Meta Selectivity in the Friedel−Crafts Reaction Induced by a Faujasite-Type Zeolite

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Zeolites comprise a broad range of both natural and synthetic microporous, crystalline aluminosilicates that are constructed from corner-sharing $SiO_{4/2}$ and $AlO_{4/2}$ tetrahedra.[1] They have a substantial potential as shape-selective catalysts. Within their micropores, only molecules of proper shape and dimension can undergo reactions. The reaction pathways can be completely different from those in solution, even for highly reactive intermediates such as carbenes.[2] Pentasil zeolites, such as ZSM-5, with their three-dimensional framework of one-dimensional channels, have often been used to obtain "linear" products. For example, *para* selectivity was observed when ethyl benzene was alkylated within this zeolite.[3] Furthermore, the *para* isomerization from *o*- and *m*-xylene catalyzed by pentasil zeolites is a major industrial process.[4]

Faujasite-type zeolites do not have linear pores, but their cavities are arranged in a tetrahedral pattern. Nevertheless, some examples of a high *para* selectivity in substitution reactions catalyzed by a faujasite exist.[5]

It is well-known that when a conventional Lewis acid, like $AlCl_3$, is added to benzyl chloride, a polymeric resin is rapidly formed.[6] Indeed, upon addition of $AlCl_3$ at room temperature, neat benzyl chloride immediately polymerizes (see Table, entry 1). However, if the dimer 1-(chloromethyl)-*x*-(phenylmethyl)benzene ($x = 2, 3, 4$) (benzylbenzyl chloride) (**1**) is sought instead of the polymer, one must employ a multistep reaction starting from another compound. But if the Friedel−Crafts reaction from benzyl chloride with a homogeneous catalyst is preferred, one should retard the polymerization process to obtain the primary product. Thus, the solution must be dilute and the reaction performed at a lower temperature. This reaction was conducted 70 years ago.[7] The authors obtained the dimer in no more than 2% isolated yield, while our yield was about 8% (see Table, entry 2). In a novel approach, we therefore tried to use a heterogeneous catalyst for this reaction (Scheme 1).

Instead of aluminum chloride, a faujasite-type zeolite can be used as a *thermal* catalyst for this reaction.[8] This zeolite contains supercages of 12 Å that can be accessed through windows of 7.5 Å diameter. Thus, the pores and cavities are large enough for benzyl chloride to be included.[9] The benzyl chloride molecules are believed to be partly "shielded" by the zeolite framework and are therefore not as freely accessible as in solution. Thus, it was hoped that the ability to polymerize should be reduced.

Indeed, compared with the solvent reaction, considerably less polymer is formed within NaY. After 2 h, only 17% was not converted into polymer in the retarded solvent reaction (Table, entry 2), whereas 73% could be isolated from the zeolite (Table, entry 4). Benzylbenzyl chloride (**1**) was obtained in yields of 12%. In addition, 53% of unreacted benzyl chloride and 2% of trimers were recovered from the zeolite. When the reaction time was prolonged, more benzyl chloride was converted into **1**, increasing the yield remarkably to 33% (Table, entry 6).

Although, with the exception of entry 6, polymer formation exceeds that of the dimer, these preliminary results show that zeolites seem destined to become the medium of choice for coupling reactions that normally lead to uncontrollable polymerization.

Without doubt, the most interesting aspect revealed by these experiments is the peculiar isomer ratio of the dimers formed. This study presents an example whereby the "banana-shaped" space created by a cage−window−cage arrangement favors formation of the "bent" *meta* product, even though electronic effects favor the *ortho* and *para* isomers. The CH_2Cl pendant in benzyl chloride has a slight electron-withdrawing inductive effect, which deactivates not only the *ortho*/*para* positions, but also, though to a smaller extent, the *meta* position. This deactivation is opposed in the *ortho*/*para* positions, but not in the *meta* position, by an activating mesomeric effect. In the case of benzyl chloride, this leads to a deactivating effect, which is most pronounced in the *meta* positions, weaker in the *ortho* positions and insignificant in the *para* position.[10] This agrees with the isomer ratio obtained from the solvent reaction (Table, entry 2). In the zeolite-catalyzed reactions, however, the *meta* isomer is always highly favored (Table, entries 4−8).

Since the *meta* isomer is generally the thermodynamically most stable isomer,[11] one could suspect that the preference for this isomer is due to thermodynamic

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[8] For the *photochemical* behavior of BnCl within NaY see: Alvaro, M.; Corma, A.; Garcia, H.; Miranda, M. A.; Primo, J. *J. Chem. Soc., Chem. Commun.* **1993**, 1041−1042. Among other products, **1** was also formed. The number of isomers of **1** as well as their ratio, however, were not reported.

[9] Approximately 2 mmol of BnCl were taken up by 1 g of activated zeolite. This corresponds to 3 molecules of BnCl per supercage! This large number can be explained by assuming that there is one molecule of BnCl in the center of each supercage, and one in every window accessing the supercages.

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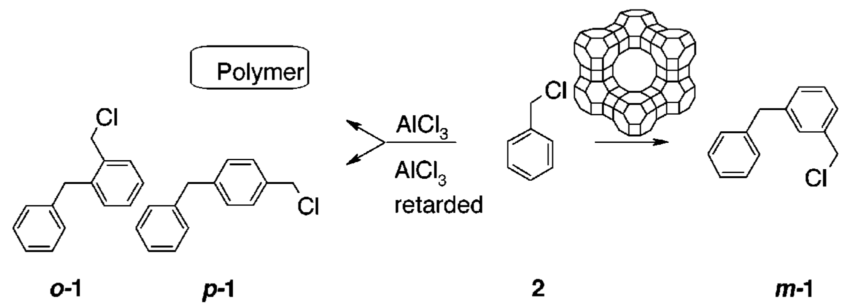
Scheme 1. Directions of Reaction Pathways



reasons. Strong Lewis acids catalyze the isomerization of alkyl benzenes, so that the thermodynamic equilibrium can be reached. However, there are three convincing arguments against this hypothesis:

First, when the reaction time is extended and if isomerization were to take place, one would expect that the share of the thermodynamically most stable isomer would increase. The isomer ratio, however, remained unchanged within the experimental error (Table, compare entry 4 with 5 and entry 7 with 8). These results also rule out the possibility that the *meta* isomer is the slowest to be converted into polymer, because also in this case, the isomer ratio would change with time. In solution, however, different polymerization rates for **1** were found.[6b]

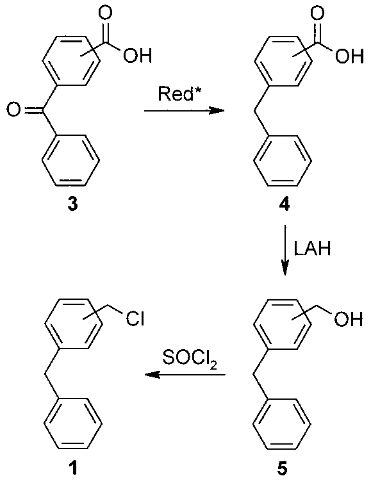
Second, the usual strategy to find the thermodynamic equilibrium is to perform the reaction at higher temperatures, so that activation energy barriers become less important. Thus, at temperatures that are high enough to reach the thermodynamic equilibrium, the main isomer obtained is the thermodynamically favored one. Raising the reaction temperature from room temperature to 35 °C did not affect the isomer ratio (Table, compare entry 4 with entry 7 and entry 5 with entry 8) within the margins of error. Because of complete polymerization it was not possible to study the isomer ratio of the reaction in solution at higher temperatures (Table, entry 3). Of course, this is not unexpected, since the thermodynamically most stable product is in fact the polymer!

Third, and most convincing, when neat *o*- or *p*-benzylbenzyl chloride (**1**) was included within NaY polymerization continues. Important is, however, that no isomerization takes place. Even after 20 h no other isomers could be extracted. Next to **1**, secondary products [mainly 1-(hydroxymethyl)-*x*-(phenylmethyl)benzene (benzylbenzyl alcohol) (**5**)] were isolated. However, these were exclusively products with the same constitution as the included **1**.

Thus, under the reaction conditions applied, no thermodynamic equilibrium is established. The reaction within the zeolite is kinetically controlled, and the preference for the formation of the *meta* isomer is therefore expected to be due to a molding effect of the zeolite.

To identify the isomers of benzylbenzyl chloride (**1**) without doubt, they were synthesized independently from commercially available benzoyl benzoic acids (**3**) (Scheme 2). The reaction sequence included a reductive Wolff–Kishner removal of the ketone to benzylbenzoic acid (**4**),[12] reduction with LAH to the corresponding benzylbenzyl alcohols (**5**),[12,13] and a substitution reaction with thionyl chloride.[13] The *ortho* isomer of **3** was converted to *o*-**4** with H_2 over a Pd/C catalyst[14] because Wolff–Kishner conditions yielded 4-phenyl-1(2*H*)-phthalazinone as the main product.[15]

Scheme 2. Independent Synthesis of 1-(Chloromethyl)-*x*-(phenylmethyl)benzene (1)



* Reduction of *o*-**3**: H_2, Pd/C
of *m*/*p*-**3**: NH_2NH_2, NaOH

In summary, the Friedel–Crafts reaction of benzyl chloride is a convincing example for the benefits of a zeolite acid catalyst over a conventional homogeneous Lewis acid catalyst. The faujasite-type zeolite considerably reduces the usual head-to-tail reaction leading to polymer. Moreover, its shape-selectivity causes the predominant formation of the *meta* dimer, which under conventional conditions, is difficult to obtain.

Experimental Section

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 250 MHz spectrometer at 300 K. Deuteriochloroform was used in all cases. UV spectra were measured on a Perkin-Elmer Lambda 7 spectrometer.

1. Classical Organic Synthesis: Friedel–Crafts Synthesis of 1-(Chloromethyl)-*x*-(phenylmethyl)benzene (1). A solution of **2** (9.0 mL, 9.1 g, 72 mmol) in nitrobenzene (33 mL) was cooled to −8 °C. $AlCl_3$ (0.15 g, 1.1 mmol) was added, and the resulting mixture was stirred for 2 h. The reaction was quenched by the addition of water (30 mL). The organic phase was separated from the aq phase and washed with CH_2Cl_2. The combined organic layers were evaporated under reduced pres-

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Table 1. Products Obtained in the Friedel–Crafts Reaction of Benzyl Chloride[a]

entry	reaction conditions[b]	*T* (°C)	time[c] (h)	BnCl (%)	dimer (%)	ratio *o*:*m*:*p*	trimer[d] (%)	other[e] (%)	solid[f] (%)
1	$AlCl_3$, no solvent[g]	RT	0.1	0	0	-	0	0	100
2	$AlCl_3$, $C_6H_5NO_2$	−8	2	8	8	35:25:40	1	0	83
3	$AlCl_3$, $C_6H_5NO_2$	RT	2	0	0	-	0	0	100
4	NaY	RT	2[h]	53	12	20:60:20	2	5	27
5	NaY	RT	24[h]	25	29	25:65:10	9	1	36
6[i]	NaY	RT	24[h]	45	33	30:60:10	9	1	12
7	NaY	35[j]	2[h]	16	24	25:65:10	8	6	46
8	NaY	35[j]	24[h]	4	23	25:65:10	3	0	70

[a] Conversions and isomer ratios were determined by GC; average of at least 3 experiments. [b] See Experimental Section for details. [c] Reaction time starts as soon as the BnCl solution is added to the catalyst. [d] Identified by GC MS. [e] Mainly benzyl alcohol and dibenzyl ether. [f] Amount of BnCl converted to polymer in the $AlCl_3$-catalyzed reactions and the amount that could not be extracted in the zeolite-catalyzed reactions. [g] 0.15 g of $AlCl_3$ added to 9 mL of BnCl. [h] Extraction times not included. [i] Scaled up by a factor of 10. [j] Reaction temperatures of 35 °C were obtained by keeping the zeolite in refluxing pentane.

sure. Afterward, unreacted **2**, and the nitrobenzene, were removed using vacuum distillation. The resulting brown residue was extracted with Et_2O. The extract was weighed and analyzed by GC MS and GC FID. Yield: 8% (not isolated).

Synthesis of 1-(Chloromethyl)-*x*-(phenylmethyl)benzene (1). The three isomers were synthesized in three steps from the corresponding *x*-benzoylbenzoic acids (**3**), which are commercially available from Aldrich.

***o*-Benzylbenzoic Acid (4).** The reduction of *o*-**3** (3.0 g, 13 mmol) was performed in acetic acid (4.5 mL) with 0.3 g of Pd/C catalysts at 65 °C and under 1 bar of H_2 gas. After 44 h, the reaction was complete. The catalyst was filtered off and washed with 25 mL of a hot Na_2CO_3 solution. Concentrated HCl was slowly dropped into the filtrate and the product precipitated. The product was washed with water and dried overnight over $CaCl_2$. Yield: 2.1 g (9.9 mmol; 76%). mp 114 °C (lit.[16] 115 °C); ^{1}H NMR δ 4.45 (s, 2 H), 7.1−7.35 (m, 7 H), 7.55 (t, 1 H), 8.05 (d, 1 H), 9.80 (s, br, 1 H); ^{13}C NMR CH_2: δ 39.6, CH: δ 125.9, 126.3, 128.3, 129.0, 131.4, 131.6, 132.6, C: δ 140.8, 143.0.

***m*- or *p*-Benzylbenzoic Acid (4).** To a suspension of **3** (1.0 g, 4.4 mmol) and 0.7 g of finely powdered NaOH in triethylene glycol (30 mL) was added 0.7 mL of aq hydrazine. The mixture was heated for 8 h at 110 °C and then for 10 h at 210 °C. The solution was cooled, and water was added until there was only one phase. The solution was washed twice with Et_2O. Concentrated HCl was dropped slowly to the water phase while stirring, and white crystals precipitated. The product was filtered off and dried. *m*-**4**: Yield: 0.74 g (3.5 mmol; 80%). mp 102−104 °C (lit.[17] 102−104 °C); ^{1}H NMR δ 4.09 (s, 2 H), 7.2−7.5 (m, 7 H), 8.0−8.1 (m, 2 H); ^{13}C NMR CH_2: δ 41.7, CH: δ 126.4, 128.59, 128.62, 128.7, 128.9, 130.6, 134.4 C: 129.5, 140.3, 141.7, 172.1; *p*-**4**: Yield: 0.76 g (3.6 mmol; 82%). mp 159 °C (lit.[18] 159 °C). ^{1}H NMR δ 4.05 (s, 2H), 7.20−7.40 (m, 7H), 8.05 (d, 2H); ^{13}C NMR CH_2: δ 42.0, CH: δ 126.4, 128.6, 129.0, 129.1, 130.5, C: 127.2, 139.9, 147.6, 172.0.

1-(Hydroxymethyl)-*x*-(phenylmethyl)benzene (5). A warm solution of **4** (0.25 g, 1.2 mmol) in 7 mL of Et_2O was added dropwise to a stirred suspension of 0.05 g LAH in 2 mL of anhyd Et_2O. After refluxing for 1 h, 1 mL of water was added to destroy the excess of LAH. The ether layer was diluted to 10 mL and washed twice with 1 mL of a 10% H_2SO_4 solution. The combined acidic aq phases were washed with 5 mL of ether. The organic phases were combined and washed twice with 2 mL of a 10% Na_2CO_3 solution. The basic aq phase was washed with 5 mL of ether. All organic phases were combined and dried overnight over anhyd $MgSO_4$. Evaporation of the solvent afforded **5**. *o*-**5**: Yield: 0.18 g (0.91 mmol; 76%) colorless oil. ^{1}H NMR δ 2.04 (s, br, 1 H), 4.13 (s, 2 H), 4.67 (s, 2 H), 7.15−7.40 (m, 8 H), 7.4−7.5 (m, 1 H); ^{13}C NMR CH_2: δ 38.4, 62.9 CH: δ 126.1, 126.7, 127.8, 128.2, 128.4, 128.6, 130.4, C: δ 138.4, 138.8, 140.4; *m*-**5**: Yield: 0.13 g (0.66 mmol; 56%) colorless oil. ^{1}H NMR δ 2.83 (s, br, 1 H), 4.04 (s, 2 H), 4.62 (s, 2 H), 7.15−7.45 (m, 9 H); ^{13}C NMR CH_2: δ 41.7, 64.8, CH: δ 124.6, 126.0, 127.4, 128.0, 128.3, 128.5, 128.8, C: δ 140.9, 141.1, 141.2; *p*-**5**: Yield: 0.11 g (0.56 mmol; 47%) white crystals. mp 41 °C (lit.[16] 42 °C); ^{1}H NMR δ 3.05 (s, br, 1 H), 4.05 (s, 2 H), 4.67 (s, 2 H), 7.20−7.45 (m, 9 H); ^{13}C NMR CH_2: δ 41.6, 64.9, CH: δ 126.0, 127.2, 128.4, 128.8, 129.0, C: δ 138.5, 140.5, 141.0.

1-(Chloromethyl)-*x*-(phenylmethyl)benzene (1). For 4 h, **5** (0.42 g, 2.1 mmol) was refluxed in 1.1 mL (15 mmol) of $SOCl_2$ and one drop of pyridine. The excess $SOCl_2$ was evaporated and the crude product cleaned by filtering through silica gel with Et_2O/petroleum ether (5:95) eluent. *o*-**1**: Yield: 0.38 g (1.8 mmol; 84%), colorless oil. ^{1}H NMR δ 4.20 (s, 2 H), 4.59 (s, 2 H), 7.14−7.43 (m, 9 H); ^{13}C NMR CH_2: δ 38.3, 44.4, CH: δ 126.3, 127.0, 128.5, 128.7, 129.3, 130.4, 130.9, C: δ 135.7, 139.6, 140.0; *m*-**1**: Yield: 0.39 g (1.8 mmol; 86%) colorless oil. ^{1}H NMR δ 4.03 (s, 2 H), 4.59 (s, 2 H), 7.13−7.40 (m, 9 H); ^{13}C NMR CH_2: δ 41.8, 46.2, CH: δ 126.2, 126.4, 128.5, 128.85, 128.92, 129.0, 129.1, C: δ 137.6, 140.6, 141.7; *p*-**1**: Yield: 0.34 g (1.6 mmol; 76%) colorless oil. ^{1}H NMR δ 4.02 (s, 2 H), 4.60 (s, 2 H), 7.18−7.38 (m, 9 H); ^{13}C NMR CH_2: δ 41.6, 46.1, CH: δ 126.2, 128.5, 128.7, 128.9, 129.3, C: δ 135.3, 141.5.

2. General Procedure: Zeolite-Mediated Organic Synthesis of 1. Zeolite NaY (2.4 g of LZ-Y52, obtained from Aldrich) was activated for 2 h in an evaporating dish at 200 °C in a muffle furnace (lost approximately 24 wt % of lattice water). After the activating period, the hot zeolite was immediately transferred into a dry flask filled with argon, and the flask was sealed. As soon as the zeolite reached room temperature, the loading solution of 870 mg of **2** in 150 mL of pentane (dried over molecular sieves prior to use) was added. The suspension was magnetically stirred during the reaction time. A drying tube containing anhyd $CaCl_2$ was mounted on the flask to keep out moisture. The guest uptake within the zeolite was monitored by UV analysis of aliquots from the supernatant solution. The signal of **2** ($\epsilon_{260\ \mathrm{nm}} = 202\ \mathrm{M^{-1}cm^{-1}}$) decreased as more guest was taken up by the zeolite. The uptake was found to be rapid: 90% of the maximum loading was reached within only 5 min and complete uptake within 15 min. Abundant **2** remaining within pentane did not react. After the reaction time, the zeolite was filtered through a glass sinter (Por. 4) and washed several times with pentane. The zeolite was continuously extracted for 18 h with hot CH_2Cl_2 using a Soxhlet apparatus. The solution obtained was evaporated under reduced pressure and the recovered material weighed and analyzed (see Table 1).

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