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A Rapid and Efficient Synthesis of Diaryl Thioureas *via* Solvent-Free Reaction Using Microwave

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Abstract: A rapid and efficient method for the preparation of diaryl thiourea compounds was reported for the first time. Twelve diaryl thiourea compounds that possessing biological activity have been synthesized in excellent yields (91-97%). The reaction proved to be extremely simple and highly efficient (in 1.5-4.5 min).

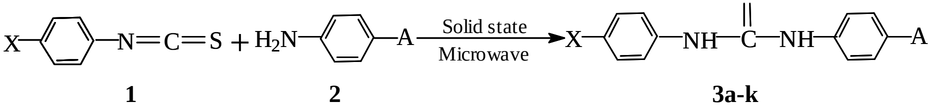
Keywords: Diaryl thiourea, microwave technique, solvent-free reaction.

The application of microwave techniques for chemical synthesis has attracted considerable interest in recent years[1-5]. The reason is that technology can enhance the selectivity and reactivity[6,7], increase the chemical yields and shorten the reaction time[8,9]. In order to provide a method that is economic, without pollution, easy to carry out, we coupled the solvent-free reaction with microwave.

As we know, thiourea compounds are associated with a serious biological activities such as antiviral[10], antituberculous[11], fungicidal[12] and herbicidal[13]. So, particularly intense interest has been directed toward the synthesis of these compounds. Generally, the preparation of these compounds has been carried out in solvents[14,15]. The shortcoming of all the existing methods is that they need a large amount of volatile and poisonous solvents, long reaction time and the yields are not high.

By this method, we have successfully synthesized twelve diaryl thioureas in excellent yields. No solvent or catalyst of complicated is involved. The reaction time is short (1.5-4.5 min). The structures of the products were characterized by IR, ^{1}HNMR

Scheme



1 **2** **3a-k**

a: X=Cl, A=CH_3
b: X=Cl, A=OCH_3
c: X=Cl, A=Cl
d: X=Cl, A=Br
e: X=Cl, A=I
f: X=Br, A=CH_3
g: X=Br, A=OCH_3
h: X=Br, A=Br
i: X=Br, A=I
j: X=OEt, A= CH_3
k: X=OEt, A=OCH_3

and elemental analysis.

Experimental section

Melting points were determined with a Kofler micro melting point apparatus and the thermometer was uncorrected. IR spectra were recorded on a SP3-300 spectro-photometer in KBr tablet. ^{1}HNMR spectra were measured on a FT-80A spectrometer using TMS as internal standard and $(CD_3)_2CO$ as solvent. Elemental analysis was performed on Carlo-Erba 1102 elemental analyzer.

Aryl isothiocyanate (1 mmol) and aromatic primary amine (1 mmol) were mixed thoroughly in an agate mortar. Then put the mixture into the Galanz household microwave oven. Turned the adjustor of the microwave oven to proper temperature (about 60°C). Then irradiate the reaction mixture for the specified time (1.5-4.5 min) under solvent-free conditions. The power of the microwave oven is 750W. The end of the reaction was tested with thin-layer chromatography. After the reaction was complete, the crude products were recrystallized with ethanol or acetone, and dried under vacuum to yield the pure products.

Table 1 Physical data and elemental analyses of **3a-k**

compd[a]	m p (^{O}C)	reaction time (min)	yields (%)	elemental analysis (found) C	H	N
3a	175-177	3	92	60.76 (60.57)	4.70 (4.48)	10.13 (10.17)
3b	176-178	1.5	96	57.44 (57.33)	4.44 (4.19)	9.57 (9.30)
3c	174-176	2.5	95	52.70 (52.44)	3.38 (3.05)	9.46 (9.21)
3d	179-181	2.5	94	45.81 (45.50)	2.94 (2.68)	8.22 (8.02)
3e	181-183	3	93	40.26 (39.97)	2.58 (2.33)	7.23 (6.99)
3f	180-182	2.5	93	52.34 (52.15)	4.05 (3.84)	8.72 (8.34)
3g	183-185	1.5	97	49.85 (49.62)	3.86 (3.59)	8.31 (8.02)
3h	188-190	4	91	40.41 (40.17)	2.59 (2.39)	7.25 (6.97)
3i	178-180	3.5	93	36.03 (35.86)	2.31 (2.03)	6.47 (6.22)
3j	138-140	4.5	92	67.13 (66.87)	6.29 (6.01)	9.79 (9.51)
3k	160-161	4.5	93	63.58 (63.31)	5.96 (5.63)	9.27 (8.97)

a) White tabular or needle crystal.

In general, using microwave method the solvent-free reactions proceed with significant decrease in reaction time, and comparable high yields. It is an efficient and convenient method for the preparation of diaryl thiourea compounds.

Table 2 IR and ^{1}HNMR spetra data of compounds **3a-k**

compd	IR (cm^{-1})	^{1}HNMR(ppm)
3a	3210, 3030, 2985, 2850, 1595, 1490, 1250, 830	2.367 (s, 3H, CH_3), 7.201~7.367 (m, 8H, Ar–H), 7.791(s, 1H, NH), 8.098(s, 1H, NH)
3b	3215, 3030, 2990, 2850, 1600, 1500, 1350, 1250, 840	3.828 (s, 3H, CH_3), 6.937~7.373 (m, 8H, Ar–H), 7.592 (s, 1H, NH), 7.877 (s, 1H, NH)
3c	3220, 3180, 3030, 1590, 1550, 1490, 1245, 820	7.303~7.402(m, 8H, Ar–H), 7.815 (s, 2H, NH)
3d	3210, 3030, 1595, 1495, 1235, 830	7.261~7.553 (m, 8H, Ar–H), 7.728 (s, 1H, NH), 7.742 (s, 1H, NH)
3e	3220, 3030, 1600, 1500, 1240, 825	7.255~7.546 (m, 8H, Ar–H), 7.723 (s, 1H, NH), 7.438 (s, 1H, NH)
3f	3220, 3030, 2990, 2850, 1600, 1495, 1350, 1245, 835	2.372(s, 3H, CH_3), 7.210~7.376(m, 8H, Ar–H), 7.801(s, 1H, NH), 8.120 (s, 1H, NH)
3g	3215, 3030, 2985, 2850, 1595, 1550, 1350, 1250, 840	3.821(s, 3H, CH_3), 6.940~7.541 (m, 8H, Ar–H), 7.546 (s, 1H, NH)
3h	3220, 3180, 3030, 1600, 1500, 1245, 825	7.290~7.392 (m, 8H, Ar–H), 7.820 (s, 2H, NH)
3i	3225, 3030, 1595, 1495, 1240, 820	7.251~7.541 (m, 8H, Ar–H), 7.720 (s, 1H, NH), 7.433 (s, 1H, NH)
3j	3210, 3030, 2995, 2930, 2890, 1600, 1530, 1400, 1250, 835	1.420 (t, 3H, J = 7.0Hz, CH_3), 2.362 (s, 3H, CH_3), 4.040 (q, 2H, J = 7.0Hz, CH_2), 6.910~7.690 (m, 8H, Ar–H), 7.640 (s, 1H, NH), 7.643 (s, 1H, NH)
3k	3215, 3030, 2995, 2895, 1600, 1500, 1355, 1250	1.417 (t, 3H, J = 7.0Hz, CH_3), 3.814 (s, 3H, CH_3), 4.032 (q, 2H, J = 7.0Hz, CH_2), 6.902~7.631 (m, 8H, Ar–H), 7.634 (s, 1H, NH), 7.637 (s, 1H, NH)

Acknowledgments

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