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A

PROJECT REPORT

ON

Synthesis of Phenacyl Bromides And Their Imidazole Derivatives

Submitted By: Mr. Shubham S. Dabhade &
Mr. Akash M. Zend

Academic Year

2020-2021

Under the Guidance of

Prof. R.D. Deshmukh

Synthesis of 1-(1H-imidazol-1-yl)-2-(4-substitutedphenyl) ethanones.

A PG Dissertation Report of a Project Carried out as a Part of Curriculum for the Degree of Master of Science in Organic Chemistry

SUBJECT CODE: 33424C
[CBOP-5 CHO-453 C]

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(M.Sc. IInd, Organic Chemistry)

Under the Guidance of
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Submitted to

Post Graduate Department of Chemistry,
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Affiliated to

SAVITRIBAI PHULE PUNE UNIVERSITY, PUNE
(2020-2021)

DECLARATION BY THE STUDENT

We declare that the dissertation entitled **"Synthesis of 1-(1H-imidazol-1-yl)-2-(4-substitutedphenyl) ethanones"** submitted by us for the degree of Master of Science in Organic Chemistry **SUBJECT CODE: 33424C [CBOP-5 CHO-453 C]** is the record of work carried out by us under the guidance of **PROF. ROHINI D. DESHMUKH** and has not formed the basis for the award of any degree, diploma, associate ship, fellowship, titles in this or any other university or other institution of higher learning. We further declare that the material obtained from other sources has been duly acknowledged in the dissertation

Date- 15/07/2021

Place- Nashik

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CERTIFICATE OF RESEARCH SUPERVISOR (GUIDE)

Certificate of the Guide CERTIFIED that the work incorporated in the PG dissertation entitled **"Synthesis of 1-(1H-imidazol-1-yl)-2-(4-substitutedphenyl)ethanones"** submitted by **MR. SHUBHAM S. DABHADE** and **MR. AKASH M. ZEND** was carried out by the candidates under my supervision/guidance. Such material has been obtained from other sources has been duly acknowledged in the dissertation.

Date: - 15/7/2021

Place: - Nashik

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EXAMINER'S CERTIFICATE

This is to certify that PG dissertation entitled **"Synthesis of 1-(1H-imidazol-1-yl)-2-(4-substitutedphenyl) ethanones"** submitted by **MR. SHUBHAM SHASHIKANT DABHADE** and **MR. AKASH MOTILAL ZEND** was carried out by the candidates under supervision of **PROF. ROHINI D. DESHMUKH**

With this understanding, we consider the fact that the PG dissertation is a well written project report, should be appreciable and the project work carried out is commendable, we recommend that the PG dissertation submitted by **MR. SHUBHAM SHASHIKANT DABHADE** and **MR. AKASH MOTILAL ZEND** be accepted in its present form for the award of Master of Science in Organic Chemistry, Savitribai Phule Pune University, Pune. They successfully defended the Viva-Voce Examination.

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Acknowledgement

In the accomplishment of this project successfully, many people have best owned upon us their blessing and the heart pledged support, this time we are utilizing to thank all the people who have been concerned with this project.

We wish to thank **Prof. Rohini. D. Deshmukh** for the supervision of this project, for their valuable and intelligent guidance and sympathy, without which it would not have been possible. We also wish to thank the teaching and non teaching staff of the department for co-operation, and **Dr. Amol H. Kategaonkar** for helpful discussions.

I would like to thanks to **Dr. S. K. KUSHARE, H.O.D. Department Of Chemistry**, Karmveer Shantarambapu Kondaji Wavare Arts, Science and Commerce College, Uttamnagar, CIDCO, Nashik. For providing us such a great environment and laboratory with all facilities like instrumentation and chemicals and also their best suggestions and instructions have served me as the major contributor towards the completion of this project.

It is our privilege to express our gratitude and sincere thanks to our family for their unconditional love prayer and moral support.

Our acknowledgement is much more what we have expressed here.

Mr. Shubham S. Dabhade &
Mr. Akash M. Zend

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1. INDRODUCTION

Phenacyl bromides, an α-bromoacetophenone is a lachrymatory compound that has found wide use as a constituent of "tear gas". It is considerably more reactive than acetophenone so that in addition to the customary reactions undergone by ketones it takes part in many others e.g. elimination. Both Phenacyl Bromides are widely used in the identification of acids with the salts of which they react to form well defined crystalline esters.[1]

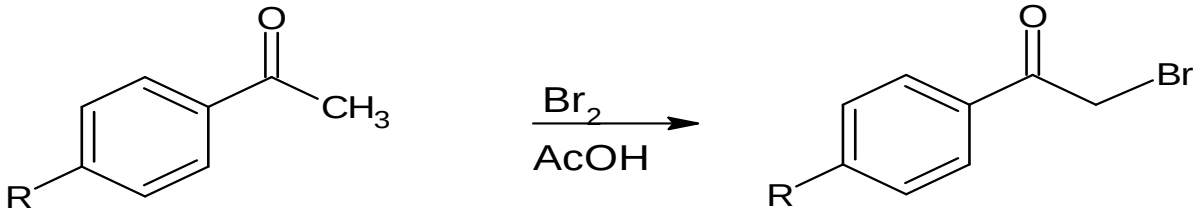
In the present work we have used the acid-catalyzed bromination of a series of substituted acetophenones in order to prepare the phenacyl bromides.[1]

Imidazole nucleus has proved to be a prolific source for a number of medicinal agents.[2] The various activities associated with the imidazole nucleus are antiprotozoal, mutagenic properties, anticancer, antiviral, enzyme inhibitory activities, H2-Antagonism, α- Adrenergic agonist and β-blocking, anticonvulsant, broad spectrum antibacterial and antifungal activities.**[3-14]**

2. Literature Review

2.1]

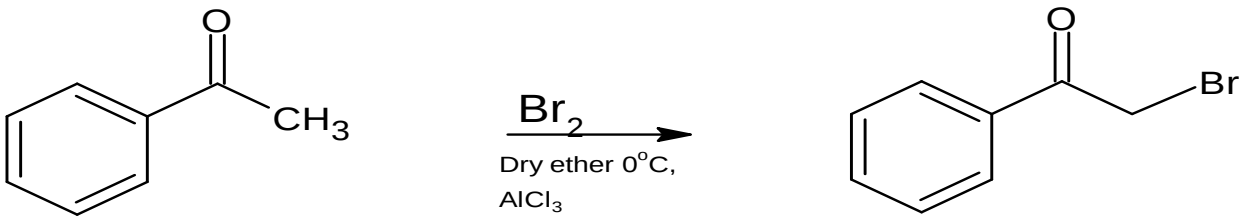
Acid catalysed bromination of p-substituted aceto phenone takes place to synthesize p- substituted phenacyl bromides by Alpha-Halogenation. **(Scheme1)[1]**



(Scheme 1)[1]

2.2]

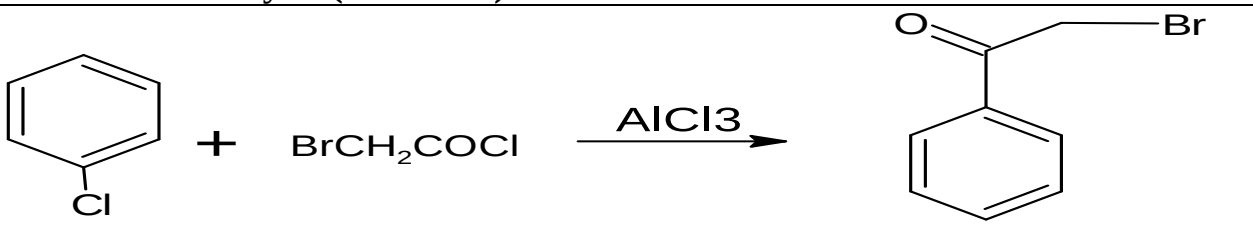
For synthetic purposes acid catalysed brominaticn has been more frequently employed. Glacial acetic acid, carbon tetrachloride, dry ether and ethyl alcohol have all been used as solvents. **(Scheme2)[1]**



(Scheme 2)[1]

2.3]

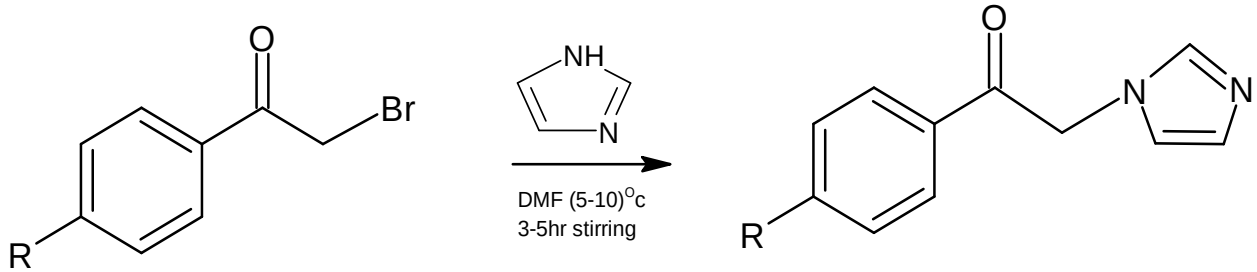
The Friedel Crafts acylation method, starting with the appropriate benzene derivative and bromoacetylchloride in the presence of aluminium chloride as catalyst. **(Scheme3)[1]**



(Scheme3)[1]

2.4]

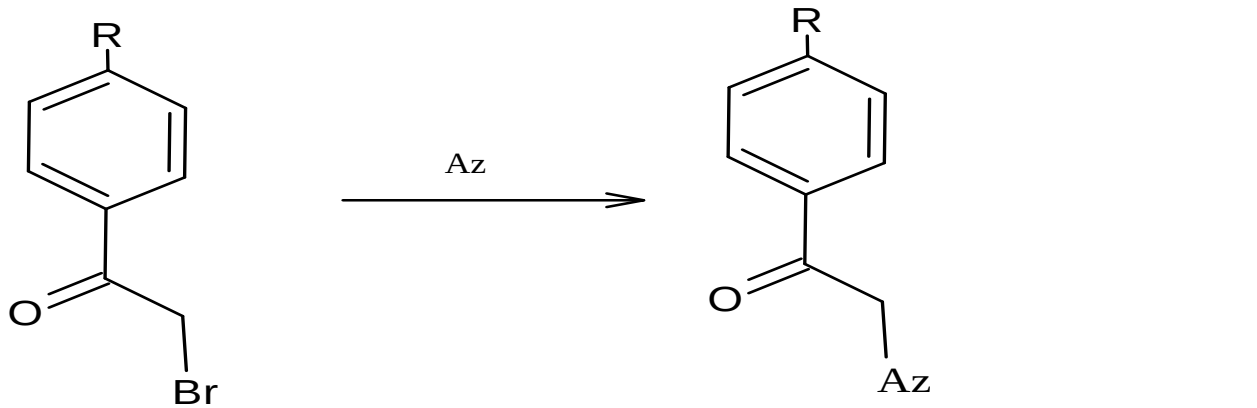
p-substituted phenacyl bromides in presence of DMF at lower temperatures were reacted with imidazole to give N-1 sustituted imidazole derivatives**.(Scheme4)**[2]



(Scheme4)[2]

2.5]

The p-substituted acetophenone precursors, were treated with imidazole in DMF to provide the 2-(lH-imidazol-1 -yl)- 1 - phenylethanones. **(Scheme5)**[14]



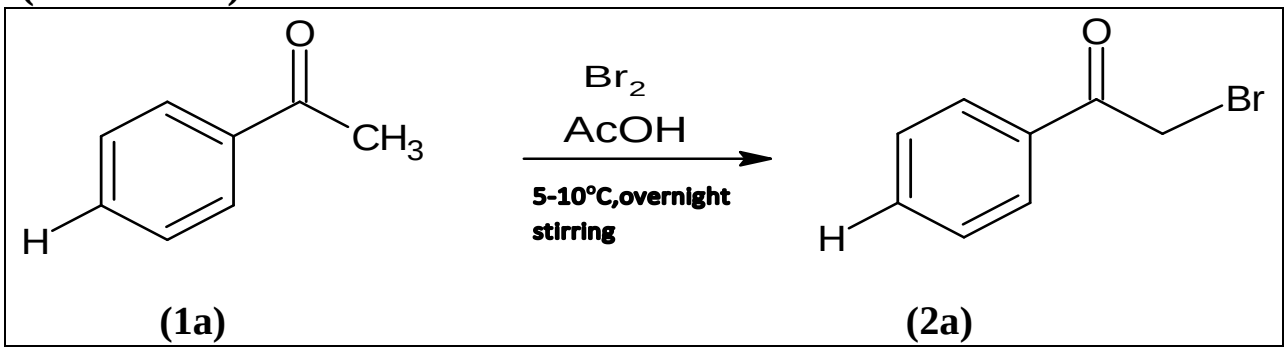
Az- Imidazole or Triazole **(Scheme5)**[14]

3. Present Work

3.1]

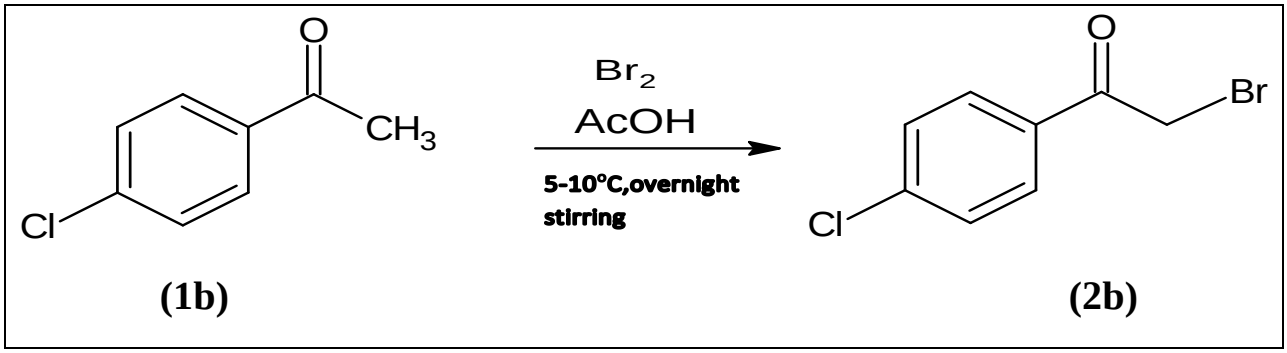
We prepared p-substitued phenacyl bromides by using acid catalysed α-halogenation of p-substituted acetophenone at lower temperature. **(Scheme 6a-c)**[1]

(Scheme 6a)



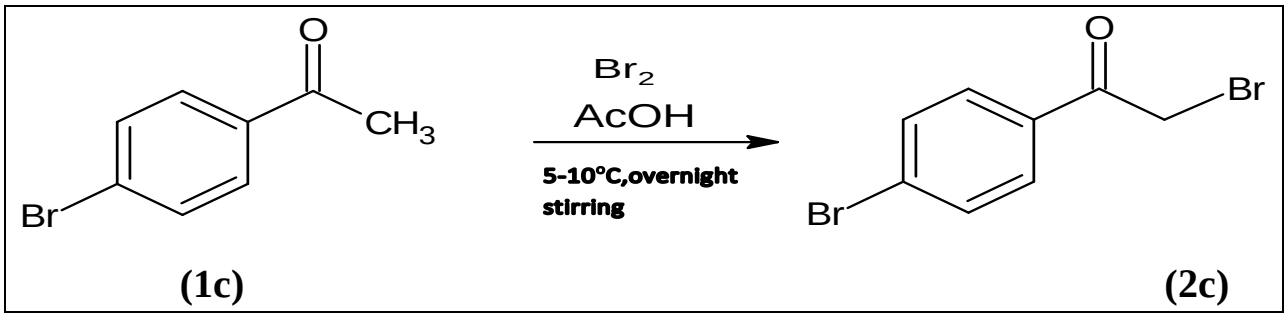
(1a) **(2a)**

(Scheme 6b)



(1b) **(2b)**

(Scheme 6c)

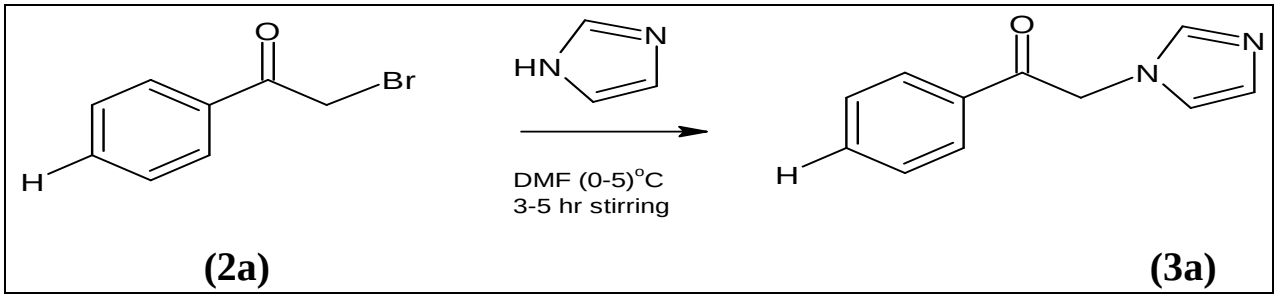


(1c) **(2c)**

3.2]

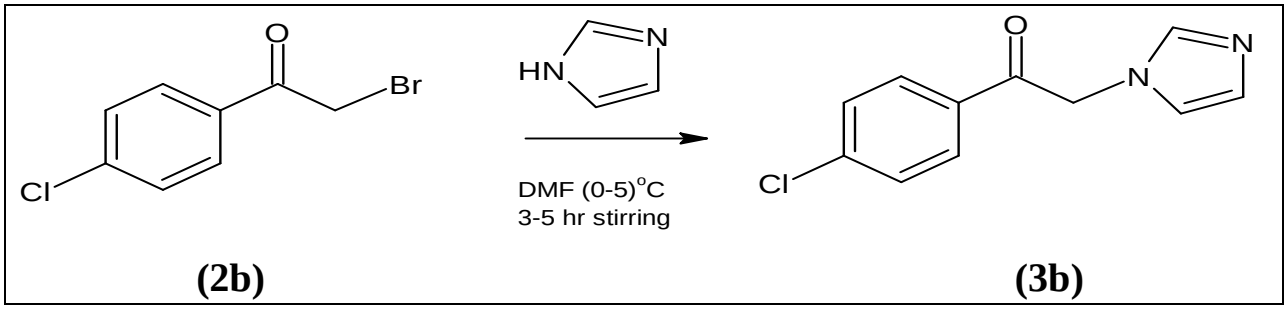
By using earlier prepared p-substitued phenacyl bromides, N-1 sustituted imidazole derivatives were prepared in presence of DMF at lower temperature. **(Scheme 7a-c)**[2,14]

(Scheme 7a)



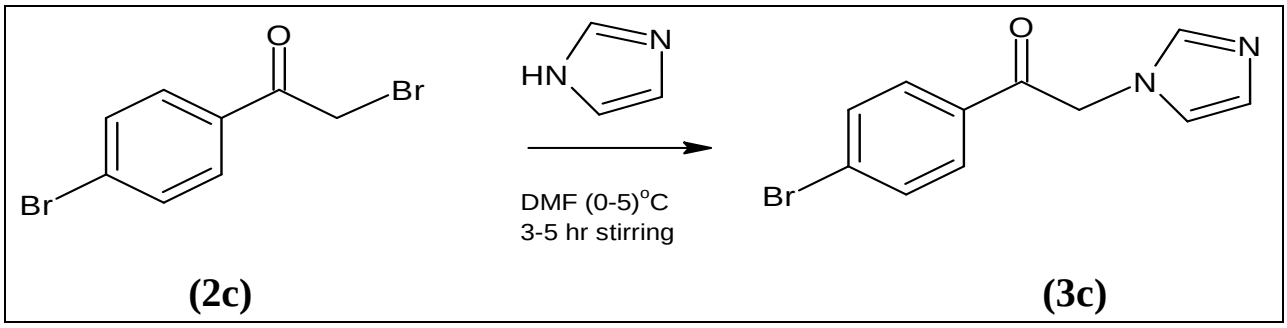
(2a) **(3a)**

(Scheme 7b)



(2b) **(3b)**

(Scheme 7c)



(2c) **(3c)**

4. Results and Discussion

Optimization of synthesis of (2a-c) & (3a-c) is tabulated as follows,

Table-01

Sr. No.	COMPOUND	R	Mol. Formula	Mol. Weight	M.P in ^{0}C		% Yield
					Obs.	Lit.	
1.	(2a)	H	C_8H_7BrO	199.047	46	50	62%
2.	(2b)	Cl	C_8H_6BrClO	233.49	96	99	73%
3.	(2c)	Br	$C_8H_6Br_2O$	277.94	104	109	65%
4.	(3a)	H	$C_{11}H_{10}N_2O$	186.21	112	117	77%
5.	(3b)	Cl	$C_{11}H_9ClN_2O$	220.66	158	160	78%
6.	(3c)	Br	$C_{11}H_9BrN_2O$	265.106	156	168	84%

We started our work by preparing phenacyl bromides **2a-c.** These precursors were obtained by the acid catalysed alpha halogenation (i.e. bromination) of different acetophenones **1a-c** using acetic acid at lower temperature (i.e. 10-12^{o}C). The products formed were filtered and dried. The desired α-bromoketones **2a-c** were recrystallize to enhance the purity of the compound by using suitable solvent**. [15]**

With the a-bromoketones precursors **2a-c** in hand, we envisaged that the reaction between **2a-c** and imidazole could be used to synthesize, *1-(Aryl)-2-(imidazol-1-yl) Ethanone* **(Scheme 7a-c).[2,14]**

5. Experimental Work

All the melting points were determined in open capillaries in a paraffin bath and are uncorrected. Identification of the compounds is done by taking IR spectra of the compounds. The progress of the reactions was monitored by TLC.

6. General Procedure

6.1] Synthesis of p-substituted phenacyl bromide:

p-substituted acetophenone (0.1 Mole) and glacial acetic acid (approx. 40 ml) were placed in a 250 ml round bottom flask. To this solution bromine (0.15 Mole) was added drop wise at 5-10°C for 2hrs and the mixture was kept for stirring overnight. After completion, the reaction mixture was worked out to separate the desired product which is then dried and purified.**[1]**

6.2] Synthesis of *1-(Aryl)-2-(imidazol-1-yl) Ethanone***:**

The solution of imidazole (0.5 mol) in DMF (10 ml) was added dropwise to a solution of appropriate p-substituted phenacyl bromides (0.1 mol) in DMF (10 ml) at a temperature of 0–5˚C with stirring for 3-4hrs, reaction is monitored by TLC. After completion, reaction

mixture was poured into ice water (20ml) with vigorous stirring till the precipitate has been developed. The product was filtered and recrystallized in Toluene.[2,14]

7. Spectral Analysis

8. Conclusion

We prepared p-substitued phenacyl bromides by using acid catalysed α-halogenation of p-substituted acetophenone at lower temperature which lachrymetric in nature ,followed by the synthesis of N-1 substituted imidazole derivatives. The derivatives **3a-c** containing imidazole moiety possesses greater anthelmintic activity. [16]

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URL: http://dx.doi.org/10.15640/jcb.v2n2a3