New Reagent Systems for Electrophilic Chlorination of Aromatic Compounds: Organic Chlorine-Containing Compounds in the Presence of Silica

Keith SMITH*, Michael BUTTERS, Walter E. PAGET

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.

In the presence of silica, a number of chlorine-containing organic compounds, such as *N,N*-dichlorourethane, dichloramine-T, and *t*-butyl hypochlorite, become active electrophilic reagents capable of controlled monochlorination of aromatic compounds under mild conditions; for example, *t*-butyl hypochlorite/silica chlorinates alkylbenzenes, naphthalene, and anisole readily at 25°C; *N,N*-dichlorourethane/silica chlorinates benzene within 2 days 50°C.

Traditional electrophilic chlorination reactions of aromatic substrates[1], with reagents such as elemental chlorine in ethanoic acid, are tedious and messy. Large volumes of ethanoic acid have to be removed by evaporation or neutralisation and the by-product, hydrogen chloride, may be deleterious to functionalities present in the substrate. The situation is improved by use of tetrachloromethane as solvent with silica as a catalyst[2], but the by-product is still hydrogen chloride, and the use of chlorine gas as the reagent presents problems of control of stoichiometry. Replacement of chlorine by sulphuryl chloride[3] allows easier metering of the reagent but still results in the production of hydrogen chloride. Furthermore, since the presence of water on the silica causes destruction of some of the reagent, without accurate knowledge of the water content of the silica the stoichiometry can again be difficult to control.

We now report that several organic chlorine-containing compounds become active electrophilic chlorinating agents in the presence of silica, and that such reagent systems are convenient to use, produce clean reactions, and do not result in the generation of hydrogen chloride.

We first became aware of such possibilities during investigations of the synthesis of chloroalkanes by the reaction of organoboranes with dichloramine-T (DCT) or *N,N*-dichlorourethane (DCU)[4]. During purification of the product mixture on silica (BDH, material for chromatography), small quantities of by-products which were not present in the initial mixture were eluted from the column. A brief survey of those components of the mixture which might be interacting with silica to form an active reagent system revealed that the chlorine-containing organic compounds (DCU or DCT) were responsible. The electrophilic nature of the reagent systems was demonstrated by the production of nuclear-chlorinated compounds in reactions with toluene. We have subsequently observed that several other chlorine-containing organic compounds, such as *t*-butyl hypochlorite, *N*-chlorosuccinimide, and *N*-chloroamines also become effective electrophilic chlorinating agents in the presence of silica, though the reactivities of the different systems vary considerably. Dichloramine-T, *N,N*-dichlorourethane, and *t*-butyl hypochlorite all give highly reactive systems capable of chlorinating toluene quantitatively within 1–4 hours at 25°C.

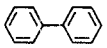
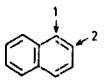
The system *t*-butyl hypochlorite/BDH silica was chosen for a study of the scope of these new chlorination reactions.

$$\text{Ar—H} \xrightarrow[70\text{-}100\%]{t\text{-}C_4H_9\text{—}OCl/SiO_2/CCl_4,\ r.t.} \text{Ar—Cl}$$

As is evident from the Table, aromatic substrates of moderate reactivity react readily with *t*-butyl hypochlorite on silica at ~25°C to give essentially quantitative yields of the monochloro derivatives with little or no tendency to polychlorination. Isomer distributions within the product reflect those produced by solution-phase electrophilic chlorinating systems quite closely[1].

Substrates of greater reactivity (e.g. *p*-xylene and especially phenol) react with *t*-butyl hypochlorite even in the absence of silica, so the latter is of little consequence, and by causing a more rapid reaction it may encourage polychlorination. Less reactive substrates such as nitrobenzene do not react significantly with these reagents even at elevated temperatures (e.g. 60°C), but a slow reaction occurs with benzene and halobenzenes. Some control over these systems is possible by appro-

Table. Chlorination of Aromatic Compounds with *t*-Butyl Hypochlorite/Silica in Tetrachloromethane (Representative Examples)

Arene	*t*-C_4H_9—OCl/Arene mol/mol	Reaction Conditions (temperature, time)	Yield[a] [%]	Product Distribution[a]
	1.0/1.0	25°C, 1 h	100	*o*/*p* = 65/35
	1.0/1.0	25°C, 6 d	86[b]	*o*/*p* = 57/43
	1.5/1.0[c] 1.0/1.0	25°C, 10 d[c] 40°C, 4 h	100 97	*o*/*p* = 44/56 *o*/*p* = 47/53
	1.0/1.0 1.5/1.0[c]	25°C, 5 d 25°C, 8 d[c]	70 100	*o*/*p* = 15/85
	1.0/1.0	25°C, 40 min	100	*o*/*p* = 30/70
	1.0/1.0 1.5/1.0[c]	25°C, 4 d 25°C, 6 d[c]	70 100	*o*/*p* = 56/44
	1.0/1.0	40°C, 3 h	93	1-/2- = 100/0

[a] All yields and product distributions were determined by G. L. C. using an added standard. Products were compared directly with authentic materials.

[b] Doubtless, these yields could be improved by use of excess reagent.

[c] The reaction was carried out with an initial 1.0/1.0 ratio; after the reaction had ceased further reagent was added. The reaction times given refer to the entire reaction. Shorter overall reaction times are possible if excess reagent is added initially, or if the temperature is increased to ~40°C.

priate choice of solvent and reagent. For example, benzene is converted into chlorobenzene in 90% yield by dichlorourethane on silica in acetonitrile at 50°C for 2 days.

The nature of the silica is important for success of the reactions. Optimal results are obtained with silica which is significantly acidic (pH of 10% aqueous slurry < 5) and which has been dried at 120°C. Malinckrodt silicic acid and BDH material for chromatography are particularly effective, and require drying only if they have been exposed to the atmosphere for a long period. Silicas which are almost neutral (e.g. Davison 57, pH 6.9), if thoroughly dried, give a slow reaction. Addition of water to reagents supported on active silicas does not destroy the reagents but causes a diminution of their rates of reaction with aromatic substrates.

For the reaction of toluene with dichloramine-T and BDH silica in tetrachloromethane, the maximum rate is obtained with a dichloramine-T/silica ratio of ~ 1/4. Reactions with other reagents were therefore performed using approximately the same molar loading as this represents. Stirrer speed does not appear to have a major effect on the reaction rate. The reaction is readily scaled up for preparative reactions (see Experimental Section).

The results reported here demonstrate that reagent systems composed of silica and (for example) *t*-butyl hypochlorite possess considerable practical advantages over traditional reagents for electrophilic chlorination reactions. The reactions are clean and high-yielding and work-up is simple. They should provide the method of choice for chlorination of aromatic substrates of moderate reactivity. Furthermore, they open up the possibility of gaining control of the regiochemistry by modification of the solid support, and we have evidence that this can be achieved[5].

Chlorination of Toluene; Typical Procedures:

Investigative-Scale Chlorination: Tetrachloromethane (10 ml), silica (3.76 g, BDH chromatography grade, 60–120 BSS mesh), toluene (0.46 g, 5.0 mmol), and *t*-butyl hypochlorite (0.54 g, 5.0 mmol) are gently stirred together at 25°C in a 50 ml round-bottomed flask. After 30 min, the mixture is filtered and the silica is washed with a little extra tetrachloromethane. G.L.C. analysis of the combined filtrates shows the presence of *o*-chlorotoluene (65%) and *p*-chlorotoluene (35%). Evaporation of the solvent leaves a liquid residue which is the essentially pure chlorination product.

Preparative-Scale Chlorination: To silica gel (95 g, BDH chromatography grade) is added dichloromethane (100 ml), toluene (9.2 g, 0.10 mol), and *t*-butyl hypochlorite (12.0 g, 0.11 mol). This solution is stirred at 25°C in a 250 ml round-bottomed flask. After 5 h, the mixture is filtered through a sintered-glass funnel, and the residual silica is washed with methanol (20 ml). The combined filtrate is washed with 1.5 molar sodium thiosulphate solution (20 ml) and water (2 × 20 ml), and then dried with magnesium sulphate. The volatile solvents are removed by fractional distillation through a 30 cm Vigreux column. The residue (25 ml) is transferred to a smaller apparatus and fractionally distilled through a 10 cm Vigreux column. The fraction distilling at 158–162°C is collected and shown by G.L.C. to be a mixture of *p*-chlorotoluene (35%) and *o*-chlorotoluene (65%); total yield: 11.03 g (87%).

We thank the SERC for a studentship (to MB) and a fellowship (to WEP).

Received: March 18, 1985

* Address for correspondence.

[1] See, for example, de la Mare, P. B. D, *Electrophilic Halogenation* Cambridge University Press, Cambridge, 1976.

[2] Yaroslavsky, C. *Tetrahedron Lett.* **1974**, 3395.

[3] Hojo, M., Masuda, R. *Synth. Commun.* **1975**, *5*, 169.

[4] Jigajinni, V. B., Paget, W. E., Smith, K. *J. Chem. Res. (S)* **1981** 376.

[5] Smith, K., Butters, M., Nay, B. *Synthesis* **1985**, 1157.