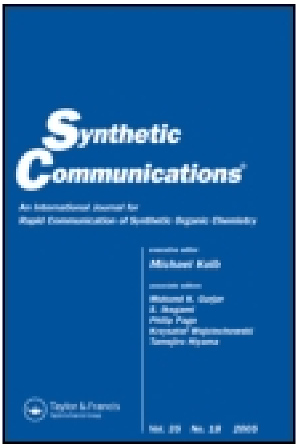

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MICHAEL ADDITION REACTION OF ANTHRONE TO NITROOLEFINS IN WATER

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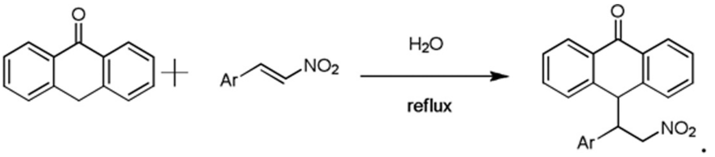
GRAPHICAL ABSTRACT



Abstract *Michael addition reaction of anthrone to nitroolefins is described in water without using any catalyst to prepare 9-(2-nitro-1-arylethyl)anthracene-10(9*H*)-ones. This method is green and efficient and gives good yields of products. The solvent effect is also investigated.*

Keywords Anthrone; Michael addition; nitroolefin; water

INTRODUCTION

Since Breslow has reported the use of water as accelerator for the Diels–Alder reaction in 2004,[1] considerable attention has been directed toward the development of organic reactions in water. Reactions in aqueous media are generally environmentally safe, devoid of any carcinogenic effects, simple to handle, cheaper to operate, and especially important in industry.[2] Also, catalyst-free reactions are desirable in synthetic pathways and processes because they reduce the hazardous materials and in some cases reduce the number of steps needed for the extraction and purification of the products.[3]

Anthrone derivatives have wide applications in medicine as antitumor, antimetastatic, antiviral, antipsoriatic, and anti-inflammatory agents.[4] Also, they have been used for determination of carbohydrates and steroids.[5]

Anthrones usually behave as reactive dienes toward a variety of dienophiles in the presence of a base in aprotic solvents.[6] On the other hand, the use of nitroalkenes as Michael acceptors,[7] which is seldom used in Diels–Alder reactions, has attracted

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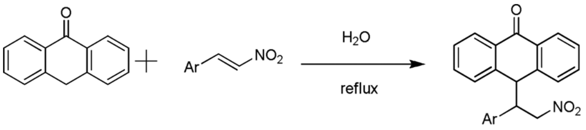
significant interest in recent years, because of the activating effect of the nitro group as well as its easy transformation to other functional groups.

RESULTS AND DISCUSSION

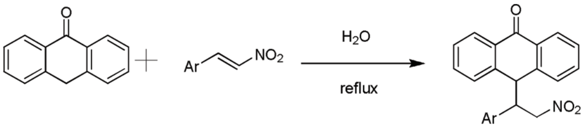
In continuation of our interest in environmentally friendly synthesis using water as solvent and catalyst for organic transformations,[8] we envisioned that the Michael addition of anthrone and nitroolefins would be possible via activation of the nitro group in the nitroolefins and the carbonyl group in anthrone via enol formation through hydrogen bonding in aqueous medium (Scheme 1).

Optimization of the reaction conditions were done by screening a range of organic solvents for the Michael addition of anthrone to nitrostyrene. As shown in Table 1 (entry 1), we found that the best yield was obtained in the presence of protic



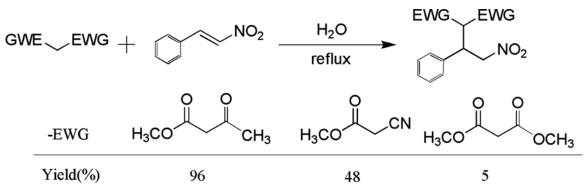
Scheme 1. Michael addition reaction of anthrone with nitroolefins in water.

Table 1. Michael addition of anthrone to nitroolefins in water



Entry	Ar	Yield(%)[a]
1	Ph (H_2O)	74[7g][b]
	(CH_3OH)	73
	(C_2H_5OH)	78
	(THF)	56
	(CH_2Cl_2)	N.R.
	(DMSO)	59
	(CH_3CN)	21
	(ether)	Trace
	(solvent-free)	10
2	4-Cl-Ph	74[7g]
3	2-Cl-Ph	83[7g]
4	2-OCH_3-Ph	65[7f]
5	3-NO_2-Ph	72[7g]
6	1-naphthyl	85[7g]
7	4-OCH_3	75[7g]
8	2-Furyl	85[7g]
9	2,4-Cl_2-Ph	85[7g]
10	2-thienyl	73[7f]
11	4-F-Ph	68[7g]

[a] Reaction condition: anthrone (1 mmol), nitroolefin (1 mmol), water (3 mL), 18 h at reflux.
[b] References for the known compounds.



Scheme 2. Michael addition reaction of other active methylene groups with nitrostyrene.

solvents such as water, methanol, and ethanol. Also, the reaction gives poor yield under solvent-free conditions. After optimization of the solvent, we studied the reaction at different temperatures and found that the best yield is obtained at reflux temperature. Also, we found that using distilled water instead of tap water does not have any considerable effect on the reaction yields.

After optimization of the reaction conditions, different nitroolefins were used under these reaction conditions. As shown in Table 1, nitroolefins with electron-withdrawing or electron-donating groups on aromatic ring do not have considerable effect on the yields of the reactions. Also, nitroolefins derived from 1-naphthaldehyde gave good yield (entry 6). Nitroolefins derived from thiophene-2-carbaldehyde and furan-2-carbaldehyde gave good yields of products (entries 8 and 10). This method is not effective for Michael addition reaction of anthrone to 2-benzylidenemalononitrile and dimethyl 2-benzylidenemalonate.

To show the efficiency of the procedure, we have used the same reaction conditions for the reaction of nitrostyrene with other activated methylene groups such as diethyl malonate, methyl cyanoacetate, and methyl acetoacetate. As shown in Scheme 2, methyl acetoacetate gave 96% of the Michael adducts, while methyl cyanoacetae and diethyl malonate gave 48% and 5% respectively.

In conclusion, we have shown an effective, mild, and green protocol for the Michael addition reaction of anthrone to nitroolefins in water without using any catalyst. The reaction gives good yields of 9-(2-nitro-1-arylethyl)anthracen-10(9*H*)-ones. The ability of protic solvents for hydrogen bonding formation may promote the reaction by activation of nitroolefins toward nucleophiles or activation of anthrone via enol formation.

EXPERIMENTAL

Material

All reactions were carried out in an atmosphere of air. Chemicals and solvents were purchased from Merck and Fluka and used as received. The ^{1}H and ^{13}C NMR spectra were recorded on 500-MHz spectrometers. Tap water was used in all reactions.

General Procedure

In a test tube equipped with magnet stirrer, nitroolefin (3 mmol), anthrone (3 mmol), and water (5 mL) were added. The reaction mixture was stirred overnight at reflux condition. Progress of the reaction was checked by thin-layer chromatography. After completion, the reaction mixture was cooled to room temperature and extracted with ethyl acetate. The organic layer was treated with anhydrous Na_2SO_4 and evaporated under reduced pressure to give the crude product. Purification has been done by column chromatography using silica gel and ethyl acetate–petroleum ether (1:9). The products were characterized by ^1H and ^{13}C NMR and compared with those reported in the literature.

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