GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF RESEARCH ADMINISTRATION

Date: 6 October 1965

RESEARCH PROJECT INITIATION

Project Title: Enolates of Unsymmetrical Ketones
Project No.: B-1501
Project Director: Dr. D. S. Coine
Sponsor: American Chemical Society
Agreement Period: From 1 June 1965 until 31 August 1966
Type Agreement: Grant 7147-2073-21, 4
Amount: $10,000.00

Grant Administrator
Research Grants and Fellowships Division
American Chemical Society
1155 Sixteenth Street N.W.
Washington 6, D. C.

Reports Required
Progress - Annually as requested by Grant Administrator
Financial - Annually as of 31 August

Assigned to: School of Chemistry

COPIES TO:
- Project Director
- School Director
- Dean of the College
- Administrator of Research
- Associate Controller (2)
- Security-Reports-Property Office
- Patent Coordinator

Other: File B-1501
RESEARCH PROJECT TERMINATION

Date: 13 December 1967

Project Title: Enolates of Unsymmetrical Ketones
Project No: B-1501
Project Director: Dr. D. S. Caine
Sponsor: Petroleum Research Fund, American Chemical Society
Termination Effective: Immediately

Charges Should Clear Accounting By: All acceptable charges have cleared.

Final report has been transmitted
Various methods of generating specific lithium enolates of unsymmetrical cyclohexanone derivatives have been investigated. Reduction-alkylation of \( \alpha-\beta \)-unsaturated cyclohexones has been applied successfully both to \( \beta \)-substituted and \( \beta \)-unsubstituted compounds (1).

Rates of alkylation of potassium and lithium enolates of 2,6- and 2,2-dimethylcyclohexanone with various alkylating agents in 1,2-dimethoxyethane have been determined and compared (2). Rates of alkylation of structurally isomeric lithium enolates of 2-methylcyclohexanone have been determined (3) and similar studies with related cyclohexanone derivatives are in progress. These studies suggest that the influence of steric and electronic factors on rates of enolate alkylations is small and that alkylation rates are related significantly to ground state energies of the species involved.


The composition of enolate mixtures produced by treating 2-alkylcyclohexanone derivatives with trityl lithium and trityl potassium in aprotic solvents under conditions of kinetic and thermodynamic control have been investigated. In all cases studied so far the less highly substituted enolate was found to be favored under kinetic conditions and the more highly substituted enolate was favored under thermodynamic conditions. Enolate mixture compositions were dependent upon the nature of the metal cation, the solvent, and the temperature. In certain systems (2-isopropylcyclohexanone and 2,6,6-trimethylcyclohexanone) the kinetic lithium enolate mixtures were found to contain greater than 95% of the less substituted isomer. The enolate mixture compositions were determined by the acetic anhydride quenching method (1). Methylolation of the lithium enolate mixtures with methyl iodide gave mixtures of methylation products which closely reflected the original enolate compositions. Thus with the ketones mentioned above only the 2,6-isomers were produced. With the potassium enolate mixtures the composition of the methylation product mixtures showed that enolate equilibration occurred during alkylation (2).

Lithium-liquid ammonia reduction and enolate trapping (3) has been extended to β substituted and β unsubstituted α, β-unsaturated cyclohexenones (4). With the β unsubstituted compounds it was found that more complete reduction was achieved if an equivalent of proton donor was employed in the reduction scheme. In all cases the only monoalkylation product formed was derived
from the specific lithium enolate produced in the reduction step.

Rates of alkylation of potassium and lithium enolates of 2,6- and 2,2-
dimethylcyclohexanone with various alkylating agents in 1,2-dimethoxyethane
have been determined and compared (5). With lithium the enolate of the un-
symmetrical ketone was found to undergo alkylation 1.6 times faster than the
enolate of the symmetrical ketone. However, with potassium the order of re-
activity was reversed with the enolate of 2,6-dimethylcyclohexanone reacting
2.8 times faster. The alkylation rates for these species were found to be
related to their ground state energies. The influence of steric and electronic
factors on the alkylation rates, although observable, appeared to be small
with these enolates.

The kinetics of alkylation of the lithium enolate of cyclohexanone and
of the isomeric lithium enolates of 2-methylcyclohexanone have been investi-
gated (6). Alkylations of these species do not follow simple kinetics in
convenient concentration ranges; the order in metal enolate approaches one
at very low concentration and zero at high concentration. This suggests that
enolate association is a complicating factor in these systems. With the
isomeric enolates of 2-methylcyclohexanone the initial alkylation rate for
the more substituted enolate was about twice that of the less substituted
one. Work with related cyclohexanone unsymmetrical derivatives which show
simpler alkylation kinetics is in progress.

1. H. O. House, V. Kramar, J. Org. Chem., 28, 3363 (1963); H. J. Ringold and

