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N-ALKYLATION OF ACRIDONE BY MEANS OF MICROWAVE IRRADIATIONS WITHOUT SOLVENT

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ABSTRACT. Using as solid support reagent KF absorbed on Al_2O_3, the *N*-alkylation of acridone under microwaves irradiation conditions has been realized. The identity of the resulting *N*-alkyl acridones was assigned on the basis of comparative literature melting points and ^{1}H–NMR spectra. Our yields, ranging between 90–96%, were similar or even higher with respect to those already reported in the literature.

Keywords: *N-acridones, microwaves irradiation, KF/Al_2O_2 catalyst, solid support.*

INTRODUCTION

N-Akylacridones are compounds of interest in organic synthesis and pharmaceutical chemistry [1, 2]. Their preparation was previously achieved by using phase transfer catalysis [3, 4], starting from acridone in reaction with various alkyl halides. In contrast with the reported results in the above classical acridone's *N*-alkylation conditions, the application of microwaves irradiation methodology, *e.g.* by using a conventional microwaves oven, in the presence of phase transfer catalysis and of $NaOH/K_2CO_3$ absorbed on Al_2O_3 is known to give better results [5]. Thus, under microwaves irradiation, some authors [5] found that the yields largely depend on the strength of base.

Taking into account this observation, we attempted at seeing whether the preparation of *N*-akylacridones could be improved in the presence of KF, as solid support reagent, absorbed on Al_2O_3 [6]. It is already known that, in these conditions, K_3AlF_6 is formed as a result of KF reaction with alumina, F^- ions being responsible for the catalytic activity of KF/Al_2O_3 system rather than O^{2-} ions which are active sites on $NaOH/K_2CO_3$ absorbed on Al_2O_3 [7].

RESULTS AND DISCUSSION

The reactions were carried out in a microwave synthesis system, by simple mixing the acridone with alkylbromides adsorbed on KF/Al_2O_3 (Scheme 1).

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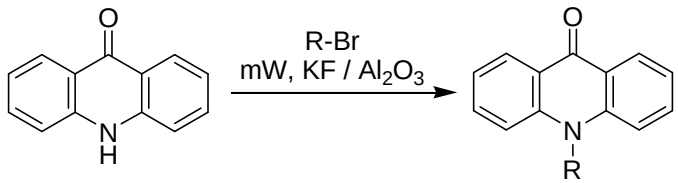

1-**6**

1: R = Me; **2**: R = Et; **3**: R = *n*-Pr
4: R = *n*-Bu; **5**: R = $(CH_2)_2CH(CH_3)_2$
6: R = Bn

Scheme 1.

The results of our experiments are shown in **Table 1**.

Table1. Preparation of *N*-alkylacridones **1**-**6** using microwave irradiation and KF/Al_2O_3 as solid support

Compd.	Molar ratio Acridone : alkylbromide	Micro-wave power (W)	Irradiation time (min.)	Yield (%) (lit.)	M.p. (^{0}C) (lit.)
1	1 : 5	300	3.0	90 (73 [5])	200-201 (210-202[4])
2	1 : 2 - 5	300	2.0	95 (81[5])	159 (158-160[4])
3	1 : 5	400	4.0	94 (88[5])	130-131 (131-132[4])
4	1 : 5	400	3.5	96 (91[5])	98-99 (97-98[4])
5	1 : 2	600	4.0	92 (91[5])	83-64 (84-86[4])
6	1 : 1.5	300	3.5	95 (89[5])	178-180 (180-181[4])

The structure of *N*-alkylacridones **1**-**6** were confirmed based on melting points (Table 1) and their ^{1}H – NMR data (Table 2).

Table 2. Relevant ^{1}H-NMR data of *N*-alkylacridones **1**-**6**.

Compound	^{1}H-NMR (DMSO-d_6)
1 (R = Me)	3.80 (3H, s); 7.23-7.26 (2H, m); 7.53-7.58 (4H, m); 8.40 (2H, d).
2 (R = Et)	1.47 (3H, t); 4.46 (2H, q); 7.20- 7.23 (2H, m); 7.60 – 7.66 (4H, m); 8.39 (2H, d).
3 (R = *n*-Pr)	1.17 (3H, t), 1.94 (2H, q), 4.32 (2H, t); 7.20-7.23 (2H, m), 7.62-7.67 (4H, m); 8.40 (2H, d).
4 (R = *n*-Bu)	1.03 (3H, t); 1.57-1.59 (2H, m); 1.78-1.96(2H, m); 4.42 (2H, t); 7.24-7.29 (2H, m); 7.63 – 7.68 (4H, m); 8.41 (2H, d).
5 [R = $(CH_2)_2$-$CH(CH_3)_2$]	0.87 (6H, d); 1.46–1.48 (2H, m); 1.74 – 1.76 (1H, m); 4.59 (2H, s); 7.23-7.27 (2H, m); 7.56-7.60 (4H, m); 8.40 (2H, d).
6 (R = Bn)	5.61 (2H, s); 7.18-7.71 (11H, m); 8.42 (2H, d).

CONCLUSIONS

We succeeded to improve the *N*-alkylation methodology of acridone, using microwave irradiation. Indeed, in comparison with the earlier reported Wang and coworkers' protocol [5], our reactions occurred with the same or even better yields without the presence of a phase transfer catalyst.

EXPERIMENTAL SECTION

M.p. are uncorrected. For *N*-alkylation reactions, a microwave synthesis system Synthos 3000, Anton Par was used. ^{1}H-NMR spectra were recorded on a NMR Bruker Avance 300 spectrometer operating at 300 MHz and 75 MHz for ^{1}H and ^{13}C nuclei respectively. No $SiMe_4$ was added, chemical shifts were measured against the solvent peak.

GENERAL PROCEDURE FOR *N*-ALKLATION OF ACRIDONE

A mixture of acridone (0.98 g, 5 mmol), alkyl bromide (7.5-25 mmol) and 4 g of solid support (KF/Al_2O_3) were irradiated for the indicated time and power, as listed in Table 1. Subsequently, the reaction mixtures were cooled at room temperature and the crude products were purified by column chromatography on silica gel, using petroleum ether-ethyl acetate-dichloromethane as eluent.

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