A Convenient Route to 3,6-Diaminofluoren-9-ones

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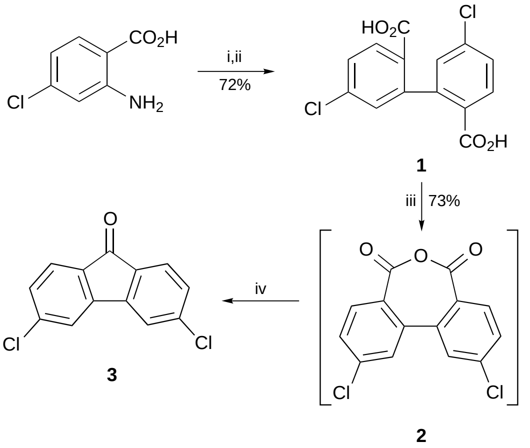
The synthesis of fluoren-9-ones having a 3,6-bis(tertiary amino) functionality is described, in which the amino groups are introduced using either cyclic secondary amines or their *N*-formylated derivatives to effect nucleophilic displacement of the halogen from 3,6-dichlorofluoren-9-one, which is derived from 4-chloroanthranilic acid.

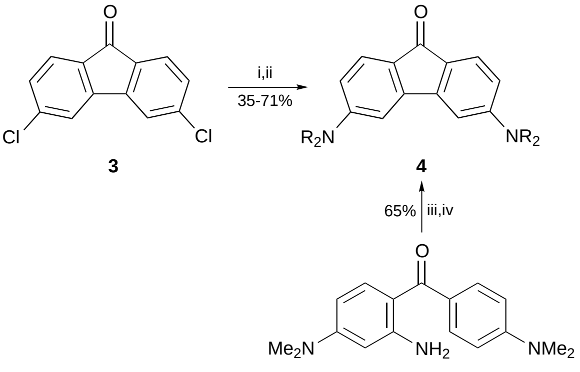
As part of our studies of di- and tri-arylmethane dyes, we have reported the synthesis of some 4,4′-diaminobenzophenones,[16] analogues of Michler's ketone, the 4,4′-bis(dimethylamino) derivative. We now describe the preparation of some cyclic analogues, 3,6-diaminofluoren-9-ones, from the commercially available 4-chloroanthranilic acid.

On treatment with a cuprammonium reagent, diazotised 4-chloroanthranilic acid underwent a self-coupling process which yielded 5,5′-dichlorobiphenyl-2,2′-dicarboxylic acid (**1**). Conversion into the anhydride **2**, achieved by boiling with acetic anhydride, was followed by *in situ* pyrolysis at *ca.* 400 °C to give 3,6-dichlorofluoren-9-one (**3**) in 53% overall yield (Scheme 1).



Scheme 1 *Reagents and conditions:* i, HCl, $NaNO_2$ (aq.), 0 °C; ii, $CuSO_4$ (aq.), NH_3 (aq.), $NH_2OH\cdot HCl$ (aq.), NaOH (aq.); iii, Ac_2O, heat; iv, 400 °C

The nucleophilic displacement of halides in an aromatic environment is known to be promoted by the presence of electron-withdrawing functionalities. However, unless such activation is particularly efficient, as for example in Sanger's reagent where the preferred halogen,[15] fluorine, is activated by two nitro groups, quite severe conditions are necessary. Cyclic secondary amines provide not only a good nucleophilic centre but also enable high reaction temperatures to be achieved and react with 4,4′-difluorobenzophenone to give the corresponding diamino ketone.[16] Although not a powerfully activated halogen, both chlorine atoms were displaced from 3,6-dichlorofluoren-9-one by a variety of amine nucleophiles in boiling sulfolane. The aminofluorenones **4b–d** were also obtained when the aminating species was derived from the corresponding *N*-formylamines under basic conditions[19] (Scheme 2).



Scheme 2 *Reagents and conditions:* i, R_2NH, sulfolane, heat; ii, R_2NCHO, KOH, heat; iii, H_2SO_4, $NaNO_2$, dil. H_2SO_4, 0–5 °C; iv, Cu bronze, Na_2SO_4, 90 °C

Although halide displacement from activated chloro compounds by boiling with *N,N*-dimethylformamide is well documented,[20] 3,6-bis(dimethylamino)fluoren-9-one (**4a**) could not be obtained in this manner. Similar failure attended the use of *N,N*-diethylformamide.

3,6-Bis(dimethylamino)fluoren-9-one (**4a**) was obtained in good yield from 2-amino-4,4′-bis(dimethylamino)benzophenone (**5**) *via* diazotisation and intramolecular coupling of the derived radicals under acidic conditions. Careful control of the conditions are essential to the success of the reaction.

Techniques used: ^1H NMR, flash chromatography

References: 25

Schemes: 2

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