COPPER(I)CHLORIDE/2,2′-BIPYRIDINE-PROMOTED REACTIONS OF SOME ETHERS, ALCOHOLS AND CONJUGATED KETONES CONTAINING A TRICHLOROMETHYL GROUP

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JULY 2009

CONTENTS

	Page No.
Certificates	i
Acknowledgements	ii
Abstract	iii
List of figures	vi
List of tables	xviii
List of abbreviations	xix
Notes	xxii

Chapter 1 The chemistry of compounds containing a trichloromethyl group

Introduction	1
1.1. Preparation of trichloromethyl compounds	3
1.2. Reactions of trichloromethyl compounds	17

Chapter 2 1,2-H Shift in copper-chlorocarbenoid intermediate during CuCl/bpy-promoted stereoselective dechlorination of 2,2,2-trichloroethyl alkylethers to (*Z*)-1-alkoxy-2-chloro-ethenes

2.1. Statement of the problem	57
2.2. Results and discussion	58
2.3. Medicinal importance of the products 1-alkoxy-2-chloroethenes	83

2.4. Conclusions 85

2.5. Experimental 87

Chapter 3 Synthesis of chloromethyl ketones from trichloromethyl carbinols by CuCl/bpy-promoted 1,2-H shift in the intermediate copper-chlorocarbenoid

3.1 Introduction 109

3.2 Statement of the problem 132

3.3 Results and discussion 132

3.4 Conclusions 139

3.5 Experimental 140

Chapter 4 Copper(I)-promoted alcoholysis of 2,2,2-trichloroethyl alkyl ethers to α-alkoxycarboxylic acid esters

4.1. Statement of the problem 154

4.2. Results and discussion 154

4.3. Importance of α-alkoxyacetic acid esters 177

4.4. Conclusions 179

4.5. Experimental 180

Chapter 5 Copper(I) chloride/bpy-promopted dechlorinative radical dimerization of 2,2,2-trichloroethylideneacetophenones and synthesis of symmetrical 2,5-diaryl-3,4-bis(2,2-dichlorovinyl)furans

5.1. Statement of the problem 205

5.2. Results and discussion 207

5.3. Conclusions 217

5.4. Experimental 218

References 232

Appendix (NMR spectra) 256

Bio-data of the author 355

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BY

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Thesis submitted

in fulfillment of the requirements of degree of

DOCTOR OF PHILOSOPHY

to the

DEPARTMENT OF CHEMISTRY

INDIAN INSTITUTE OF TECHNOLOGY, DELHI

JULY 2009

Dedicated to my parents

Certificates

This is to certify that the thesis entitled "Copper(I)chloride/2,2′-bipyridine-promoted reactions of some ethers, alcohols and conjugated ketones containing a trichloromethyl group", being submitted by Mr. Manoj T. P, to the Indian Institute of Technology, Delhi, for the award of the degree of "Doctor of Philosophy" in chemistry is a record of bonafide research carried out by him. Mr. Manoj T.P has worked under my guidance and supervision, and has fulfilled the requirements for the submission of this thesis, which to my knowledge has reached the requisite standard.

The results contained in this dissertation have not been submitted in part or full, to any other university or institute for the award of any degree or diploma.

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July, 2009

ACKNOWLEDGEMENTS

I wish to express my deep sense of gratitude to my research supervisor ***Dr. Ram N. Ram***, Professor, Department of Chemistry, Indian Institute of Technology, Delhi, for his guidance, interest and encouragement, which made this work possible.

I would like to thanks Head of the Department of Chemistry, Prof. B Jayaram and the ex-Heads of the Department of Chemistry, Prof. H. M Chowla and Late Prof. U. K Nadir for providing the essential facilities for carrying out my research. I also extend my gratitude to Prof. Veena Choudhary, ex-Dean of the student Prof. S. M Istiaque and all other faculty members of the Department of Chemistry for their kind help and support.

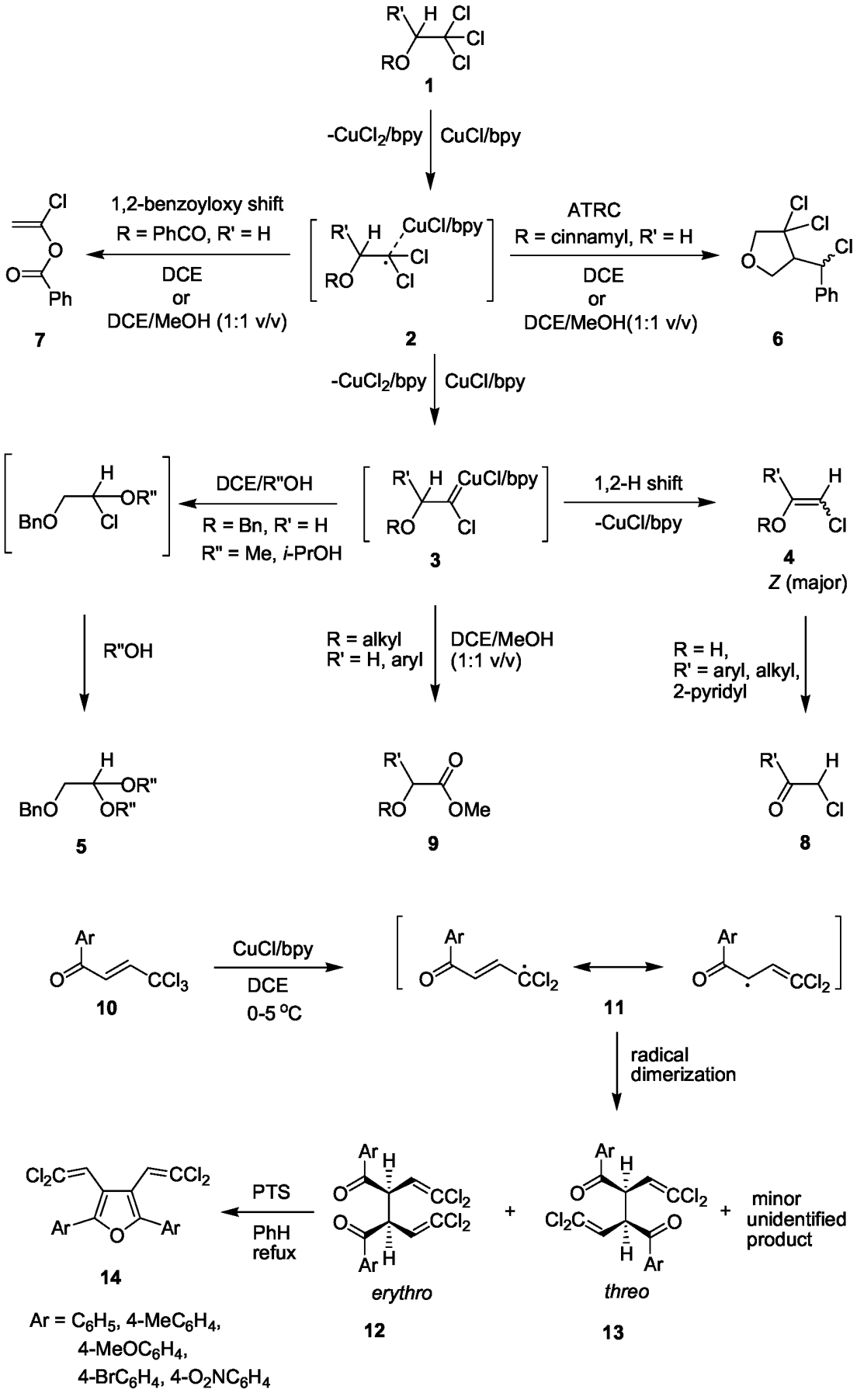
I would like to express many thanks to my laboratory colleagues, Dr. Arif Ali Khan, Dr. Nabin Kumar Mehar, Ashish Kumar Gupta, Mr. Virinder Sing, Mr. Ram Kumar Tittal, Mr. Neeraj Jain, Mr. Vineet Soni and Mr. Dharmendhra Kumar Gupta for their fruitful advices, moral support and uninhibited help from time to time. It is my great pleasure to express many thanks to my friends particularly, Titto Varugheese, Purnendhu Paari, Prosenjit Chattopadhyaya, Raghavendra Panjangam, Venkidesh, Nabhakrishna Behra, Senthil Muthayya, Prince Ashok, Sathyanarayana Sahu, Rahul Sreevastava, Vijay Kathri, Sebastian Joseph, Vinay Kumaar, Prakashan K, Robin Joseph, Renu john and Anith Nelleri for their well wishes and kind help during the tough time at IIT-D life. I would like to express many thanks to all other friends and well wishers for their help and support. The help rendered by the technical staff of the department is duly appreciated.

Lastly and most importantly, I take this opportunity to express my heartfelt affection, love and thanks to my parents and other family members.

Manoj T. P

ABSTRACT

The introductory chapter 1 of the thesis describes some known chlorination and non-chlorination methods of preparation of compounds containing a trichloromethyl group and their reactions, highlighting the solvolytic stability of the trichloromethyl group and its propensity to form radical and carbenoid intermediates by reaction with transition metals, which are relevant to the new work presented in the succeeding chapters 2-5. The new work is concerned with CuCl/bpy-promoted reactions of 2,2,2-trichloroethyl alkyl ethers **1** (R = alkyl in the following scheme), trichloromethyl carbinols **1** (R = H) and β-trichloromethyl-α,β-unsaturated aryl ketones **10**. In aprotic solvents such as DCE, the 2,2,2-trichloroethyl alkyl ethers **1** (R = alkyl) underwent dechlorinative intramolecular 1,2-H shift in copper chlorocarbenoid intermediate **3** produced by successive abstraction of two chlorine atoms by CuCl/bpy to afford predominantly *Z*-enol ethers **4** stereoselectively in good yields. The intramolecular nature of the 1,2-H shift was demonstrated by deuterium labeling experiments. The intermediacy of the chlorocarbenoid **3** was inferred by trapping it as acetals **5** in the presence of methanol and isopropanol in the reaction of a representative substrate, 2,2,2-trichloroethyl benzyl ether **1** (R = Bn, R' = H). In the presence of an easier available pathway for a radical reaction, such as chlorine atom transfer radical cyclization (ATRC) in 2,2,2-trichloroethyl cinnamyl ether **1** (R = cinnamyl, R' = H) and 1,2-benzoyloxy shift in 2,2,2-trichloroethyl benzoate **1** (R = benzoyl, R' = H), the intervening radical intermediate **2** diverted the reaction along these pathways to form **6** and **7,** respectively even in the presence of excess of methanol.


1
-CuCl2/bpy
CuCl/bpy
1,2-benzoyloxy shift
R = PhCO, R' = H
DCE
or
DCE/MeOH (1:1 v/v)
7
CuCl/bpy
2
ATRC
R = cinnamyl, R' = H
DCE
or
DCE/MeOH(1:1 v/v)
6
-CuCl2/bpy
CuCl/bpy
DCE/R"OH
R = Bn, R' = H
R" = Me, i-PrOH
3
1,2-H shift
-CuCl/bpy
4
Z (major)
R"OH
R = alkyl
R' = H, aryl
DCE/MeOH
(1:1 v/v)
R = H,
R' = aryl, alkyl,
2-pyridyl
5
9
8
10
CuCl/bpy
DCE
0-5 °C
11
radical
dimerization
PTS
PhH
refux
14
Ar = C6H5, 4-MeC6H4,
4-MeOC6H4,
4-BrC6H4, 4-O2NC6H4
erythro
12
threo
13
minor
unidentified
product

Application of the reaction to trichloromethyl carbinols **1** (R =H) offered a simple, high yielding, regiospecific, chemoselective and fairly general method for the preparation of chloromethyl ketones **8**, which are important synthetic intermediates. The trichloromethyl group of the 2,2,2-trichloroethyl ethers **1** was converted to a methoxycarbonyl group to yield α-alkoxycarboxylic acid methyl esters **9** predominantly when the reaction was performed in DCE/MeOH (1:1 v/v). The finer details of the mechanism of this alcoholysis reaction are not clear, though involvement of the copper chlorocarbenoid intermediate **3** was strongly indicated. In these reactions, involvement of the initially formed radical intermediate in the key step or a carbocationic intermediate was ruled out on the basis of some other experimental facts. In contrast, the β-trichloromethyl-α,β-unsaturated aryl ketones **10** underwent dechlorinative dimerization to yield a mixture of *erythro* **12** and *threo* **13** 1,4-diaryl-2,3-bis(2,2-dichlorovinyl)butane-1,4-diones in DCE or DCE/MeOH by symmetrical coupling of the allylic radical intermediate **11** with carbon-carbon double bond shift. These 1,4-diketones were cyclodehydrated in the presence of a catalytic amount of PTS to furnish new seemingly useful symmetrically tetrasubstituted furans **14** which exhibited unusual stability towards hydrolysis under acidic conditions.