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Facile Synthesis of 1, 2-Diazepine Derivatives under Microwave Irradiation

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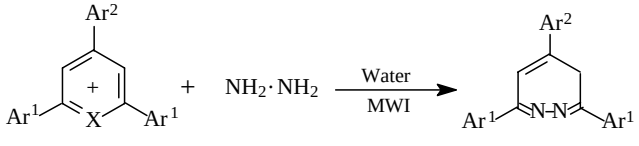
Abstract: An efficient and convenient synthesis of 3, 5, 7-triaryl-4H-1, 2-diazepine from 2, 4, 6-triarylpyrylium salts and hydrazine in water under microwave irradiation is reported. The same reaction can be conducted using 2, 4, 6-triarylthiopyrylium salts and hydrazine.

Keywords: 2, 4, 6-Triarylpyryliums, hydrazine, 1, 2-diazepine derivatives, microwave irradiation.

Seven-membered heterocyclic ring compounds have received much attention in the past few years owing to its wide range of biological activity. Diazepine derivatives are this class of compounds possessing a wide variety of medicinal properties[1]. Introduction of substituted group in the diazepine segment is expected to improve their pharmacological propertied. Also, the facile acylation of symmetrically aryl substituted 1, 2-4H-diazepines[2] into the corresponding 1, 2-1H-diazepine derivatives provides a useful alternative route to photochemical method for the synthesis of this class of heterocyclic compounds[3]. It was reported that 2, 4, 6-triarylpyrylium is converted by hydrazine in ethanol leads to 1, 2-4H-diazepine derivatives[4], but the scope of this reaction has not been explored and this reaction suffers from long reaction time. In connection with a program aimed at studying the reaction of 2, 4, 6-triarylpyrylium salts with nucleophilic reagents under microwave irradiation conditions, we examined the reaction of 2, 4, 6-triarylpyrylium salts and 2, 4, 6-triarylthiopyrylium salts with hydrazine in water under microwave irradiation.

Now, we report that it is a neat reaction producing a single product in excellent yield (**Scheme 1**) and the corresponding results are shown in **Table 1**.

Scheme 1



1 X = O, S **2** **3**

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To determine the optimum condition of this reaction, we investigated the effects of microwave irradiation power and time. It was found that the highest yield of compound **3** can be obtained in 225W for 30~60s irradiation. Water can be used as reaction medium instead of ethanol.

In summary, the application of microwave and water as solvent offers a simple, mild, inexpensive, eco-friendly and practical method for rapid synthesis of 3, 5, 7-triaryl-4H-1, 2-diazepine.

Table 1 The results of 2,4,6-triarylpyrylium and 2,4,6-triarylthiopyrylium with hydrazine under microwave irradiation [b]

3	Ar^1	Ar^2	Yield (%) [a]	mp (Lit) / ℃
a	C_6H_5	C_6H_5	90	192-193 (191-192[4a])
b	*p*-ClC_6H_4	C_6H_5	94	229-230
c	*p*-$CH_3C_6H_4$	*p*-ClC_6H_4	96	207-208
d	C_6H_5	*p*-ClC_6H_4	93	189-190 (189-190[4b])
e	*p*-BrC_6H_4	*p*-ClC_6H_4	97	243-244
f	*p*-$CH_3C_6H_4$	*p*-ClC_6H_4	96	222-223
g	*p*-ClC_6H_4	*p*-ClC_6H_4	97	217-218
h	*p*-$CH_3C_6H_4$	*p*-$CH_3OC_6H_4$	88	185-186
i	*p*-ClC_6H_4	*p*-$CH_3OC_6H_4$	89	184-186
j	*p*-ClC_6H_4	*p*-$CH_3C_6H_4$	96	214-215
k	*p*-BrC_6H_4	*o*-ClC_6H_4	86	244-245

a: Isolated yield; b: All the products were characterized by ^1H NMR, MS and Elemental analysis.

General procedure: 2,4,6-Triarylpyrylium (1 mmol) suspended in water (15 mL), followed by the addition of hydrazine hydrate (2.5 mmol). Then, the mixture was irradiated in microwave (225 W) in an open flask for 30~60 s. After the conversion was completed as indicated by TLC, the reaction mixture left to cool to room temperature and the diazepine crystallized. The diazepines were filtered and recrystallized once or twice from ethanol to analytical purity.

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