

Reactions of hydroxymethylferrocenes with C-acids catalyzed by Ca^{2+} -montmorillonite

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Dedicated to Professor RNDr. V. Sutoris, CSc., in honour of his 60th birthday

It was found that Ca^{2+} -montmorillonite and Ca^{2+} -bentonite can be used as catalysts for the reactions of hydroxymethylferrocenes with ethyl malonate, ethyl formamidomalonate, acetylacetone, and aniline. The reaction can find synthetical utilization because the 40—60 % yields of products have been obtained without optimization.

Обнаружено, что Ca^{2+} -монтморильтонит и Ca^{2+} -бентонит могут быть использованы в качестве катализаторов в реакциях гидроксиметилферроценов с этилмалонатом, этилформамидомалонатом, ацетилацетоном и анилином. Эта реакция может использоваться в синтетических целях, поскольку и без оптимизации были достигнуты 40—60 % выходы продуктов.

Ferrocenylmethylammonium salts [1—3] are usually applied as the alkylating agents for the introduction of ferrocenylmethyl group into various substrates, and the reactions are performed at higher temperatures in anhydrous medium. As an alkylating agent, hydroxymethylferrocene or dialkylaminoferrocene can be also used, from which ferrocenylmethyl cation is generated by the action of acids [4—7] (CF_3COOH , HBF_4 , HClO_4 , POCl_3 , etc.). This method has some limitation — the nucleophile must be sufficiently stable in the acidic medium.

Great attention has been paid recently to the utilization of inorganic carriers of agents in organic synthesis [8, 9]. Different homoionic forms of montmorillonite also rank among them. Using them, the stable triarylmethyl cations [10, 11] have been generated but their reactions have not been studied.

The aim of the present work was to study possibility of utilization of homoionic forms of montmorillonite or bentonite as catalysts for ferrocenylmethylation of different substrates with hydroxymethylferrocenes.

Experimental

Bentonite from the locality, Jelšový Potok used in this work, contained ca. 80 % of mineral montmorillonite. Montmorillonite was prepared from this bentonite according

to [12]. Ca^{2+} -Bentonite and Ca^{2+} -montmorillonite were prepared by sixfold washing of natural bentonite resp. montmorillonite with 0.1 mol dm^{-3} solution of CaCl_2 according to [12]. Hydroxymethylferrocene was prepared by [13, 14], α -hydroxybenzylferrocene and bis(phenylferrocenylmethyl) ether by [15].

Melting points of the prepared compounds were determined on a Kofler hot-stage and are uncorrected. ^1H NMR spectra were measured on a Tesla BS 487 instrument using working frequency of 80 MHz. The spectra of compounds were taken in C^3HCl_3 (99 % of ^2H -isotope) solution and tetramethylsilane was used as internal standard.

Attempted preparation of methoxymethylferrocene

To a stirred solution of hydroxymethylferrocene (0.3 g ; 1 mmol) in *n*-heptane (120 cm^3), Ca^{2+} -bentonite (10 g) was added. After adsorption of hydroxymethylferrocene on bentonite (solution remains colourless), bentonite was filtered off and dried at $65\text{--}70^\circ\text{C}$ for 2 h. After drying, bentonite was quenched with methanol, which extracted organic compound. Methanol was evaporated under vacuum leaving 0.15 g of compound which was chromatographed on Al_2O_3 using benzene as eluent. Only 0.05 g (17 %) of pure bis(ferrocenylmethyl) ether, having m.p. (petroleum ether) = $126\text{--}128^\circ\text{C}$ (Ref. [16] gives $134\text{--}136^\circ\text{C}$), was isolated.

Note: During experiments with other homoionic forms of bentonite (Cu^{2+} , Fe^{3+} , Al^{3+} , Co^{2+}) prepared according to [12], ferrocene derivative decomposed. Therefore, all further experiments were carried out using Ca^{2+} -bentonite.

Ferrocenylmethylation of C-acids

To a stirred solution of corresponding hydroxymethylferrocene (3 mmol) in benzene (50 cm^3), substrate (C-acid, 3 mmol) and 8 g of Ca^{2+} -bentonite (Procedure A) or Ca^{2+} -montmorillonite (Procedure B) was added. The reaction mixture was stirred under reflux for 6 h during what time the colour of catalyst has changed from white to grey-black. After cooling, catalyst was filtered off and benzene was evaporated under vacuum. From the catalyst, organic material was extracted by ethanol. The residue, leaving after vacuum evaporation, combined with the residue remaining after evaporation of benzene was chromatographed on Al_2O_3 or SiO_2 , using benzene as eluent. Small amount of yellow, unidentified compound, resp. bis(ferrocenylmethyl) ether was usually isolated from the first band and the reaction product was isolated from the second band.

The results of experiments are summarized in Table 1 and the ^1H NMR spectra of prepared compounds are given in Table 2.

Results and discussion

Reaction of hydroxymethylferrocene with ethyl malonate has been chosen as a model reaction for study of the influence of exchangeable ion in montmorillonite. We examined Cu^{2+} -, Al^{3+} -, Fe^{3+} -, Co^{2+} -, and Ca^{2+} -montmorillonite. Except for the last, no product has been isolated, because an oxidative decomposition of

Table 1. Results of ferrocenylmethylation of *C*-acids catalyzed by Ca^{2+} -bentonite (*A*), resp. Ca^{2+} -montmorillonite (*B*)

Experiment No.	Alkylating agent	Substrate	Catalyst	Compound	Yield	M.p.	M.p.	Ref.
					%	°C	°C	
1	FcCH_2OH	$\text{CH}_2(\text{COOC}_2\text{H}_5)_2$	<i>A</i>	<i>I</i>	43.5	Yellow oil	Oil [2]	
2	FcCH_2OH	$\text{CH}_2(\text{COCH}_3)_2$	<i>A</i>	<i>II</i>	46.7	Red oil	Oil [2]	
3	FcCH_2OH	$\text{CH}_2 \begin{array}{c} \diagup \text{CO} \diagdown \\ \diagdown \text{CO} \diagup \end{array} (\text{CH}_2)_3$	<i>A</i>	<i>III</i>	18.6	300	<i>a</i>	
4	FcCH_2OH	$\text{OHCNHCH}(\text{COOC}_2\text{H}_5)_2$	<i>A</i> ^b	<i>IV</i>	16.2	84—86	84—86 [17]	
5	$\begin{array}{c} \text{OH} \\ \\ \text{FcCHC}_6\text{H}_5 \end{array}$	$\text{CH}_2(\text{COOC}_2\text{H}_5)_2$	<i>B</i>	<i>V</i>	27	78—80	80 [18]	
6	$\begin{array}{c} \text{OH} \\ \\ \text{FcCHC}_6\text{H}_5 \end{array}$	$\text{CH}_2(\text{COOC}_2\text{H}_5)_2$	<i>A</i>	<i>V</i>	60.8	78—80	80 [18]	
7	$\begin{array}{c} \text{OH} \\ \\ \text{FcCHC}_6\text{H}_5 \end{array}$	$\text{CH}_2(\text{COCH}_3)_2$	<i>B</i> ^c	<i>VI</i>	33.5	110—114	115—117 [20]	
8	FcCH_2OH	$\text{C}_6\text{H}_5\text{NH}_2$	<i>B</i>	<i>VII</i>	24.7	118—120	115—116 [19]	
				<i>VIII</i>	24.7	102—105	107—108 [19]	
9	$\left(\begin{array}{c} \text{Fc} \\ \\ \text{C}_6\text{H}_5 \end{array} \text{CH} \right)_2\text{O}$	$\text{CH}_2(\text{COOC}_2\text{H}_5)_2$	<i>B</i>	<i>V</i>	26.3	78—80	80 [18]	
10	$\left(\begin{array}{c} \text{Fc} \\ \\ \text{C}_6\text{H}_5 \end{array} \text{CH} \right)_2\text{O}$	$\text{CH}_2(\text{COOC}_2\text{H}_5)_2$	<i>B</i> ^d	<i>V</i>	27	78—80	80 [18]	

a) For $\text{C}_{17}\text{H}_{18}\text{FeO}_2$ ($M_r=310.18$) $w_i(\text{calc.})$: 65.82 % C, 5.8 % H, 18.0 % Fe; $w_i(\text{found})$: 65.55 % C, 5.75 % H, 17.96 % Fe. *b*) The yield did not change either at the ratio $n(\text{FcCH}_2\text{OH}) : n(\text{OHCNHCH}(\text{COOC}_2\text{H}_5)_2) = 1 : 2$. *c*) 1.7 g of *B* for 3 mmol of $\begin{array}{c} \text{OH} \\ | \\ \text{FcCHC}_6\text{H}_5 \end{array}$. *d*) 4 g of *B* for 3 mmol of

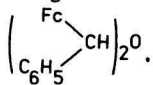


Table 2

¹H NMR chemical shifts (δ/ppm) of the prepared compounds I—VIII

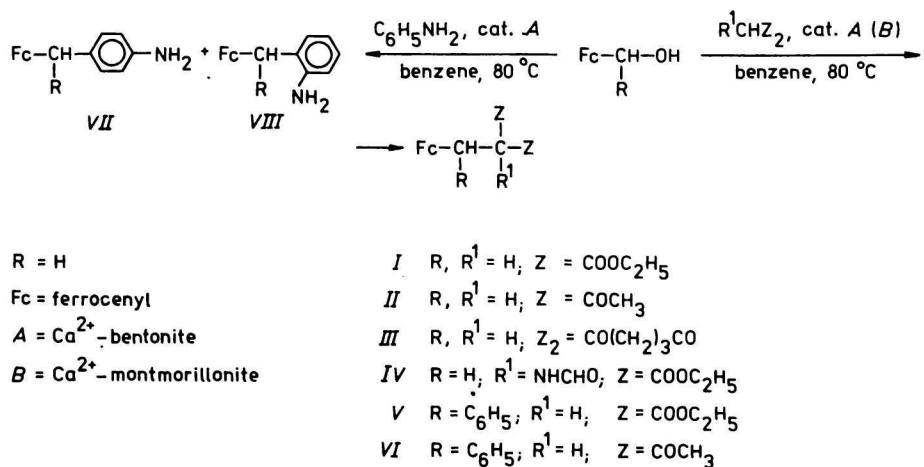
I	4.30—4.05 (m, 13H, Fc, OCH ₂), 3.42 (t, 1H, CH), 2.95 (d, 2H, FcCH ₂), 1.25 (t, 6H, CH ₃)
II	4.8 (t, 1H, CH), 4.6 (s, 4H, C ₃ H ₄), 4.3—4.1 (m, 7H, C ₃ H ₅ , CH ₂), 2.1 (s, 6H, CH ₃)
III	4.07 (s, 5H, C ₆ H ₅), 3.97 (m, 4H, C ₃ H ₄ , CH), 2.92 (bs, 2H, FcCH ₂), 1.95 (t, 4H, COCH ₂), 1.50 (m, 2H, CH ₂)
IV	8.01 (bs, 1H, CHO), 6.75 (bs, 1H, NH), 4.13 (q, 4H, OCH ₂), 4.12 (s, 9H, Fc), 3.45 (t, 2H, FcCH ₂), 1.25 (t, 6H, CH ₃)
V	7.32 (bs, 5H, C ₆ H ₅), 4.42 (t, 2H, H _a), 4.0 (m, 7H, H _β , CH, OCH ₂), 3.82 (s, 5H, C ₃ H ₅), 3.25 (bs, 1H, C ₆ H ₅ CH), 1.01 (t, 3H, CH ₃), 0.92 (t, 3H, CH ₃)
VI	7.37 (s, 5H, C ₆ H ₅), 4.40 (bs, 2H, CH—CH), 4.05 (m, 2H, H _a), 3.92 (m, 2H, H _β), 3.82 (s, 5H, C ₃ H ₅), 2.00 (s, 3H, CH ₃), 1.87 (s, 3H, CH ₃)
VII	6.95 (d, 2H, C ₆ H ₄ , H _m), 6.30 (d, 2H, C ₆ H ₄ , H _o), 4.05 (bs, 9H, Fc), 3.55 (s, 2H, NH ₂), 1.25 (s, 2H, CH ₂)
VIII	7.05—6.6 (m, 4H, C ₆ H ₄), 4.10 (bs, 9H, Fc), 3.60 (s, 2H, NH ₂), 1.25 (s, 2H, CH ₂)

H_m — proton in the *meta* position.H_o — proton in the *ortho* position.

ferrocene derivative occurred. Otherwise, Mg^{2+} -montmorillonite does not cause decomposition of ferrocene derivative but not even catalyze the alkylation.

The oxidative decomposition of hydroxymethylferrocene occurred during attempting to generate ferrocenylmethyl cation on Ca^{2+} -montmorillonite on the dry way, performed analogically as done by *Helsen* [10] when generating triphenylmethyl cation. The experiment proved that the reaction takes place in interlayer of montmorillonite because methoxymethylferrocene was not formed during the quenching of carrier with methanol, but bis(ferrocenylmethyl) ether was isolated (17 %). Ferrocenylmethyl cation reacted with water present in the interlayer of montmorillonite even before quenching with methanol.

All further experiments were carried out under catalysis of Ca^{2+} -bentonite (A), resp. Ca^{2+} -montmorillonite (B). The course of reactions is depicted in Scheme 1 and the results are given in Table 1.



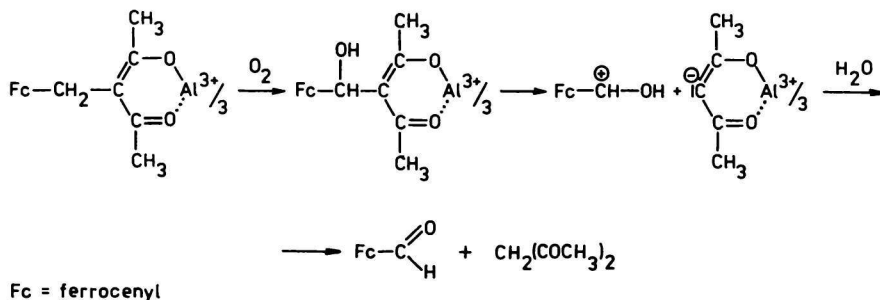
Scheme 1

Based on the results, it is evident that product of alkylation was isolated from 16 % (ethyl formamidomalonate) up to 47 % (acetylacetone) yields in all cases. Ferrocenylalkylations worked better with hydroxymethylferrocene than with α -hydroxybenzylferrocene. No starting ferrocene derivative was isolated from the reactions, indicating that its decomposition occurs and so low yields of products result. We performed therefore an experiment using half amount of catalyst. However, it did not affect the yields of reaction (*cf.* with the experiment No. 9 and 10). In the next experiment (No. 6) we lowered the amount of catalyst even more markedly. For 0.5 g (1.7 mmol) of ferrocene derivative, we used 1 g of

Ca^{2+} -bentonite and the reaction time was shortened to 2.5 h. The yield of product increased to 60.8 %. Our results are similar to those obtained by Postnov and coworkers [18] in the case of ferrocenylalkylation of ethyl acetoacetate and ethyl malonate under catalysis by zeolite.

Lombardo *et al.* [19] found that aniline can be ferrocenylmethylated by the help of ferrocenylmethyltrimethylammonium iodide. Using lower temperatures (95 °C), product of kinetically controlled reaction is formed, *i.e.* alkylation took place on the nitrogen atom. At the higher temperature (180 °C), products of thermodynamically controlled reaction, *i.e.* a mixture of *o*- and *p*-ferrocenylmethylanilines, were obtained. We decided to carry out an attempt to ferrocenylmethylate aniline at our conditions. Despite of the fact that the reaction temperature is only 80 °C, we obtained a mixture of *o*- and *p*-ferrocenylmethylanilines in the ratio of 1 : 1 and the total yield was 50 %.

In some cases, the small amounts of bis(phenylferrocenylmethyl) ether were observed during experiments with α -hydroxybenzylferrocene. We decided therefore to verify whether this ether can be utilized as an alkylating agent. We found that ethyl (ferrocenylmethyl)malonate is produced by the reaction with ethyl malonate in the same yield (27 %) as from α -hydroxybenzylferrocene. Attempted chromatography on Al_2O_3 of ferrocenylmethylation products of acetylacetone showed strong adsorption of product and gradual change in colour of the corresponding band. Instead of 2-(ferrocenylmethyl)-1,3-pentanedione, ferrocenecarbaldehyde was isolated after chromatography. Nesmeyanov and coworkers [21] observed analogical cleavage of the C—C bond in ferrocenylmethyl derivatives of 1,3-diketones caused by the action of the Lewis acids (anhydrous MgBr_2 , ZnCl_2 , and SnCl_2). In our case, Al_2O_3 takes over the function of the Lewis acid, and the reaction can be depicted by Scheme 2.



Scheme 2

The performed experiments prove that after further optimalization, catalysis of ferrocenylmethylation by Ca^{2+} -montmorillonite resp. Ca^{2+} -bentonite can be useful in organic synthesis. It can be expected that Ca^{2+} -bentonite will be of use

also in alkylations of different C- nucleophiles by some benzyl alcohols, from which stable carbocations can be formed and which are not sensitive toward oxidative decomposition.

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