Chapter 17

C-H ACTIVATION AND FUNCTIONALIZATION OF ALKANES AND ARENES

1. INTRODUCTION

Although alkanes are considered to be inert, some classical reactions have been known for a long time, for instance with halogens, reactive radicals and superacids. The C-H bond that is cleaved in such reactions is the weakest one, i.e. reaction occurs at the most substituted carbon. Thus, the radicals R• or carbocations R+ formed react at their most substituted carbon atom giving branched products. The selectivity in the above reactions always is: tertiary > secondary > primary.

In Chap. 3, we have examined the addition of an alkane C-H bond to a 16-electron metal center M giving a transient 18-electron metal-alkane intermediate M(RH) that ultimately gives oxidative addition of the C-H bond to M(R)(H). In this organometallic reaction, activation of the C-H bond occurs at the less substituted carbon for steric reasons. For instance, a linear alkane yields an n-alkyl-metal species via C-H activation at a terminal methyl group. The selectivity is thus primary > secondary > tertiary. This opens the valuable possibility of generating linear alkyl-functionalized products if such an oxidative addition mechanism can be made catalytic:

However, in addition to facing the functionalization of the strongest C-H bond (the terminal one) of the alkane molecule, it is necessary to overcome the fact that the monofunctional products are usually more reactive than the alkane starting material. Alcohols tend to form ketones, aldehyde and CO₂, and monohalogenated alkanes may react further to give gem-dihalogenated products. Finally, most reactions of alkanes such as carbonylation and dehydrogenation are endergonic. Thus, in view of these problems, the goal of selective terminal alkane functionalization is very challenging. In fact, no industrial alkane functionalization process is based on alkane oxidative addition.

Yet, it is of great interest to now examine what these remarkable organometallic concepts of oxidative addition and σ-bond metathesis elaborated in the early 1980s
have brought in terms of practical catalytic functionalization of alkanes and
arenes.\textsuperscript{17.1} It is also essential to include all the types of systems that can activate
C-H bonds by metals by extending our scope to include non-classical organomet-
allic systems, which allows comparison, mutual enrichment and confrontation of
hypotheses.\textsuperscript{17.1}

Thus, as in the case of alkenes in the preceding chapter, we start with the radical
type of activation that is much older. Transition-metal compounds play a key role in
radical activation, because they provide very strong oxidants that can oxidize
hydrocarbons either by (reversible) electron transfer or H-atom transfer (more rarely
by hydride transfer). Biological oxidation of hydrocarbons involves reactive metal-
oxo species in methane mono-oxygenases and many related synthetic models, and a
number of simple metal-oxo complexes also work. The clear criterion of distinction
between an organometallic C-H activation and a radical activation is the above
selectivity in activated C-H bonds.

Finally, as we move to arenes, it is found that C-H activation is more facile than
with alkanes, because arenes are more electron rich than the latter, i.e. for instance
they are easier to oxidize by single electron transfer (their oxidation potential is
lower than that of alkanes), and they react more readily than alkanes with electrophiles. They can also coordinate more strongly than alkanes to transition
metals, because of their ability to accept much more backbonding from transition
metals than alkanes do, which facilitates further activation. Electrophilic activation
of C-H bonds known from Friedel-Crafts reactions with organic electrophiles, has
also been known with metal electrophiles since the end of the xixth century and now
provide really efficient catalytic C-H activation reactions. Finally, given the
richness and variety of the C-H activation field, it is not surprising that organic
chemists have focused on the possibility of functionalizing alkane segments in
complex organic substrates, in particular via coordination-directed C-H bond
activation.\textsuperscript{17.1b,c}

\section*{2. Alkanes and Cycloalkanes}

\subsection*{2.1. Radical-type Oxidation}

The direct oxidation of methane and alkanes by very strong oxidants according to a
single electron-transfer pathway is followed by deprotonation of the extremely
acidic radical cationic species RH\textsuperscript{++}:

\[ \text{RH} \rightarrow \text{RH}^{++} \rightarrow \text{R}^{+} \rightarrow \text{products} \]

For instance, peroxodisulfate oxidizes methane to alcohols in the absence of a metal
at 105-115°C. Metal complexes can be used as mediators for such reactions which
permits carrying out the reactions at lower reaction temperatures.\textsuperscript{17.1} In the case of
cycloalkanes, strongly electrophilic and oxidizing transition-metal ions play an
irreplaceable role in the initiation step.