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One-pot α-ferrocenylalkylation of amines and alcohols with α-ferrocenyl substituted alcohols under acid-free conditions

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ABSTRACT

One-pot reaction of FcCH(R)OH with equimolar quantities of Bu^nLi and EtOCOCl followed by an excess of amine produces *N*-(α-ferrocenylalkyl)amines in up to 98% yields. Nitrogen heteroaryl amines undergo the α-ferrocenylalkylation at the amino group. The α-ferrocenylalkylation of alcohols and phenols (R'OH) leads to a formation of ethers FcCH(R)OR′ in lower yields. The reactions proceed *via* an intermediate formation of α-ferrocenylalkyl carbonates FcCH(R)OCOOEt. The side reactions associated with this protocol are discussed.

1. Introduction

In addition to their use in chemistry, ferrocene derivatives have found the applications in medicine [1], agriculture [2], and material sciences [3]. α-Ferrocenylalkylation is an important reaction in the chemistry of ferrocene for it provides preparations of a variety of ferrocene derivatives [4]. Typically, either quaternary ammonium salts derived from α-ferrocenylalkyl amines or α-ferrocenyl substituted alcohols are used as the α-ferrocenylalkylating reagents (Scheme 1) [4]. With the ammonium salts, the α-ferrocenylalkylation proceeds as a nucleophilic substitution at the C_α atom. The use of α-ferrocenyl substituted alcohols FcC(OH)RR' (Fc = ferrocenyl) as the ferrocenylalkylating agents is based on their ability to readily generate the α-ferrocenyl carbocations FcC^+RR' on the action of an acid, typically HBF_4 (aq.) [4,5].

Some other α-ferrocenylalkylation procedures reported up to date include the reactions of FcC(OH)RR′ in the presence of Lewis acids [**6**, 7], or cerium(IV) ammonium nitrate (CAN) [8], or "on water" [7]. In addition, the α-ferrocenylalkylation of azoles have been carried out by the reactions of FcC(OH)RR′ with *N,N*-carbonyldiimidazole [9,10], *N,N′*-thionyldiimidazole [10] or *N,N′*-thionyldibenzimidazole [10].

We have recently reported that α-ferrocenylalkyl carbonates **2** readily generated *in situ* from the α-ferrocenyl substituted alcohols **1** on the sequential action of the equimolar quantities of Bu^nLi and an alkyl chloroformate are ferrocenylalkylating reagents acting under acid-free conditions (Scheme 2) [11].

The α-ferrocenylalkylation with carbonates **2** is based on the spontaneous heterolytical breakdown of the C—O bond furnishing carbocation **3** and carbonate anion **4** (Scheme 2) [11]. The last one reversibly releases a carbon dioxide molecule yielding alkoxide anion **5** which deprotonates a pre-nucleophile NuH thus generating the nucleophile Nu^- (**6**) that reacts with carbocation **3** to form ferrocenylalkylation product **7**. All transformations above excepting the last stage are reversible. As one can see from Scheme 2, both the decay of the ferrocenyl carbonate and further transformations occur without the addition of an external base or acid, i. e. under acid-free conditions. This allows using the substrates NuH sensitive to acids in the reaction.

However, what about the substrates that are nucleophiles as is? Amines, alcohols, nitrogen heterocycles, etc. need not necessary to be deprotonated to enter the alkylation reactions. According to Scheme 2, when alkylating such substrates with ferrocenyl carbonates **2**, several nucleophiles ($R'O^-$, NuH, Nu^-) can

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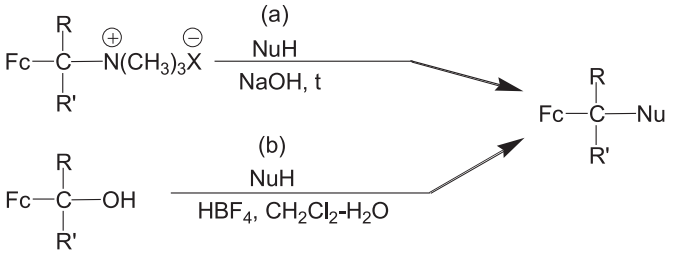
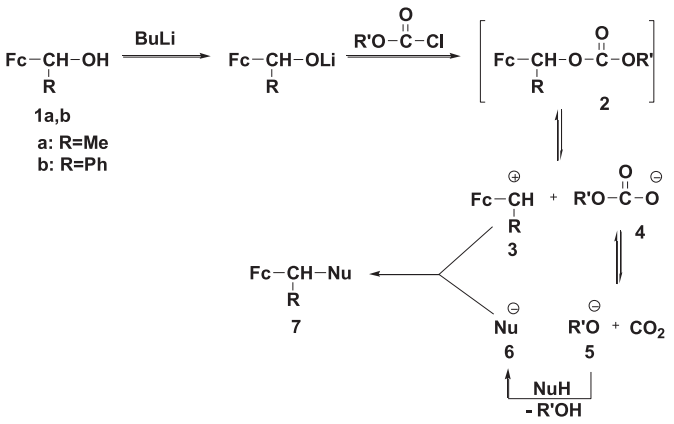


Scheme 1. α-Ferrocenylalkylation reactions using α-ferrocenylalkylammonium salts (*a*) or α-ferrocenyl substituted alcohols (*b*) (Nu – nucleophile).



Scheme 2. α-Ferrocenylalkylations with α-ferrocenylalkyl carbonates **2**.

simultaneously present in the reaction mixture, which can lead to the formation of a mixture of the products.

Herein, we report the use of ferrocenyl alcohols **1** for the one-pot α-ferrocenylalkylation of amines and alcohols *via* an intermediate formation of the (α-ferrocenylalkyl) carbonates **2** and discuss the unwanted competitive side processes accompanying the alkylation reactions.

2. Results and discussion

2.1. α-Ferrocenylalkylation of alcohols and amines

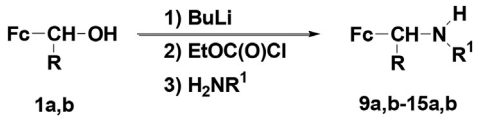
2.1.1. α-Ferrocenylalkylation of amines

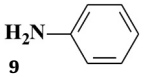
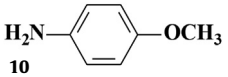
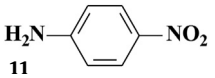
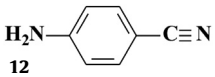
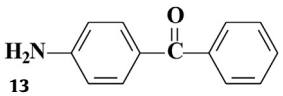
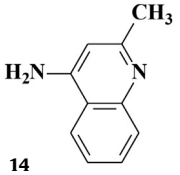
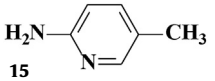
α-Ferrocenylalkylation of amines is a method for preparation of amines bearing a ferrocenyl group. Ferrocenyl substituted aromatic amines can be prepared from ferrocenyl carbinols and aniline or substituted anilines at elevated temperature [12] or by the reactions catalysed by an acid [13], $[(Cp)Fe(CO)_2]^+[OTf]^-$ [14], Bi(III) salts [15], cerium ammonium nitrate (CAN) [16] or Ca^{2+}-bentonite [17].

Aliphatic α-ferrocenylalkyl amines can be obtained by a direct aminomethylation of ferrocene [18], or by a nucleophilic substitution of either the acetoxy group in esters FcCH(R)OAc on the action of amines [19–21] or the cyano group in $FcCH(CN)NMe_2$ on the action of MeMgI [22]. In addition, the reductive amination of acetylferrocene with secondary amines in the presence of $Ti(OPr^i)_4$ or $NaBH_4$ also affords aliphatic α-ferrocenylalkyl amines [23].

In this paper, we report a one-pot preparation of α-ferrocenylalkyl amines from α-ferrocenyl substituted alcohols **1** under acid-free conditions. The reaction proceeds at room temperature *via* the intermediate formation of ethyl carbonates FcCH(R)OC(O)OEt (**8**). Since the reaction proceeds in a acid-free medium, this method avoids a protonation of the amine in a course of the reaction.

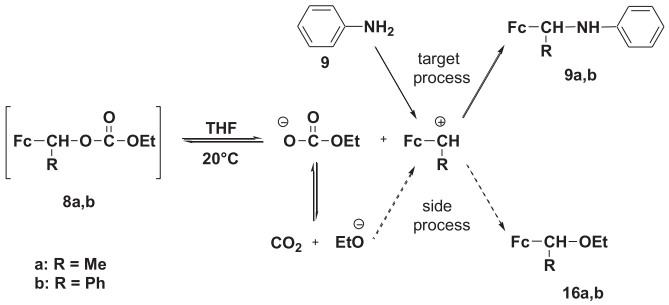
Table 1
One-pot α-ferrocenylalkylation of aryl and heteroaryl amines with ferrocenyl alcohols **1a,b**.



Entry	1	R	H_2NR^1	Product	Yield (%)[a]
1	**1a**	Me		**9a**	96 (98)
2	**1b**	Ph		**9b**	87 (96)
3	**1a**	Me		**10a**	54 (55)
4	**1b**	Ph		**10b**	80 (70)
5	**1a**	Me		**11a**	60 (85)
6	**1b**	Ph		**11b**	62 (65)
7	**1a**	Me		**12a**	67 (40)
8	**1b**	Ph		**12b**	67 (71)
9	**1a**	Me		**13a**	55 (42)[b]
10	**1b**	Ph		**13b**	47 (49)
11	**1a**	Me		**14a**	50 (59)
12	**1b**	Ph		**14b**	76 (34)
13	**1a**	Me		**15a**	39 (37)
14	**1b**	Ph		**15b**	65 (50)

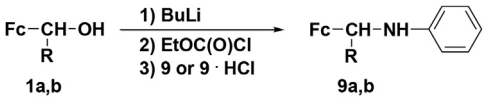
[a] Conditions: 2 eq. of amine, room temperature, 24 h, in THF. A yield of the product in the presence of $KHSO_4$ (2 eq.) is given in parentheses.
[b] Isolated as hydrochloride **13a**.HCl.

The results of α-ferrocenylalkylations of aryl and heteroaryl amines **9**–**15** substituted with both electron donating and withdrawing groups are summarized in Table 1. According to ^{1}H NMR data, the alkylation of heteroaryl amines **14,15** proceeds at the amino function. Specifically, the peaks of CH proton in $FcCHCH_3$ and FcCHPh moieties of heterocyclic derivatives **14a**, **15a** (4.54, 4.62 ppm) and **14b**, **15b** (5.35, 5.34 ppm) are very similar to that ones of the aniline derivatives **9a** and **9b** (4.40 and 5.14 ppm, respectively). In addition, unlike the quadruplet signal of CH in **9a**, the corresponding peaks of CH in **14a** and **15a** appears as



Scheme 3. The competitive target and side processes on the decomposition of FcCH(R)OC(O)OEt (**8a,b**) in the presence of $PhNH_2$ (**9**).

Table 2
α-Ferrocenylalkylation of $PhNH_2$ (**9**).



Entry	1	R	Substrate	Amount of 9 or 9 · HCl, eq.	t°C	Product	Yield (%)[a]
1	**1b**	Ph	9	1	20	**9b**	15
2	**1b**	Ph	9 · HCl	1	20	**9b**	19
3	**1a**	Me	9	2	20	**9a**	96 (98[b])
4	**1b**	Ph	9	2	20	**9b**	87 (96[b])
5	**1a**	Me	9 · HCl	2	20	**9a**	15
6	**1b**	Ph	9 · HCl	2	20	**9b**	40
7	**1b**	Ph	9	2	66	**9b**	55
8	**1b**	Ph	9 · HCl	2	66	**9b**	38

[a] In THF, 24 h.
[b] In the presence of $KHSO_4$ (2 eq.).

multiplets. Besides that, the signal of NH (5.56 ppm) in the spectrum of **14b** appears as the dublet.

One of the synthetic problems associated with this protocol of α-ferrocenylalkylation of amines is exemplified in Scheme 3 by the decomposition process of carbonates **8a,b** in the presence of **9**. As one can see, two nucleophiles, EtO^- and $PhNH_2$, are simultaneously present in the reaction mixture in this case. These nucleophiles are able to compete with each other for carbocation $Fc(R)CH^+$. Moreover, anion EtO^- can very effectively compete with the neutral $PhNH_2$ molecule in the nucleophilic attack. This should lead to a formation of ether FcCH(R)OEt (**16**) along with the target amine **9a** or **9b**. And this is the case.

The equimolar alkylation of **9** with **1b** produces amine **9b** in only 15% yield (Table 2). To avoid the side reaction, aniline hydrochloride (**9**·HCl) was taken instead of the free amine. It was assumed that EtO^- formed in the course of decomposition of the intermediate carbonate **8b** must first deprotonate the hydrochloride, thereby disappearing from the reaction mixture and releasing amine **9**, which would attack the carbocation **3** to give the desired product. However, with an equimolar ratio of the reagents, this resulted in only a slight increase in the yield of amine **9b** (19%). The use of a 2-fold excess of **9**·HCl notably increased the yield of **9b** (40%). However, much more effective was found to be the use of a 2-fold excess of amine **9** that resulted in 87% yield of **9b**. The reaction of **1b** with 2 eq. of **9** in the presence of 2 eq. of $KHSO_4$, which was supposed to protonate EtO^-, likewise **9**·HCl, lead to increasing the yield of **9b** to 96%. The reaction of **1a** with 2 eq. of **9** resulted in a formation of the alkylation product **9a** in 98% yield.

It should be specially stressed that the almost quantitative yields of the target amines **9a,b** in the reactions of **1a,b** with **9** is the conclusive proof that the *in situ* generation of carbonates **8a,b** from the parent alcohols **1a,b** occurs also quantitatively. This fact is important for a correct understanding that the alcohols FcCH(R)OH found out among the products of the α-ferrocenylalkylation reactions are not the parent alcohols **1a,b**, but arise in the course of unwanted side reactions (see below).

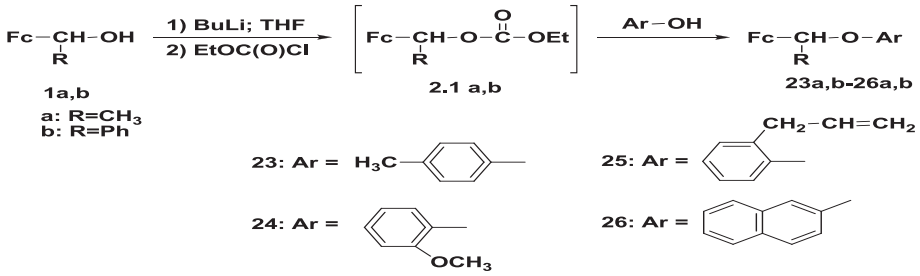
The α-ferrocenylalkylations of amines at higher temperature lead in the lower yields of the products.

The α-ferrocenylalkylation reactions of aliphatic amines (Et_2NH, Me_2NH) with alcohols **1a,b** (Table 3) furnish the corresponding ferrocenyl amines $FcCH(R)NR'_2$ (**17**, **18**). As one can see from Table 3, the yields of amines **17a,b** only slightly increase on going from 2-fold excess to 20-fold excess of Et_2NH. The alkylation products **18a,b** were obtained in higher yields than **17a,b**.

Table 3
α-Ferrocenylalkylation of aliphatic amines (Et_2NH, Me_2NH).

Entry	FcCH(R)OH	R	R′	FcCH(R)OH/amine molar ratio	Product	Yield[a], %
1	**1a**	Me	Et	1:2	**17a**	35
2	**1a**	Me	Et	1:2	**17a**	31[b]
3	**1a**	Me	Et	1:20	**17a**	38(67)
4	**1a**	Me	Et	1:20	**17a**	34(69)[b]
5	**1a**	Me	Me	1:20	**18a**	46(62)
6	**1a**	Me	Me	1:20	**18a**	47(73)[b]
7	**1b**	Ph	Et	1:2	**17b**	43
8	**1b**	Ph	Et	1:2	**17b**	51[b]
9	**1b**	Ph	Et	1:20	**17b**	49
10	**1b**	Ph	Et	1:20	**17b**	55[b]
11	**1b**	Ph	Me	1:20	**18b**	67(80)
12	**1b**	Ph	Me	1:20	**18b**	70(93)[b]

[a] Isolated yield, room temperature, 24 h, in THF. The yield calculated from the ^1H NMR spectrum of the reaction mixture after the hydrolytic workup followed by an extraction of the products is given in parentheses.
[b] A yield of the product in the presence of $KHSO_4$ (2 eq.).



Scheme 4. α-Ferrocenylalkylation of ArOH.

All in all, the use of 2-fold excess of the starting amine is sufficient to obtain the highest achievable yield of the α-ferrocenylalkylation product. As for $KHSO_4$, this salt only slightly and ambiguously affects on the yields of the alkylation products both in the case aromatic (Tables 1 and 2) and aliphatic amines (Table 3). This may be due to the poor solubility of $KHSO_4$ in THF.

2.1.2. α-Ferrocenylalkylation of alcohols

α-Ferrocenylalkylation of alcohols R'OH produces the corresponding ethers FcCH(R)OR'. To date, several methods for the preparation of such ethers have been reported.

The reactions of (*N,N*-dimethylaminomethyl)ferrocene iodomethylate with alcohols and phenols or alcoholates thereof at 90 °C produce the corresponding ethers in 40–80% yields [24,25]. Another reported method is the reaction of **1b** with a neat aliphatic alcohol in the presence of AcOH [13] or CAN [16]. However, in both cases, the reactions with branched alcohols (Pr^iOH, Bu^tOH) produced the symmetric ether, FcCH(Ph)OCH(Ph)Fc, solely. The authors explained this result by steric hindrances caused by bulky nucleophiles [16]. In addition, the ferrocenyl substituted ethers can be obtained by the reactions of ferrocenylcarbinols with alcohols and phenols catalysed by $[(Cp)Fe(CO)_2]^+[OTf]^-$ [26], $Yb(OTf)_3$ [27] or $InBr_3$ [6] along with the reaction of $FcCH_2OH$ with ArOH and diethyl azodicarboxylate in the presence of PPh_3 (Mitsunobu reaction) [28]. Ethers FcCH(R)OR' and $(FcCH(R))_2O$ have been reported to form in the reactions of $FcCH_2OCH=CH_2$ with alcohols and phenols in the presence of CF_3COOH [29] and, as the by-products, in the synthesis of ferrocenyl esters FcCH(R)OCH(R′)COOMe (R = H, Me, Ph) [30].

We studied the one-pot synthesis of FcCH(R)OR′ from **1a,b** and R'OH (R' = alkyl, aryl) in THF (20 °C, 24 h). Reactions of **1a,b** with ArOH (Scheme 4) produced aryl ethers FcCH(R)OAr (**19**) along with alcohols FcCH(R)OH and the traces of ethers FcCH(R)OCH(R)Fc (**20a,b**) as the by-products (^1H NMR data).

Aryl ethers **19** were found to undergo a partial decomposition during the column chromatography on Al_2O_3 (for a decomposition of ethers FcCH(R)OR' during a chromatography on silica gel see also: [16]). This may be due to the heterolytic breakdown of the C–O bond in these molecules resulting in a formation of relatively stable $Fc(R)CH^+$ and ArO^- ions. As a result, only 4-tolyl ethers **19** (Ar = 4-MeC_6H_4) were isolated in moderate yields (47% for R = Ph; 56% for R = Me). Aryl ether **19** (Ar = 2-$MeOC_6H_4$, R = Ph) was isolated in 29% yield. All our attempts to isolate pure products **19** (Ar = 2-(allyl)C_6H_4, 2-naphthyl; R = Me, Ph) from the reactions with 2-allylphenol and β-naphthol failed.

In the reactions with ArOH (Scheme 4), the intermediate anion EtO^- rapidly and irreversibly deprotonates ArOH (i. e. NuH) acting as base **5** in Scheme 2. Thus, three nucleophiles (EtOH, ArOH, ArO^-) capable to compete with each other in nucleophilic reactions are simultaneously present in the reaction mixture. The absence of ethers **16a,b** among the reaction products indicates that EtOH can not effectively compete as the nucleophile with ArO^- and ArOH.

Unlike the reactions with ArOH, there is the next equilibrium in the reactions of **1a,b** with alkyl alcohols AlkOH:

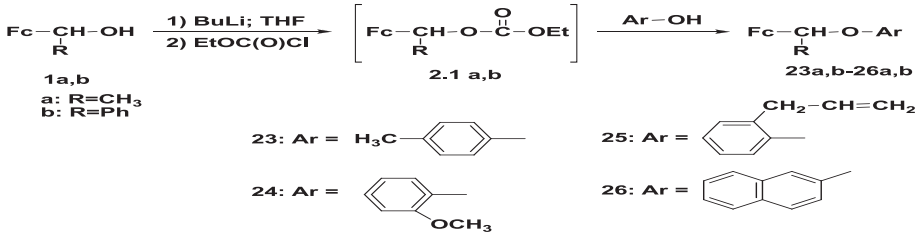
$$EtO^- + \rightleftarrows EtOH + AlkO^-$$

with the balance depending on the relative basicity of EtO^- and $AlkO^-$. As a result, four nucleophiles (EtO-, AlkO-, AlkOH and EtOH) that can compete with each other for the carbocation **3** (Scheme 2) are simultaneously present in the reaction mixture. Therefore, it is imperative for the α-ferrocenylalkylation of AlkOH to use a large excess of AlkOH to increase the selectivity of the reaction and obtain higher yields of the target ethers FcCH(R)OAlk.

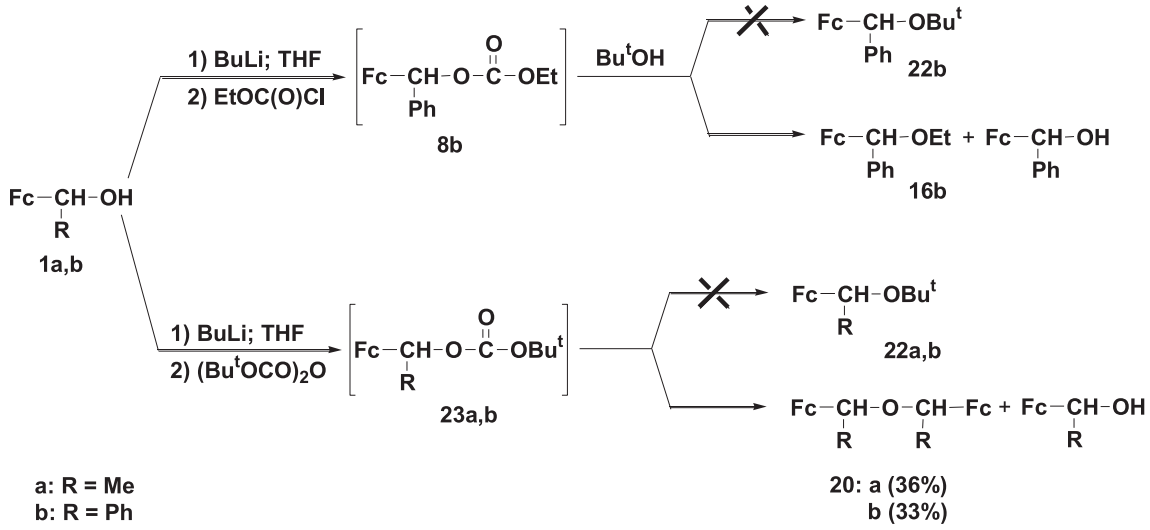
Therefore, 25-fold excess of Pr^iOH was used in its reaction with **1a,b** to obtain ethers $FcCH(R)OPr^i$ (**21a,b**) in good yields (Scheme 5). The result shows an applicability of this protocol for a preparation of ferrocenyl ethers from AlkOH including the alcohols with branched alkyl groups. In the reaction of **1a,b** with Pr^iOH, anion EtO^- generated *in situ* from the intermediate carbonates **8a,b** does not significantly compete with Pr^iOH for carbocation **3**, apparently, because of the low concentration of EtO^- in the reaction mixture compared to that one of Pr^iOH.

We also tried to synthesise *tert*-butyl ethers $FcCH(R)OBu^t$ (**22**) that have not been reported up to date. However, the reaction of **1b** with Bu^tOH (Scheme 6) furnished the mixture of **16b** and FcCH(Ph)OH instead of **22b**. Ether **16b** is formed from the intermediate carbonate **8b** as a result of the side process depicted in Scheme 3; as for FcCH(Ph)OH, see below section 2.1.3.

So, an attempt was made to prepare ethers **22** by a decomposition of *tert*-butyl carbonates **23a,b** (Scheme 6) in the absence of



Scheme 5. α-Ferrocenylalkylation of Pr^iOH.



Scheme 6. The unsuccessful attempts to prepare FcCH(R)OBu^t (**22**).

an external nucleophile. It was expected that the interaction of alkoxide anion **5** (R' = Bu^t) with carbocation **3** (Scheme 2) should lead to a formation of ethers **22** similar to a formation of ethers **16** on the decomposition of carbonates **2** (R' = Et) in the absence of NuH [11]. However, the decomposition of carbonates **23** generated *in situ* from FcCH(R)OLi and Boc_2O furnished the mixture of ethers **20** and FcCH(R)OH (Scheme 6). The mechanism of their formation is discussed in section 2.1.3.

Unlike aryl ethers **19**, alkyl ethers FcCH(R)OAlk do not decompose on chromatography and can be easily separated from the other reaction products by chromatography on Al_2O_3.

2.1.3. Ferrocenylalkylation and competitive side reactions

Thus, ferrocenylalkylations *via* the intermediate formation of α-ferrocenylalkyl carbonates result in the target products along with some by-products. This is because of the transformations depicted in Scheme 2 can be accompanied by a spectrum of side processes. These side reactions are of particular significance in the case of such substrates NuH as alcohols, amines, etc., which exhibit nucleophilic properties without preliminary deprotonation and can react with carbocations **3** as is. In these cases, two nucleophiles, NuH and alcoholate ion **5**, are simultaneously present in the reaction mixture and compete with each other both for α-ferrocenylcarbocation **3** and for participation in side processes.

An overview of the α-ferrocenylalkylations using reagents of general formulae FcCH(R)OC(O)X **(24)** including α-ferrocenylalkyl carbonates and relative compounds prone to the heterolytic decay producing cation **3** and anion XC(O)O$^-$ (**25**) along with the competitive side reactions are shown in Scheme 7. It is required of X that it would ensure that CO_2 to be released from **25** furnishing anion X$^-$ possessing strong both basic and nucleophilic properties (RO$^-$, R_2N^-, etc.). Then, the possible side reactions (paths *a*-*e*) accompanying the α-ferrocenylalkylation process and the corresponding products are as follows:

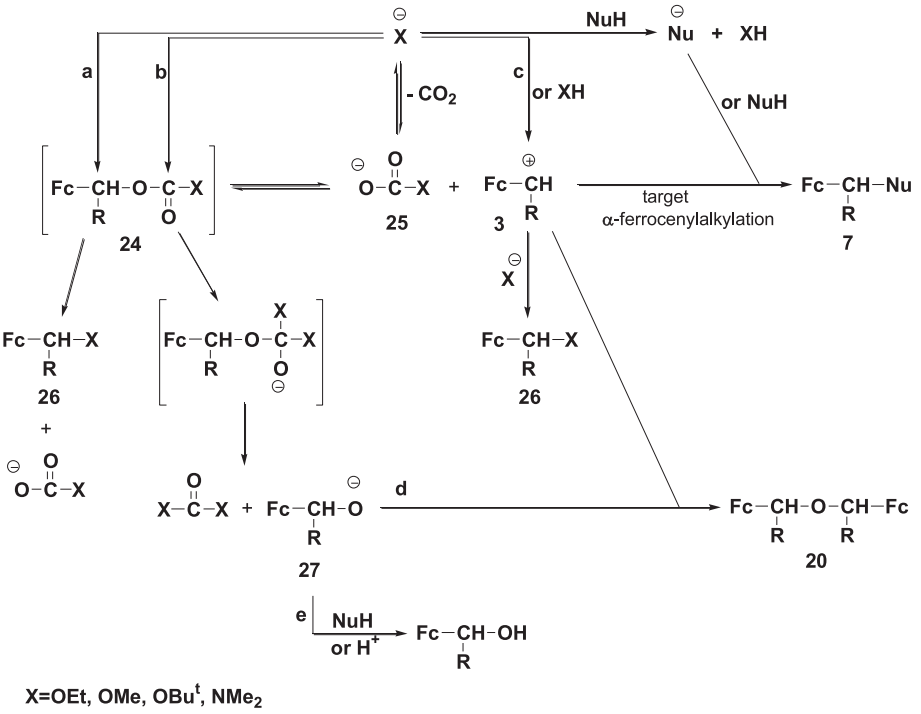
(a) the nucleophilic attack of anion X$^-$ on the C_α carbon atom in carbonyl compound **24** resulting in product **26**. This process is more likely to occur at the earlier stages of the ferrocenylalkylation reaction when the concentration of compound **24** in the reaction mixture is still high;
(b) the nucleophilic attack of X$^-$ on the carbonyl carbon in compound **24** resulting in the release of alcoholate anion FcCH(R)O$^-$ (**27**) that produces FcCH(R)OH on the subsequent hydrolytic work-up of the reaction mixture (see also path *e*). As one can see, product FcCH(R)OH is identical to starting alcohol **1** taken for the *in situ* generation of reagent **24**. Thus, this process explains the presence of FcCH(R)OH among the reaction products after a hydrolysis of the reaction mixture despite the quantitative formation of carbonyl reagents **24** (see above);
(c) reacting the anion X$^-$ (or XH) with carbocation **3** resulting in the formation of product **26** (i. e. ether or amine, if reactant **24** is a carbonate or carbamate);
(d) reacting of alcoholate anion **27** with carbocation **3** resulting in the formation of bisferrocenyl ether **20**;
(e) in addition, anion **27** can deprotonate the pre-nucleophile NuH to form nucleophile Nu$^-$ and alcohol FcCH(R)OH identical to the product of path *b*.

Both a composition and ratio of the products in the α-ferrocenylalkylation reactions can be easily monitored by ^{1}H NMR spectra of the reaction mixtures after hydrolysis, extraction of the products, and evaporation of the solvent. In various experiments, we actually identified the products of all side reactions mentioned above.

For example, the reactions of **1a,b** with 2 eq. of Et_2NH proceeding through the intermediate formation of carbonates **8a,b** produced the mixture of **17a,b** and FcCH(R)OH in 1: 0.58 (for **17a**) and 1: 0.16 (for **17b**) ratios along with the traces of **16a,b** (**a:** R = Me; **b:** R = Ph) and FcCH = CH_2 (in the case of **1a**), the product of an elimination of the proton from the intermediate carbocation Fc$(CH_3)CH^+$.

In the reaction of **1a** with Et_2NH, the use of 20 eq. of the amine increased the FcCH(Me)NEt$_2$: FcCH(Me)OH ratio up to 1: 0.49. Further increase took place in the presence of 2 eq. of $KHSO_4$ (1: 0.37). The similar results were obtained with Me_2NH. Thus, an excess of the amine increases the efficiency of the target alkylation, and the presence of $KHSO_4$, a proton donor, hinders the competitive reaction of anion EtO$^-$ (Scheme 3, path *b*). The results are consistent with what is expected.

It is obviously that a composition of the products of the α-ferrocenylalkylation process must depend on the ratio of the rates of the target and side reactions, as well as on the ratio of the rates of the forward and reverse reactions in the reversible stages. Specifically, the composition of the reaction products must be affected by



Scheme 7. α-Ferrocenylalkylation of NuH with FcCH(R)OC(O)X and competitive side reactions.

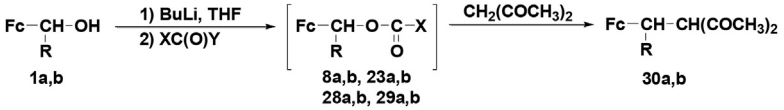
the nucleophilicity of X^-, the base formed on the decomposition of the intermediate carbonyl compound **24**, because of its nucleophilicity should influence the decay rates of both the carbonyl compound **24** and anion **25**. In addition, the basicity and nucleophilicity of X^- should affect the NuH deprotonation rate and the equilibrium position in the reversible stages, as well as the efficiency of the side reactions involving X^-.

To demonstrate the influence of the nature of base X^- on the side reactions and, hence, the composition of the products, methyl carbonates **28a,b**, ethyl carbonates **8a,b**, *tert*-butyl carbonates **23a,b**, and carbamates **29a,b** generated *in situ* by an addition to a solution of **1a,b** in THF of the equimolar quantities of Bu^nLi followed by MeOC(O)Cl, EtOC(O)Cl, Boc_2O or $Me_2NC(O)Cl$, respectively, were entered the reaction with acetylacetone that was chosen as the pre-nucleophile NuH (Table 4).

Any of the bases X^- (MeO^-, EtO^-, Bu^tO^-, Me_2N^-) appearing in the reaction mixture during the decomposition of the intermediate carbonyl compounds can easily deprotonate acetylacetone with a formation of the nucleophilic anion. Thus, the nature of the base should not affect the deprotonation stage, but it have to affect some stages of both the target α-ferrocenylalkylation (for example, a decay of anion $XC(O)O^-$ into X^- and CO_2) and side processes (Scheme 7). As show the data from Table 4, the nature of anion X^- has a pronounced effect on the yield of the ferrocenylalkylation products. The highest yields of the target products were achieved in the case of ethyl carbonates **8a,b**. Excepting methyl carbonate **28a,b**, the higher the nucleophilicity of X^-, the lower the yields of the α-ferrocenylalkylation products regardless of the group R, which is due to the occurrence of the side reactions. Obviously, the higher nucleophilicity of Bu^tO^- and Me_2N^- hinders the decay of the corresponding carbonate and carbamate anions **25** but facilitates the nucleophilic attacks of these anions on the carbonyl group of compounds **24** (Scheme 7, path *b*) leading to a formation of anion **27** that can not participate in a formation of target product **7**.

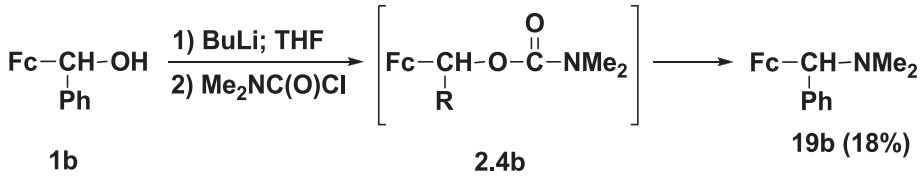
As for the methyl carbonates **28a,b**, anion MeO^- is a weaker nucleophile than EtO^-. Therefore, anion $MeOCOO^-$ formed as a

Table 4
α-Ferrocenylalkylation of acetylacetone with carbonyl compounds **8a,b**, **23a,b, 28a,b, 29a.b**.



Entry	FcCH(R)OH	R	X	Y	Carbonyl interme-diate	Product	Yield[a], %
1	**1a**	Me	OEt	Cl	**8a**	**30a**	70
2	**1b**	Ph	OEt	Cl	**8b**	**30b**	76
3	**1a**	Me	OMe	Cl	**28a**	**30a**	43
4	**1b**	Ph	OMe	Cl	**28b**	**30b**	46
5	**1a**	Me	OBu^t	$OC(O)OBu^t$	**23a**	**30a**	14
6	**1b**	Ph	OBu^t	$OC(O)OBu^t$	**23b**	**30b**	18
7	**1a**	Me	NMe_2	Cl	**29a**	**30a**	traces
8	**1b**	Ph	NMe_2	Cl	**29b**	**30b**	traces

[a] Conditions: 3 eq. of acetylacetone, room temperature, 24 h, in THF.



Scheme 8. Decomposition of carbamate **30b** in the absence of an external nucleophile.

result of the heterolylic decay of **28a,b** (see Scheme 7) dissociates to CO_2 and MeO^- faster than does anion $EtOCOO^-$ in the case of ethyl carbonates **8a,b**. In addition, the equilibrium in a reversible process: $R'OCOO^- \leftrightarrow R'O^- + CO_2$ is shifted more right for R' = Me than for R' = Et. So, MeO^- appears in the reaction mixture at the earlier stage of the reaction than EtO^- (i. e. at higher concentration of the undissociated parent carbonate **28** in the reaction mixture) and, in addition, its concentration is higher than that one of EtO^-. All of these make the side nucleophilic attack of MeO^- on the carbonyl group in the parent carbonate **23** more effective than in the case of EtO^-, thus leading to a higher yield of the "starting" alcohol FcCH(R)OH and, hence, to a lower yield of the α-ferrocenylalkylation product **30**.

Thus, it is most preferable to use ethyl carbonates in the α-ferrocenylalkylation reactions.

"Hard" amide ion Me_2N^- is the strongest nucleophile among the discussed X^-. This increases the efficiency of its attack on the carbonyl group (Scheme 7, path *b*). As a result, alcohol FcCH(R)OH is the major reaction product, amine $FcCH(R)NMe_2$ is the minor one, and the target ferrocenylalkylation product **30** is formed in traces. Meanwhile, spontaneous decomposition (20 °C, 24 h) of carbamate **29b** in the absence of an external nucleophile (Scheme 8) leads to a formation of amine **18** (18%) along with alcohol FcCH(R)OH and traces of ether **20** (R = Ph).

Path *d* (Scheme 7) leading to a formation of bisferrocenyl ethers **20a,b** is illustrated by a decomposition of *tert*-butyl carbonates **23a,b** in the absence of an external nucleophile (Scheme 6).

3. Conclusion

Thus, one-pot reactions of α-ferrocenylalkyl alcohols **1a,b** with Bu^nLi, EtOCOCl and an excess of amine, phenol or alcohol result in a formation of the corresponding *N*-(α-ferrocenylalkyl) amines or ethers in moderate to 98% yields. The reactions proceed *via* the intermediate formation of α-ferrocenylalkyl carbonates **8a,b** under acid-free conditions at the α-ferrocenylalkylation step. Nitrogen heteroaryl amines undergo the selective α-ferrocenylalkylation at the amino group. The competitive side reactions associated with this protocol were discussed and their occurrence was proved by the identification of the predicted side products in the reaction mixtures.

4. Experimental section

4.1. General

^1H and ^{13}C NMR spectra were recorded on a Bruker Avance™400 spectrometer (400.13 MHz for ^1H). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform: δ 7.28 ppm for ^1H and 77.0 ppm for ^{13}C). Data are reported as follows: chemical shifts (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (*J*, Hz). Mass spectra were recorded on a Finnigan Polaris Q instrument (EI, 70 eV, ion trap). Elemental analyses (excepting Fe) were performed using a Carlo-Erba CE-1106 elemental analyzer; the contents of Fe were determined by an X-ray fluorescence (XRF) method using a VRA-30 XRF-spectrometer. Melting points were determined with an Electrothermal 1002 MEL-TEMP® capillary melting point apparatus and are uncorrected. TLC was performed on Silufol UV-254 plates; the spots were visualized in camera with iodine. Column chromatography was performed using aluminum oxide (Brockmann Activity III).

All reactions were carried out in an argon atmosphere. All solvents were purified (dried and distilled) before use according to literature methods. EtOCOCl, MeOCOCl, Boc_2O, Me_2NCOCl, $HNEt_2$, Pr^iOH, 2-methoxyphenol, 2-naphthol, 2-allylphenol and compounds **9**–**15** are commercially available (Aldrich). Alcohols **1a,b** were prepared by a reduction of the corresponding carbonyl compounds with $LiAlH_4$ in Et_2O [31,32].

4.2. α-Ferrocenylalkylation of amines with *1a,b*

4.2.1. α-Ferrocenylalkylation of Et_2NH

A hexane solution of Bu^nLi (1 eq.) was added to a solution of **1a,b** (150 mg) in THF (15 ml) and the mixture was stirred for 5 min. Ethyl chloroformate (1 eq.) was added to the mixture in one portion followed by 5 min stirring and, if specified, addition of $KHSO_4$. Diethyl amine (2 eq.) was added after 5 min stirring and the mixture was stirred for additional 24 h at room temperature. The reaction mixture was quenched with 5% aqueous solution of HCl (15 ml) and diethyl ether (10 ml) was added. The organic layer was separated and washed with 5% aqueous solution of HCl (3 × 15 ml). The combined acidic solutions were extracted with diethyl ether (20 ml), alkalized with aqueous ammonia to pH = 10 and extracted with diethyl ether (3 × 15 ml). The ether extracts were combined, dried over Na_2SO_4 and the solvent was evaporated to afford pure product.

*4.2.1.1. Diethyl(1-ferrocenylethyl)amine (**17a**) [23].* Product **17a** was obtained from the reaction without $KHSO_4$ (65 mg, 35%) or in the presence of $KHSO_4$ (55 mg, 31%) as brown oil. The same reaction with 20 eq. of Et_2NH afforded 71 mg (38%) of **17a** in the absence of $KHSO_4$ and 63 mg (34%) of **17a** in the presence of $KHSO_4$. ^1H NMR: 0.98 (t, 6H, $^3J = 7.1$, **CH₃**–CH_2–N); 1.40 (d, 3H, $^3J = 6.8$, **CH₃**–CH); 2.14–2.22 (m, 2H, CH_3–**CH₂**–N); 2.37–2.46 (m, 2H, CH_3–**CH₂**–N); 3.86 (q, 1H, $^3J = 6.8$, CH_3–**CH**); 4.09 (s, 5H, Fc); 4.09–4.18 (m, 4H, Fc). ^{13}C NMR: 14.21, 16.47, 43.68, 53.65, 66.98, 67.02, 67.34, 68.31, 68.59, 68.96. MS spectrum: 285(M^+), 213 ($Fc(CH_3)CH^+$).

*4.2.1.2. Diethyl(α-ferrocenylbenzyl)amine (**17b**).* Product **17b** was obtained from the reaction without $KHSO_4$ (76 mg, 43%) or in the presence of $KHSO_4$ (90 mg, 51%) as brown oil. The same reaction with 20 eq. of Et_2NH afforded 88 mg (49%) of **17b** in the absence of $KHSO_4$ and 98 mg (55%) of **17b** in the presence of $KHSO_4$. ^1H NMR: 0.93 (t, 6H, $^3J = 6.9$, **CH₃**–CH_2–N); 2.35–2.40 (m, 2H, CH_3–**CH₂**–N); 2.50–2.57 (m, 2H, CH_3–**CH₂**–N); 4.12–4.32 (m, 4H, Fc); 4.25 (s, 5H, Fc); 4.55 (s, 1H, **CH**-Ph); 7.31–7.50 (m, 5H, Ph). ^{13}C NMR: 11.70, 43.29, 66.57, 68.11, 68.21, 68.55, 68.80, 70.03, 126.86, 127.85, 128.26, 128.94. MS spectrum: 347(M^+), 275 ($Fc(Ph)CH^+$).

4.2.2. α-Ferrocenylalkylation of Me_2NH

A hexane solution of Bu^nLi (1 eq.) was added to a solution of **1a,b** (150 mg) in THF (15 ml) and the mixture was stirred for 5 min. Ethyl chloroformate (1 eq.) was added to the mixture in one portion followed by 5 min stirring and, if specified, addition of $KHSO_4$. The mixture was added by the pressure of argon at −5°C to the bulb charged with dimethyl amine 5 ml (20 eq.), the mixture was stirred for 24 h at room temperature. The reaction mixture was quenched with water (20 ml) and extracted with diethyl ether (2 × 20 ml). The combined extracts were washed with water (20 ml) and dried over Na_2SO_4. Evaporation of the solvent afforded oily residue which was dissolved in diethyl ether (10 ml) the solution was washed with 5% aqueous HCl (2 × 15 ml). The acidic solutions were combined, washed with diethyl ether (20 ml) and alkalized with aqueous ammonia to pH = 10 and extracted with diethyl ether (3 × 15 ml). The ether extracts were combined, dried over Na_2SO_4 and the solvent was evaporated to afford pure product.

*4.2.2.1. (1-Ferrocenylethyl)dimethylamine (**18a**) [18].* Product **18a** was obtained from the reaction without $KHSO_4$ (78 mg, 46%) or in the presence of $KHSO_4$ (79 mg, 47%) as brown oil. ^{1}H NMR: 1.46 (d, 3H, ^{3}J = 6.8, **CH$_3$**–CH); 2.09 (s, 6H, **CH$_3$**); 3.61 (q, 1H, ^{3}J = 6.8, **CH**–CH_3); 4.13–4.15 (m, Fc). ^{13}C NMR: 69.38, 68.59, 67.37, 67.23, 66.89, 58.62, 40.69, 16.13. MS spectrum: 257 (M^+), 213 ($FcCHPh^+$).

*4.2.2.2. (α-Ferrocenylbenzyl)dimethylamine (**18b**) [20].* Product **18b** was obtained from the reaction without $KHSO_4$ (109 mg, 67%) or in the presence of $KHSO_4$ (115 mg, 70%) as orange crystalline solid, m. p. 60-61°C. ^{1}H NMR: 2.11 (s, 6H, CH_3); 3.75 (s, 5H, Fc); 3.80 + 4.13+4.18 (s + s + s, H + H + H, Fc); 4.25 (s, 2H, Fc + CH); 7.33–7.54 (m, 5H, Ph). ^{13}C NMR: 44.57, 66.48, 67.27, 68.61, 68.74, 70.55, 72.41, 90.37, 127.11, 128.04, 128.51, 143.47. MS spectrum: 319 (M^+), 275 ($FcCHPh^+$).

4.2.3. α-Ferrocenylalkylation of $PhNH_2$

A hexane solution of Bu^nLi (1 eq.) was added to a solution of **1a,b** (150 mg) in THF (15 ml) and the mixture was stirred for 5 min. Ethyl chloroformate (1 eq.) was added to the mixture in one portion followed by 5 min stirring and, if specified, addition of $KHSO_4$ (2 eq.). Aniline or aniline hydrochloride (the quantities are shown in Table 2) was added after 5 min stirring and the mixture was stirred for additional 24 h at the temperature indicated in Table 2. The reaction mixture was passed through a layer of SiO_2 (4 cm; eluent: ethyl acetate). An evaporation of the solvent produced brown oily residue, which was kept at 120 °C/1 mm Hg for 30 min to afford pure amine 9. The yields are shown in Table 2.

*4.2.3.1. N-(1-ferrocenylethyl)aniline (**9a**) [13,16].* Brown oil. ^{1}H NMR: 1,56 (d, 3H, ^{3}J = 6.2, **CH$_3$**–CH); 3.97 (s_{br}, 1H, NH); 4.15–4.26 (m, 4H, Fc); 4,25 (s, 5H, Fc); 4.36 (q, 1H, ^{3}J = 6.2, **CH**–CH_3); 4.59 (s, 1H, **CH**-Ph); 6.69–7.28 (m, 5H, Ph). ^{13}C NMR: 21.10, 47.18, 66.38, 67.24, 67.74, 67.98, 68.51, 68.62, 93.69, 113.35, 117.30, 129.56.

*4.2.3.2. N-(α-ferrocenylbenzyl)aniline (**9b**) [13].* Brown oil. ^{1}H NMR: 4.11–4.24 (m, 4H, Fc); 4,28 (s, 5H, Fc); 4.85 (s_{br}, 1H, NH); 5.14 (s, 1H, **CH**-Ph); 6.94–7.55 (m, 10H, Ph + Ph). ^{13}C NMR: 57.59, 66.84, 67.54, 67.95, 68.16, 68.84, 113.55, 117.68, 126.88, 127.25, 128.64, 129.41, 143.18, 147.62.

*4.2.4. General procedure for α-ferrocenylalkylation of aryl or heteroaryl amines with **1a,b***

A hexane solution of Bu^nLi (1 eq.) was added to a solution of **1a,b** (150 mg) in THF (15 ml) and the mixture was stirred for 5 min. Ethyl chloroformate (1 eq.) was added to the mixture in one portion followed by 5 min stirring and, if specified, addition of $KHSO_4$ (2 eq.). The amine (2 eq.) was added after 5 min stirring and the mixture was stirred for additional 24 h at room temperature. Aluminum oxide (3 g, for chromatography, Brockmann Activity III) was added to the reaction mixture ant the solvent was rotatory evaporated to dryness. The residue was placed on the top of the chromatography column (Al_2O_3, 2 × 15 cm) and the products were separated by elution with petroleum ether (to remove ethers **26**) followed by the mixture petroleum ether – ethyl acetate.

*4.2.4.1. N-(1-ferrocenylethyl)-4-methoxyaniline (**10a**) [13,16].* Product **10a** was eluted with petroleum ether – ethyl acetate (50:1); orange oil. The yields are 118 mg (54%) from the reaction without $KHSO_4$ or 119 mg (55%) in the presence of $KHSO_4$. ^{1}H NMR: 1.55 (d, 3H, ^{3}J = 6.2, **CH$_3$**–CH); 3.82 (s, 3H, OCH_3); 4.19–4.29 (m, 4H, Fc); 4.25 (s, 5H, Fc); 4.29–4.32 (m, 1H, **CH**–CH_3); 6.70 + 6.87 (d + d, 2H+2H, ^{3}J = 8.9, C_6H_4). ^{13}C NMR: 21.28, 48.42, 55.88, 66.27, 67.20, 67.61, 67.85, 68.56, 93.83, 115.06, 141.94, 152.12. IR (KBr pellet, cm^{-1}): 3394 (NH). Anal. Calc. for $C_{19}H_{21}NOFe$: C, 67.86; H, 6.25; N, 4.17; Fe, 16.96. Found: C, 67.89; H, 6.32; N, 4.14; Fe, 16.50%.

*4.2.4.2. N-(α-ferrocenylbenzyl)-4-methoxyaniline (**10b**) [13].* Product **10b** was eluted with petroleum ether – ethyl acetate (50:1); orange oil. The yields are 163 mg (80%) from the reaction without $KHSO_4$ or 143 mg (70%) in the presence of $KHSO_4$. ^{1}H NMR: 3.77 (s, 3H, OCH_3); 4.15–4.23 (m, 4H, Fc); 4.27 (s, 5H, Fc); 4.62 (s_{br}, 1H, NH); 5.06 (s, 1H, CH); 6.61 + 6.80 (d + d, 2H+2H, ^{3}J = 8.9, C_6H_4); 7.29–7.54 (m, 5H, Ph). ^{13}C NMR: 55.85, 66.57, 58.50, 67.55, 67.85, 68.09, 68.79, 69.87, 94.50, 114.68, 114.98, 126.87, 127.18, 128.61, 142.02, 143.59. IR (KBr pellet, cm^{-1}): 3394 (NH). Anal. Calc. for $C_{24}H_{23}NOFe$: C, 72.52; H, 5.79; N, 3.53; O, 4.03; Fe, 14.10. Found: C, 72.58; H, 5.83; N, 3.53; Fe, 14.10%.

*4.2.4.3. N-(1-ferrocenylethyl)-4-nitroaniline (**11a**) [13,16].* Product **11a** was eluted with petroleum ether – ethyl acetate (8:1) and recrystallized from hexane to afford orange crystalline solid, m. p. 115–116 °C. The yields are 142 mg (62%) from the reaction without $KHSO_4$ or 194 mg (85%) in the presence of $KHSO_4$. ^{1}H NMR: 1.58 (d, 3H, ^{3}J = 6.5, **CH$_3$**–CH); 4.20–4.24 (m, 4H, Fc); 4.24 (s, 5H, Fc); 4.44–4.48 (m, 1H, **CH**–CH_3); 4.96 (s_{br}, 1H, NH); 6.58 + 8.11 (d + d, 2H+2H, ^{3}J = 9.2, Ph). ^{13}C NMR: 20.40, 47.02, 66.02, 67.24, 68.07, 68.33, 68.64, 91.61, 111.27, 126.59, 152.32. IR (KBr pellet, cm^{-1}): 3395 (NH), 1307 (NO).

*4.2.4.4. N-(α-ferrocenylbenzyl)-4-nitroaniline (**11b**) [13].* Product **11b** was eluted with petroleum ether – ethyl acetate (8:1); orange crystalline solid, m. p. 99–100 °C. The yields are 132 mg (62%) from the reaction without $KHSO_4$ or 137 mg (65%) in the presence of $KHSO_4$. ^{1}H NMR: 4.05–4.26 (m, 4H, Fc); 4.23 (s, 5H, Fc); 5.25 (d, 1H, ^{3}J = 4.9, **CH**–NH); 5.64 (s_{br}, 1H, NH); 6.54 + 8.05 (d + d, 2H+2H, ^{3}J = 9.2, C_6H_4); 7.31–7.46 (m, 5H, Ph). ^{13}C NMR: 56.96, 67.38, 68.41, 68.54, 68.71, 68.96, 92.20, 112.11, 126.46, 126.83, 127.81, 128.84, 138.13, 141.09, 152.16. IR (KBr pellet, cm^{-1}): 3394 (NH), 1310 (NO).

*4.2.4.5. 4-Cyano-N-(1-ferrocenylethyl)aniline (**12a**).* Product **12a** was eluted with petroleum ether – ethyl acetate (8:1) and recrystallized from petroleum ether to afford orange crystalline solid, m. p. 76–77 °C. The yields are 145 mg (67%) from the reaction without $KHSO_4$ or 85 mg (40%) in the presence of $KHSO_4$. ^{1}H NMR: 1.53 (d, 3H, ^{3}J = 6.5, **CH$_3$**–CH); 4.18–4.23 (m, 4H, Fc); 4,22 (s, 5H, Fc); 4.36–4.42 (m, 1H, **CH**–CH_3); 4.58 (s_{br}, 1H, NH); 6.61 + 7.45 (d + d, 2H+2H, ^{3}J = 8.4, C_6H_4). ^{13}C NMR: 20.53, 46.66, 66.09, 67.15, 67.90, 68.18, 68.60, 92.08, 98.05, 112.44, 120.72, 133.86, 150.43. IR (KBr pellet, cm^{-1}): 3394 (NH), 2201 (CN). Anal. Calc. for $C_{19}H_{18}N_2Fe$: C, 69.09; H, 5.46; N, 8.49; Fe, 16.97. Found: C, 69.01; H, 5.49; N, 8.50;

Fe, 17.20%.

*4.2.4.6. 4-Cyano-N-(α-ferrocenylbenzyl)aniline (**12b**).* Product **12b** was eluted with petroleum ether – ethyl acetate (8:1) as orange oil, which was washed with hot hexane to afford orange solid, m. p. 163 °C. The yields are 136 mg (67%) from the reaction without $KHSO_4$ or 144 mg (71%) in the presence of $KHSO_4$. ^{1}H NMR: 4.04–4.26 (m, 4H, Fc); 4.27 (s, 5H, Fc); 5.18 (s, 1H, CH); 5.35 (s_{br}, 1H, NH); 6.57–7.48 (m, 10H; C_6H_4 + Ph). ^{13}C NMR: 56.74, 67.17, 67.20, 68.18, 68.28, 68.74, 92.74, 113.03, 126.65, 127.62, 128.68, 133.69, 141.21, 150.06. IR (KBr pellet, cm^{-1}): 3369 (NH), 2206 (CN). Anal. Calc. for $C_{24}H_{20}N_2Fe$: C, 73.47; H, 5.10; N, 7.14; Fe, 14.29. Found: C, 73.45; H, 5.43; N, 6.97; Fe, 14.30%.

*4.2.4.7. 4-Benzoyl-N-(1-ferrocenylethyl)aniline hydrochloride (**13a·HCl**).* Product **13a** eluted from the column with petroleum ether – ethyl acetate (50:1) contained the impurity of **1a**. The mixture was obtained after an evaporation of the solvent as orange oil, which was dissolved in diethyl ether and acidified with HCl (aq.). The precipitate was washed with diethyl ether and dried in vacuo to afford orange solid **13a**·HCl, m. p. 120 °C. The yields are 151 mg (55%) from the reaction without $KHSO_4$ or 112 mg (42%) in the presence of $KHSO_4$. ^{1}H NMR: 1.57 (d, 3H, $^3J = 6.5$, **CH$_3$**–CH); 4.19–4.24 (m, 4H, Fc); 4.24 (s, 5H, Fc); 4.43–4.49 (m, 1H, **CH**–CH_3); 4.58 (s_{br}, 1H, NH); 6.65 + 7.81 (d + d, 2H+2H, $^3J = 8.4$, C_6H_4); 7.47–7.78 (m, 5H, **Ph**-C=O). ^{13}C NMR: 17.70, 41.77, 67.22, 68.91, 69.98, 76.77, 77.09, 77.40, 128.22, 128.41, 129.71, 129.96, 131.16, 132.52, 132.68, 137.16, 195.30. IR (KBr pellet, cm^{-1}): 2449–2919 (NH_2), 1659 (CO). Anal. Calc. for $C_{25}H_{24}NOFeCl$: C, 67.29; H, 5.38; N, 3.14; O, 3.59; Fe, 12.56; Cl, 7.96. Found: C, 67.21; H, 5.32; N, 3.13; Fe, 12.55; Cl, 7.89%.

*4.2.4.8. 4-Benzoyl-N-(α-ferrocenylbenzyl)aniline (**13b**).* Product **13b** was eluted with petroleum ether – ethyl acetate (8:1) and recrystallized from hexane to afford yellow solid, m. p. 150 °C (dec.). The yields are 113 mg (47%) from the reaction without $KHSO_4$ or 119 mg (49%) in the presence of $KHSO_4$. ^{1}H NMR: 4.07–4.25 (m, 4H, Fc); 4.25 (s, 5H, Fc); 5.24 (s, 1H, CH); 5.40 (s_{br}, 1H, NH); 6.61–7.76 (m, 10H, C_6H_4 + Ph). ^{13}C NMR: 56.77, 67.11, 67.25, 68.10, 68.20, 68.73, 93.02, 112.19, 126.70, 127.47, 128.03, 128.62, 129.47, 131.25, 132.95, 139.04, 141.67, 150.82, 195.17. IR (KBr pellet, cm^{-1}): 3386 (NH), 1636 (CO). Anal. Calc. for $C_{30}H_{25}NOFe$: C, 76.27; H, 5.30; N, 2.97; O, 3.39; Fe, 11.86. Found: C, 76.25; H, 5.31; N, 3.19; Fe, 11.85%.

*4.2.4.9. 4-[(1-Ferrocenylethyl)amino]-2-methylquinoline (**14a**).* Product **14a** was eluted with petroleum ether – ethyl acetate (8:1). Yellow crystalline solid, m. p. 171 °C. The yields are 121 mg (50%) from the reaction without $KHSO_4$ or 142 mg (59%) in the presence of $KHSO_4$. ^{1}H NMR: 1.60 (d, 3H, $^3J = 6.4$, **CH$_3$**–CH); 2.66 (s, 3H, CH_3); 4.19–4.26 (m, 4H, Fc); 4.26 (s, 5H, Fc); 4.50–4.57 (m, 1H, **CH**–CH_3); 5.42 (s_{br}, 1H, NH); 6.44 (s, 1H, C_5HN); 7.40 (t, 1H, $^3J = 7.6$, C_6H_4); 7.62 (t, 1H, $^3J = 7.6$, C_6H_4); 7.71 (d, 1H, $^3J = 8.4$, C_6H_4); 7.97 (d, 1H, $^3J = 8.4$, C_6H_4). ^{13}C NMR: 19.98, 25.84, 46.25, 66.11, 67.16, 68.06, 68.26, 68.34, 68.53, 92.18, 99.05, 117.36, 118.95, 124.00, 129.13, 129.23, 148.43, 159.57. IR (KBr pellet, cm^{-1}): 3426 (NH). Anal. Calc. for $C_{22}H_{22}N_2Fe$: C, 71.16; H, 5.93; N, 7.55; Fe, 15.36. Found: C, 69.89; H, 5.95; N 7.05; Fe, 14.3%.

*4.2.4.10. 4-[(α-Ferrocenylbenzyl))amino]-2-methylquinoline (**14b**).* Product **14b** was eluted with petroleum ether – ethyl acetate (8:1). Yellow crystalline solid, m. p. 175 °C (dec.). The yields are 240 mg (76%) from the reaction without $KHSO_4$ or 76 mg (34%) in the presence of $KHSO_4$. ^{1}H NMR: 2.50 (s, 3H, CH_3); 4.04–4.26 (m, 4H, Fc); 4.29 (s, 5H, Fc); 4.50–4.57 (m, 1H, **CH**–CH_3); 5.33 (d, 1H, $^3J = 4.7$, **CH**–NH); 6.09 (d_{br}, 1H, NH); 6.16 (s, 1H, C_5HN); 7.30–7.41 (m, 3H, C_6H_4); 7.48–7.53 (m, 3H, C_6H_4); 7.66–7.69 (t, 1H, $^3J = 7.1$, C_6H_4); 7.92–8.00 (m, 2H, C_6H_4). ^{13}C NMR: 25.72, 56.24, 67.01, 67.30, 68.33, 68.73, 93.02, 100.89, 117.47, 118.82, 124.30, 126.60, 127.62, 128.65, 129.15, 129.36, 140.87, 148.18, 159.53. IR (KBr pellet, cm^{-1}): 3445 (NH). Anal. Calc. for $C_{27}H_{24}N_2Fe$: C, 75.00; H, 5.56; N, 6.48; Fe, 12.96. Found: C, 74.98; H, 5.55; N, 6.51; Fe, 12.94%.

*4.2.4.11. 2-[(1-Ferrocenylethyl)amino]-5-methylpyridine (**15a**).* Product **15a** was eluted with petroleum ether – ethyl acetate (50:1); yellow oil. The yields are 82 mg (39%) from the reaction without $KHSO_4$ or 78 mg (37%) in the presence of $KHSO_4$. ^{1}H NMR: 1.54 (d, 3H, $^3J = 6.2$, **CH$_3$**–CH); 2.21 (s, 3H, CH_3); 4.13–4.23 (m, 4H, Fc); 4.23 (s, 5H, Fc); 4.61–4.70 (m, 1H+1H, **CH**–CH_3+NH); 6.37 + 7.28 (d + d, 1H+1H, $^3J = 8.4$, C_5H_3N); 7.97 (s, 1H, C_5H_3N). ^{13}C NMR: 17.44, 21.23, 45.62, 66.04, 66.98, 67.52, 67.78, 68.48, 106.97, 121.42, 138.48, 147.76, 156.28. IR (KBr pellet, cm^{-1}): 3255 (NH). Anal. Calc. for $C_{27}H_{24}N_2Fe$: C, 67.50; H, 6.25; N, 8.75; Fe, 17.50. Found: C, 67.52; H, 6.26; N, 8.77; Fe, 17.54%.

*4.2.4.12. 2-[(α-Ferrocenylbenzyl))amino]-5-methylpyridine (**15b**).* Product **15b** was eluted with petroleum ether – ethyl acetate (8:1); yellow oil. The yields are 134 mg (65%) from the reaction without $KHSO_4$ or 105 mg (50%) in the presence of $KHSO_4$. ^{1}H NMR: 2.23 (s, 3H, CH_3); 4.21–4.32 (m, 4H, Fc); 4.32 (s, 5H, Fc); 5.36 (d. 1H, $^3J = 5.4$, CH); 5.55 (d_{br}. 1H, $^3J = 5.1$, NH); 6.20 (d, 1H, C_5H_3N); 7.19–7.50 (m, 6H, C_5H_3N + Ph); 8.00 (s, 1H, C_5H_3N). ^{13}C NMR: 17.46, 55.73, 66.80, 67.07, 67.88, 67.94, 68.77, 69.89, 93.16, 106.33, 122.08, 126.79, 127.13, 128.39, 138.57, 142.81, 147.99, 156.19. IR (KBr pellet, cm^{-1}): 3412 (NH). Anal. Calc. for $C_{23}H_{22}N_2Fe$: C, 72.23; H, 5.76; N, 7.33; Fe, 14.65. Found: C, 72.25; H, 5.79; N, 7.35; Fe, 14.70%.

*4.3. General procedure for α-ferrocenylalkylation of phenols and alcohols with **1a,b***

A solution of n-BuLi (1 eq.) in hexane was added to a solution of **1a,b** (150 mg) in THF (15 ml). The mixture was stirred for 5 min and EtOC(O)Cl was added followed by 5 min stirring and addition of R'OH. The mixture was stirred for 24 h at room temperature.

*4.3.1. α-Ferrocenylbenzyl 2-methoxyphenyl ether **19** (Ar = 2-MeOC$_6$H$_4$, R = Ph)*

The reaction mixture obtained from **1b** and **20** (3 eq.) was quenched with 0.1 M aqueous solution of NaOH (20 ml) and extracted with ether (3 × 15 ml). The combined extracts were washed with water (3 × 15 ml) and dried over Na_2SO_4. Evaporation of the solvent afforded **20b** (49 mg, 29%) as yellow oil. ^{1}H NMR: 3.89 (s, 3H, CH_3); 4.0–4.17 (m, 9H, Fc); 5.82 (s, 1H, CH); 6.66–6.79 (m, 4H, C_6H_4); 7.20–7.29 (m, 5H, Ph). ^{13}C NMR: 43.93, 56.00, 67.25, 67.70, 68.56, 68.75, 69.28, 91.43, 108.29, 119.03, 122.01, 127.84, 125.93, 128.81, 131.36, 144.43.

*4.3.2. 1-Ferrocenylethyl isopropyl ether (**21a**) [16]*

The reaction mixture obtained from **1a** and Pr^{i}OH (25 eq.) was evaporated. The products were separated by column chromatography (Al_2O_3, petroleum ether) to afford **24a** (80 mg, 47%) as orange oil. ^{1}H NMR: 1.10–1.12 (d, 3H, $^3J = 6.2$, **CH$_3$**CHO); 1.15–1.17 (d, 3H, $^3J = 6.3$, **CH$_3$**–CH); 3.70–3.76 (m, 1H, **CH**$(CH_3)_2$; 4.13–4.23 (m, 9H, Fc); 4.38–4.40 (m, 1H, **CH**–CH_3). ^{13}C NMR: 21.48, 22.52, 23.08, 65.83, 67.52, 67.81, 68.26, 68.54, 68.62, 70.49. Anal. Calc. for $C_{15}H_{20}OFe$: C, 66.23; H, 7.36; Fe, 20.53. Found: C, 66.27; H, 7.41; Fe, 20.50%.

*4.3.3. α-Ferrocenylbenzyl isopropyl ether (**21b**) [13]*

The reaction mixture obtained from **1b** and Pr^{i}OH (25 eq.) was evaporated. The products were separated by column

chromatograpy (Al_2O_3, petroleum ether: ethyl acetate = 16: 1) to afford **24b** (100 mg, 58%) as orange oil. ^{1}H NMR: 1.10–1.12 (d, 3H, ^{3}J = 6.2, **CH$_3$**CHO); 1.15–1.17 (d, 3H, ^{3}J = 6.3, **CH$_3$**–CH); 3.70–3.76 (m, 1H, **CH**$(CH_3)_2$; 4.13–4.23 (m, 9H, Fc); 4.38–4.40 (m, 1H, **CH**–CH_3). ^{13}C NMR: 21.48, 22.52, 23.08, 65.83, 67.52, 67.81, 68.26, 68.54, 68.62, 70.49. Anal. Calc. for $C_{15}H_{20}$OFe: C, 66.23; H, 7.36; Fe, 20.53. Found: C, 66.27; H, 7.41; Fe, 20.50%.

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Appendix A. Supplementary data

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