APPLICATION OF PHASE TRANSFER CATALYSIS IN THE ACRIDINE SERIES. VII (1). SYNTHESIS OF 9-CYANOACRIDINE DERIVATIVES

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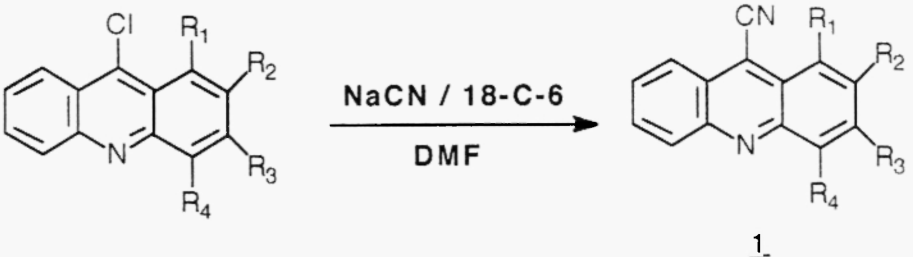
Abstract : A new method using solid-liquid PTC for preparing 9-cyanoacridine derivatives in high yields under mild conditions is described.

Some procedures for the synthesis of 9-cyanoacridine derivatives have been developed which use reactions of acridine (2,3,9), 9-choloroacridine (4,5,7,10), 9-methoxyacridine hydrate (6) or 3,9-dichloroacridine with sodium or potassium cyanide (2-9) or anhydrous hydrogen cyanide in the absence (6) or presence of benzoylchloride (7).

When 9-chloroacridine is used as starting material, reaction conditions are rather hard (heating in a sealed tube for 4 hours at 160-170°C with potassium and cuprous cyanine) except when the reaction takes place in the presence of p-toluene sulfinate or methane sulfinate as catalyst (10). For this reason, we propose to prepare 9-cyanoacridine derivatives starting from the corresponding 9-chloroacridines and using sodium cyanide under liquid-solid phase transfer catalysis conditions.



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Experimental

M.p. are given uncorrected. IR spectra of KBr pellets were recorded on a UNICAM SP 200 spectrophotometer. TLC analyses were run on plates covered with silica gel, eluted with benzene ether 4:1 (v/v), and iodine was used as visualising agent.

General Synthetic Procedure

The 9-chloroacridine derivative (2.5 mmoles), NaCN (0.25 g, 5 mmoles) and 18-crown-6 (0,02 mmoles) is added in anhydrous DMF (10 mL). The mixture is stirred and heated at 90°C under nitrogen atmosphere for 24 h. The cooled mixture is then poured into water and the precipitate filtered, dried and recrystallized from ethanol (compounds **1a** - **1b**) or acetic acid (compounds **1e**).

Results and discussion

Results are gathered in the following Table.

Compound	R_1	R_2	R_3	R_4	Yields % (lit.)	m.p. (lit.)	IR cm^{-1} ν_{CN}
1a	H	H	H	H	90-95 (80-85[7])	180-182 (181[7])	2245
1b	H	CH_3	H	H	70 (48[6])	176-177 (179[6])	2244
1c	H	OCH_3	H	H	75-80 (55[6])	185-187 (185[6])	2240
1d	H	H	Cl	H	75	204-205 (202.5[9])	2237
1e	H	H	H	NO_2	80	214-216 (216[1])	2240

It must be noted that reaction failed when it was carried out in the presence of water or aqueous alkaline solution and using quaternary ammonium salts or crown ethers as catalysts. In contrast the highest yields were obtained using DMF as solvent and 18-crown-6 ether as catalyst.

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