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Direct fluorination of toluene using elemental fluorine in gas/liquid microreactors

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Dedicated to late Professor Schiemann on the occasion of the 100th anniversary of his birth

Abstract

Direct fluorination of toluene, pure or dissolved in either acetonitrile or methanol, using elemental fluorine was investigated in gas/liquid microreactors, namely a falling film microreactor and a micro bubble column. The experiments included measurements at high substrate concentrations and at high fluorine contents diluted in a nitrogen carrier gas, e.g. up to 50 vol.% fluorine. Results obtained were compared to the performance of a laboratory bubble column which served as a technological benchmark.

Due to the formation of liquid layers of only a few tens of micrometers thickness, the microreactors provide very large interfacial areas, e.g. up to 40,000 m^2/m^3. These values exceed by far those of the laboratory bubble column as well as all other devices applied in practice.

The potential for enhancing mass and heat transfer was verified by several experiments resulting in an increase in conversion and selectivity for the microreactors compared to the laboratory benchmark. For the falling film microreactor, yields of up to 28% of monofluorinated ortho and para products for a degree of toluene conversion of 76% were obtained. These values are of the same order as described for the industrially applied Schiemann process. Space-time yields of the microreactors, when referred to the reaction channel volume, were orders of magnitude higher than those of the laboratory bubble column. Taking into account the construction material needed, the corresponding figures of merit, for an idealized geometry as well as the existing total reactor geometry, still indicate technological and economic benefits.

A variation of operating conditions for the direct fluorination revealed that conversion can be increased in the microreactors by using higher fluorine-to-toluene ratios and reaction temperatures. The choice of solvent is also essential, with acetonitrile yielding much better results than methanol.

Keywords: Fluorination; Toluene; Elemental fluorine; Falling film microreactor; Micro bubble column

1. Introduction

The direct fluorination of aromatics with pure fluorine on a technical scale is a problem still unsolved to date. For the synthesis of the vast majority of fluorinated compounds multi-step processes such as the Schiemann reaction are employed. In this process, aromatic amines are converted into diazonium tetrafluoroborates, which thermally decompose with formation of monofluorinated aromatic compounds in reasonable yields [1].

On the laboratory scale, a number of experiments using elemental fluorine as a fluorination agent have been carried out. For instance, the fluorination of toluene was performed by a gas phase process as described by Schiemann et al. in 1968 [2]. However, selectivities turned out to be very low.

Other authors investigated direct fluorination of aromatic compounds in the liquid phase. In the very early attempts using conventional reactors, direct fluorination experiments were characterized by the formation of undefined products and often led to explosions [3] due to too large heat release. In the last 30 years, substantial efforts have been focused on the development of more advanced processing routes, e.g. improved heat transfer characteristics, allowing the desired electrophilic substitution path to proceed. By operation at extremely low temperatures, e.g. −70°C, and reactant concentrations, e.g. down to 0.01 mol/l, the proof of feasibility for performing direct fluorination was given for aromatic substrates like benzene, toluene and phenol [4–7].

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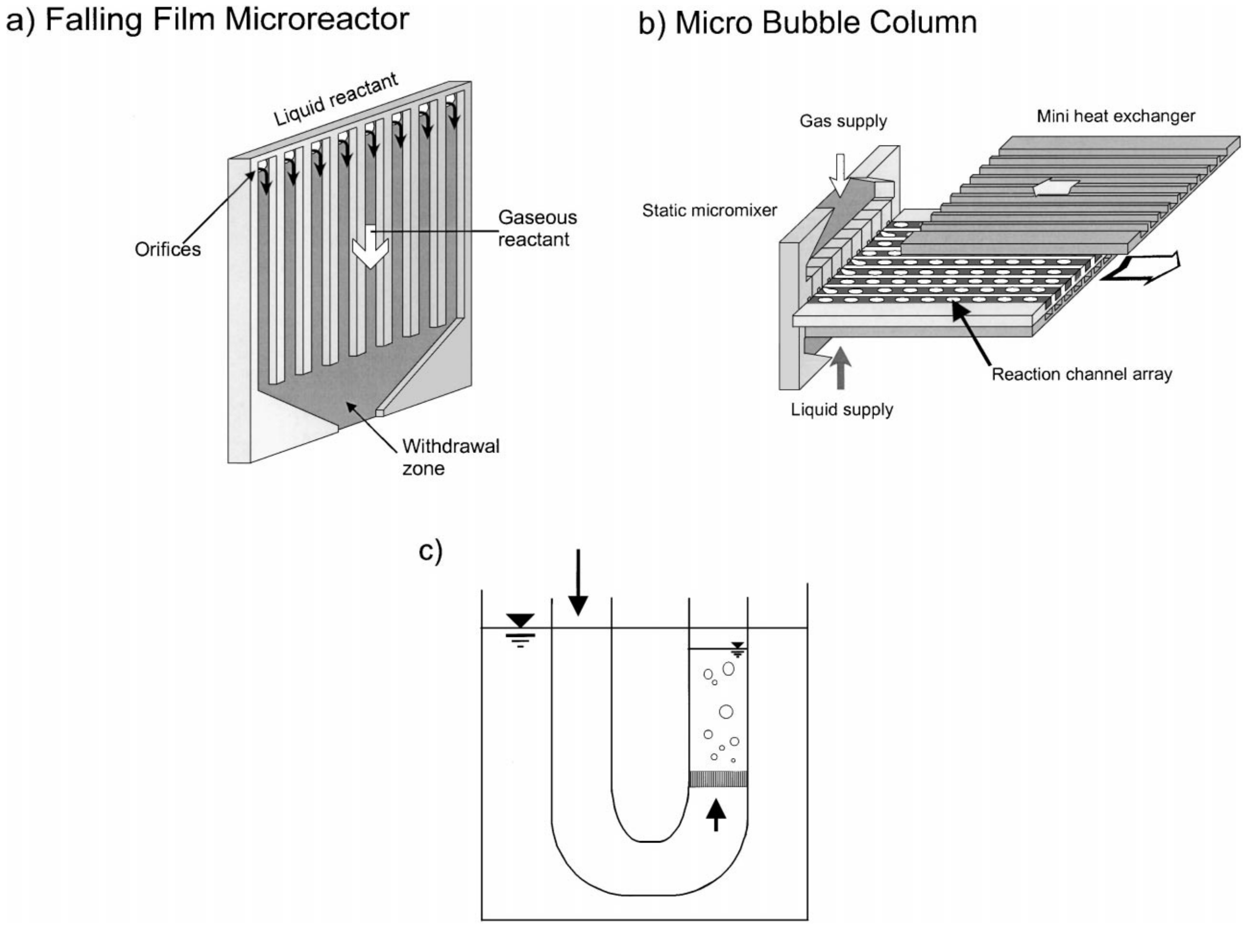


Fig. 1. Schematic diagram of a falling film microreactor, a micro bubble column and a laboratory bubble column. (a) Vertically oriented falling film microreactor, a thin liquid film is fed through orifices into the reaction channels, generating a relatively large surface for contact to the gas. (b) Micro bubble column the liquid and gaseous reactants are contacted through a static micromixer, and, subsequently, fed into the reaction channels. (c) In the laboratory bubble column the gas is dispersed through a porous frit into the liquid.

Even greater control over reaction temperature and, in addition, reactant mixing should be achievable by using microfabricated reaction devices, so-called microreactors, since high gradients for heat and mass transfer can be utilized, due to small diffusion distances within the microchannels [8]. These transport enhancements, in general, allow improvement in the performance of reactions which are not carried out under a kinetically controlled regime, e.g. fast reactions coupled to fast side reactions. If the reaction is run in a multiphase system, the potential benefit of using microreactors may even be amplified. This scenario ideally holds for gas phase reactions on solid catalysts and the resulting improvements have been demonstrated recently by many authors and for a large variety of applications [9,10].

The criteria sketched above obviously are also met by gas/liquid reactions. Two approaches paved the way for further investigations in this field. In the first reference, a selection of possible microreactor designs for efficient gas/liquid contacting was presented and their potential applications were outlined [11]. The second paper aimed at giving a sound theoretical basis for this field by analyzing various cases of diffusion hindrance [12]. This was completed by a first proof of feasibility using existing contacting components, originally designed for liquid/liquid extraction. Based on this knowledge, the first integrated gas/liquid microreaction systems were built, termed a falling film microreactor (FFMR) and a micro bubble column (MBC) [11,13] (see Fig. 1a and b) made of stainless steel. In the meantime Chambers et al. [14] have successfully tested a simple microreactor for the direct fluorination of 1,3-dicarbonyl compounds, but no yield or selectivity data have been reported.

The FFMR, developed for this study, generates a thin falling film of several 10 μm thickness flowing by means of gravity forces. This is performed on a platelet comprising a large number of microchannels of 100 μm×300 μm cross-section. By changing volume flow, control can be exerted over film thickness. The micro bubble column consists of a mixing and a reaction unit. Various mixers containing interdigital channel arrays of dimensions from a few micrometers to a few tens of micrometers were tested. For the experiments described in this article, only one device was used equipped with 20 μm deep gas and liquid feeding channels 7 and 20 μm wide, respectively. For the reaction unit comprising an array of parallel microchannels, two types were utilized, namely platelets of 50 μm×50 μm and 300 μm×100 μm channel cross-section, in the following referred to as 'narrow' and 'wide' channels. More details on design criteria and microreactor assembly are given in reference [13].

It is the aim of the following discussion to give a detailed analysis of the reaction performance of the microreactors with regard to direct fluorination of toluene and to compare the respective results to technical benchmarks. In addition, it is aimed to gather first hints for a performance optimization of the microreactors by means of variation of operating conditions. In this context, considerable efforts were made in order to get precise analytical data on conversion, yield, and selectivity.

2. Experimental

Fluorinations were performed at two sites, namely the Institut für Angewandte Chemie at Berlin-Adlershof (ACA) and the Institut für Mikrostrukturtechnik in Karlsruhe. Using the equipment at the former site, only fluorinations with fluorine contents up to 10 vol.% could be carried out, whilst at Karlsruhe much higher contents could be utilized. Due to this difference in operating parameters, the corresponding measurements have been split in two groups, named series A and B. A complete list of all experimental parameters in both experimental series is given in Tables 1–4.

In all experiments, the liquid volume flow in the microreactors was controlled using a HPLC pump (L-6200A). Temperature was monitored by resistance thermometers and the gas flow was set by mass flow controllers.

Conversion, yield and selectivity were not referred to the non-stoichiometric component, i.e. fluorine, although in most experiments fluorine-to-toluene ratios below one were used. This was caused by a lack of experimental instrumentation for a quantitative determination of excess fluorine remaining in the gas phase after reaction. Therefore, the corresponding definitions had to be based on toluene:

$$X = \frac{n_{\text{Toluene},0} - n_{\text{Toluene},\text{R}}}{n_{\text{Toluene},0}} \times 100\ (\%),$$

$$Y = \frac{n_{\text{mono-F-toluene}}}{n_{\text{Toluene},0}} \times 100\ (\%),$$

$$S = \frac{n_{\text{mono-F-toluene}}}{n_{\text{Toluene},0} - n_{\text{Toluene},\text{R}}} \times 100\ (\%)$$

where X the is conversion (%); S is the selectivity (%); Y is the yield (%); $n_{\text{Toluene, 0}}$ is the amount of toluene before reaction (mol); $n_{\text{Toluene, R}}$ is the amount of toluene after reaction (mol); and $n_{\text{mono-F-toluene}}$ is the amount of monofluorinated products (ortho, meta, para) (mol).

The majority of data presented were based on single experiments. For control of accuracy, two consecutive measurements were performed for selected experiments. These measurements confirmed a reproducibility of the experiments within a range of about 5%.

During the experimental investigations, considerable efforts had to be made to establish suitable analytical methods for gathering reliable data. For series A, it turned out that by using high performance liquid chromatography (HPLC) and gas chromatography (GC) most of the reaction products could be identified. Moreover, quantitative data on toluene consumption and generation of monofluorinated products were obtained. In case of series B, fourier transform infrared spectroscopy (FTIR) analysis based on a

Table 1
Series A: FFMR

Experimental no.	Molar ratio mol F_2/mol C_7H_8 (%)	Liquid volume flow (1.1 mmol C_7H_8 in 1 ml solvent) (ml/h)	Temperature (°C)	Conversion X (%)	Yield Y (%)	Selectivity S (%)
Acetonitrile						
3D2	40	11.6	−16	30	11	37
3D3	54	11.6	−16	38	14	37
3D4	92.5	11.6	−16	50	20	40
3G1	40	11.6	−21	23	12	52
3G2	40	11.6	−42	15	5	33
3C1	20	19.6	−15	15	8	53
3C2	20	19.6	−15	14	8	57
3C3	40	19.6	−15	29	13	45
Methanol						
4D1	20	19.6	−17	15	3	20
4D3	30	19.6	−17	36	5	14
4D2	40	19.6	−17	12	7	58
4D4	54	19.6	−17	24	10	42
4E2	40	11.1	−17	42	4	9
4E3	54	11.1	−17	18	9	50
4E4	92.5	11.1	−17	34	14	41

Table 2
Series A: MBC[a]

Experimental no.	Molar ratio mol F_2/mol C_7H_8 (%)	Liquid volume flow (1.1 mmol C_7H_8 in 1 ml CH_3CN) (ml/h)	Gas volume flow (10% F_2 in N_2) (ml/min)	Conversion X (%)	Yield Y (%)	Selectivity S (%)
Version I						
3L4, 304	20	13	12.1	4	3	75
3M4, 3P4	40	13	24.2	12	6	50
3N4, 3Q4	54	13	32.7	26	11	42
3R4	83	13	50.0	28	6	21
Version II						
3R2/3T3/3V3	20	13	12.1	9	2	22
3R5/3T4/3V5	40	13	24.2	18	5	28
3R7/3T6/3V7	54	13	32.7	25	7	28
3U3/3V9	83	13	50.0	41	11	27

[a] LM: acetonitrile; temperature: −15°C.

Table 3
Series A: LBC[a]

Experimental no.	Molar ratio mol F_2/mol C_7H_8 (%)	Liquid batch (1.1 mmol C_7H_8 in 1 ml CH_3CN or CH_3OH) (ml)	Gas volume flow (10% F_2 in N_2) (ml/min)	Conversion X (%)	Yield Y (%)	Selectivity S (%)
Acetonitrile						
3E1	40	20	50	7	2	29
3E2	54	20	50	8	3	38
3H2	40	20	20	17	3	18
3H3	54	20	20	23	4	17
3J2/3K2	40	20	20	6	6	50
3J3/3K3	54	20	20	13	4	30
3J4/3K4	80	20	20	25	7	28
3J5/3K5	100	20	20	34	8	22
Methanol						
4K1	40	20	50	6	1	17
4K2	54	20	50	8	1	13

[a] Temperature: −17°C.

Table 4
Series B: FFMR

Molar ratio mol F_2/mol C_7H_8 (%)	Molar ratio mol C_7H_8/mol CH_3C (%)	Liquid volume flow (ml/h)	Temperature (°C)	Conversion X (%)	Yield Y (%)	Selectivity S (%)
40	10	19.6	−16	37	15	40
100	10	19.6	−16	62	19	31
200	10	19.6	−16	76	28	37
100	100	19.6	−16	7	3	43

attenuated total reflection (ATR) technique was applied to quantify the product composition. This was used for measurements performed at fluorine contents higher than 10 vol.% and substrate concentrations exceeding 1.1 mol/l.

For GC analysis, a HP 5890 instrument (Series II plus, Hewlett Packard, Palo Alto, USA) was employed, using a separation capillary coated with Stabilwax DA of 0.25 mm film thickness. HPLC analysis was made using an instrument equipped with a UV-detector L-4000A (Merck/Hitachi, Darmstadt, Germany). FTIR analysis was carried out with a spectrometer IFS 88 (Bruker, Karlsruhe) including a ATR-circular cell with a ZnSe crystal.

3. Discussion

3.1. Hydrodynamics: falling film and segmented flow

For a precise interpretation of data for direct fluorination, some information with respect to the hydrodynamics of the

Table 5

Reactor type	FFMR	MBC (I)	MBC (II)	Bubble columns [15,16]	Impinging jets [15,16]
Specific interfacial area (m^2/m^3 reactor)	27,000	9800	14,800	50–600	90–2050

microreactors was already obtained prior to this publication [13] and has been completed during the present study. Specific interfacial areas were calculated using assumptions from film theory [15] and from measurements performed in millimeter wide capillaries [16]. Experimental data were gathered by means of an optical analysis technique [13] and a chemical method, sulfite oxidation [17]. As a technical benchmark, published data from conventional gas/liquid contacting reactors, e.g. bubble or spray columns, were used [18,19]. Table 5 lists data of interfacial areas measured for the microreactors investigated and compared to the technical benchmarks.

It was shown in previous experiments that films down to 25 μm thickness can be generated in the falling film microreactor, using isopropanol as liquid. As shown in Table 5, the corresponding specific interfacial area amounts to 40,000 m^2/m^3 which is far larger than for conventional gas/liquid contacting equipment [18,19]. In the experiments described here, acetonitrile films of about 30–37 μm were utilized corresponding to a specific interfacial area of about 33,000 and 27,000 m^2/m^3, respectively.

Investigations concerning the micro bubble column focused on the determination of the flow pattern. From measurements in capillaries, it was likely that a segmented flow pattern (referred to as Taylor flow or bubble train flow) is established, i.e. bubbles of a cross-section close to that of the channels separated by liquid plugs and surrounded by thin liquid films. First measurements using the micro bubble column with wide channels (300 μm×100 μm) show that this flow pattern is found at low gas superficial velocities (see Fig. 2).

Increasing the gas superficial velocity, the flow pattern changes to a gaseous core surrounded by a thin liquid film referred to as so-called annular flow. Both regimes are separated by a relatively large transition region comprising zones of both segmented and annular flow in different channels.

4. Fluorination of toluene

One series of experiments (A) was aimed at proving the feasibility of the fluorination of toluene (1.1 mol toluene/1 l solvent) using elemental fluorine (10% F_2 in N_2) in microreactors. In addition, the impact of the variation of selected process conditions on target values was investigated. In this context, selectivity and conversion were monitored as a function of fluorine-to-toluene ratio, volume flow rate, temperature, and solvent. These data were utilized to gather selectivity-conversion diagrams and space-time yields for comparison of reactor performance and economics. In addition to the variation of process conditions, geometric parameters, such as the width and depth of the microchannels of the micro bubble column, were changed. In all these experiments, data from a laboratory bubble column served as a benchmark for standard laboratory equipment.

In another series of experiments (B), fluorination with significantly increased toluene and fluorine concentrations was carried out. The corresponding measurements were only performed in the falling film microreactor. Tables 1–4 lists all data from both series of experiments.

The results of toluene fluorination in microreactors were compared to fluorination data achieved by using a macro-

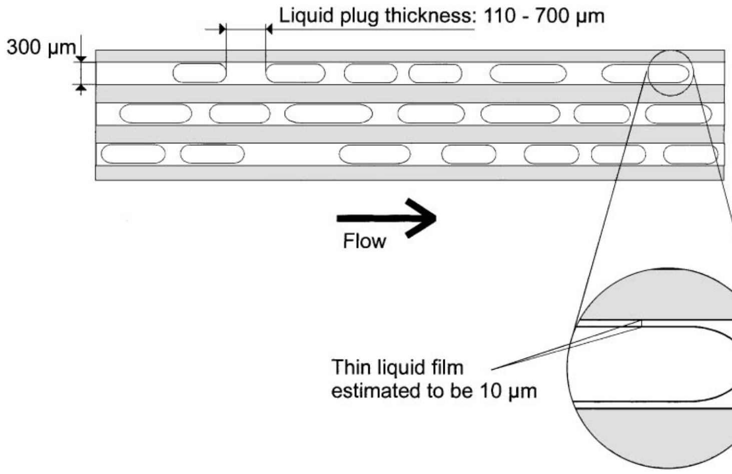


Fig. 2. Drawing of a measured segmented flow pattern in the micro bubble column (MBC I) at a gas velocity of 10 ml/min. The contrast of the real photographic image is too low for representation within this article.

scopic gas/liquid contactor, i.e. a laboratory bubble column. This column consists of a U-tube with a fine porous quartz glass frit, and a reaction volume of 25 ml cooled by a thermostatic bath (see Fig. 1c). Similar devices have been used in the vast majority of relevant scientific investigations described in this field [4–7]. Much more elaborate conventional gas/liquid devices exist which are used both on an industrial and laboratory scale, however, the fact is that there is no example of using such a device for direct fluorination. Most likely, this is strongly prohibited for reasons of process safety.

4.1. Product composition and substitution pattern

According to the reaction mechanisms expected, being either radical or electrophilic [4,5], four isomers may contribute, in principle, to the product composition. Radical substitution may result in side chain or ring fluorination, whereas both mechanisms lead to ortho, meta and para isomers, usually of defined distribution, the so-called substitution pattern. Moreover, di- or polyfluorinated side chain or ring products could potentially be synthesized.

In Fig. 3, a typical GC plot corresponding to a product mixture of the falling film microreactor obtained at fluorine contents of 10 vol.% is shown. Apart from the three monofluorinated isomers, peaks corresponding to a difluorinated product, 2,4-difluoro toluene, by-products, toluene, and acetonitrile were found. As to be expected from results performed previously [3–7], a number of by-products were detected, most likely generated by radical addition and polymerisation mechanisms [4,5].

A quantitative analysis of the three well-resolved monofluorinated isomers yields a substitution pattern of 5:1:3, with respect to the ortho, meta and para product. This ratio is in accordance with an electrophilic substitution mechanism [20,21]. By increasing the fluorine content in the gaseous phase from 10 to 50 vol.%, para products are predominantly formed. By FTIR analysis, it could be shown that the corresponding ratio of ortho to para products amounts to approximately 1:4. The wave numbers of the detected compounds are given for the FTIR in Table 6.

Table 6

Compound	Wave number (cm^{-1})
Acetonitrile	1038, 918
Toluene	1378, 736
o-Fluorinated toluene	1232, 1186, 838, 703
p-Fluorinated toluene	1220, 1156, 813

On the basis of this information, maximum yields of about 7% of the ortho isomer and 21% of the para isomer were achieved, when applying the optimum set of process parameters for the falling film microreactor (see series B, Table 4). These values have to be compared to yields for various monofluorinated products, including *ortho*- and *para*-fluoro toluene, achieved using the Schiemann reaction, the technologically applied process [22].

Whilst the direct fluorination results in the predominant formation of two isomers and non-negligible amounts of impurities of by-products, the large-scale route via diazotization of aromatic amines yields only one isomer that alone has to be separated from the crude product. For the latter process, yields of this one isomer typically range from 20 to 27% which equals the sum of the yields, referring to the three isomers, achieved in the microreactor. Thus, the expenditure for product separation is, at present, higher for the microreactors which, on the other hand, seem to

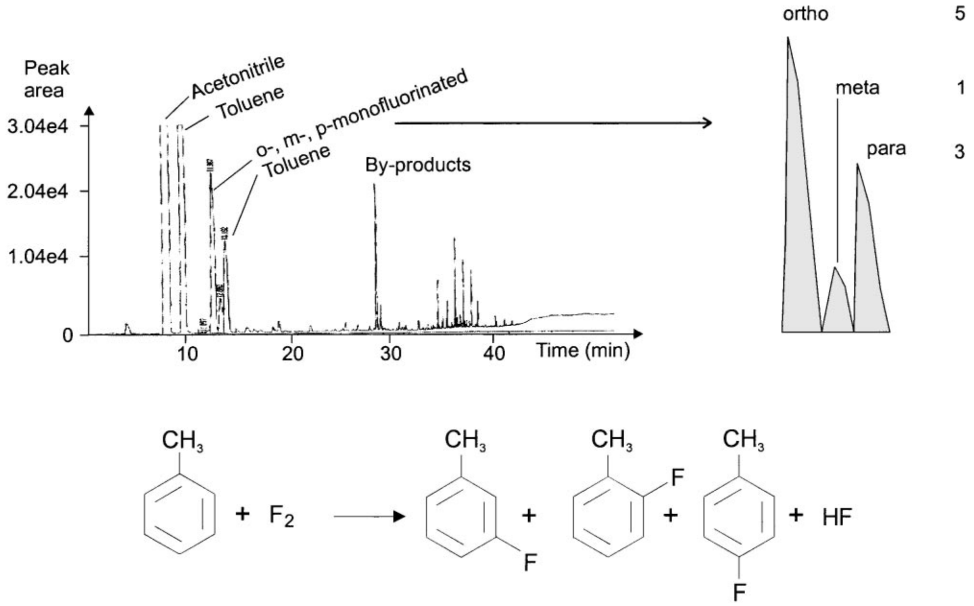


Fig. 3. A typical gas chromatography plot of a product mixture, obtained by direct fluorination of toluene in the falling film microreactor.

benefit from simpler processing and less waste generation compared to the multi-step technical process.

4.2. Conversion and selectivity

For various operating conditions, conversions, yields and selectivities were determined for the micro bubble column using two types of reaction platelets ('narrow/wide'), the falling film microreactor, and the laboratory bubble column. In more than 20 experiments performed in these microreactors, the feasibility of toluene fluorination could be demonstrated by high yields of monofluorinated products. Moreover, the yields of the falling film microreactor exceed for a wide range of operating conditions, with the exception of one experiment, those of the laboratory bubble column. The maximum yields of monofluorinated products determined in the two series, amounting to 20 and 28%, are more than two to three times larger than the benchmark. The yields obtained using the two types of platelets of the micro bubble column do exceed this standard, but to a minor extent.

Selectivities achieved by performing the fluorination in the microreactors range from approximately 30 to 50%, i.e. the content of by-products in the product mixture is equal to or double that of the target products. Although such a ratio would be unacceptable for the majority of organic syntheses, product selectivities measured are comparable to the best values reported for toluene fluorination in the literature [4–7].

Referring to these investigations, differences of operating conditions with respect to the present study must be mentioned. Only in case of using the microreactors, was processing performed at high toluene concentrations and high molar ratios of toluene to fluorine as well as using high fluorine contents in the inert gas and with elevated reaction temperatures. In earlier experiments, at least one of these parameters was set to a notably lower value [4–7] or a more complex experimental protocol was applied, e.g. by addition of protic or Lewis acids. Hence, the results of the microreactors indicate that efficient temperature control and mass transfer was exerted, thereby, avoiding hot spots. Any local increase in temperature would ultimately result in the formation of fluorine radicals [4] which will induce side reactions such as addition or polymerization.

4.3. Selectivity-conversion diagram

For a detailed analysis of the performance of the reactors, the representation of the experimental data as a selectivity-conversion diagram or space-time yield is recommended [22]. The first type of analysis solely reflects the influence of reaction engineering on the underlying chemistry, whereas an economic evaluation, in terms of reactor throughput, can be given in the second case.

In Fig. 4, a selectivity-conversion diagram is given for the falling film microreactor, the micro bubble column utilizing the narrow (50 μm×50 μm) and wide (100 μm×300 μm) microchannels, and the laboratory bubble column (series A, Tables 1–3). Nearly constant selectivities are found for the first two microreactors, whereas the corresponding data decrease with conversion for the micro bubble column using wide channels and the laboratory bubble column. Remarkably, the performance of the falling film microreactor is clearly superior to that of the laboratory benchmark. In contrast, the micro bubble column using narrow channels exceeds the selectivities of the laboratory bubble column only at high conversion.

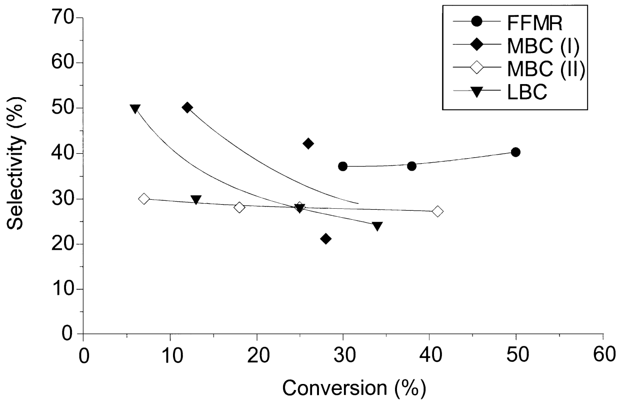


Fig. 4. Selectivity-conversion diagram of direct fluorination of toluene for the falling film microreactor (FFMR), micro bubble column (MBC (I) and (II)) and laboratory bubble column (LBC) based on the experiments listed in Tables 1–3, series A.

The diagram for the micro bubble column equipped with wide channels is not well understood currently for the following reasons. Since the corresponding diffusion distances for mass and heat transport increase when using larger channels, it was expected that measurements with this device should result in lower conversions and selectivities. Surprisingly, the selectivities are higher than for the micro bubble column with narrow channels when comparing values obtained at fixed conversions. For conversion, the smaller bubble column gives superior performance, even though the residence times applied were shorter. However, the origin of the low selectivities remains unclear and requires more detailed information on hydrodynamics and transport phenomena.

The same holds for one data point, referring to the highest conversion, of the micro bubble column using the wide channels. The corresponding selectivity seems to be unusually low and might be caused by a change of the flow pattern. Although this information can, for experimental reasons, not be easily obtained for the fluorine/acetonitrile system, a flow pattern map determined using isopropanol as liquid indicates a transition between segmented and annular flow for a corresponding set of operating conditions. For these reasons, it was decided to omit the data record of this microreactor from the following plots. However, it has to be emphasized that, concerning the conclusions drawn below, this device gave qualitatively similar results as the other microreactors when compared to the laboratory benchmark.

4.4. Space-time yields

To date, a large part of the microreactor volume has to be designated to achieve fluid tightness. In a first step, a practicable solution was provided by applying flat sealing techniques which inevitably need large areas for build-up of sealing pressure. The resulting large contribution of parts, not related to chemical reaction, to the overall reactor volume is typical for present microreactors, whereas for conventional reactors this can be neglected. Therefore, different definitions of space-time yields are used in Fig. 5, based on experiments of series A.

The first approach solely refers to the channel volume, i.e. the volume where reaction takes place (see Fig. 5a). Due to the principle of yielding small fluid thicknesses, inherent to microreactors, the reaction channels are separated from each other by channel walls. Taking this volume and that of the micromixing unit into account, giving an idealized reactor geometry, space-time yield data corrected for the reactor construction material result (see Fig. 5b). This idealized reactor geometry, however, represents not the current state-of-the-art design, but corresponds to a miniaturized prototype of future fabrication generation. Data corrected according to the overall volume of the current design will be discussed as well, but are not shown in Fig. 5.

Space-time yields, based on the real reaction volume (see Fig. 5a) of both microreactors are orders of magnitude higher than those of the laboratory benchmark. This increase is mainly caused by much lower residence times achievable by using these microreactors, the volume corrected yields of both types of devices being in the same range. While for completion of the reaction about 3 h are needed in case of the laboratory bubble column, enhancement of heat and mass transfer by miniaturization enables fluorination to proceed in a few seconds.

Even when correcting the data with respect to the idealized reactor geometry, a significant improvement of

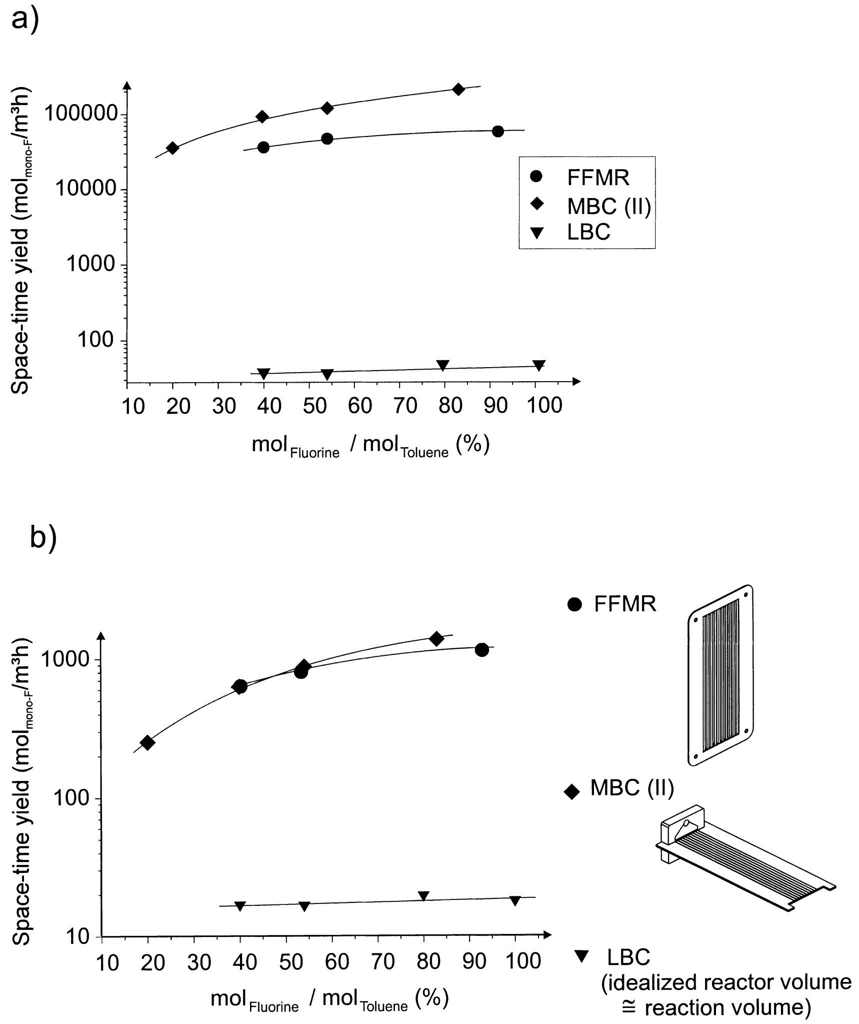


Fig. 5. Comparison of space-time yields of direct fluorination of toluene for the falling film microreactor (FFMR), micro bubble column (MBC (II)) and laboratory bubble column (LBC) (a) referred to the reaction volume, (b) referred to an idealized reactor geometry.

performance by using microreactors remains (see Fig. 5b). Moreover, the current state-of-the-art microreactor design, far from being optimized regarding system size miniaturization, still has space-time yields, comparable to those of the laboratory bubble column, when referred to the overall reactor volume. Concerning safety issues, the use of microreactors allows reduction of the technical expenditure for laboratory experiments, which handle only small sample volumes, e.g. for gathering analytical data.

The space-time yield of the microreactors is dependent on the set of operating conditions chosen. The most important parameters for an optimization of this figure are the ratio of gaseous to liquid reactant, temperature, solvent, residence time as well as fluorine and substrate concentration. The influence of the variation of these parameters on target values such as conversion or selectivity, being proportional to the space-time yield, is discussed below.

4.5. Variation of fluorine-to-toluene ratio

In Fig. 6a, toluene conversions are given as a function of the fluorine-to-toluene ratio, achieved by variation of fluorine volume flow at a fixed liquid flow rate (series A, Tables 1–3). The measurements show an increase in conversion both for the microreactors and the laboratory bubble column. This indicates that transport hindrances, if present at high fluorine concentrations, do not play a dominant role when using either devices, e.g. by prohibiting further performance improvements.

However, there seems to be a small, but distinct difference between the three types of reactors investigated. This refers to the amount of fluorine contributing to conversion relative to that introduced in the gas. This figure, yet another measure of reactor efficiency, is small at low fluorine-to-toluene ratios for the laboratory benchmark (see Fig. 6b). For instance, only 6% of the fluorine molecules react if a 40% stoichiometric ratio is applied yielding an efficiency of about 15%. In contrast, about 50–75% efficiency results for the two microreactors. For all operating conditions investigated, the efficiencies of the microreactors exceed those of the laboratory bubble column, mostly because of the huge differences in interfacial areas.

In the case of the miniaturized and macroscopic bubble columns, efficiency slightly increases when fluorine volume flow is enhanced. For the falling film microreactor, however, performance decreases. This indicates that mass transport limitations exist at high fluorine-to-toluene ratios, i.e. at high fluorine volume flows. Film thickness and interfacial area being constant, this can only be caused by the decrease in residence time of the gas molecules. The time scale of gas transport to the interface seems to be high compared to that of transport phenomena in the liquid film. By reduction of the height of the gas chamber of the falling film microreactor, a simple optimization strategy for reactor efficiency at high fluorine-to-toluene ratios is possible.

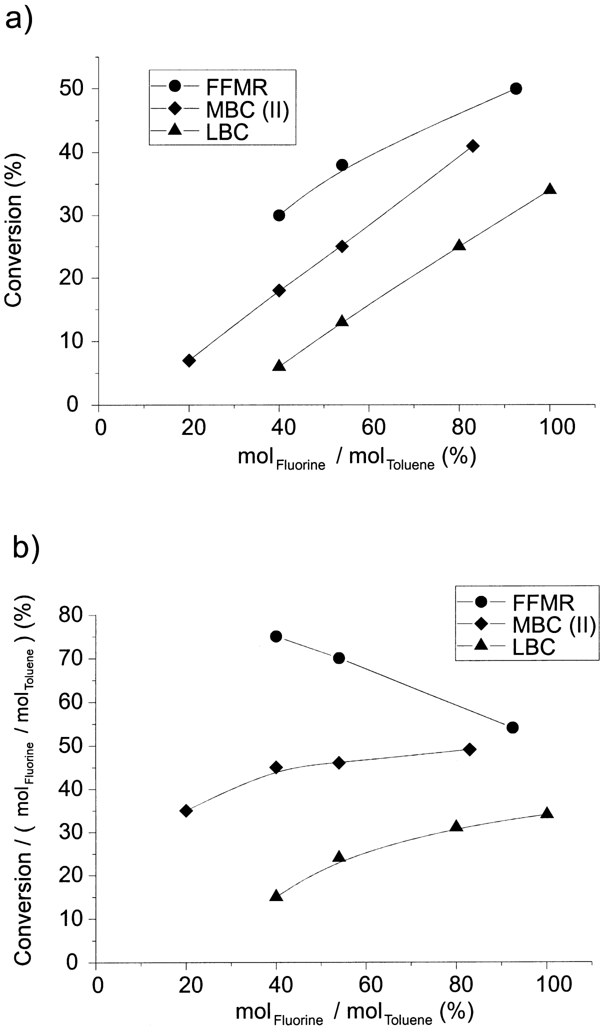


Fig. 6. (a) Conversion of direct fluorination of toluene in the three reactor types (FFM, MBC (II) and LBC) as a function of the molar ratio of fluorine-to-toluene. (b) Efficiency of the reactors, defined as conversion normalized by the molar ratio of fluorine-to-toluene, as a function of the molar ratio of fluorine-to-toluene.

4.6. Variation of temperature

The effect of increasing temperature on conversion and selectivity was investigated for several fluorination reactions [4–7]. As a common result for different aromatic compounds, it was found that, due to increased radical formation, conversion increases, whereas selectivity decreases. In the framework of the feasibility experiments presented here (series A, Tables 1–3), the dependence of these parameters were analyzed in the temperature range of about −40 to −15°C using the falling film microreactor at a fluorine-to-toluene ratio of 40% (see Fig. 7). It turned out that for the conversions measured the expected relationship was detected, conversion increased from 15 to 30%. The temperature dependency on selectivity is less clear, showing scattered data in the range from 33 to 52%. The origin of this

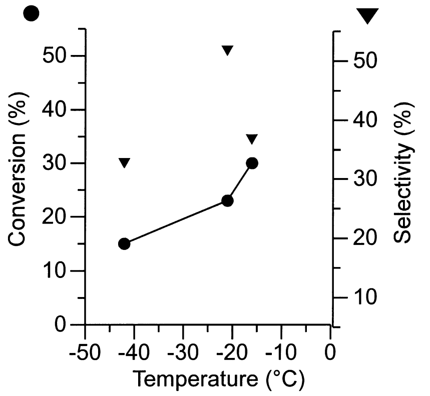


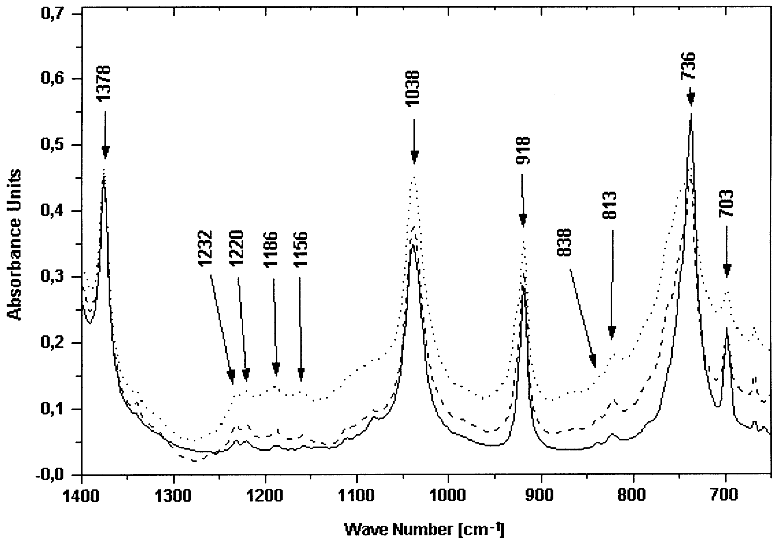
Fig. 7. Conversion (●) and selectivity (▲) of direct fluorination of toluene in the falling film microreactor as a function of temperature.

effect is presently not well understood, and further experimental data are needed.

4.7. Variation of solvent

The choice of solvent mainly affects fluorine solubility, thereby increasing conversion, while its influence on selectivity is more difficult to predict. In this context, several authors described an increase in product yield by increasing solvent polarity as well as the use of ingredients such as acids or bases via polarization of the fluorine molecule [5,6,23].

In order to investigate this, fluorinations of toluene were performed in the falling film microreactor and laboratory bubble column using the protic, polar solvent methanol in



Acetonitrile: 1038 cm^{-1}, 918 cm^{-1}; Toluene: 1378 cm^{-1}, 736 cm^{-1};
o-monofluorinated Toluene: 1232 cm^{-1}, 1186 cm^{-1}, 838 cm^{-1}, 703 cm^{-1};
p-monofluorinated Toluene: 1220 cm^{-1}, 1156 cm^{-1}, 813 cm^{-1}

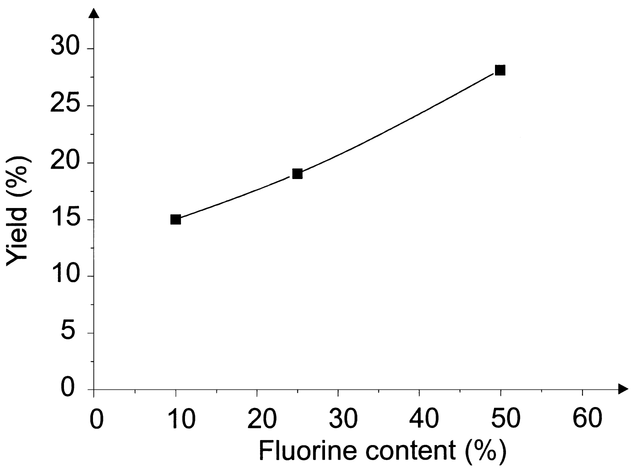


Fig. 8. Yield as a function of fluorine content in educt gas.

addition to the aprotic, polar acetonitrile (series A, Tables 1–3). The results in terms of yields and selectivities for methanol were worse for both types of reactors. In particular, the range of selectivities measured in the microreactor is large and the dependency on the molar ratio of fluorine-to-toluene is not clear. At least, for one set of operating conditions a relatively high yield of about 14% was found which also notably exceeds the nearly negligible formation of monofluorinated isomers of only 1% in case of the laboratory benchmark.

4.8. Variation of residence time

Variation of the liquid volume flow for the falling film microreactor affects the residence time of the flowing liquid. Since the measurements in series A were limited to only two values, no general conclusions but only tentative hints can be given. Increasing the volume flow from 11.6 to 19.6 ml/h has no effect on toluene conversion, thereby, possibly indicating that gas diffusion is not limiting for this parameter range (see Tables 1–4). Selectivity increases slightly which might be caused by allowing the reaction and, correspondingly, the heat release to proceed more slowly.

4.9. Fluorine and substrate concentration

Fluorinations were performed at fluorine contents of 10, 25 and 50 vol.% (series B, Table 4). This increase in fluorine concentrations has a remarkable influence on the substitution pattern which has already been discussed. Moreover, a nearly linear increase in yield with the fluorine content is found (see Fig. 8).

This increase is mainly due to an enhancement of conversion, the selectivities being relatively constant (see Tables 1–4).

In addition to an increase of the concentration of the gaseous reactant, one experiment was run at a toluene concentration of 100%, i.e. without any solvent (see Tables 1–4). Although the yields and conversions obtained were relatively small, amounting to only a few percentage, the corresponding selectivities did not decrease compared to the values obtained at diluted toluene concentrations.

Apart from this quantitative analysis of reactor performance, this experiment as well as the fluorinations using high fluorine contents demonstrated that in microreactors even very explosive mixtures can be safely handled. At no time were explosions or clogging recorded, e.g. prohibiting a further analysis. In this context, the microreactors proved to be a useful and precise measuring tool for process regimes, which are not accessible for conventional laboratory reactors.

5. Conclusions

The feasibility of performing direct fluorination using elemental fluorine in the falling film microreactor and micro bubble column was demonstrated. Moreover, the reactor performance, expressed as space-time yield and selectivity-conversion diagram, is by far superior compared to the laboratory benchmark. The yields obtained are in the same order compared to the technically performed Schiemann process. A further optimization of reactor efficiency was indicated by monitoring the dependence of target quantities, e.g. conversion and selectivity, as a function of various operating conditions. It is expected that future experiments utilizing still higher fluorine contents, e.g. up to 100% fluorine without any inert gas, at ambient temperatures may be even superior to technical benchmarks.

The experiments performed for the direct fluorination of toluene in this microreactors are not an entirely systematic study. To completely survey the field of direct fluorination the following studies have to be performed in future.

- The influence of substrate on the performance of direct fluorination.
- The solvent used, e.g. polar and non-polar solvents.
- The substrate concentration, e.g. up to 100%.
- The fluorine concentration in the gas phase, e.g. up to 100%.
- The reaction temperature, especially use of room temperature.
- The use of Lewis acids as a catalyst in direct fluorination.

In order to return this technological potential into real economic benefit, numbering-up concepts, e.g. a number of microreactors in parallel for scale-up, have to be developed, in particular, referring to more compact systems, i.e. devices with an improved ratio of reaction to construction volume. Especially, for a significant minimization of the areas needed for interconnection, the use of irreversible connection techniques, e.g. laser welding, is a promising approach for microreactors of the next generation. Special attention has to be paid for the development of suitable microfluidic structures for manifolding and microstructuring techniques capable of mass fabrication.

At present, the reaction volume fills only a small part of the overall reactor size, since the residual volume is needed to guarantee fluid tight interconnection. Thus, the current systems are restricted to laboratory purposes, e.g. for process development and optimization. Due to the precise setting of operating conditions and hydrodynamics, e.g. interfacial areas, accurate data concerning reaction kinetics as well as mass and heat transport are obtainable, thereby, providing an excellent basis for simulation and reactor modeling. First experiments for this purpose are underway.

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