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Anodic α-Cleavage of Ketones

James Y. Becker, Larry L. Miller,*[1] and Theodore M. Siegel

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

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Abstract: Ketones with branching at the α position were potentiostatically oxidized at platinum gauze. The anolyte was acetonitrile–lithium perchlorate and the reference electrode Ag|0.1 M $AgNO_3$. α-Cleavage was observed to be the main route of these oxidations. 2,2-Dimethyl-3-butanone, 2,2-dimethyl-3-hexanone, acetyladamantane, 2-methyl-3-butanone, and 2,5-dimethyl-3-pentanone of the general formula RCOR′ gave α-cleavage products of the type $RNHCOCH_3$ and R′COOH. 2,2-Dimethylpropanal and 2,2,4,4-tetramethyl-3-pentanone gave acetylpivaloylimide in addition to acid and amide products. It was found that small amounts of water are necessary for the obtention of high amide ($RNHCOCH_3$) yields. A mechanism involving generation of carbonium ions from α-cleavage of a ketone cation radical is proposed, and analogies with photochemistry and mass spectrometry are drawn.

The simplest mechanistic paradigm for most anodic organic reactions involves initial electron transfer from substrate to the electrode followed by reactions of the resultant cation radical. This paradigm suggests that there should be analogies between mass spectrometry and anodic chemistry, because both processes are controlled by formation and reaction of cation radicals. Verification of this analogism would provide some unusual solution phase chemistry with synthetic ramifications, and this has been a goal of our recent research.

Although there is a surprisingly general correlation between gas-phase ionization potentials and electrochemical oxidation potentials,[2] there are presently few meaningful analogies between anodic and mass spectral chemistry. A primary reason for this dissimilarity appears to be that bimolecular reactions are favored in solution. Thus, cation radicals in solution typically give dimeric products or products resulting from attack by nucleophiles.[3] These processes are extremely unlikely in a dilute gas. Recent explorations in this laboratory using direct anodic oxidation in acetonitrile solvent have, however, revealed fragmentation reactions which mimic mass spectral chemistry.[4,5] In this paper, we report several examples of α-cleavage of carbonyl compounds. This is a very common reaction in the mass spectrometer.[6] It is also common in ketone photochemistry (Norrish Type I process).[7] In the following paper, results from ketones without α-branching are presented.[8] The oxidation products in these cases are ketoamides produced by hydrogen abstraction. The abstraction appears to be intramolecular so that these reactions are also reminiscent of mass spectral and photochemical processes.

Experimental Section

Equipment. A Perkin-Elmer 457 ir spectrometer, Varian A-60A and T-60 nmr spectrometers, and an AEI MS-12 mass spectrometer were used for structure determination. Gas–liquid chromatographic (glc) analyses were performed on a Bendix 2300 or an F&M 720 gas chromatograph equipped with thermal conductivity detectors. The potentiostats employed were a Wenking Model 70 HV 1/90 or a Princeton Applied Research Model 373. Coulometry during preparative electrolysis was performed with a counter constructed from an Acromag integrator-totalizer. An Exact Model 126-VCF function generator was used to pulse the anode potential during preparative oxidations. Cyclic voltammograms (cv) were run on a Princeton Applied Research Model 170 instrument.

Materials. Acetonitrile (Eastman 0.01% water or Fisher 0.03% water) was freshly purified by distillation from phosphorus pentoxide under nitrogen and stored over 4A molecular sieves. Purification involving an initial distillation from permanganate, followed

Table I. Oxidation Products[a]

Reactant (mmol)	E, V[b]	n,[c] Faradays/mol	Product (% yield)[d]
Acetyladamantane (1.2)	2.10	2.2	1-Adamantylacetamide (85); CH_3CO_2H
(1.2)	2.30	2.3	1-Adamantylacetamide (40); CH_3CO_2H
$(CH_3)_3CCOCH_3$ (2.4)	2.15	2.1	$(CH_3)_3CNHCOCH_3$ (**1**) (80); CH_3CO_2H (25)
$(CH_3)_3CCOCH_2CH_2CH_3$ (4.0)	2.08	2.1	**1** (65); $CH_3CH_2CH_2CO_2H$ (10)
$(CH_3)_3CCOCH_2C(CH_3)_3$[e] (0.5)	2.30	2.2	**1** (40); $(CH_3)_3CCH_2CO_2H$ (45)[f]
$(CH_3)_3CCOC(CH_3)_3$[e] (1.5)	2.10	1.9	**1** (24); $(CH_3)_3CCO_2H$ (45); $(CH_3)_3CCONHCOCH_3$ (6); $(CH_3)_3CCOCH_2C(NHCOCH_3)(CH_3)_2$ (14)
$(CH_3)_3CCHO$[e] (2.3)	2.45	2.0	**1** (24); $(CH_3)_3CCO_2H$ (42); $(CH_3)_3CCONHCOCH_3$ (4)
$(CH_3)_2CHCOCH_3$ (2.8)	2.15	1.8	$(CH_3)_2CHNHCOCH_3$ (**2**) (46); CH_3CO_2H; $(CH_3)_2C(NHCOCH_3)COCH_3$ (15)
$(CH_3)_2CHCOCH(CH_3)_2$ (2.1)	2.10	2.2	**2** (59); $(CH_3)_2CHCO_2H$ (59); $(CH_3)_2C(NHCOCH_3)COCH(CH_3)_2$ (20)

[a] Oxidation with $LiClO_4$ electrolyte. Work-up by continuous extraction except where noted. [b] Potential for preparative electrolysis. [c] Preparative scale coulometry. [d] Yield based on amount of ketone added. In case of mixtures nmr and glc analyses were used for quantitation. [e] Work-up with regular chloroform extraction. [f] A small amount (~5%) of a ketoamide tentatively identified as $(CH_3)_3CCOCH_2C(CH_3)(C_2H_5)NHCOCH_3$ was also isolated.

by distillation from phosphorus pentoxide, did not give qualitatively different results. Anhydrous lithium perchlorate (G. F. Smith) was used without purification. This material is, however, extremely wet as demonstrated by ir analysis. Tetraethylammonium perchlorate was purified by recrystallization and dried at 100°. All ketones, except 2,2,5,5-tetramethyl-3-hexanone, were commercial samples. The latter was prepared from 2,2,5,5-tetramethyl-3-hexanol by chromium trioxide oxidation.[9]

Preparative Electrolysis. A three-compartment cell which has been previously described[10] was employed. The reference electrode was a silver wire immersed in 0.1 *M* $AgNO_3$, acetonitrile solution. The anolyte and catholyte were 0.1 *M* electrolyte in acetonitrile. A stainless steel cathode and platinum (4 × 4 cm) gauze anode was used, and the anolyte (100 ml) was stirred magnetically. The anode compartment was kept under an atmosphere of dry nitrogen. In some preparative oxidations, the anode potential was pulsed to ~0 V for 1 sec each 100 sec. This was generally unnecessary, however, and had no discernible effect on the product.

A background i,E curve was recorded before addition of ketone. Exact electrical data are recorded in the tables, but in general the potential was set, and electrolysis was carried out until either 2 Faradays/mol of ketone added was passed or the current dropped to some low value near the original background level. Some irreproducibility in initial current was seen due to the differing placement of anode and reference electrode. This indicates that the actual potential may vary somewhat from run to run because of variable electrode placement and ir drop.

After completion of the oxidation (reaction time 0.5-2 hr), the anolyte was concentrated. (*Caution:* If perchlorate electrolyte is used, the anolyte contains perchloric acid!) Aqueous sodium bicarbonate (10%) was added, and the solution was extracted three times into chloroform. The chloroform extract was dried over anhydrous $MgSO_4$, filtered, and evaporated to an oil and analyzed. Acidification of the aqueous fraction, followed by chloroform extraction and evaporation, gave the carboxylic acid products.

A second work-up procedure involved concentration of the anolyte, addition of 15-20 ml of water, and continuous extraction for 3 hr with chloroform. Continuous extraction for longer times did not improve recovery. If tetraalkylammonium salts were employed, the chloroform extract contained this electrolyte. It was precipitated from chloroform with ether.

The products isolated (Table I) were identified by nmr and glc comparisons with authentic samples. A 7-ft column packed with 15% Carbowax 20M or a 5-ft column packed with 10% SE-30 on Chromosorb W was used for glc analyses.

The isolated yields of small carboxylic acids, *e.g.*, acetic acid, are expected to be low because of their volatility and water solubility, and in general these acids were not carefully assayed. Some variability in yields depending upon work-up method was observed. In general, continuous extraction appeared somewhat better than ordinary extraction. An exception was the 2,2,5,5-tetramethyl-3-hexanone product mixture. There were a number of minor products obtained in this case by continuous extraction not obtained otherwise, and the yields of major products were actually lower.

Acetylpivaloylimide. This imide was isolated from the oxidation of di-*tert*-butyl ketone and pivaldehyde by preparative glc: nmr 1.28 (s, 9 H), 2.51 (s, 3 H), 8.2 (broad singlet, 1 H); mass spectrum 143 ($M\cdot^+$), 128, 115, 110, 100, 86, 58, 57, 43; ir 3280, 3260, 1730, 1695, 1665, 1540, 1470, 1415.

5-Acetamido-2,2,5-trimethyl-3-hexanone. The ketoamide was isolated by glc from the oxidation of di-*tert*-butyl ketone: nmr 1.13 (s, 9 H), 1.43 (s, 3 H), 1.93 (s, 3 H), 2.98 (s, 2 H), 6.15 (broad singlet, 1 H); mass spectrum 199 ($M\cdot^+$), 184, 143, 142, 125, 115, 114, 100, 83, 72, 60, 58, 43; ir 3450-3300, 1705, 1655, 1550, 1475.

Cyclic Voltammetry. Voltammograms were recorded for each ketone in twice-distilled acetonitrile. The cell volume was 10 ml. The Ag|0.1 *M* $AgNO_3$ reference electrode was separated from the working electrode by a glass frit. The auxiliary electrode was a platinum wire, and the working electrode a platinum wire sealed in glass and ground smooth making a small platinum button.

All the voltammograms showed no cathodic peak corresponding to reduction of an initially formed cation radical. In several cases, a sweep rate of 100 V/sec was employed to look for this peak.

Results and Discussion

Preparative Electrolyses. This study has revealed that the general reaction of α-branched ketones in damp acetonitrile at platinum is α-cleavage (Table I).

$$RCOR' \xrightarrow[\text{anode}]{CH_3CN,\ H_2O} RNHCOCH_3 + R'CO_2H + R'CONHCOCH_3$$

$$R = \text{tertiary or secondary alkyl}$$

Acetyladamantane oxidation is extremely clean. The tertiary 1-adamantyl group is converted into the corresponding acetamide in 85% yield. Some unreacted acetyladamantane is also present. The acetic acid was not quantified because of its water solubility and volatility. Somewhat lower yields (~40%) were obtained at 2.3 V.[5] Coulometry at 2.1 V shows about 2.2 Faradays/mol indicating that the conversion of interest has $n = 2$. The current falls almost logarithmically with time. There is, however, a reproducible deviation from the theoretical i,t curve toward higher current just after the oxidation is initiated.

Several *tert*-butyl ketones were oxidized. *tert*-Butyl methyl ketone and *tert*-butyl propyl ketone gave high yields of *tert*-butylacetamide (**1**) and some acetic and propionic acids, respectively. No evidence for isobutylene or the imides, pivaloylacetylimide or diacetylimide, was found. As discussed below, the electrolyte had little effect on the products as long as the water content was sufficient. An oxidation of *tert*-butyl methyl ketone at −22° gave the same products as a room temperature oxidation. The yield from *tert*-butyl isobutyl ketone was somewhat lower, but the potential employed was 2.3 V. At this potential, acetyladamantane and *tert*-butyl methyl ketone gave comparably lower yields.

Pivaldehyde was the only aldehyde examined. It also gave α-cleavage of the *tert*-butyl moiety but led primarily to pivalic acid. It should be noted that the anolyte was under nitrogen to avoid autoxidation of the aldehyde.

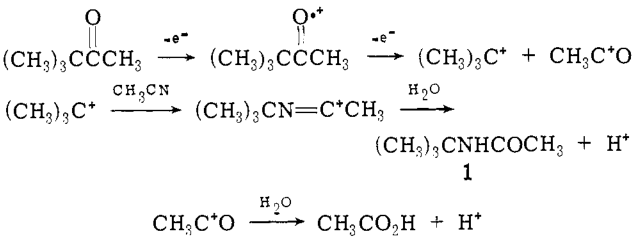
We have shown that unbranched ketones oxidatively give substitution of acetamide for hydrogen, producing ketoamides. This substitution reaction also intrudes in certain oxidations where α-cleavage is the primary reaction. Thus in the case *tert*-butyl neopentyl ketone, a small amount of ketoamide was isolated. Its structure is tentatively assigned by nmr as $(CH_3)_3CCOCH_2C(CH_3)(C_2H_5)NHCOCH_3$. This would result from γ-hydrogen loss, rearrangement, and acetamidation. Di-*tert*-butyl ketone also gave some ketoamide product. In this case the imide, $(CH_3)_3CCONHCOCH_3$, was also isolated.

Ketones with secondary α groups give both α-cleavage and substitution. Since α and β substitution are generally unfavorable,[8] diisopropyl ketone and isopropyl methyl ketone give reasonable yields of cleavage products, *i.e.*, isopropylacetamide (**2**). Larger ketones like dicyclohexyl ketone do not give cleavage but form ketoamides by substitution.

In all the cases, the current decayed with time, but the decay was generally nonlogarithmic with higher than expected currents at the beginning. This was traced to the poor cell geometry. The oxidation of iodide to iodine in acetonitrile behaved similarly at high concentrations (high currents) but at lower currents gave proper behavior. This was also observed for *tert*-butyl methyl ketone. The explanation is that the measured, controlled potential contains a considerable iR contribution. This is most serious at the beginning of the reaction where i is highest and decreases as the current drops. For this reason the i,t curves will not be considered further. The coulometry was near 1.5–2.5 electrons/molecule in each case, but it was clearly not 2.0 electrons/molecule in many cases. Isopropyl methyl ketone, for example, consistently gave n = 1.4–1.8 for exhaustive electrolysis. Diisopropyl ketone, on the other hand, gave $n \simeq 2.2$.

Mechanism. Consideration of the voltammetric characteristics and products leads to mechanistic Scheme I, illustrated for *tert*-butyl methyl ketone. Although this scheme cannot explain all the data, certain parts of it are adequate, and it provides a vehicle for the discussion. All these ketones oxidize well below the onset of background processes and show well-defined cyclic voltammetry peaks (Table II). The current is roughly proportional to ketone concentration, and it is concluded that electron transfer from the ketone is involved in the rate-determining step. This electron should come from a nonbonding oxygen orbital. The photoelectron spectra of *tert*-butyl methyl ketone demonstrates that in the gas phase the HOMO is nonbonding oxygen.[11] The E_p values for ketones fall on the correlation line for E_p *vs.* I_p, and there is a general resemblance of the gas and solution phase chemistry, so there is some reason to believe that the initial electrode process resembles that in the gas phase. These arguments are, however, equivocal, and we have no direct evidence for a free cation radical intermediate with the hole in a nonbonding oxygen orbital. In the case of isopropyl ketones, enol formation could have interceded. Oxidation of an enol does not, however, seem to be important. No wave is seen near 1.5 V which we judge to be the region of enol oxidation. Enol ethers[12] and enol esters[13] have been shown to be oxidized in this range.

Scheme I



$$(CH_3)_3C\overset{\overset{O}{\|}}{C}CH_3 \xrightarrow{-e^-} (CH_3)_3C\overset{\overset{O^{\cdot+}}{\|}}{C}CH_3 \xrightarrow{-e^-} (CH_3)_3C^+ + CH_3C^+O$$

$$(CH_3)_3C^+ \xrightarrow{CH_3CN} (CH_3)_3CN{=}C^+CH_3 \xrightarrow{H_2O} \underset{\mathbf{1}}{(CH_3)_3CNHCOCH_3} + H^+$$

$$CH_3C^+O \xrightarrow{H_2O} CH_3CO_2H + H^+$$

Table II. Cyclic Voltammetry Data, Lithium Perchlorate[a]

Substrate	Concn, mM	E_p, V	I_p, μA[b]
$(CH_3)_3CCOCH_3$	24	2.33	68
$(CH_3)_2CHCOCH_3$	28	2.36	60
$(CH_3)_2CHCOCH(CH_3)_2$	22	2.35	64
$(CH_3)_3CCHO$	26	2.50	63
$(CH_3)_3CCOC(CH_3)_3$	17	2.20	48
$(CH_3)_3CCH_2COC(CH_3)_3$	16	2.15	50
$(C_5H_5)_2Fe$	20		32

[a] 0.1 M $LiClO_4$ in acetonitrile. Sweep rate 200 mV/sec. [b] I_p from a ferrocene standard is the last entry.

The formation of alkyl acetamide and carboxylic acid is most easily rationalized in terms of the cationic intermediates shown. This requires a net two-electron process in agreement with the voltammetry and coulometry in the cases with high yields of cleavage products. We have independently demonstrated that alkyl radicals do not give acetamidated products in acetonitrile.[8]

The observation that tertiary ketones give preferential cleavage, while substitution competes with fragmentation for secondary ketones and is the exclusive pathway for primary ketones, can be explained in terms of cation radical reactivity. Tertiary fragments (radical or cation) are most stable and, therefore, formed rapidly. As the rate of cleavage goes down for secondary ketones (*e.g.*, isopropyl methyl ketone), remote substitution starts to compete. An alternate explanation would be that remote substitution is slowest for tertiary ketones, and the cleavage rate is relatively insensitive to branching. In order to test this *tert*-butyl neopentyl ketone was oxidized. If the latter proposition was correct, substitution would be preferred. The former proposition would predict cleavage, and this is in agreement with the result.

Mechanisms involving a nucleophilic attack on the α carbon of a cation radical or dication displacing the acetyl group are ruled out since the bulky tertiary groups (especially, adamantane with no possibility of backside displacement) should be displaced slowest not fastest. It seems likely, therefore, that the fragment which appears as acetamide arises *via* an alkyl cation. These carbonium ion intermediates might have been expected to produce alkenes or alcohols in addition to the acetamide. No *tert*-butyl alcohol or isobutylene was, however, detected in the *tert*-butyl methyl ketone product mixture. If one discounts the possibility of modifying the reactivity of a cation with a highly positively charged anode, *i.e.*, adsorbed cations, one is then left with the proposition that alkene, if formed, is converted to acetamide in a Ritter reaction. This is especially probable near the anode surface where a high acid concentration must exist. Such acid catalyzed processes converting alcohol or alkene to acetamide are not uncommon under these conditions.[14]

$$\begin{tikzcd} ROH \arrow[r, shift left, "H_2O"] & R^+ \arrow[l, shift left, "H^+"] \arrow[r] \arrow[d, shift left] & RNHCOCH_3 \\ & \text{alkene} \arrow[u, shift left, "-H^+"'] & \end{tikzcd}$$

Table III. Effect of Water on Yields of Acetamides[a]

Substrate	Added [H_2O], m*M*	Electrolyte	Current, mA[b] Bkg	Current, mA[b] Init	Current, mA[b] Final	*n*,[c] Faradays/mol	Product (yield, %)
$(CH_3)_3CCOCH_3$[d]	28	TEAP[e]	18	340	13	2.0	**1** (74)
	0	TEAP	4	250	38	1.1	(0)[f]
	28	TEAF$_4$[g]	20	270	50	2.1	**1** (39)
	0	$LiClO_4$	8	200	15	2.2	**1** (80)
$(CH_3)_2CHCOCH_3$[h]	0	$LiClO_4$	6	250	16	1.8	**2** (46)
	0	TEAP	3	220	70	2.0	**2** (17)
	28	TEAP	15	220	7	1.8	**2** (44)

[a] Results at 2.15 V. [b] Bkg is background current. Init is initial current with added ketone. Final is current when oxidation was terminated. [c] Faradays/mol during preparative run. [d] 2.4 mmol. [e] Tetraethylammonium perchlorate. [f] **1** was not formed; a small amount of $CH_3CONHC(CH_3)(CH_2CH_3)COCH_3$ was isolated. [g] Tetraethylammonium fluoroborate. [h] 2.8 mmol.

Table IV. Cyclic Voltammetry Data. Tetraethylammonium Perchlorate with Added Water[a]

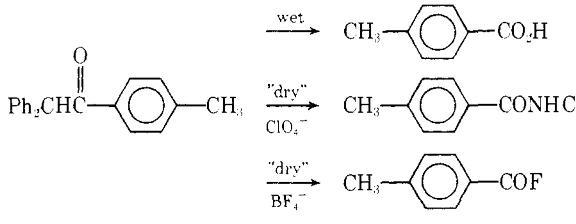
Substrate (concn, m*M*)	Added [H_2O], m*M*	E_p, V	$E_{p/2}$, V	I_p, A
$(CH_3)_3CCOCH_3$ (2.4)	0	2.24	2.09	25
	2.8	2.36	2.12	33
	5.6	2.38	2.14	34
$(CH_3)_2CHCOCH_3$ (2.8)	0	2.34	2.18	34
	2.8	2.43	2.24	45
$(CH_3)_2CHCOCH(CH_3)_2$ (2.1)	0	2.24, 2.50	2.07	33
	2.8	2.34	2.12	45

[a] 0.1 *M* tetraethylammonium perchlorate in acetonitrile, Ag|0.1 *M* $AgNO_3$ reference, sweep rate 0.2 V/sec.

The carboxylic acid fragment could reasonably be formed from an acylium ion if trapping by water was more effective than that by acetonitrile. Small amounts of the imide formed by acetonitrile trapping were detected when the imide was not too water soluble, *i.e.*, acetyl pivaloylimide from di-*tert*-butyl ketone. This product is, of course, consistent with acylium ion formation. It may well be true that water traps both halves preferentially, but the carboxylic acids are stable, while the alcohols are chemically converted to amides. This would explain the low yields of imide compared with those of amide. A different explanation may be required, however, since water has a large effect on the chemistry.

Evidence for acylium ions was sought in the oxidation of di-*tert*-butyl ketone. Although even this pivaloyl cation has an activation energy of 15 kcal/mol for decarbonylation,[14] it was thought that some might be detected. The experimental results are, however, inconclusive.

A comparison with the anodic chemistry of benzyl ketones is in order. These oxidations performed under the same conditions also give cleavage to amides *via* relatively stable benzyl cations. In the case of *p*-tolyl benzhydryl ketone, some indirect evidence for acylium ions was obtained.[15] In dry acetonitrile perchlorate, an imide was formed. In dry acetonitrile fluoroborate, acyl fluoride was formed, and in wet acetonitrile, carboxylic acid was formed. All these product variations are consistent with acylium ion formation.



Water. Small amounts of water in acetonitrile have often been suspected of affecting the outcome of electrochemical oxidations.[16,17] The data in Tables III and IV demonstrate its essential role in the α-cleavage of ketones. Lithium perchlorate was used in most oxidations, and it is extremely wet. In an attempt to use a relatively dry system, tetraethylammonium perchlorate was used with carefully and freshly dried acetonitrile. Although even this system contains some water, the change in the products was dramatic in that no *tert*-butylacetamide was formed from *tert*-butyl methyl ketone. On the other hand, 100 ml of dry acetonitrile-TEAP spiked with 2.8 mmol of water as anolyte gave the same product yield as lithium perchlorate electrolyte. Similar results are reported for isopropyl methyl ketone in Table III.

Water also has a definite effect on the cyclic voltammetry of ketones (Tables II and IV). Testing several ketones, the peak current (I_p) and potential E_p for lithium perchlorate electrolyte are the same as those for TEAP with added water. In dry TEAP-acetonitrile, the I_p is significantly lower, and the E_p is shifted very slightly positively. The higher currents are reflected to a certain extent in the coulometry measured during preparative oxidations (Table III).

We have no satisfactory explanation for these results. Water could enter into the reaction scheme at any number of points. Thus, it could change the electrode surface, it could directly scavenge cation radicals, or it could act as a buffer and prevent reactions of cations and initially formed products. Because of the paucity of pertinent data, speculation will be deferred.

Conclusion

Fragmentation has been shown to be an important reaction pathway for α-branched ketones. This reaction shows great similarities to mass spectral and photochemical α-cleavage reactions. The mass spectral reaction is assumed to involve a cation radical with the vacancy in the nonbonding oxygen orbital, the photochemistry generally proceeds *via* n $\rightarrow \pi^*$ states with a vacancy in this orbital, and it is probable that the electrochemistry involves a similar species. Assignment of the detailed mechanism is, however, premature, especially in light of the involvement of water in the reaction.

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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.

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Abstract: Ketones which lacked branching at the α position were oxidized at $\sim$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 $\sim$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-

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