Two-step regioselective synthesis of 1,2-difluorobenzenes from chlorotrifluoroethylene and buta-1,3-dienes*

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The gas-phase copyrolysis of chlorotrifluoroethylene with buta-1,3-diene, penta-1,3-diene, or isoprene in a flow reactor at 440—480 °C gave 4-chloro-4,5,5-trifluorocyclohex-1-enes. The latter treated with aqueous KOH under condition of phase-transfer catalysis were selectively converted into 1,2-difluorobenzene, 2,3-difluorotoluene, or 3,4-difluorotoluene.

Key words: chlorotrifluoroethylene, buta-1,3-diene, isoprene, penta-1,3-diene, cycloaddition, (alkenyl)chlorotrifluorocyclobutanes, chlorotrifluorocyclohexenes, 1,2-difluorobenzene, 3,4-difluorotoluene, 2,3-difluorotoluene.

The unique effect of fluorine atom on the biological and physicochemical properties of organic compounds attracts an increased attention to the development of new syntheses of organofluorine compounds of various classes.[1—7] Of particular interest are fluoroaromatic compounds, which are used in the synthesis of more than 100 modern drugs and agrochemicals and are intensively explored in the search for new biologically active substances, components of liquid crystals, and discovery of new materials.[1—7] The conventional approaches to fluorine-containing aromatic compounds implemented in industry and most of the described new laboratory procedures involve nucleophilic or electrophilic substitution of hydrogen or appropriate functional groups pre-introduced into the aromatic ring with fluorine using different fluorinating agents.[1,2,8—11] An alternative methodology for production of fluoroarenes is also being developed. It consists in the synthetic assembly of fluorobenzoid structures from reactive fluorine-containing synthons (fluorinated carbenes, olefins, dienes, and acetylenes), which can simultaneously act as building blocks and sources of fluorine bonded to the C atom.[12—27] In the present work, we report on the possibilities of efficient application of this methodology for the regioselective synthesis of 1,2-difluorobenzenes using thermal cycloaddition of chlorotrifluoroethylene to buta-1,3-dienes.

The most common approach to construct C_6 cyclic carbon skeleton is the Diels—Alder [2+4] cycloaddition of olefins to 1,3-dienes. However, this reaction is not typical of fluorinated olefins. The thermal reactions of tetrafluoroethylene, chlorotrifluoroethylene, trifluoroethylene, and hexafluoropropylene with buta-1,3-dienes proceed either almost exclusively or predominantly as [2+2] cycloaddition to form vinylcyclobutanes.[28—32] Nevertheless, thermal cycloaddition of polyfluoroolefins to dienes turned out to be quite applicable for obtaining cyclohexenes and arenes due to the ability of fluorinated vinylcyclobutanes to undergo thermal rearrangement with ring expansion and aromatization.[15—20,24—27]

Earlier, we[16—20] and DuPont researchers[25] showed the fundamental possibility of the synthesis of chlorotrifluorocyclohexenes and difluorobenzenes under conditions of gas-phase pyrolysis of 2-chloro-1,2,2-trifluoro-3-vinylcyclobutanes obtained by thermal cycloaddition of chlorotrifluoroethylene (CTFE) to buta-1,3-diene and its derivatives. Herein we described the detailed studies on optimization of these processes.

The pyrolysis of an equimolar mixture of CTFE and buta-1,3-diene (**1a**) in a flow reactor at 410 °C leads to isomeric 2-chloro-1,2,2-trifluoro-3-vinylcyclobutanes (**2a**) ((2*S**,3*S**)-**2a** : (2*S**,3*R**)-**2a** = 1 : 1)) in 57% yield, as well as to 4-chloro-4,5,5-trifluorocyclohex-1-ene (**3a**) (6% yield) and 1,2-difluorobenzene (**4a**) (1% yield) (Scheme 1, Table 1). An increase in the pyrolysis temperature in the range of 410—470 °C is accompanied by the increase in the fractions of cyclohexene **3a** and difluorobenzene **4a** with a simultaneous decrease in the fraction of cyclobutane **2a**. Under optimal conditions, cyclohexene **3a** can be obtained in 39% isolated yield.

The data obtained are consistent with the results of pyrolysis of cyclobutane **2a** at the same temperature range (Table 2) confirming the sequence of the reaction steps of formation of **2a** and its isomerization to cyclohexene **3a** under the reaction conditions. Pyrolysis of cyclobutane **2a** at 450—480 °C gives chlorotrifluorocyclohexene **3a** as

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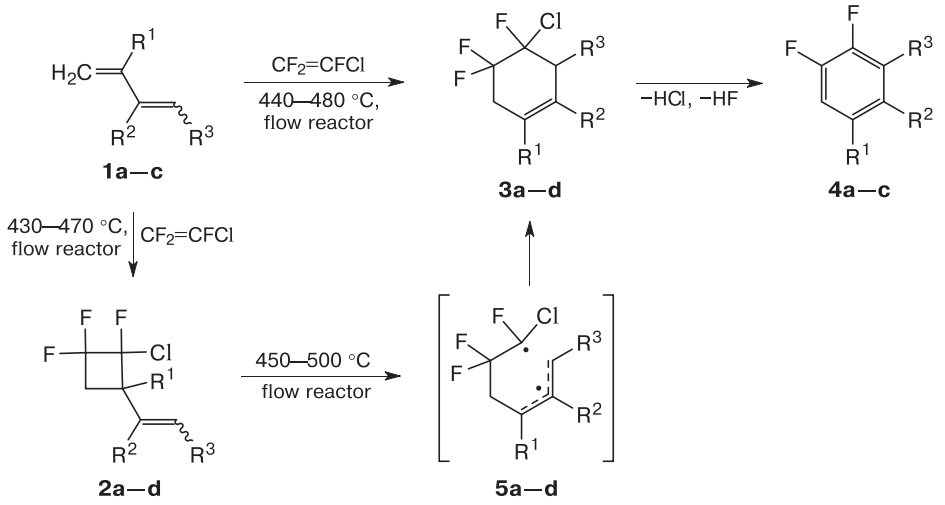
Scheme 1



1—5: $R^1 = R^2 = R^3 = H$ (**a**); $R^1 = R^2 = H$, $R^3 = Me$ (**b**); $R^1 = Me$, $R^2 = R^3 = H$ (**c**); $R^1 = R^3 = H$, $R^2 = Me$ (**d**)

the main product, which is likely a result of homolytic cleavage of the C(2)—C(3) cyclobutane bond and subsequent C_6 cyclization of the biradical intermediate **5a** stabilized by the allyl fragment (see Scheme 1). The expected alternative route of the rearrangement of **2a** through the ring opening at the C(3)—C(4) bond and intermediate **6a**, which should lead to chlorotrifluorocyclohexene **7a** (Scheme 2), seems to have a small contribution to the process due to the lower stability of intermediate **6a** compared to intermediate **5a** additionally stabilized by the chlorine atom.

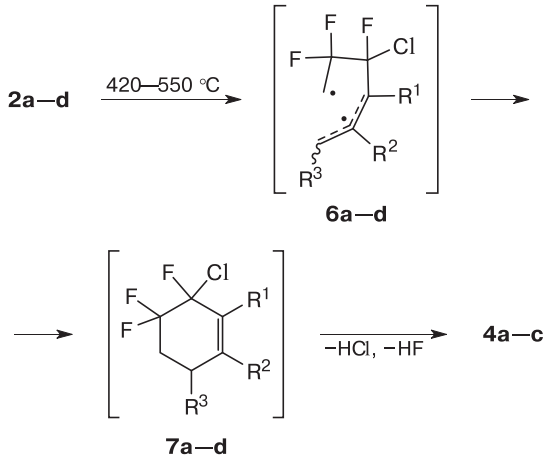
It should be noted that similar thermal rearrangements of 1,1,2,2-tetrafluoro-3-vinylcyclobutane,[15—18] in contrast to rearrangements of compound **2a**, proceed mainly *via* the ring opening at the C(3)—C(4) bond to give 3,3,4,4-tetrafluorocyclohexene (Scheme 2). In this case, the contribution of an alternative rearrangement pathway (see Scheme 1) leading to 4,4,5,5-tetrafluorocyclohexene is significantly lower.

Table 1. Composition and yield of copyrolysis products of chlorotrifluoroethylene (CTFE) and buta-1,3-dienes **1a—c** at various temperatures[a]

Diene	*T*/°C	Products (yield[b] (%))
1a	410	**2a** (62), (57)[c] + **3a** (9), (6)[c] + **4a** (1)
1a	435	**2a** (29) + **3a** (37), (31)[c] + **4a** (3)
1a	450	**2a** (18) + **3a** (45), (39)[c] + **4a** (6)
1a	470	**2a** (12) + **3a** (41), (32)[c] + **4a** (8)
1a	500	**2a** (8) + **3a** (31) + **4a** (10)
1a	580	**2a** (4) + **3a** (19) + **4a** (18)
1b	410	**2b** (57), (52)[c] + **3b** (7) + **4b** (1) + **4c** (1)
1b	435	**2b** (25), (20)[c] + **3b** (32), (27)[c] + **4b** (4) + **4c** (2)
1b	450	**2b** (18) + **3b** (36), (31)[c] + **4b** (7) + **4c** (2)
1b	470	**2b** (14) + **3b** (35) (29)[c] + **4b** (9) + **4c** (2)
1b	500	**2b** (10) + **3b** (30) + **4b** (12) + **4c** (3)
1c	400	**2c** (39), (34)[c] + **2d** (26) (19)[c] + **3c,d** (10), (6)[c] + **4c** (0.5) + **4b** (0.3)
1c	420	**2c** (22) + **2d** (16) + **3c,d** (34), (28)[c] + **4c** (2) + **4b** (1)
1c	440	**2c** (6) + **2d** (8) + **3c,d** (46), (41)[c] + **4c** (5) + **4b** (1)
1c	460	**2c** (4) + **2d** (6) + **3c,d** (42), (35)[c] + **4c** (7) + **4b** (3)
1c	480	**2c** (3) + **2d** (5) + **3c,d** (38), (32)[c] + **4c** (9) + **4b** (3)

[a] Conditions: a flow reactor, flow rate of CTFE 0.54 mol h^{-1}, flow rate of **1a—c** 0.54 mol h^{-1}.
[b] The yield in mixtures was calculated according to the analysis of the pyrolysate by GC and NMR spectroscopy.
[c] Isolated yield after distillation of the pyrolysate.

Scheme 2



2, 6, 7: $R^1 = R^2 = R^3 = H$ (**a**), $R^1 = R^2 = H$, $R^3 = Me$ (**b**), $R^1 = Me$, $R^2 = R^3 = H$ (**c**), $R^1 = R^3 = H$, $R^2 = Me$ (**d**)

Similar results were obtained for the thermal reactions of CTFE with penta-1,3-diene (**1b**) and isoprene **1c**. Thus, the copyrolysis of CTFE with penta-1,3-diene (**1b**) (a mixture of *E*-**1b** : Z-**1b** = 1.6 : 1) at 410 °C results in four expected stereoisomeric 2-chloro-1,1,2-trifluoro-3-(prop-1-en-1-yl)cyclobutanes (**2b**) (52% total isolated yield, ratio of isomers 1.6 : 1.5 : 1 : 1) as the main products, the expected products of their isomerization, methylcyclohexenes **3b** (a mixture of two isomers in a ratio of 1.3 : 1, 7% total yield), and small amounts of 2,3-difluorotoluene (**4b**) and 3,4-difluorotoluene (**4c**) (see Table 1). Cyclohexenes **3b** become the main products at temperatures of 435—470 °C and can be obtained in 27—31% isolated yields by fractional distillation of pyrolysates. Copyrolysis of CTFE and **1b** at higher temperatures does not increase the yield of cyclohexenes **3b** due to an increase in the contribution of the side processes of aromatization and resinification.

Cyclohexenes **3b** can also be obtained according to a two-step scheme involving preliminary synthesis of cyclobutanes **2b** by copyrolysis of CTFE with pentadiene **1b** at 410 °C and their subsequent isomerization under pyrolysis conditions at 450—500 °C (see Table 2). The highest isolated yield of compound **3b** (38%) was achieved by the pyrolysis of cyclobutane **2b** at 480 °C. When temperature is decreased or increased, the yield of cyclohexenes **3b** decreases due to lowering of the conversion of cyclobutanes **2b** or an increase in the contribution of aromatization of cyclohexenes **3b** and resinification. It should be noted that the highest yields of cyclohexenes **3b** are noticeably lower than those observed for similar rearrangements of compound **2a**, which is probably explained by the unfavorable steric effect of the methyl group on the C_6 cyclization of intermediate **5b**.

It is important to note that the pyrolysis of cyclobutanes **2b** gives along with 2,3-difluorotoluene (**4b**) the expected

Table 2. Composition and yield of pyrolysis products of 3-alkenyl-2-chloro-1,1,2-trifluorocyclobutanes **2a—d** at various temperatures[a]

Cyclobutane	*T*/°C	Conversion of **2a—d** (%)	Products (yield[b] (%))
2a	420	23	**3a** (14) + **4a** (1)
2a	450	78	**3a** (48), (42)[c] + **4a** (4)
2a	480	89	**3a** (56), (50)[c] + **4a** (8)
2a	580	96	**3a** (29) **4a** (20) (14)[c]
2b	420	22	**3b** (13) + **4b** (1) + **4c** (1)
2b	450	70	**3b** (39), (32)[c] + **4b** (4) + **4c** (1)
2b	480	85	**3b** (44), (38)[c] + **4b** (7) + **4c** (2)
2b	500	90	**3b** (40), (34)[c] + **4b** (10) + **4c** (2)
2b	580	95	**3b** (26) + **4b** (17) + **4c** (3)
2c	420	35	**3c** (23) + **4c** (1) + **4b** (1)
2c	450	82	**3c** (50), (44)[c] + **4c** (4) + **4b** (2)
2c	470	90	**3c** (56), (51)[c] + **4c** (7) + **4b** (2)
2c	550	98	**3c** (31) + **4c** (15) + **4b** (2)
2d	450	77	**3d** (44), (38)[c] + **4c** (5) + **4b** (—)
2d	475	89	**3d** (54), (48)[c] + **4c** (9) + **4b** (—)
2d	580	98	**3d** (28) + **4c** (19) (13)[c] + **4b** (—)
2c,d	450	78—83	**3c,d** (47) (41)[c] + **4c** (5)+ **4b** (2)
2c,d	470	88—92	**3c,d** (55), (50)[c] + **4c** (7) + **4b** (3)
2c,d	600	95—98	**3c,d** (18) + **4c** (17) + **4b** (4)

[a] Conditions: a flow reactor, flow rate of **2a—d** 0.54 mol h^{-1}; flow rate of N_2 13.0 L h^{-1}.
[b] The yield in mixtures was calculated according to the analysis of the pyrolysate by GC and NMR spectroscopy.
[c] Isolated yield after distillation of the pyrolysate.

product of dehydrohalogenation of cyclohexenes **3b** (see Scheme 1), and fair amounts of isomeric 3,4-difluorotoluene (**4c**). The formation of product **4c** is consistent with possible competitive isomerization of **2b** to cyclohexene **7b** and aromatization of the latter (see Scheme 2).

The cycloaddition of CTFE to isoprene **1c** under the copyrolysis conditions at 400 °C proceeds at both multiple bonds resulting in the corresponding [2+2] cycloadducts **2c** and **2d** (in a ratio of 1.5 : 1). These compounds can be separated using a distillation column and obtained in 34 and 19% isolated yields, respectively (see Table 1). Pyrolysis of cyclobutane **2c** at 450—470 °C gives cyclohexene **3c** in 50—56% yield (GC data) (44—51% isolated yield) and difluorotoluenes **4c** and **4b** (6—9% total yield) (see Table 2). 3,4-Difluorotoluene (**4c**) obviously results from dehydrohalogenation of cyclohexene **3c** (see Scheme 1), while the presence of 2,3-difluorotoluene (**4b**) in the pyrolysate, as in the case of aromatization of cyclobutane **2b**, can be explained by partial rearrangement of cyclobutane **2c** following the competitive Scheme 2.

Cyclobutane **2d** under similar conditions at 450—475 °C isomerizes to cyclohexene **3d** (38—48% isolated yield) with minor (5—9%) formation of 3,4-difluorotoluene (**4c**) (see Table 2). At 580 °C, the yield of arene **4c** increases to 19% with no formation of 2,3-difluorotoluene being observed, which is consistent with the fact that both competitive routes of isomerization of cyclobutane **2d** (see Schemes 1 and 2) should lead to compound **4c** *via* dehydrohalogenation of cyclohexenes **3d** or **7d**.

Cyclohexenes **3c** and **3d** can also be obtained by pyrolysis of a mixture of **2c** and **2d** at 450—470 °C in 41—50% total isolated yield or in a single step by copyrolysis of CTFE and isoprene **1c** at 440—460 °C (35—41% total yield, ratio **3c** : **3d** = 2.1 : 1) (see Table 1).

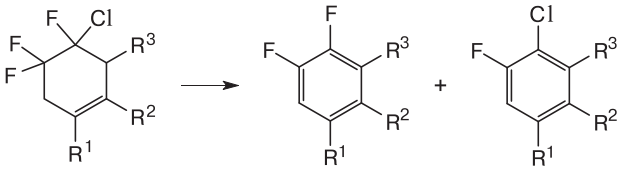
A comparison of the results presented in Tables 1 and 2 allows us to conclude that in terms of the yields of chlorotrifluorocyclohexenes **3** the one-step version is more preferable than the alternative two-step procedure. At the same time, to obtain pure cyclohexenes **3c** and **3d**, which have very close boiling points, only a two-step procedure is suitable *via* a preliminary synthesis of the mixtures of **2c** and **2d** from CTFE and isoprene, separation of compounds **2c** and **2d**, and their subsequent isomerization.

The yields of difluoroarenes **4a—c** obtained by pyrolysis of cyclobutanes **2a—d** at 420—500 °C do not exceed 5—10% because of the low rate of thermal dehydrohalogenation of cyclohexenes **3a—d** at this temperature range. When the temperature of pyrolysis is increased to 550—600 °C, the yield of difluoroarenes increases insignificantly, only up to 15—20%, because of a decrease in the selectivity of **2** → **3** rearrangements and a sharp increase in the contribution of resinification.

Aromatization of cyclobutanes **2a—d** by gas-phase heterogeneous pyrolysis in the presence of SiC or metal oxides (Al_2O_3, ZnO/Al_2O_3, V_2O_5/Al_2O_3) at 400—500 °C suggested earlier[25,27] turned out to be ineffective. The transformations **2a** → **4a** under these conditions provided 22—35% yields, while pyrolysis of compounds **2b** and **2c,d** led to inseparable mixtures of 2,3-difluorotoluene (**4b**) and 3,4-difluorotoluene (**4c**) in 12—15% total yield. Moreover, significant amounts of fluoro- and chlorofluorobenzenes were formed in all the cases.

We found a much more efficient procedure for synthesizing difluoroarenes, which consists in the isolation of chlorotrifluorocyclohexenes **3a—d** from the mixtures of pyrolysis products and their subsequent aromatization by water-alkaline dehydrohalogenation under phase-transfer catalysis conditions (Scheme 3). Thus, the reaction of chlorotrifluorocyclohexene **3a** with a 3—4-fold molar excess of 50% aqueous KOH in the presence of catalytic amounts of triethylbenzylammonium chloride (TEBAC) at 85—95 °C gives 1,2-difluorobenzene (**4a**) in 83% isolated yield. 2-Chloro-1-fluorobenzene (**8a**) is formed as a by-product (7% yield).

Scheme 3



3, 4, 8: $R^1 = R^2 = R^3 = H$ (**a**); $R^1 = R^2 = H$, $R^3 = Me$ (**b**); $R^1 = Me$, $R^2 = R^3 = H$ (**c**); $R^1 = R^3 = H$, $R^2 = Me$ (**d**)

Reagents and conditions: KOH, H_2O, Et_3NBnCl, 85—95 °C.

2,3-Difluorotoluene (**4b**) and 2-chloro-3-fluorotoluene (**8b**) (82% and 6% yield, respectively) were obtained from cyclohexene **3b** under similar conditions. The alkaline aromatization of cyclohexenes **3c** and **3d** gave 3,4-difluorotoluene (**4c**) in 82—83% yield with 4-chloro-3-fluorotoluene (**8c**) and 3-chloro-4-fluorotoluene (**8d**) being formed as the minor products. A mixture of cyclohexenes **3c** and **3d** obtained by copyrolysis of CTFE and isoprene can also be used as a starting material for selective synthesis of **4c** in 84% yield. Dehydrohalogenation can be carried out solvent-free by addition of aqueous alkali to cyclohexenes **3a—d**, stirring the reaction mixture at 85—95 °C for 3—4 h, and subsequent steam distillation to separate the products.

In conclusion, thermal cycloaddition reactions of commercially available monomers of chlorotrifluoroethylene, buta-1,3-diene, penta-1,3-diene, and isoprene were used to accomplish a simple two- or three-step regioselective synthesis of 1,2-difluorobenzene, 2,3-difluorotoluene, or 3,4-difluorotoluene, respectively. We showed the pos-

sibility to scale-up these procedures by obtaining kilogram amounts of these products under laboratory conditions, which were used as the starting compounds for the development of new technologies for the synthesis of a series of fluoroquinolone antibacterial drugs (pefloxacin, ciprofloxacin, and their analogs).

Experimental

Commercially available chlorotrifluoroethylene (99.5%) (Poly-Trade, Russia), buta-1,3-diene (99.0%), isoprene (99.0%), and penta-1,3-diene (98.0%) (Sintez-Kauchuk, Russia) were used. Isoprene and penta-1,3-diene were additionally distilled to separate from the polymer products formed during storage. Commercially available KOH (85%), triethylbenzylammonium chloride (TEBAC) (99%), 1,2-difluorobenzene, and 3,4-difluorotoluene (Sigma-Aldrich) were used as purchased.

GC analysis was performed on Kristal 2000M (Macherey-Nagel OPTIMA-1 capillary column, 30 m×0.25 mm, carrier gas helium, flame-ionizing detector) and LHhM-8MD (steel column 3.0 m×0.5 cm, 5% SE-30 on Chromaton N-AW-DMCS, carrier gas helium, a katharometer) chromatographs. ^{1}H and ^{19}F NMR spectra were recorded on a Bruker AC-200 spectrometer (200.1 (^{1}H) and 188.3 MHz (^{19}F)) in $CDCl_3$ containing 0.05% of Me_4Si (an internal standard). ^{19}F NMR chemical shifts are given relative to $CClF_3$ (an external standard). Mass spectra were recorded on a Trace GC Ultra instrument equipped with a Finnigan MAT DSQII mass detector (EI, 70 eV, an ion trap as an ion source, 200 °C) and a Thermo TR-5ms SQC capillary chromatographic column (15000×0.25 mm). Fischer HMS-500 and Fischer MMS-255 distillation apparatus were used to separate products with close boiling points.

Gas-phase pyrolytic processes (general procedure). A tubular quartz reactor with an inner diameter of 30 mm and a length of 1000 mm with a coaxially inserted quartz rod 16 mm in diameter and 1000 mm long was used. The reactor was placed in a tubular electric heating furnace with a heated zone length of 750 mm. The length of the measured, conditionally isothermal, heating zone of the reactor (with a temperature variation of ±5 °C from the set) was 380—390 mm. The reaction temperature was evaluated by the readings of a thermocouple placed in a special quartz pocket installed in the center of the reaction zone. The reactor was heated to a pre-set temperature in a stream of nitrogen, then the starting substrates were fed into the reactor at a constant flow rate controlled by rheometers (for gases) or a microdosing pump (for liquids).

Copyrolysis of CTFE and buta-1,3-diene (1a). The gas flows of CTFE at a constant flow rate of 13.0 L h^{-1} (0.54 mol h^{-1}) and buta-1,3-diene (**1a**) at a constant flow rate of 13.0 L h^{-1} (0.54 mol h^{-1}) were passed through a tubular reactor heated to 410 °C for 9 h. The pyrolysis products leaving the reactor were cooled in a water condenser and then collected in two sequentially connected traps cooled with ice—water mixture and dry ice—ethanol mixture. The resulting crude pyrolysate was steam distilled to separate resins, gaseous components, and inorganic products. The obtained distillate was washed with water and dried with $CaCl_2$ to give 630.8 g of the product mixture containing (GC and NMR spectroscopy data) 1.1% of butadiene **1a**, 80.9% of cyclobutane **2a**, 11.6% of cyclohexene **3a**, 1.8% of difluorobenzene **4a**, and 4.6% (total) of unidentified products. Distillation of this mixture afforded 467.4 g (57%) of 3-chloro-1,1,2-trifluoro-3-vinylcyclobutane **2a** ((2*S**,3*S**)-**2a** : (2*S**,3*R**)-**2a** = = 1 : 1), b.p. 114—115 °C. Liquified products (140.2 g) collected in the trap cooled with dry ice—ethanol mixture contained 64% of CTFE and 26% of butadiene **1a**.

Similar copyrolysis procedure (450 °C) of CTFE and diene **1a** at a flow rate of 0.54 mol h^{-1} of each reactant for 9 h and subsequent treatment of the crude pyrolysate gave 629.8 g of a product mixture containing 1.1% of butadiene **1a**, 23.5% of cyclobutanes **2a**, 58.7% of cyclohexene **3a**, 5.9% of difluorobenzene **4a**, and 10.8% (total) of unidentified products. Vacuum distillation of this mixture using a rectification apparatus afforded 320.6 g (39%) of cyclohexene **3a**, b.p. 83—85 °C (130 Torr). Liquified products (94.4 g) collected in the trap cooled with dry ice—ethanol mixture contained 63% of CTFE and 22% of butadiene **1a**.

Similar copyrolysis procedure (410 °C) of CTFE and penta-1,3-diene (**1b**) (a mixture of *E*-**1b** : *Z*-**1b** = 1.6 : 1) at a flow rate of 0.54 mol h^{-1} of each reactant for 10 h and subsequent treatment of the crude pyrolysate gave 785.2 g of a product mixture containing 5.8% of pentadiene **1b**, 72.7% of cyclobutanes **2b**, 9.1% of a mixture of cyclohexenes **3b**, 1.9% of a mixture of difluorotoluenes **4b**,**c**, and 10.5% (total) of unidentified products. Distillation of this mixture using a rectification apparatus afforded 520.3 g (52%) of cyclobutanes **2b** (a mixture of four isomers: (2*S**,3*S**)- and (2*S**,3*R**)-3-chloro-1,1,2-trifluoro-3-(*E*-prop-1-en-1-yl)cyclobutanes and (2*S**,3*S**)- and (2*S**,3*R**)-3-chloro-1,1,2-trifluoro-3-(*Z*-prop-1-en-1-yl)cyclobutanes in the ratio of 1.6 : 1.5 : 1 : 1), b.p. 139—142 °C. Liquified products (120.2 g) collected in the trap cooled with dry ice—ethanol mixture contained 82% of CTFE and 9% of pentadiene **1b**.

Similar copyrolysis procedure (450 °C) of CTFE and pentadiene **1b** at a flow rate of 0.54 mol h^{-1} of each reactant for 10 h and subsequent treatment of the crude pyrolysate gave 739.2 g of a product mixture containing 5.2% of pentadiene **1b**, 25.6% of cyclobutanes **2b**, 48.6% of a mixture of cyclohexenes **3b**, 8.5% of a mixture of difluorotoluenes **4b** and **4c**, and 7.5% (total) of unidentified products. Vacuum distillation of this mixture using a rectification apparatus afforded 308.8 g (31%) of cyclohexenes **3b** (a mixture of *cis*-**3b** and *trans*-**3b**, 1 : 1.3), b.p. 68—69 °C (44 Torr). Liquified products (115.2 g) collected in the trap cooled with dry ice—ethanol mixture contained 79% of CTFE and 9% of pentadiene **1b**.

Similar copyrolysis procedure (400 °C) of CTFE and isoprene **1c** (flow rate of each reactant 0.54 mol h^{-1}) for 10 h gave 820.21 g of a product mixture containing 3.9% of isoprene **1c**, 47.7% of cyclobutane **2c**, 31.4% of cyclobutane **2d**, 11.8% of a mixture of cyclohexenes **3c,d**, 1.1% of difluorotoluenes **4b,c**, and 4.1% (total) of unidentified products. Distillation of this mixture using a rectification apparatus afforded 340.12 g (34%) of 2-chloro-1,1,2-trifluoro-3-methyl-3-vinylcyclobutane (**2c**) ((2*S**,3*R**)-**2c** : (2*S**,3*S**)-**2c** = 1 : 1), b.p. 129—130 °C, and 184.21 g (19%) of 2-chloro-1,1,2-trifluoro-3-isopropenylcyclobutane (**2d**) ((2*S**,3*R**)-**2d** : (2*S**,3*S**)-**2d** = 1.7 : 1), b.p. 139—142 °C. Liquified products (103.3 g) collected in the trap cooled with dry ice—ethanol mixture contained 82% of CTFE and 11% of isoprene.

Similar copyrolysis procedure (440 °C) of CTFE and isoprene **1c** (flow rate of each reactant 0.54 mol h^{-1}) for 10 h and subsequent steam distillation of the crude pyrolysate gave 752.31 g of a product mixture containing (GC and NMR spectroscopy data)

4.1% of isoprene **1c**, 7.9% of cyclobutane **2c**, 10.6% of cyclobutane **2d**, 60.9% of cyclohexenes **3c,d**, 5.8% of difluorotoluenes **4b,c**, and 10.7% (total) of unidentified products. Vacuum distillation of this mixture afforded 407.8 g (40%) of a mixture of cyclohexenes **3c,d** (**3c** : **3d** = 2.1 : 1), b.p. 84—88 °C (70 Torr). Liquified products (116.2 g) collected in the trap cooled with dry ice—ethanol mixture contained 81% of CTFE and 9% of isoprene.

Pyrolysis of 3-alkenyl-2-chloro-1,1,2-trifluorocyclobutanes 2a—d. 2-Chloro-1,1,2-trifluoro-3-vinylcyclobutane (**2a**) ((2*S**,3*S**)-**2a** : (2*S**,3*R**)-**2a** = 1 : 1) (460.3 g, 2.70 mol) at a constant flow rate of 1.53 g min^{-1} and a gas flow of nitrogen (220 mL min^{-1}) were passed through a tubular reactor heated to 480 °C for 5 h. The pyrolysis products leaving the reactor were cooled in a water condenser and then collected in two sequentially connected traps cooled with ice—water mixture and dry ice—ethanol mixture. Steam distillation and drying of the liquid pyrolysate gave 363.1 g of a mixture containing 13.8% of cyclobutane **2a**, 71.1% of cyclohexene **3a**, 6.9% of difluorobenzene **4a**, 0.7% of butadiene, and 7.5% of unidentified products. Vacuum distillation of this mixture afforded 230.3 g (50%) of 4-chloro-4,5,5-trifluorocyclohex-1-ene (**3a**), b.p. 83—85 °C (130 Torr). Liquified products (65.4 g) collected in the trap cooled with dry ice—ethanol mixture contained 69% of CTFE and 24% of butadiene **1a**.

Similar pyrolysis (480 °C) of cyclobutane **2b** (a mixture of four isomers: (2*S**,3*S**)- and (2*S**,3*R**)-3-chloro-1,1,2-trifluoro-3-(*E*-prop-1-en-1-yl)cyclobutanes and (2*S**,3*S**)- and (2*S**,3*R**)-3-chloro-1,1,2-trifluoro-3-(*Z*-prop-1-en-1-yl)cyclobutanes in the ratio of 1.6 : 1.5 : 1 : 1) (199.2 g, 1.08 mol) at a constant flow rate of 1.66 g min^{-1} in a flow of nitrogen (220 mL min^{-1}) for 2 h gave 173.1 g of the liquid pyrolysate, steam distillation and drying of which gave 156.1 g of a product mixture containing 19.2% of cyclobutanes **2b**, 56.4% of cyclohexenes **3b**, 6.3% of difluorotoluene **4b**, 2.7% of difluorotoluene **4c**, 5.1% of pentadiene **1b**, and 10.3% (total) of unidentified products. Vacuum distillation of this mixture afforded 75.96 g (38%) of cyclohexenes **3b** (a mixture of *cis*-**3b** and *trans*-**3b** in the ratio of 1 : 1.4), b.p. 66—69 °C (44 Torr). Liquified products (18.1 g) collected in the trap cooled with dry ice—ethanol mixture contained 81% of CTFE and 6% of pentadiene **1b**.

Similar pyrolysis (470 °C) of cyclobutane **2c** (99.62 g, 0.540 mol) (flow rate 1.66 g min^{-1}) in a flow of nitrogen (220 mL min^{-1}) for 1 h gave 90.32 g of the liquid pyrolysate, steam distillation and drying of which gave 82.21 g of a product mixture containing 12.1% of cyclobutane **2c**, 67.9% of cyclohexene **3c**, 6.1% of difluorotoluene **4c**, 2.1% of difluorotoluene **4b**, 1.8% of isoprene, and 9.8% (total) of unidentified products. Vacuum distillation of this mixture afforded 50.79 g (51%) of 4-chloro-4,5,5-trifluoro-1-methylcyclohex-1-ene (**3c**), b.p. 85—87 °C (70 Torr). Liquified products (7.9 g) collected in the trap cooled with dry ice—ethanol mixture contained 79% of CTFE and 9% of isoprene **1c**.

Similar pyrolysis (475 °C) of cyclobutane **2d** (99.63 g, 0.540 mol) at a constant flow rate of 1.66 g min^{-1} in a flow of nitrogen (220 mL min^{-1}) for 1 h gave 86.42 g of the liquid pyrolysate, which was steam distilled and dried to give 79.41 g of a product mixture containing 13.7% of cyclobutane **2d**, 67.8% of cyclohexene **3d**, 7.8% of difluorotoluene **4c**, 1.9% of isoprene, and 8.8% (total) of unidentified products. Vacuum distillation of this mixture afforded 47.78 g (48%) of cyclohexene **3d**, b.p. 85—87 °C (70 Torr). Liquified products (8.7 g) collected in the trap cooled with dry ice—ethanol mixture contained 81% of CTFE and 5% of isoprene **1c**.

Similar pyrolysis (470 °C) of a 1.5 : 1 mixture of cyclobutanes **2c** and **2d** (199.26 g, 1.08 mol) at a constant flow rate of 1.66 g min^{-1} in a flow of nitrogen (220 mL min^{-1}) for 2 h gave 174.8 g of the crude liquid pyrolysate, which was steam distilled and dried to give 160.8 g of a product mixture containing 5.9% of cyclobutane **2c**, 6.5% of cyclobutane **2d**, 68.2% of cyclohexenes **3c,d**, 5.4% of difluorotoluene **4c**, 2.3% of difluorotoluene **4d**, 1.9% of isoprene, and 9.8% (total) of unidentified products. Vacuum distillation of this mixture afforded 98.8 g (50%) of a 1.9 : 1 mixture of cyclohexenes **3c** and **3d**, b.p. 84—86 °C (70 Torr). Liquified products (15.2 g) collected in the trap cooled with dry ice—ethanol mixture contained 81% of CTFE and 5% of isoprene.

2-Chloro-1,1,2-trifluoro-3-vinylcyclobutane (2a)[33,34] (a 1 : 1 mixture of (2*S**,3*R**)- and (2*S**,3*S**)-2-chloro-1,1,2-trifluoro-3-vinylcyclobutanes). ^{1}H NMR ($CDCl_3$), δ: 2.20—2.93 (m, 2 H, CH_2); 3.17—3.48 (m, 1 H, CH); 5.18—5.45 (m, 2 H, C=CH_2); 5.29—6.00 (m, 1 H, C=CH). ^{19}F NMR (for (2*S**,3*S**)-**2a**) ($CDCl_3$), δ: −98.3, −117.1 (both br.d, 1 F each, CF_2, J = 196 Hz); −110.0 (br.s, 1 F, CFCl). ^{19}F NMR (for (2*S**,3*R**)-**2a**) ($CDCl_3$), δ: −104.7, −109.1 (both br.d, 1 F each, CF_2, J = 199 Hz); −134.1 (br.s, 1 F, CFCl)). MS, m/z (I_{rel} (%)): 170 $[M]^+$ (2), 135 (45), 106 (16), 54 (100), 53 (40).

2-Chloro-1,1,2-trifluoro-3-((*Z*)-prop-1-en-1-yl)cyclobutane (*Z*-2b)[25] (a 1 : 1 mixture of (2*S**,3*R**)-*Z*-**2b** and (2*S**,3*S**)-*Z*-**2b**). ^{1}H NMR ($CDCl_3$), δ: 1.71 (dd, 3 H, CH_3, J = 5.0 Hz, J = 1.8 Hz); 2.08—2.37 (m, 2 H, CH_2); 3.33—3.71 (m, 1 H, CH); 5.30—5.90 (m, 2 H, HC=CH). ^{19}F NMR (for (2*S**,3*S**)-*Z*-**2b**) ($CDCl_3$), δ: −98.2, −117.8 (both br.d, 1 F each, CF_2, J = 194 Hz); −108.9 (br.s, 1 F, CFCl). ^{19}F NMR (for (2*S**,3*R**)-*Z*-**2b**) ($CDCl_3$), δ: −106.2, −108.0 (both br.d, 1 F each, CF_2, J = 194 Hz); −134.5 (br.s, 1 F, CFCl). MS (for the mixture of *Z*-**2b** and *E*-**2b**), m/z (I_{rel} (%)): 184 $[M]^+$ (2), 149 (42), 120 (18), 85 (32), 68 (100), 67 (44), 53 (18), 39 (19).

2-Chloro-1,1,2-trifluoro-3-((*E*)-prop-1-en-1-yl)cyclobutane (*E*-2b)[25] (a 1 : 1.1 mixture of (2*S**,3*R**)-*E*-**2b** and (2*S**,3*S**)-*E*-**2b**). ^{1}H NMR ($CDCl_3$), δ: 1.76 (d, 3 H, CH_3, J = 6.3 Hz); 2.38—2.95 (m, 2 H, CH_2); 3.01—3.32 (m, 1 H, CH); 5.30—5.90 (m, 2 H, HC=CH). ^{19}F NMR (for (2*S**,3*S**)-*E*-**2b**) ($CDCl_3$), δ: −98.9, −117.8 (both br.d, 1 F each, CF_2, J = 194 Hz); −110.2 (br.s, 1 F, CFCl). ^{19}F NMR (for (2*S**,3*R**)-*E*-**2b**) ($CDCl_3$), δ: −107.1, −108.7 (both br.d, 1 F each, CF_2, J = 194 Hz); −134.9 (br.s, 1 F, CFCl). MS (for the mixture of *Z*-**2b** and *E*-**2b**), m/z (I_{rel} (%)): 184 $[M]^+$ (2), 149 (42), 120 (18), 85 (32), 68 (100), 67 (44), 53 (18), 39 (19).

2-Chloro-1,1,2-trifluoro-3-methyl-3-vinylcyclobutane (2c)[35] (a 1 : 1 mixture of (2*S**,3*R**)-**2c** and (2*S**,3*S**)-**2c**). ^{1}H NMR ($CDCl_3$), δ: 1.35—1.45 (m, 3 H, CH_3); 2.30—2.53 (m, 1 H, CH_2); 2.55—2.91 (m, 1 H, CH_2); 5.08—5.37 (m, 2 H, =CH_2); 5.92—6.12 (m, 1 H, =CH—). ^{19}F NMR (for (2*S**,3*S**)-**2c**) ($CDCl_3$), δ: −98.8, −109.3 (both br.d, 1 F each, CF_2, J = 202 Hz); −123.5 (1 F, CF). ^{19}F NMR (for (2*S**,3*R**)-**2c**) ($CDCl_3$), δ: −101.9, −107.8 (both br.d, 1 F each, CF_2, J = 202 Hz); −126.7 (br.s, 1 F, CFCl). MS, m/z (I_{rel} (%)): 184 $[M]^+$ (2), 149 (17), 120 (22), 85 (27), 68 (100), 67 (63), 53 (28), 39 (26).

2-Chloro-1,1,2-trifluoro-3-isopropenylcyclobutane (2d)[35] (a 1.7 : 1 mixture of (2*S**,3*R**)-**2d** and (2*S**,3*S**)-**2d**). ^{1}H NMR ($CDCl_3$), δ: 1.87 (m, 3 H, CH_3); 2.29—2.62 (m, 1 H, CH_2); 2.63—2.84 (m, 1 H, CH_2); 4.71—4.87 (m, 1 H, =CH_2); 5.06—5.14

(m, 1 H, =CH_2). ^{19}F NMR (for (2*S**,3*S**)-**2d**) ($CDCl_3$), δ: −99.0, −119.0 (both br.d, 1 F each, CF_2, J = 202 Hz); −108.8 (br.s, 1 F, CFCl). ^{19}F NMR (for (2*S**,3*R**)-**2d**) ($CDCl_3$), δ: −107.7 (br.s, 2 F, CF_2); −138.2 (br.s, 1 F, CFCl). MS, m/z (I_{rel} (%)): 184 $[M]^+$ (2), 149 (18), 120 (24), 85 (28), 68 (100), 67 (66), 53 (30), 39 (27).

4-Chloro-4,5,5-trifluorocyclohex-1-ene (3a).[19,25,36] B.p. 83—85 °C (130 Torr). ^{1}H NMR ($CDCl_3$), δ: 2.72—2.94 (m, 2 H, CH_2); 2.95—3.13 (m, 2 H, CH_2); 5.53—5.72 (m, 2 H, HC=CH). ^{19}F NMR ($CDCl_3$), δ: −111.2, −113.4 (both br.d, 1 F each, CF_2, J = 245 Hz); −122.2 (br.s, 1 F, CFCl). MS, m/z (I_{rel} (%)): 172 and 170 $[M]^+$ (12 and 38), 135 (55), 134 (91), 115 (92), 106 (60), 95 (51), 90 (58), 84 (45), 57(37), 51(44), 39 (100).

4-Chloro-4,5,5-trifluoro-3-methylcyclohex-2-ene (3b)[19,25] (a 1 : 1.3 mixture of *cis*-**3b** and *trans*-**3b**). MS (a mixture of *cis*-**3b** and *trans*-**3b**), m/z (I_{rel} (%)): 186 and 184 $[M]^+$ (5 and 16), 149 (100), 133 (12), 129 (22), 120 (22), 109 (18), 85 (22), 68 (20), 65 (16), 39 (12).

Major isomer. ^{1}H NMR ($CDCl_3$), δ: 1.31 (d, 3 H, CH_3, J = 6.4 Hz); 2.67—3.02 (m, 2 H, CH_2); 3.03—3.25 (m, 1 H, CH); 5.36—5.67 (m, 2 H, HC=CH). ^{19}F NMR ($CDCl_3$), δ: −110.4, −115.6 (both br.d, 1 F each, CF_2, J = 244 Hz); −132.4 (br.s, 1 F, CFCl).

Minor isomer. ^{1}H NMR ($CDCl_3$), δ: 1.34 (d, 3 H, CH_3, J = 6.4 Hz); 2.67—3.02 (m, 2 H, CH_2); 3.03—3.25 (m, 1 H, CH); 5.36—5.67 (m, 2 H, HC=CH). ^{19}F NMR ($CDCl_3$), δ: −108.0, −111.2 (both br.d, 1 F each, CF_2, J = 244 Hz); −134.2 (br.s, 1 F, CFCl).

4-Chloro-4,5,5-trifluoro-1-methylcyclohex-1-ene (3c).[19,25] ^{1}H NMR ($CDCl_3$), δ: 1.75 (m, 3 H, CH_3); 2.60—2.82 (m, 2 H, CH_2); 2.84—3.08 (m, 2 H, CH_2); 5.24—5.34 (m, 1 H, =CH). ^{19}F NMR ($CDCl_3$), δ: −110.5, −112.7 (both br.d, 1 F each, CF_2, J = 246 Hz); −124.0 (br.s, 1 F, CFCl). MS, m/z (I_{rel} (%)): 186 and 184 $[M]^+$ (17 and 53), 149 (100), 133 (28), 129 (53), 109 (15), 85 (47), 68 (55).

5-Chloro-4,4,5-trifluoro-1-methylcyclohex-1-ene (3d).[19,25] ^{1}H NMR ($CDCl_3$), δ: 1.75 (m, 3 H, CH_3); 2.63—2.85 (m, 2 H, CH_2); 2.86—3.04 (m, 2 H, CH_2); 5.26—5.38 (m, 1 H, =CH). ^{19}F NMR ($CDCl_3$), δ: −111.8, −114.6 (both br.d, 1 F each, CF_2, J = 246 Hz); −122.4 (br.s, 1 F, CFCl). MS, m/z (I_{rel} (%)): 186 and 184 $[M]^+$ (19 and 58), 149 (100), 133 (32), 129 (57), 109 (16), 85 (48), 68 (57).

Water-alkaline aromatization of chlorotrifluorocyclohexenes 3a—d. A 50% aqueous KOH (392.0 g, 3.50 mol) was added to a mixture of cyclohexene **3a** (170.5 g, 1.0 mol) and TEBAC (7.0 g) at 75—85 °C (oil bath) with stirring over 90 min, then the mixture was stirred for 3 h at 85—95 °C. Steam distillation of the resulting mixture gave a mixture of organic products, which was dried with $CaCl_2$. The dried mixture of product (110.8 g) contained 86.1% of 1,2-difluorobenzene (**4a**) and 9.2% of 2-chloro-1-fluorobenzene (**8a**). Distillation of this mixture afforded 94.91 g (83%) of 1,2-difluorobenzene (**4a**), b.p. 92—92.5 °C, and 9.22 g (7%) of chlorofluorobenzene **8a**, b.p. 137—138 °C.

Similar dehydrohalogenation of cyclohexene **3b** (a 1 : 1.3 mixture of *cis*-**3b** and *trans*-**3b**) (243.93 g, 1.32 mol) by treatment with 50% aqueous KOH (535.0 g) in the presence of TEBAC (10.0 g) gave 170.17 g of a product mixture containing 85.1% of 2,3-difluorotoluene (**4b**) and 8.4% of 2-chloro-3-fluorotoluene (**8b**). Distillation afforded 138.92 g (82%) of 2,3-difluorotoluene (**4b**), b.p. 124—125 °C.

Similar dehydrohalogenation of cyclohexene **3c** (24.42 g, 0.132 mol) by treatment with 50% aqueous KOH (64.0 g) in the presence of TEBAC (1.0 g) gave 17.42 g of a product mixture containing 85.9% of 3,4-difluorotoluene (**4c**) and 8.5% of 4-chloro-3-fluorotoluene (**8c**). Distillation afforded 14.03 g (83%) of 3,4-difluorotoluene (**4c**), b.p. 123—124 °C.

Similar dehydrohalogenation of cyclohexene **3d** (22.54 g, 0.122 mol) by treatment with 50% aqueous KOH (50.0 g) in the presence of TEBAC (1.0 g) gave 15.96 g of a product mixture containing 85.1% of 3,4-difluorotoluene (**4c**) and 9.1% of 3-chloro-4-fluorotoluene (**8d**). Distillation afforded 12.81 g (82%) of 3,4-difluorotoluene (**4c**), b.p. 123—124 °C.

Similar dehydrohalogenation of a mixture of cyclohexenes **3c,d** (**3c** : **3d** = 2.1 : 1) (293.31 g, 1.59 mol) by treatment with 50% aqueous KOH (640.0 g) in the presence of TEBAC (12.0 g) gave 205.9 g of a product mixture containing 86.1% of 3,4-difluorotoluene (**4c**), 6.2% of 4-chloro-3-fluorotoluene (**8c**), and 2.9% of 3-chloro-4-fluorotoluene (**8d**). Distillation afforded 170.42 g (84%) of 3,4-difluorotoluene (**4c**) and 16.82 g (7%) of a 2.1 : 1 mixture of chlorofluorotoluenes **8c** and **8d**, b.p. 156—160 °C.

1,2-Difluorobenzene (4a). ^{1}H NMR ($CDCl_3$), δ: 7.05—7.25 (m, 4 H, arom.). ^{19}F NMR ($CDCl_3$), δ: −137.5 (m, 2 F, arom.). MS, m/z (I_{rel} (%)): 114 $[M]^+$ (100), 95 (7), 88 (30), 63 (35), 56 (17), 50 (14).

Spectral data of compound **4a** are identical to those of a commercially available sample of 1,2-difluorobenzene (Sigma-Aldrich).

2,3-Difluorotoluene (4b).[19,37] ^{1}H NMR ($CDCl_3$), δ: 2.31 (br.s, 3 H, CH_3); 6.83—7.10 (m, 3 H, Ar). ^{19}F NMR ($CDCl_3$), δ: −139.1 (m, 1 F); −142.6 (m, 1 F). MS, m/z (I_{rel} (%)): 128 $[M]^+$ (58), 127 (100), 109 (7), 107 (8), 101 (10), 75 (6), 57 (6), 51 (6).

3,4-Difluorotoluene (4c).[19] ^{1}H NMR ($CDCl_3$), δ: 2.32 (s, 3 H, CH_3); 6.85—7.12 (m, 3 H, Ar). ^{19}F NMR ($CDCl_3$), δ: −138.7 (m, 1 F); −143.0 (m, 1 F). MS, m/z (I_{rel} (%)): 128 $[M]^+$ (46), 127 (100), 109 (9), 107 (7), 101 (13), 75 (7), 57 (8), 51 (9).

Spectral data of compound **4a** are identical to those of a commercially available sample of 3,4-difluorotoluene (Sigma-Aldrich).

1-Chloro-2-fluorobenzene (8a).[38] ^{1}H NMR ($CDCl_3$), δ: 7.03—7.12 (m, 2 H, Ar); 7.17—7.24 (m, 1 H, Ar); 7.34—7.38 (m, 1 H, arom.). ^{19}F NMR ($CDCl_3$), δ: −109.7 (m, 1 F).

2-Chloro-3-fluorotoluene (8b).[39] ^{1}H NMR ($CDCl_3$), δ: 2.39 (s, 3 H, CH_3); 6.89—7.08 (m, 3 H, Ar). ^{19}F NMR ($CDCl_3$), δ: −113.8 (m, 1 F). MS, m/z (I_{rel} (%)): 146 and 144 $[M]^+$ (15 and 45), 109 (100), 107 (14), 83 (12).

4-Chloro-3-fluorotoluene (8c).[14] ^{1}H NMR ($CDCl_3$), δ: 2.21 (s, 3 H, CH_3); 7.20—7.26 (m, 3 H, Ar). ^{19}F NMR ($CDCl_3$), δ: −115.2 (m, 1 F). MS, m/z (I_{rel} (%)): 146 and 144 $[M]^+$ (13 and 42), 109 (100), 107 (13), 83 (11).

3-Chloro-4-fluorotoluene (8d).[14,40] ^{1}H NMR ($CDCl_3$), δ: 2.30 (s, 3 H, CH_3); 6.99—7.20 (m, 3 H, Ar). ^{19}F NMR ($CDCl_3$), δ: −119.6 (m, 1 F). MS, m/z (I_{rel} (%)): 146 and 144 $[M]^+$ (16 and 49), 109 (100), 107 (17), 83 (15).

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