Selective alkylation of methylbenzenes with cyclohexene catalyzed by solid acids

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The synthesis of mixtures of cyclohexyltoluenes from cyclohexene and toluene, catalyzed by solid-acid catalysts, such as zeolites (H-USY, H-BEA, H-Mor) or activated clays (e.g. Filtrol-24), was studied. The *ortho/meta/para* ratio of these mixtures strongly depends on the structure of the catalysts involved. With zeolite H-USY and Filtrol-24 as the catalysts the *meta/para* ratio is found to be about 2:1, in agreement with the thermodynamic equilibrium, and the *ortho*-isomer is absent. As H-USY appeared to be a good isomerization catalyst for the cyclohexyltoluenes, the mechanism might involve *ortho/meta/para*-alkylation followed by isomerization. In this way a new route has been developed to the expensive intermediate 3-methylbiphenyl. The reaction of cyclohexene with xylenes or mesitylene, catalyzed by the zeolite H-USY or the clay Filtrol-24, gives mixtures of cyclohexylxylenes or cyclohexylmesitylene, respectively.

KEY WORDS: alkylation; alkylbenzenes; aromatic substitution; cyclohexene; solid-acid catalysts.

1. Introduction

Alkylated biphenyl compounds can be prepared by Friedel–Crafts alkylation of biphenyl or by cyclohexylation of alkylbenzenes, followed by dehydrogenation.

Dialkylbiphenyls are precursors of dihydroxy- and dicarboxy-biphenyls which are valuable monomers [1] yielding thermostable polymers. 4,4′-Di-isopropylbiphenyl can be synthesized by shape-selective isopropylation of biphenyl by propene over de-aluminated mordenite [2]. 2,4-Dimethylbiphenyl, a precursor of 2,4-biphenyldicarboxylic acid, has been prepared by cyclohexylation of *m*-xylene in the presence of concentrated sulfuric acid followed by dehydrogenation and separation of the mixture of 2,4-, 2,6- and 3,5-dimethylbiphenyl by vacuum distillation [3].

3-Methylbiphenyl is an expensive chemical, used in the pharmaceutical industry. Conventional routes for the preparation of 3-methylbiphenyl are the Vilsmeyer reaction of 2-methyl-4-phenyl-1-penten-4-ol with phosphoryl chloride in dimethylformamide [4] and the palladium-catalyzed reaction of phenylboronic acid with 3-bromotoluene in benzene under alkaline conditions [5].

A relatively inexpensive new route would include cyclohexylation of toluene, separation of isomers, dehydrogenation of the 3-isomer and recycling of the 2- and 4-isomer.

For example, in the reaction of cyclohexene with toluene, catalyzed by HF, a mixture of cyclohexyltoluenes with a ratio of 33% *ortho*-isomer, 18% *meta*-isomer and 49% *para*-isomer was obtained [6]. Because the boiling points of the isomers [7] are close to one another the pure compounds were not isolated, and the mixture of isomers was subjected to catalytic dehydrogenation.

In recent years considerable attention has been paid to the potential of zeolites to act as heterogeneous and regenerable catalysts in electrophilic aromatic substitutions [8]. The tunability of many properties such as hydrophobicity, acidity and the range of pore sizes make zeolites interesting alternatives for conventional non-regenerable catalysts.

The reaction of cyclohexene with toluene catalyzed by zeolites has been described by Espeel [9], but under his conditions a considerable percentage of *ortho*-substitution was observed. 1,3-Dimethyl-5-*tert*-butylbenzene was selectively obtained by the alkylation of *m*-xylene with isobutene, catalyzed by Filtrol-24, an acid-activated clay [10]. These examples of steric constraints prompted us to investigate the selective alkylation of the aromatic nucleus with cyclohexene catalyzed by zeolites and also by the acid-activated clay Filtrol-24.

2. Experimental

2.1. Catalysts

Zeolite H-BEA (Si/Al = 13.5) was purchased from Uetikon AG (Switzerland) and the zeolites H-BEA (Si/Al = 25) and H-BEA (Si/Al = 50) from Süd-Chemie. Zeolite Na-USY (Si/Al = 2.5) and a silica–alumina catalyst (HA-HPV, Si/Al = 2) were kindly donated by AKZO-Nobel Chemicals, Amsterdam. The zeolite Na-USY was ion-exchanged three times with 1 M aqueous ammonium acetate at 70 °C. The resulting NH_4-USY was

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converted to H-USY by calcination at 550 °C. Zeolite H-Mordenite (Si/Al = 50) was purchased from Süd-Chemie. The zeolites were activated before use by heating at 400 °C for 2 h. Filtrol-24 (Engelhard) and Al-pillared montmorillonite (Süd-Chemie) were partly dried by azeotropic removal of water by reflux in the appropriate alkylbenzene. For comparison with the zeolites, Filtrol-24 was also dried by heating at 400 °C for 2 h. Amberlyst-15 was purchased from Aldrich. Silica-occluded heteropoly-acid (SiO_2–$H_3PW_{12}O_{40}$) was prepared according to the directions of Izumi *et al.* [11]. 3-Methyl- and 4-methylbiphenyl were purchased from Acros Chemicals.

2.2. *Analyses*

^{1}H and ^{13}C NMR spectra of the isolated mixtures were recorded with a Varian VXR-400 S spectrometer at 25 °C, with tetramethylsilane (TMS) as internal reference. IR spectra were obtained of the mixtures (neat) using a Beckman IR 4210 infrared spectrophotometer. GC–MS analyses were performed using a VG 70-250 mass spectrometer, coupled to a Sil 5 (25 m × 0.25 mm, df = 0.4) column. Gas chromatograpic analyses were performed using a Varian Star 3600 gas chromatograph with a flame ionization detector and a CP Sil 5 CB (50 m × 0.50 mm, df = 2) column.

2.3. *Reaction procedures*

Procedure I. After addition of 2.5 g of activated zeolite to a solution of 2.05 g (25 mmol) of cyclohexene in 33 ml of toluene (or alkylbenzene) the reaction mixture was heated with stirring for 3 h at 110 °C. Isolation of the reaction product was performed by filtering the solid catalyst from the hot reaction mixture, washing the catalyst and evaporating the solvent at reduced pressure.

Procedure II. With Filtrol-24 as the catalyst some of the water present in the layers was removed by azeotropic distillation of a mixture of 2.5 g of clay and 30 ml of toluene (or higher aromatic) for 2.5 h in a batch reactor, equipped with a Dean–Stark condenser for water removal. After cooling to 75 °C a solution of 2.05 g of cyclohexene in 3 ml of solvent/reactant was added within 15 min and the reaction mixture was heated while stirring for 3 h at 110 °C. The same work-up as described in Procedure I was performed.

GC and GC–MS of the residues gave the percentages of the isomers and the dialkylated products. Assignments the GC peaks of the isomers were checked after aromatization of a mixture of cyclohexyltoluenes, followed by comparison with the retention times found for authentic 3-methylbiphenyl and 4-methylbiphenyl, respectively. The mass of the peaks in combination with the IR spectra and also the NMR analyses of the mixtures completed the assignments of the chemical structures to the compounds present in the mixtures.

3. Results and discussion

3.1. *Reaction of cyclohexene and toluene*

Table 1 lists the results of the reaction of cyclohexene with toluene (excess) catalyzed by solid-acid catalysts. The selectivity of the reaction of cyclohexene and toluene depends strongly on the structure of the catalysts involved.

More or less similar results as to regioselectivity were obtained with the following catalysts: Amberlyst-15, SiO_2–$H_3PW_{12}O_{40}$, HA-HPV and the zeolite H-MOR. The percentages of the *ortho*-isomer found are between 12 and 20%, those of the *meta*-isomer are in the range 14–16%, while the *para*-isomer is the main product with an average of 50–60%. These percentages are in agreement with those found in the reaction of cyclohexene with toluene catalyzed by the conventional homogeneous Friedel–Crafts catalysts.

Table 1
Reaction of cyclohexene with toluene (excess) catalysed by solid catalysts[a]

Catalyst/procedure[b]	Conversion (%)	Cyclohexyltoluene			Dicyclohexyltoluene (3,4 or 3,5)	Dimer
		Ortho	*Meta*	*Para*		
H-BEA (13,5)/I	77	tr	15	66	18	1
H-BEA (25)/I	75	tr	14	63	22	1
H-BEA (50)/I	73	tr	14	63	20	1
H-USY/I	94	tr	64	34	2	tr
H-MOR/I	18	12	14	62	1	12
Filtrol-24/II	95	tr	65	30	5	tr
Filtrol-24/I	98	tr	50	44	5	–
Al-pillared clay/II	96	–	43	42	15	–
HA-HPV/I	52	20	14	60	2	4
Amberlyst-15/I	68	19	16	50	8	5
SiO_2–$H_3PW_{12}O_{40}$/I	73	19	16	56	6	2

[a] Reaction conditions: 2.05 g (25 mmol) cyclohexene in 33 ml of toluene was refluxed with 2.5 g catalyst for 3 h.

[b] See section 2.3.

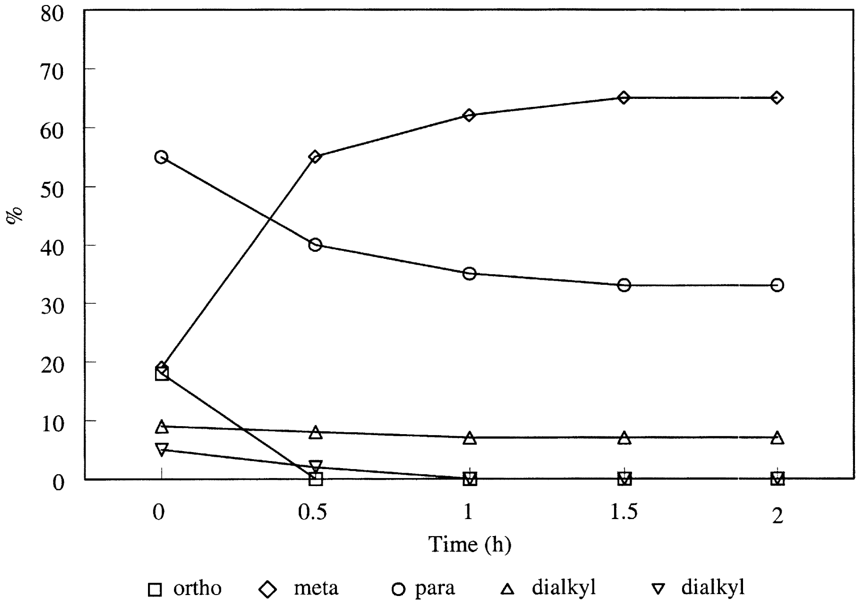


Figure 1. Isomerization of a cyclohexyltoluene mixture with an *ortho*/*meta*/*para* ratio of about 1 : 1 : 3 over zeolite H-USY.

Formation of the *meta*-isomer as the main product is found with the catalysts H-USY and the activated clay Filtrol-24, while with these catalysts the *ortho*-isomer is essentially absent. The *meta*/*para* ratio is found to be about 2 : 1, in agreement with the thermodynamic equilibrium. The amount of dicyclohexyltoluenes is very low.

Two explanations can be considered: (i) the zeolite H-USY and the clay catalyst exert shape selectivity in the alkylation, resulting in the regioselectivity observed; and (ii) initially an *ortho*/*meta*/*para* mixture is obtained with *p*-cyclohexyltoluene dominating, but due to the isomerization activity of the catalysts the thermodynamic mixture is formed. In view of the observed catalytic isomerization of the cyclohexyltoluenes (*cf.* section 3.2) we adhere to the second explanation.

With the zeolite H-BEA as the catalyst the results of the reaction of cyclohexene with toluene are independent of the Si/Al ratio, while the formation of the *para*-isomer and also the dialkylation reaction is more pronounced. The strained *ortho*-isomer is almost absent, which may due to limited space at the active sites of Beta. On the other hand, the formation of dicyclohexyltoluenes is assumed to take place on the large outer surface of Beta. An increase of the amount of dicyclohexyltoluenes is also observed in the reaction of cyclohexene with toluene catalyzed by the Al-pillared montmorillonite. This may be caused by the increase of the layer distances within the clay structure.

3.2. *Isomerization of a mixture of cyclohexyltoluenes*

Figure 1 shows the isomerization of a cyclohexyltoluene mixture with an *ortho*/*meta*/*para* ratio of about 1 : 1 : 3 after addition of the zeolite H-USY to a solution of the mixture in *n*-heptane–toluene (4 : 1), followed by reflux while stirring.

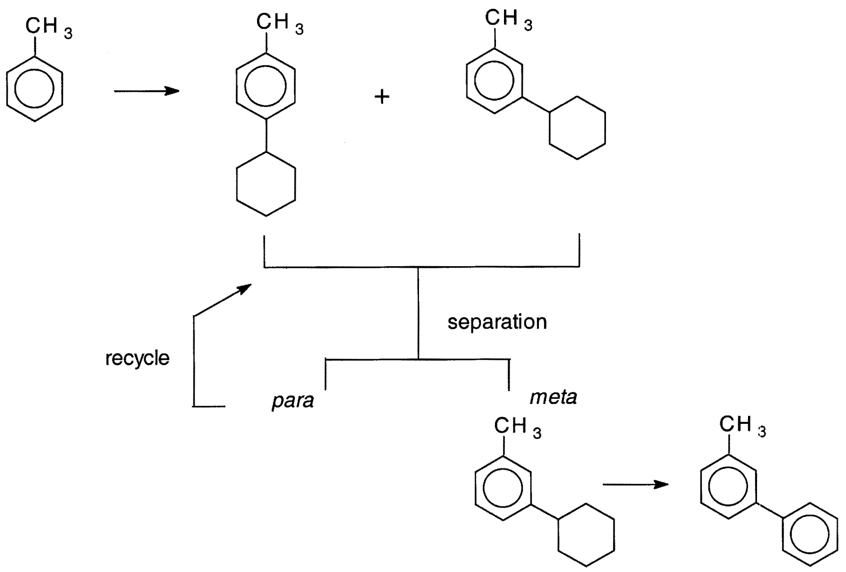
The *meta*/*para* ratio of the mixture is found to be about 2 : 1 after 1 h of reaction, while the concentration of *ortho*-isomer is essentially zero, which means that the isomerization of the cyclohexyltoluene mixture can easily take place during alkylation over zeolite H-USY as the catalyst. After separation [12] of the *meta*-isomer from the mixture the resulting fraction of *p*-cyclohexyltoluene can be isomerized to the starting mixture (scheme 1) while the *meta*-isomer can be dehydrogenated over Pt or Pd to yield the target compound: 3-methylbiphenyl.

Schemes 1 and 2 show the new and the conventional approaches to the synthesis of 3-methylbiphenyl. The conventional synthesis of 3-methylbiphenyl [5] involves the coupling of 3-bromotoluene (obtained in a multi-step synthesis from toluene via 4-nitro- and 4-aminotoluene) and benzene boronic acid (obtained in a two-step synthesis from benzene). Coupling (the Suzuki reaction) is catalyzed by $Pd(Ph)_4$ and is carried out in the presence of Na_2CO_3. Side products of the reaction sequence are *o*-nitrotoluene in the first step and inorganics in the bromination and deamination step. For the final step the *E*-factor [13] is estimated to be about 4.

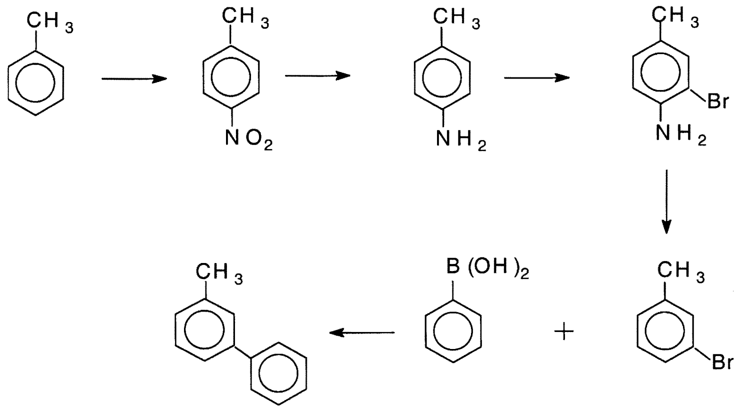
The alkylation/separation/dehydrogenation sequence outlined in the present work is essentially waste free.

3.3. *Regeneration of the catalysts*

Table 2 illustrates the reusability of the zeolite H-USY and the activated clay Filtrol-24. After the reaction the zeolite was filtrated from the solution and washed with the solvent. Subsequently the zeolite was dried and



Scheme 1.



Scheme 2.

reactivated at 400 °C for the next catalytic cycle. After three cycles no loss of catalytic activity was detected. With Filtrol-24 the reactivation was executed by azeotropic distillation in fresh toluene for 1 h. After three cycles the conversion to the mixture of cyclohexyltoluenes was constant, but the *meta*/*para* ratio was changed in favor of the *para*-isomer, indicating some decrease in isomerisation activity.

3.4. Reaction of cyclohexene with alkylbenzenes

Table 3 shows the results of the reaction of cyclohexene with the xylenes and mesitylene, catalyzed by H-USY and Filtrol-24. These substrates are electronically activated for alkylation.

With H-USY as the catalyst practically pure 4-cyclohexyl-1,2-dimethylbenzene was formed in the reaction of

Table 2
Regenerability of the catalysts in the reaction of cyclohexene with toluene

Catalyst	Cycle	Conversion (%)	Cyclohexyltoluene		Dicyclohexyltoluene
			Meta	*Para*	
H-USY	1	91	67	31	2
	2	91	65	34	1
	3	91	65	33	2
Filtrol-24	1	95	65	30	5
	2	95	59	32	8
	3	91	44	47	9

Table 3
Reaction of cyclohexene with alkylbenzenes over H-USY and Filtrol-24[a]

Catalyst	Alkylbenzene	Conversion (%)	Selectivity (%)			
			Monocyclohexyl	Dicyclohexyl	Substituted biphenyl	Other
H-USY	*o*-Xylene	98	98 (4-cyclohexyl), 2 (3-c)	–	–	–
Filtrol-24	*o*-Xylene	99	69 (4-cyclohexyl), 17 (3-c)	10	2	2
H-USY	*m*-Xylene	98	91 (5-cyclohexyl), 9 (4-c)	–	–	–
Filtrol-24	*m*-Xylene	98	67 (5-cyclohexyl), 31 (4-c)	1	1	–
H-USY	*p*-Xylene	96	80 (2-cyclohexyl)	3	9	3[b]; 2[c]
Filtrol-24	*p*-Xylene	93	88 (2-cyclohexyl)	2	4	3[b]; 2[c]
H-USY	Mesitylene	91	76 (2-cyclohexyl), 11 (1,2,4,5-c)	tr	11	2
Filtrol-24	Mesitylene	99	68 (2-cyclohexyl), 11 (1,2,4,5-c)	tr	19	1

[a] Reaction conditions: 2.05 g (25 mmol) cyclohexene in 33 ml of alkylbenzene was stirred at 110 °C with 2.5 g catalyst for 3 h.
[b] *m*-Cyclohexyltoluene.
[c] *p*-Cyclohexyltoluene.

cyclohexene and *o*-xylene. By contrast a considerable amount of 3-cyclohexyl-1,2-dimethylbenzene and also other side-products were produced with Filtrol-24 as the catalyst. Also, in the reaction of cyclohexene with *m*-xylene H-USY is the more selective catalyst. Predominantly 5-cyclohexyl-1,3-dimethylbenzene is obtained over H-USY, while with Filtrol-24 the ratio 5-/4-cyclohexyl-1,3-dimethylbenzene is about 2 : 1. The reaction of cyclohexene with *p*-xylene gives with H-USY as well as with Filtrol-24 as the catalyst predominantly 2-cyclohexyl-1,4-dimethylbenzene, but the formation of side-products, among which *m*- and *p*-cyclohexyltoluene were identified, is considerable.

The reaction of cyclohexene with mesitylene results in the formation of 2-cyclohexyl-1,3,5-trimethylbenzene as the main product, but isomerization to 5-cyclohexyl-1,2,4-trimethylbenzene is also observed with both catalysts. Moreover the reaction of two moles of mesitylene resulting in the formation of a symmetric biphenyl derivative is noteworthy.

4. Conclusions

The synthesis of cyclohexyltoluenes in the liquid phase by alkylation of toluenes with cyclohexene, catalyzed by regenerable solid-acid catalysts, depends strongly on the nature of the catalysts involved. With zeolite H-USY as the catalyst the thermodynamic equilibrium of *meta*- and *para*-isomers is obtained, the *ortho*-isomer being absent. This opens the way to a new low-waste route to 3-methylbiphenyl. After separation of the isomers the *para*-isomer can be isomerized to the starting mixture with the same catalyst. Filtrol-24 can also produce the thermodynamic equilibrium in the same reaction, but H-USY is the preferred catalyst over Filtrol-24 because of its excellent regenerability.

The reaction of cyclohexene with *o*-, *m*- and *p*-xylenes is also catalyzed by the zeolite H-USY and leads selectively to the 4-, the 5- and the 2-cyclohexyl derivative, respectively. Formation of the symmetric biphenyl compound from two moles of mesitylene catalyzed by the zeolite H-USY and the activated clay Filtrol-24 is noteworthy.

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