



SYNTHESIS OF 3-HALO FLVONES FROM 2-HYDROXY-3-5-DISUBSTITUTED ACETOPHENONE

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ABSTRACT

Substituted acetophenone was reacted with substituted benzoic acid in pyridine medium as base in presence of phosphoryl chloride for five hours and the thick mass was decomposed by 1 : 1 HCl to get substituted benzoyloxy substituted acetophenone. This product was further subjected to BVT reaction to get substituted dibenzoyl methane. Substituted dibenzoyl methane is treated with iodine monochlorides in DMF medium gives 3-halo flavones.

Key words: Flvones, Diketones, Dibenzoyl methane, Synthesis.

INTRODUCTION

β -Diketone is useful starting compounds for synthesis of various important compounds viz. hormones¹, oxygen and nitrogen containing heterocycles, pyrazoles^{2,3}, isooxazoles⁴, 3-bromo flavone^{5,6}, 3-chloroflavones⁷, propane 1-3-dione reacts with dibromide to give 3-bromoflavone⁷; β -dicarbonyl compounds have been effectively chlorinated using sulphuryl chloride to form 3-chloro flavones.

Acetyl acetone has been chlorinated with sulphuryl chloride in acetic acid⁸. Dibenzoyl methane gives α -chloro dibenzoyl methane with sulphuryl chloride in dioxane medium⁹. 3-chloro flavones were prepared by action of thionyl chloride or sulphuryl chloride with flavones¹⁰⁻¹². Various 3-halo flavones were prepared by reaction of corresponding flavones derivatives with $R_4NBr/Ph/(OAc)_2$ system under mild reaction conditions¹³. 1, 3 diketones was transformed into 7-hydroxy-6-nitro flavone¹⁴. Dibenzoyl methane reacts in DMF medium or with bromine in DMF to give 3-halo flavones¹⁵.

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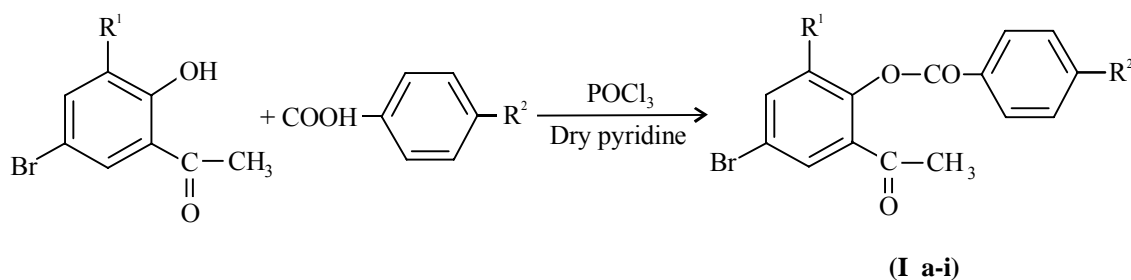
EXPERIMENTAL

The melting points were taken in an open capillary tube, IR spectra were recorded in Nujol, ^1H NMR spectra were recorded in CDCl_3 with TMS as an internal standard. The purity of synthesized compounds was checked by TLC.

Preparation of 2-(4'-nitro)-benzoyloxy-3,5-dibromo acetophenone (I a)

2-hydroxy-3,5-dibromo acetophenone (0.04 moles) together with p-nitro benzoic acid (0.05 moles) were dissolved in 40 mL of pyridine. To this ice-cold mixture 3 mL of POCl_3 was drop wise added with constant stirring. The temperature was maintained below 40°C , allowed to stand for 4 to 5 hrs. Thick mass was decomposed with 1 : 1 HCl. The product was washed with 10% Na_2CO_3 solution. Finally with 1% NaOH solution. Then with water. It was then crystallized from ethanol to get 2-(4'-nitro) benzoyloxy-3,5-dibromo acetophenone (I a) m.p. 156°C . It shows negative ferric chloride showing absence of phenolic $-\text{OH}$ group.

Similarly other compounds (I b –i) were prepared by above method.



Scheme of compounds (I a-i)

Table 1: Spectral Analysis of compound (I a-i)

S. No.	IR Data (cm^{-1})	^1H NMR Data (in CDCl_3)
1	2943.5 (C-H, stretching)	2.3 δ (s, 3H, = C- CH_3).
2	1747 (C=O, stretching)	7.6 – 8.2 δ (m, 6H, Ar-H).
3	1654 (C- NO_2 , asymmetric stretching)	
4	1607, 1507 & 1460 (-C=C-, stretching)	
5	1320 (C- NO_2 symmetric stretching)	
6	711 (C-Br stretching)	

Table 2: Physical data of synthesized acetophenones (I a-i)

S. No.	Compounds	R ₁	R ₂	M.P (°C)	Yields (%)
1	I a	Br	NO ₂	156	76
2	I b	Br	Cl	111	72
3	I c	Br	NH ₂	96	78
4	I d	NO ₂	NO ₂	179	68
5	I e	NO ₂	Cl	125	75
6	I f	NO ₂	NH ₂	182	70
7	I g	H	NO ₂	95	72
8	I h	H	Cl	109	75
9	I i	H	NH ₂	183	73

Preparation of 2-hydroxy-3, 5 dibromo -4'-nitro dibenzoyl methane (II a)

2-(4'-nitro) benzoyloxy-3, 5 dibromo acetophenone (0.01 mole) was dissolved in 40 mL pyridine. It is then treated with pulverize KOH (0.3 mole). The mixture was kept as such for 5-6 hours. It was then decomposed with ice-cold acetic acid. The crude mass was washed with 10% Na₂CO₃ solution and then washed with water. It was then crystallized with mixture of 1 : 1 ethanol and acetic acid to get 2-hydroxy-3,5 dibromo-4'-nitro dibenzoyl methane (II a). M.P.-142°C. The red coloration with natural FeCl₃ solution indicate the presence of phenolic –OH group.

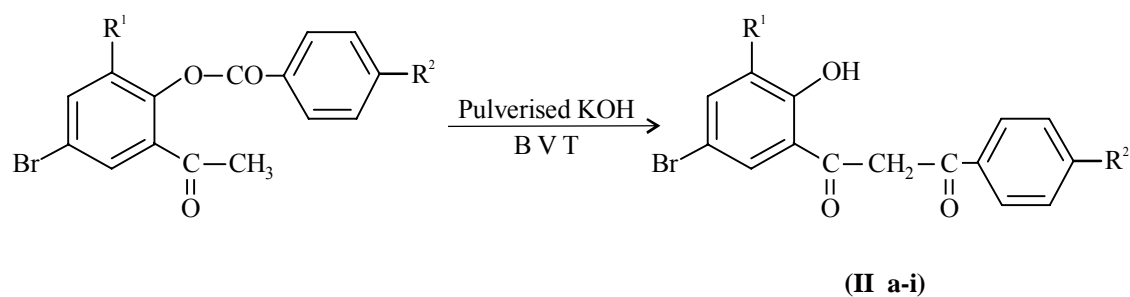
**Scheme of compounds (II a-i)**

Table 3: Spectral analysis of compound (II a-i)

S. No.	IR Data (cm ⁻¹)	¹ HNMR Data (in CDCl ₃)
1	2930 – 2850 (C – H, stretching in CH ₂)	4.4 δ (S, 2H, -CH ₂)
2	1648 (C = O, stretching in 1,3diketones)	7.26 δ (m, 6H, Ar-H)
3	827 – 762 (1, 3 disubstituted benzene)	12.84 δ (S, 1H, -OH)
4	600 – 500 (-C-Br bending)	

Table 4: Physical data of synthesized diketones (II a-i)

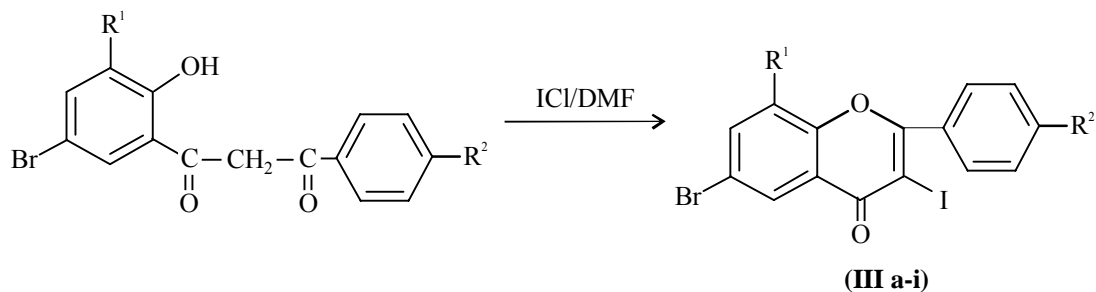
S. No.	Compounds	R ₁	R ₂	M.P (°C)	Yields (%)
1	II a	Br	NO ₂	142	70
2	II b	Br	Cl	175	65
3	II c	Br	NH ₂	110	65
4	II d	NO ₂	NO ₂	125	72
5	II e	NO ₂	Cl	118	67
6	II f	NO ₂	NH ₂	122	62
7	II g	H	NO ₂	206	59
8	II h	H	Cl	115	68
9	II i	H	NH ₂	181	65

Preparation of 2-(4'-nitrophenyl)-3-iodo-6-8-dibromo flavones (III A)

2- hydroxy-3, 5-dibromo-4'nitro dibenzoyl methane (0.01 moles) was dissolved in dimethyl formamide (DMF) and pure iodine mono chloride (0.01 moles) was added. The mixture was refluxed for 1 : 3 hours. Then cooled, diluted with ice-cold water and crystallized from alcohol-acetic acid mixture to get 2-(4'-nitrophenyl)-3-iodo-6, 8-dibromo flavones (III a), m.p. -169°C.

It show negative ferric chloride solution test indicate the involvement of phenolic -OH group in cyclization.

Similarly other compounds (III a-i) were prepared by above method.

**Scheme of compounds (III a-i)****Table 5: Spectral analysis of compound (III a-i)**

S. No.	IR Data (cm ⁻¹)	¹ H NMR Data (in CDCl ₃)
1	1663 (C = O, stretching)	6.80 – 8.20 δ (m, 6H, Ar-H)
2	1595, 1555 & 1459 (C = C stretching aromaticity)	
3	1284 (Ar-O, stretching)	
4	763 (-C-Cl, stretching)	
5	702 (-C-Br bending)	
6	546 (-C-I, bending)	

Table 6: Physical data of synthesized Flavones (III a-i)

S. No.	Compounds	R ₁	R ₂	R ₃	M.P (°C)	Yields (%)
1	III a	Br	NO ₂	I	169	75
2	III b	Br	Cl	I	206	69
3	III c	Br	NH ₂	I	176	65
4	III d	NO ₂	NO ₂	I	194	72
5	III e	NO ₂	Cl	I	132	78
6	III f	NO ₂	NH ₂	I	143	79
7	III g	H	NO ₂	I	296	76
8	III h	H	Cl	I	241	77
9	III i	H	NH ₂	I	319(D)	77

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Revised : 11.02.2012

Accepted : 14.02.2012