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Research Note

A Novel Synthesis of 2-(Alkylamino) and 2-(Arylamino)- 4(3H) Quinazolinones by Heterotrocyclization of 2-Aminobenzamide with Isothiocyanates (or Isocyanates) under Microwave Irradiation

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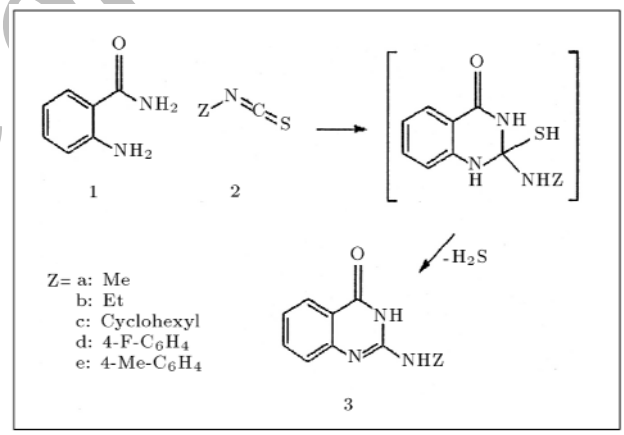
A convenient one-pot preparation of 2-(alkylamino) and 2-(arylamino)-4(3H) quinazolinones in high yields has been developed by microwave induced heterocyclization of 2-aminobenzamide with isothiocyanates (or Isocyanates) in solvent-free conditions. In comparison, the reactions are faster under microwave irradiation and the yields are much higher than those by/of conventional heating (under reflux in toluene)

INTRODUCTION

An interest in the preparation of heterocyclic compounds with potential biological activity [1] has encouraged one to look for specific routes to derivatives of 2-(alkylamino) and 2-(arylamino)-4(3H) quinazolinones. These are very interesting compounds with wide ranging biological activities [2-4]. In spite of several works on the synthesis of these compounds (see, for example, [5-7]), heterocyclization of 2-aminobenzamide with isothiocyanates has been largely overlooked.

Here, a convenient one-pot preparation of 2-(alkylamino) and 2-(arylamino)-4(3H) quinazolinones 3 in synthetically useful yields is reported. The approach is based on the reaction of isothiocyanates with 2-aminobenzamide. The title compounds were prepared via a route described in Scheme 1. When treated with one equivalent of isothiocyanate in toluene under reflux, for the indicated time (Table 1), 2-aminobenzamide is directly converted into corresponding 2-substitutedamino-4(3H) quinazolinones 3 in moderate yields (40-55%). The mixture was then subjected to microwave irradiation for the indicated time (Table 1).



Scheme 1. A simple route to 2-substitute 2- 4(3H) quinazolinones.

It can be concluded that high yields (78-98%) have been observed by microwave irradiation.

Compounds 3 were substantiated by their analytical and spectral data (Table 2). In the ^{1}HNMR spectra of compounds 3, the chemical shifts of -CONH- groups are characteristic at δ 10.87-12.94, which are in good agreement with the reported values for this type of compound. The IR spectra of these compounds show a strong absorption band at 1690-1650 cm $^{-1}$, attributable to -CO- stretching. The presence of the secondary amino group is confirmed by the absorption band around 3300-3200 cm $^{-1}$.

Mass spectra show that the expected molecular

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Table 1. Comparison of time and yields on formation of compounds 3 a-e using microwave irradiation and conventional heating.

Under Reflex in Toluene				Microwave Heating		
Product	**R**	**Time/Min**	**Yield (%)**	**Power/W**	**t/min**	**Yield (%)**
3a	$-CH_3$	120	40	300	3	78
3b	$-C_2H_5$	210	48	300	3	80
3c		60	60	300	3	98
3d		270	42	300	4	88
3e		180	55	300	3	82

Table 2. 2-(alkylamino) and 2-(arylamino)-4(3H) quinazolinones.

Spectral Data	M.P. (°C)	R	Entry
^{1}HNMR: (acetone-d6), δ 12.8-13.2 (s, 1H, NH, amide), 6.28-8.1 (m, 4H aromatic), 3.6-3.8 (s, 3H, Me); IR (KBr disk): ν, C=O, 1700 cm $^{-1}$, NH, 3200 cm $^{-1}$, m/z, 175 (M)	241	$-CH_3$	3a
^{1}HNMR: (acetone-d6), δ 11.46-11.70 (s, 1H, NH, amide), 7.3-8.2 (m, 4H aromatic), 4.2-4.7 (q, 2H, CH_2) 1.21-1.42 (t,3H,Me); IR (KBr disk): ν , C=O, 1700 cm $^{-1}$, NH, 3200 cm $^{-1}$, m/z, 189 (M)	250	$-C_2H_5$	3b
^{1}HNMR: (acetone-d6), δ 11.11-11.29 (s, 1H, NH, amide), 7.1-7.9 (m, 4H aromatic), 5.5-6.2 (d, 1H, NH amine), 1.38-1.51 (m,11H, cyclohexyl); IR (KBr disk): ν, C=O, 1640 cm $^{-1}$, NH, 3300 cm $^{-1}$, m/z, 240 (M)	225		3c
^{1}HNMR: (acetone-d6), δ 10.80-10.98 (s, 1H, NH, amide), 8.9 (s, 1H, NH amine), 6.8-8.6 (m, 8H aromatic); IR (KBr disk): ν , C=O, 1645 cm $^{-1}$, NH, 3250 cm $^{-1}$, m/z, 255 (M)	208		3d
^{1}HNMR: (acetone-d6), δ 10.75-10.90 (s, 1H, NH, amide), 7.0-8.9 (m, 8H aromatic), 2.94-2.88 (s, 1H, NH, amino), 2.20-2.38 (s, 3H, Me); IR (KBr disk): ν , C=O, 1650 cm $^{-1}$, NH, 3300 cm $^{-1}$, m/z, 251 (M)	263		3e

ion peak and the fragmentation pattern is in accordance with the proposed structure.

In summary, the 2-substitutedamino-4(3H) quinazolinones have been synthesized by a convenient route and their structures were proved via spectral data.

Experimental

Melting points were recorded on an electrothermal type 9100 melting point apparatus.

The IR spectra were obtained on a 4300 Shimadzu Spectrometer. The ^{1}HNMR (100 MHz) spectra were recorded on a Bruker AC 100 Spectrometer. Mass spectra were obtained from Varian CH-7 at 70 eV.

GENERAL PROCEDURE FOR THE PREPARATION OF 2-(ALKYLAMINO) AND 2-(ARYLAMINO)-4(3H) QUINAZOLINONES 3

2-Aminobenzamide (1) (2.5 mmoles) was mixed with isothiocyanates (or isocyanates) 3a-e (2.5 mmoles). The reaction was either in toluene (15 ml), heated under reflux for 1-4.5 hours, or exposed to microwave.

(Microwave technical information: National 700 w output - Power (IEC-706) variable power levels (80-700 w).) irradiation for 3-4 minutes (see Table 1). The solid material was crystallized from EtOH.

CONCLUSION

It can be concluded that the synthesis of compounds 3a-e under microwave irradiation is faster and that the yields are higher than those of conventional heating methods. Thus, a simple, efficient, fast and practical method has been developed for one-pat conversion of 2-Aminobenzamide with isothiocyanate into 2-(alkylamino) and 2-(arylamino) -4(3H) quinazolinones, by applying microwave irradiation in solvent free conditions.

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