Project #: CONTR
Center #: R6345-1A0
Contract #: R45-86-06-D2
Prime:

Cost share #: Center shr #:

Subprojects #: N
Main project #:

Project unit: CHEM
Unit code: 02.010.136

Sponsor/division names: NIH/PHS/NIH
Sponsor/division codes:

Award period: 06/07/89 to 09/30/89 (performance) 09/30/89 (report)

Sponsor amount New this change Total to date
Contract value 123,842.00 123,842.00 123,842.00
Funded 123,842.00 123,842.00
Cost sharing amount 0.00 0.00

Does subcontracting plan apply #: N

OXIDATION OF AROMATIC HYDROCARBONS

PROJECT ADMINISTRATION DATA

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Security class (U,C,S,TS): Defense priority rating: Equipment title vests with:

Administrative comments - INITIATION

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supplemental sheet

GIT X
NOTICE OF PROJECT CLOSEOUT

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

Date 8/24/89

Project No. G-33-614
Center No. R6345-1A0

Project Director L. M. Tolbert

School/Lab Chemistry

Grant/Grant No. 5 RO1 CA43806-02

GTRC XX GIT

Contract No. N/A

Biooxidation of Arylalkyl Hydrocarbons

Active Completion Date 6/30/89 (Performance) 9/30/89 (Reports)

Closeout Actions Required:

None

Final Invoice or Copy of Last Invoice

Final Report of Inventions and/or Subcontracts

Government Property Inventory & Related Certificate

Classified Material Certificate

Release and Assignment

Other

Subproject No(s). 

Project Under Main Project No.

Subproject Project No. G-33-606 Continued by Project No. G-33-666

Distribution:

Project Director
Administrative Network
Accounting
Procurement/GTRI Supply Services
Research Property Management
Research Security Services

X Reports Coordinator (OCA)

GTRC

Project File

Contract Support Division (OCA)

Other

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SECTION IV
PROGRESS REPORT SUMMARY

GRANT N. CA43806-03

M. Tolbert

Georgia Tech Research Corporation

July 1, 1989 June 30, 1990

TITLE OF PROJECT (Repeat title shown in item 1 on first page)

Bio-oxidation of Arylalkyl Hydrocarbons

1. Proposed Research. No significant changes in the scope of the research are anticipated from that proposed in the original application and as modified in the 1988 report. This reflects our progress in achieving the aims of developing models for side-chain vs. ring attach in radical cation intermediates. However, we will complete studies on pyridine nucleophiles which provide insight into the role of nucleophile basicity in the partition. Also, in order to provide a complete picture of the decomposition pathways, we will further investigate the reaction manifold which results in dealkylation of 9,10-dialkylanthracenes to yield anthraquinone as the ultimate oxidized product.

Progress. As outlined in our 1988 report, we have included additional oxidants in our studies, particularly those used as model compounds for cytochrome P450. These particularly include (tetraphenylporphinato)iron oxide (TTP-Fe=O), the so-called "ferryl complex." We have discovered significant differences between reaction pathways with this oxidant and with tris(phenanthroline)iron(III) (Fe(phen)_3), our model one-electron oxidant. These differences, however, show up at the secondary oxidation stage, that is, in the oxidation of the initially formed hydroxymethyl intermediate. This intermediate undergoes further oxidation by Fe(phen)_3 in non-aqueous solvents to yield formaldehyde and 10-methylanthrone. The significance of this result rests in the requirement that such reaction involve carbon-carbon bond cleavage. These studies are preliminary, and the biological relevance of formaldehyde generation in the overall mutagenicity of dimethylanthracene derivatives has not yet been ascertained. However, we do observe that TPP-Fe=O also produces oxidative demethylation with formaldehyde formation as well. We previously had noted an anomalous irreversible cyclic voltammetric wave in the oxidation of 9-(hydroxymethyl)-10-methylanthracene, which we attributed to an internal solvation to yield a spiroepoxide intermediate. This additional evidence for anomalous chemical reactivity for the hydroxymethyl compound has relevance to the whole issue of mechanism in arene epoxidation, which we are currently elaborating through product studies.

The product of oxidative carbon-carbon bond cleavage, i.e., 10-methyl-9-anthrone undergoes further oxidation to 10-methyl-10-hydroxy-9-anthrone and 9,10-anthraquinone, the latter involving a second demethylation step. Obviously, such demethylation is a salient feature of metabolism of meso-alkylanthracene derivatives, and we are elucidating the details of this reaction pathway as a function of oxidant.

As part of our studies on the partition between side-chain deprotonation and ring attack, we have investigated the effect of basicity on that partition, using pyridines as our basic nucleophiles. This takes advantage of some work of Cavalieri, who observed such duality in the reaction of 9-methylanthracene with pyridine to yield either 9-(N-pyridinium)-10-methylanthracene or 9-(N-pyridiniummethyl)anthracene. By using substituted pyridines, we were able to obtain a correlation of the log ratio of products to the Hammett substituent constant and thus evaluate the effect of basicity on the partition. This correlation is also dependent upon the quality of the pyridines, which yield one ratio with anhydrous material and another ratio with wet material. We believe that water acts as an intermediate proton relay in this reaction.
Our studies in 1,4-dialkynaphthalene oxidations have been straightforward, if less surprising. Due to a lack of steric inhibition to planarity, the reaction pathway is dominated by proton loss from the side chain and formation of hydroxylalkyl products.

In summary, our focus on radical-cation deprotonation reactions continues to provide a useful framework for investigating both enzymatic and biomimetic oxidation of anthracenes. Our goal, to develop a dependable chemical model for radical cation reactivity in enzyme active sites, appears attainable.

Publications (from NIH support):


Meetings and Symposia: (from NIH support)


"Regioselectivity in 1,4-Dialkynaphthalene Deprotonations", 40th Southeast Regional Meeting, American Chemical Society, Atlanta, GA, September 9, 1988.

