phenyl ketones by (+) tris[(*S*)-2-methylbutyl]aluminum diethyl etherate proceeds through mechanistic pathways different from those invoked for the reduction by (+) tris[(*S*)-2-methylbutyl]aluminum.

Our previous findings have shown that, in the reductions by organoaluminum etherate, the ether ligand takes part in the transition state of the reaction.[4a] The electronegativity of the aluminum atom in Al2MB·OEt$_2$ should operate to make the cyclic transition state looser. The increased distance between the aluminum atom and the carbonyl oxygen atom should imply that the interactions among the groups are relatively weaker.[4a] So the restrictions to the conformational mobility and consequently the activation entropy should be similar in both diastereomeric states. On the other hand, the ligand, by itself exerting a certain compression on the groups, should modify the steric requirements of the transition states with respect to those involved in the reduction of ketones by Al2MB.

In this context the different values of $\Delta\Delta H^\ddagger$ and $\Delta\Delta S^\ddagger$, calculated for the asymmetric reduction of isopropyl phenyl ketone by (+)(*S*)Al2MB and by (+)(*S*)Al2MB·OEt$_2$, really appear very significant.

**Acknowledgment.** The authors wish to thank Professor S. Cabani (Istituto di Chimica Fisica, Università di Pisa) for helpful and stimulating discussion of the results.

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(10) Since the most important contributions to $\Delta S^\ddagger$ come from losses in internal motions, the positive difference of the activation entropies, when the alkyl group in the ketone is *i*-Pr and *t*-Bu, should reasonably fit this hypothesis. On this basis, the high symmetry of the *t*-Bu group could explain why $\Delta\Delta S^\ddagger$ is lower in this case rather than in that of the asymmetric reduction of isopropyl phenyl ketone[4a] (Table II).

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# Anodic Cleavages of Secondary and Tertiary Alkylphenylcarbinols

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**Abstract:** The oxidation of secondary alkylphenylcarbinols PhC(R$_1$)(R$_2$)OH (R$_1$ = H; R$_2$ = methyl, ethyl, isopropyl or *tert*-butyl) in acetonitrile-tetra-*n*-butylammonium fluoroborate at platinum led to the formation of carbonyl compounds. When R$_2$ = methyl or ethyl, acetophenone or propiophenone were respectively formed. For R$_2$ = isopropyl or *tert*-butyl, benzaldehyde and either *N*-isopropyl- or *tert*-butylacetamide were isolated. Tertiary alkylphenylcarbinols (R$_1$, R$_2$ = methyl, ethyl, isopropyl, or *tert*-butyl) were found to cleave to yield ketones and either gases or *N*-alkylacetamides from the corresponding alkyl fragments. The relative leaving group abilities were methyl < ethyl < isopropyl < *tert*-butyl. An ECE mechanism is proposed in which the initial step is oxidation of the aromatic ring (E) to form a cation radical, then followed by loss of a proton or an alkyl radical (C) by the cation radical, and finally oxidation of the alkyl or alkylphenylcarbinol radical (E). Of the alkyl radicals, only the methyl radical failed to undergo further oxidation.

The chemical oxidation of *tert*-alkylphenylcarbinols has been reported,[1] but there has been only one previous study on its electrochemical oxidation. Maruyama and Murakami[2] investigated the electrochemical oxidation of various *tert*-alkylphenylcarbinols in water–dioxane–sodium hydroxide, utilizing a platinum electrode and constant current. With this alkaline solvent system, the *tert*-alkylphenylalkoxide was proposed as the species undergoing oxidation, yielding the *tert*-alkylphenylalkoxy radical which cleaved to produce alkyl phenyl ketones and alkyl radicals. The relative leaving group abilities were then measured by determining the ratio of the two possible alkyl phenyl ketones. The relative leaving group abilities were allyl > *sec*-butyl > isopropyl > ethyl > *n*-propyl > *n*-butyl > *n*-pentyl > isobutyl > methyl, implying the hyperconjugative effect of the $\beta$ hydrogen was the most important factor in determining which group was cleaved. Hydrocarbons, C$_2$ to C$_5$, derived from the alkyl fragment, were also detected. The determination of the mechanism is, however, complicated by the oxidation of the solvent since a large quantity of oxygen was detected, and therefore a chemical reaction, i.e., radical abstraction, between an electrochemically generated species and the *tert*-alkylphenylcarbinol cannot be eliminated.

Benzylic ethers, esters, alcohols, and phenyl epoxides have been previously reported to yield carbonyl compounds upon anodic oxidation in acetonitrile at a platinum electrode.[3] It, therefore, became of interest to examine the electrochemical behavior of such carbinols in acetonitrile since it would be the carbinol and not the alkoxide which would be oxidized, and solvent decomposition could be eliminated.

## Results

All the oxidations were controlled potential electrolyses and conducted with platinum electrodes in a divided cell. The electrolyte was 0.2 *M* tetra-*n*-butylammonium fluoroborate in acetonitrile, and cyclic voltammetry indicated no substantial oxidation up to +3.0 V vs. Ag$^+$|Ag (Figure 1). Generally 1.0–0.5 g of substrate and 2.0 g of anhydrous sodium carbonate were added. The potential was pulsed to

**Table I.** Oxidation Reactants and Products

| $R_1$<br>X-Ph-C-OH<br>$R_2$ | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $R_1$ | $R_2$ | X | Bp, °C | $E_{p_1}{}^a$ | $E_{p_2}$ | $E_{ox}{}^d$ | Product (%)$^b$ | $n^c$ |
| H | $CH_3$ | H | 85 (10 mm) | 2.01 | 2.49 | 2.20 | $PhCOCH_3$ (82.5) | 2.37 |
| H | $CH_2CH_3$ | H | 100 (8 mm) | 2.08 | 2.60 | 2.20 | $PhCOCH_2CH_3$ (74.9) | 2.68 |
| H | $CH(CH_3)_2$ | H | 102 (9 mm) | 1.97 | 2.47 | 2.20 | PhCHO (62.8)<br>$(CH_3)_2CHNHCOCH_3$ (33.3) | 2.64 |
| H | $C(CH_3)_3$ | H | 112–115 (15 mm) | 1.96 | 2.50 | 2.20 | PhCHO (61.1)<br>$(CH_3)_3CNHCOCH_3$ (46.8) | 2.97 |
| H | $CH_3$ | $CH_3$ | 109–110 (9 mm) | 1.80 | 2.25 | 2.0 | $CH_3PhCOCH_3$ (76.5) | 2.57 |
| $CH_3$ | $CH_3$ | H | 91 (15 mm) | 2.15 | 2.68 | 2.30 | $PhCOCH_3$ (72.2) | 6.2 |
| $CH_3$ | $CH_2CH_3$ | H | 101–102 (15 mm) | 2.04 | 2.42 | 2.30 | $PhCOCH_3$ (73.9)<br>$CH_3CH_2NHCOCH_3$ (9.4) | 2.3 |
| $CH_2CH_3$ | $CH_2CH_3$ | H | 103–104 (8 mm) | 2.10 | 2.48 | 2.20 | $PhCOCH_2CH_3$ (71.3)<br>$CH_3CH_2NHCOCH_3$ (12.9) | 2.51 |
| $CH_2CH_3$ | $CH(CH_3)_2$ | H | 112 (11 mm) | 1.99 | 2.39 | 2.20 | $PhCOCH_2CH_3$ (81.9)<br>$(CH_3)_2CHNHCOCH_3$ (48.9) | 2.18 |

$^a$ Versus $Ag^+|Ag$. Conditions are those used for controlled potential electrolysis. $^b$ Based on starting material reacted. $^c$ Based on product isolated. $^d$ Potential used for controlled potential electrolysis.

approximately 0.0 V, utilizing a square wave function with a 10/1 duty time. This served to keep the electrode from becoming fouled. Table I lists the compounds oxidized and the products isolated as determined by VPC and spectroscopic data.

It can be seen the conversion to carbonyl compounds is fairly good, and the alkyl fragment produced the corresponding *N*-alkylacetamide. However, for cumyl alcohol ($R_1$, $R_2$ = methyl), no acetamide was found, and gas analysis indicated both methane and ethane were formed. Quantitative analysis was not performed, but there was approximately twice as much methane as ethane produced. A similar experiment was performed with 3-phenyl-3-pentanol ($R_1$, $R_2$ = ethyl), and the gas analysis indicated the presence of only ethylene.

## Discussion

Since all of the *tert*-alkylphenylcarbinols oxidize in the same potential region as dibenzyl ether, $E_p = +1.98$ vs. $Ag^+|Ag$, it is the carbinol and not the alkoxide being oxidized. Typical alkoxides, sodium methoxide and ethoxide, have been reported to oxidize at +1.0 V vs. $Ag^+|Ag$.[4] Also, the cyclic voltammograms before and after the addition of the sodium carbonate were identical. The addition of the carbonate was necessary to scavenge the electrochemically produced protons since the carbinols and possibly the products should be sensitive to acid catalysis.[5]

Since the carbinol has been established as the species undergoing oxidation, there are two possible sites within the carbinol from which the electron may be removed, the $\pi$ electrons of the aromatic ring and the nonbonding electrons on the oxygen atom. For benzylic ethers, esters, and alcohols, it has been established, utilizing the ionization and oxidation potentials of toluene vs. methanol, that the $\pi$ electrons are removed more easily.[3] From a representative cyclic voltammogram (Figure 1), it is apparent that *tert*-alkylphenylcarbinols follow the same pattern since these oxidize in the same region necessary to oxidize toluene, $E_{1/2}$ = 1.96 V vs. $Ag^+|Ag$.[6] The electrochemical data revealed the height of the first peak varied linearly with concentration, and no reversibility was observed up to 50 V/sec. The current function, $i_p/v^{1/2}C^*$, where $i_p$ is the peak current, $v$ the scan rate, and $C^*$ the concentration of the carbinol, decreased, and $E_p$ shifted more positive with increasing scan rate. Controlled potential electrolysis indicated that $n \approx 2$. All of the preceding data are consistent with a very rapid ECE mechanism.[7] The second oxidation peak was attributed to the oxidation of the carbonyl product produced since cyclic voltammograms of the ketones or aldehyde alone had identical oxidation potentials. Also, after completion of the electrolysis, the first oxidation peak was not observed, but the second with increased height was. Cyclic voltammetry revealed the height of the second peak did not decrease with increasing scan rate implying very fast chemical and electrochemical kinetics for the production of the carbonyl compound.[8]

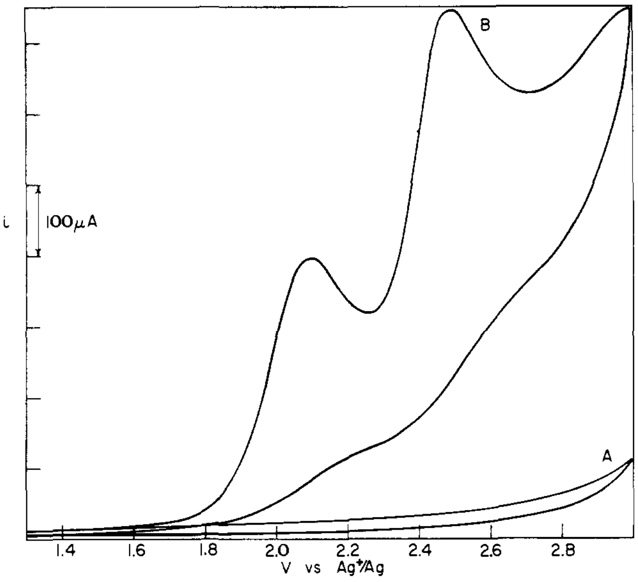
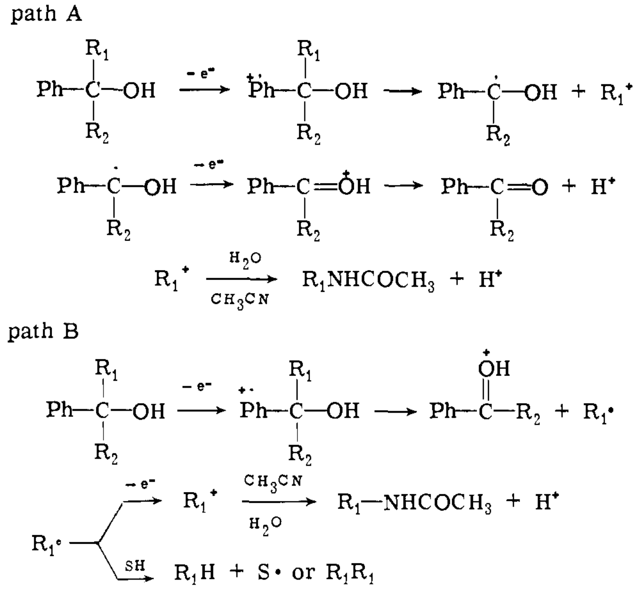


**Figure 1.** Cyclic voltammograms of (A) background, acetonitrile–tetra-*n*-butylammonium fluoroborate–sodium carbonate and (B) 0.081 *M* 3-phenyl-3-pentanol.

The next aspect is to determine the fate of the aryl cation radical. There are numerous examples which indicate such cation radicals undergo chemical reactions,[9] and the two most probable reactions are illustrated in the sequence shown in Scheme I.

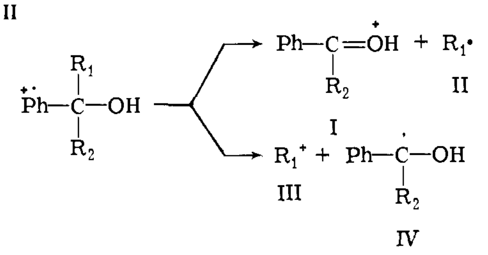
Since *N*-methylacetamide was not isolated from the oxidation of cumyl alcohol, path A can be eliminated, thus leaving path B as the most probable mechanism for this carbinol. It can be argued from a thermodynamic viewpoint that the formation of the carbonyl group is the dominating

Scheme I



factor in the choice between path A and B, and so the alkyl radical cleavage mechanism should be valid for all *tert*-alkylphenylcarbinols. Scheme II illustrates this argument.

Scheme II



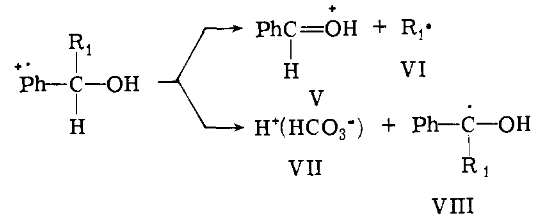
There is a stability difference in the radicals II and IV, but it is small when compared with the difference between the carbonium ions I and III. The difference between the methyl and *tert*-butyl radical is 11 kcal/mol while, for the respective carbonium ions, it is approximately 77 kcal/mol. The latter difference was obtained by utilizing the ionization potentials of the radicals in the gas phase. Solvation energies should lower this difference, but it still should be greater than for the radicals. Therefore the decomposition is determined by the production of the more stable carbonium ion I. The fate and therefore the product distribution of the alkyl fragment depends upon whether it is able to undergo further oxidation. It seems ethyl, isopropyl, and *tert*-butyl radicals are capable of further oxidation, while the methyl is not. A similar observation has been made in the Kolbe reaction, the oxidation of carboxylate anion to yield carbon dioxide and an alkyl radical. Eberson has proposed that those radicals which have an ionization potential lower than 8.0 eV should undergo oxidation.[10] The ionization potentials for methyl, ethyl, isopropyl, and *tert*-butyl radicals are respectively 9.84, 8.38,7.55, and 6.93 eV.[11] From the products isolated, methyl, isopropyl, and *tert*-butyl radicals follow the prescribed behavior, but the ethyl does not. According to Eberson's proposal, the ethyl radical should not be oxidized, but the gassing experiment of 3-phenyl-3-pentanol showed no evidence of ethane. Ethylene, however, was found which would indicate the ethyl radical was oxidized, and the resulting carbonium ion eliminated a proton faster than nucleophilic trapping by acetonitrile. This would also explain the low yield of *N*-ethylacetamide. The apparent discrepancy between the Kolbe reaction and this study can be explained by the differences in the oxidation potentials required for each study. Geske found the peak potential for tetra-*n*-butylammonium acetate at platinum in sodium perchlorate-acetonitrile to be +1.8 V vs. $Ag^+|Ag$.[12] The carbinols oxidize at +2.0 V vs. $Ag^+|Ag$, and the bulk electrolyses are done at +2.2-2.3 V vs. $Ag^+|Ag$ so that this increase in potential is sufficient to oxidize the ethyl radical.

An attempt was made to oxidize the methyl radical by making the potential more positive. Cumyl alcohol was oxidized at +2.80 V vs. $Ag^+|Ag$, but methane and ethane were still produced. From the ionization potential, this potential should be sufficient to oxidize the methyl radical, but it is apparent that the rate of hydrogen abstraction is much more favorable. It should also be pointed out that the coulometric *n* value is rather high for cumyl alcohol. Since the methyl radical must abstract a hydrogen atom to form methane, it may be the subsequent oxidation of this new radical and products derived from it that yield the high *n* value.

For the *tert*-alkylphenylcarbinols, the rates of cleavage follow the relative stabilities of the alkyl radicals, but the magnitude of the difference is somewhat larger than for radicals. The difference between a methyl and ethyl radical is only 2 kcal/mol, which implies approximately a 10/1 product ratio. Since only one of the two possible alkyl phenyl ketones was isolated, the larger difference may be attributed to a polarized transition state in which the cleaving alkyl group has obtained a substantial positive charge. Polarized transition states have been observed for many types of radical reactions,[13] in particular, the decomposition of *tert*-alkylalkoxy radicals.[14] If such a transition state is important in the neutral free radical cleavage, it should be equally, if not more, important in the cleavage of a cation radical since delocalization of the charge can occur.

For secondary alkylphenylcarbinols, the mechanism can be either path A or B depending upon the alkyl leaving group ability relative to a proton. When $R_2$ = isopropyl or *tert*-butyl, the leaving group is an alkyl radical which by further oxidation and nucleophilic trapping by acetonitrile yields the *N*-alkylacetamide. The dominating factor again for alkyl radical cleavage is the formation of a carbonyl group. If $R_2$ = methyl or ethyl, however, the cation radical loses a proton faster than an alkyl group, and the alkylphenylcarbinol radical is oxidized to yield the corresponding ketone. The gain in energy by formation of a carbonyl group is apparently not sufficient to overcome the instability of the methyl and ethyl radical relative to a proton so the latter becomes the favored pathway. This perhaps may be seen from Scheme III. The major difference between this scheme and the previous one for *tert*-alkylphenylcarbinols is the much smaller stability difference between the cations V and VII. So the radicals become more important in determining which pathway is taken. This dichotomy has also been observed in the chemical oxidation of secondary alkylphenylcarbinols.[1]

Scheme III



It is now apparent that anodic cleavage of tertiary and secondary alkylphenylcarbinols and cleavage of the respective alkoxy radicals are mechanistically related, even though different reactive intermediates are involved.

## Experimental Section

Ir analyses, neat for liquids and potassium bromide pellets for solids, were done with a Perkin-Elmer 237 B spectrophotometer. NMR analyses were performed with a Perkin-Elmer R-12 spectrometer. A F & M Research Model 720 gas chromatograph with a 6-ft 10% SE 30 on 60–80 diatport S was used for VPC analyses. Melting points were taken with a Melt-temp apparatus and are uncorrected.

A divided electrochemical cell was used and has been previously described.[15] The working and auxiliary electrodes were 5.56 $cm^2$ platinum sheets. The reference electrode was 0.1 *N* $AgNO_3$|Ag in acetonitrile which was contained in a separate glass fritted compartment. A platinum disk, 0.0186 $cm^2$, was used for cyclic studies. A Princeton Applied Research Model 170 electrochemistry unit was used for cyclic voltammetry and controlled potential electrolysis studies. Eastman Kodak acetonitrile was purified by distillation using the method proposed by Mann.[16] Tetra-*n*-butylammonium fluoroborate was prepared by the previously reported synthesis,[17] and Baker anhydrous sodium carbonate was used.

All of the compounds were synthesized by either lithium aluminum hydride reduction of the corresponding ketone, by the corresponding alkyl Grignard and benzaldehyde, or by a phenyl Grignard and the corresponding aliphatic ketone. The compounds were purified by distillation, and Table I lists the pertinent physical constants.

A typical experiment was as follows. The fluoroborate, 8.50 g, was dissolved in 125 ml of acetonitrile and then placed into the cell. The electrodes were put in place and the substrate, 1.0–0.5 g, and anhydrous sodium carbonate, 2.0 g, added. After the electrolysis was completed, the anolyte was placed in a round-bottomed flask and the acetonitrile distilled with the aid of a water pump. The residue was then extracted several times with ether. The ether layer was then dried with magnesium sulfate, filtered, and then concentrated by distillation. The residue was placed in a volumetric flask and analyzed by VPC. Quantitative and qualitative analyses were done with standard solutions of authentic samples. Further spectroscopic analyses were done by collecting the appropriate fraction from the VPC.

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# Reactions of Crowded Molecules under High Pressure. Reactions of 2,6-Di-*tert*-butylpyridine with Methyl Iodide and Methyl Fluorosulfonate under High Pressure

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**Abstract:** 2,6-Di-*tert*-butylpyridine (**1**) was reacted with methyl iodide in dioxane under 5000–6000 atm of pressure at 90° for 10–15 hr. The reaction gave two main products, 2,6-di-*tert*-butyl-*N*-methylpyridinium iodide (**2**) and 2,6-di-*tert*-butylpyridinium hydrogen iodide (**3**). The ratio of these products was about 2 to 8, respectively. Under similar conditions, both **1** and 2,4,6-tri-*tert*-butylpyridine (**4**) were found to react with methyl fluorosulfonate. The solid products from these reactions were also mixtures of the *N*-methyl and protonated compounds. However, the ratio of these products was about 8 to 2, respectively. 4,5-Dimethylacridine was also reacted with methyl fluorosulfonate under high pressure to yield 4,5-dimethyl-*N*-methylacridinium fluorosulfonate. The *N*-methyl compounds of **1** and **4** were thermally very stable and did not decompose at temperatures of up to 300°. The unusual stability of the compounds was accounted for by invoking the steric hindrance of the *tert*-butyl groups. Low-field chemical shifts of methyl and *tert*-butyl protons in the $^1H$ NMR of **2** and 2,4,6-tri-*tert*-butyl-*N*-methylpyridinium fluorosulfonate (**8**) were discussed and compared with those of their sterical homomorphs in the benzene series.

Menschutkin reactions—typical SN2-type reactions of alkyl halides with amines to form quaternary ammonium salt—have been widely investigated for steric effects.[1] Generally, reaction rates decrease sharply with increased steric hindrance at the reaction site. For example, the reaction rate of pyridine with alkyl iodides decreases sharply as the alkyl iodide is changed through methyl, ethyl, to isopropyl. The activation energy in this case shows a corresponding increase. Introduction of alkyl groups into the 2 and 6 positions of pyridine also results in a decrease in the rate of reaction with alkyl halides which becomes more and more pronounced as the size of the alkyl group increases.