# Polyhalogenonitrobenzenes and Derived Compounds. Part 2.[1] Reactions of 1,2,3,4-Tetrachloro-5,6-dinitrobenzene with Aliphatic Amines under Phase-transfer Conditions

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The reactions of acyclic and cyclic aliphatic amines with 1,2,3,4-tetrachloro-5,6-dinitrobenzene have been investigated under phase-transfer conditions (toluene–water in the presence of Aliquat 336). In comparison with the corresponding reactions in toluene alone as solvent, overall reactivity was increased, and there was an enhanced preference for chlorine rather than nitro-group displacement. An explanation for this is advanced.

We have previously investigated the relationship between amine structure and the nature of the products of the reaction between 1,2,3,4-tetrachloro-5,6-dinitrobenzene (TCDNB) and amines[1] in toluene. Primary amines displace a nitro group giving a product of structure (**1**), whereas acyclic secondary amines tend to replace a chlorine, leading to a product having structure (**2**). In all cases it is the chlorine *ortho* to a nitro group which is replaced. Cyclic secondary amines tend to give a mixture of products arising from both chlorine and nitro-group replacement. In some cases disubstituted products [(**3**) or (**4**)] were also isolated.

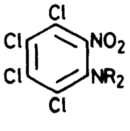
This paper reports the results of a complementary study in which the same aliphatic amines have been treated with 1,2,3,4-tetrachloro-5,6-dinitrobenzene in a two-phase solvent system (water–toluene) in the presence of a phase-transfer catalyst. It was of interest to see whether the phase-transfer conditions (*a*) increased the reactivity of the system and/or (*b*) altered the preference for chlorine or nitro-group displacement for a particular amine.

Since the pioneering work of Makosza,[2] phase-transfer catalysis has become a major area of organic chemistry. This has been due to the ability of phase-transfer catalysts to increase reactivity and selectivity in many reactions; in some cases by bringing together incompatable reagents in such a way that reaction occurs. Many of these reactions have been nucleophilic substitutions, but in nearly all cases the nucleophile has been a charged species, *e.g.* $CN^-$. Quaternary ammonium salts have been shown to have a real catalytic effect on the reactions of amines with activated aromatic compounds.[3] We have, therefore, studied the reactions of TCDNB with amines in toluene–water (1:1) in the presence of a quaternary ammonium salt as a phase-transfer catalyst. Initially the efficiencies of four different phase-transfer catalysts were investigated. These were (i) cetyltrimethylammonium bromide (CTAB) (ii) benzyl(dimethyl)-2-{2-[4-(1,1,3,3-tetramethylbutyl)phenoxy]ethoxy}ethylammonium chloride monohydrate (Hyamine 1622), (iii) tetrabutylammonium iodide (TBAI), and (iv) trioctylmethylammonium chloride (Aliquat 336). Although each of these effected reaction between TCDNB and the amines, practical difficulties were encountered with reaction mixtures containing CTAB and Hyamine 1622 because emulsions were formed which were difficult to break down. Aliquat 336 was a slightly more effective catalyst than TBAI and was therefore used in the reactions reported here. Table 1 summarises the results obtained and, for comparison, the results obtained using toluene alone as solvent (*i.e.* under non-phase-transfer conditions).

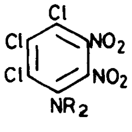
**Table 1.** Reaction of TCDNB with aliphatic amines under phase-transfer[a] and (in braces) non-phase-transfer conditions

| Amine | Conditions | Products [% yield] |
|---|---|---|
| n-Butylamine | 1 h reflux | (1) [80] |
| | {1 h reflux | (1) [78]} |
| t-Butylamine | 1 h reflux | (1) [75] |
| | {1 h reflux | No reaction} |
| Dimethylamine | 1 h reflux | (1) [25], (2) [51] |
| | {1.25 h reflux | (1) [41], (2) [18]} |
| Diethylamine | 1 h reflux | (2) [65] |
| | {1 h reflux in acetonitrile | (2) [22]} |
| Pyrrolidine | 1 h reflux | (1) [63], (2) [16] |
| | {1 h reflux | (1) [53]} |
| Piperidine | 1 h reflux | (1) [21], (2) [61], (4) [7] |
| | {1 h reflux | (1) [31], (2) [37], (4) [2]} |
| Morpholine | 1 h reflux | (2) [60][b] |
| | {1 h reflux in dichloromethane–water | (2) [18], pentachloronitrobenzene [40]} |
| | {1 h reflux | (2) [1], (4) [4]} |

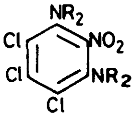
[a] The figures quoted refer to reactions in which Aliquat 336 was the phase-transfer catalyst. [b] Only main fraction from column chromatography isolated.



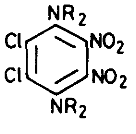
(1)



(2)



(3)



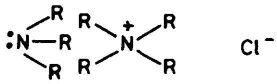
(4)

At the end of each reaction the catalyst was removed, either during recrystallisation of the product (catalyst remained in mother liquor) or column chromatography (catalyst not eluted). Products were identified by t.l.c., g.l.c., and i.r. comparisons plus mixed m.p. determination with authentic samples.[1] The results show that changing to phase-transfer conditions has a significant effect on both reactivity and the preference for chlorine *versus* nitro-group replacement. For all amines studied overall reactivity is increased: a slight increase is observed for amines which were already very reactive, *e.g.* n-butylamine, and a dramatic increase for amines which previously had shown little reactivity, *e.g.* t-butylamine and morpholine.

The results also show the increased preference for chlorine rather than nitro-group displacement, *i.e.* production of product

**(2)** at the expense of product **(1)** (*e.g.* reactions of dimethylamine, piperidine, and pyrrolidine). We previously reported[1] that primary amines and pyrrolidine show a marked preference to displace a nitro group in TCDNB, whereas acyclic secondary amines tend to displace chlorine. Other cyclic secondary amines, *e.g.* morpholine and piperidine, gave both chlorine and nitro-group displacement. These differences were ascribed to the fact that the carbon atoms bearing chlorine are less sterically hindered than those bearing a nitro group. Hence as the size of the attacking amine increases (primary→secondary) attack at a chlorine-bearing carbon atom should be enhanced. Hydrogen bonding between the amine and a nitro group of TCDNB was the explanation for the observation that it was always a chlorine *ortho* to a nitro group which was displaced. The increased tendency towards chlorine displacement under phase-transfer conditions suggests, therefore, that the size of the attacking nucleophile has been increased.

Although further work is necessary to establish the precise role of the phase-transfer catalyst, the following speculative explanation is proposed at this stage. In the absence of catalyst, the amines studied are all soluble to varying extents in both toluene and water. After a stirred solution of TCDNB and amine in toluene–water was heated under reflux for 1 h, no reaction was observed. (Note that the reaction temperature here is lower than for a refluxing solution in toluene alone: *ca.* 83 °C rather than 110 °C.) The effect of the catalyst may be explained in terms of its association with the nucleophile to form a species such as (A). As a kinetic effect, this type of species would enhance the amine's oleophilicity, and therefore increase its solubility in the organic phase where reaction occurs. It may also remove $Cl^-$ and/or $NO_2^-$ products into the aqueous phase. These processes would aid product formation. As a thermodynamic effect, this associated species might increase reactivity by lowering activation energies and entropies in the system, *via* (i) enhancing nucleophilicity of the amine, (ii) excluding water of solvation of the amine, and/or (iii) facilitating departure of the leaving group from TCDNB. Note that association also produces a much bulkier nucleophile than would be found in toluene alone as solvent; the experimental results are consistent with a larger attacking species in the presence of phase-transfer catalyst.



(A)

The actual position of attack on TCDNB is determined by a balance between electronic and steric factors. Electronically the most favoured position of attack is the 5-position (*i.e.* a carbon atom bearing a nitro group). However, this is more sterically hindered than the 2- or the 1-position (both carbon atoms bearing a chlorine). Therefore, the increased tendency to chlorine displacement under phase-transfer conditions is a consequence of the increased size of the attacking amine due to its association with the phase-transfer catalyst as shown in (A). The marked preference for attack at the 1-position over the 2-position is again ascribed to hydrogen bonding of the amine N–H with a nitro group of TCDNB.

**Table 2.** p$K_b$ Values of amines[4]

| Amine | p$K_b$ |
|---|---|
| n-Butylamine | 3.39 |
| t-Butylamine | 3.55 |
| Dimethylamine | 3.23 |
| Diethylamine | 3.07 |
| Pyrrolidine | 2.89 |
| Piperidine | 2.80 |
| Morpholine | 5.60 |

With regard to the relative reactivities of the amines studied, there is a parallel between an amine's basicity and its reactivity. Table 2 lists the p$K_b$ values. Since, however, reactivity here depends on steric factors as well as nucleophilicity (of which the p$K_b$ values may be taken as a rough measure) it is appropriate to consider the amines in three groups. Of the two primary amines the n-butylamine is, as expected from its higher basicity and small size, more reactive than t-butylamine. Being primary amines they both displace exclusively a nitro group. For the two acyclic secondary amines the steric factor now dominates with the bulkier diethylamine giving only chlorine displacement whereas dimethylamine gives both chlorine and nitro displacement but with a marked preference for the former (contrast this with the situation in toluene alone as solvent). Finally, of the three cyclic secondary amines, piperidine (the most basic of all the amines studied) is the only one sufficiently reactive to produce some disubstituted product, although monosubstituted products predominate with a strong preference for the chlorine-substituted product. In contrast, pyrrolidine, due to its smaller size, is able preferentially to attack the more reactive carbon atom bearing a nitro group. This is accompanied by only a small amount of chlorine displacement. Morpholine, the least basic of all the amines, is not sufficiently reactive to overcome its steric problems and, therefore, only attacks at the chlorine-bearing carbon atom. When the solvent system was changed to dichloromethane–water chlorine displacement again took place, but the major product turned out to be pentachloronitrobenzene. The latter arises from attack by the chloride ion (available from the catalyst and from displacement by morpholine from TCDNB) on TCDNB in competition with the poorly reactive morpholine. In support of this we have observed that lithium chloride reacts with TCDNB (in acetone) also to give pentachloronitrobenzene.

## Experimental

T.l.c. was carried out on precoated silica gel plates (0.25 mm). G.l.c. was carried out with a Pye 104 instrument equipped with a flame-ionisation detector and an OV17 column at 250 °C. Mass spectra were recorded with a V. G. Micromass 16B instrument.

The following description is typical of the method used.

*Reaction with t-Butylamine.*—t-Butylamine (1.06 g) in water (25 cm$^3$) was added to a stirred solution of TCDNB (2.0 g) in toluene (25 cm$^3$). Aliquat 336 (0.2 g) was added and the stirred mixture heated under reflux for 1 h. After cooling, the organic phase was separated, dried ($MgSO_4$), and filtered. Removal of the solvent under vacuum gave an orange oil. This was purified by column chromatography [silica gel (35—70 mesh); light petroleum (b.p. 60—80 °C)] and recrystallised from methanol to give the yellow *1,2,3,4-tetrachloro-5-nitro-6-t-butylaminobenzene* (1.62 g, 75%), m.p. 76—78 °C, *m/z* 336 ($M^+$ for $^{37}Cl$) (Found: C, 36.2; H, 2.9; Cl, 42.4; N, 8.55. $C_{10}H_{10}Cl_4NO_2$ requires C, 36.15; H, 3.0; Cl, 42.8; N, 8.4%).

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