

THE EFFECT OF THE SUBSTITUENTS ON THE ACID-CATALYZED CHALCONE FORMATION

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The condensation of *p*-substituted acetophenones with benzaldehydes has been carried out in abs. ethanol containing 30% hydrogen chloride as the catalyst. On the basis of the yields of chalcones qualitative conclusions have been drawn regarding the influence of the substituents on the condensation. It has been found that the electron-releasing substituents of benzaldehyde and the electron-withdrawing substituents of acetophenone are favourable for the condensation.

We have reported previously that *p*-hydroxy- and *p*-methoxybenzaldehyde with nitro-, hydroxy- and nitro-hydroxyacetophenones in abs. ethanol containing 30% hydrogen chloride gave better yields of corresponding chalcones than *p*-nitrobenzaldehyde [1]. On the basis of these results the effect of the substituents on the acid-catalyzed chalcone formation has been examined more extensively in the present work.

The acid-catalyzed reactions of the substituted acetophenones with benzaldehydes were carried out by allowing the equimolecular amounts of the reactants to stand at room temperature in abs. ethanol containing 30% hydrogen chloride. Two runs of the condensations were effected. The reaction time of the one run was two and that of the other five hours.

The expected chalcones obtained in these experiments are listed in Table I.

Table II shows the yields of the above chalcones in the two runs of the condensation.

It is seen that the yields are highest with *p*-hydroxy- and *p*-methoxybenzaldehyde and lowest with *p*-nitrobenzaldehyde. It is striking that benzaldehyde gives lower yields with substituted acetophenones than *p*-chlorobenzaldehyde with acetophenones, and the yields are much better than with benzaldehyde. However in the condensations of benzaldehyde there is a possibility for the addition of hydrogen chloride [2]. As concluded from the yields *p*-methoxy-, *p*-hydroxy-*p*-chloro- and *p*-methylbenzaldehyde have almost equivalent effects on the condensation. The

Table I
Chalcones from the acid-catalyzed chalcone formation

chalcone	Formula	Molar weight	Carbon		Hydrogen		Nitrogen		Melting point °C	
			Calcd.	Found %	Calcd.	Found %	Calcd.	Found %	Found.	Liter.
4', 4-dinitro	$C_{16}H_1O_5N_2$	298.2	60.3	—	3.3	—	9.3	9.5	209	209
4'-nitro-4-chloro	$C_{15}H_1O_3NCl$	287.7	62.6	—	3.5	—	4.8	5.0	165	164
4'-nitro-4-methyl	$C_{16}H_{13}O_3N$	267.2	71.8	—	4.9	—	5.2	5.3	166	168
4'-nitro-4-hidroxy	$C_{15}H_{11}O_4N$	269.2	67.9	—	4.2	—	5.3	5.3	202	202
4'-nitro-4-methoxy	$C_{16}H_{13}O_4N$	283.2	67.8	—	4.6	—	4.9	4.8	180	179
4'-chloro-4-nitro	$C_{15}H_1O_3NCl$	287.6	62.2	—	3.5	—	4.8	5.0	163	164
4',-4-dichloro	$C_{15}H_1OCl_2$	277.0	65.0	65.2	3.6	3.7	—	—	157	157
4'-chloro-	$C_{15}H_{11}OCl$	242.6	72.2	72.2	4.5	4.6	—	—	98	98
4'-chloro-4-methyl	$C_{16}H_{13}OCl$	256.7	74.8	74.6	5.1	5.3	—	—	161	165
4'-chloro-4-hidroxy	$C_{15}H_{11}O_2Cl$	258.6	69.6	69.9	4.2	4.4	—	—	178	174
4'-chloro-4-methoxy	$C_{16}H_{13}O_2Cl$	272.7	70.4	70.4	4.8	4.9	—	—	125	128
4-nitro	$C_{15}H_{11}O_3N$	253.2	71.1	—	4.3	—	5.5	5.7	164	162
4-chloro	$C_{15}H_{11}OCl$	242.6	72.2	72.4	4.5	4.8	—	—	116	116
4-methyl	$C_{16}H_{14}O$	222.2	86.4	86.3	6.3	6.1	—	—	85	90—101
4-hydroxy	$C_{15}H_{12}O_2$	224.2	80.3	80.4	5.2	5.4	—	—	185	183
4'-methyl-4-nitro	$C_{16}H_{13}O_3N$	267.2	71.8	—	4.9	—	5.2	5.5	160	163
4'-methyl-4-chloro	$C_{16}H_{13}OCl$	256.7	74.8	74.6	5.1	5.2	—	—	124	122
4'-methyl	$C_{16}H_{14}O$	268.1	86.4	86.6	6.3	6.5	—	—	96	96
4',-dimethyl	$C_{17}H_{16}O$	254.2	86.4	86.6	6.8	6.7	—	—	123	129
4'-methyl-4-hidroxy	$C_{16}H_{14}O_2$	252.1	80.6	80.7	5.9	5.7	—	—	160	—
4'-methyl-4-methoxy	$C_{17}H_{16}O_2$	238.2	76.1	80.6	6.3	6.4	—	—	98	91—126
4'-hidroxy-4-chloro	$C_{15}H_{11}O_2Cl$	272.7	75.5	69.8	4.2	4.4	—	—	190	190
4'-hidroxy	$C_{15}H_{12}O_2$	254.2	80.9	80.4	6.0	6.1	—	—	176	177
4'-hidroxy-4-methyl	$C_{16}H_{14}O_2$	240.2	80.6	80.6	5.5	5.6	—	—	193	143
4', 4-dihidroxy	$C_{15}H_{12}O_3$	238.2	70.4	76.3	6.3	6.4	—	—	203	203
4'-hidroxy-4-methoxy	$C_{16}H_{14}O_3$	224.2	75.5	75.8	5.9	5.7	—	—	189	187
4'-methoxy-4-chloro	$C_{16}H_{13}O_2Cl$	272.7	70.4	70.3	4.8	4.9	—	—	129	131
4'-methoxy	$C_{16}H_{14}O_2$	238.2	80.6	80.8	5.9	5.7	—	—	106	108
4'-methoxy-4-methyl	$C_{17}H_{16}O_2$	257.1	80.9	80.7	6.3	6.4	—	—	117	126
4'-methoxy-4-hidroxy	$C_{16}H_{14}O_3$	254.2	75.5	75.8	5.5	5.6	—	—	184	188
4', 4-dimethoxy	$C_{17}H_{16}O_3$	268.1	76.1	76.3	6.0	6.1	—	—	107	97—103

likely interpretation of this fact is that in the case of *p*-chlorobenzaldehyde the +M effect is dominant in the acidic medium.

The above facts mean that the electron-releasing substituents of benzaldehydes are favourable, while the electron-withdrawing substituents are disadvantageous in the acid-catalyzed chalcone formation of substituted benzaldehydes with acetophenones, in accordance with earlier observations [1-5]. This effect of the substituents can be interpreted on the basis of the reaction mechanism [6, 7];

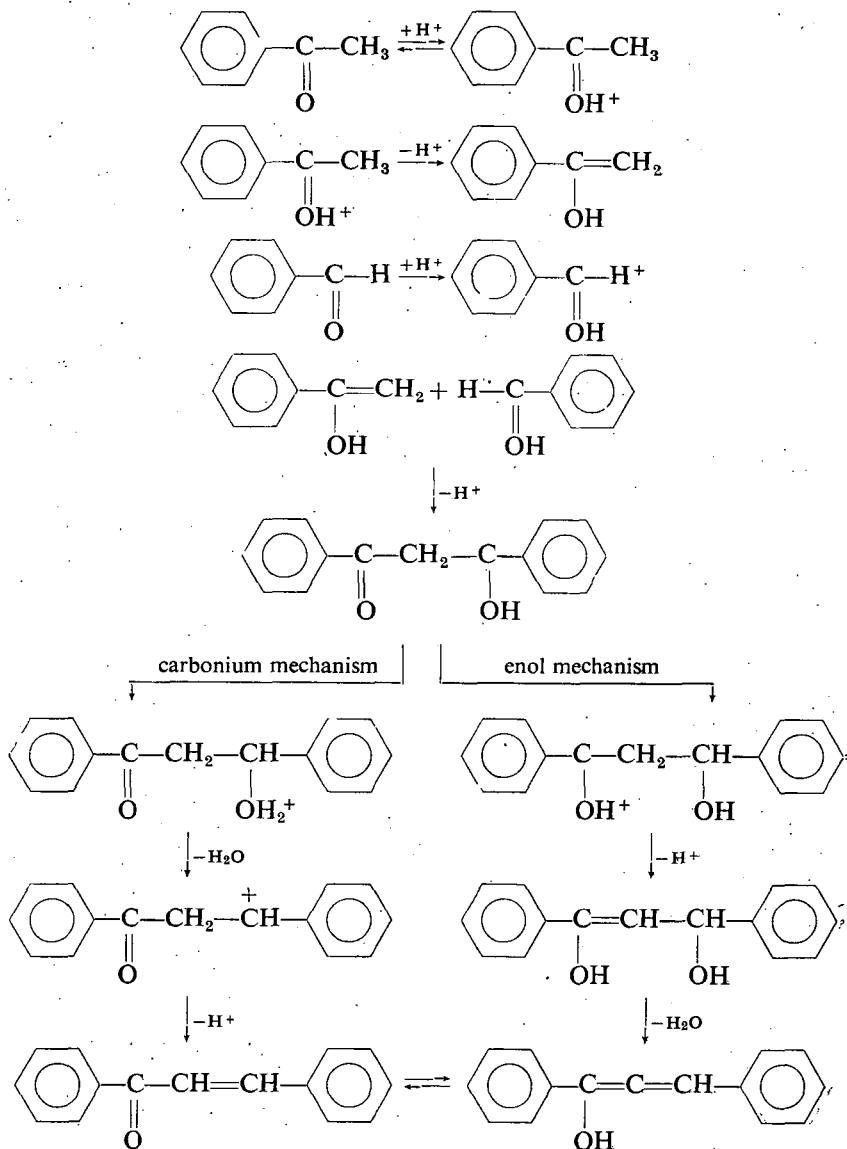


Table II
The yields (%) of chalcones

acetophenone	Reaction components	-benzaldehyde											
		p-nitro		p-chloro		p-methoxy		p-hydroxy		p-methyl		benz-aldehyde	
	Reaction time hours	5	2	5	2	5	2	5	2	5	2	5	2
	p-nitro	20	13	71	55	80	76	68	45	86	75	60	40
	p-chloro	12	10	67	33	66	50	84	83	82	74	41	20
	p-methoxy	—	—	26	23	43	36	72	71	46	60	29	11
	p-hydroxy	—	—	40	30	78	72	82	78	78	58	43	19
	p-methyl	13	9	57	34	48	33	55	41	53	24	38	29
	acetophenone	12	4	21	8	39	28	81	51	46	10	36	26

NOYCE supposed, that the likely explanation of the favourable effect of the electron-releasing methoxyl substituent may be founded upon the increase of the basicity of benzaldehyde in the condensation step [8]. Because of this increase the concentration of the protonic salt of aldehyde thus increase the ease of the condensation. Besides it is presumable that the electron-releasing substituents facilitate the separation of the hydroxyl ion in the final step of the condensation. Hence the electron-releasing substituents promote the reaction both in the condensation and the dehydration step.

Concerning the effect of the substituents of the acetophenone component on the condensation may be similarly derived from Table II. *p*-Nitro- and *p*-chloro-acetophenone gave generally better yields with substituted benzaldehydes than the other acetophenones. From this fact it can be concluded that the electron-withdrawing nitro and chloro substituents of the acetophenone component favour the condensation. They promote the enolization of the ketone component in the first reaction step and the elimination of the proton in the final step of the reaction.

Our results concerning the effect of the substituents of the acetophenone component are in accordance with LYLE's observations [2].

EXPERIMENTAL

Cold abs. ethanol was saturated with gaseous hydrogen chloride and the solution was diluted to the required 30 percent. 10 ml of this catalyst solution was used to effect the condensation of the reactants in amounts of 1 mmole each. After the reaction had been completed, the mixture was diluted with cold water to 40–50 ml and neutralized with a cold solution of sodium hydroxid to p_{H} 7. After allowing the mixture to stand several days at room temperature, the precipitate was filtered off and recrystallized from aqueous ethanol or acetone.

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ВЛИЯНИЕ ЗАМЕСТИТЕЛЕЙ НА ОБРАЗОВАНИЕ КАЛЬКОНА КАТАЛИЗОВАННОЕ КИСЛОТАМИ

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Конденсация с бензальдегидами пара-замещенных сульфонов была осуществлена в абсолютном спирте содержащем 30% хлористого водорода как катализатора. На основе данных выпуска выводы были сделаны о влиянии заместителей оказанном на конденсацию. Получилось, что заместители бензальдегида которые выпускают и те ацетофеноны которые притягивают электроны, выгодно влияют на конденсацию.