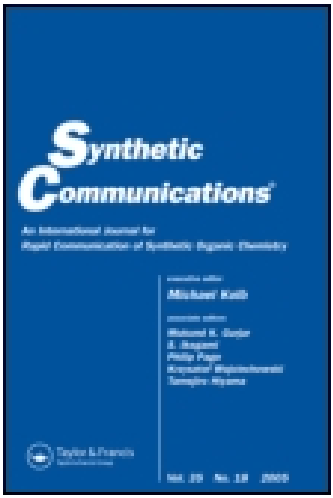

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Synthesis of 2,4-Difluoroaniline and 1,3-Difluorobenzene from 1,2,4-Trichlorbenzene

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SYNTHESIS OF 2,4-DIFLUOROANILINE AND 1,3-DIFLUOROBENZENE FROM 1,2,4-TRICHLORBENZENE

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Abstract
Nitration of inexpensive 1,2,4-trichlorobenzene gave 2,4,5-trichloronitrobenzene (90%) which was treated with KF to form 2,4-difluoro-5-chloronitrobenzene (70%). This was selectively hydrogenated over Pd / C to give 2,4-difluoroaniline (80%). Deamination afforded 1,3-difluorobenzene. The sequence avoids the need for costly 1,3-dichlorobenzene.

INTRODUCTION

Although (V), (IIIa) and (IV) are valuable intermediates [1,2,3], their manufacture poses problems. Derivation of (V) by diazotisation methods from 1,3-dinitrobenzene usually requires several steps[4] because the double fluorodeamination of 1,3-diaminobenzene is low yielding[5,6,7]. Similarly, direct fluorination of fluorobenzene gives very little of the meta-isomer[8].

Halogen exchange is more appropriate. Thus, both chlorine atoms of (IIa) are activated towards displacement by fluoride[9] and the subsequent reduction and deamination steps give good yields[6,10] (Scheme).

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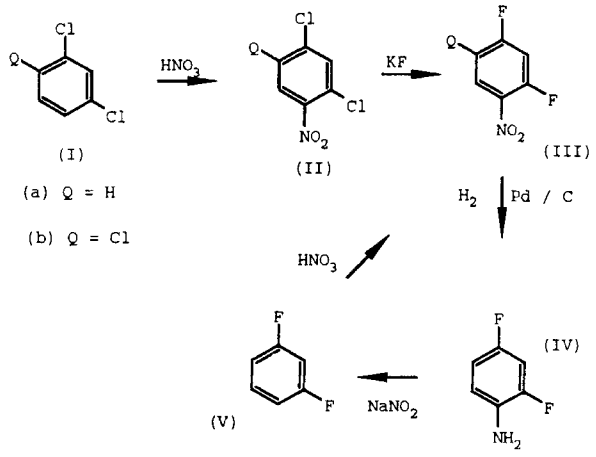
SCHEME



Unfortunately, (Ia) is itself rather difficult to make and relatively expensive[11]. We now report that (V) can be made in good yield from inexpensive precursor (Ib).

DISCUSSION

Chlorination of benzene gives little (Ia) but further reaction affords mostly (Ib)[12]. (Ib) also results cleanly upon dehydrochlorination of unwanted stereo-isomers of benzene hexachloride after isolation of the insecticidal gamma-form (Lindane)[13]. Thus, (Ib) is a cheap source of the 1,3-dichlorobenzene substructure.

Selective nitration of (Ib) to (IIb) has been reported[14], the halogen exchange gave (IIIb) cleanly (70%), and hydrodeamination of (IV) to (V) was staightforward[10].

The reduction of (IIIb) to (IV) was not expected to be easy. Chambers noted that the polarity of the aromatic C-F bond leads to special reactivity towards replacement by nucleophiles[15]. Moreover, in (IIIb) the fluorine atoms, but not the chlorine atom, are activated by the nitro group. Hydrogenolysis depends greatly on the

position of an activating nitro group, decreasing in the order ortho > para > meta[16]. Therefore, hydrodefluorination of (IIIb) might be expected to accompany the required hydrodechlorination and nitro reduction. However, mild catalytic hydrogenation of (IIIb) gave (IV) selectively (80% yield). The reactions of the Scheme were completed by deamination[10] (80% yield) and nitration of the resulting (V) to give (IIIa) (60%)[7].

EXPERIMENTAL

Materials

Spray dried potassium fluoride was from Laporte and 5% palladium on carbon was from Engelhard. Anhydrous DMF and all other chemicals were from Aldrich.

GC Analysis

This was performed on 30m capillary columns of DB-624 and CP WAX-52-CB at 100 to 200°. **Halogen Exchange**

Potassium fluoride (31.8g, 0.55 mol), n-hexadecyl trimethylammonium bromide (5.6g) and DMF (110 ml) were dried by removal of about 30ml of DMF under reduced pressure. (IIb) (45.3g, 0.2 mol) was added and the stirred mixture was heated at 125° overnight. GC showed almost total conversion to a single volatile product of m/e 223 (1 Cl). Aqueous work-up gave crude (IIIb)(43.7g). $C_6H_2ClF_2NO_2$ needs C 37.0, H 1.0, Cl 18.3, F 19.5, N 7.2, found C 36.2, H 1.4, Cl 20.9, F 17.2, N 7.8. Pure (IIIb) (28g, 70% yield) was isolated by distillation b = 85° at 0.5 torr. NMR in $CDCl_3$, δ 7.25(1H), 8.25(1H); ^{13}C 107.8, 161.4, 118.0, 128.3, 134.2, 155.1 ppm; ^{19}F 113.5, -99.5 ppm.

Catalytic Hydrogenation

Stirring of (IIIb) in ethanol containing 5% Pd / C under hydrogen (7 bar) at 80° for 6h gave (IV) (80%) which was identical to authentic 2,4-difluoroaniline (m/e 129).

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