclohexane, thus generating the cyclohexyl radical. Another *tert*-butyl peroxide molecule reacts with iron(II) to give iron(III) *tert*-butoxide **230**, which deprotonates the NH_2 group of sulfonamide **226a** yielding complex **231**. In the final step, this complex reacts with cyclohexyl radical **232** to give *N*-cyclohexyl-substituted amide **227a** with regeneration of Fe^{II} to continue the cycle.

Li and Cai [101] proposed an unusual method for *N*-methylation of aniline (**200a**) and aromatic amides **218** and **226** using *tert*-butyl peroxybenzoate (TBPB) as the methylating agent. Compounds **202a**, **233** and **234** were isolated as the major products (Scheme 87).

Scheme 87

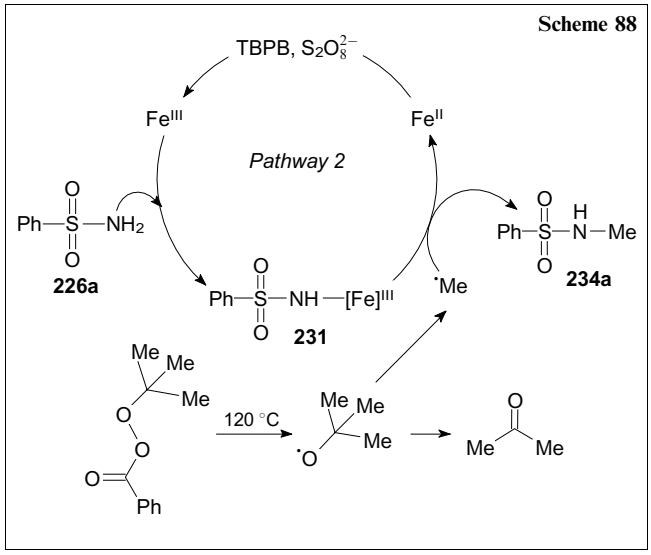


(*a*) Fe(acac)$_3$ (20 mol.%), TBPB (2 equiv.), $K_2S_2O_8$ (1 equiv.), PhCl, 120 °C, 24 h; X = C(O) (**218**, **233**), SO_2 (**226**, **234**); R = H, Me, Br

The authors proposed a probable reaction mechanism (Scheme 88), according to which the reaction started with thermal decomposition of *tert*-butyl peroxybenzoate to give, first, the *tert*-butyl and then the methyl radicals; the role of the catalyst was to form complex **231** by metallation of the NH_2 group of the starting amide **226a**.

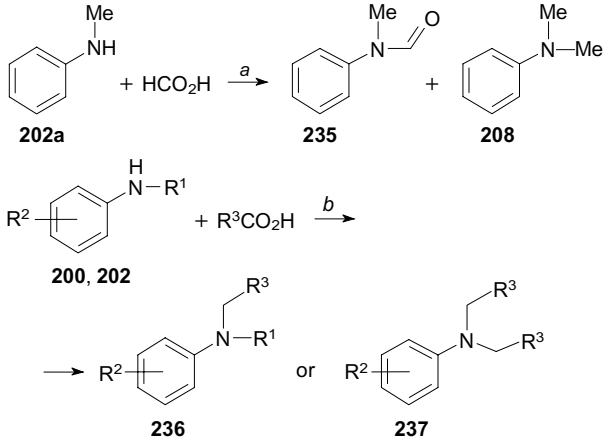
Qiao *et al.*[102] described iron-catalyzed *N*-alkylation of anilines with formic and acetic acids as sources of the methyl and ethyl groups, which are formed from formic and acetic acids, respectively, upon the reduction with phenylsilane. The following iron compounds were tested as catalysts for this reaction: $Fe(acac)_2$, $Fe(acac)_3$, $Fe(\eta\text{-}C_5H_5)_2$, $Fe(BF_4)_2 \cdot 6H_2O$, $FeCl_2 \cdot 4H_2O$, $FeCl_3$, $Fe_2(CO)_9$, $Fe_3(CO)_{12}$. The best results in the alkylation of *N*-methylaniline (**202a**) with formic acid were attained when iron carbonyls $Fe_2(CO)_9$ and $Fe_3(CO)_{12}$ were used; these catalysts ensured the formation of *N*,*N*-dimethylaniline (**208**) in 95% and 93% yields, respectively. In the case of

Scheme 88



Fe(acac)$_2$, Fe(acac)$_3$, $Fe(\eta\text{-}C_5H_5)_2$, $Fe(BF_4)_2 \cdot 6H_2O$, $FeCl_2 \cdot 4H_2O$ and $FeCl_3$, the reaction follows a different pathway and gives *N*-methylformanilide (**235**) in 24% – 80% yields (Scheme 89). Similarly, reactions of substrates **200** and **202** (0.5 mmol) with various carboxylic acids (0.57–1.5 mmol) in the presence of $Fe_2(CO)_9$ and phenylsilane (1.5–3 mmol) provided the synthesis of a series of alkylated anilines **236** and **237** (28% – 94% yield).

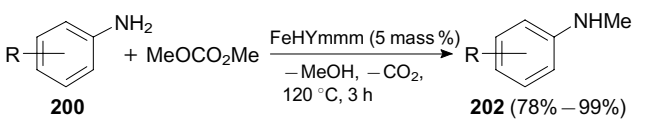
Scheme 89



(*a*) [Fe], $PhSiH_3$, 100 °C, 1 – 12 h;
(*b*) $Fe_2(CO)_9$ (5 mol.%), $PhSiH_3$, PhMe, 100 °C, 1 – 12 h;
R^1 = H, Me, Et, Pr^i, $(CH_2)_2OH$, All, Bn; R^2 = H, 4-Me, 4-OMe, 4-F, 4-Cl, 4-Br; R^3 = H, Et, Pr^n, Bu^i, n-C_8H_{17}, All, CH_2CF_3

It was found [103] that dimethyl carbonate is an efficient *N*-methylating agent for anilines **200**; methylation of aniline, toluidines and chloro- and bromoanilines in the presence of FeHYmmm (3% – 5% Fe) at 120 °C for 3 h gave monomethyl derivatives **202** in high yields (Scheme 90).

Scheme 90



R = H, 2-Me, 3-Me, 4-Me, 2-Cl, 4-Cl, 4-Br

7. Iron-containing catalysts in the synthesis of imines

It was found [104, 105] that heating of benzylamine (**201a**) in CCl_4 in the presence of iron-containing catalysts — $FeCl_3 \cdot 6H_2O$, $FeCl_3$, $FeCl_2 \cdot 4H_2O$, $Fe(\eta\text{-}C_2H_5)_2$, $Fe(acac)_3$, $Fe(OAc)_2$, $Fe_2(CO)_9$ — affords *N*-benzylidenebenzylamine (**238a**) in 92% – 96% yield (Scheme 91).

Scheme 91

$$\underset{\textbf{201a}}{PhCH_2NH_2} \xrightarrow[80-85\ ^\circ C,\ 8\ h]{[Fe],\ CCl_4} \underset{\textbf{238a}}{PhCH{=}NCH_2Ph}$$

The authors analyzed the composition of the reaction mixture in which, apart from imine **238a**, they detected chloroform, benzonitrile (< 1%), HCl, ammonium ions and active chlorine. This allowed them to propose a probable pathway to product formation, the key step of which is chlorination of benzylamine with CCl_4 catalyzed by an iron compound [reaction (1) in Scheme 92]. *N*-Chlorobenzylamine (**239**) thus formed eliminates HCl to be converted to imine **240a** [reaction (2)], which attacks the next benzylamine molecule [reaction (3)].

Scheme 92

$$\underset{\textbf{201a}}{PhCH_2NH_2} + CCl_4 \xrightarrow{[Fe]} PhCH_2NHCl + CHCl_3 \quad (1)$$

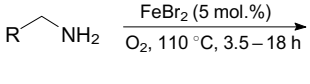
$$\underset{\textbf{239}}{PhCH_2NHCl} \longrightarrow \underset{\textbf{240a}}{PhCH{=}NH} + HCl \quad (2)$$

$$\underset{\textbf{240a}}{PhCH{=}NH} + \underset{\textbf{201a}}{PhCH_2NH_2} \longrightarrow \underset{\textbf{238a}}{PhCH{=}NCH_2Ph} + NH_3 \quad (3)$$

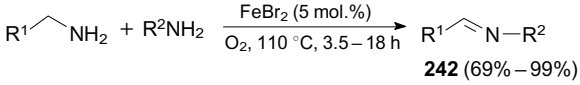
$$NH_3 + HCl \longrightarrow NH_4Cl \quad (4)$$

The formation of imines **238** (R = Ar), **241** (R = Alk) and **242** by oxidative self-condensation or cross-condensation of various primary amines is catalyzed by the following iron compounds: FeF_2, $FeCl_2$, $FeBr_2$, $FeSO_4$, $Fe(NO_3)_3$, $Fe(ClO_4)_2 \cdot xH_2O$, $FeCl_3$, $FeBr_3$ and $Fe(acac)_3$. Iron(II) bromide $FeBr_2$ proved to be the catalyst of choice. Oxygen is used, most often, as the oxidant (Scheme 93).[106]

Scheme 93



238, **241** (53% – 99%)

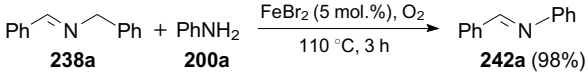


242 (69% – 99%)

241: R = n-C_7H_{15}, Cy; **238**: R = $X_nC_6H_{5-n}$ [X_n = H, 4-Me, 4-OMe, 4-F, 2-Cl, 3,4-Cl_2, 3,5-$(CF_3)_2$], *etc.*; **242**: R^1 = $X_nC_6H_{5-n}$ (X_n = H, 4-Me, 4-OMe, 4-F, 2-Cl, 3,4-Cl_2); R^2 = Bu^n, n-C_8H_{17}, Cy, 1-Naph, $Y_nC_6H_{5-n}$ (Y_n = H, 4-Me, 2-Me, 4-Pr^i, 4-OMe, 4-F, 4-Cl, 3,4-Cl_2)

N-Benzylideneaniline (**242a**) was obtained in a quantitative yield by transamination of *N*-benzylidenebenzylamine (**238a**) with aniline (**200a**) catalyzed by $FeBr_2$ (Scheme 94). In the absence of a catalyst (110 °C, 3 h), imine **242a** is not formed. When the reaction time is increased to 40 h, imines **238a** and **242a** in 3 : 1 ratio are detected in the reaction mixture by NMR spectroscopy. Hence, $FeBr_2$ catalyzes the self- and cross-condensation of both amines.

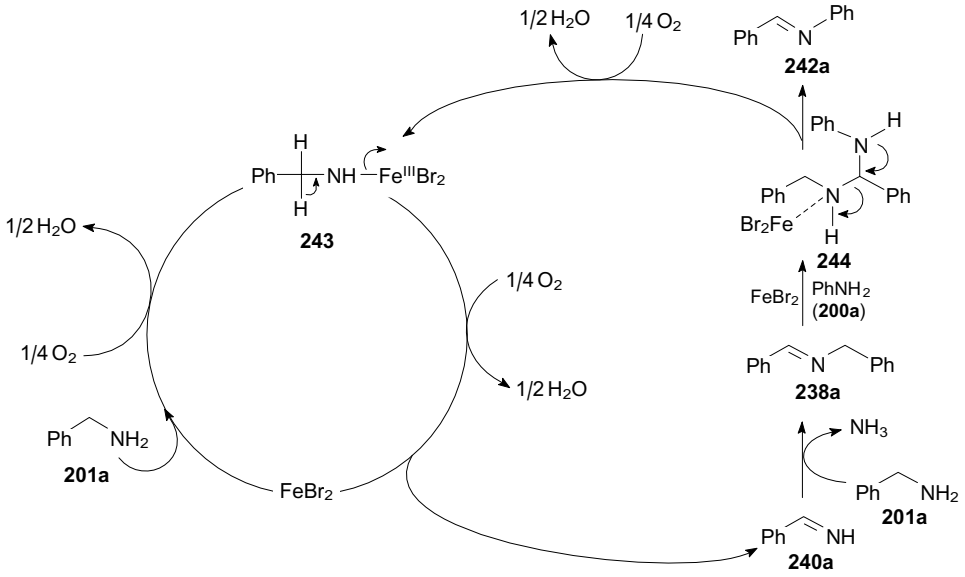
Scheme 94



238a **200a** **242a** (98%)

Scheme 95 shows a probable reaction mechanism. Presumably, the first step is the formation of Fe – amide complex **243** comprising the amine, $FeBr_2$ and oxygen. The subsequent oxidation of complex **243** with oxygen affords benzylimine (**240a**) and regenerates iron(II) bromide for the next catalytic cycle. Then benzylimine **240a** reacts with benzylamine to give benzylidenebenzylamine **238a** and ammonia. This is followed by nucleophilic addition of aniline to imine **238a** catalyzed by iron(II) bromide, giving rise to complex **244**. Finally, the latter decomposes to benzylidenephenylamine (**242a**) and complex **243**, which continues the cycle.

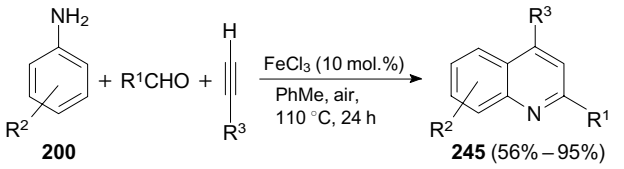
Scheme 95



8. Synthesis of quinolines in the presence of Fe-containing catalysts

Iron compounds and complexes are efficient catalysts for the synthesis of quinolines from anilines. A benefit of iron catalysts is the broad range of substrates applicable as 'partners' for anilines to construct a quinoline ring. For example, it was found [107] that $FeCl_3$ catalyzes the multicomponent reaction of anilines **200** with aldehydes and alkynes to give 2,4-disubstituted quinolines **245** (Scheme 96).

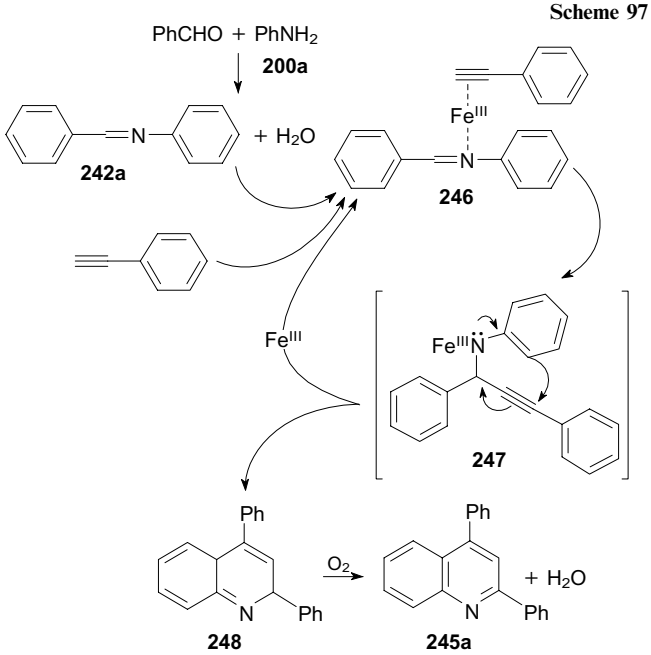
Scheme 96



R^1 = XC_6H_4 (X = H, 4-Me, 4-OMe, 4-Cl, 2-CF_3), 1-Naph, 3-Th;
R^2 = H, 6-Me, 6-OMe, 6-Cl, 8-Cl;
R^3 = Ph, 4-$MeOC_6H_4$, 4-$F_3CC_6H_4$, 3-Th

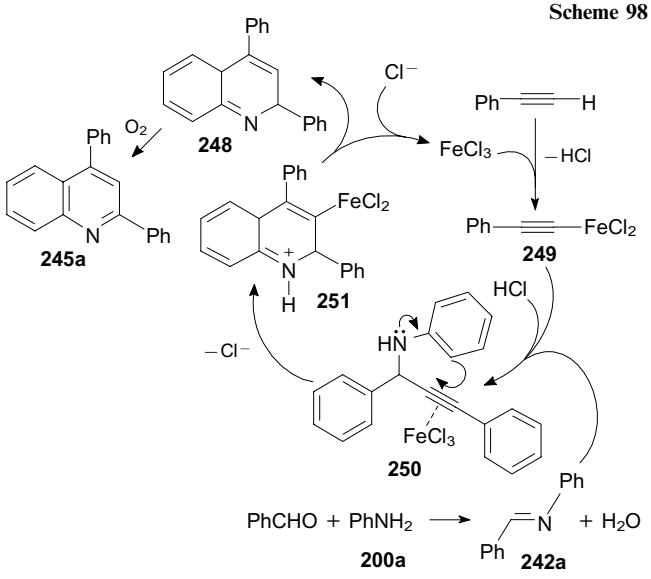
Cao *et al.*[107] proposed a reaction mechanism (Scheme 97), according to which aniline first reacts with the aldehyde to give Schiff base **242a**. This is followed by the formation of iron complex **246** comprising alkyne and imine and by conversion of complex **246** to complex **247**. The next step is cyclization of complex **247** to be converted to dihydroquinoline **248**. The formation of complex **247** is a fast reaction; therefore, the authors failed to detect it in the reaction mixture. In the final step, dihydroquinoline **248** is converted to quinoline **245a** upon oxidation with air oxygen.

Scheme 97



According to Zhang *et al.*,[108] an alternative mechanism is possible for this reaction (Scheme 98). The authors assumed the initial formation of Fe^{III}–alkynyl complex **249**, which adds to the imine, generated *in situ* from the aldehyde and the aniline, giving complex **250**. Then $FeCl_3$

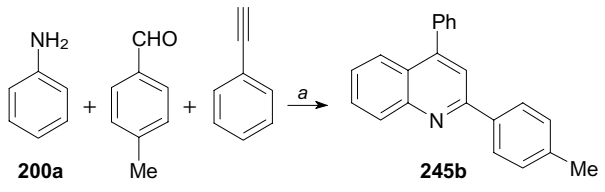
Scheme 98



coordinated to the triple bond promotes the intramolecular nucleophilic attack on the *ortho*-position of the aniline benzene ring, thus participating in the formation of complex **251**. The latter decomposes to dihydroquinoline **248** and $FeCl_3$, which continues the catalytic cycle. The oxidation of dihydroquinoline **248** with air oxygen furnishes the target quinoline **245a**.

The heterocyclization of aniline with *p*-tolualdehyde and phenylacetylene is more efficiently catalyzed by iron(III) triflate than by $FeCl_3$. The yield of 2-(*p*-tolyl)-4-phenylquinoline (**245b**) in the iron(III) triflate-catalyzed reaction can reach 82% (Scheme 99). High yields of the corresponding quinolines (77%–88%) were also obtained in the heterocyclization of *p*-toluidine with phenylacetylene and 4-chloro-, 4-bromo-, 4-fluoro-, 3,4-dichloro- or 3,4-dimethoxybenzaldehydes. The yields of 2,4-diaryl-substituted quinolines in the reactions of aniline or 4-chloroaniline with benzaldehyde (4-chloro- or 2-hydroxybenzaldehyde) and phenylacetylene (4-fluoro- or 4-acetylarylacetylene) in the presence of $Fe(OTf)_3$ are 66%–87%.[109] Tetra-n-butylammonium hydroxide markedly increases the activity of a Fe-containing catalyst, in particular $Fe(acac)_3$, towards aniline heterocyclization with aldehydes and acetylenes.[110]

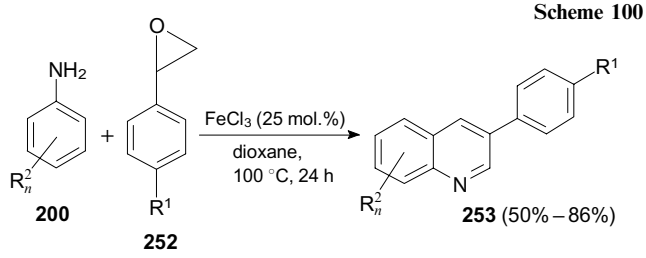
Scheme 99



(*a*) [Fe] (10 mol.%), PhMe, air, 110 °C, 24 h;
[Fe] = $FeCl_3$ (72%), $Fe(OTf)_3$ (75%), $Fe(OTf)_2$ (47%), $FeSO_4$ (29%), $Fe(NO_3)_3$ (< 1%), $Fe_2(SO_4)_3$ (< 1%), $Fe(OTf)_3$ (5 mol.%, 100 °C, 2.5 h, 82%)

Styrene epoxides **252**, taken in a twofold excess, can act as one more component in the quinoline synthesis catalyzed by iron compounds, for example, $FeCl_3$ (Scheme 100). This reaction, proceeding *via* C–O bond cleavage and C–H bond activation, results in the formation of 3-aryl derivatives **253**.[111]

Scheme 100



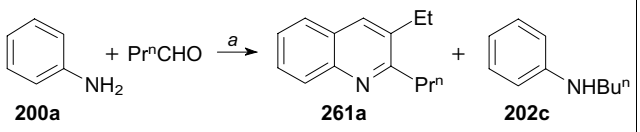
R^1 = H, Me, F, Cl, Br; R^2_n = H, 6-Me, 7-Me, 8-Me, 6-OMe, 7-Cl, 8-Cl, 6-Br, 8-Br, 6-F, 6-CF_3, 6-Me-8-Br, 7,8-Me_2, 6,8-Me_2, 5,8-Me_2, 5,7-Me_2, 5,6,7-Cl_3 (substituent positions are indicated for the product)

The mechanism of this reaction was considered in relation to the reaction of aniline (**200a**) with styrene epoxide (**252a**) (Scheme 101). The first step is $FeCl_3$-catalyzed aniline condensation with the epoxide yielding β-amino alcohol **254**. In the second step, amino alcohol **254** eliminates water, being converted to enamine **255**, which reacts with another molecule of epoxide **252a** under the action of $FeCl_3$ to give complex **256**. This complex decomposes with the release of $HFeCl_2$ and ketone **257**. In turn, $HFeCl_2$ degrades to HCl and [FeCl]. The coordinatively unsaturated intermediate [FeCl] attacks the *ortho*-C – H bond of ketone **257** to give Fe hydride complex **258**, which eliminates benzaldehyde to be converted to seven-membered complex **259**. The reductive elimination of intermediate **259** with the release of [FeCl] leads to dihydroquinoline **260**, which is oxidized to quinoline **253a**. Benzaldehyde and amino alcohol **254**, which are formed in the reaction, were detected by HPLC.

The salt $FeCl_3 \cdot 6H_2O$ serves as the catalyst in the classical method for the synthesis of quinoline **261a** by condensation of aniline (**200a**) with butyraldehyde, giving the product in a quantitative yield (Scheme 102).[112]

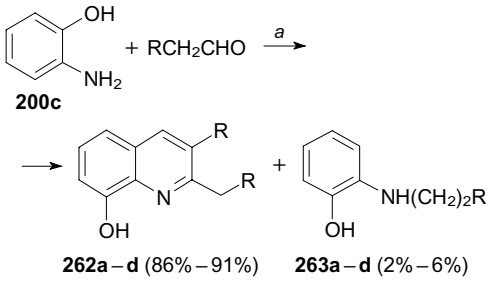
Shepetov *et al.*[113] synthesized substituted hydroxyquinolines **262a – d** by condensation of *o*-aminophenol (**200c**) with aliphatic aldehydes using the $FeCl_3 - PPh_3 - DMF$ catalytic system (Scheme 103). Anilines **263a – d** were isolated as by-products. It was found that the promoting metal additives (Ni, Co, Al, Zn, Cu) used together with this catalytic system reduce the yields of resinous products, while high conversion of aminophenol (80% – 88%) and selectivity to quinolines (72% – 81%) are retained. The authors assumed that the addition of metal powders increases the lifetime of catalytically active species by attaching them to the surface of promoting additives; therefore, the starting monomers are almost completely consumed in the desired condensation reaction, thus preventing compaction reactions and decreasing the fraction of resinous products.[114] The reaction is performed using 20 mmol of substrate **200c**, 44 mmol of aldehyde and 7 mL of a DMF – ethanol solvent mixture (1 : 6).

Scheme 102



(*a*) $FeCl_3 \cdot 6H_2O$ (0.2 mol.%), DMF or EtOH, 20 °C, 3 – 5 min

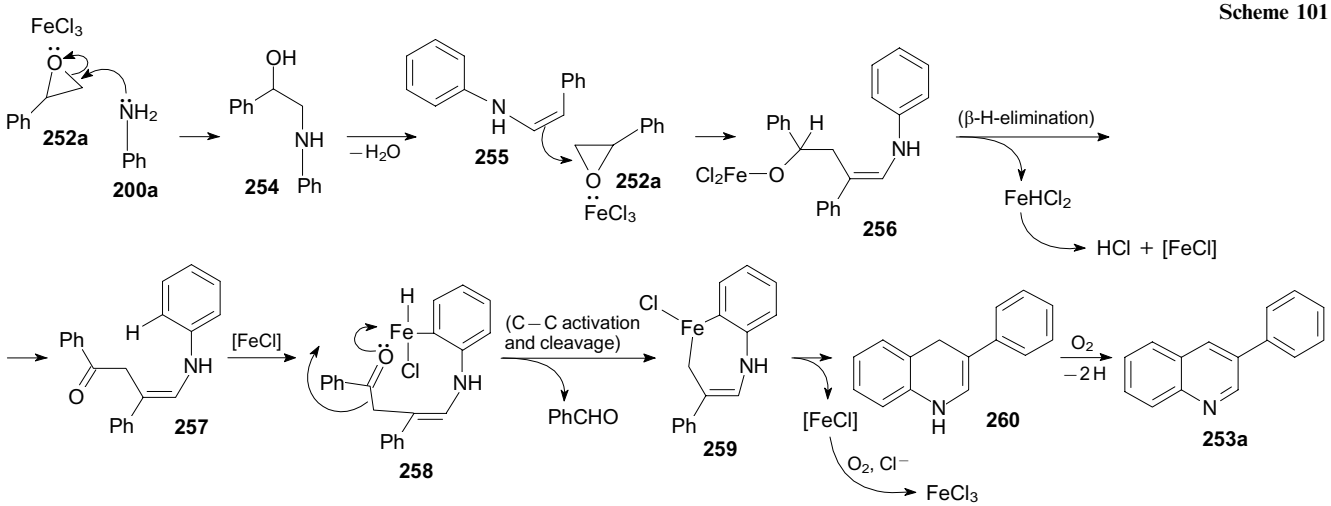
Scheme 103



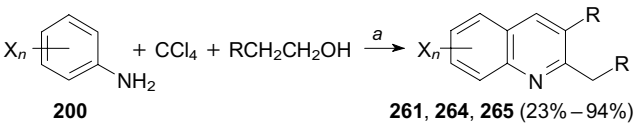
(*a*) $FeCl_3$ (2 mol.%), PPh_3 (6 mol.%), DMF, EtOH, 125 °C, 6 h; **262**, **263**: R = Et (**a**), Pr^n (**b**), Pr^i (**c**), Bu^n (**d**)

The syntheses of tri- and tetrasubstituted quinolines by reactions of anilines with alcohols rather than with carbonyl compounds has also been reported.[115 – 117] The reactions of aniline derivatives $X_nC_6H_4NH_2$ (where X = Me and Cl in various positions, 2-Et, 4-OMe) with ethyl, n-propyl and n-butyl alcohols in the presence of iron-containing catalysts afford substituted quinolines **261**, **264** and **265** (Scheme 104; substituent positions in the product are indicated). The compounds tested as catalysts include $FeCl_3 \cdot 6H_2O$, $FeCl_3$, $FeCl_2 \cdot 4H_2O$, $Fe(\eta\text{-}C_5H_5)_2$, $Fe(acac)_3$, $Fe(OAc)_2$ and $Fe_2(CO)_9$; the best results were attained using $FeCl_3 \cdot 6H_2O$. It is noteworthy that one more reagent, carbon tetrachloride, is needed for the formation of quinolines, apart from alcohol and aniline. The optimal catalyst : aniline : CCl_4 : ROH ratio is 1 : 50 : 100 : 200. In some cases, the reaction is non-selective and gives mixtures of isomers (see Scheme 104).

Scheme 101



Scheme 104



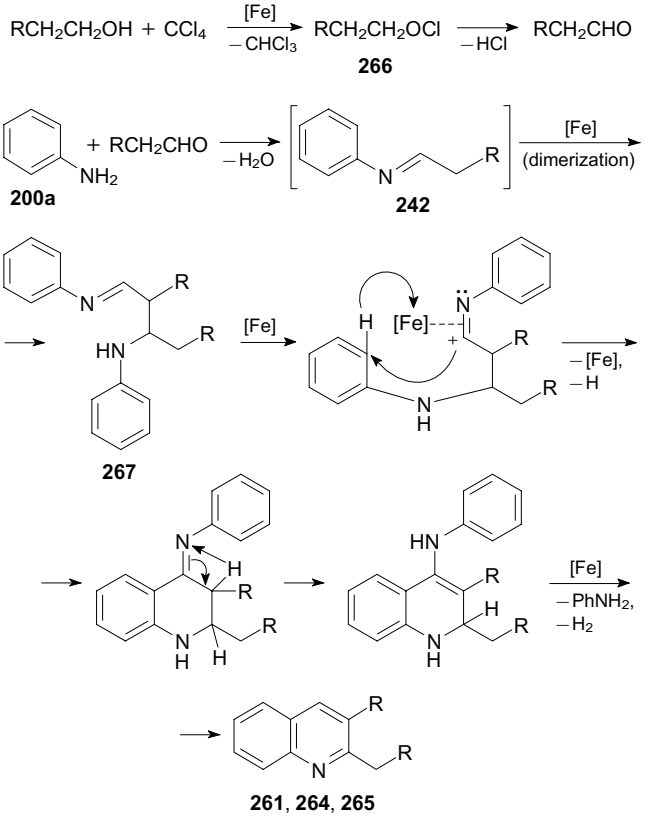
200 **261**, **264**, **265** (23% – 94%)

(*a*) $FeCl_3 \cdot 6H_2O$, 140°C, 4 h (two-step loading);
264: R = H: X_n = H, 6-Me, 7-Me, 8-Me, 8-Et, 6-Cl, 8-Cl, 5- and 7-Cl (1 : 7), 6-OMe, 5,6- and 6,7-Cl_2 (1 : 1);
265: R = Me: X_n = H, 6-Me, 8-Me, 5- and 7-Me (1 : 4), 8-Et, 6-Cl, 8-Cl, 5- и 7-Cl (1 : 5), 6-OMe, 5,6- and 6,7-Cl_2 (1 : 1.5);
261: R = Et: X_n = H, 6-Me, 8-Me, 5- and 7-Me (1 : 5), 8-Et, 6-Cl, 8-Cl, 5- and 7-Cl (1 : 4), 6-OMe, 5,6- and 6,7-Cl_2 (1 : 2)

High yields of quinolines in this reaction are observed for 4-methyl-, 4-methoxy- and 4-chloro-substituted anilines. Meanwhile, 2-, 3- and 4-aminophenols; 2- and 3-methoxyanilines; 2-nitroaniline; 2-amino- and 4-aminobenzoic acids; and 5-aminosalicyclic acid do not react with CCl_4 and alcohols. The lack of reactivity of these compounds can be attributed to catalyst deactivation due to complex formation with the functional group of the aniline substrate.

An important advantage of Fe-containing catalysts is high selectivity to quinolines and the absence of *N*-monoalkyl- and *N*,*N*-dialkylanilines among the reaction products. Khusnutdinov *et al.*[115] proposed a reaction mechanism, which includes oxidation of the alcohol under the action of CCl_4 to give alkyl hypochlorite **266**, as was confirmed by iodometric titration. Then compound **266** decomposes, thus generating aldehyde and HCl. The next step is condensation of the aldehyde and aniline to give Schiff base **242**, which is dimerized under the reaction conditions. Dimer **267** undergoes heterocyclization and dehydrogenation under the action of the catalyst to be converted to quinoline **261**, **264** or **265**, depending on the substituent R (Scheme 105).

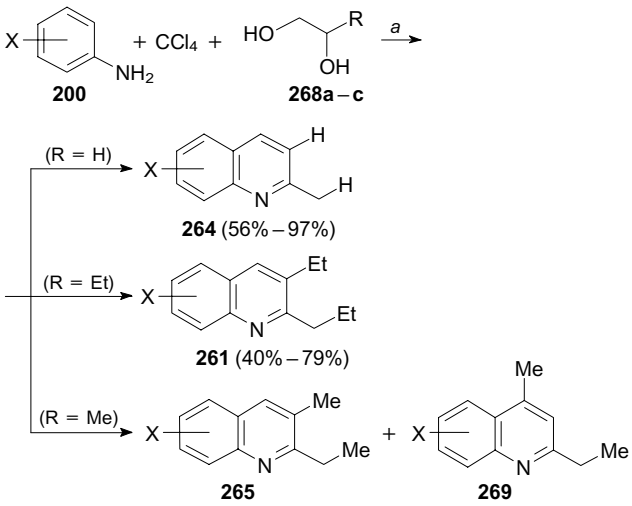
Scheme 105



266 **200a** **242** **267** **261**, **264**, **265**

It was found[118,119] that iron compounds catalyze the reaction of anilines **200** with 1,2-diols **268a – c** to afford quinolines **261**, **264**, **265** and **269** (Scheme 106). This reaction is efficiently catalyzed by the following iron compounds and complexes: $FeCl_3 \cdot 6H_2O$, $FeCl_3$, $FeCl_2 \cdot 4H_2O$, $Fe(OAc)_2$, $Fe(acac)_3$, $Fe(\eta\text{-}C_5H_5)_2$ and $Fe_2(CO)_9$. The best result was attained using $FeCl_3 \cdot 6H_2O$. Indeed, the condensation of aniline with propane-1,2-diol **265c** (R = Me) catalyzed by $FeCl_3 \cdot 6H_2O$ furnished 2-ethyl-3-methyl- (**265**) and 2-ethyl-4-methylquinolines **269** (75% – 94% yield; 2 : 1 ratio). The reaction was conducted in CCl_4 for 8 h at 150 °C, with the catalyst : aniline : CCl_4 : propane-1,2-diol molar ratio being 1 : 100 : 200 : 400.

Scheme 106



200 **268a – c** **264** (56% – 97%) **261** (40% – 79%) **265** **269**

(*a*) $FeCl_3 \cdot 6H_2O$ (1 mol.%), 150 °C, 8 h;
268: R = Et (**a**), H (**b**), Me (**c**); X = H, 2-Me, 3-Me, 4-Me, 2-Et, 2-Cl, 3-Cl, 4-Cl, 4-OMe (substituent positions are indicated for the substrate)

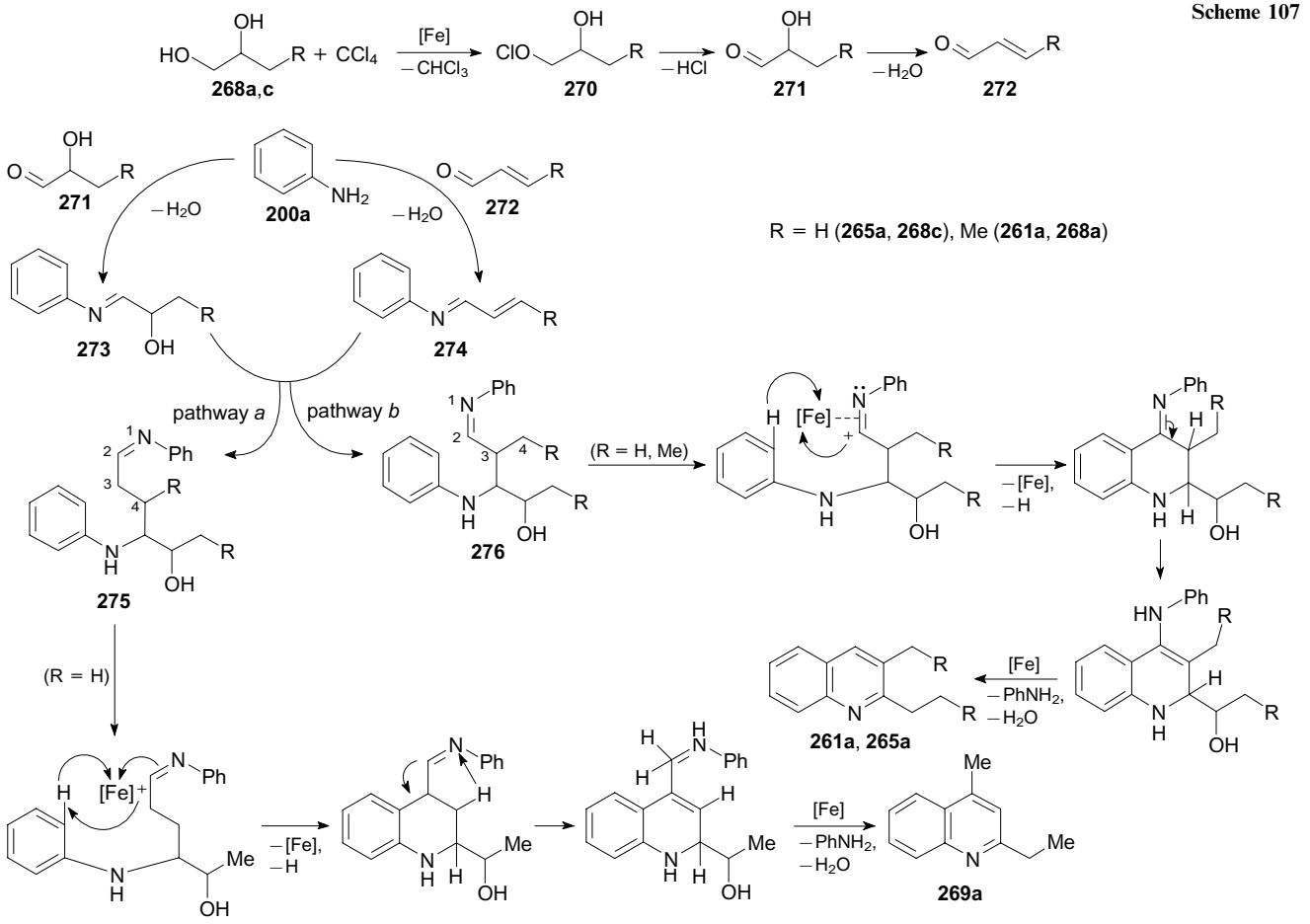
Similar reactions can also smoothly occur for other 1,2-diols: ethylene glycol and butane-1,2-diol; this affords the corresponding 2-methylquinolines **264** and 3-ethyl-2-n-propylquinolines **261**.

The yields of quinolines obtained upon the reactions of 1,2-diols with anilines depend substantially on the nature and position of substituents in the aniline molecule. In particular, the closer the substituent to the amino group, the stronger the deactivating effect of the substituent on the reaction. It was shown that the *ortho*-substituted anilines that have one position for closing the heterocyclic moiety form 2,3,8- and 2,4,8-substituted quinolines. Cyclization of anilines with *para*-substituents involves both *ortho*-positions and gives 2,3,6- and 2,4,6-substituted quinolines, while *meta*-substituted anilines are converted to mixtures of the 2,3(4),5- and 2,3(4),7-isomers in 1 : (3 – 6) ratio.

In order to elucidate the role CCl_4, which is necessary for the reaction to proceed, analysis of the reaction mixture was carried out.[118] This showed the presence of chloroform (with the complete absence of CCl_4) and HCl; the concentration of the latter increased by the end of experiment and could reach 274 mg mL^{-1}.

Considering the composition of by-products and the known possibility of catalytic oxidation of alcohols with CCl_4 to aldehydes *via* hypochlorite, Khusnutdinov *et al.*[96] proposed the following mechanism of quinoline formation

Scheme 107



from aniline and propane- and butane-1,2-diols **268a**,**c** [Scheme 107; in relation to aniline (**200a**)].[118] In the first step, diol **268** is oxidized by CCl_4 at the primary alcohol group to give, first, hypochlorite **270** and then hydroxy aldehyde **271**. The latter, in turn, can be dehydrated to give unsaturated aldehyde **272**. In the first step, aldehydes **271** and **272** react with aniline to afford Schiff bases **273** and **274**, respectively. This is followed by co-dimerization, resulting in the formation of two isomeric intermediates **275** [pathway *a*: addition to C(4)] and **276** [pathway *b*: addition to C(3)]. Heterocyclization, dehydrogenation, dehydration and deamination of compounds **275** and **276** in the presence of an iron catalyst furnishes the target 2,3- (**261a**, **265a**) and 2,4-disubstituted quinolines (**269a**).

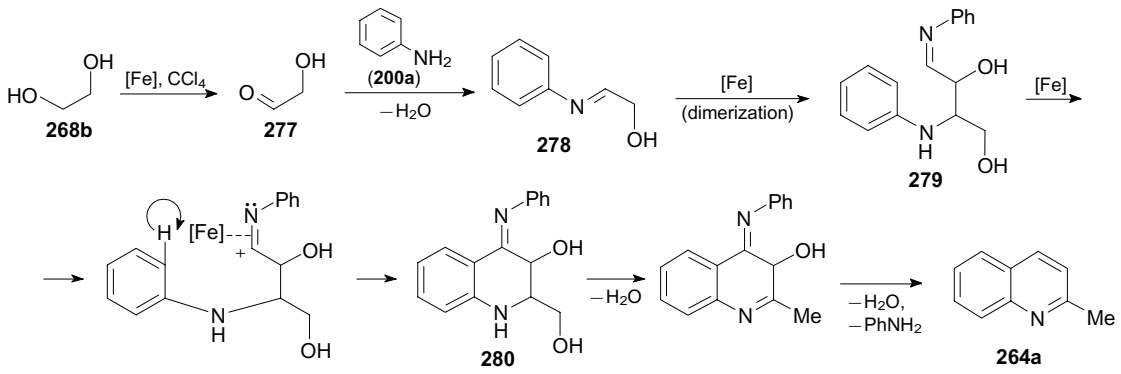
It is noteworthy that butane-2,3-diol does not react with aniline.

In the light of these data, mention should be made of the outcome of the reaction of ethane-1,2-diol (**268b**) with aniline catalyzed by $FeCl_3 \cdot 6H_2O$ in CCl_4: the reaction selectively gives 2-methylquinoline (**264a**) in 97% yield, but does not give the expected indole. A probable reaction mechanism was reported,[118] according to which the reaction starts with the oxidation of one hydroxyl group of ethylene glycol to give glycolaldehyde (**277**), which reacts with aniline to give Schiff base **278**. Dimer **279** formed from compound **278** undergoes cyclization to compound **280**, which is converted to 2-methylquinoline (**264a**) (Scheme 108). The reaction gives off three water molecules (according to the Fischer titration data), which is evidence in favour of the proposed mechanism.[118]

Ethylene glycol readily reacts with *o*-, *m*-, *p*-toluidines, *o*-, *m*-, *p*-chloroanilines, *p*-anisidine and *o*-hydroxy- and *o*-ethylanilines. The yields of the corresponding quinolines are 42% – 90%.

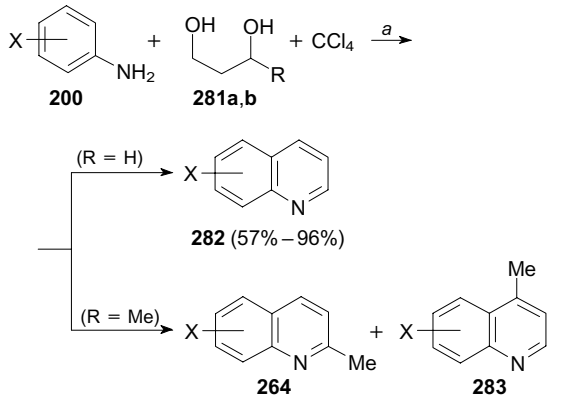
The iron compounds $FeCl_3 \cdot 6H_2O$, $FeCl_3$, $FeCl_2 \cdot 4H_2O$, $Fe(\eta\text{-}C_5H_5)_2$, $Fe(acac)_3$, $Fe(OAc)_2$ and

Scheme 108



$Fe_2(CO)_9$ proved to be efficient catalysts for quinoline synthesis by the reaction of anilines **200** with propane-1,3-diol (**281a**) (Scheme 109).[120, 121] $FeCl_3 \cdot 6H_2O$ was found to be the best catalyst in this series. Quinolines **282** are formed in CCl_4 within for 8 h at 150 °C. Under similar conditions, the reaction of aniline with butane-1,3-diol (**281b**) produces a mixture of 2-methyl- (**264a**) and 4-methylquinolines **283a**.[121, 122] When other aniline derivatives are used in this reaction, mixtures of 2- and 4-methylquinolines **264** and **283** in 1 : (1–3) ratio are formed in 78%–95% total yield. In the case of *meta*-substituted anilines, the composition of the reaction mixture is more complicated, because isomeric 5- and 7-substituted 2-methylquinolines are formed (1 : 2 ratio).

Scheme 109



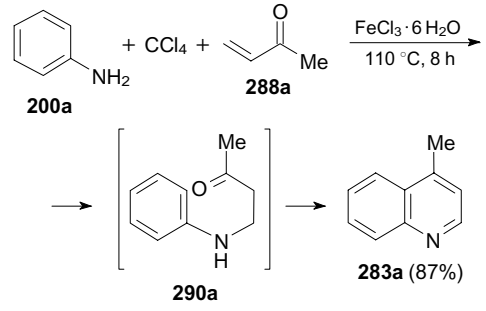
(*a*) $FeCl_3 \cdot 6H_2O$ (1 mol.%), 150 °C, 8 h;
R = H (**a**), Me (**b**); X = H, 2-Me, 3-Me, 4-Me, 2-Et, 2-Cl, 3-Cl, 4-Cl, 4-OMe (substituent positions are indicated for the substrate)

Two mechanisms have been proposed for the formation of 2-methyl- (**264a**) and 4-methylquinolines (**283a**) from aniline and butane-1,3-diol **281b** (R = Me) (Scheme 110).[122] According to one mechanism, the reaction starts with oxidation of 1,3-diol **281b** involving one hydroxyl group, which gives 2-hydroxybutanal (**284**) and 4-hydroxybutan-2-one (**285**). Next, these reactions react with aniline to form Schiff bases **286** and **287**. The subsequent heterocyclization, dehydration and dehydrogenation afford products **264a** and **283a**.

An alternative reaction pathway is possible: first, butane-1,3-diol is oxidized and dehydrated to give but-2-enal **272** and methyl vinyl ketone **288**, which subsequently react with aniline along two pathways, producting either compounds **289** and **290** (*in situ* Michael reaction) or Schiff bases **291** and **292**. Intermediates **289**–**292** undergo heterocyclization, dehydration and dehydrogenation to be converted to 2-methyl- (**264a**) and 4-methylquinolines (**283a**) (see Scheme 110).[122, 123] Similarly, the reaction of propane-1,3-diol gives unsubstituted quinoline **282a** as the only product.

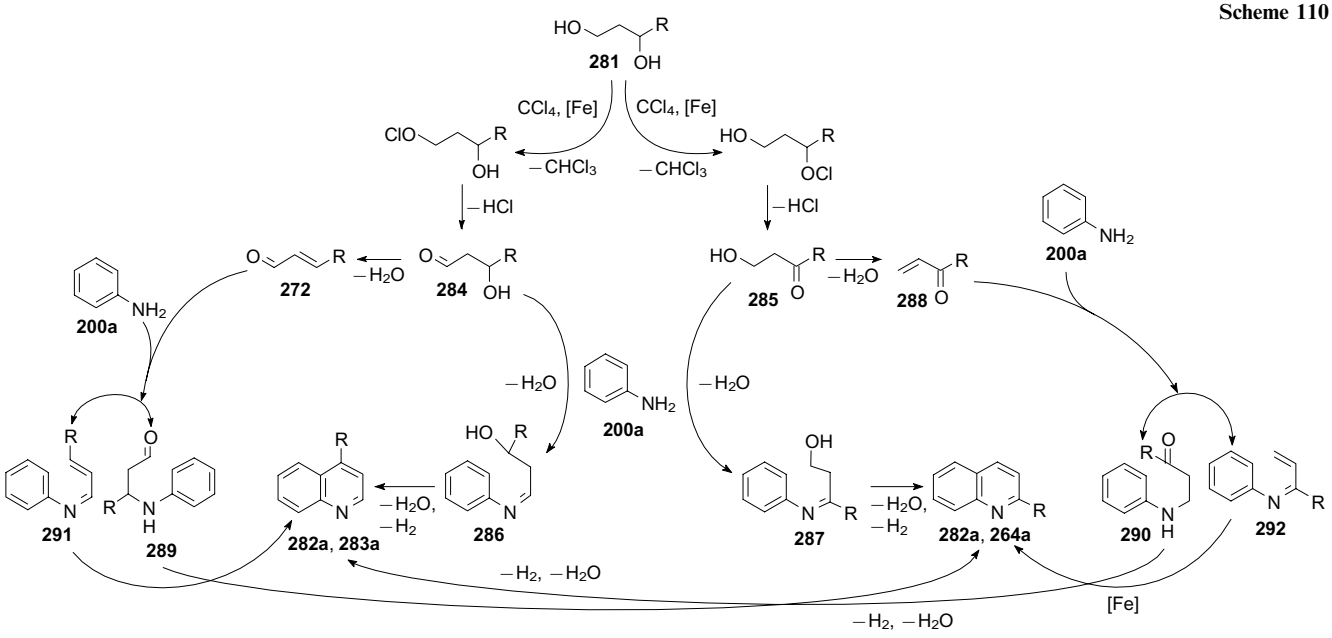
The control experiment with introduction of methyl vinyl ketone (**288a**) into the reaction afforded 4-methylquinoline (**283a**) in a high yield; this attests to the above-described reaction mechanism, which implies the formation of intermediate **290a** (Scheme 111).

Scheme 111

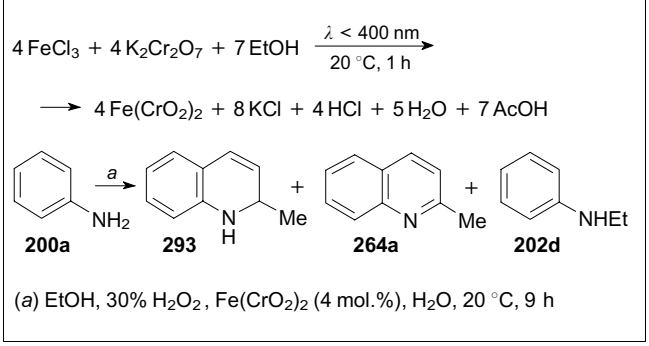


A one-pot tandem method was developed for the synthesis of substituted quinolines; the process includes selective catalytic oxidation of primary alcohols to aldehydes and their condensation with arylamines under the action of a suspension of $Fe(CrO_2)_2$ and 30% H_2O_2 at room temperature (Scheme 112).[124] Photoactivation was applied to accelerate the catalytic oxidation of alcohols. The $Fe(CrO_2)_2$ catalyst was obtained by photochemical synthesis. Under these conditions, aniline (**200a**) and ethanol react to give dihydroquinoline **293**, quinoline **264a** and *N*-ethylaniline (**202d**).

Scheme 110

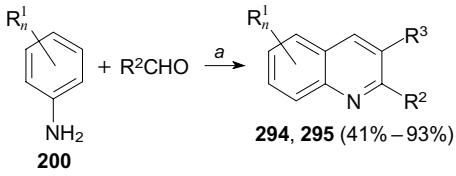


Scheme 112



Li *et al.*[125] proposed an atom-economic efficient method for the synthesis of 2-arylquinolines **294** and **295** by a multicomponent reaction of anilines **200** with aldehydes and alcohols catalyzed by iron compounds (Scheme 113). Among the tested catalysts [$Fe(acac)_3$, $FeCl_2$, $FeCl_3 \cdot 6H_2O$, $Fe(OTf)_2$], iron(III) chloride hydrate was the catalyst of choice. The reaction takes place in the presence of *p*-toluenesulfonic acid and KI, which are necessary to convert EtOH to EtI. The reaction is conducted using 0.66 mmol of aniline **200**, 0.30 mmol of aldehyde and 3 mL of ethanol or n-propanol.

Scheme 113



(*a*) R^3OH, $FeCl_3 \cdot 6H_2O$ (10 mol.%), TsOH (20 mol.%), KI (20 mol.%), O_2 (1 atm), 140 °C, 12 h; R^3 = Et, Pr^n; R^1 = 4-Cl: $R^2 = R^3_nC_6H_{5-n}$ (R^3_n = H, 4-Me, 4-OMe, 2-OMe, 4-Cl, 4-Br, 3-NO_2, 4-CN, 2,6-Cl_2, 3,4-$(OMe)_2$, 3,5-$(OMe)_2$), 2-Naph, 2-Th, 4-Py; R^2 = 4-$MeOC_6H_4$: R^1 = H, 4-Me, 2-Me, 4-OMe, 4-OPh, 4-F, 3-Cl, 4-CO_2Et, 4-NO_2, 3,4-Me_2 (substituent positions are indicated for the substrate); R^3 = H (**294**), Me (**295**)

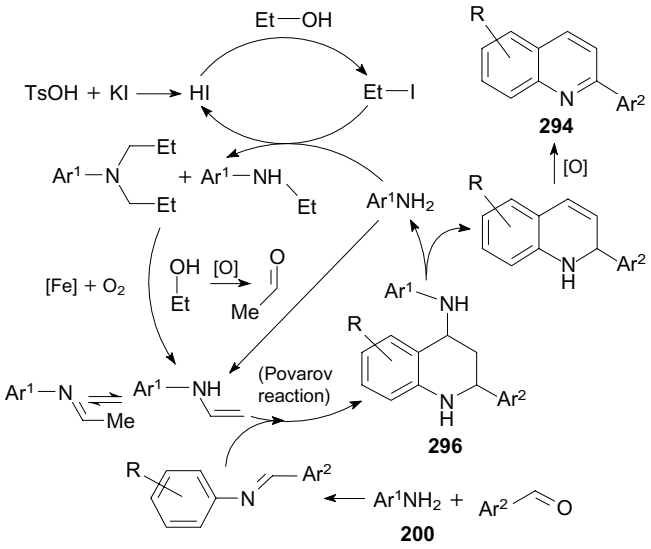
The process includes the following transformations: *N*-alkylation, alcohol oxidation to aldehyde with oxygen catalyzed by $FeCl_3 \cdot 6H_2O$ and the Povarov reaction to give compound **296** (Scheme 114). During the reaction, ethanol and n-propanol can be oxidized to aldehydes or converted to EtI and Pr^nI. Apart from the direct participation in the formation of substituted quinolines, EtOH and Pr^nOH act as solvents.

2-Phenyl-substituted quinolines **294a** and **295a**,**b** were synthesized by a $FeCl_3 \cdot 6H_2O$-catalyzed multicomponent reaction of benzylamine (**201a**), aniline (**200a**) and the corresponding alcohols in CCl_4 (Scheme 115).[126, 127]

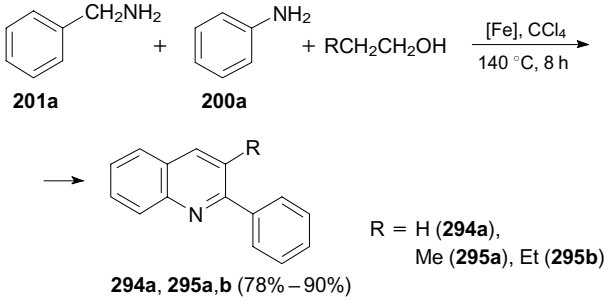
The authors believe that, by analogy with *N*-benzylidenebenzylamine **238a**,[103] the reaction of aniline (**200a**) with benzylimine **240a** *in situ* forms *N*-benzylideneaniline (**242a**), which reacts with aldehyde, also formed *in situ* upon the alcohol oxidation with CCl_4 under the action of the catalyst (Scheme 116).

Gopalaiah *et al.*[128] reported the development of a new approach to the design of 2-aryl- and 2-hetarylquinazolines **297**, which is based on the iron-catalyzed cascade reaction of 2-aminobenzylic alcohols **298** with benzyl- (**201**) and (hetarylmethyl)amines (**299**) in the presence of oxygen as the oxidant (Scheme 117). In the series of tested

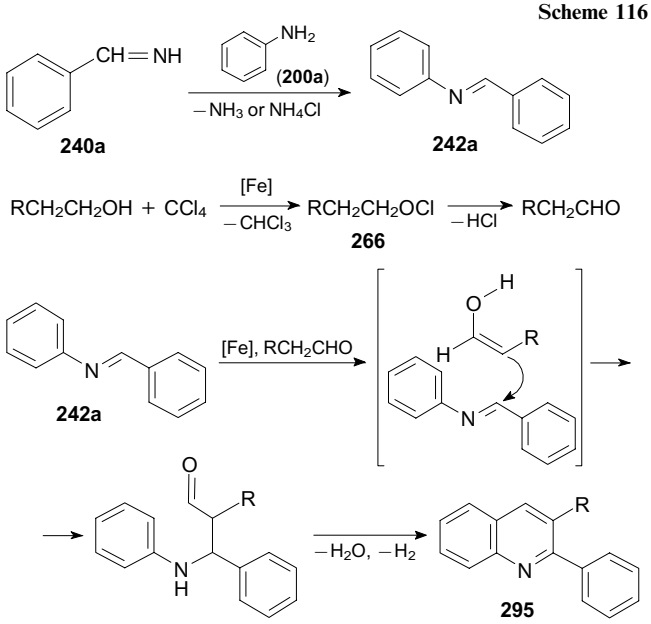
Scheme 114



Scheme 115

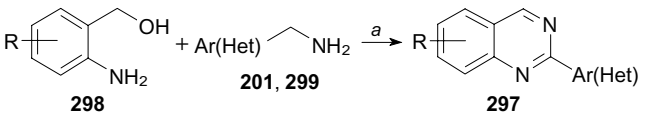


Scheme 116



iron-containing catalysts [FeF_2, $FeCl_2$, $FeBr_2$, $Fe(ClO_4)_2 \cdot xH_2O$, $FeCl_3$, $FeBr_3$, $Fe(acac)_3$], the best results were obtained for $FeBr_2$. In the case of iron(III) salts, the yield of quinazolines **297** did not exceed 35%. The reactions readily proceed in chlorobenzene (90% yield in 16 h) and toluene (76% yield in 24 h), while no reaction is observed in DMF or DMSO.

Scheme 117



(*a*) O_2, $FeBr_2$ (10 mol.%), PhCl, 110 °C, 16 – 24 h;
R = H, Alk, Hal (in different positions)

Scheme 118 depicts a putative reaction mechanism, which includes six steps. In the first step, condensation of benzylamine (**201a**) takes place to give benzylidenebenzylamine **238a** and ammonia. The latter is not removed from the system, but participates in the fourth step of the reaction, which affords bis-imine **300**.[128]

9. Unusual cyclization reactions

The application of iron-containing catalysts made it possible to perform quite a few unusual cyclizations giving not only quinolines, but also heterocyclic structures of other types.

Maiti *et al.*[129] prepared polyfunctional pyrroles **301** (Scheme 119). The four-component coupling of appropriate reactants — 1,3-dicarbonyl compounds, amines, aromatic aldehydes and nitroalkanes — is catalyzed by iron(III) salts.

Iron porphyrin complexes {[Fe(TPP)]X, **302**} catalyze the cycloaddition of aziridines **303** to aldehydes and ketones under mild conditions (25 – 60 °C, 1 h), giving rise to oxazolidines **304** (Scheme 120). The yields and the ratios of diastereometric products depend on the counter-ion (Note that the highest yield of product **304a** and stereoselectivity of the reaction, 97% and ~90%, respectively, were attained when the phenyl substituent in the porphyrin *meso*-positions was replaced by Ar = 3,5-$Bu^t_2C_6H_3$). The salts $FeCl_3$, $FeCl_2$ and $Fe(OAc)_2$ are inactive in this reaction, while $Fe(OTf)_2$ promotes the formation of an equimolar mixture of diastereomers.[130] When SbF_6 is used as the counter-ion (conditions *b*), the stereoselectivity of formation of oxazolidines **304** is 89% – 100%.

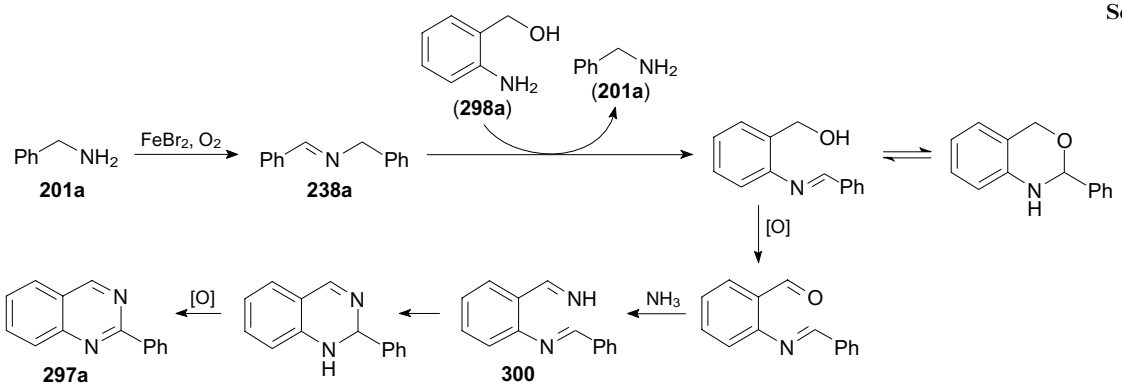
In the authors' opinion, cross-cyclization of aziridines **303** with aldehydes and ketones can follow a concerted or a stepwise mechanism (Scheme 121).

It was shown[131] that $Fe(OTf)_3$ promotes direct intramolecular dehydration of enantiomerically enriched secondary and tertiary alcohols **305** containing O-, N- and S-centred nucleophilic groups; the reaction results in the formation of practically valuable five- and six-membered heterocyclic compounds **306** with retention of 80% – 99% of the chirality (Scheme 122). The high value of this strategy was demonstrated in relation to the total synthesis of (+)-lentiginosine (**307**) — a competitive inhibitor of the enzyme amyloglucosidase — from D-glucose, where $Fe(OTf)_3$ was used at the key step.

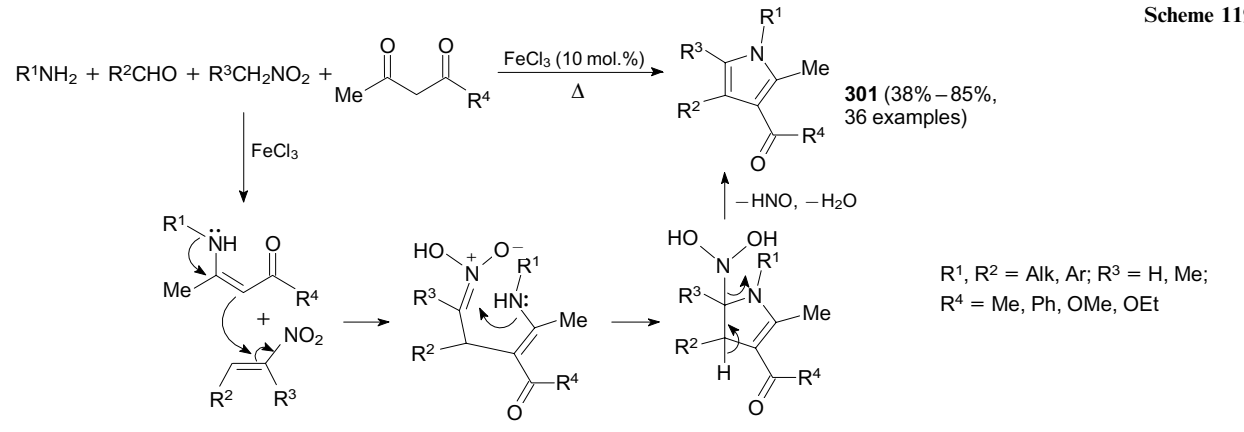
Yan *et al.*[93] carried out the synthesis of saturated nitrogen heterocycles **308** – **311** by the reaction of benzylamines **201** and *o*-phenylenediamine (**200d**) with diols **312a** – **c** and **268b** in the presence of iron complex **86** (Scheme 123).

The $FeCl_3 \cdot 6H_2O$-catalyzed reactions of butane-1,4- and pentane-1,5-diols with anilines **200** afford *N*-arylpyrrolidines **313** and *N*-arylpiperidines **314** in up to 88% yields (Scheme 124). The highest yields of products obtained on heating the reactants at 180 °C for 6 h were obtained in the case of aniline (R = H): 88% and 85% for compounds **313a**

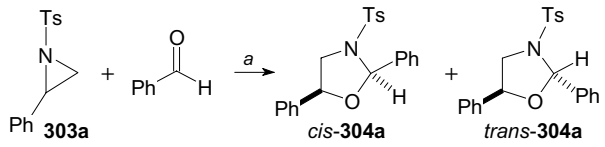
Scheme 118



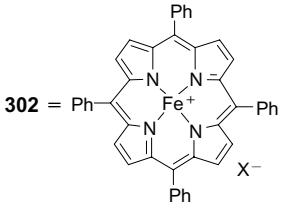
Scheme 119

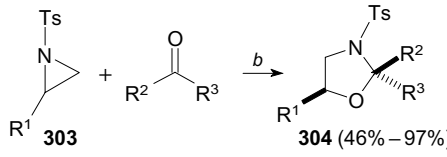


Scheme 120



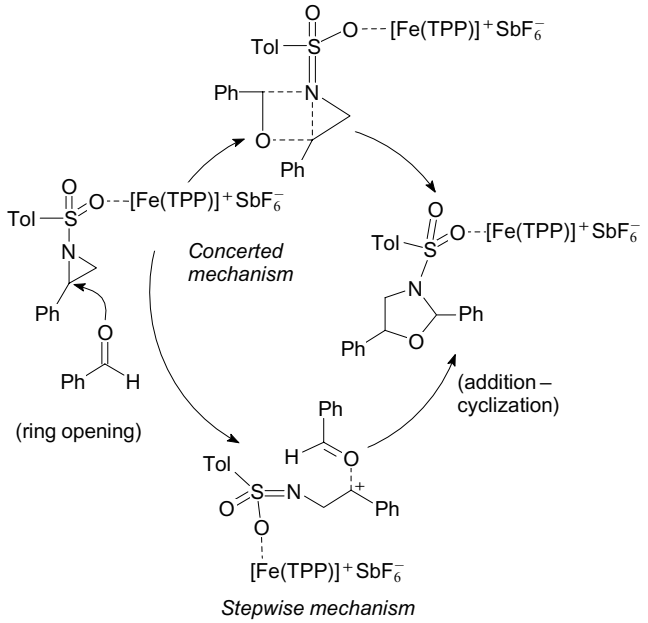
(*a*) **302** (1 mol.%), CH_2Cl_2, 25 °C, 1 h;
X = SbF_6 (87%, *cis* : *trans* = 50 : 1), OTf (30%, 20 : 1), ClO_4 (18%, 20 : 1), BF_4 (24%, 20 : 1), Cl (< 1%);





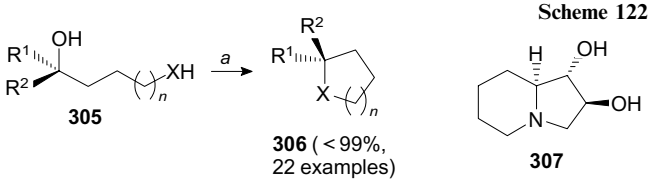
(*b*) $[Fe(TPP)]SbF_6$ (**302a**, 10 mol.%), CH_2Cl_2, 25 – 60 °C, 1 – 7 h;
R^1 = Me, Ph, 4-MeC_6H_4, 4-ClC_6H_4; R^3 = H: R^2 = H, Me, Et, Bu^t, Cy, Bn, Ph, 4-$MeOC_6H_4$, 4-ClC_6H_4, 4-$O_2NC_6H_4$;
$R^2 - R^3 = (CH_2)_n$ (n = 4 – 6)

Scheme 121



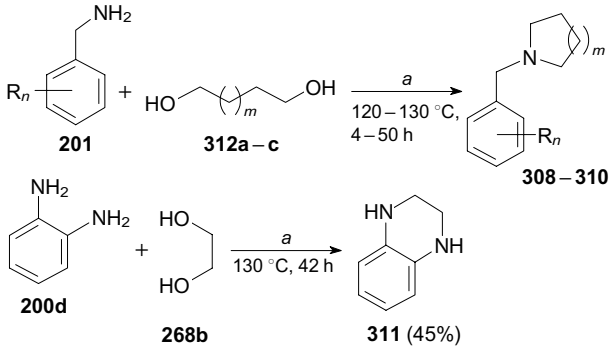
Tol = 4-MeC_6H_4

Scheme 122



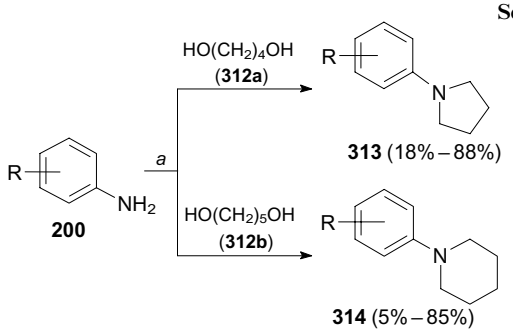
(*a*) $Fe(OTf)_3$, MS 3 Å ($-H_2O$); R^1 = Alk, Ar, propargyl;
R^2 = H, Alk, Ar; X = NAr, O, S; n = 1, 2; MS are molecular sieves

Scheme 123



(*a*) **86** (5 mol.%), Me_3NO (10 mol.%), CPME; m = 1 (**308**, **312a**), 2 (**309**, **312b**), 3 (**310**, **312c**); R_n = 3-F: m = 1 (60%), 2 (62%), 3 (67%); m = 3: R_n = 3-Cl (85%), 3-CF_3 (68%), 3-CF_3-5-Cl (66%)

Scheme 124



(*a*) $FeCl_3 \cdot 6H_2O$, CCl_4, 180 °C, 6 – 12 h; R = H, 2-Me, 3-Me, 4-Me, 2-Et, 2-Cl, 3-Cl, 4-Cl, 4-F, 3-OH, 3-OMe, 4-OMe

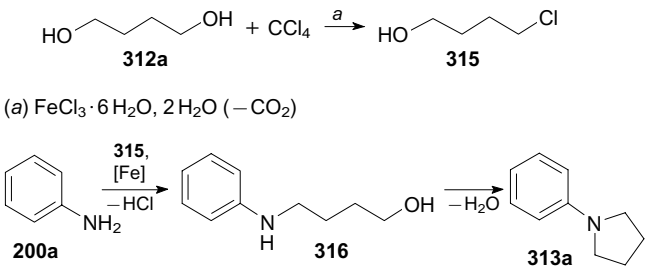
and **314a**, respectively. Aniline derivatives are less active in this reaction, irrespective of the electronic properties of substituents (electron-donating or -withdrawing ones).[132, 133] The catalyst : $PhNH_2$: diol : CCl_4 ratio is 0.5 : 100 : 200 : 30.

The heterocyclization with butane-1,4- and pentane-1,5-diols is most difficult for *p*-anisidine, which was attributed to its ability to chelate the iron ion through the NH_2 and OMe groups.

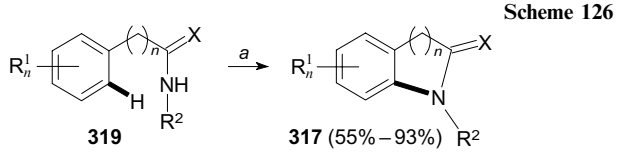
In view of detection of 4-chlorobutanol (**315**) in the reaction mixture, the authors proposed a mechanism that implies partial chlorination of butane-1,4-diol with carbon tetrachloride (Scheme 125). In the next step, chlorohydrin **315** reacts with aniline in the presence of $FeCl_3 \cdot 6H_2O$ to give *N*-phenylaminobutanol **316**, which undergoes intramolecular dehydration to give one mole of water and *N*-phenylpyrrolidine (**313a**). This mechanism is also supported by the control experiment with authentic chlorohydrin **315**, which reacts with aniline in the presence of the $FeCl_3 \cdot 6H_2O$ catalyst to give *N*-phenylpyrrolidine in a quantitative yield.

Henry *et al.*[134] described an efficient two-step method for the synthesis of benzoannulated heterocyclic systems **317**, **318** from arenes **319**, **320** (Scheme 126). In the first step, functionally substituted arenes **319** and **320** are iodinated at the *ortho*-position with *N*-iodosuccinimide (NIS) in the presence of $Fe(NTf_2)_3$. Then the intermediate iodoarenes **321** undergo intramolecular dehydroiodination under the action of CuI in the presence of a base (Cs_2CO_3) to give the corresponding indolines, dihydrobenzofurans and their six-membered analogues (Scheme 127; for X = 2 H, n = 1).

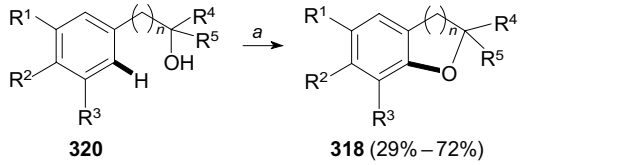
Scheme 125



Scheme 126

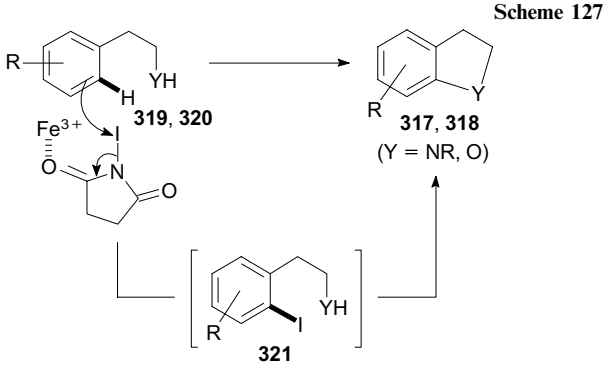


n = 1, 2; R^1_n = 3-OMe, 3,4-$(OMe)_2$, 3,5-$(OMe)_2$, 3,4,5-$(OMe)_3$, 3-OMe-4-Me, 3-NH_2, 3-NH_2-4-Cl, 3-NHAc, 3-NHAc-4-Cl; R^2 = H, Ac, Bz, Cbz, Boc, Ms, Ts; Ms is methanesulfonyl (mesyl)

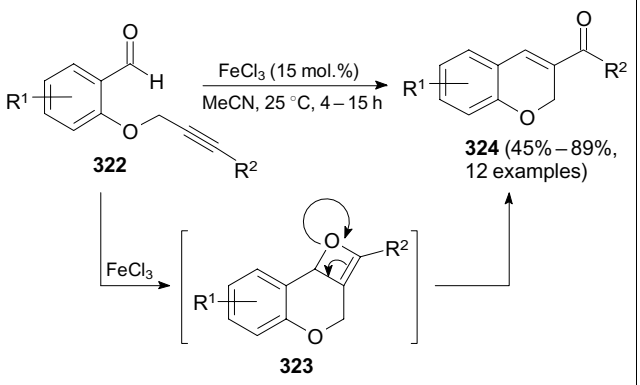


n = 1, 2; R^1 = OMe, NHAc; R^2, R^3 = H, OMe; $R^1 - R^2$ = OCH_2O, $O(CH_2)_2O$; R^4 = H, Me; R^5 = H, Me, Ph, 4-$MeOC_6H_4$, 4-ClC_6H_4; (*a*) 1) $FeCl_3$ (2.5 mol.%), [Bmim]NTf_2 (7.5 mol.%), NIS, PhMe, 40 °C, 5 h; 2) CuI (10 mol.%), DMEDA (20 mol.%), Cs_2CO_3, H_2O, 130 °C, 18 – 24 h; DMEDA is 1,2-dimethylethylenediamine

Scheme 127

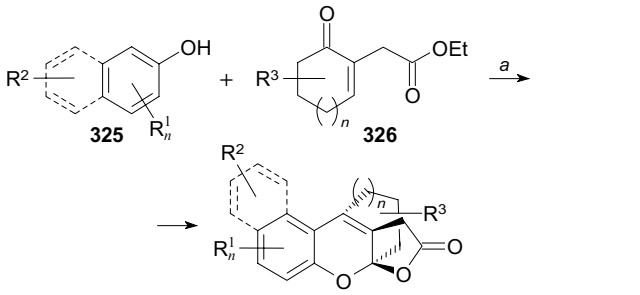


Scheme 128

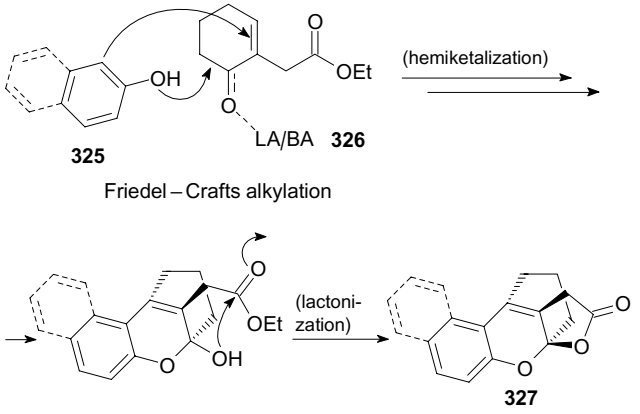


R^1 = Ph, OMe, Cl, Br (in different positions); R^2 = Alk, Ar

Scheme 129



(*a*) $Fe(OTf)_3$ (20 mol.%), DCE, 90 °C, 4 h; R^1_n = H, 4-Ph, 4-(1-Ad), 4-OMe, 3,4-$(OMe)_2$; R^2 = H, 6-OH, 6-Br, Alk; R^3 = H, Me; n = 0 – 2



LA is Lewis acid, BA is Lewis base

Bera *et al.*[135] reported a unique example of intramolecular alkyne – aldehyde metathesis of alkynyl ethers of salicylaldehyde **322** (Scheme 128). The $FeCl_3$-catalyzed reaction proceeds under mild conditions (at room temperature) and gives functionalized 2*H*-chromenes **324** *via* tricyclic intermediates **323**.

According to Borade *et al.*,[136] iron-containing catalysts induce cyclization of phenols and naphthols **325** and cyclic keto esters **326** to give polycyclic lactones **327** (Scheme 129). The formation of the latter includes the successive Friedel – Crafts alkylation of the aromatic ring – hemiketalization – lactonization (see Scheme 129 for $R^1 - R^3$ = H). The $Fe(OTf)_3$-catalyzed reaction includes the formation of three new chemical bonds, two new rings and three stereocentres. The yields of polycyclic bridged lactones **327** reach 76% – 87%.

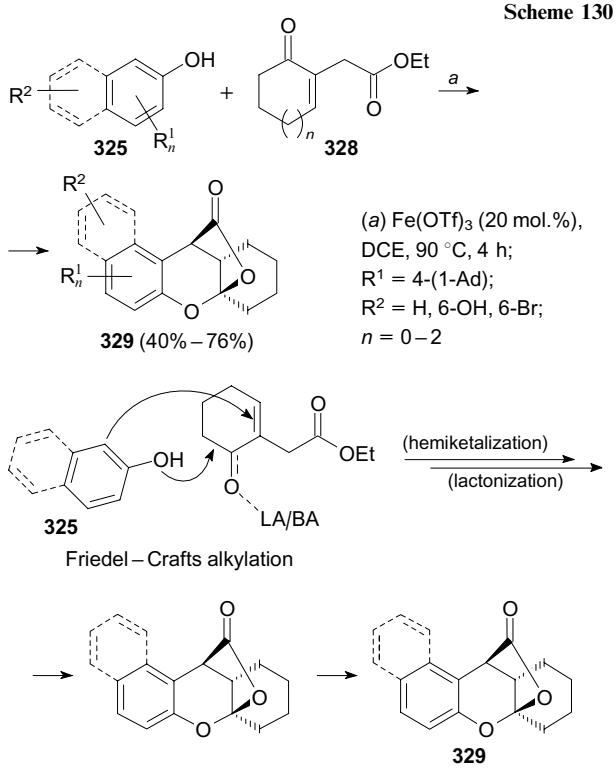
Under analogous conditions, cyclic keto esters **328** were converted to polycyclic lactones **329** (Scheme 130).

Iron(III) chloride catalyzes the one-pot regio- and diastereoselective [4 + 2]-cyclization of 2-hydroxy ketoxime ethers **330** with indol-2-ylamides **331** under mild conditions (Scheme 131). The reaction leads to the formation of 2-piperidone ring **332**.[137]

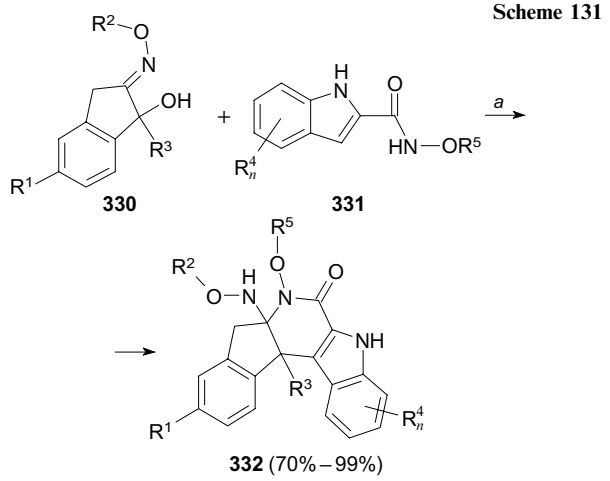
10. Iron-containing catalysts in the amidation reactions

Iron trichloride hexahydrate catalyzes the amidation of norbornene (**333**) on treatment with nitriles of various

Scheme 130



Scheme 131

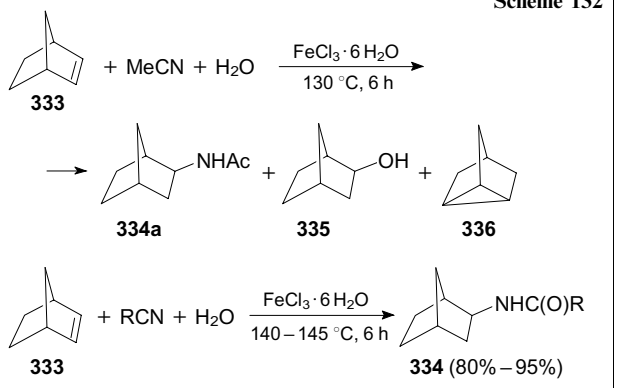


(*a*) $FeCl_3$ (5 mol.%), CH_2Cl_2, 40 °C, 3 – 30 min; R^1 = H, Br; R^2 = Me, TBS; R^3 = Me, XC_6H_4 (X = H, 3-Me, 4-Bu^t, 3-OMe, 4-Cl, 4-CF_3); R^4_n = H, 5-Me, 5-OMe, 5,6-$(OMe)_2$, 5-Cl, 5-F; R^5 = Me, Bn; TBS is *tert*-butyldimethylsilyl

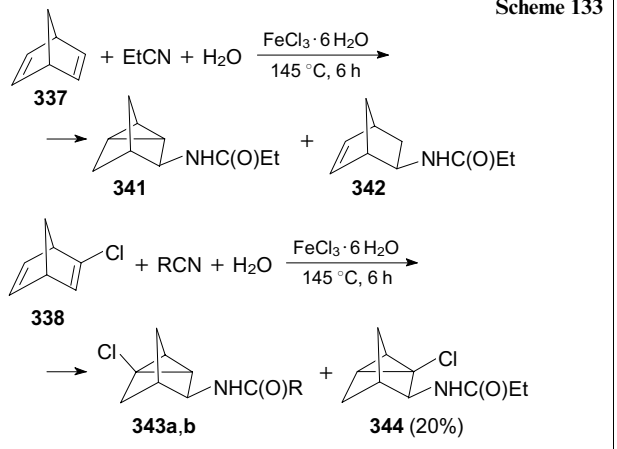
nature and water to give *N*-(*exo*-2-norbornyl)acylamides **334** (Scheme 132).[138] In the case of acetonitrile, the formation of compound **334a** was accompanied by formation of by-products **335** and **336** (total yield of 84%; **334a** : **335** : **336** = 10 : 1 : 1).

The $FeCl_3 \cdot 6H_2O$-catalyzed Ritter amidation with nitriles and water actively proceeds for norbornane type dienes: norbornadiene (**337**), 2-chloronorbornadiene (**338**), *exo-exo*-tetracyclo[6.2.1.1^{3,6}0^{2,7}]dodeca-4,9-diene (**339**), *endo-trans-exo*- and *exo-trans-exo*-pentacyclo[8.2.1.1^{4,7}.0^{2,9}.0^{3,8}]tetradecadienes **340** (Schemes 133, 134). The reactions occur at 145 °C within 6 h and give amides **341** and **342** (80% yield, 6 : 1) and **343a**,**b** and **344**, **345**, **346** in 35% to 87% yields.[139]

Scheme 132



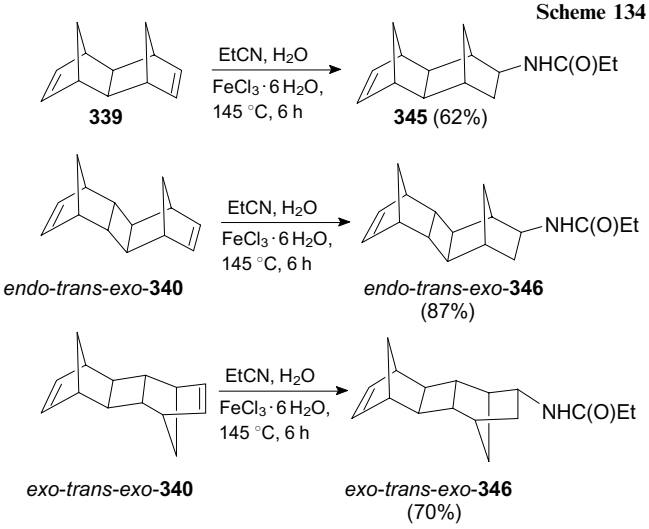
Scheme 133



It is noteworthy that amidation of 1,6- and 1,7-dienes selectively involves only one double bond despite their remote positions (Scheme 134).

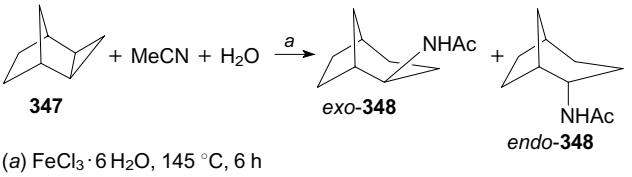
The $FeCl_3 \cdot 6H_2O$ catalyst proved to be efficient for the amidation of one more class of compounds, cyclopropane-containing polycyclic hydrocarbons, on treatment with organic nitriles. It is known that due to the internal strain, the three-carbon ring, has partial p character and easily forms a carbocation, which can attack RCN to give the corresponding amide.

Scheme 134



The amidation of tricyclo[3.2.1.$0^{2,4}$]octane (**347**) with acetonitrile and water in the presence of $FeCl_3 \cdot 6H_2O$ affords isomeric 2-*exo*- and 2-*endo*-acetamidobicyclo[3.2.1]octanes **348** in 1.25 : 1 ratio in a total yield of 90% (Scheme 135).[140]

Scheme 135

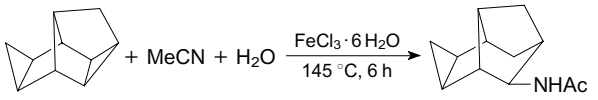


347 *exo*-**348** *endo*-**348**

(*a*) $FeCl_3 \cdot 6H_2O$, 145 °C, 6 h

Pentacyclo[4.4.0.0^{2,4}.0^{3,7}.0^{8,10}]decane (**349**), containing di- and trisubstituted cyclopropane moieties, behaves in an unusual way (Scheme 136). The amidation of this compound selectively involves the trisubstituted cyclopropane with C(2) – C(3) bond cleavage to give 2-acetamidotetracyclo[5.2.1.0^{3,8}.0^{4,6}]decane (**350**) with only *exo*-configuration.[140]

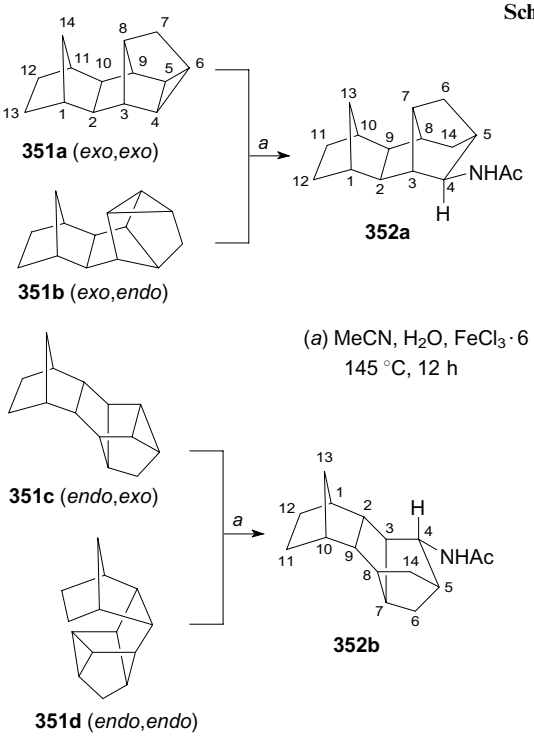
Scheme 136



349 **350** (71%)

The salt $FeCl_3 \cdot 6H_2O$ efficiently catalyzes the amidation of hexacyclo[9.2.1.0^{2,10}.0^{3,8}.0^{4,6}.0^{5,9}]tetradecanes (hydrogenated norbornadiene [4 + 2]-dimers) **351a – d** with acetonitrile. The reaction gives 4-*exo*-acetamidopentacyclo[8.2.1.1^{5,8}.0^{2,9}.0^{3,7}]tetradecanes **352a**,**b** (Scheme 137), which are formed upon selective C(4) – C(5) bond cleavage in the cyclopropane moiety of the substrates. It is noteworthy that hydrocarbons **351a**,**c** react with acetonitrile and water in the presence of $FeCl_3 \cdot 6H_2O$ without a skeletal isomerization and afford amides **352a**,**b** in 80% and 94% yields, respectively. Meanwhile, hydrocarbons **351b**,**d** containing the most shielded cyclopropane moiety undergo a skeletal rearrangement during the reaction to give the same amides **352a**,**b** (75% and 87% yields).[140]

Scheme 137



351a (*exo*,*exo*) **352a**

351b (*exo*,*endo*)

(*a*) MeCN, H_2O, $FeCl_3 \cdot 6H_2O$, 145 °C, 12 h

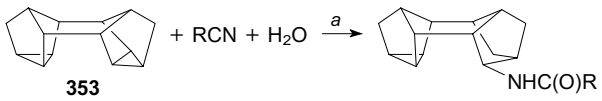
351c (*endo*,*exo*)

352b

351d (*endo*,*endo*)

Khusnutdinov *et al.*[141] reported the amidation of the heptacyclic norbornadiene dimer, binor-S (**353**), with acetonitrile, propionitrile, valeronitrile and benzonitrile in the presence of $FeCl_3 \cdot 6H_2O$ at 140 °C (Scheme 138). Although the binor-S molecule contains two three-membered rings, the reaction involves regioselective cleavage of the C(4) – C(5) bond in one of them and gives the corresponding *N*-substituted amides **354** in a good yield. The structure of the amides was established by X-ray diffraction. The binor-S : nitrile : water : catalyst ratio used by the authors was 20 : 300 : 20 : 1.

Scheme 138

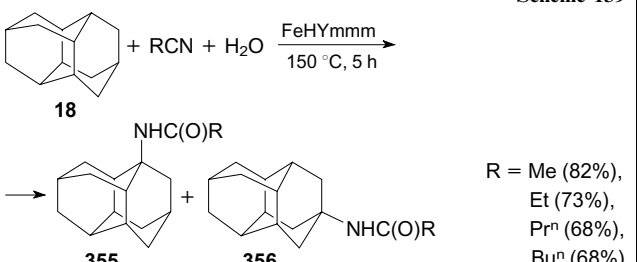


353 **354** (75% – 93%)

(*a*) $FeCl_3 \cdot 6H_2O$, 140 °C, 6 h;
R = Me, Et, Pr^n, Ph

Using iron compounds, the Ritter reaction could be extended to saturated hydrocarbons,[142] in particular to the second representative of the series of diamondoids, diamantane; similar reactions of this compound were considered in a review.[143] For example, FeHYmmm catalyzes the amidation of diamantane (**18**) with organic nitriles and water on heating to 150 °C (Scheme 139). The reaction proceeds in the presence of CBr_4 and gives isomeric amides **355** and **356** in 11 : 1 ratio.

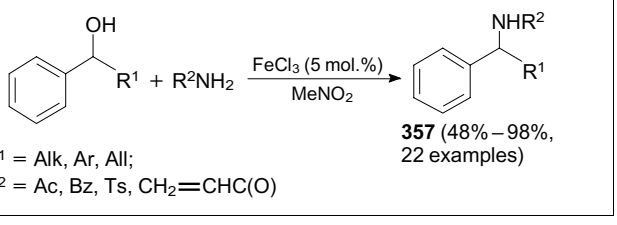
Scheme 139



18 **355** **356**

Iron(III) chloride catalyzes the amidation of benzylic and allylic alcohols with primary amides, which leads to the synthesis of compound **357** (Scheme 140).[144]

Scheme 140



357 (48% – 98%, 22 examples)

R^1 = Alk, Ar, All;
R^2 = Ac, Bz, Ts, CH_2=CHC(O)

11. Conclusion

The material presented in this review is a good illustration of abundant potential of iron compounds in the catalysis of

organic reactions. In view of the versatility, ready availability and low toxicity of iron compounds, one can hope that the scope of their application for the catalysis of known reactions and development of new reactions would be further expanded.

Evidently, the efforts of researchers would be directed towards increasing the activity and productivity of Fe-containing catalysts. As follows from this review, most of the considered reactions are catalyzed by iron compounds soluble in organic media taken in amounts of 1 mol.% – 10 mol.% relative to the reactants; this precludes separation of the catalyst from the reaction mixture components and reuse of the catalyst. The activity and productivity of iron-containing catalysts can be increased by using more efficient ligands, in particular *N*-heterocyclic carbene ligands, and by using immobilized forms prepared by deposition of iron compounds on solid supports — silica gels and zeolites of various types.

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