for SN1 reactions (α-methylallyl chloride) and negative values for SN2 reactions (β-methylallyl chloride).

Effect of Reaction Impurities on the Heat Capacity of Activation. Some preliminary work done on unpurified samples of the allylic halides studied in this research points up the effect which certain impurities can have on derived thermodynamic parameters, particularly on the heat capacity of activation. In the present study this is most apparent in results obtained using a sample of *trans*-γ-methylallyl chloride which was later found to contain 6% of the *cis* isomer as an impurity. This has the effect of making the observed value of $\Delta H^{\ddagger}$ decrease more rapidly with increasing temperature than the true value does. Thus an erroneous value of $\Delta C_p^{\ddagger}$ of -170 cal/mol deg was obtained from these data.

The preceding case is one in which it was quite apparent from an inspection of the kinetic data that the results were in error. In general this will be the case if a significant impurity is at least twofold slower reacting or twofold faster reacting than the compound of interest.

A situation in which the presence of an impurity is less easily detected kinetically occurs when the impurity reacts at nearly the same rate as the compound of interest. This situation was encountered in preliminary work on the hydrolysis of a sample of α-methylallyl chloride which was later found to contain a 10% impurity of *trans*-γ-methylallyl chloride. The experimental results were observed to deviate noticeably from the first-order rate law at the high end of the temperature range, but to a much lesser extent than in the preceding case. Even so, the effect on the derived value of $\Delta C_p^{\ddagger}$ was considerable; a value of -125 cal/mol deg was obtained from these data compared to the value of -92 cal/mol deg (see Table II) obtained on a purified sample.

In summary we make the following suggestions for examining kinetic data in order to detect the presence of kinetically significant impurities. (1) The first-order plot should be examined for indications of nonrandom deviations from true first-order behavior. Clearly deviations are more likely to be apparent in the later part of the main reaction (*i.e.*, beyond 3–4 half-lives). (2) Where a conductance bridge accurate to $^1/_{5000}$ is used and $\Delta t^0 = 0.002°$, relative standard deviations for pure compounds are usually $<0.01\%$ provided adsorption of ions on the cell walls is minimized.

Mechanism of Electron Transfer Oxidation of Alkyl Radicals by Copper(II) Complexes

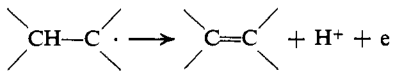
J. K. Kochi, A. Bemis, and C. L. Jenkins

Contribution from the Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106. *Received February 1, 1968*

Abstract: The rates of oxidation of *n*-butyl, isopropyl, and neopentyl radicals by carboxylatocopper(II) complexes have been determined in acetonitrile–acetic acid solutions. The neopentyl radical is oxidized significantly slower than other alkyl radicals. Polar substituents have large effects on the relative rates of oxidative elimination and substitution of β-arylethyl radicals. Thus, the ratio of second-order rate constants k_e/k_s for oxidative elimination and oxidative substitution for a series of substituted β-phenethyl radicals varies from 50 for *m*-methoxy, 33 for hydrogen, 1.3 for *p*-methyl to 0.014 for *p*-methoxy. The rate of oxidative substitution is enhanced by electron-releasing substituents, but oxidative elimination is retarded by these polar groups. The *total rate* of oxidation (k_e/k_s) of these β-arylethyl radicals, however, is remarkably constant. We conclude that the rate-limiting step for oxidation of alkyl radicals by Cu^{II} precedes and is separate from the product-determining step. An alkylcopper intermediate which is reversibly formed is postulated. Oxidative substitution results from heterolysis of this organocopper species to Cu^{I} and a carbonium ion. (The β-arylethyl acetates isolated from the oxidation of β-phenethyl-β,β-d_2 and β-anisylethyl-α,α-d_2 radicals show complete equilibration of the α- and β-carbon atoms.) Oxidative elimination as a competing process also proceeds from the alkylcopper intermediate. Carbonium ions, as such, are not relevant to oxidative eliminations, since the styrenes which accompany the β-arylethyl acetates are not rearranged. The β-deuterium kinetic isotope effect in oxidative elimination of β-phenethyl radical is 2.8–2.9. We conclude that electron transfer to Cu^{II} has proceeded further than heterolysis of the β-proton in the transition state for oxidative elimination.

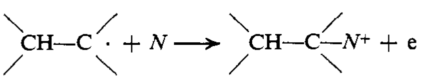
The electron-transfer oxidation of alkyl radicals by a variety of metal oxidants in solution generates alkenes and alkyl derivatives as the two principal types of products.[1-3] The standard (half-cell) reactions for oxidation of alkyl radicals can be represented by eq 1 and 2. The associated reduction of the metal oxidant

Oxidative elimination



(1)

Oxidative substitution



(2)

N = nucleophile = HOAc, HOR, CH$_3$CN, ArH, etc.

---

(1) J. Kochi and A. Bemis, *J. Amer. Chem. Soc.*, **90**, 4038 (1968).
(2) J. Kochi, J. Bacha, and T. Bethea, *ibid.*, **89**, 6538 (1967).
(3) J. Bacha and J. Kochi, *J. Org. Chem.*, **33**, 83 (1968).

is given by a general reaction such as eq 3.[4] These

$$\mathrm{M}^{n+}(\mathrm{OAc}^-)_n + \mathrm{e} \longrightarrow \mathrm{M}^{(n-1)+}(\mathrm{OAc}^-)_n \qquad (3)$$

standard reactions together (eq 1 or 2 and 3) constitute important processes in the catalytic sequence of many oxidation–reduction reactions.[5-8]

Cu^{II} complexes have been particularly useful for examining structural effects of the alkyl moiety on the rate and the nature of the transition state in oxidative processes.[1,3,5,9-12] The oxidative elimination (eq 1) and substitution (eq 2) of alkyl radicals by copper(II) carboxylates can be parallel routes. Thus, benzylic, homoallylic, and β-arylethyl radicals generate mixtures of alkenes and alkyl acetates on oxidation by Cu^{II} complexes in acetic acid.[1,2,13] On the other hand, simple alkyl radicals, such as *n*-butyl, *sec*-butyl, and *t*-butyl radicals, with readily available β-hydrogens, are oxidized at similar rates, and they afford alkenes as principal (and often exclusive) products.[9,11] At the other extreme, allylic radicals on oxidation yield only substitution products.[14]

In our previous paper[1] we showed that carbonium ions formed by electron transfer from the alkyl radical to the metal oxidant were intermediates in oxidative substitution. Alkenes by oxidative elimination of alkyl radicals were considered separately. Heretofore, no direct evidence has been presented for a coherent mechanism for the oxidation of alkyl radicals by electron-transfer processes.

In this paper we applied kinetic studies in order to resolve the dichotomy between oxidative substitution and oxidative elimination. We chose *n*-butyl, isopropyl, and neopentyl radicals together with the series of ring-substituted β-phenethyl radicals to ascertain the magnitude of structural effects and direction of polar effects in these competing processes. Deuterium substitution was used to determine kinetic isotope effects and also as an isotopic tracer for rearrangement during oxidation. A mechanism for electron-transfer oxidation of alkyl radicals consistent with these kinetic consequences are reconciled with the earlier product studies.[1]

Results and Discussion

Competitive Kinetics for Oxidation of Alkyl Radicals. All oxidation studies were carried out in solutions of acetic acid and acetonitrile. The former served as a suitable protic solvent that diverted intermediates to stable alkyl acetates which could be readily analyzed. Acetonitrile exerted a stabilizing influence on Cu^I species, and promoted the catalytic reactions used in the generation of alkyl radicals.[15]

Alkyl (R·) radicals are the prime chain-carrying species in the copper-catalyzed decomposition of diacyl peroxides, $(RCO_2)_2$.[9,10] In the presence of a hydrogen donor (SH), these radicals are reduced to alkane (RH, eq 4) or suffer oxidation by Cu^{II} (R_{ox}, eq 5).

$$\mathrm{R}\cdot + \mathrm{SH} \xrightarrow{k_\mathrm{H}} \mathrm{RH} + \mathrm{S}\cdot \qquad (4)$$

$$\mathrm{R}\cdot + \mathrm{Cu^{II}} \xrightarrow{k_\mathrm{ox}} \mathrm{R_{ox}} + \mathrm{Cu^{I}} + \mathrm{H^+} \qquad (5)$$

Since the radical chain decomposition is a catalytic process, the concentrations of Cu^I and Cu^{II} species remain invariant throughout the reaction.[12] The latter exists in acetonitrile–acetic acid solutions as a mixture of monomeric and dimeric Cu^{II} complexes (eq 6), but it

$$\mathrm{Cu^{II}}_2(\mathrm{OAc})_4 \overset{K}{\rightleftarrows} 2\mathrm{Cu^{II}}(\mathrm{OAc})_2 \qquad (6)$$

is only the monomeric form which oxidizes alkyl radicals. Under these conditions, the dissociation constant, K, of the dimeric Cu^{II} species, and the second-order rate constants for oxidation, k_{ox}, and reduction, k_H, are related to the measured excess of SH and the total Cu^{II} concentrations, (Cu_t), according to eq 7.[16]

$$\frac{(\mathrm{Cu_t})(\mathrm{RH})}{(\mathrm{SH})(\mathrm{R_{ox}})} = 2K^{-1}\left(\frac{k_\mathrm{H}}{k_\mathrm{ox}}\right)^2\frac{(\mathrm{R_{ox}})}{(\mathrm{RH})}(\mathrm{SH}) + \frac{k_\mathrm{H}}{k_\mathrm{ox}} \qquad (7)$$

Kinetics of Oxidation of *n*-Butyl and Isopropyl Radicals by Cu^{II} Complexes. The catalyzed decomposition of valeryl peroxide, $(n\text{-}C_4H_9CO_2)_2$, by copper salts in acetonitrile–acetic acid solutions generated *n-butyl radicals*, which afforded *n*-butane in the presence of

$$(n\text{-}\mathrm{C_4H_9CO_2})_2 + \mathrm{Cu^I} \longrightarrow n\text{-}\mathrm{C_4H_9CO_2Cu^{II}} + \mathrm{CO_2} + n\text{-}\mathrm{C_4H_9}\cdot$$

isobutyraldehyde (eq 8) or underwent oxidation by Cu^{II} to butene-1 (eq 9). The variation of butane and butene-1

$$n\mathrm{C_4H_9}\cdot + \mathrm{(CH_3)_2CHCHO} \xrightarrow{k_\mathrm{H}} n\text{-}\mathrm{C_4H_{10}} + \mathrm{(CH_3)_2CH\dot{C}O} \qquad (8)$$

$$n\text{-}\mathrm{C_4H_9}\cdot + \mathrm{Cu^{II}} \xrightarrow{k_\mathrm{e}} \mathrm{CH_3CH_2CH{=}CH_2} + \mathrm{Cu^I} + \mathrm{H^+} \qquad (9)$$

produced over a range of concentrations of isobutyraldehyde and Cu^{II} could be correlated by eq 7 (RH = butane, R_{ox} = butene-1, SH = isobutyraldehyde, $k_{ox} = k_e$). A typical plot is shown in Figure 1. The values of K and k_H/k_e obtained in this manner in acetonitrile–acetic acid solutions of various compositions are presented in Table I.

Table I. Dissociation Constants for Copper(II) Acetate Dimer and Second-Order Rate Constants for Hydrogen Transfer and Oxidation of *n*-Butyl and Isopropyl Radicals in Acetic Acid–Acetonitrile Solutions[a]

Solvent HOAc–CH_3CN, v/v	Isopropyl radical K, mol/l.	Isopropyl radical k_H/k_e	*n*-Butyl radical K, mol/l.	*n*-Butyl radical k_H/k_e
100:0	...	...	9.1×10^{-5} [b]	0.99×10^{-3} [c]
93:7	1.2×10^{-3}	0.32×10^{-3}	2.0×10^{-3}	1.2×10^{-3}
76:24	1.5×10^{-1}	1.3×10^{-3}	1.2×10^{-1}	3.7×10^{-3}
60:40	5.5×10^{-2}	1.0×10^{-3}	5.6×10^{-2}	3.2×10^{-3}
20:80	8.4×10^{-2}	0.8×10^{-3}	8.6×10^{-2}	2.9×10^{-3}

[a] At 25.5° from valeryl peroxide and isobutyraldehyde, using copper(I,II) acetates. [b] Extrapolated from data in ref 16. [c] From ref 12, value at 57°.

---

(4) In the following presentation, coordination around the metal atom will be omitted unless required for discussion.

(5) J. Kochi, *Rec. Chem. Progr.*, **27**, 209 (1966).

(6) (a) The problem of matching oxidation states of oxidants and reductants in redox processes has been considered extensively in inorganic systems. (b) *Cf.* T. Turney, "Oxidation Mechanisms," Butterworth and Co., Ltd., London, 1965, p 9 ff. (c) J. Halpern, *Quart. Rev.* (London), **15**, 207 (1961).

(7) (a) J. Kochi, *J. Amer. Chem. Soc.*, **87**, 3609 (1965); (b) *J. Org. Chem.*, **30**, 3265 (1965).

(8) J. Kochi and T. Bethea, *ibid.*, **33**, 75 (1968).

(9) J. Kochi, *J. Amer. Chem. Soc.*, **85**, 1958 (1963).

(10) J. Kochi and R. Gilliom, *ibid.*, **86**, 5251 (1964).

(11) H. DeLaMare, F. Rust, and J. Kochi, *ibid.*, **83**, 2013 (1961).

(12) J. Kochi and R. Subramanian, *ibid.*, **87**, 4855 (1965).

(13) J. Kochi and J. Bacha, *J. Org. Chem.*, **33**, 2746 (1968).

(14) (a) J. Kochi, *J. Amer. Chem. Soc.*, **84**, 774, 3271 (1962); (b) J. Kochi and H. Mains, *J. Org. Chem.*, **30**, 1862 (1965).

(15) J. Kochi and A. Bemis, *Tetrahedron*, in press.

(16) J. Kochi and R. Subramanian, *Inorg. Chem.*, **4**, 1527 (1965).

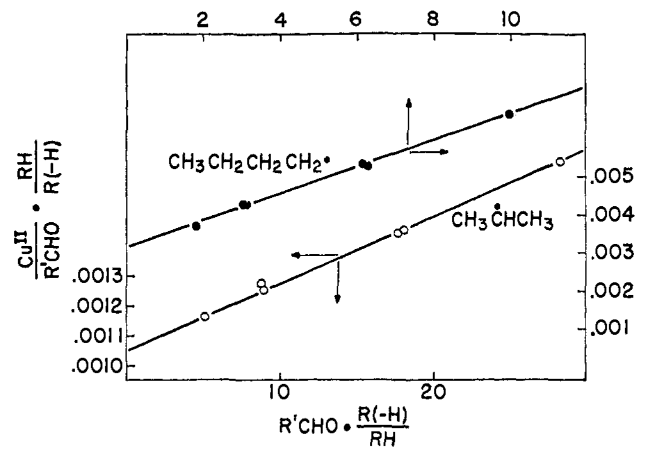


Figure 1. Determination of the dissociation constant K for $Cu^{II}OAc$ dimer and the ratio of second-order rate constants (k_H/k_e) for hydrogen transfer and oxidative elimination for n-butyl (●, R(–H) = butene-1, RH = n-butane) and isopropyl radicals (○, R(–H) = propylene, RH = propane) in 40 vol % acetonitrile–acetic acid at 25.5° using isobutyraldehyde (R′CHO) as hydrogen donor.

When isobutyraldehyde was used as hydrogen donor, *isopropyl radicals* were useful by-products as a result of decarbonylation (eq 10) of the isobutyryl radicals

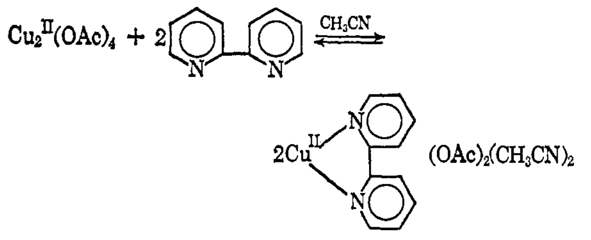
$$(CH_3)_2CH\dot{C}O \longrightarrow (CH_3)_2CH\cdot + CO \qquad (10)$$

produced in eq 8. Isopropyl radicals formed in this manner were susceptible to hydrogen transfer with isobutyraldehyde and oxidation with Cu^{II} in the same way[15] as n-butyl radicals derived from valeryl peroxide. The values of k_H/k_e for isopropyl radicals in acetonitrile–acetic acid solutions are presented in Table I.

Independent values of the dissociation constant K of the dimeric Cu^{II} species could also be obtained in the same medium by analysis of the propane–propylene and butane–butene-1 mixtures. Despite the inherent sensitivity[16] of this method of determining K, the values reported in Table I agree remarkably well. It is interesting to note that K increased by a factor of 1000, as approximately 20% by volume of the glacial acetic acid was replaced by acetonitrile. Further addition of acetonitrile caused only a slight decrease in K. The same change in solvent had only a minor effect on the values of k_H/k_e. The change in dissociation constant of the dimer could be associated with the formation of acetonitrilecopper(II) complexes.[17] Pyridine effected similar changes.[15]

$$Cu^{II}_2(OAc)_4 + CH_3CN \rightleftarrows 2(CH_3CN)_4Cu^{II}(OAc)_2 \qquad (11)$$

In a similar manner, the addition of α,α'-bipyridine in stoichiometric amounts increased the dissociation of the cupric acetate dimer in 40 vol % acetonitrile–acetic acid to a point that at 10^{-2} M it was completely dissociated. The bipyridinecopper(II) acetate complex formed under these conditions was a more powerful oxidant than the acetonitrilecopper(II) acetate since the value of k_H/k_e for n-butyl radicals decreased to 5.8×10^{-4} (compared to 3.2×10^{-3}).



(12)

Kinetics of Oxidation of Neopentyl Radicals. Neopentyl radicals were generated in a similar manner from the catalyzed decomposition of t-butylacetyl peroxide. The rate of oxidation by Cu^{II}, relative to hydrogen transfer with isobutyraldehyde (eq 13),[13]

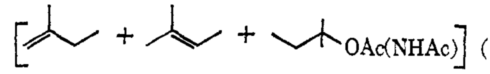
$$[(CH_3)_3CCH_2CO_2]_2 + Cu^I \longrightarrow (CH_3)_3CCH_2CO_2Cu^{II} + CO_2 + (CH_3)_3CCH_2\cdot$$

was determined by the technique described in the previous section.

$$(CH_3)_3CCH_2\cdot + (CH_3)_2CHCHO \xrightarrow{k_H} (CH_3)_4C + (CH_3)_2CH\dot{C}O \qquad (13)$$

In contrast to n-butyl radicals, which produced butene-1 as the sole product of oxidation by Cu^{II}, neopentyl radical afforded four oxidation products: 2-methylbutene-1 and -2, t-amyl acetate, and acetamide (eq 14).[1,9] The relative yields of these products in

$$(CH_3)_3CCH_2\cdot + Cu^{II} \xrightarrow[CH_3CN-HOAc]{k_{ox}} Cu^I + H^+ +$$



(14)

acetonitrile–acetic acid solutions were shown to be invariant with the nature of the Cu^{II} oxidant. In eq 7, (R_{ox}) was taken as the sum of all four products. The value k_H/k_{ox} (eq 13/14) was obtained by measuring neopentane at various concentrations of isobutyraldehyde and Cu^{II} oxidant.

The value of k_H/k_{ox} for neopentyl radicals in 40 vol % acetonitrile–acetic acid was 2.2×10^{-2} when cupric acetate was the oxidant. This value was almost 10 times larger ($k_H/k_{ox} = 3.9 \times 10^{-1}$) when α,α'-bipyridinecopper(II) acetate was employed. Neopentyl radicals, thus, were oxidized by bipyridinecopper(II) complexes more slowly than they were by acetonitrilecopper(II) complexes. This order of reactivity of copper(II) complexes was exactly reversed from their behavior toward n-butyl and isopropyl radicals.[18] Similar observations were made in the catalysis obtained by these copper(II) complexes in the decomposition of n-valeryl[15] and t-butylacetyl peroxides.[1]

Kinetics of Oxidation of β-Arylethyl Radicals. β-Arylethyl radicals (substituted in the ring) were derived from the catalyzed decomposition of substituted hydrocinnamoyl peroxides.[1] Oxidation of these β-arylethyl

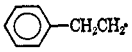
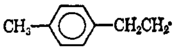
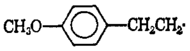
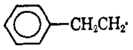
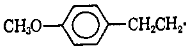
$$(ArCH_2CH_2CO_2)_2 + Cu^I \longrightarrow ArCH_2CH_2CO_2Cu^{II} + CO_2 + ArCH_2CH_2\cdot \qquad (15)$$

---

(17) C. Addison, B. Hathaway, N. Logan, and A. Walker, *J. Chem. Soc.*, 4308 (1960).

(18) There are a number of reasons why neopentyl and n-butyl radicals behave differently toward acetonitrilecopper(II) and bipyridinecopper(II) acetates. Oxidative elimination and substitution have different requirements (*vide infra*). Since neopentyl radical can only undergo the latter and n-butyl radicals only suffer oxidative elimination, the difference may reflect the effect of ligands on these two reactions (see ref 1 and 13 for further discussion of this point).

Table II. Relative Rates of Hydrogen Transfer and Oxidative Elimination or Substitution of β-Arylethyl Radicals[a,b]

Oxidant	Radical	$k_H/(k_e + k_s)$	k_H/k_e	k_H/k_s
$Cu^{II}(NCCH_3)_4$[c]		5.95×10^{-3}	6.05×10^{-3}	2.00×10^{-1}
$Cu^{II}(NCCH_3)_4$[c]		5.90×10^{-3}	9.53×10^{-3}	1.24×10^{-2}
$Cu^{II}(NCCH_3)_4$[c]		6.66×10^{-3}	4.76×10^{-1}	6.44×10^{-3}
$Cu^{II}(Bipy)$[d]		6.7×10^{-4}	7.0×10^{-4}	1.2×10^{-2}
$Cu^{II}(Bipy)$[d]		6.4×10^{-4}	3.3×10^{-3}	8.0×10^{-5}

[a] At 25.5° from β-arylpropionyl peroxide and isobutyraldehyde using copper(I,II) acetates in 40 vol % acetonitrile–acetic acid solution. [b] $k_H/(k_e + k_s)$ was determined separately from k_H/k_e and k_H/k_s. [c] Copper(II) acetate in 40 vol % acetonitrile–acetic acid. [d] Copper(I,II) acetates plus 1 molar equiv of α,α′-bipyridine in 40 vol % acetonitrile–acetic acid.

radicals with Cu^{II} gave mixtures of elimination (styrenes) and substitution (β-arylethyl acetates) products. The relative amounts of acetate and styrene represented the relative rates of oxidative substitution, k_s, and elimination, k_e, respectively. These values of k_s/k_e varied with the ring substituent and the Cu^{II} oxidant. In particular, the amount of ester (eq 16) derived relative to styrene (eq 17), k_s/k_e, was optimum with β-anisylethyl

$$ArCH_2CH_2\cdot + HOAc + Cu^{II} \xrightarrow{k_s} ArCH_2CH_2OAc + H^+ + Cu^I \quad (16)$$

$$ArCH_2CH_2\cdot + Cu^{II} \xrightarrow{k_e} ArCH{=}CH_2 + H^+ + Cu^I \quad (17)$$

radical. It generally correlated with electron release at the *para* position of the aryl group. However, the latter conclusion is not necessarily valid since the relative rates of oxidative substitution and elimination really only measure *differences* in polar effects of these two competing reactions.

In order to evaluate polar effects on oxidative substitution and elimination *separately*, we measured the rate of oxidation of β-arylethyl radicals relative to hydrogen transfer (to isobutyraldehyde, eq 18). The

$$ArCH_2CH_2\cdot + (CH_3)_2CHCHO \xrightarrow{k_H} ArCH_2CH_3 + (CH_3)_2CH\dot{C}O \quad (18)$$

yields of the substituted styrene as well as the β-arylethyl acetate were each determined relative to the corresponding ethylbenzene at various concentrations of isobutyraldehyde and Cu^{II} applicable in eq 7. In this manner, it was possible to obtain values of k_e/k_H (*i.e.*, eq 17/18; R_{ox} = $ArCH{=}CH_2$, $k_{ox} = k_e$ in eq 7), and k_s/k_H (eq 16/18; R_{ox} = $ArCH_2CH_2OAc$, $k_{ox} = k_s$ in eq 7) for each β-arylethyl radical.[19] These relative rates are tabulated in Table II, together with the relative rates of total oxidation and hydrogen transfer [$k_H/(k_e + k_s)$; R_{ox} = $[ArCH{=}CH_2 + ArCH_2CH_2OAc]$, $k_{ox} = k_e + k_s$ in eq 7].

Rates of Oxidation of *n*-Butyl, Isopropyl, and Neopentyl Radicals by Cu^{II}. The values of k_H/k_e obtained for *n*-butyl, isopropyl, neopentyl, and β-arylethyl radicals examined in this study were all based on isobutyraldehyde as the single hydrogen donor. To obtain rates of oxidation, it was necessary independently to know values of k_H of each of these radicals with isobutyraldehyde (eq 19). The latter have not been mea-

$$R\cdot + (CH_3)_2CHCHO \longrightarrow RH + (CH_3)_2CH\dot{C}O \quad (19)$$

sured, but we estimated these rates by assuming that they are little affected by minor changes in the structure of the aldehyde. Thus, Trotman-Dickenson found that acetaldehyde, propionaldehyde, and *n*- and isobutyraldehydes, as well as pivaldehyde, all reacted with methyl radicals at the same rate.[20] In the same manner we assumed that the rate of hydrogen transfer between alkyl radicals and isobutyraldehyde (eq 19) was the same as that with the parent aldehyde. The values of k_H given in Table III were calculated on this basis from the activation parameters reported by Trotman-Dickenson.[21] These values for *n*-butyl radical and *n*-valeraldehyde are E_a = 5.4 kcal/mol and $A = 10^{7.9}$ l./mol sec and for isopropyl radicals and isobutyraldehyde E_a = 6.3 kcal/mol and $A = 10^{8.3}$ l./mol sec. The rate of hydrogen transfer by neopentyl radical was assumed to be the same as that with *n*-butyl radicals since the relevant dissociation energies of neopentane and *n*-butane are the same within experimental error.[22] The second-order rate constants, k_e, given in Table III for oxidation of *n*-butyl, isopropyl, and neopentyl radicals by Cu^{II} complexes were calculated from values of k_H/k_e (Table I) and k_H discussed above.

Table III. Rates of Oxidation of Alkyl Radicals by $Cu^{II}(NCCH_3)_4$ Complexes[a]

Oxidant	Alkyl radical	k_H/k_e[b]	$k_H \times 10^{-4}$, l./mol sec	$k_e \times 10^{-6}$, l./mol sec
$Cu^{II}(NCCH_3)_4$	*n*-Butyl	3.2×10^{-3}	1.0	3.1
$Cu^{II}(NCCH_3)_4$	Isopropyl	1.0×10^{-3}	0.50	5.0
$Cu^{II}(NCCH_3)_4$	Neopentyl	2.2×10^{-2}	1.0	0.45
$Cu^{II}(Bipy)$[c]	*n*-Butyl	5.8×10^{-4}	1.0	17
$Cu^{II}(Bipy)$[c]	Neopentyl	3.9×10^{-1}	1.0	0.025

[a] In 40 vol % acetonitrile–acetic acid solutions at 25.5° using isobutyraldehyde as hydrogen donor. [b] k_H/k_e for neopentyl radicals included 2-methylbutenes, *t*-amyl acetate, and acetamide as oxidation products only. [c] α,α′-Bipyridine: total copper (Cu^I, Cu^{II}) was 1 in 40 vol % acetonitrile–acetic acid.

---

[19] The small amount of N-β-anisylethylacetamide formed in 40 vol % acetonitrile–acetic acid solutions was not included in these calculations of k_s/k_H. Proper inclusion would lead to approximately 6–8% higher values of k_s for β-anisylethyl radicals.

[20] (a) R. Birrell and A. Trotman-Dickenson, *J. Chem. Soc.*, 2059 (1960); (b) see also D. Applequist and L. Kaplan, *J. Am. Chem. Soc.*, 87, 2194 (1965).

[21] J. Kerr and A. Trotman-Dickenson, *Progr. Reaction Kinetics*, 1, 107 (1961).

[22] R. Taubert and F. Lossing, *J. Amer. Chem. Soc.*, 84, 1523 (1962).

Table IV. Polar Effects on the Rates of Oxidation of Substituted β-Phenethyl Radicals by Cu^{II} Complexes[a]

Oxidant	$Y\text{-}C_6H_4CH_2CH_2\cdot$	$k_e \times 10^{-6}$ [b]	$k_s \times 10^{-6}$ [c]	$(k_e + k_s) \times 10^{-6}$ [d]	k_e/k_s
$Cu^{II}(NCCN_3)_4$	*m*-Methoxy	...	...	...	~50
$Cu^{II}(NCCH_3)_4$	H	1.6	0.050	1.7 (1.7)	33
$Cu^{II}(NCCH_3)_4$	*p*-Methyl	1.0	0.81	1.7 (1.8)	1.3
$Cu^{II}(NCCH_3)_4$	*p*-Methoxy	0.021	1.6	1.5 (1.6)	0.014
$Cu^{II}(Bipy)$[e]	H	14	0.83	15 (15)	17
$Cu^{II}(Bipy)$[e]	*p*-Methoxy	3.0	13	16 (16)	0.24

[a] In 40 vol % acetonitrile–acetic acid at 25.5° using isobutyraldehyde as hydrogen donor. [b] Second-order rate constant (l./mol sec) for oxidative elimination (eq 17). [c] Second-order rate constant for oxidative substitution (eq 16). [d] Second-order rate constant (l./mol sec) for total oxidation. Values in parentheses are sum of columns 3 and 4 and represent internal consistency. [e] Oxidant is mono-α,α'-bipyridinecopper(II) in 40 vol % acetonitrile–acetic acid.

The rates of oxidation of *n*-butyl and isopropyl radicals by Cu^{II} are both approximately ten times faster than the rate of oxidation of neopentyl radical. The discrepancy in rates of oxidation between *n*-butyl and neopentyl radicals shows up even more strikingly with Cu^{II} (Bipy) where the factor in rates is approximately 100.[18]

Rates of Oxidation of β-Arylethyl Radicals by Cu^{II}. The rates of oxidation of β-arylethyl radicals can also be evaluated from their measured values of k_H/k_e provided values of k_H (eq 18) were known. Szwarc and coworkers have shown by the toluene carrier method that the bond dissociation energies of the benzyl–bromine bond are rather insensitive to ring substituents.[23] Insulation of the radical center out of direct conjugation with the aromatic nucleus by interposition of the methylene group should greatly attenuate substituent effects in phenethyl radicals compared to benzyl radicals. Moreover, in the analog, allylcarbinyl radical, no evidence has been adduced heretofore for any homoconjugative interaction between the π bond and the primary radical center.[24] We expect, therefore, that heats of formation of phenethyl radicals would be independent of minor changes in ring substitution. In a series of closely related alkyl radicals, Kerr has shown that the Evans–Polyani equation, relating heats of formation to activation energies, is generally applicable to homolytic processes.[25] From these correlations, we postulate that the rate of hydrogen transfer from isobutyraldehyde to β-phenethyl radical is the same as its *p*-methyl and *m*- and *p*-methoxy derivatives. The oxidation rates of these radicals listed in Table IV were calculated from data in Table II using the value of k_H for *n*-butyl radical. The absolute value of k_H is not particularly pertinent, since here we are more interested in the *relative* effect of substituents on the rates of oxidation of phenethyl radicals.

Mechanisms for Oxidation of Alkyl Radicals by Cu^{II}. On examination of Table IV it is noteworthy that the total rate of oxidation of β-arylethyl radicals given by $(k_e + k_s)$ *is remarkably constant for a series of substituents*. On the other hand, in varying the substituent from hydrogen to *p*-methoxy, the rate of oxidative elimination decreases by a factor of approximately 80, whereas the rate of oxidative substitution increases by about a factor of 30. At the same time the relative rates of elimination and substitution change by a factor of 2400. We conclude that *the rate-limiting step for oxidation precedes and is separate from the product-forming step.*

This conclusion militates against a mechanism (I) in which elimination and substitution occur by two independent and parallel processes. It would be highly fortuitous for such concurrent reactions as (20) and (21) to proceed at widely varying rates, which compensate one another on ring substitution in such a fashion that the total rate $(k_e + k_s)$ remained invariant.

Mechanism I

$$R\cdot + Cu^{II} \xrightarrow{k_e} R(-H) + H^+ + Cu^I \qquad (20)$$

$$R\cdot + HOAc + Cu^{II} \xrightarrow{k_s} R\text{—}OAc + H^+ + Cu^I \qquad (21)$$

Two alternative mechanisms which are compatible with these kinetic constraints are II, a rate-limiting electron-transfer (outer sphere) process, or III, a rate-limiting reaction between alkyl radical and Cu^{II}.[26] In both mechanisms II and III, products are formed in a step subsequent to the formation of an intermediate generated in a rate-limiting step.[27] Relative amounts of elimination and substitution products would then be determined by competing routes for decomposition of the intermediate.

In mechanism II, an alkyl cation (eq 22) could satisfy these requirements. Loss of a β-proton (eq 23) or solvolysis (eq 24) are well-established routes to alkenes and substitution products from carbonium ions generated as intermediates in a variety of reactions.[28] However, if carbonium ions were direct precursors to both alkene and ester, we would not expect the relative rates of oxidative elimination and substitution, k_e/k_s, to vary with the nature of the Cu^{II} oxidant. However, in the majority of cases in which both oxidative elimination and substitution have been observed, the relative

Mechanism II

$$R\cdot + Cu^{II} \xrightarrow{k_e + k_s} [R^+] + Cu^I \qquad (22)$$

$$[R^+] \longrightarrow R(-H) + H^+ \qquad (23)$$

$$[R^+] \xrightarrow[HOAc]{} ROAc + H^+ \qquad (24)$$

---

(23) (a) M. Szwarc, C. Leigh, and A. Sehon, *Proc. Roy. Soc.* (London), **A209**, 97 (1951); (b) *cf.* also J. Kochi and D. Davis, *Nature*, **202**, 690 (1964).

(24) (a) L. Montgomery and J. Matt, *J. Amer. Chem. Soc.*, **89**, 6556 (1967); (b) L. Montgomery, J. Matt, and J. Webster, *ibid.*, **89**, 923 (1967).

(25) J. Kerr, *Chem. Rev.*, **66**, 465 (1966).

(26) We would expect the association of an alkyl radical and the paramagnetic Cu^{II} species to be very fast. If the alkylcopper intermediate is metastable and formed reversibly, the term *rate limiting* is a misnomer and should be replaced by *preequilibrium* (*vide infra*).

(27) Mechanisms II and III are the simplest, in that they involve the fewest intermediates and steps consistent with the observations. Others are, no doubt, possible.

(28) For general discussions, see (a) D. Banthorpe, "Elimination Reactions," Elsevier Publishing Co., New York, N. Y., 1963; (b) C. Bunton, "Nucleophilic Substitution at a Saturated Carbon Atom," Elsevier Publishing Co., New York, N. Y., 1963.

rates *are* dependent on the Cu^{II} species (*cf.* Table IV and ref 1 and 13). Neopentyl radical is the outstanding exception. In this radical, however, rearrangement must precede the formation of products[1] (*vide infra*).

The influence of Cu^{II} on the relative rates of oxidative elimination and substitution indicates that it must also be associated with the alkyl moiety in the product-determining step. Mechanism III accommodates both of these important limitations. The alkylcopper intermediate is best represented as an inner-sphere complex.[29]

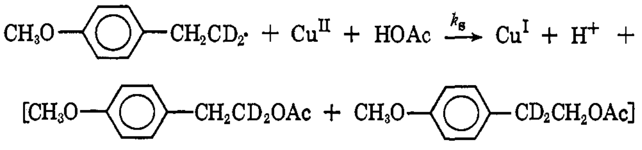
Mechanism III

$$R\cdot + Cu^{II} \overset{k_e + k_s}{\rightleftharpoons} [RCu] \qquad (25)$$

$$[RCu]\begin{cases} \longrightarrow Cu^{I} + H^{+} + R(-H) & (26) \\ \xrightarrow[(a)]{} Cu^{I} + [R^{+}] \xrightarrow[(b)]{HOAc} ROAc + H^{+} & (27) \end{cases}$$

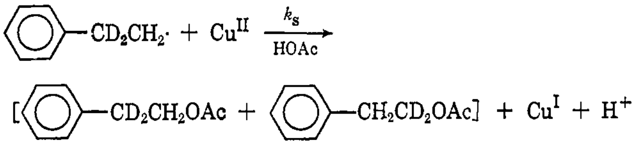
The Mechanism of Oxidative Substitution. We associate substitution products with heterolysis of the alkylcopper intermediate to Cu^{I} and a carbonium ion (eq 27a), followed by solvation (eq 27b). The importance of this oxidative fragmentation is generally related to the cationic stability of the alkyl fragment and, thus, constitutes the more important process with cyclobutyl,[1,13] *p*-methoxybenzyl,[2] β-anisylethyl, and similar radicals.[1] The properties of the resultant carbonium ion (rearrangement, selectivity in solvation, elimination, etc.) are essentially those observed in facile SN1-E1 solvolyses of the corresponding alkyl tosylates and halides under comparable conditions.[28]

The presence of cationic intermediates in the formation of substitution products can be shown by deuterium labeling. Thus, *oxidation of β-anisylethyl radicals by copper(II)* acetate from the catalyzed decomposition of *p*-methoxyhydrocinnamoyl peroxide afforded β-anisylethyl acetate in excellent yields (>90%), together with small amounts (~1%) of *p*-methoxystyrene.[1] The α- and β-carbon atoms were scrambled during oxidative substitution, since β-anisylethyl-α,α-d_2 radicals yielded an equimolar mixture of β-anisylethyl-α,α-d_2 and β-anisylethyl-β,β-d_2 acetates (eq 28).



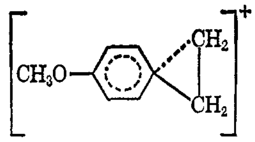
(50%) (50%) (28)

Even the unsubstituted *β-phenethyl radical on oxidation by Cu^{II}* affords β-phenethyl acetate in which the α- and β-carbon atoms have been completely equilibrated. The ester fraction isolated in 15% yield from the copper-catalyzed decomposition of hydrocinnamoyl-β,β-d_2 peroxide consisted of both β-phenethyl-α,α-d_2 and -β,β-d_2 acetates (eq 29) in equimolar amounts.

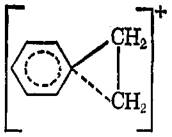


(50%) (50%) (29)

We attribute the loss of identity of the α- and β-carbon atoms during oxidative substitution of β-arylethyl radicals to the formation of bridged cationic intermediates IV and V.[30] The corresponding β-arylethyl radicals do not rearrange under these conditions.



IV



V

Complete equilibration of the α- and β-carbon atoms of the β-anisylethyl moiety during solvolysis of the tosylate derivative has been attributed to the intervention of delocalized cation IV.[30,31] There is significantly less driving force for the formation of the analogous ethylenephenonium ion V in the solvolysis of the tosylate.[32] Convincing support for the ethylenephenonium ion V has only recently been found through solvolytic studies in trifluoroacetic acid.[33]

A heterolysis of an organometallic species similar to oxidative substitution (presented in eq 27) has been noted in the solvolysis of organomercurials by Jensen and Ouellette.[34a] In these cases, alkylmercurium species can be generated by ligand exchange. SN1 solvolysis (eq 30) exhibits great sensitivity to changes in

$$RHg^{+}Y^{-} \longrightarrow R^{+} + Hg^{0} + Y^{-} \text{ etc.} \qquad (30)$$

structure of the alkyl moiety and to neighboring group participation. The latter are indicative of carbonium ions as intermediates or a high degree of carbonium ion character in the transition state.[34b] The driving force in these reactions is undoubtedly derived from the formation of Hg^{0}; Cu^{I} plays a similar role in oxidation of alkyl radicals with Cu^{II} (eq 27). Interestingly, the acetolysis of the β-phenethylmercury ion leads to 90% scrambling of the α and β positions.[35]

The Mechanism of Oxidative Elimination. The more common route obtained in the oxidation of alkyl radicals by Cu^{II} is elimination (eq 26). A discrete carbonium ion does not appear to be directly involved in this process. Thus oxidative elimination of alkyl radicals occurs with no rearrangement (of either the carbon skeleton or the hydrogens) diagnostic of other

---

(29) (a) An allylcopper species was presented as a possible intermediate in an earlier study of the oxidation of allylic radicals by Cu^{II} (J. Kochi, *J. Amer. Chem. Soc.*, **84**, 774 (1962)). (b) The formal oxidation state of copper in these complexes has been deliberately omitted. (c) For radical–metal complexes see J. Koch and F. Rust, *J. Amer. Chem. Soc.*, **83**, 2017 (1961).

(30) (a) S. Winstein, C. Lindegren, H. Marshall, and L. Ingraham, *ibid.*, **75**, 147 (1953); (b) H. Brown, R. Bernheimer, C. Kim, and S. Schepple, *ibid.*, **89**, 370 (1967); (c) H. Brown, K. Morgan, and F. Chloupek, *ibid.*, **87**, 2137 (1965); (d) E. Jenny and S. Winstein, *Helv. Chim. Acta*, **41**, 807 (1958); (e) G. Olah, M. Comisarow, E. Namenworth, and B. Ramsey, *J. Amer. Chem. Soc.*, **89**, 711 (1967).

(31) Equilibration of α and β carbon atoms cannot be used alone as definitive evidence for bridged carbonium ions. For a recent discussion of localized and delocalized β-aralkyl cations, see H. Brown and C. Kim, *J. Amer. Chem. Soc.*, **90**, 2082 (1968).

(32) (a) W. Saunders, S. Asperger, and D. Edison, *ibid.*, **80**, 2423 (1958); (b) C. Lee, G. Slater, and J. Spinks, *Can. J. Chem.*, **35**, 1417 (1957); **39**, 1510 (1961); *Tetrahedron*, **7**, 206 (1959); (c) L. Eberson, J. Petrovich, R. Baird, D. Dyckes, and S. Winstein, *J. Amer. Chem. Soc.* **87**, 3504 (1965); (d) M. Bentley and M. Dewar, *ibid.*, **90**, 1075 (1968).

(33) J. Nordlander and W. Deadman, *ibid.*, **90**, 1590 (1968); *Tetrahedron Lett.*, 4409 (1967); R. Jablonski and E. Snyder, *ibid.*, 1103 (1968).

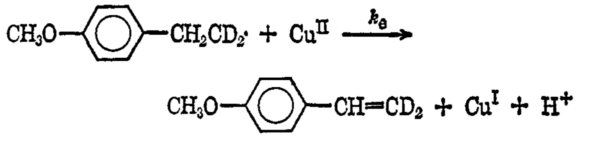
(34) (a) F. Jensen and R. Ouellette, *J. Amer. Chem. Soc.*, **83**, 4488, 4478 (1961); **85**, 363 (1963); (b) F. Jensen and R. Ouellette, *ibid.*, **85**, 367 (1963).

(35) C. Lee and R. Tewari, *Can. J. Chem.*, **45**, 2256 (1967).

carbonium ion processes. For example, primary alkyl radicals afford only terminal alkenes, and isobutyl radicals generate only isobutylene (no butene-1 or -2). Furthermore, radicals such as cyclobutyl and 2-norbornyl afford significant amounts of cyclobutene[13] and norbornene,[36] respectively, whereas solvolysis or deamination of the corresponding tosylates and amines gives little or none of these products.[37]

Neither β-anisylethyl-α,α-d_2 nor β-phenethyl-β,β-d_2 radicals shows any evidence of rearrangement during oxidative elimination by $\mathrm{Cu^{II}}$ to *p*-methoxystyrene or styrene, respectively. This is true in spite of the extensive scrambling of the α- and β-carbon atoms observed in the products derived by oxidative substitution.

p-Methoxystyrene is the minor product from oxidation of β-anisylethyl radical by $\mathrm{Cu^{II}}$ in acetonitrile–acetic acid solutions. The amounts of *p*-methoxystyrene were too small for us to isolate and characterize. However, solvent studies[13] showed that the relative amounts of oxidative elimination of radicals by $\mathrm{Cu^{II}}$ can be enhanced by carrying out the reactions in benzene solutions. Under these conditions, oxidation of β-anisylethyl radicals by $\mathrm{Cu^{II}}$ produced much higher yields (∼65%) of *p*-methoxystyrene and less β-anisylethyl acetate, together with dimeric adducts.[38] Examination of the nuclear magnetic resonance spectrum of *p*-methoxystyrene isolated from the copper-catalyzed decomposition of *p*-methoxyhydrocinnamoyl-α,α-d_2 peroxide in benzene showed that β-anisylethyl-α,α-d_2 radicals were oxidatively eliminated by $\mathrm{Cu^{II}}$ without rearrangement (eq 31). As expected, the β-anisylethyl acetate formed concomitantly by oxidative substitution was completely rearranged (eq 28), as shown earlier in acetonitrile–acetic acid solutions.[1]



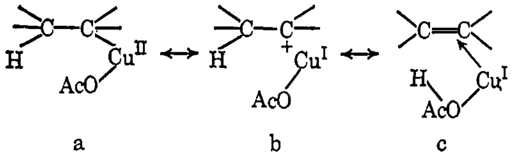
(31)

Styrene is the major product from the oxidation of β-phenethyl radicals by $\mathrm{Cu^{II}}$ in acetonitrile–acetic acid solutions. The unrearranged styrene-α-*d* was also isolated as the exclusive product of oxidative elimination of β-phenethyl-β,β-d_2 radical by $\mathrm{Cu^{II}}$ (eq 32).

$$\mathrm{PhCD_2CH_2\cdot + Cu^{II} \xrightarrow{k_e} PhCD{=}CH_2 + Cu^{I} + D^+} \qquad (32)$$

We conclude that alkenes are formed in oxidative elimination from an alkylcopper intermediate (eq 25) by loss of a β-proton synchronously with electron transfer (eq 26). A possible transition state for such a process is represented in Scheme I.

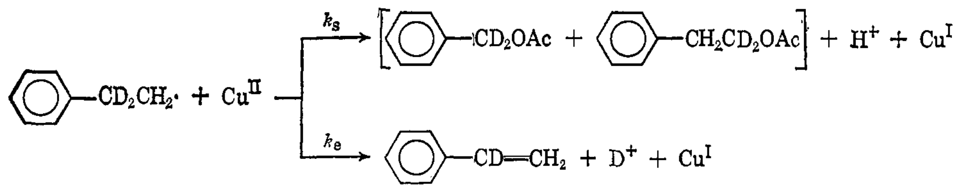
Scheme I. A Transition State for Oxidative Elimination of Alkyl Radicals by $\mathrm{Cu^{II}}$ Complexes



Oxidative Elimination *vs.* Oxidative Substitution. Various solvents and ligands can be employed to alter the relative amounts of oxidative elimination and substitution. Thus acetonitrile and tetramethylene sulfone are solvents which are particularly good in enhancing the yields of oxidative substitution products. For example, the oxidation of β-anisylethyl radicals by $\mathrm{Cu^{II}}$ in acetonitrile–acetic acid solutions affords β-anisylethyl acetate in greater than 90% yield, whereas equivalent oxidations in benzene–acetic acid solutions generate *p*-methoxystyrene in excellent yields.[39] A similar dichotomy has been noted with cyclobutyl radicals.[13] Furthermore, the oxidation of neopentyl radicals by $\mathrm{Cu^{II}}$ in benzene is significantly slower than in acetic acid solutions.[1,9] These changes in rates of reaction may be partly attributed to a general solvent effect. Specific coordination[40] to the copper species to generate a $\mathrm{Cu^{I}}$ complex which is a better leaving group in the heterolysis step (eq 27a)[14] is an important function of the solvent.

The oxidation of β-arylethyl radicals further illustrates the difference between elimination and substitution processes. Deuterium labeling has shown that the α- and β-carbon atoms are completely scrambled in the β-arylethyl acetate, whereas no such scrambling occurs in the styrene. The importance of such a synchronous elimination of a β-hydrogen is also shown by the kinetic isotope effect in the oxidation of β-phenethyl-β,β-d_2 radical.

The ratio of the second-order rate constants for oxidative elimination and substitution given by k_e/k_s was readily determined from the relative amounts of styrene and β-phenethyl acetate formed (Table V). This value was 33 for the oxidation of β-phenethyl radical by $\mathrm{Cu^{II}}$ in 40 vol % acetonitrile–acetic acid, and 12 for β-phenethyl-β,β-d_2 radical under equivalent conditions. We expect the isotope effect in oxidative substitution (eq 33) to be small and negligible.[41] The observed differences in rates are attributed solely to effects of deuterium substitution in oxidative elimination (eq 34). On this basis, the kinetic isotope effect



(33)

(34)

---

(36) R. Gilliom, unpublished results.

(37) (a) S. Winstein and D. Trifan, *J. Amer. Chem. Soc.*, 74, 1147, 1154 (1952); (b) E. Corey, J. Casanova, P. Vatakencherry, and R. Winter, *ibid.*, **85**, 169 (1963); (c) R. Roberts, W. Bennett, and R. Armstrong, *ibid.*, 72, 3121, 3329 (1950).

(38) 1,4-Dianisylbutene-1 and butyl acetate are typical dimeric products when styrenes are formed in major amounts.[1] They were not characterized further.

(39) Unpublished results. See Experimental Section.

(40) V. Gutmann, *Coord. Chem. Rev.*, 2, 239 (1967); (b) J. Kochi and H. Mains, *J. Org. Chem.*, **30**, 1862 (1965); (c) L. Katzin, *Transition Metal Chem.*, 3, 56 (1966).

(41) (a) We expect this to be certainly less than 10% because the effect is secondary or less; (b) *cf.* E. Thornton, "Solvolysis Mechanisms," Ronald Press Co., New York, N. Y., 1964, p 209 ff.

Table V. Catalyzed Decomposition of Hydrocinnamoyl and Hydrocinnamoyl-β,β-d_2 Peroxide[a]

Per- oxide[b]	Cu^{I}, mequiv	Cu^{II}, mequiv	Cu^{I}/Cu^{II}	Ligand[c] added, mequiv	Products, mol %: CO$_2$	Ethyl- benzene	Styrene	Phenethyl acetate	Styrene[d]/ phenethyl acetate	k_e(H)/ k_e(D)
H	0.26	5.0	0.052		90	0.0160	0.540	0.0735	9.8	2.9
D	0.26	5.0	0.052		92	0.0165	0.440	0.1850	3.4	
H	0.20	2.0	0.10		99	0.0210	0.497	0.097	7.1	2.8
H	0.20	2.0	0.10		100	0.0260	0.497	0.099	7.0	
D	0.20	2.0	0.10		97	0.0230	0.351	0.203	2.8	
D	0.20	2.0	0.10		97	0.0250	0.364	0.217	2.4	
H	0.45	2.0	0.230		100	*e*	0.505	0.070	10.4	
H	0.25	1.0	0.25		99	0.0365	0.475	0.0695	10	2.9
D	0.25	1.0	0.25		100	0.0255	0.320	0.1540	3.7	
H	0.95	2.0	0.45		100	*e*	0.490	0.057	13	
H	1.5	2.0	0.75		100	*e*	0.480	0.0360	20	
H	3.0	2.0	1.50		100	*e*	0.490	0.0300	25	
H	1.4	1.0	1.40		99	0.0390	0.410	0.0310	22	2.8
D	1.4	1.0	1.40		100	0.0390	0.387	0.0840	8	
H	0.20	2.0	0.10	Py 2.2	103	*f*	0.700	0.060	14	
H	0.20	2.0	0.10	Py 2.2	105	*f*	0.715	0.050	16	2.3
D	0.20	2.0	0.10	Py 2.2	98	*f*	0.520	0.109	6.5	
D	0.20	2.0	0.10	Py 2.2	103	*f*	0.550	0.109	6.6	
H	0.20	2.0	0.10	Bipy 2.2	98	*f*	0.680	0.031	26	
H	0.20	2.0	0.10	Bipy 2.2	102	*f*	0.670	0.024	34	
D	0.20	2.0	0.10	Bipy 2.2	100	*f*	0.492	0.079	8.9	3.5[g]
D	0.20	2.0	0.10	Bipy 2.2	101	*f*	0.490	0.085	8.2	

[a] In 25-ml solutions of 40 vol % acetonitrile–acetic acid containing 1 mmol of peroxide at 0°. [b] H = hydrocinnamoyl peroxide; D = hydrocinnamoyl-β,β-d_2 peroxide. [c] Py = pyridine; Bipy = α,α'-bipyridine. [d] Styrene corrected for dimer formation (see ref 1). [e] Not determined. [f] Too small to measure. [g] Error large, due to small amounts of ester formed.

for the oxidative elimination of β-phenethyl radical is 2.8. The relatively small isotope effect observed is consistent with a high degree of electron transfer (structure b, Scheme I) in the transition state for oxidative elimination. This conclusion is also in accord with the rather random loss of β-hydrogens during oxidation of *sec*-butyl radicals discussed previously.[42] Furthermore, the *magnitude* of the β-deuterium isotope effect for oxidative elimination is intermediate between values observed for the base-promoted elimination of a variety of β-arylethyl derivatives[43] and for the unimolecular elimination (substitution) of analogous systems.[44] E2 and E1 (S$_N$1) reactions commonly represent extremes of rupture of the β-hydrogen bond in the transition state for elimination.[45]

The factors which influence the partitioning of the alkylcopper intermediate merit further discussion. No doubt the stability of the carbonium ion formed by heterolysis influences the yield of substitution products, since excellent yields are obtained with those alkyl moieties which generate stable carbonium ions. However, the contrary is not valid, since primary and secondary alkyl radicals such as *n*-butyl and isopropyl, which do not produce stable cations, are oxidized as readily as (in fact, slightly faster than) the β-anisylethyl radical. Oxidative elimination is, thus, a kinetically (and energetically) equivalent route for decomposition of the alkylcopper intermediate.

Polar substituents exert diametrically opposed effects on oxidative substitution and elimination of β-arylethyl radicals. The rates shown in Table IV do not conform to a Hammett correlation.[45c] However, from the trend in rates, it is apparent that the substitution process is enhanced by electron-releasing substituents, and oxidative elimination is favored by electron-attractive substituents. Oxidative substitution is easily associated with a transition state in which the arylethyl moiety takes on cationic character.[46] On the other hand, the charge requirements in oxidative elimination parallel those observed in proton transfers and base-promoted E2 reactions. Thus, rates of proton exchange from substituted toluene[43c] and rates of elimination of β-arylethyl derivatives[43a,b] are affected by substituents in a manner opposite to their cationic counterparts.

If mechanism III is applicable, strict quantitative correlations between polar substituent effects and relative rates of oxidative substitution and elimination cannot be made, since they are mutually interdependent processes (*via* a common alkylcopper intermediate).

---

(42) (a) J. Kochi, *J. Amer. Chem. Soc.*, **85**, 1958 (1963). (b) However, it is possible that such a statistical distribution of butenes was completely fortuitous. The thermodynamically less-favored isomer, butene-1 (and to a lesser extent *cis*-butene-2), also forms stronger π complexes with Cu^{I} [O. Chaltykyan, "Copper-Catalytic Reactions," Consultants Bureau, New York, N. Y., 1966]. This may lend additional driving force (structure c, Scheme I) for the formation of these isomers, which are ordinarily the less-favored ones. The observed distribution must then be rationalized on the basis of a rather complex interplay of various factors often discussed in ionic elimination processes.[28]

(43) (a) A. Cockerill, S. Rottschaefer, and W. Saunders, *J. Amer. Chem. Soc.*, **89**, 901, 4985 (1967); **90**, 1775 (1968); (b) L. Steffa and E. Thornton, *ibid.*, **89**, 6149 (1967); D. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, p 27 ff; (c) A. Streitwieser, Jr., and J. Hammons, *Progr. Phys. Org. Chem.*, **5**, 60 (1965).

(44) (a) D. Kevill and J. Dorsey, *Chem. Ind.* (London), 2174 (1967); (b) G. Frisone and E. Thornton, *J. Amer. Chem. Soc.*, **90**, 1211 (1968); (c) V. Shiner, W. Buddenbaum, B. Murr, and G. Lamaty, *ibid.*, **90**, 418 (1968).

(45) (a) W. Saunders, "Chemistry of Alkenes," S. Patai, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 149 ff; (b) E. Thornton, "Solvolysis Mechanisms," Ronald Press, New York, N. Y., 1964, p 207 ff; (c) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 105 ff.

(46) (a) H. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, **80**, 4979 (1958); (b) L. Stock and H. Brown, *ibid.*, **81**, 3323 (1959); (c) J. Kochi and G. Hammond, *ibid.*, **75**, 3446 (1953).

Reversibility as a Factor in Alkylcopper Formation. According to the preferred mechanism III, the source of the product composition lies in the competition between elimination (eq 26) and fragmentation of the alkylcopper intermediate (eq 27a).[47] The total rate of oxidation ($k_e + k_s$) should be independent of this dichotomy, except insofar as the formation of the alkylcopper species is reversible. We think the latter is especially important when the alkyl radical has no β-hydrogen atoms and/or the corresponding cation is not readily formed.[48] A case in point is the neopentyl radical. We observe that its rate of oxidation is significantly less than that of *n*-butyl radical which has a similar value for the ionization potential.[22] The neopentylcopper intermediate has, as its only recourse for oxidation, fragmentation to a relatively unfavored primary neopentyl cation (eq 36). Reversibility (eq 35) is probably optimum in such a situation.

$$(CH_3)_3CCH_2\cdot + Cu^{II} \rightleftarrows [(CH_3)_3CCH_2Cu] \qquad (35)$$

$$[(CH_3)_3CCH_2Cu] \longrightarrow Cu^{I} + (CH_3)_3CCH_2^{+} \text{ etc.} \qquad (36)$$

The reversible formation of a neopentylcopper intermediate as in eq 35 is indicated by preliminary studies of temperature dependence on the oxidation of alkyl radicals by Cu^{II}. Earlier, we showed that the oxidation of *n*-butyl radicals by Cu^{II} had an apparent activation energy of 2.0 ± 0.6 kcal/mol in acetic acid solutions. This value is not significantly altered in acetonitrile–acetic acid solutions. The oxidation of neopentyl radical, on the other hand, shows a slight negative apparent activation energy. A similar temperature effect was found by Dainton and coworkers[49] during their examination of the oxidation of polyacrylamide radicals. The most readily acceptable explanation for this negative temperature coefficient is one which includes a preequilibrium step such as eq 35.[49] The enthalpy change for such an associative process is expected to be negative.

Reversibility becomes especially relevant with those radicals, such as neopentyl and cyclopropyl, which do not enjoy (for one reason or another) facile routes for decomposition (elimination, eq 26, or ionization, eq 27). The extent to which reversibility is a factor with other readily oxidized radicals is indeterminant.[50] For this reason, the measurement of apparent activation energies for the oxidation of alkyl radicals are of tenuous significance.

We sought to demonstrate reversibility from the cation stage by attempting to generate carbonium ions in the presence of Cu^{I}. Diazoneopentane was generated from the salt of *t*-butylacetaldehyde tosylhydrozone[51] and was treated with copper(I) acetate in acetonitrile–acetic acid solutions (eq 37). Heretofore, we have

$$(CH_3)_3CCHN_2 + Cu^{I} + HOAc \longrightarrow (CH_3)_3CCH_2CuOAc + N_2 \qquad (37)$$

found only traces of neopentane and are unable, at the present time, to produce a more convincing case for reversibility.

$$(CH_3)_3CCH_2CuOAc \longrightarrow (CH_3)_3CCH_2\cdot + Cu^{II}OAc \text{ etc.} \qquad (38)$$

Summary and Conclusions. *n*-Butyl, neopentyl, and β-arylethyl radicals represent three classes of alkyl radicals from which distinctive kinetic information has been obtained about electron-transfer oxidation by Cu^{II} complexes. *n*-Butyl radicals undergo oxidative elimination exclusively, whereas neopentyl radicals, by virtue of the lack of β-hydrogens, can only undergo oxidative substitution. Oxidative elimination and substitution are competing processes during reaction of β-arylethyl radicals with Cu^{II} complexes. Electron-releasing substituents in the ring markedly enhance oxidative substitution, but deter oxidative elimination. These processes do not occur independently, since the total rate of oxidation is relatively constant. From these kinetic constraints we conclude that oxidative elimination and substitution occur from a common alkylcopper intermediate subsequent to the rate-limiting step (mechanism III). Oxidative substitution is largely associated with ionization of the alkylcopper intermediate to a carbonium ion[1] and a Cu^{I} species (eq 27). Subsequent reactions of the carbonium ion are rearrangement, addition, solvolysis, etc., characteristic of carbonium ions generated by other processes. Oxidative elimination proceeds from the alkylcopper intermediate by a molecular mechanism in which loss of a β-hydrogen occurs synchronously with electron transfer to the copper atom (eq 26).

The relative rates of oxidative elimination and substitution with a particular radical are largely determined by the stability of the carbonium ion, except with those radicals where elimination is unfavored (cyclopropyl) or not possible (neopentyl). In the latter cases, reversibility in the formation of the alkylcopper intermediate is pronounced.

Mechanism III allows for a number of previous anomalies observed in the oxidation of radicals to be accommodated. Among these are (a) the small spread in reactivities of primary compared to tertiary alkyl radicals despite significant differences in ionization potentials;[12] (b) the rather random loss of β-hydrogens in the oxidative elimination of *sec*-butyl radicals;[9] (c) the apparently large negative ρ value in the oxidation of ring-substituted benzyl radicals;[3] (d) the marked polar effect on oxidative substitution and elimination of β-arylethyl radicals;[1] (e) the solvent effect on oxidation of homoallylic radicals by Cu^{II} complexes;[13] (f) the formation of carbonium ions as intermediates in the oxidation of certain radicals;[1] (g) absence of cationic rearrangements during oxidative elimination; (h) electrophilic addition (substitution) of the alkyl moiety to nitriles, arenes, and other weak nucleophiles.

---

(47) We do not wish to imply that substitution products can only arise *via* a route such as eq 27, and elimination only by concerted loss of a β-proton and electron transfer (eq 26). For a discussion of this point see ref 1 and 13.

(48) (a) Cyclopropyl radicals also fit into this category. Though they have β-hydrogens, loss would lead to a highly strained cyclopropene system. (b) It is interesting to note that cyclobutyl radicals, although secondary, give excellent yields of substitution products in acetonitrile–acetic acid solutions. In this regard it is akin to β-anisylethyl and *p*-methoxybenzyl, and quite unlike *sec*-butyl and even *t*-butyl. If the rationalization we propose is correct, this indicates that cyclobutyl cation is reasonably highly stabilized, and would lend support to a nonclassical structure. (For a discussion of this point see P. Bartlett, "Nonclassical Ions," W. A. Benjamin, Inc., New York, N. Y., 1954.)

(49) E. Collinson, F. Dainton, B. Mile, S. Tazuke, and D. Smith, *Nature*, **198**, 26 (1963).

(50) In the foregoing discussion k_e and k_s have been used to represent rate constants for oxidative elimination and substitution, respectively.[26] To an extent to which the formation of the alkylcopper species is reversible, these should be modified by a preequilibrium constant. See Tables II and IV especially.

(51) (a) G. Kaufman, J. Smith, C. Van der Stouw, and H. Shechter, *J. Amer. Chem. Soc.*, 87, 935 (1965). (b) We wish to thank Dr. J. Bayless for the sodium *t*-butylacetaldehyde tosylhydrazonide.

Experimental Section

Most of the materials used in this study were described previously.[1] Isobutyraldehyde (Matheson Coleman and Bell, reagent grade) was distilled immediately before use, bp 64.0–64.4°.

Kinetic Procedure. A stock solution of cupric acetate in acetonitrile–acetic acid solutions of the desired composition was prepared. Cuprous acetate and diacyl peroxide were separately prepared in the solvent of the same composition and contained in flasks capped with a gas-tight rubber septum and flushed free of air with oxygen-free nitrogen introduced with a hypodermic needle. The reaction was carried out in a 125-ml erlenmeyer flask by first introducing an aliquot of stock solution of cupric acetate, together with a measured amount of isobutyraldehyde and acetonitrile–acetic acid as solvent. The flask was capped with a self-sealing rubber septum (previously washed in toluene, acetone, and water to remove inhibitors and then dried). After chilling in an ice bath, the flask was swept with a stream of pure nitrogen or helium introduced with a hypodermic needle. To commence reaction, an aliquot of cuprous acetate solution followed by an aliquot of diacyl peroxide was added with a hypodermic syringe. The rate of the reaction was followed by evolution of carbon dioxide. The latter was determined by gas chromatography using ethane as an internal standard (Porapak Q at room temperature). Ethane was added prior to the addition of peroxide when the rates of decomposition were rapid. The system was carefully calibrated with standard mixtures of gases and appropriate amounts of the solvent with copper salts to simulate reaction conditions as closely as possible.

After completion of the reaction, standard amounts of marker were added and the reaction was analyzed in the usual manner.[1,15] In all cases, the system was calibrated under reaction conditions in order to obviate problems due to fractionation in the work-up or analysis. The products derived from the alkyl portion of the diacyl peroxide analyzed in this manner were alkane (R–H), alkene [R(–H)], and alkyl acetate (R–OAc).[1] The derivation of values of k_H/k_e, k_H/k_s, k_H/k_{ox} (rates of second-order rate constants for hydrogen transfer and oxidative elimination, oxidative substitution, and total oxidation, respectively) and K (dissociation constant of $\mathrm{Cu^{II}OAc}$ dimer) from these products with changes in $\mathrm{Cu^{II}OAc}$ and isobutyraldehyde concentrations was described previously.[12,16]

***p*-Methoxystyrene from *p*-Methoxyhydrocinnamoyl-α,α-d_2 Peroxide.** A solution of 0.040 *M* *p*-methoxyhydrocinnamoyl-α,α-d_2 peroxide in benzene was treated with a mixture of $\mathrm{Cu^{II}OAc}$ and $\mathrm{Cu^{I}OAc}$ described previously.[1] The reaction was slower than usually encountered in acetonitrile–acetic acid solutions. The mixture was poured into water, washed several times with dilute hydrochloric acid, dried, and then concentrated. *p*-Methoxystyrene was separated by gas–liquid partition chromatography and collected from the effluent stream.

The nuclear magnetic resonance spectrum of *p*-methoxystyrene in carbon tetrachloride showed proton resonances (δ scale) for methoxy (3.8 ppm), two pairs of multiplets for the two β protons (5.3 and 5.8 ppm), the multiplet for the α protons (6.7 ppm), and the aromatic multiplets (7.2 ppm). The latter were not sufficiently well resolved to distinguish completely, and we have taken the simple expediency of lumping the aromatic with the α protons and integrating relative to the methoxy and/or β protons. These intensities were in the expected ratio 5:2:3. The analysis of the nmr spectrum of styrene[52] forms the basis for these assignments.

The *p*-methoxystyrene-d_2 obtained from the oxidation of β-anisylethyl-α,α-d_2 radical showed no proton resonances between 5 and 6 ppm characteristic of the β-protons in *p*-methoxystyrene. Furthermore, the integrated intensities of the methoxy protons relative to the sum of the aromatic and α-protons were in the expected ratio of 3.0:5.1 for *p*-methoxystyrene-β,β-d_2. The nmr spectrum of β-anisylethyl-d_2 acetate isolated in the same manner was identical with that of the acetate obtained from the decomposition of the peroxide in acetonitrile–acetic acid described earlier.[1]

Hydrocinnamoyl-β,β-d_2 Peroxide. Benzyl-α,α-d_2 alcohol was prepared from ethyl benzoate by reduction with lithium aluminum deuteride (E. Merck AG, 99% min D). It was converted into benzyl-α,α-d_2 tosylate *via* the sodium salt.[53] The nmr spectrum of the tosylate showed no resonances at 5 ppm (δ scale) characteristic of benzyl protons. Sodium diethylmalonate (0.15 mol) was benzylated in 70 vol % dimethyl sulfoxide–ethanol by addition of benzyl tosylate (0.13 mol) to a solution containing a 200% excess of diethyl malonate. Crude diethyl benzylmalonate was isolated by diluting the reaction mixture with water, extracting with ether, and drying with sodium sulfate, followed by rotary evaporation of ether under vacuum. Distillation yielded 26 g of diethyl benzylmalonate-d_2 boiling at 108–113° (1 mm). It was saponified by treating with 2.2 molar equiv of aqueous potassium hydroxide at 100° for 3 hr, acidified with dilute sulfuric acid, and decarboxylated by heating at 100° for 2 hr. The acid was extracted with pentane and on crystallization afforded 8 g of hydrocinnamic-β,β-d_2 acid, mp 47.8–48.2°.

The nmr spectrum in carbon tetrachloride showed aromatic resonance (7.1 ppm) and the broadened α-methylene protons (2.6 ppm). The integrated intensities of the aromatic protons relative to the methylene protons were in the ratio 5:2 expected for hydrocinnamic-d_2 acid. The acid was also analyzed by combustion followed by the falling drop method for deuterium.[54] *Anal.* Calcd for $C_9H_8D_2O_2$: C, 71.0; H, 5.3; D, 2.7. Found: C, 71.5; H, 5.5; D, 2.6; 1.96, 1.99 atoms of D/molecule.

Hydrocinnamic-β,β-d_2 acid was converted into hydrocinnamoyl-β,β-d_2 peroxide with hydrogen peroxide (threefold excess) and dicyclohexylcarbodiimide in 85% yield.[55]

Catalyzed Decomposition of Hydrocinnamoyl-β,β-d_2 Peroxide. A solution of 0.040 *M* hydrocinnamoyl-β,β-d_2 peroxide in 40 vol % acetonitrile–acetic acid was catalytically decomposed by copper salts at 0.5° by the procedure described previously.[15] The yields of products derived from the protiated and deuterated peroxides were determined under a variety of conditions given in Table V.

Styrene from the deuterated peroxide was trapped from the effluent of the gas chromatograph. Its nmr spectrum in carbon tetrachloride showed no proton resonances between 6.5 and 7.1 ppm expected for the α-hydrogen. The β-hydrogens appeared as a multiplet at 5.2 and 5.7 ppm and were each broadened by deuterium. The integrated intensities of the aromatic and the two β protons were in the expected ratio of 5:1:1. Within these experimental limitations (5%), no deuteriums were scrambled into the β position during oxidative elimination.

The nmr spectrum of the isolated β-phenethyl acetate was the same as that of an authentic undeuterated sample, except for the pair of methylene triplets which were broadened by deuterium and replaced by a pair of poorly resolved multiplets centered at the same frequencies. The areas (planimeter) of the α- and β-methylene resonances under high amplification were in the ratio 1.08 ± 0.02 and 0.92 ± 0.02, respectively. The integrated areas of the pair of methylene triplets in authentic β-phenethyl acetate were (α) 2.15 ± 0.04 and (β) 1.85 ± 0.04 under identical operating conditions. We conclude that the deuterated β-phenethyl acetate isolated from the reaction mixture consisted of equimolar quantities of both isomers. The extent of methylene scrambling decreased when either pyridine or α,α′-bipyridine was employed as ligand. The latter phenomenon will be elaborated further.

Acknowledgment. We wish to thank the National Science Foundation for generous financial support of this work.

---

[52] J. Pople, W. Schneider, and H. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p 238 ff.

[53] J. Kochi and G. Hammond, *J. Amer. Chem. Soc.*, **75**, 3443 (1953).

[54] Analysis performed by Mr. J. Németh, University of Illinois.

[55] F. Greene and J. Kazan, *J. Org. Chem.*, **28**, 2168 (1963).