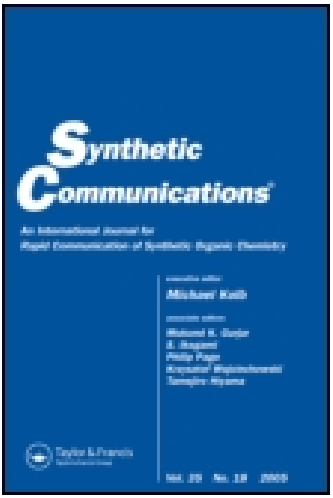

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Facile N-Alkylation of Anilines with Alcohols Over Raney Nickle Under Microwave Irradiation

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FACILE N-ALKYLATION OF ANILINES WITH ALCOHOLS OVER RANEY NICKLE UNDER MICROWAVE IRRADIATION

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ABSTRACT The anilines could be easily and selectively N-alkylated with alcohols in the presence of a small amount of Raney nickel and with a greatly shortened period under microwave irradiation. A purely non-thermal effect of microwave was observed in the reaction.

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Table 1. N-Alkylation of aniline with n-propanol in the presence of Raney Ni by various methods.

Entry	Method	Molar Ratio[a]	Temp. (℃)	Time (h)	Yield[b] (%)
1	Reflux n-PrOH	1.00:4.67:0.39	102	16	82
2	Reflux n-PrOH	1.00:1.50:0.30	102	24	98
3	Reflux n-PrOH	1.00:3.00:0.10	102	24	0
4	Autoclave	1.00:3.00:0.10	180	20	87
5	Microwave Open Vessels[c]	1.00:3.00:0.10	102	4	91
6	Microwave Closed Vessels[d]	1.00:3.00:0.10	—	0.5	91

[a]Aniline : n-propanol : Raney Ni. [b]Product isolated. Microwave irradiation: [c]630W,[d]300W.

N-Alkylation of anilines with alcohols catalyzed by Raney nickel had been found for several decades,[1,2] but there was no decisive improvement for practical use.[3] Unfortunately, such reaction had been devaluated due to a comparatively appreciable amount of catalyst consumed, longer reaction time required and restriction on the straight chain primary alcohols other than methanol.[4] Thus, microwave[5,6] was attempted to promote the reaction and reduce the harshers of experimental conditions, which provided both thermal effect[7] and non-thermal effect[8,9] during the reactions; the sealed tube reaction was applied to progmatize the reaction at relative higher temperature and internal pressure with no loss of either the substrates or products.[10]

Typically, aniline 0.372 g(4 mmol), n-propanol 0.72 g(12 mmol) and Raney nickel W-2, 0.024 g(0.4 mmol) were put in a 10 ml Pyrex tube and sealed off. The sealed tube protected by a Teflon tube was placed in a domestic microwave oven (630 W) and heated for 30 minitues. The mixture was then cooled to room temperature, filtered to remove the catalyst and poured into 10 mL water. The mixture was extracted with diethyl ether(3×10 mL). The organic extract was washed with water (1×10 mL) and dried with anhydrous sodium sulface. The solvent evaporated in vacuum and the product chromatogrphed through a short column of silica gel (70-230 mesh) using benzene/ethyl acetate as an eluant. The fractions containing the N-n-propylaniline were collected

Table 2. N-Alkylation of anilines with alcohols in the presence of Raney Ni and in sealed tubes under microwave irradiation[a].

Entry	Anilines	Alcohols	Power (W)	Time (min)	Yield[b] (%)
1	$C_6H_5NH_2$	CH_3OH	560	45	19
2	$C_6H_5NH_2$	C_2H_5OH	560	50	77
3	$C_6H_5NH_2$	C_2H_5OH	630	30	91
4	$C_6H_5NH_2$	n-C_3H_7OH	560	60	91
5	$C_6H_5NH_2$	i-C_3H_7OH	560	30	23
6	$C_6H_5NH_2$	n-C_4H_9OH	630	30	83
7	$C_6H_5NH_2$	$C_6H_5CH_2OH$	560	30	86
8	2-$CH_3C_6H_4NH_2$	C_2H_5OH	630	30	66
9	3-$CH_3C_6H_4NH_2$	C_2H_5OH	630	30	80
10	4-$CH_3C_6H_4NH_2$	C_2H_5OH	630	30	91
11	2-$CH_3OC_6H_4NH_2$	C_2H_5OH	630	30	60
12	4-$CH_3OC_6H_4NH_2$	C_2H_5OH	630	30	89

[a]Aniline(4 mmol), alcohol(12 mmol), Raney Ni(W-2, 0.4 mmol, 0.024g). [b] Product isolated.

and rectified in vacuum to give the product: 0.49 g(91%); b. p. 104-106 ℃/20 mmHg(Lit.[11] 112-113 ℃/26 mmHg).

The results in **Table 1** show the high efficiency of the N-n-propylation with a small amount Raney Ni under microwave irradiation. The results also suggest the purely non-thermal effect of microwave activation existing in this kind of microwave mediated reaction (Entry 5, 102℃), in contrast to that being carried in a reflux reaction (Entry 3, 102℃). The effect of microwave would be still further reinforced when the reaction was carried out in a sealed tube (Entry 6), the enhancement of reaction rate by microwave irradiation is 48-fold, in comparsion the reaction rate in Entry 2 with that in Entry 6. The results in **Table 2** illuminate that a variety of N-alkylated anilines could be rapidly prepared by simple reactions of anilines with alcohols in the presence of Raney nickel and in selaed tubes under microwave irradiation, including N-methylaniline and N-iso-propylaniline in good yield which couldn't be synthesized by conventional heating even

with such great amount of catalyst and alcohols as described in literature.[4] Although the substituted groups such as methyl and methoxy at the para position of anilines wouldn't affect the reactions, those at the ortho position would considerably retard the reactions, due to the hindrance of the ortho groups.

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