Indian Journal of Chemistry
Vol. 37B, October 1998, pp. 963 - 964

Rapid Communication

A novel enzymatic synthesis of 2-substituted naphtho[2,1-*b*]-pyran-3-ones using microwaves

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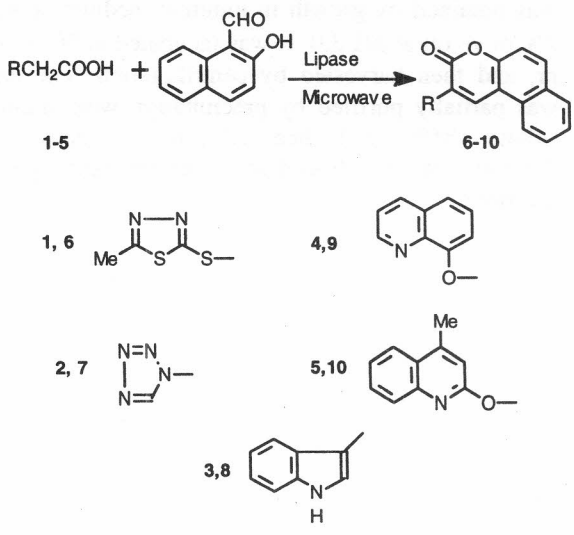
Received 19 May 1998; accepted (revised) 10 August 1998

2-Substituted naphtho[2,1-*b*]pyran-3-ones **6-10** have been synthesised by a novel one-pot environment friendly method which involves cyclocondensation of 2-hydroxy-1-naphthaldehyde using microwaves with 5-methyl-1,3,4-thiadiazol-2-ylsulfanyl-, 1*H*-1,2,3,4-tetrazol-1-yl-, 1*H*-indol-3-yl-, quinolin-8-yloxy- and 4-methylquinolin-2-yloxy-acetic acids **1-5** in the presence of DMF, 1,8-diazabicyclo[5.4.0]-undecene-7 (DBU) and an acidic lipase from *Pseudomonas* species.

Novel approaches to ecofriendly chemistry demands usage of domestic microwave oven for the synthesis of heterocycles, a practically convenient safe and rapid methodology.[1] Thiadiazole,[2] tetrazole,[2] indole,[3-4] and quinoline[5] derivatives are pharmocologically important. Naphtho [2,1-*b*]pyran-3-ones are associated with diverse biological activities.[6-8] Keeping in view the potential of microwave[9] and the biological importance of the above mentioned moieties, it was thought worthwhile to develop a new enzymatic[10] method for the synthesis of the title compounds using *Pseudomonas* lipase under microwave activation. This is the first report on the synthesis using enzyme under microwave irradiation. The use of environment friendly enzymes[11] in synthesis is being adopted with increasing and enthusiastic alacrity.

5-Methyl-1,3,4- thiadiazol-2-ylsulfanyl-, quinolin-8-yloxy- and 4-methylquinolin-2-yloxy-acetic acids **1**, **4**, and **5** were prepared starting from 5-methyl-1,3,4-thiadiazole-2-thiol, 8-hydroxyquinoline and 2-hydroxy-4-methylquinoline respectively by treatment with ethyl bromoacetate[12] followed by hydrolysis of the ester to the corresponding acid (**1**,**4**,**5**). 1*H*-1,2,3,4-Tetrazol-1-yl- and 1*H*-Indol-3-ylacetic-acids (**2**,**3**) were purchased.

We report herein a novel enzymatic route to the synthesis of 2-(5-methyl-1,3,4-thiadiazol-2-yl-sulfanyl)-, 2-(1*H*-1,2,3,4-tetrazol-1-yl)-, 2-(1*H*-indol-3-yl)-, 2-(quinolin-8-yloxy), and 2-(4-methylquinolin-2-yloxy)-naphtho[2,1-*b*]pyran-3-ones **6-10** (**Scheme I; Table I**) in the presence of DMF, DBU and an acidic lipase from *Pseudomonas* species under microwave irradiation. This lipase had an optimum activity at *p*H 3.0 and 50 °C. It was thermostable at 100 °C for 30 minutes and was active on saturated fatty acids. It was also stable in various organic solvents. The title compounds were characterised and compared with authentic samples (TLC, mp, ^{1}H NMR and IR).[13] The IR spectra showed an absorption band at 1710-1730 cm^{-1} due to lactone of the coumarin ring. In the ^{1}H NMR spectra, a singlet at δ 8.3-8.5 was assigned to the 1*H*-proton of the naphtho-[2,1-*b*]pyran-3-one ring.



Scheme I

Table I — Physical and spectral data of compounds **6-10**

Compd	mp (°C)	Yield (%)	^{1}H NMR ($CDCl_3$+DMSO-d_6)
6	213	65	2.72 (s, 3H, CH_3 ring), 7.15-8.19 (m, 6H, Ar-H), 8.41 (s, 1H, 1-H)
7	234	63	7.12-8.31 (m, 6H, Ar-H), 8.53 (s, 1H, 1-H), 9.51 (s, 1H, 5′ -H of tetrazole ring)
8	207-8	60	7.18-8.19 (m, 11H, Ar-H), 8.35 (1H, brs NH), 8.50 (s, 1H, 1-H)
9	179	68	7.13-8.21 (m, 12H, Ar-H), 8.32 (s, 1H, 1-H)
10	201	62	2.40 (s, 3H, CH_3 ring), 7.18-8.06 (m, 11H, Ar-H), 8.5 (s, 1H, 1-H)

Experimental Section

General. Melting points were recorded on an electrothermal apparatus and are uncorrected. IR spectra (ν_{max} in cm^{-1}) were recorded on a Perkin-Elmer 1710 spectrophotometer, and ^{1}H NMR spectra on a Hitachi R-600 FT spectrophotometer using Me_4Si as internal standard (chemical shifts in δ, ppm). Mass spectra were recorded on a JEOL-JMS-Dx 303 mass spectrophotometer at 70eV. Purity of the compounds was checked by TLC over silica gel coated Al plates (Merck). Irradiations were carried out in a Padmini essentia microwave oven model Brownie (2450 MHz) at low power setting.

Enzyme source. Lipase from *Pseudomonas* species was obtained by growth in minimal medium containing 2% olive oil at *p*H 3.0. It was incubated at 50 °C for 48 hr, and then harvested by centrifugation. The enzyme was partially purified by precipitation with ammonium sulfate (85%) and then subjected to dialysis. The dialysate was lyophilized and used for carrying out the reactions.

Procedure for the synthesis of naphtho[2,1-*b*]pyran-3-ones 6-10. 2-Hydroxy-1-naphthaldehyde (5 mmoles, 0.86 g), the appropriate substituted acetic acid (6.25 mmoles), DBU (1 mmole), and the enzyme acidic lipase from *Pseudomonas* species (0.5 g) were mixed in DMF (15 mL) in a conical flask covered with a funnel. The reaction mixture was irradiated in a microwave oven at 40 °C. TLC was run after every 30 sec. to check the progress of the reaction. Once the reaction was complete in (4-6 min.), the reaction mixture was filtered off to remove the enzyme which was used as a catalyst, and the filtrate poured into ice water. The resultant solid was filtered, and washed with water to afford the corresponding naphtho[2,1-*b*]pyran-3-ones (cf. **Table I**).

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