Highly *para*-Selective Mono-Chlorination of Aromatic Compounds Under Mild Conditions by *t*-Butyl Hypochlorite in the Presence of Zeolites

Keith SMITH*, Michael BUTTERS

Department of Chemistry, University College of Swansea, Swansea SA2 8PP, U.K.

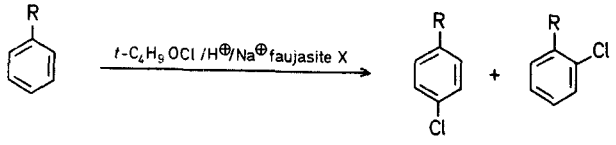
Barry NAY

New Reactions Branch, BP Research Centre, Chertsey Road, Sunbury-on-Thames, Middlesex TW16 7LN, U.K.

t-Butyl hypochlorite supported on $H^{\oplus}$, $Na^{\oplus}$ faujasite X (zeolite X) produces *para*-selective monchlorination of alkyl-, phenyl-, and halobenzenes under mild conditions; for example, chlorobenzene in acetonitrile (at 40 °C) is chlorinated in high yield of isolated product (92%) to give dichlorobenzene with an isomer ratio 97% *para*/3% *ortho*.

Much attention has been paid to organic reactions effected by reagents immobilised on highly-divided solids[1]. In our preceding communication[2], we reported that several organic chlorine-containing compounds, when deposited on silica gel, become powerful electrophilic chlorinating agents, even at room temperature. Unfortunately, the regioselectivity in these reactions is poor, comparable to that found with chlorine and a catalyst in the liquid phase[3]. In an effort to manipulate the regioselectivity we turned our attention to well-defined, crystalline aluminosilicate zeolites[4] as inorganic supports[5]. The majority of active sites in these microporous solids are embedded within pores or cavities of molecular dimensions. Thus, in certain cases the lattice structure is able to discriminate between the structural shapes of reactants or products. Despite this, few studies have been made of the ability of zeolites to control organic reactions under normal liquid-phase conditions[6].

We now report a high degree of regioselectivity in the chlorination of aromatic substrates with *t*-butyl hypochlorite[7] in the presence of partially proton-exchanged sodium faujasite X ($H^{\oplus}$, $Na^{\oplus}$ faujasite X). Chlorination of a range of monoalkyl-, phenyl-, and halobenzenes **(1)** results in highly selective formation of the *para*-chloro isomers **(2)**. For example, toluene is chlorinated at 25 °C using this reagent system (slight excess) in dichloromethane/ether (1/3) to give a quantitative yield of monochlorotoluenes with a *p*:*o* isomer ratio of 91:9. As far as we are aware, there is no other known system that can chlorinate toluene with the same degree of *para* selectivity[8]. The greater the proportion of ether in the solvent mixture, the higher is the *para* selectivity. Unfortunately, the use of ether as a solvent or co-solvent is not practical with less reactive aromatic substrates because reaction of *t*-butyl hypochlorite with the ether then becomes competitive. Thus, in general other solvents are appropriate.



1a-g **2a-g** (major) **3a-g** (minor)

The reagent has been applied to chlorination of a series of aromatic substrates. For comparison, all results listed in the Table refer to reactions in acetonitrile. It is clear that this reagent gives much better *para* selectivity than either *t*-butyl hypochlorite on silica[2] or molecular chlorine in acetic acid[9]. It is most effective for alkyl-, phenyl-, and halobenzenes, giving high *para* selectivity in all cases. Benzenes with deactivating substituents (for example benzonitrile, benzoic acid, methyl benzoate, and nitrobenzene) could not be chlorinated even at elevated temperatures. Phenols react with *t*-butyl hypochlorite even in the absence of the inorganic support, so no control is possible. Similarly, anisole is chlorinated in acetonitrile at the same rate whether in the presence or absence of a support, but in this case considerable regioselective control is possible using partially proton-exchanged sodium faujasite X in tetrachloromethane, to give a *p*/*o* isomer ratio of 82/18 (whereas a *p*/*o* ratio of 70/30 is obtained when silica is the support).

We have applied all of the organic chlorine-containing reagents reported in our previous communication[2] over zeolitic supports instead of silica, and molecular chlorine has previously been tried[10]. However, *t*-butyl hypochlorite is far superior to the other reagents. For example, molecular chlorine gives an inferior selectivity, rate of reaction, and yield of products, together with the undesirable evolution of hydrogen chloride which causes structural deformation of the zeolite lattice. Sulphuryl chloride and several organic chlorine-containing compounds are not effective chlorinating agents in the presence of zeolites although effective in the presence of silica[2].

We have tried a variety of other zeolites with *t*-butyl hypochlorite, including different cation-exchanged forms: $Na^{\oplus}$ZSM-5; $H^{\oplus}$ZSM-5; $K^{\oplus}$ zeolite L; silicalite-1; $H^{\oplus}$, $Na^{\oplus}$ large port mordenite (ex Norton); $Na^{\oplus}$ zeolite X; $H^{\oplus}$, $Na^{\oplus}$, $Ca^{2\oplus}$ zeolite X; $H^{\oplus}$, $Na^{\oplus}$, $Ca^{2\oplus}$, $La^{3\oplus}$ zeolite X; $Na^{\oplus}$, $Ca^{2\oplus}$ zeolite X; $H^{\oplus}$, $Na^{\oplus}$, $Fe^{3\oplus}$ zeolite X; $Na^{\oplus}$ zeolite Y; $H^{\oplus}$, $Na^{\oplus}$ zeolite Y. However, partially proton-exchanged sodium faujasite X appears to be the best. Studies involving faujasites with a series of different Si/Al ratios revealed that proton-exchanged forms of faujasites with a low aluminium content (Si/Al > 2.4) gave by-products resulting from Friedel-Crafts type alkylation reactions[11]. The optimum Si/Al ratio for clean chlorination reactions is ~ 1.2. Presumably, relatively weak acid sites favour aromatic chlorinations.

A wide range of solvents has been employed in these reactions, including pentane, tetrachlormethane, dichloromethane, acetonitrile, ether, methanol, and others found to be inferior or reactive [1,4-dioxan, tetrahydrofuran, 1,2-dimethoxyethane, dimethylformamide, tetramethylethanediamine (TMEDA), pyridine, and piperidine]. However, the yields, rates of reaction, and degree of *para* selectivity generally appeared to be optimum in acetonitrile. Preparative-scale reactions to chlorinate chlorobenzene (at 40 °C) and toluene were very successful, giving yields of isolated (distilled) products in the region of 90% with considerable regioselectivity.

$H^{\oplus}$, $Na^{\oplus}$ Faujasite X that had previously been employed in a *para*-dichlorobenzene preparation could easily be reactivated and used in another reaction with no detrimental effect. Likewise, a "physically-supported" reagent was prepared (composed of *t*-butyl hypochlorite; $H^{\oplus}$, $Na^{\oplus}$ faujasite X; and trace amounts of dichloromethane solvent) and showed little loss in activity even after two weeks at room temperature. Such findings suggest that the reaction could be applicable to large-scale work.

A possible reaction mechanism could involve the *t*-butyl hypochlorite oxonium cation[12].

Table. Yields and *para/ortho* Selectivities in the Chlorination of Mono-substituted Benzenes with *t*-Butyl Hypochlorite over $H^{\oplus}$, $Na^{\oplus}$ Faujasite® X, in Comparison with the Selectivities obtained over BDH Silica[2] and to Those obtained with Chlorine in Acetic Acid[9]

1, 2, 3	R	*t*-C_4H_9—OCl/$H^{\oplus}$, $Na^{\oplus}$ X in Acetonitrile		*t*-C_4H_9—OCl/SiO_2 in CCl_4	Cl_2/AcOH
		Yield[a] **2** + **3** [%]	**2**/**3** (*p*/*o*)	**2**/**3** (*p*/*o*)	**2**/**3**/*meta* (*p*/*o*/*m*)
a	CH_3	100	82/18[b]	35/65	42/58/0
b	C_2H_5	100	90/10	43/57	48/52/0
c	*i*-C_3H_7	90	80/20	56/44	63/37/0
d	*t*-C_4H_9	99	98/(2)[c]	85/(15)[c]	76/22/2
e	C_6H_5	86	86/14	44/56	50/50/0
f	Cl	95	97/3	little reaction	55/39/6
g	Br	75	97/3	little reaction	52/42/6

[a] As estimated by G.L.C. with reference to undecane added as a standard after removal of organic products from the zeolite (2.5 mmol scale reaction); reaction periods vary from ~1 h at 25 °C for toluene to ~2 weeks at 40 °C for halobenzenes.

[b] Note that toluene may be chlorinated in dichloromethane/ether (1/3) to effect a selectivity of 91% *para*/9% *ortho*.

[c] Data in parentheses indicate that the *ortho* and *meta* isomers were not distinguished.

Partially Proton-Exchanged Sodium Faujasite X:

Sodium faujasite X (BDH powdered 13X molecular sieve, 20 g) is heated at 100 °C with stirring for 1 h with aqueous 1 molar ammonium chloride solution (200 ml). After this time the solid is filtered, washed several times with distilled water, and then dried in a furnace at 500 °C. After cooling, the material is stored under dry conditions in a sealed container.

Chlorination of Toluene; Typical Procedures:

Investigative-Scale Chlorination: To a mixture of dichloromethane (7.5 ml), diethyl ether (2.5 ml), toluene (**1a**; 0.23 g, 2.5 mmol), and *t*-butyl hypochlorite (2.6 mmol, estimated by iodimetry), gently stirred in a 50 ml round-bottomed flask, is added partially proton-exchanged sodium faujasite X (1.5 g), prepared as above. The mixture is stirred at 25 °C for 2 h and then filtered. The solid is washed with a little extra dichloromethane and the filtrates are combined. G.L.C. analysis indicates the presence of *p*-chlorotoluene (**2a**; 91%) and *o*-chlorotoluene (**3a**; 9%) confirmed by comparison with authentic materials. This mixture can be obtained essentially pure simply by removal of the solvent.

This procedure is representative except for variations in solvents, reaction temperatures, or reaction times (see Table).

Preparative-Scale Chlorination: To partially proton-exchanged sodium faujasite X (60 g, finely powdered) prepared as above and contained in a 500 ml round-bottomed flask, is added dichloromethane (200 ml), diethyl ether (200 ml), and toluene (**1a**; 9.2 g, 0.10 mol). After addition is complete, *t*-butyl hypochlorite (14 g, 0.12 mol) is added and the resultant mixture stirred in a constant temperature bath at 25 °C. After 1 h, the mixture is filtered through a sintered-glass funnel, and the zeolite residue is washed with methanol (50 ml). The volatile solvents are removed by fractional distillation through a 30 cm Vigreux column. The resultant residue (25 ml) is transferred to a smaller apparatus and further purified by fractional distillation through a 10 cm Vigreux column. The fraction of boiling range 158 °C - 162 °C consists of *p*-chlorotoluene (**2a**; 90%) and *o*-chlorotoluene (**3a**; 10%) according to G.L.C. analysis; yield of **2a** + **3a**: 11.13 g (88%). G.L.C. analysis of the forerun reveales a further 2% yield of chlorotoluenes.

1,4-Dichlorobenzene (2f):

To partially proton-exchanged sodium faujasite X (20 g), prepared as above, is added acetonitrile (54 ml) and chlorobenzene (**1f**; 3.83 g, 34 mmol). In a separate vessel, *t*-butyl hypochlorite (34 mmol, estimated by iodimetry) is dissolved in acetonitrile (82 ml). This solution is added to the first mixture, the flask is fitted with a reflux condenser, and the mixture is heated to 40 °C in a thermostatically controlled water bath, whilst gentle stirring is maintained. After 14 days, the mixture is cooled and filtered. The separated solid is washed with more acetonitrile (50 ml), pentane (2 × 50 ml), and water (50 ml) and the combined filtrates are placed in a separating funnel. The pentane layer is separated and then washed with water (2 × 20 ml) and dried with magnesium sulphate. Evaporation of the solvent under reduced pressure gives a white semi-solid material in almost quantitative yield. G.L.C. analysis shows the material to consist of 1,4-dichlorobenzene (**2f**; 97%) and 1,2-dichlorobenzene (**3f**; 3%). This material is further purified by kugelrohr distillation (~ 55 °C/10 torr) to give a colourless crystalline distillate which, according to G.L.C. analysis, is almost pure 1,4-dichlorobenzene (**2f**) containing just a trace of 1,2-dichlorobenzene (**3f**); yield: 4.60 g (92%); m.p. 50–51 °C (Ref.[13], m.p. 53 °C).

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* Address for correspondence.

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