Polyhalogenoaromatic Compounds; 51[1]. Substitution of Polychloro- and Polybromoaromatic Compounds by Potassium *t*-Butoxide

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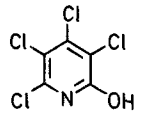
Polyhalogenoaromatic compounds undergo substitution by a variety of nucleophilic reagents, including alkoxides. These reactions occur readily with polyfluoroaromatic compounds[2], but polychloro- and polybromoaromatic compounds require more vigorous conditions[3,4], an important reason being steric hindrance. It has generally been supposed that the *t*-butoxide ion is too large to penetrate to a ring carbon atom of these compounds, or that even if it does, vigorous conditions are required and the product immediately decomposes, either thermally or by reaction with a protic solvent, to give the corresponding phenol. For example, whereas reaction of hexafluorobenzene with potassium hydroxide in ethanol gave ethoxypentafluorobenzene, the analogous reaction in *t*-butanol gave pentafluorophenol[5]; and reaction of pentachloropyridine with sodium hydroxide in aqueous *t*-butanol gave tetrachloro-6-hydroxypyridine **(1)** in 78% yield[6]. The latter example provides a good illustration of the influence of steric hindrance, since, in general, small nucleophiles attack the 4-position in pentachloropyridine, whereas with large nucleophiles attack occurs partly or mainly in the 2-(6-)position[3]. On the other hand, in the reaction of tetrabromo-4-methanesulphonylpyridine **(2)** with potassium *t*-butoxide in *t*-butanol, the sulphonyl group was displaced, giving tetrabromo-4-hydroxypyridine and isobutene[7].



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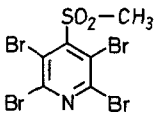

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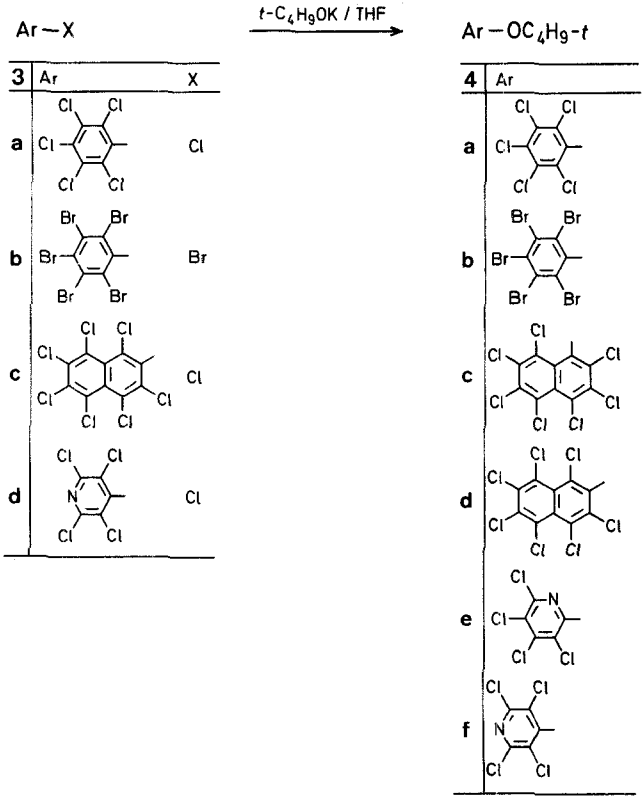
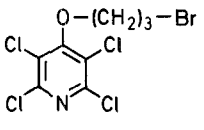
We now report that, contrary to expectations, potassium *t*-butoxide reacts with polyhaloaromatic compounds **3** in tetrahydrofuran solution rapidly and under mild conditions, to give the appropriate *t*-butoxyderivates **4**, and that the products are, in most cases, stable and readily isolable (Table).

The reactions with octachloronaphthalene **(3c)** and pentachloropyridine **(3d)** demonstrate remarkable insensitivity to steric hindrance, since a considerable proportion of substitution occurred at the hindered *peri*-position in the former and 4-position in the latter. This insensitivity to steric hindrance, and the mild conditions required for the reactions, suggested that they might proceed by single electron transfer mechanisms[8,9]. However, preliminary experiments failed to provide



evidence: no E.S.R. signals were observed from the reaction with hexachlorobenzene; and a reaction with the 3-bromopropoxypyridine **(5)** gave a multicomponent mixture of products, which did not include the pyranopyridine **6** (*cf.* Ref.[10]). Reactions of pentachloropyridine **(3d)** with two or three equivalents of potassium *t*-butoxide gave 2,4-di-*t*-butoxytrichloropyridine **(7)**.



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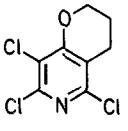

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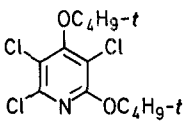

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Preliminary experiments on partly chlorinated pyridines indicate that reaction can occur at least in part by formal displacement of hydride rather than of chloride[11]. It has recently been reported that nitrobenzenes react similarly with potassium *t*-butoxide in tetrahydrofuran[12].

Potassium *t*-butoxide was commercial material, described as >97% pure. Tetrahydrofuran was distilled from potassium benzophenone ketyl.

***t*-Butoxypentachlorobenzene (4a); Typical Procedure:**

Potassium *t*-butoxide (0.40 g, 3.5 mmol) is added to a stirred solution of hexachlorobenzene (**3a**; 1.0 g, 3.5 mmol) in tetrahydrofuran (30 ml). The mixture is stirred until the exothermic reaction subsides and the mixture cools to room temperature (~25 min in all). The mixture is poured into water (50 ml). The aqueous solution is saturated with sodium chloride and extracted with chloroform (3 × 50 ml). Conventional work-up of the extract, followed by chromatography on silica (gradient elution with chloroform in light petroleum), gives hexachlorobenzene; yield: 0.25 g (25%) and *t*-butoxypentachlorobenzene **(4a)**; yield: 0.75 g (67%).

The other reactions are carried out with minor variations, as follows:

Hexabromobenzene **(3b)**: total reaction time 2 h; the main product **4b** cannot be freed from traces of an impurity, apparently disubstituted.

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Table. Reactions of Polyhaloaromatic Compounds **3** with Potassium *t*-Butoxide

Substrate	Product	Yield [%]	m.p. [°C]	Molecular formula[a]	M.S. *m/e* (M^+)[b]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ [ppm]	^{13}C-N.M.R. ($CDCl_3$/TMS) δ [ppm]
3a	**4a**	67	40–42°	$C_{10}H_9Cl_5O$ (322.4)	320	1.6 (s)	29.7; 88.0; 128.4; 130.3; 131.5; 150.1
3b	**4b**	45	oil[c]	$C_{10}H_9Br_5O$ (544.7)	—	1.6 (s)	—
3c	**4c+4d**	82[d]	131–133°	$C_{14}H_9Cl_7O$ (441.4)	438	**4c:** 1.3 (s) **4d:** 1.5 (s)	—
3d	**4e**	33	70–72°	$C_9H_9Cl_4NO$ (289.0)	287	1.5 (s)	28.1; 84.0; 118.3; 120.8; 143.1; 156.3[e]
3d	**4f**	30	75–77° (dec)	$C_9H_9Cl_4NO$ (289.0)	—	1.6 (s)	29.8; 90.8; 127.2; 146.6; 160.5[e]
3d	**7**	74	oil[f]	$C_{13}H_{18}Cl_3NO_2$ (326.7)	325	1.5 (s); 1.6 (s)	28.2; 29.7; 82.9; 88.3; 115.3; 119.5; 143.2; 157.1; 159.7[e]

[a] Satisfactory microanalyses obtained: C ±0.10, H ±0.10, N ±0.05; exceptions: **4b** and **4f** which could not be adequately purified.
[b] Ions containing ^{35}Cl or ^{79}Br only are given; appropriate isotope clusters were observed.
[c] Decomposed on attempted distillation.
[d] Mixture, see text.
[e] For ^{13}C-N.M.R. spectra of the methoxy analogues, see Ref.[14].
[f] b.p. (Kugelrohr): 120 °C/1 torr.

Octachloronaphthalene **(3c):** the mixture of 1- **(4c)** and 2-*t*-butoxyheptachloronaphthalene **(4d)** cannot be separated. They are identified by cleavage to the naphthols, followed by methylation to the known heptachloro-(methoxy)-naphthalenes[13].

Pentachloropyridine **(3d):** the products **4e** and **4f** are separated by chromatography on neutral alumina; chromatography on silica gave the 2-*t*-butoxypyridine **(4e)** and tetrachloro-4-hydroxypyridine (eluted with methanol); m.p. and mixture m.p. 230–232 °C.

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