(5) V. R. Koch and L. L. Miller, *J. Amer. Chem. Soc.*, **95,** 8631 (1973).

(6) H. Budzikiewicz, C. Djerassi, and D. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, Chapter 3.

(7) R. O. Kan, "Organic Photochemistry," McGraw-Hill, New York, N.Y., 1966, Chapter 3.

(8) J. Y. Becker, L. R. Byrd, L. L. Miller, and Y.-H. So, *J. Amer. Chem. Soc.*, **97,** 853 (1975).

(9) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

(10) E. A. Mayeda, L. L. Miller, and J. F. Wolf, *J. Amer. Chem. Soc.*, **94,** 6812 (1972).

(11) L. L. Miller, V. R. Koch, M. Tuttle, and T. Koenig, *J. Amer. Chem. Soc.*, **95,** 5075 (1973).

(12) M. Katz, P. Riemenschneider, and H. Wendt, *Electrochim. Acta*, **17,** 1595 (1972).

(13) Y.-H. So, unpublished work.

(14) H. Hogeveen and C. F. Roobeck, *Recl. Trav. Chim. Pays-Bas*, **89,** 1121 (1970).

(15) V. R. Koch, *et al.*, *Electroanal. Chem. Interfacial Electrochem.*, **43,** 318 (1973).

(16) E. A. Mayeda and L. L. Miller, *Tetrahedron*, **28,** 3375 (1972).

(17) See, for example, O. Hammerich and V. D. Parker, *J. Chem. Soc., Chem. Commun.*, 245 (1974).

# Remote Anodic Substitution of Ketones

**James Y. Becker, Larry R. Byrd, Larry L. Miller,*[1] and Ying-Hung So**

*Contribution from the Department of Chemistry, Colorado State University, Fort Collins, Colorado 80521.*

*Received July 15, 1974*

**Abstract:** Ketones which lacked branching at the α position were oxidized at ~2.2 V *vs.* Ag|0.1 *M* $AgNO_3$ in acetonitrile. The anolyte was acetonitrile–lithium perchlorate, and the anode was platinum. Substitution of acetamide for hydrogen at remote (γ, δ, ε) positions was observed for straight-chain ketones. 2-Hexanone produced 5-acetamido-2-hexanone, 2-heptanone gave mainly 6-acetamido-2-heptanone, and 2-octanone led to a mixture of 5-, 6-, and 7-acetamido-2-octanones. Ketones with branching at the β position gave rearranged ketoamides under these conditions. 4,4-Dimethyl-2-pentanone, for example, gave only 4-acetamido-4-methyl-2-hexanone. The oxidation of 4-deuterio-4-methyl-2-pentanone produced two products: 1-deuterio-2-acetamido-2-methyl-4-pentanone by deuteride migration and 4-deuterio-4-acetamido-2-hexanone by methyl migration. A mechanism involving intramolecular hydrogen abstraction by a ketone cation radical and carbonium ion formation is proposed.

Certain anodic systems provide extremely powerful reagents. A platinum electrode in acetonitrile–tetraethylammonium fluoroborate can, for example, be polarized to +3.0 V *vs.* Ag|$AgNO_3$ without substantial oxidation of the electrolyte mixture. Within this potential range, molecules as inert as alkanes can be oxidized. A comparison with the aqueous permanganate–manganous couple indicates that the above anodic system is capable of performing electron-transfer reactions some 40 kcal/mol more endothermic than those achievable with aqueous permanganate. Recent work in our laboratories has aimed at elucidating the chemistry obtained at these high potentials with simple aliphatic substrates.[2-4] This work has indicated interesting correlations between mass spectrometry and anodic reactivity, and it was of considerable interest to see if this relationship would hold for carbonyl compounds. Initial studies with α-branched ketones[5] showed that α-cleavage occurred anodically in analogy to the mass spectral and photochemical reactions. In the present case, we set out to determine if γ-hydrogen abstraction as found in McLafferty rearrangements and Norrish type II reactions would occur with suitable ketones at an anode.[6]

## Experimental Section

**General.** Spectrometers and electrochemical equipment have been described previously.[7] Reactant ketones were with one exception commercial samples whose purity was ascertained by glc.

**4-Deuterio-4-methyl-2-pentanone.** Spectroscopic grade acetone (5.5 g) was reduced with $LiAlD_4$ (1 g)[8] in 5 ml of dry diglyme[9] to produce 2-deuterio-2-propanol (4.8 g), bp 77–78°. This alcohol (3 g) was allowed to react with 47% HI, and 4.5 g (53%) of 2-deuterio-2-iodopropane was obtained. This product (350 mg, 2 mmol) was treated with 1.05 mmol of π-(2-methoxyallyl)nickel bromide in 12 ml of dry DMF under an argon atmosphere.[10] The resulting deuterio ketone was purified by glc on a 5-ft column packed with 10% SE-30 on Chromosorb W: nmr 0.95 (t, 6 H, *J* = 0.5 Hz), 2.08 (s, 3 H), 2.40 (t, 2 H, *J* = 0.5 Hz). The isotopic purity was >98% as determined from mass spectrometry.

**Preparative Oxidations.** The cell and general procedure[5,7] have been described. Oxidations in $CH_3CN$, 0.1 *M* $LiClO_4$ were performed at controlled potentials as indicated in Table I. The reactions were arbitrarily terminated, usually after passage of ~2 Faradays/mol of added ketone. The work-up procedure consisted of evaporation of much of the acetonitrile (*caution*: perchlorate), addition of water, and extraction with chloroform or ether. Chloroform generally gave better recovery. The products (Table I) were purified by chromatography on silica gel and characterized spectroscopically as detailed in Table II. In the cases where isomeric amides were produced, isolation was made by preparative glc, and yields were estimated by integration of the glc trace.

A number of experiments examined the feasibility of intermolecular substitution. These experiments employed a ketone and another compound, *e.g.*, a hydrocarbon. The other compound was selected to be electroinactive at the potential used for ketone oxidation. As Table III indicates, an indirect substitution reaction on the electroinactive substance is possible in certain cases. It should be noted that in all these reactions a large excess of hydrocarbon or ester was employed. Short-chain ketones, acetone and 3-pentanone are not acetamidated at this potential but do lead to substitution, albeit in low yield, on 2,3-dimethylbutane, 2-methylbutane, and ethyl 3-methylbutyrate. In contrast, 4,4-dimethyl-2-pentanone did not give any detectable indirect attack on 2,3-dimethylbutane present in tenfold excess. Instead, the usual intermolecular substitution was observed; 4-acetamido-4-methyl-2-hexanone was produced in 40% yield.

## Results

As Table I demonstrates, aliphatic ketones which lack α branching are oxidized at platinum in acetonitrile to produce ketoacetamides. In general 60–80% of the starting material could be accounted for as recovered reactant plus ketoamide(s). All the ketoacetamides had ir bands at 3300, 1710, 1660, and 1550 $cm^{-1}$ in agreement with the proposed structures. In each case, the mass and nmr spectra dis-

**Table I.** Preparative Oxidation Conditions and Products

| Substrate (mmol) | *E*, V[a] | $n$[b] | Product (% yield)[c] |
|---|---|---|---|
| 2-Hexanone (1.6) | 2.3 | 2.2 | 5-Acetamido-2-hexanone (40) |
| 2-Heptanone (3.3) | 2.3 | 2.0 | 6-Acetamido-2-heptanone (30)[d] |
| 2-Octanone (4.0) | 2.4 | 2.0 | 7-Acetamido-2-octanone (21) |
| | | | 6-Acetamido-2-octanone (30) |
| | | | 5-Acetamido-2-octanone (7) |
| 4-Heptanone (6.0) | 2.3 | 2.0 | 2-Acetamido-4-heptanone (31) |
| 2-Methyl-4-pentanone (5.3) | 2.2 | 2.0 | 2-Acetamido-2-methyl-4-pentanone (20) |
| | | | 4-Acetamido-2-hexanone (20) |
| 2,6-Dimethyl-4-heptanone (3.6) | 2.25 | 2.0 | 2-Acetamido-2,6-dimethyl-4-heptanone (20) |
| | | | 6-Acetamido-2-methyl-4-octanone (20) |
| 2-Deuterio-2-methyl-4-pentanone (0.3) | 2.2 | 2.2 | 1-Deuterio-2-acetamido-2-methyl-4-pentanone (20)[e] |
| | | | 4-Deuterio-4-acetamido-2-hexanone (10)[e] |
| 2,5-Dimethyl-3-hexanone (4.0) | 2.2 | 2.2 | 5-Acetamido-2,5-dimethyl-3-hexanone (35) |
| | | | 5-Acetamido-2-methyl-3-heptanone (25) |
| 4,4-Dimethyl-2-pentanone (4.0) | 2.25 | 2.2 | 4-Acetamido-4-methyl-2-hexanone (50) |
| (2.0) | 2.3 | 3.3 | 5-Acetamido-4-methyl-2-hexanone (40) |

[a] The controlled potential *vs.* Ag|0.1 *M* $AgNO_3$ in $CH_3CN$. [b] Faradays/mol of added ketone. [c] Yields based on isolated products compared with added reactant. [d] A minor (~5%) component suspected to be a ketoamide was not isolated. [e] The crude product was analyzed directly by glc–mass spectrometry and nmr. Both glc and nmr integrations gave the same yield.

**Table II.** Spectroscopic Data of Electrooxidation Products

| Product | Nmr[a] and mass spectra |
|---|---|
| 5-Acetamido-2-hexanone | Nmr 0.75 (t, 3 H), 1.27 (s, 3 H), 1.80 (oct, 2 H, $J$ = 2.5 Hz), 1.85 (s, 3 H), 1.91 (s, 3 H), 2.88 (AB quartet, 2 H, $J$ = 16.5 Hz), 5.91 (s,[b] 1 H); ms 171.1277 ($M\cdot^+$), 156, 142, 128, 114, 113, 100, 86, 58, 57, 43 |
| 6-Acetamido-2-heptanone | Nmr 1.1 (d, 3 H, $J$ = 6.5 Hz), 1.45 (m, 4 H), 1.9 (s, 3 H), 2.1 (s, 3 H), 2.45 (t, 2 H, $J$ = 6.4 Hz), 4.0 (m, 1 H), 5.4 (s,[b] 1 H); ms 171 ($M\cdot^+$), 156, 128, 114, 86, 58, 43 (100%) |
| 7-Acetamido-2-octanone | Nmr 1.1 (d, 3 H, $J$ = 7 Hz), 1.2–1.9 (m, 6 H), 1.96 (s, 3 H), 2.18 (s, 3 H), 2.5 (t, 2 H, $J$ = 7 Hz), 3.9 (m, 1 H), 5.4 (s,[b] 1 H); ms 185 ($M\cdot^+$), 142, 128, 114, 100, 86 (100%), 58, 43 |
| 6-Acetamido-2-octanone | Nmr 0.9 (t, 3 H, $J$ = 6.4 Hz), 1.5 (m, 6 H), 2.0 (s, 3 H), 2.18 (s, 3 H), 2.5 (t, 3 H), 3.9 (m, 1 H), 5.4 (s,[b] 1 H); ms 185 ($M\cdot^+$), 156, 142, 128, 114, 100, 58 (100%), 43 |
| 5-Acetamido-2-octanone | Nmr 0.95 (t, 3 H), 1.2–1.8 (m, 6 H), 1.96 (s, 3 H), 2.1 (s, 3 H), 2.52 (t, 2 H), 3.95 (m, 1 H), 5.4 (s,[b] 1 H); ms 185 ($M\cdot^+$), 142, 140, 128, 126, 114, 100 (100%), 72, 58, 43 |
| 2-Acetamido-4-heptanone | Nmr 0.85 (t, 3 H, $J$ = 7 Hz), 1.0 (d, 3 H, $J$ = 7.4 Hz), 1.3–1.8 (m, 2 H), 1.95 (s, 3 H), 2.3–2.7 (m, 4 H), 3.9 (m, 1 H), 5.6 (s,[b] 1 H); ms 171.1258 ($M\cdot^+$), 143, 128, 100, 86, 58 (100%), 43 |
| 2-Acetamido-2-methyl-4-pentanone | Nmr 1.40 (s, 6 H), 1.95 (s, 3 H), 2.10 (2, 3 H), 2.98 (s, 2 H), 6.20 (s,[b] 1 H); ms 157.1090 ($M\cdot^+$), 114, 100, 58, 57, 43 |
| 4-Acetamido-2-hexanone | Nmr 0.9 (t, 3 H), 1.5 (m, 2 H), 2.0 (s, 3 H), 2.2 (s, 3 H), 2.65 (d, 2 H), 4.2 (m, 1 H), 6.2 (s,[b] 1 H); ms 157.1111 ($M\cdot^+$), 128, 114, 100, 58, 43 |
| 2-Acetamido-2,6-dimethyl-4-heptanone | Nmr 0.9 (d, 3 H), 1.4 (s, 6 H), 1.95 (s, 3 H), 2.0–2.4 (m, 3 H); 2.9 (s, 2 H), 6.8 (s,[b] 1 H); ms 199 ($M\cdot^+$), 184, 157, 142, 114, 100, 58, 43 (100%) |
| 6-Acetamido-2-methyl-4-octanone | Nmr 0.8–1.1 (m, 9 H), 1.5 (m, 2 H), 1.98 (s, 3 H), 2.3 (3 H), 2.65 (d, 2 H), 4.1 (m, 1 H), 6.2 (s,[b] 1 H); ms 199 ($M\cdot^+$), 170, 157, 142, 128, 114, 100, 86 ,58 (100%), 43 |
| 1-Deuterio-2-acetamido-2-methyl-4-pentanone | Nmr 1.4 (s, 5 H + D), 1.95 (s, 3 H), 2.15 (s, 3 H), 2.95 (s, 2 H), 6.2 (s,[b] 1 H); ms 158 ($M\cdot^+$), 143, 142, 115, 101, 100, 59, 44, 42 |
| 4-Deuterio-4-acetamido-2-hexanone | Nmr 0.9 (t, 3 H), 1.45 (m, 2 H), 2.0 (s, 3 H), 2.17 (s, 3 H), 2.7 (t, 2 H, $J$ = 0.5 Hz), (s,[b] 1 H); ms 158 ($M\cdot^+$), 129, 115, 101, 100, 87, 73, 59, 58, 42 |
| 5-Acetamido-2,5-dimethyl-3-hexanone | Nmr 0.9 (t, 3 H, $J$ = 7.5 Hz), 1.1 (d, 6 H, $J$ = 7 Hz), 1.5 (m, 2 H), 1.98 (s, 3 H), 2.3–2.9 (m, 3 H), 4.1 (m, 1 H), 6.2 (s, 1 H); ms 185 ($M\cdot^+$), 156, 142, 126, 114, 100, 86, 84, 72, 58, 43 |
| 5-Acetamido-2-methyl-3-heptanone | Nmr 1.05 (d, 6 H, $J$ = 7 Hz), 1.4 (s, 6 H), 1.9 (s, 3 H), 2.6 (heptet, 1 H, $J$ = 7 Hz), 2.95 (s. 2 H), 6.1 (s,[b] 1 H); ms 185 ($M\cdot^+$), 170, 142, 128, 114, 100, 84, 83, 71, 60, 58, 43 |
| 4-Acetamido-4-methyl-2-hexanone | Nmr 1.17 (d, 3 H), 1.93 (s, 3 H), 2.18 (s, 3 H), 1.57–2.17 (m, 2 H), 2.37–2.77 (m, 2 H), 3.65–3.93 (m, 1 H), 6.10 (s,[b] 1 H); ms 157 ($M\cdot^+$), 114, 100, 86, 58, 57, 43 |

[a] Nmr data are given in parts per million. Samples were run in $CDCl_3$ with TMS as internal reference. [b] Broad.

**Table III.** Acetamidation *via* Ketone Oxidation[a]

| Substrate (mmol) | Ketone (mmol) | *E*, V[b] | Electrolyte, (0.14 *M*) | mFaradays | Product (% yield)[c] |
|---|---|---|---|---|---|
| 2,3-Dimethylbutane (10) | Acetone (2.4) | 2.55 | $LiClO_4$ | 5.3 | 2-Acetamido-2,3-dimethylbutane (11) |
| 2,3-Dimethylbutane (10) | Acetone (1.38) | 2.55 | $Et_4NBF_4$ | 3.0 | 2-Acetamido-2,3-dimethylbutane (4) |
| 2,3-Dimethylbutane (10) | 4,4-Dimethyl-2-pentanone (1.0) | 2.25 | $LiClO_4$ | 2.2 | 4-Acetamido-4-methyl-2-hexanone (40) |
| 2-Methylbutane (17) | Acetone (2.8) | 2.55 | $Et_4NBF_4$ | 5.6 | 2-Acetamido-2-methylbutane (10) |
| Ethyl 3-methylbutyrate (17) | 3-Pentanone (1.2) | 2.42 | $Et_4NBF_4$ | 2.5 | Ethyl 3-acetamido-3-methylbutyrate (13) |

[a] Anolyte 100 ml of $CH_3CN$. Background current with the hydrocarbon or ester, but without ketone present was ~2% of the initial current with ketone. [b] Ag|0.1 *M* $AgNO_3$ reference electrode. [c] Current yield.

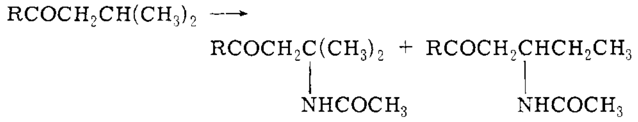
cussed below provided a definitive structure proof. The substitution of acetamide for hydrogen is shown to occur preferentially at positions remote from the carbonyl, and in branched-chain ketones, rearrangement of the carbon skeleton is observed.

**Unbranched Ketones.** 2-Hexanone, 2-heptanone, 4-heptanone, and 2-octanone were examined. Each of the first three compounds led to one major ketoamide found by acetamide substitution at the carbon next to the end of the chain ($\omega - 1$). This isomer is readily identified by nmr since the $\omega$-methyl group appears as a doublet (all other unbranched isomers give a triplet). This structural assignment is confirmed by the mass spectrum. It has been found that the mass spectra of the ketoamides generally have a base peak at *m/e* 43 or 58 due $CH_3CO^+$ or $CH_3CONH^+$, respectively, as well as peaks from fragmentation $\alpha$ to the nitrogen and $\alpha$ to the carbonyl. In the spectra in question, peaks are observed for an ion of apparent composition $CH_3CH^+NHCOCH_3$, *m/e* 86. This cleavage indicates that the acetamide is attached at $\omega - 1$ since other isomers give different $\alpha$-cleavage ions.

2-Octanone oxidation produced three products in an approximate ratio of 3:4:1. The three products were collected (glc, Carbowax 20M) and analyzed by nmr and mass spectrum. The compound with the longest retention time was identified as the $\omega - 1$ ketoamide, 7-acetamido-2-octanone. The isomeric identification was evident from the methyl doublet in the nmr spectrum. The mass spectrum of this isomer showed peaks of special interest at *m/e* 114, 100, and 86 ($CH_3C^+HNHCOCH_3$). The compound with intermediate retention time was the $\omega - 2$ isomer, 5-acetamido-2-octanone. The methyl terminating the heptyl chain appears as a triplet, and the mass spectrum shows *m/e* 114, 100 ($CH_3CH_2C^+HNHCOCH_3$), but no 86. The compound with the shortest retention time showed a very similar nmr spectrum to the $\omega - 2$ and *m/e* 114. It was assigned the structure of 5-acetamido-2-octanone. In each case, the total nmr and mass spectrum could be rationalized on the basis of the proposed structures. In order to further confirm these assignments, a crude mixture of ketoacetamides was reduced using the Huang-Minlon modification of the Wolff-Kishner reduction.[12] The resulting products were primarily octylamines from reduction of the carbonyl and hydrolysis of the amide. This mixture was then treated with acetic anhydride and then analyzed by glc. The three products were identified, by coinjections with authentic samples,[11] as 2-, 3-, and 4-octylacetamides.

The 2-octanone oxidation was also performed using tetraethylammonium fluoroborate as the electrolyte. The isomer ratio was similar to that found using lithium perchlorate. In a reaction at 2.4 V terminated after 2.0 Faradays/mol, the molar ratio was: $\omega - 1$ (11), $\omega - 2$ (14), $\omega - 3$ (3). In another oxidation carried to 4.2 Faradays/mol, the molar ratio was: $\omega - 1$ (5), $\omega - 2$ (9), $\omega - 3$ (1). At higher values of *n*, the yields were somewhat lower, even though more ketone was consumed. This is most probably due to oxidation of the ketoacetamide.

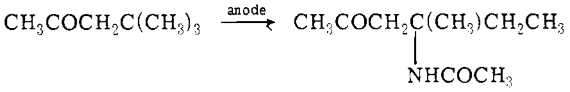
**Branched Ketones.** The isobutyl ketones, 2-methyl-4-pentanone, 2,6-dimethyl-4-heptanone, and 2,5-dimethyl-3-hexanone were oxidized. In each case, two major products, ketoacetamides, were formed, *i.e.*



$$\mathrm{RCOCH_2CH(CH_3)_2} \longrightarrow \mathrm{RCOCH_2\underset{\displaystyle NHCOCH_3}{\underset{|}{C}}(CH_3)_2} + \mathrm{RCOCH_2\underset{\displaystyle NHCOCH_3}{\underset{|}{C}}HCH_2CH_3}$$

All six products gave readily interpreted nmr and mass spectra which unequivocally demonstrated that one isomer was rearranged in each reaction. In the case of 2,5-dimethyl-3-hexanone, products from substitution in the 2-propyl group were present in less than 5% yield.

The oxidation of 4,4-dimethyl-2-pentanone was one of the cleanest and also involved rearrangements since 4-acetamido-4-methyl-2-hexanone was produced.



$$\mathrm{CH_3COCH_2C(CH_3)_3} \xrightarrow{\text{anode}} \mathrm{CH_3COCH_2\underset{\displaystyle NHCOCH_3}{\underset{|}{C}}(CH_3)CH_2CH_3}$$

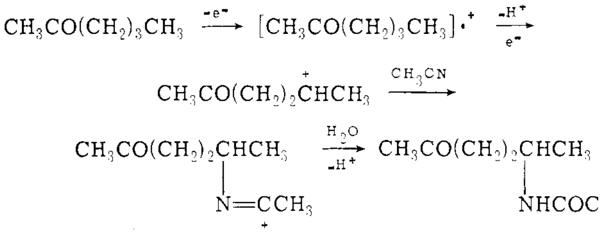
## Discussion

Two types of anodic reactions are observed for ketones. $\alpha$-Cleavage reactions are favored for $\alpha$-branched ketones and remote substitution for ketones lacking $\alpha$ branching. As discussed before,[5] this is rational, because $\alpha$-cleavage to form relatively stable tertiary, secondary, or benzylic fragments (presumably radicals or cations) will be more facile than the formation of a primary fragment. In the latter case, substitution becomes the dominant reaction mode. This change from fragmentation to substitution is also observed in going from branched to normal alkane oxidations.[3,13]

These substitution reactions are unique in that unactivated methylene and methyl groups are converted to carbonium ion-like species. In this sense, the closest analog would be a hydride abstraction reaction. It should be noted, however, that even potent hydride abstractors, like an $AlBr_3$ sludge, appear not to attack methyl groups.[14] The reasons for this extreme anodic reactivity are undoubtedly based on the very high anode potentials employed.

**Mechanism.** Several mechanistic aspects have been elucidated. Taken together these points allow a working hypothesis to be formulated which is useful in understanding the various transformations. This hypothetical mechanism involves (1) direct oxidation of the ketone, (2) an intramolecular attack on the remote hydrogen-carbon bond by oxygen and a second electron transfer, and (3) trapping, or rearrangement and trapping reactions of the resulting carbonium ions. This can be envisaged for 2-hexanone as shown in Scheme I. A direct oxidation of substrate at the electrode is indicated since background current at 2.3 V is only ~2% of that due to added ketone. Also, if the concentration of ketone is increased, the initial current increases proportionately. Although no evidence for a discrete cation radical is in hand, its formation by loss of a nonbonding oxygen electron provides a useful rationale for the chemistry. This has also been proposed as the initial step in $\alpha$-branched ketone oxidations.[5,15]

**Scheme I**



$$\mathrm{CH_3CO(CH_2)_3CH_3} \xrightarrow{-e^-} [\mathrm{CH_3CO(CH_2)_3CH_3}]\cdot^+ \xrightarrow[e^-]{-H^+} \mathrm{CH_3CO(CH_2)_2\overset{+}{C}HCH_3} \xrightarrow{\mathrm{CH_3CN}}$$

$$\mathrm{CH_3CO(CH_2)_2\underset{\displaystyle N{=}\underset{+}{C}CH_3}{\underset{|}{C}}HCH_3} \xrightarrow[-H^+]{\mathrm{H_2O}} \mathrm{CH_3CO(CH_2)_2\underset{\displaystyle NHCOCH_3}{\underset{|}{C}}HCH_3}$$

Two classes of mechanism for reaction of this cation radical were considered. One intermolecular mechanism involves attack of the cation radical or some derived species on a neutral ketone molecule. The second (labeled intramolecular) is typified by not involving a neutral ketone molecule in this step. The former mechanism can be rendered improbable in at least one case by the following experiment. 4,4-Dimethyl-2-pentanone was oxidized at 2.3 V in the presence of a tenfold excess of 2,3-dimethylbutane. The hydrocarbon is not oxidized at this potential. Careful examination of the products did not reveal any

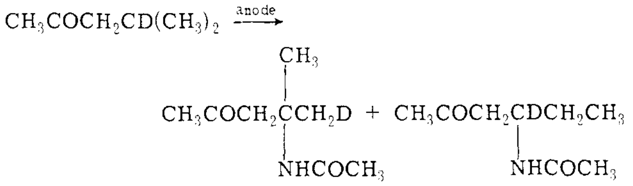
$(CH_3)_2CHC(CH_3)_2\text{-}]_2$ or any amides derived from the hydrocarbon, *e.g.*, $(CH_3)_2CHC(CH_3)_2NHCOCH_3$. The ketoamide was instead formed in essentially the same yield as found in the absence of hydrocarbon. Since intermolecular abstraction is not competitive when this high concentration of hydrocarbon is used, it seems unlikely to be important for the ketone mechanism.

Concerning the intimate mechanism of the intramolecular reaction of a ketone cation radical, two possibilities can again be imagined. In one, the oxygen with its half-filled nonbonding orbital participates through space in the substitution at carbon. One member of this mechanistic set is a McLafferty,[16] Norrish type II[17] $\gamma$-hydrogen transfer from carbon to oxygen. In the second, the only function of the oxygen is to activate the molecule by acquiring a positive charge. No direct attack by oxygen on the C–H bond occurs. Instead, displacement of hydrogen could be assisted by acetonitrile. An obvious test of this pair of possibilities is to examine the positional selectivity for hydrogen loss. The former Norrish-type mechanism would require attack only at spacially accessible hydrogens. The latter would have unknown selectivity depending on the exact mode of interaction of the orbitals and perhaps the electrode surface, but presumably it would not be prerequisite to have the abstractable hydrogen easily accessible to the oxygen. Examination of the data indicates that the Norrish-type mechanism is more attractive, but the decision is equivocal because there is no clear-cut preference for substitution on a certain position in straight-chain ketones. Thus, although $\alpha$ and $\beta$ substitution are not observed in these cases, 2-hexanone gives exclusive $\gamma$, 2-heptanone preferential $\delta$, and 2-octanone preferential $\delta$ and $\epsilon$ acetamidation. In the branched chain molecules, $\gamma$ abstraction is observed to predominate over $\alpha$ and $\beta$, but there is no chance for $\delta$ or $\epsilon$ substitution. It must be realized, furthermore, that the products may not accurately reflect the initial point of hydrogen departure because of hydride shifts.[18] A through-space mechanism explains the discrimination against $\alpha,\beta$ attack because of the strain inherent in forming small, cyclic transition states, and this hypothesis is acceptable if there is low positional selectivity in remote attacks. The feasibility of direct attack of a ketone cation radical on C–H bonds was demonstrated by oxidizing mixtures of ketones, which have only $\alpha,\beta$ hydrogens and cannot readily react intramolecularly, and electroinactive substrates (Table III). Acetone does not produce any ketoamide when 4.0 Faradays/mol of charge is passed at 2.5 V. It will, however, indirectly cause the acetamidation of 2,3-dimethylbutane, 2-methylbutane, or methyl butyrate. In these experiments, the potential is held so that acetone or 3-pentanone are oxidized, and the much higher concentration of hydrocarbon or ester is not. Since the intermediate(s) formed during ketone oxidation *can* lead to substitution by attack on the C–H bond (albeit inefficiently in these intermolecular cases), it seems likely that this is involved in the intramolecular mechanism. This provides a tidy intellectual package because of the mass spectral,[16] photochemical[17] analogy, but experiments with geometrically rigid ketones will be required to really answer this question.

Proceeding now to the final stages of the mechanism, it is required that somewhere in the process a second electron is lost. The timing of this step is not known, but it is clearly needed to generate acetamide products and account for the rearrangements. The intermediacy of secondary and tertiary carbonium ions can explain the formation of acetamides[2,19] as shown in Scheme I. A reasonable alternative in several cases is, however, a concerted loss of hydrogen and attack by acetonitrile on carbon. It seems unlikely that acetamidation occurs *via* acetonitrile trapping of radicals. Benzoyl peroxide was decomposed at 70° in acetonitrile containing cyclohexane, and no cyclohexylacetamide was formed.

The rearrangement reaction observed with 4,4-dimethyl-2-pentanone indicates that real or incipient primary cations are generated efficiently from methyl groups. The rearrangement of neopentyl-type radicals is known not to occur.[20] The corresponding cations, however, rearrange as they are formed producing the more stable tertiary cations.[20] The efficiency of this abstraction from methyl is remarkable since methyl groups are normally quite inert. It suggests that the abstracting intermediate is extremely reactive. If one considers the high potentials at which these processes occur, this is perhaps not surprising.

In light of the above result, it was considered likely that the isobutyl ketones were also reacting by preferential $\gamma$ abstraction and rearrangement. This was tested by oxidizing 2-deuterio-2-methyl-4-pentanone. Two ketoacetamides were formed as expected. These were identified by nmr and gc-ms in accordance with the following reaction:



$$CH_3COCH_2CD(CH_3)_2 \xrightarrow{\text{anode}} CH_3COCH_2\overset{\displaystyle CH_3}{\underset{\displaystyle NHCOCH_3}{C}}CH_2D + CH_3COCH_2\underset{\displaystyle NHCOCH_3}{C}DCH_2CH_3$$

Within the accuracy of the determination, the unrearranged product results only from $\gamma$ abstraction and a deuteride shift. Nmr integration (methyls equal 5 H), the molecular ion, and $CH_3C^+(CH_2D)NHCOCH_3$, *m/e* 87 ion (no *m/e* 86) demonstrate this conclusively. Also loss of $CH_2D$ and $CH_3$ is observed in the mass spectrum. The rearranged product also has retained the deuterium as indicated from the mass spectrum, and the absence of the methine proton in the nmr spectrum shows the deuterium position.

**Acknowledgment.** This work was supported by the Donors of the Petroleum Research Fund, administered by the American Chemical Society. $\pi$-(2-Methoxyallyl)nickel bromide was supplied by L. S. Hegedus.

## References and Notes

(1) Fellow of the A. P. Sloan Foundation, 1972–1974.
(2) V. R. Koch and L. L. Miller, *J. Amer. Chem. Soc.*, **95**, 8631 (1973).
(3) T. M. Siegel, L. L. Miller, and J. Y. Becker, *J. Chem. Soc., Chem. Commun.*, 341 (1974).
(4) L. L. Miller and V. Ramachandran, *J. Org. Chem.*, **39**, 369 (1974).
(5) J. Y. Becker, L. L. Miller, and T. Siegel, *J. Amer. Chem. Soc.*, **97**, 849 (1975).
(6) Preliminary communication: J. Y. Becker, L. R. Byrd, and L. L. Miller, *J. Amer. Chem. Soc.*, **96**, 4718 (1974).
(7) E. A. Mayeda, L. L. Miller, and J. F. Wolf, *J. Amer. Chem. Soc.*, **94**, 6812 (1972).
(8) C. Djerassi, *et al.*, *J. Amer. Chem. Soc.*, **92**, 3084 (1970).
(9) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," Vol. I, Wiley, New York, N.Y., 1967, p 255.
(10) L. S. Hegedus and R. K. Stiverson, *J. Amer. Chem. Soc.*, **96**, 3250 (1974).
(11) B. Watkins, unpublished work.
(12) A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed, Wiley, New York, N.Y., 1956, p 516.
(13) D. Clark, M. Fleischmann, and D. Pletcher, *J. Chem. Soc., Perkin Trans. 2*, 1578 (1973).
(14) H. Pines and N. C. Hoffmann, "Friedel-Crafts and Related Reactions," Vol. II, G. A. Olah, Ed., Interscience, New York, N.Y., 1964, p 1222.
(15) L. L. Miller, V. R. Koch, T. Koenig, and M. Tuttle, *J. Amer. Chem. Soc.*, **95**, 5075 (1973).
(16) H. Budzikiewicz, C. Djerassi, and D. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, Chapter 3.
(17) R. O. Kan, "Organic Photochemistry," McGraw-Hill, New York, N.Y., 1966.
(18) It has been found[11] that 2-octyl cations generated under very similar conditions rearrange to 3-octyl cations to the extent of ~15% before trapping.
(19) J. J. Ritter and P. P. Minieri, *J. Amer. Chem. Soc.*, **70**, 4645 (1948).
(20) P. DeMayo, "Molecular Rearrangements," Vol. I, Interscience, New York, N.Y., 1963.