Vilsmeier Formylation of *para*-Substituted *tert*-Anilines Results in Dibenzo[1,5]diazocines or Quinazolinium salts: a Remarkable Example of the '*t*-Amino Effect'†

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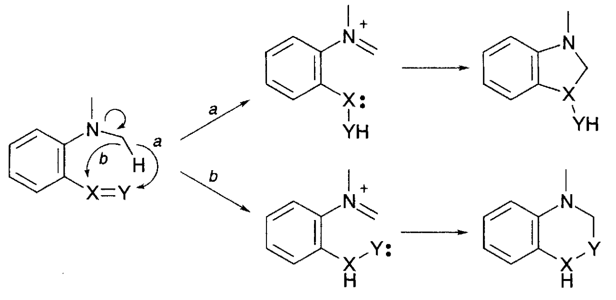
Formylation of *para*-substituted *tert*-anilines with various *N*-formylated *sec*-anilines† in phosphoryl chloride results in *ortho*-formylation followed by cyclisation of the iminium salt to the adjacent *tert*-amino α-position by way of the '*t*-amino effect' giving dibenzo[*b,f*][1,5]diazocines; in a similar manner, with *N*-formylated *sec*-aliphatic amines, quinazolinium salts are formed while bulky formanilides give the expected *ortho*-formylated *tert*-aniline.

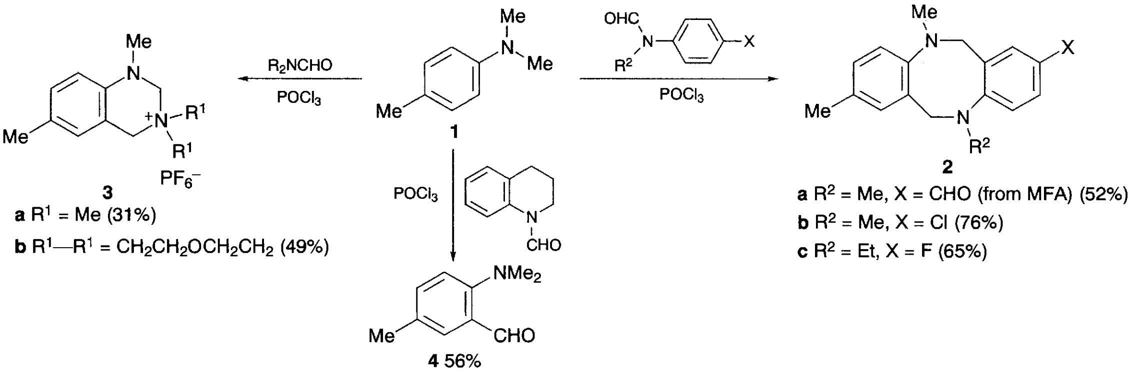
When a tertiary aniline contains an *ortho*-substituent containing a doubly bonded function (X=Y), a concerted thermal hydrogen migration to X=Y from the α-position of the *tert*-amine can occur leading to cyclisation, a process referred to[1] as the '*t*-amino effect' (*e.g.* Scheme 1). Either group X or Y can be the terminus of the hydrogen shift and either the X or the Y group can then cyclise onto the resulting iminium group, leading to 5- or 6-membered products. Following our discovery of this surprisingly general phenomenon,[1] new examples were developed, particularly by Reinhoudt and coworkers[2] who also showed that the reaction proceeded with enamines, and more recently further examples have been added by others.[3] The reaction often proceeds best either with acid catalysis or with electron deficient groups on the X=Y function.



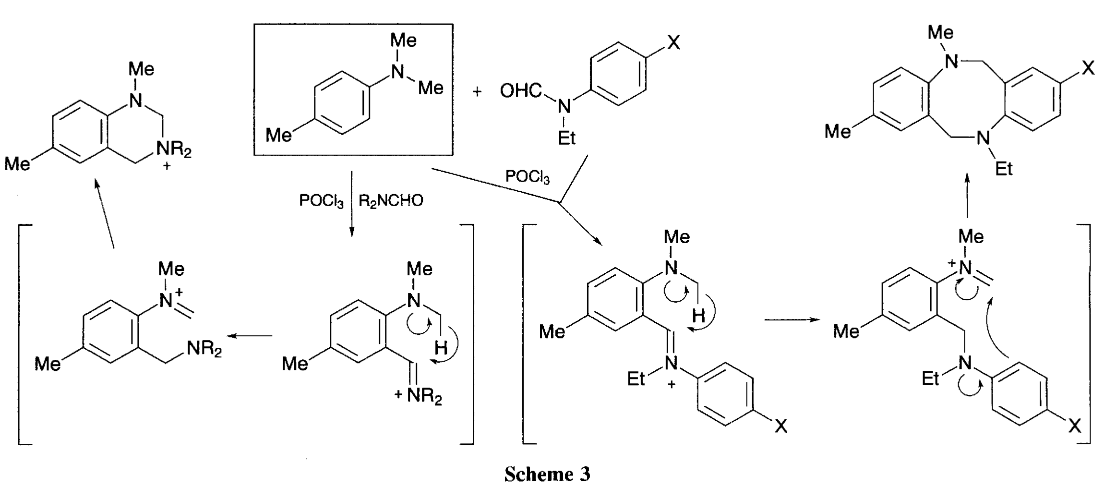
Scheme 1 The '*t*-amino effect'

We now report a remarkable reaction whereby the interaction of a *p*-substituted *tert*-aniline **1** with *N*-formyl-*N*-substituted arylamides in $POCl_3$ gives a dibenzo[1,5]diazocine **2** while the use of *N*-formylated *sec*-aliphatic amines leads to quinazolinium salts **3**[4] (Scheme 2). However, if a slightly bulky formamide derivative (*e.g.* *N*-formyltetrahydroquinoline) is utilised, the same *tert*-aniline is *ortho*-formylated in the expected manner to give **4**.

The reaction proceeds by Vilsmeier formylation *ortho* to the dimethylamino group followed by hydrogen migration (1,5-sigmatropic shift). The resulting new iminium ion then is positioned ideally to attack the adjacent aromatic ring or nitrogen atom (Scheme 3). The aliphatic formamide may be acyclic or cyclic (*e.g.* *N*-formylmorpholine), in the latter case giving a spiroquinazolinium salt. If *N*-methylformanilide is used in the reaction the product diazocine is further formylated



Scheme 2



Scheme 3

para to the formanilide nitrogen. Although dibenzo-1,5-diazocines are known[5] routes to unsymmetrical derivatives are very limited. Our simple approach makes these interesting systems with potential as psychotropic drug intermediates, readily available with unsymmetrical substitution patterns. The extension of these reactions to new systems is under active investigation.

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Footnote

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† *tert*-Aniline = *N,N*-disubstituted aniline, *t*-Amino = *N,N*-disubstituted amino, *sec*-aniline = *N*-monosubstituted aniline.

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