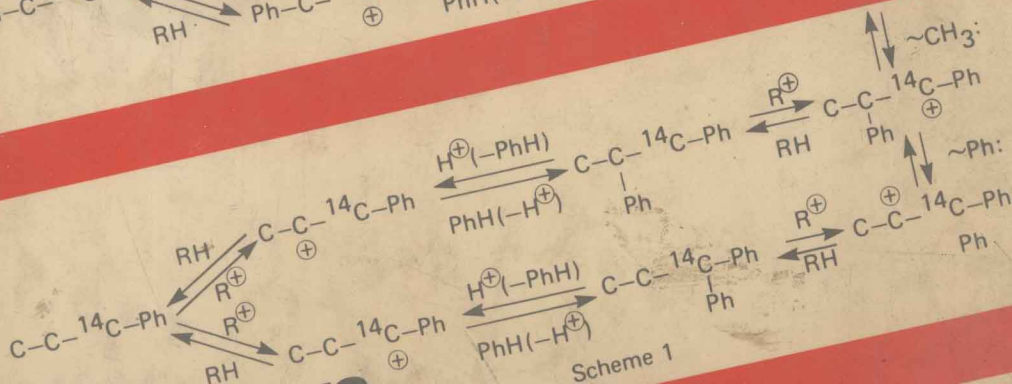


GILBERT
A CENTURY OF DISCOVERY

$RH \rightleftharpoons Ph-\overset{\oplus}{C}-^{14}C-C \rightleftharpoons H^{\oplus}-(PhH) \rightleftharpoons PhH-(H^{\oplus})$



Scheme 1

RH
ROYSTON M. ROBERTS
ALI ALI KHALAF 

FRIEDEL-CRAFTS ALKYLATION CHEMISTRY

A CENTURY OF DISCOVERY

ROYSTON M. ROBERTS

*The University of Texas at Austin
Austin, Texas*

ALI ALI KHALAF

*The University of Assiut
Assiut, Egypt*

MARCEL DEKKER, INC.

New York and Basel

Library of Congress Cataloging in Publication Data

Roberts, Royston M.

Friedel-Crafts alkylation chemistry.

Includes bibliographical references and index.

1. Friedel-Crafts reaction. I. Khalaf, Ali Ali,

[date] . II. Title.

QD281.A5R63 1984 547'.21 84-4265

ISBN 0-8247-6433-1

COPYRIGHT © 1984 by MARCEL DEKKER, INC. ALL RIGHTS RESERVED

Neither this book nor any part may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, microfilming, and recording, or by any information storage and retrieval system, without permission in writing from the publisher.

MARCEL DEKKER, INC.

270 Madison Avenue, New York, New York 10016

Current printing (last digit):

10 9 8 7 6 5 4 3 2 1

PRINTED IN THE UNITED STATES OF AMERICA

This Book is Dedicated to
PROFESSORS
COSTIN D. NENITZESCU
and
ECATERINA CIORANESCU-NENITZESCU
with
Appreciation and Affection

Preface

A comprehensive treatise, *Friedel-Crafts and Related Reactions*, edited by George A. Olah, appeared in 1963-1965. One of the present authors (R.M.R.), with the collaboration of G. J. Fonken, contributed a chapter to that work, and in 1965 he wrote a short review which appeared in *Chemical & Engineering News* (January 25, 1965) under the title "Friedel-Crafts Chemistry." Shortly after its appearance, Dr. Maurits Dekker suggested that an expansion of that review into a monograph which would represent "the heart of Friedel-Crafts chemistry" would be valuable, because the size of the Olah treatise made it impractical for the working chemist, from the viewpoint of both convenience and expense.

This project was initiated with enthusiasm, and its prospects for success were augmented when Dr. Khalaf agreed to become a collaborator; however, other commitments of both authors delayed its completion. In the meantime, Professor Olah updated portions of his contributions to the comprehensive treatise and combined them with some new material to produce a monograph which borrowed with our blessing the title of the 1965 *Chemical & Engineering News* review, "Friedel-Crafts Chemistry." Owing to the differences in viewpoint and interest, it turned out that there was little duplication between Olah's 1973 monograph and our manuscript in preparation, and we concluded that there was still a need for our contribution. One way of subdividing "Friedel-Crafts chemistry" is in terms of *alkylation* and *acylation* reactions. This book is concerned almost entirely with the first category, the larger and more interesting area of alkylation reactions and the competing processes that accompany them, hence the title *Friedel-Crafts Alkylation Chemistry*.

To the average organic chemist, "the Friedel-Crafts reaction" is most likely to bring to mind the reaction of an alkyl halide with benzene in the presence of aluminum chloride catalyst. He or she is also likely to be aware that the alkylbenzene so produced may be of uncertain structure because of the possibility of isomerization, but may not know exactly what the facts are, or where to learn them. This situation is a reasonable one, even at the present time. Rearrangements accompanying Friedel-Crafts alkylations were recognized at a very early date, but many of the early reports were incorrect or at least incomplete because of the lack of modern analytical techniques, and the resultant errors and misconceptions have been perpetuated throughout most of the reviews and textbooks up to the present time.

Although alkylations with alkyl halides have been central to Friedel-Crafts chemistry since the first observations of Friedel and Crafts, the chapter on this subject in the large Olah treatise was far from complete and contained several errors with regard to rearrangements accompanying alkylations. This chapter was not one of the four brought up to date by Olah for his 1973 monograph. In the last two decades, through research in our own laborator-

ies and those of others, most of the mysteries surrounding the rearrangements and other competing processes accompanying Friedel-Crafts alkylations have been cleared up, so that a definitive picture of their relationship to the rest of Friedel-Crafts chemistry may now be given.

This book begins in Chapter 1 with a brief introduction and overview of the whole area of Friedel-Crafts alkylation chemistry. The complications produced by rearrangements and by competing reactions occurring before, during, and/or after alkylation are outlined briefly here. Chapter 2 treats in detail the most common complication, the rearrangement of an alkylating agent preceding its attachment to an aromatic substrate. This chapter includes a survey of the generation and chemistry of carbocations in superacid media.

Chapter 3 is a comprehensive survey of alkylations of arenes with all types of alkyl halides, in which the errors and inconsistencies of the older literature and even textbooks published in very recent years are sorted out and corrected.

Chapters 4 and 5 will probably be of special interest to industrial and other practicing organic chemists. In Chapter 4 alkylations by alkenes, alcohols, and other industrially useful alkylating agents are cataloged and described in detail and, in Chapter 5, a similar extensive treatment is given to alkylations by di- and polyfunctional alkylating agents.

Cyclialkylations make up a wide and important area of Friedel-Crafts alkylation chemistry. Some of the di- and polyfunctional reagents described in Chapter 5 lead to bicyclic and polycyclic products, so that their reactions may be considered to be cyclialkylations. Chapter 6 is devoted to the additional large group of cyclialkylations that occur through intramolecular ring closures of arylhaloalkanes, arylhydroxyalkanes, and arylalkenes.

The last two chapters describe those major complications to Friedel-Crafts alkylations other than the rearrangements of the alkylating agents that occur before or simultaneously with the alkylation step. In Chapter 7 the trans-alkylations and reorientations which have long been known to accompany alkylations are described and interpreted in modern mechanistic terms. In Chapter 8 the more recently recognized rearrangements, dealkylations, and fragmentations that arenes undergo in the presence of Friedel-Crafts catalysts are described, so that the effects of these reactions as complications to desired alkylations may be seen.

We are pleased to acknowledge the continuing encouragement given for this project by Dr. Maurits Dekker, without which the book would never have been completed. We are grateful to Terry Parsons Smith for editorial and technical assistance at an early stage of the work, and to the University of Texas Research Institute for a grant which made this assistance possible. We are indebted to Dr. Thomas L. Gibson, Jr., for similar excellent assistance at a later stage, and we thank him and other former graduate students and post-doctoral associates for their contributions to the research reported in this monograph. Their names will be found in association with those of the authors in references throughout the book. One other person who was invaluable to the completion of the project was Susie Pruett, who typed most of the text and drew most of the figures. Her ability to transform illegible and sometimes slightly Arabic script into clear typescript was a major miracle.

Preliminary planning for the book was done during a summer visit at the Philipps University of Marburg and further organization of material was carried out during a semester spent at the Polytechnic Institute of Bucharest. For these opportunities, one of us (R.M.R.), expresses his appreciation to the Fulbright-Hayes program and to the host institutions, and he also wishes

especially to thank Professor Karl Dimroth (Marburg) and Professors A. T. Balaban and E. Cioranescu-Nenitzescu (Bucharest) for their hospitality during these visits. A.A.K. is grateful for support from Assiut University (Assiut, Egypt) and from King Abdulaziz University (Jeddah, Saudi Arabia).

Both authors are greatly indebted to the Robert A. Welch Foundation for generous support in the form of fellowships and other financial aid to the research at the University of Texas at Austin. We believe that it may be seen that this research has resulted in significant contributions to the new Friedel-Crafts alkylation chemistry described in this book.

Finally, we wish to thank our wives, Phyllis and Magida, for their unselfish encouragement and their understanding of the neglect they uncomplainingly encountered during the long gestation period of the book.

Royston M. Roberts
Ali Ali Khalaf

Contents

Preface	v
1 INTRODUCTION AND SCOPE	1
I. Discovery of the Friedel-Crafts Reaction	1
II. Rearrangements Accompanying Alkylation	1
III. Types of Alkylating Agents	2
IV. Cyclialkylations	3
V. Transalkylations and Reorientations	4
VI. Rearrangements of Arenes	4
VII. Dealkylations and Fragmentations of Arenes	5
References	6
2 REARRANGEMENTS OF ALKYLATING AGENTS	7
I. Rearrangements of Alkylating Agents in the Presence of Metal Halide Catalysts	8
II. Rearrangements of Alkylating Agents and Related Compounds in the Presence of Superacids	44
III. Mechanistic Aspects	103
References	108
3 ALKYLATIONS OF ARENES WITH ALKYL HALIDES	122
I. Alkylations with Methyl and Benzyl Halides	122
II. Alkylations with Linear Primary Alkyl Halides	138
III. Alkylations with Linear Secondary Alkyl Halides	164
IV. Alkylations with Branched Alkyl Halides	181
V. Alkylations with Cycloalkyl and Related Halides	204
Summary	213
References	215
4 ALKYLATIONS OF ARENES WITH ALCOHOLS, ETHERS, ESTERS, AND ALKENES	228
I. Introduction	228
II. Alkylations with Linear Primary Alcohols, Ethers, and Esters	228
III. Alkylations of Arenes with Linear Alkenes and Linear Secondary Alcohols, Ethers, and Esters in the Presence of Various Catalysts	249
IV. Alkylations of Arenes with Branched Alkenes, Alcohols, Ethers, and Esters	291
V. Alkylations of Arenes with Cycloalkenes and Cycloalkanols	330
VI. Alkylations of Arenes with Heterocyclic Derivatives	347
References	378
	ix

5	ALKYLATIONS WITH DI- AND POLYFUNCTIONAL ALKYLATING AGENTS	404
	I. Alkylations with Di- and Polyhaloalkanes	404
	II. Alkylations with Unsaturated Alkyl Halides, Alcohols, and Ethers	457
	III. Alkylations of Aromatics with Dienes	488
	IV. Alkylations with Miscellaneous Di- and Polyfunctional Reagents	502
	References	507
6	FRIEDEL-CRAFTS CYCLIALKYLATION REACTIONS	521
	I. Introduction	521
	II. Cyclialkylations of Arylhaloalkanes and Related Systems	521
	III. Cyclialkylations of Arylalkanols, Arylalkenes and Related Systems	570
	References	661
7	TRANSALKYLATIONS AND REORIENTATIONS OF ARENES INDUCED BY FRIEDEL-CRAFTS CATALYSTS	673
	I. Early Reports of Transalkylations and Reorientations of Methyl-, Ethyl-, and <i>n</i> -Propylbenzene	673
	II. Transalkylations and Reorientations of Methylarenes	674
	III. Higher Alkylarenes: Intra- and Intermolecular Mechanisms of Transalkylations and Reorientations	676
	References	697
8	REARRANGEMENTS, DEALKYLATIONS, AND FRAGMENTATIONS OF ARENES INDUCED BY FRIEDEL-CRAFTS CATALYSTS	701
	I. Rearrangements of Arenes	701
	II. Dealkylations of Arenes	726
	III. Fragmentations of Arenes	747
	References	760
	Index	763

Introduction and Scope

I. DISCOVERY OF THE FRIEDEL-CRAFTS REACTION

The reaction of benzene with "amyl chloride" in the presence of aluminum chloride to produce "amylbenzene" was carried out by Charles Friedel and his American collaborator James Mason Crafts in Paris on May 14, 1877, and the results were reported orally to the Chemical Society of France a few days later [1]. This was apparently the first typical Friedel-Crafts alkylation reaction, although Friedel and Crafts had earlier tested the behavior of various combinations of aluminum, aluminum chloride, organic halides, and hydrocarbons. Their oral report contained the statement: "With a mixture of chloride and hydrocarbon, the formation is established, in good yield, of hydrocarbons from the residues of the hydrocarbon less H and from the chloride less Cl. It is thus that ethylbenzene, amylbenzene, benzophenone, etc., are obtained" [1]. Thus in their first communication they described products of both alkylation and acylation. Friedel and Crafts recognized the practical importance of their discovery, as is shown by the fact that they immediately secured patents in both France and England on procedures for preparing hydrocarbons and ketones. Their judgment was accurate; probably no other reaction has been of more practical value. Major processes for the production of high-octane gasoline, synthetic rubber, plastics, and synthetic detergents are applications of *Friedel-Crafts chemistry*. Aside from its commercial importance, this area of organic chemistry encompasses classic examples of some of the most interesting aspects of modern organic theory: electrophilic aromatic substitution and carbocation formation and rearrangement. In the following chapters we examine both the practical and theoretical aspects of Friedel-Crafts chemistry.

II. REARRANGEMENTS ACCOMPANYING ALKYLATION

Within a matter of months after its discovery, one of the limitations to the alkylation reactions as a synthetic method was revealed by the Russian chemist G. Gustavson [2]: the same product, isopropylbenzene, was obtained from either *n*-propyl bromide or isopropyl bromide and benzene and aluminum chloride. This was the first indication that the alkyl group being attached to the aromatic ring may suffer a structural rearrangement. (It is now known that the reaction with *n*-propyl bromide gives some *n*-propylbenzene as well as the major product, isopropylbenzene, but the presence of the normal product went undetected in the early work.) The formation of isopropylbenzene was attributed to the isomerization of *n*-propyl bromide, brought about by the effect of the catalyst prior to alkylation. This isomerization of the alkylating agent was demonstrated separately [3]. *sec*-Butylbenzene was reported to be the alkylation product from *n*-butyl chloride, and *t*-butylbenzene the product

from both *t*-butyl and isobutyl chlorides. In the reaction of the latter halide, a gaseous hydrocarbon thought to be isobutylene was observed and this was assumed to be the intermediate for the rearranged product [4]. Interestingly, unchanged isobutyl chloride was recovered from one of the reaction mixtures.

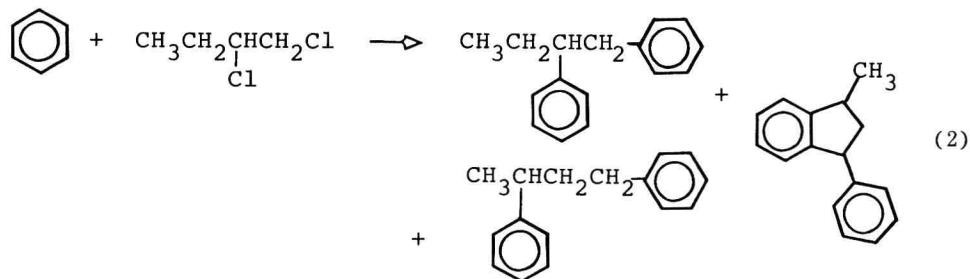
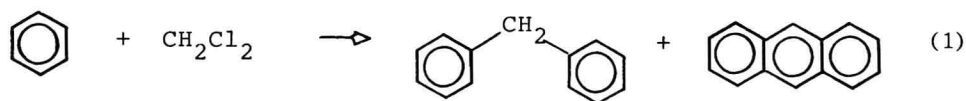
Although these particular early examples of rearrangement have been checked and confirmed by modern analytical techniques, quite a number of incorrect accounts of rearrangements have appeared in the literature. On the basis of both correct and incorrect reports, generalizations and extrapolations have been made that range from misleading to downright incorrect, and some of these fallacies have carried over into even recent publications [5]. Specific cases will be examined in detail in the following chapters, but we shall try to set the record straight briefly at this point.

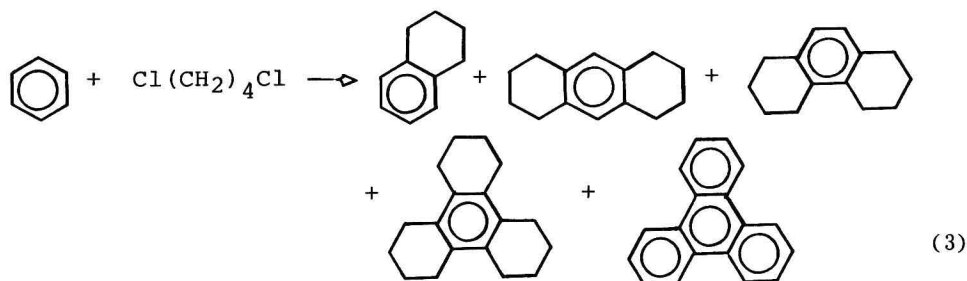
The generalization that "the usual tendency in rearrangement of the alkyl groups during alkylation is in the direction primary \rightarrow secondary \rightarrow tertiary" [5-(c)-(e)] is only partially correct, because although primary groups usually rearrange to secondary, secondary groups do not usually rearrange to tertiary. *n*-Butyl halides lead to *sec*-butyl groups, but not usually to *t*-butyl [5(a),(b)]. *t*-Alkyl halides do not always form *t*-alkylbenzenes [5(c)], but may indeed produce *sec*-alkylbenzenes. Thus it may be seen that the generalization which has perhaps made the strongest impression, "regardless of the configuration of the alkyl halide, the final product contains an alkyl group of the highest possible branching" [5(a)], is nevertheless wrong.

III. TYPES OF ALKYLATING AGENTS

Although the alkylating agents involved in the discovery of the Friedel-Crafts reaction were alkyl halides, and these compounds are most commonly used in textbook examples of the reaction, many other types of alkylating agents have been used. In fact, some of the most important commercial applications employ alkenes, such as the synthesis of styrene from ethylene and cumene from propylene. Alcohols and ethers are also useful types of alkylating agents. Alkylations with alkyl halides are discussed in Chap. 3 and those involving the other alkylating agents are discussed in Chap. 4.

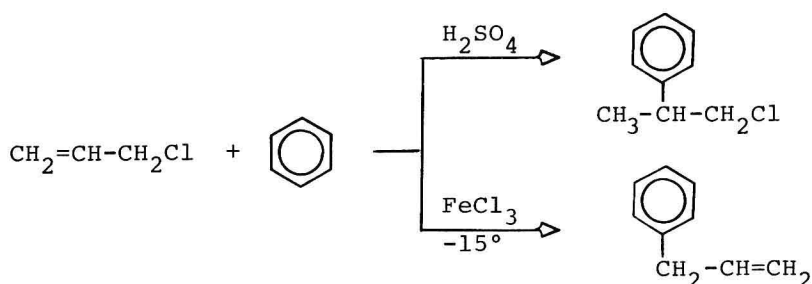
Some of the most interesting and useful applications of the Friedel-Crafts reaction are those in which di- and polyfunctional alkylating agents are em-





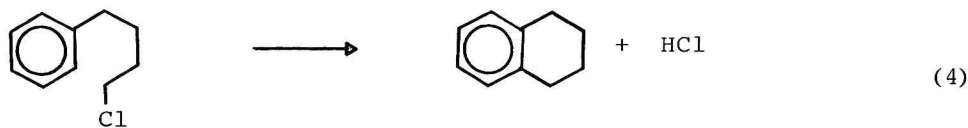
ployed with arene substrates. Reactions with dihalides may lead to a wide variety of products, such as diarylalkanes, polycyclic arenes, indans, tetralins, and other alicyclic arenes, as shown in Eqs. (1) to (3).

The reaction of an unsaturated alkyl halide with an arene may take place at either or both of the reactive sites, that is, the halide and/or the double bond, depending on the type of catalyst and the conditions. In general, protonic catalysts favor reaction of the double bond and metal halides favor reaction at the halide site:



IV. CYCLIALKYLATIONS

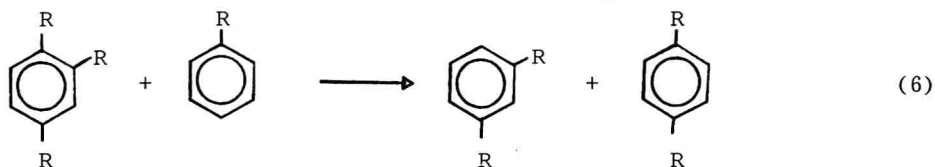
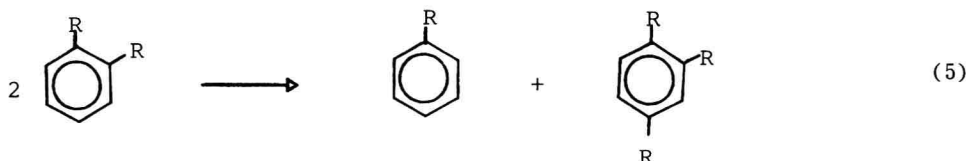
Some of the products in Eqs. (1) to (3) are formed by processes in which the difunctional alkylating agent first reacts with the arene to yield an aryl-substituted monofunctional compound, which then undergoes an intramolecular alkylation to produce the alicyclic ring. Although the term *cyclialkylation* has been applied more generally (to any Friedel-Crafts alkylation of arenes with difunctional compounds such as dichlorides, diols, and dienes in which a new ring is formed), we shall use it in the more limited sense to describe intramolecular ring closures such as that of an arylhaloalkane (Eq. 4).



Reactions of di- and polyfunctional alkylating agents with arenes (some of which produce cyclizations) are described in Chap. 5 and cyclialkylations are described in Chap. 6.

V. TRANSALKYLATIONS AND REORIENTATIONS

Another feature of Friedel-Crafts alkylation observed from the start was polyalkylation. Alkylation of benzene did not stop with the introduction of one alkyl group onto the ring; di-, tri-, and higher-alkylated benzenes were produced, although their production could be controlled to some extent by using a molar excess of benzene and by variations in other experimental parameters. It was also shown that alkyl groups could be transferred from one aromatic ring to another by the catalytic effect of aluminum chloride. For example, when ethylbenzene was heated with the catalyst, a mixture of benzene, ethylbenzene, diethylbenzene (mainly *m* and *p* isomers), and higher-boiling material was produced [6]. An unusual feature of both polyalkylations and transalkylations (also called disproportionations) was the rather high proportions of *meta*- and 1,3,5-oriented isomers produced. These have been explained in terms of the dealkylation of a 1,2,4-trialkyl derivative (to produce an *m*-dialkylbenzene) or the reorientation of 1,2-, 1,4-, and 1,2,4-derivatives in the presence of an excess of catalyst. As discussed in detail in Chap. 7, the type of Friedel-Crafts rearrangement represented by a reorientation of an *ortho*- or a *para*-dialkylbenzene to a *meta*-dialkylbenzene is intimately related to the transalkylation reaction: the reorientation of most dialkylbenzenes cannot be demonstrated without the concurrent production of transalkylation products. Thus it is possible that some observed reorientations take place by an intermolecular transalkylation process rather than by a true intramolecular reorientation (Eqs. 5 and 6).

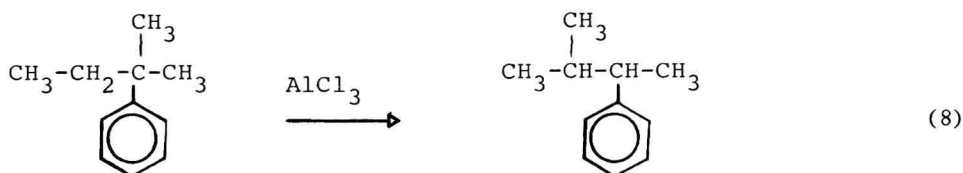
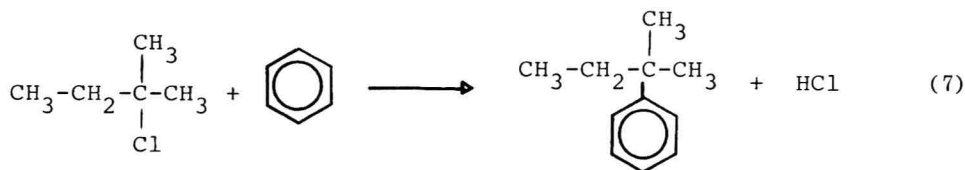


VI. REARRANGEMENTS OF ARENES

Although the Friedel-Crafts alkylation reaction has been widely used as a synthetic procedure, as we have already noted there are inherent limitations which have complicated its practical applications. These include polyalkylation, which can be controlled without too much difficulty, the problem of producing the desired orientation of the alkyl group, or groups, when more than one is introduced, and the possible rearrangement of the alkyl group whenever it is larger than ethyl. The latter two complications cannot be controlled in some cases, but if they are correctly recognized, the utility and reliability of Friedel-Crafts alkylation procedures are little impaired.

More recently an additional complication has been discovered, the isomerization of the side chain of an alkylbenzene *after* attachment to the aromatic ring [7]. This new reaction has been called the *alkylbenzene rearrangement*. It is the occurrence of this unexpected rearrangement which is responsible for some of the fallacies in the generalizations mentioned in Sec. II. For ex-

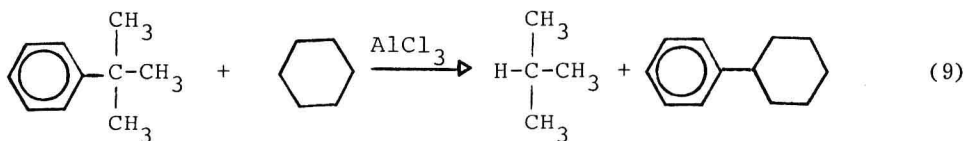
ample, alkylation of benzene with *t*-pentyl chloride and aluminum chloride gives the secondary alkylbenzene 2-methyl-3-phenylbutane as the major product, because the initially formed *t*-pentylbenzene undergoes a subsequent rearrangement (Eqs. 7 and 8).



Details of this and of other alkylbenzene rearrangements are given in Chap. 8.

VII. DEALKYLATIONS AND FRAGMENTATIONS OF ARENES

True reversibility of Friedel-Crafts alkylation implies dissociation of an alkylbenzene into benzene and alkene, or alkyl halide, etc. Under ordinary alkylating conditions the thermodynamic equilibrium is so far on the side of alkylation that the reaction is irreversible for all practical purposes. However, some of the early workers in Friedel-Crafts chemistry observed the evolution of saturated hydrocarbon gases from reaction mixtures in which an alkylbenzene was heated with aluminum chloride. In 1886 Anschutz [6] reported that a saturated gas, free of chlorine, was produced from cymene, and toluene was found among the liquid products of the reaction. The gas was later identified as propane [8]. The evolution of propane from cymene suggests that a transient isopropyl cation is formed and may abstract a hydride ion from some source in a fast step that diverts it from the alkylation equilibrium. This hypothesis was supported by results of experiments in which cycloalkanes (as sources of hydride ions) were added to various alkylbenzenes in the presence of aluminum chloride [9]. Alkanes corresponding to the side chains of the alkylbenzenes were evolved in an order of ease in conformity with carbocation stability: *t*-butyl > *sec*-butyl > isopropyl (ethyl and methyl were not cleaved).



Actually, secondary and tertiary alkylbenzenes require no added source of hydride ions for dealkylation by aluminum chloride, and even primary alkylbenzenes such as *n*-butylbenzene undergo some (ca. %5) dealkylation at 100°C [10]. The obvious source of the hydride ion necessary for the formation of an alkane after cleavage from the side chain of an alkylbenzene molecule is the side chain of another molecule; the secondary and tertiary

benzylic hydrogens should be especially susceptible to abstraction. Other sources of hydride exchange are possible and will be discussed when mechanisms for dealkylation are described in detail in Chap. 8.

Ipatieff and Pines [9] reported that dealkylation of *sec*-butylbenzene produced only *n*-butane. With the added capability of gas chromatography, more recently it was possible to demonstrate that isobutane was also produced from *sec*-butylbenzene, and the dealkylation product from 2-phenylpentane was found to be almost entirely (96%) isopentane. Thus we see here another type of Friedel-Crafts rearrangement—the rearrangement of an alkyl group accompanying the dealkylation reaction.

The development of sensitive and convenient analytical methods in recent years has led to the recognition of one further type of reaction of alkylbenzenes that takes place when they are heated with Friedel-Crafts catalysts, especially at higher temperatures. Whereas dealkylation applies to a reaction producing an alkane corresponding to the side chain of an alkylbenzene, the term *fragmentation* may be used for the process that produces alkanes with fewer carbon atoms than the original alkylbenzene. Only a few scattered observations of such reactions were noted until recently. However, gas chromatography has made it easy to demonstrate that almost a complete spectrum of lower alkanes and alkylbenzenes is produced by heating an alkylbenzene with aluminum chloride at 100°C for a short time [10].

It is probably impossible to study fragmentation as an individual reaction, because the required conditions are more vigorous than those for dealkylation, rearrangement, transalkylation, and reorientation. In fact, there is evidence that common intermediates are involved in several of these reactions. The interrelationship of these reactions is explored in Chap. 8.

REFERENCES

1. Fridel, C., and J. M. Crafts, *Bull. Soc. Chim. Fr.*, (2), 27, 530 (1877).
2. Gustavson, G., *J. Russ. Phys.-Chem. Soc.*, 10, 269 (1877); *Chem. Ber.*, 11, 1251 (1878).
3. Kekule, A., and H. Schrötter, *Chem. Ber.*, 12, 2279 (1879); Gustavson, G., *Chem. Ber.*, 16, 958 (1883).
4. Schramm, J., *Monatsh. Chem.*, 9, 613 (1888).
5. (a) Calloway, N. O., *Chem. Rev.*, 17, 332, 367 (1935); (b) Gilman, H., and R. M. Meals, *J. Org. Chem.*, 8, 135 (1943); (c) Drahowzal, F. A., in *Friedel-Crafts and Related Reactions*, (G. A. Olah, ed.), Vol. 2, Part 1, Wiley-Interscience, New York, 1964, p. 446; (d) Olah, G. A., in *Friedel-Crafts and Related Reactions*, Vol. 1, (G. A. Olah, ed.), Wiley-Interscience, New York, 1963, p. 68; (e) Olah, G. A., *Friedel-Crafts Chemistry*, Wiley-Interscience, New York, 1973, p. 68; (f) Hendrickson, J. B., D. J. Cram, and G. S. Hammond, *Organic Chemistry*, 3rd ed., McGraw-Hill, New York, 1970, p. 670.
6. Anschütz, R., *Justus Liebigs Ann. Chem.*, 235, 177 (1886).
7. (a) Schmerling, L., and J. P. West, *J. Am. Chem. Soc.*, 76, 1917 (1954); (b) Roberts, R. M., and S. G. Brandenberger, *Chem. Ind.*, 227 (1955); Roberts, R. M., *Intra-Sci. Chem. Rep.*, 6(2), 89 (1972), and references given there.
8. Schorger, A. W., *J. Am. Chem. Soc.*, 39, 2671 (1917).
9. Ipatieff, V. N., and H. Pines, *J. Am. Chem. Soc.*, 59, 56 (1937).
10. Roberts, R. M., E. K. Baylis, and G. J. Fonken, *J. Am. Chem. Soc.*, 85, 3454 (1963).

Rearrangements of Alkylating Agents

The whole field of Friedel-Crafts chemistry began with a report by Friedel and Crafts on the action of aluminum chloride on alkyl chlorides. In 1877, these pioneers made two preliminary oral communications to the Chemical Society of France describing their experiences relating to the action of aluminum chloride on alkyl chlorides particularly "amyl chloride" [1,2]. They stated that the interaction of amyl chloride with aluminum chloride in the cold "gave rise to an intense evolution of hydrogen chloride, to some combustible gases from saturated hydrocarbons, and to some condensed products."

A month later, Friedel and Crafts published a more detailed account of their findings in which they emphasized that the active catalyst in these reactions was the metal chloride [3]. In these reports, however, there is no indication that they were aware of the isomerizing effect of the catalyst on the alkyl chloride.

In fact, the real interest in the study of the rearrangements of alkyl halides by metal halide catalysts arose after Gustavson claimed that the reaction of benzene with either *n*-propyl or isopropyl bromide in the presence of aluminum chloride resulted only in the formation of isopropylbenzene [4]. The first explanation of Gustavson's claim was given in terms of isomerization of *n*-propyl to isopropyl bromide prior to the alkylation process itself. This type of explanation inspired numerous chemists to investigate the behavior of alkylating agents under the influence of Friedel-Crafts catalysts in order to understand the results of alkylations utilizing these agents. More important, in recent years a great deal of effort has been devoted toward elucidating the complex nature of the rearrangements of alkylating agents under Friedel-Crafts conditions; e.g., to resolve the question of whether or not these rearrangements occur concurrent with or consecutive to substrate ionization, and to seek evidence for or against the involvement of intermediates such as alkenes, protonated cyclopropanes, and primary carbocations. The present chapter concentrates on understanding the various isomerization processes observed when Friedel-Crafts alkylating agents such as halides and alcohols are subjected to the action of Friedel-Crafts catalysts.

In discussing these rearrangements we shall distinguish between two types: (1) those induced by metal halides, which will be discussed first; and (2) those induced by strong acids.

1. REARRANGEMENTS OF ALKYLATING AGENTS IN THE PRESENCE OF METAL HALIDE CATALYSTS

A. Rearrangements in Acyclic Systems

1. Rearrangements in linear acyclic systems

a. Ethyl rearrangements

Studies on the isomerization of ethyl halides similar to those of propyl halides are made possible by labeling one of the carbon atoms with carbon 13 or carbon 14. The case of ethyl halide rearrangement is of particular importance because, first, it presents an ideal model to determine whether or not primary to primary carbocation rearrangements may occur, and second, as will be evident later, it gives more insight into the mechanism of Friedel-Crafts alkylation.

The finding that labeled ethyl halide can be rearranged in the presence of aluminum halide was first reported by Roberts et al. [5]. These workers found that ethyl- β - ^{14}C chloride was almost completely isomerized by standing over aluminum chloride at room temperature for 1 hr. The same workers also reported that the Friedel-Crafts alkylation of benzene with ethyl- β - ^{14}C chloride gave ethylbenzene with no isotope-position rearrangement in the ethyl side chain, if the ethyl- β - ^{14}C chloride was added to a mixture of benzene and aluminum chloride.

The authors used the alkylation reaction as a means of determining the extent of isotopic rearrangement produced in ethyl- β - ^{14}C chloride by treatment with aluminum chloride in the absence of benzene. Thus the ethyl chloride recovered after standing over aluminum chloride for 1 hr was used to alkylate benzene, the ethylbenzene obtained was oxidized to benzoic acid, and the molar radioactivity of the latter was measured.

A more detailed study of a similar isotopic isomerization was conducted by Sixma and Hendriks [6]. These investigators carried out the isomerization of ethyl- α - ^{14}C bromide with and without solvents using aluminum bromide as catalyst. They found that the rate of isomerization was lower in nitrobenzene than in carbon disulfide, and still lower in nitromethane. The isomerization was much faster in the absence of solvents. From measurements of the reaction rate at temperatures between 25 and 50°C, Sixma and Hendriks calculated the apparent activation energy of the reaction as 19.1 kcal/mol. Interestingly, these authors also pointed out that the isomerization of ethyl bromide by aluminum bromide does not take place via elimination and readdition, since no appreciable amounts of hydrogen are exchanged for deuterium in the presence of deuterium bromide.

The isomerization of ethyl- β - ^{14}C iodide in the presence of aluminum chloride was similarly investigated by Lee et al. [7]. Since ethylation of benzene with ethyl- β - ^{14}C iodide was also shown to proceed with no detectable rearrangement, the investigators applied the alkylation-oxidation procedure previously used by Roberts et al. [5] as a means of measuring the rearrangement of the ^{14}C -labeled atoms from the β to the α positions of the ethyl iodide.

As in the cases of ethyl chloride and bromide, the degree of isotope-position rearrangement induced by aluminum chloride on ethyl- β - ^{14}C iodide was shown to be dependent on temperature, contact time, and ratio of the catalyst to the ethyl iodide.

It is of interest to point out here that analysis of the data obtained by the various groups of workers on the isotopic rearrangement of radioactive ethyl halides [5-7], together with those of Brown and Wallace [8] on the addition compounds of aluminum halides with alkyl halides, reveals that the apparent