Examination of the Perkin Reaction under Microwave Irradiation

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The microwave irradiation shortened the reaction time of the Perkin reaction by 60-fold over classical heating. Cesium salts (acetate, carbonate, fluoride) with a small amount of pyridine were found to be the best catalysts under all conditions tested.

The first reports of the application of commercial microwave ovens to the synthesis of small organic molecules appeared in 1986 [1, 2]. Microwave irradiation proved then to be extremely useful for promoting and simplifying of many condensation reactions which can be carried both in the solvent and solvent-free conditions [3—7].

The classical Perkin reaction of the cinnamic acids consists of prolonged (8—10 h) heating of the benzaldehyde, the acetic anhydride, and a catalyst to 180 °C [8—13]. We describe herein the attempts to perform efficient Perkin reaction in the microwave oven. The goal of this work was to examine the catalyst effect and to study the influence of the substituents on the course and yields of this reaction.

RESULTS AND DISCUSSION

To start our investigation we performed the study of different catalyst effect on the course of reaction of benzaldehyde with acetic anhydride. The control experiments with commercial heating were performed also with the same catalyst. From the results given in Table 1 it follows that the most frequently used catalyst sodium acetate was not effective in microwave experiments. Only the starting compounds were isolated after 1 h heating and no products were observed on TLC. Just low yields of products were isolated both with sodium and potassium acetate after conventional heating (10 h, 180 °C). This is in contradiction with the literature [9—13] and therefore the experiments were repeated three times, but with the same results. The similar observation was mentioned as the footnote on pages 218 and 249 in [14]. We found that the best catalysts are different cesium salts especially when a small amount of pyridine was used to rise their catalytic activity. The reaction time in microwave oven reactions is 60—80 times shorter than at conventional heating and the yields of isolated products are usually 5—10 % higher. No difference in the course of microwave reaction was observed at scaling up the experiments from 0.01 mol to 0.1 mol of benzaldehyde.

Table 1. Synthesis of Cinnamic Acid under Various Conditions

Catalyst	Microwave) (800 W)		Classical heating (10 h)
	Reaction time/min	Yield/%	Yield/%
CH_3CO_2Na	60	–	15
CH_3CO_2K	30	31	24
CH_3CO_2Cs	10	37	48
CH_3CO_2Na/pyr	60	–	17
CH_3CO_2K/pyr	20	40	27
CH_3CO_2Cs/pyr	10	45	47
KF/pyr	15	4	–
CsF/pyr	10	47	–
Cs_2CO_3/pyr	10	51	–

From the data given in Table 2 it may be seen that very good results were obtained using the substituted benzaldehydes as a starting material. The reaction was very rapid and high yields of the pure products were isolated especially when bromo, chloro, and hydroxy derivatives were used. These results indicate that the activity of substituted benzaldehydes in the Perkin reaction performed under microwave irradiation is similar to the activity observed in the classical conditions. Cinnamaldehyde gives excellent result under usual conditions of the Perkin reaction, but α-styrylacrylic acid (*XIII*) was prepared only in 18 % yield under microwave activation. Although we have expected some problems with stability of furan-2-carbaldehyde under microwave conditions, it was converted to the corresponding acrylic acid (*XIV*) in satisfactory yield.

In the next part of the work we decided to examine the possibility to change the anhydride in the Perkin reaction. Propionic and butyric anhydrides gave just small yields of the expected α-

Table 2. Synthesis of Substituted Cinnamic Acids under Microwave Irradiation

Compound	Substituent	Time/min	Yield/%	M.p./°C	M.p./°C Ref.
I	2-Nitro	15			240 [15]
III	3-Phenoxy	10	75	244—246	187 [16]
IV	2-Methoxy	15	41	184—186	185—186 [15]
V	2,4-Dimethoxy	20	30	190—193	184 [17]
VI	2,4-Dichloro	3	88	233—236	235—236 [15]
VII	2-Bromo	3	64	208—211	215—216 [15]
VIII	3-Bromo	3	56	176—179	178—179 [15]
IX	4-Bromo	3	80	261—263	257 [15]
X	2-Hydroxy	3	48[a]	65	70 [15]
XI	3-Hydroxy	5	76	194—199	191 [15]
XII	4-Hydroxy	11	85	202—203	210—213 [15]
XIII	Cinnamaldehyde	2	18	165—166	165—166 [15]
XIV	Furfural	20	44	139—142	141 [15]

a) Coumarine.

Table 3. Synthesis of α-Substituted Cinnamic Acids under Microwave Irradiation

Compound	Anhydride	Time/min	Yield/%	M.p./°C	M.p./°C Ref.
XV	Propionic	10	11	77—80	82 [15]
XVI	n-Butyric	10	14	102	104 [15]
XVII	Phenylacetic	8	89	168	173 [15]

methyl- or α-ethylcinnamic acids (*XV, XVI*) in the microwave reaction with benzaldehyde. Cesium fluoride had to be used as the catalyst. On the other hand, more reactive phenylacetic acid anhydride afforded α-phenylcinnamic acid (*XVII*) in excellent yield (89 %) when cesium acetate was used as the catalyst (Table 3).

EXPERIMENTAL

All reactions were carried out in the Milestone LAVIS 1000 Basic Microwave. Melting points were determined on a Kofler hot-stage and are uncorrected. The ^{1}H NMR spectra were recorded with a Tesla BS 487 C apparatus operating at 80 MHz: tetramethylsilane was the internal reference for measurements in $CDCl_3$ (compounds *I, VIII, X, XIII, XVI, XVII*) and hexamethyldisiloxane for those in DMSO-d_6 (compounds *II—VII, IX, XI, XII, XIV, XV*).

Benzaldehyde and acetic anhydride were purified according to Ref. [9]. The catalysts were fused on a hot plate, or dried in the microwave oven at 270 W for 5 min.

Synthesis of the Cinnamic Acid (*I*) under Microwaves

A mixture of freshly distilled benzaldehyde (0.05 mol), acetic anhydride (0.1 mol), and the freshly fused catalyst (0.05 mol) was heated in the microwave oven at 800 W for the time given in Table 1. The reaction mixture was then poured into 100 cm^3 of 5 % $NaHCO_3$ and the unreacted aldehyde was removed by steam-distillation or extracted three times into 150 cm^3 of diethyl ether. The residual liquid was filtered, the clear filtrate was heated to boiling and acidified to pH 2 by addition of HCl. The crystalline product (m.p. = 133—134 °C) was filtered off, washed with cold water and dried. As a control, an identical mixture was heated on the oil bath for 10 h at 180 °C. The workup and isolation was the same as described above. The results are given in Table 1.

The substituted cinnamic acids (*I—XII*) were prepared similarly from corresponding substituted benzaldehydes using cesium acetate and two drops of pyridine as the catalyst. The experiments were performed in microwave oven at 270 W. The results are given in Table 2.

The substituted cinnamic acids (*XV—XVII*) were prepared similarly from benzaldehyde, appropriate anhydride, and appropriate catalyst. Anhydrides and yields are given in Table 3.

^{1}H NMR Spectra of Synthesized Compounds

I: δ: 6.50 (d, 1H, =CH_A), 7.44—7.64 (m, 5H, H_{arom}), 7.76 (d, 1H, =CH_B), 12.37 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

II: δ: 6.58 (d, 1H, =CH_A), 7.66—8.14 (m, 4H, H_{arom}), 7.82 (d, 1H, =CH_B), 12.70 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

III: δ: 6.58 (d, 1H, =CH_A), 6.99—7.44 (m, 9H, H_{arom}), 7.45 (d, 1H, =CH_B), 12.48 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

IV: δ: 3.87 (s, 3H, CH_3O), 6.56 (d, 1H, =CH_A),

7.32—7.72 (m, 4H, H_{arom}), 7.80 (d, 1H, $=CH_B$), 12.24 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

V: δ: 3.82 (s, 3H, CH_3O), 3.87 (s, 3H, CH_3O), 6.42 (d, 1H, $=CH_A$), 6.53—7.55 (m, 3H, H_{arom}), 7.71 (d, 1H, $=CH_B$), 12.05 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

VI: δ: 6.68 (d, 1H, $=CH_A$), 7.41—8.02 (m, 3H, H_{arom}), 7.57 (d, 1H, $=CH_B$), 12.68 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

VII: δ: 6. 62 (d, 1H, $=CH_A$), 7.26—7.94 (m, 4H, H_{arom}), 7.82 (d, 1H, $=CH_B$), 12.71 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

VIII: δ: 6.49 (d, 1H, $=CH_A$), 7.17—7.70 (m, 4H, H_{arom}), 7.66 (d, 1H, $=CH_B$), 12.67 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

IX: δ: 61 (d, 1H, $=CH_A$), 7.48—7.75 (m, 4H, H_{arom}), 7.53 (d, 1H, $=CH_B$), 12.49 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

X: δ: 6.43 (d, 1H, $=CH_A$), 6.94—7.78 (m, 4H, H_{arom}), 8.05 (d, 1H, $=CH_B$), $J_{A,B}$ = 10.5 Hz.

XI: δ: 6.47 (d, 1H, $=CH_A$), 6.77—7.65 (m, 4H, H_{arom}), 7.49 (d, 1H, $=CH_B$), 9.72 (s, 1H, OH), 12.19 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

XII: δ: 6.33 (d, 1H, $=CH_A$), 6.74—7.57 (m, 4H, H_{arom}), 7.46 (d, 1H, $=CH_B$), 9.99 (s, 1H, OH), 11.96 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

XIII: δ: 6.05 (d, 1H, $=CH_A$), 6.96 (t, 2H, $=CH_{B,C}$), 7.30—7.59 (m, 5H, H_{arom}), 7.44 (d, 1H, $=CH_D$).

XIV: δ: 6.23 (d, 1H, $=CH_A$), 6.60—7.83 (m, 3H, H_{arom}), 7.34 (d, 1H, $=CH_B$), 12.37 (s, 1H, COOH), $J_{A,B}$ = 15.8 Hz.

XV: δ: 2.06 (d, 3H, CH_3), 7.36—7.52 (m, 5H, H_{arom}), 7.64 (s, 1H, =CH), 12.52 (s, 1H, COOH).

XVI: δ: 1.22 (t, 3H, (CH_3)), 2.58 (q, 2H, CH_2), 7.40 (s, 5H, H_{arom}), 7.92 (s, 1H, =CH), 10.14 (s, 1H, COOH).

XVII: δ: 7.08—7.54 (m, 10H, H_{arom}), 7.96 (s, 1H, =CH), 10.07 (s, 1H, COOH).

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