The synthesis of alkylamino-N-alkylnaphthalic-1,8-imides from 2- and 4-nitronaphthalic anhydrides by nitro group displacement

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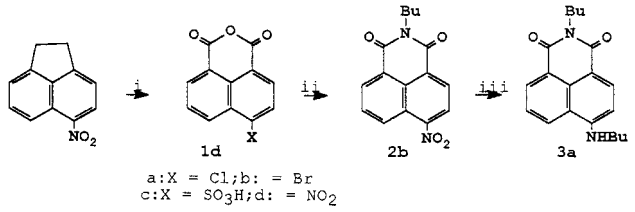
4-Alkylamino-N-alkylnaphthalic-1,8-imides and 2-alkylamino isomers have been synthesised by the reaction of 4-nitro- and 2-nitronaphthalic anhydrides respectively with primary amines in aprotic solvents in which reaction the nitro group in 3-nitronaphthalic anhydride is unreactive. Unsymmetrical compounds in the 2- and 4-series are derived from either the appropriate 4-nitro-N-alkylnaphthalic-1,8-imide or for 4-dialkylamino compounds from 4-nitronaphthalic anhydride by reaction with a secondary amine and then the 4-dialkylaminonaphthalic anhydride with a primary amine.

The fluorescence of the 4-alkylamino-N-alkylnaphthalic-1,8-imides **3(a-i)** notably **3a** has been of interest for many decades since their early preparation from 4-sulphonaphthalic anhydride[1] **(1c)** and subsequently from 4-halonaphthalic anhydrides[2] **(1a,b)** Their intense fluorescence has led to a vast variety of industrial, technical, electronic and medical uses in non-destructive testing (NDT) for crack detection[3,4] in aircraft metal and in ceramics, for their laser activity,[5] as luminescent sensors and switches,[6] fluorescent probes for hypoxic cells in cancer studies,[7] and with the 3-bromo derivative[8] of **3a** a photochemically activated antiviral substance more effective than AZT against (HIV-1).

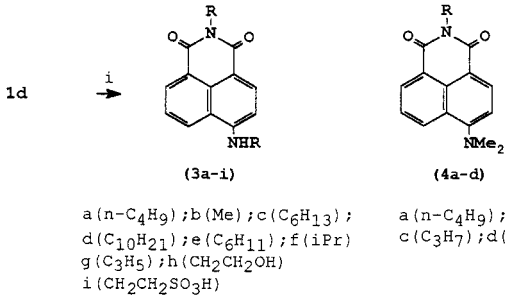
In connection with work on the relationship[9] between structure and fluorescence involved in NDT we were interested to synthesise 4-butylamino-N-butylnaphthalic-1,8-imide (**3a**) by an improved route since 4-sulphonaphthalic-1,8-anhydride[1] (**1c**) and 4-halo derivatives[2] (**1a,1b**) were not in our experience satisfactory starting materials in that either excessive pressure with a low conversions or tarry products resulted respectively. Accordingly it seemed probable that 4-nitronaphthalic-1,8-anhydride (**1d**) readily obtainable from acenaphthene by conversion to the N-butylimide and thence catalytic reductive alkylation with butanal would afford an alternative approach.



Scheme 1 Synthesis of 4-butylamino-N-butylnaphthalic-1,8-imide
Reagents and conditions: (i) AcOH, $Na_2Cr_2O_7$ (ii) $BuNH_2$, 0°C, (iii) C_3H_7CHO, Pd-C, H_2

Although the reaction of 4-nitronaphthalic anhydride (**1d**) with n-butylamine in methanol has been described[10] as giving 4-nitro-N-butylnaphthalic-1,8-imide we found the reaction to occur substantially at the nitro group to give a highly fluorescent mixture containing the required compound 4-butylamino-N-butylnaphthalic-1,8-imide (**3a**) by partial displacement of the nitro group. Aprotic solvents gave better yields and in hot dimethylformamide (DMF) with primary amines a range of symmetrical compounds (**3a–i**) as shown in Scheme 2 was obtained.[11] The product was accompanied in many cases by the 4-dimethylamino-N-alkylnaphthalic-1,8-imide (**4a–d**) resulting from aqueous hydrolysis of the DMF at the imide formation stage. This side reaction was avoided with dibutylformamide as solvent which simplified the purification but not the yield of product.

Subsequently we found[12] that 4-halonaphthalic-1,8-anhydrides

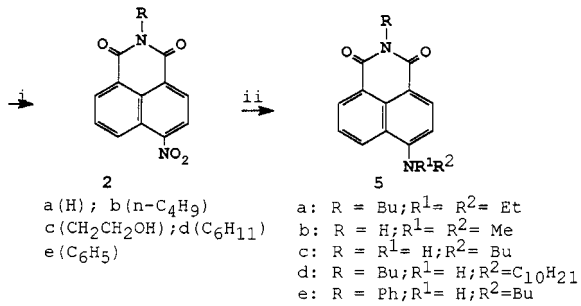


Scheme 2 Synthesis of symmetrical 4-alkyamino-N-alkylnaphthalic-1,8-imides
Reagents and conditions: (i) $BuNH_2$, DMF, 80°C

(**1a,b**) gave excellent yields of (**3a**) and analogues in the solvent N-methylpyrrolidinone and enabled products to be purified by crystallisation without the need for chromatography.

The uv-visible spectra, fluorescence intensity and quantum yields of a range of symmetrical and unsymmetrical isomeric alkyl-N-alkylnaphthalic-1,8-imides which were prepared prior to the use of N-methylpyrrolidinone have been described[12] although no preparative details were given. This present account records these syntheses.

Unsymmetrical compounds such as (**5a–e**) were derived from 4-nitronaphthalic-1,8-anhydride in DMF with ammonia or primary amines at 0-10°C through reaction solely at the anhydride group to afford 4-nitro-N-alkylnaphthalic-1,8-imides (**2a–e**) which were then reacted with primary or secondary amines as shown in Scheme 3.

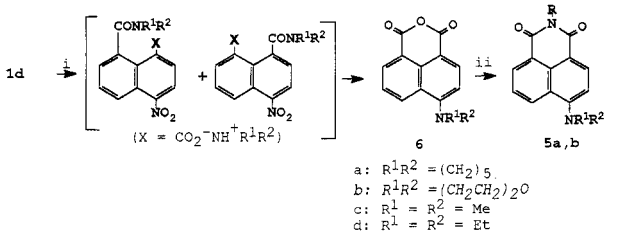


Scheme 3 Synthesis of unsymmetyrical 4-alkylamino and 4-dialkylamino-N-alkylnaphthalic-1,8-imides.
Reagents and conditions: (i) RNH_2 , DMF (or DMSO/THF), 0°C (ii) R^1R^2NH, DMSO.

As an alterrnative sequence to Scheme 3, 4-nitronaphthalic-1,8-anhydride with secondary amines in DMF underwent nitro group displacement to give the 4-dialkylaminonaphthalic anhydride, as shown in Scheme 4, (**6a–d**) accompanied by varying proportions of ring-opened products (characterised in the case of the diethyl compound **6d**) which then by ring closure during work-up gave

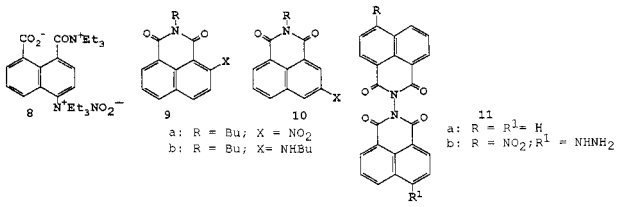
* To receive any correspondence.

the same 4-dialkylaminonaphthalic anhydride and thence another procedure for compounds of structure **(5)**. Thus by reaction of **(6c)** and of **(6d)** with butylamine and with ammonia respectively the unsymmetrical compounds (**5a)** and (**5b**) were obtained also available by preliminary reaction at the anhydride group followed by nitro group displacement. We were not able to prepare 4-alkylaminonaphthalic anhydrides by virtue of preferential formation of the N-alkyl imide.



Scheme 4 Synthesis of 4-dialkylaminonaphthalic anhydrides and of 4-dialkylamino-N-alkylnaphthalic-1,8-imides. Reagents and conditions: (i) R^1R^2NH, DMF, (ii) RNH_2 , DMF, _.

Triethylamine and 4-nitronaphthalic formed salt-like products one of which is believed to be (**8**) having undergone nitro group displacement to yield products devoid of fluorescence.



Formulae (8), (9a,b), (10a,10b), (11a,11b)

2-Nitronaphthalic-1.8-anhydride in DMF gave by nitro group displacement with butylamine the symmetrical 2-butylamino-N-butylnaphthalic-1,8-imide (**9b**) and with secondary amines access to a range of unsymmetrical analogued. By contrast with the nitro group nucleophilic activity of the 2- and 4-nitro series, 3-nitronaphthalic-1,8-anhydride showed no displacement of the nitro group and merely afforded 3-nitro-N-butylnaphthalic-1,8-imide (**10a**) catalytic reductive alkylation of which in ethanol solution containing palladised charcoal with butanal gave (**10b**), 3-butylamino-N-butylnaphthalic-1,8-imide.

With hydrazine several products resulted including two *bis* imides, one (**11b**) where partial nitro group displacement had taken place and another (**11a**) where total reductive displacement had evidently occurred probably through the action of diimide generated *in situ*.

In the case of 4-nitronaphthalic-1,8-anhydrides in reaction with the primary amine RNH_2 the seven predictable intermediate Meisenheimer-type transition states (Fig. 1a) contain three contributors with an intact benzeoid ring while with 2-nitronaphthalic-1.8-anhydride there are two contributors (Fig 1b). In the case of 3-nitronaphthalic anhydride there are five contributors (Fig 1c) none of which retain the benzenoid ring and the transition state is thus inherently more unstable.

The reaction mechanism (Fig.2) for nitro group displacement in the 2- and 4-series after formation of the Meisenheimer intermediate, is considered to be deprotonation and final removal of nitrite ion as RNH_3^+ NO_2^- which was readily chemically detected.

In our experience nitro group displacement in the bicyclic naphthalic series was more facile than from 4-nitrophthalic anhydride but less than with the tricyclic 1-nitroanthraquinone.[14] It is probably associated with relative ease of Meisenheimer complex

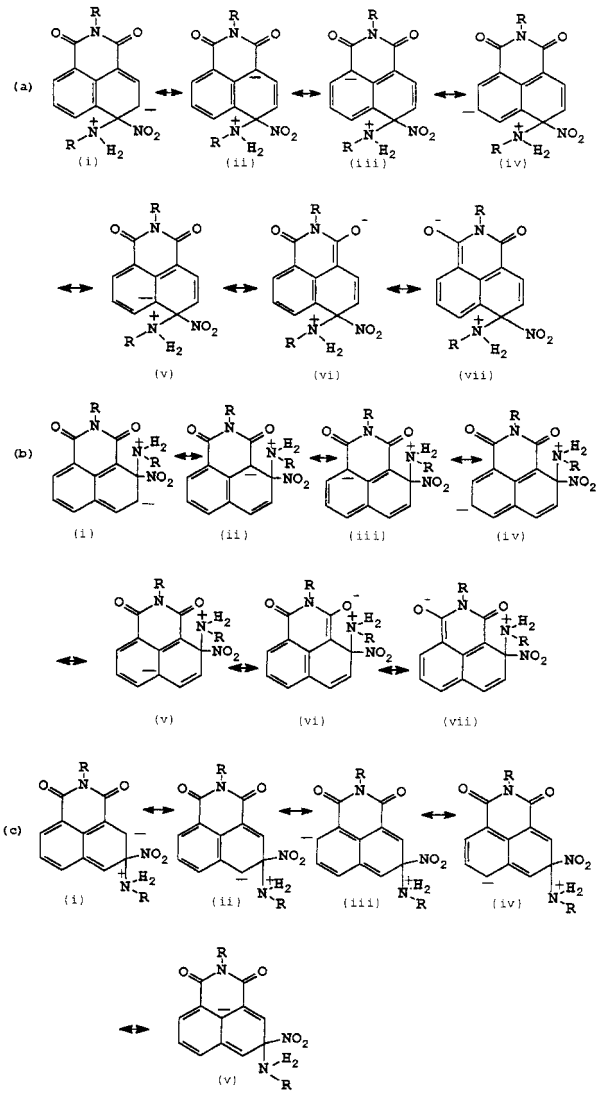


Fig. 1a,b,c Mesomeric Meisenheimer complexes in the reaction of RNH_2 with isomeric nitronaphthalic anhydrides.

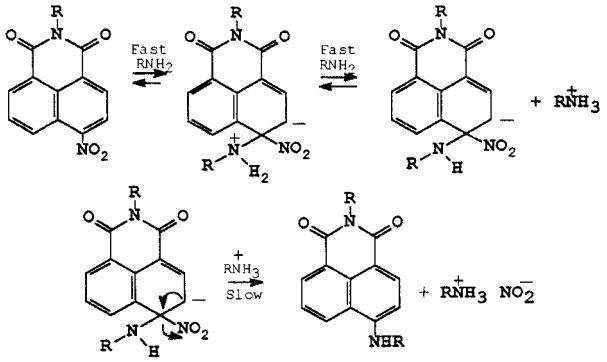


Fig. 2 Reaction sequences in the Reaction of RNH_2 with nitronaphthalic anhydrides.

formation which has been examined in the mono and bicyclic serres.[18] Nitro group displacement in benzenoid compounds has been reviewed.[21]

Techniques used. ^1H NMR., MS, TLC, UV, IR.

Schemes: 1,2,3,4 Figures: 1a,b,c; 2

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