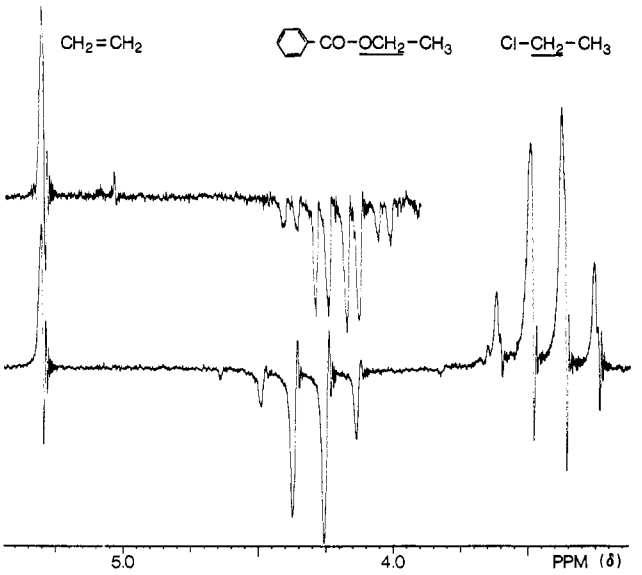

Figure 2. CH_2 resonances during the decomposition of a mixture of BPPO and CBPPO in CCl_4 without shift reagents, and in presence of $Pr(fod)_3$ (upper trace).

in Figure 1.2 and 1.3 correspond to a molar ratio between the shift reagent and the ester of 7.5×10^{-3}. Whereas such low concentrations of the shift reagents cause only small reductions of the CIDNP intensities of the complexing products, higher molar ratios ($>5 \times 10^{-2}$) will eventually quench them.

The CIDNP intensities of the other products which complex less are also reduced less, so that adding shift reagents can be used to simplify CIDNP spectra by removing certain enhanced resonance lines selectively. However, this means a loss of information, and shifting the resonance lines while retaining their CIDNP is more desirable. We found that even if products give coinciding resonances, shift reagents may lift their degeneracy by complexing better with one of the products. We have demonstrated this fact by decomposing equivalent amounts of *m*-chlorobenzoyl propionyl peroxide (CBPPO) and BPPO in CCl_4. Without shift reagents the emission quartets of ethyl *m*-chlorobenzoate (II) and I have identical chemical shifts and coupling constants (Figure 2 lower trace). Upon addition of $Pr(fod)_3$, the quartet of I is shifted to higher magnetic fields more than that of II so that the two resonances can be distinguished (Figure 2 upper trace). Figure 3 shows the case where I was added to a solution of decomposing CBPPO. Whereas I gives an unenhanced absorption quartet, the reaction product II causes an emission quartet. Normally the two quartets overlap and, as their relative intensities have been chosen so that they are equal during the decomposition, emission and absorption cancel (Figure 3.1). In the presence of $Eu(fod)_3$ the degeneracy is removed and the emission and the absorption quartet can be analyzed separately (Figure 3.2). Similarly, $Pr(fod)_3$ shifts the absorption quartet more upfield than the emission quartet (Figure 3.3).

During the reactions the line positions of the shifted lines change, *i.e.*, they approach their original chemical shifts. This is partly explained by the change in ratio between shift reagents and the products with increasing conversion of the reactants. Unfortunately, as some lines move, time-averaging methods cannot be used if

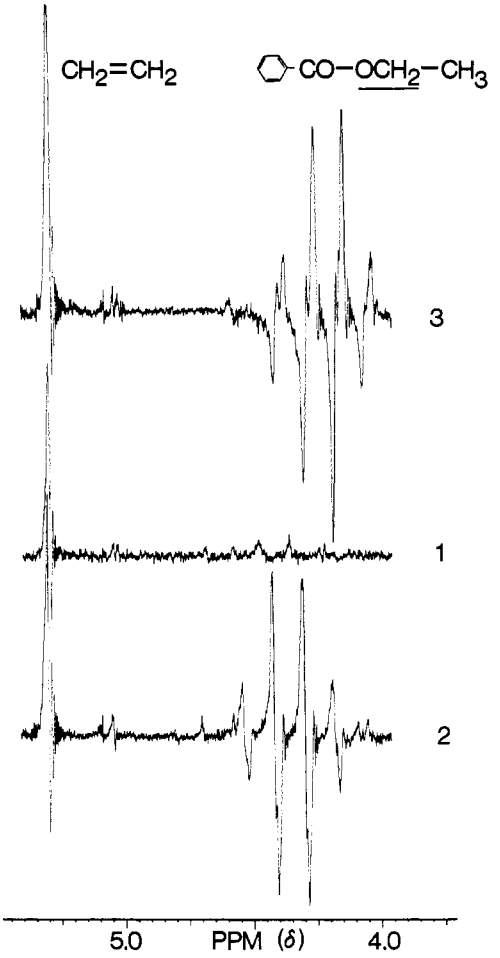

Figure 3. Emission quartet of ethyl benzoate and absorption quartet of ethyl *m*-chlorobenzoate without shift reagent (1), with $Eu(fod)_3$ (2), and with $Pr(fod)_3$ (3).

shift reagents are present. However, the actual line positions reflect the extent of conversion of the reactants. Therefore, the line positions, if calibrated, allow the determination of enhancement factors, which are often difficult to obtain otherwise.

Shift reagent poisons, for example acids, resulting from some reactions as products have to be avoided, since they destroy the lanthanides. Thus during the decomposition of certain benzoyl peroxides a precipitate is formed, and the CIDNP is quenched. The fate of the shift reagents can conveniently be studied by following the shifts of their own resonances during the reactions.

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Structure and Absolute Stereochemistry of Everheptose

Sir:

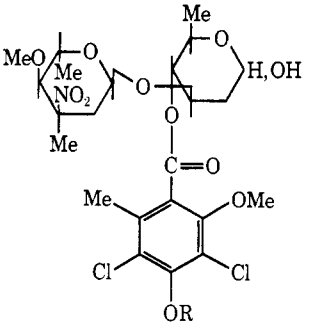
Everninomicins[1] are oligosaccharide antibiotics and perhaps related to curamycins[2] and avilamycins.[3] Due

(1) G. H. Wagman, G. M. Luedemann, and M. J. Weinstein, *Antimicrob. Ag. Chemother.*, 33 (1964).
(2) O. L. Galmarini and V. Duelofeu, *Tetrahedron*, **15**, 76 (1962).
(3) E. Gäumann, *et al.*, German Patent, 1,116,864 (Nov 9, 1961).

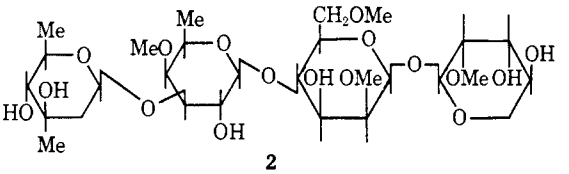
to their inherent complexity, the structural elucidation of this group of antibiotics has been rather slow. They are amorphous compounds of high molecular weight and have many asymmetric centers. In this communication we wish to disclose the structure of everheptose, a seven sugar fragment of everninomicin D.

Everninomicin D on hydrolysis with aqueous acid yields a mixture of products from which everheptose was isolated in a pure state using preparative tlc. Everheptose is an amorphous solid: $C_{57}H_{89}NO_{31}Cl_2$; $[\alpha]D$ $-59.2°$; ν_{max} 1538 (nitro), 1730 cm^{-1} (carbonyl); λ_{max} 208 nm (25,800). It formed a heptaacetate: $C_{71}H_{102}NO_{38}Cl_2$; $[\alpha]D$ $-59.9°$; ν_{max} 1538 cm^{-1} (nitro). In everheptose the nitro absorption in the ir was weaker in intensity compared to the carbonyl absorption, whereas in everninonitrose (**1**) the nitro absorption is much stronger than the carbonyl absorption. It was therefore evident that everheptose has an extra carbonyl group (probably an ester) compared with everninonitrose. A methanolic solution of everheptose when treated with ethereal diazomethane underwent smooth cleavage to yield a mixture of two compounds (as evidenced by tlc). These were isolated using preparative tlc. The more polar component was shown to be identical with evertetrose[4] (**2**) by direct comparison with an authentic sample. The less polar component **3** from the above reaction mixture always seemed to be transformed to a small extent to another still less polar component **4** on tlc. Compound **3** when stirred in acetone solution with silica gel was completely converted into **4**. Alternatively a methanolic solution of **4** when treated with *p*-toluenesulfonic acid was converted completely into **3**. It is clear, therefore, that **3** is a hydroxy ester which is easily converted to the lactone **4**.

Compound **4** is a colorless crystalline solid: $C_{30}H_{41}O_{14}NCl_2$ (M^+ 709); mp 186–188°; $[\alpha]D$ $-57.9°$; λ_{max} 287 (978) and 210 nm (36,159); ν_{max} 1754 (carbonyl), 1555 (nitro), and 3472 cm^{-1} (hydroxyl). It formed an amorphous monoacetate **5** ($C_{32}H_{43}NCl_2O_{15}$ (M^+ 751); $[\alpha]D$ $-47.9°$; λ_{max} 287 (924) and 208 nm (35,931)) and in the ir there was no hydroxyl absorption. Besides showing an acetate methyl absorption and characteristic resonances of everninonitrose (**1**), the nmr spectrum of **5** showed absorption at δ 1.46 (d, J = 6.5 Hz, C_6 methyl), 4.25 (octet, J = 6.5 and 8 Hz, H_5), 3.65 (q, J = 8 and 3 Hz, H_4), 5.49 (d of t, J = 4.8 and 3 Hz, H_3), 2.67 and 2.95 (J_{gem} = 16 Hz, H_2). The chemical shift of H_5 in the parent compound **4** appeared at δ 4.18 and did not change significantly on acetylation to **5**, confirming that **4** was a δ-lactone. The relative stereochemistry at C_3 (axial hydroxyl), C_4, and C_5 followed from the above $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ values. Although the nmr spectrum of **4** was consistent with the major part of the structure, it showed abnormal $J_{2,3}$ = 7 and 8 Hz and $J_{3,4}$ = 8 Hz values perhaps indicating that (a) the compound **4** exists in equilibrium with an open-chain hydroxy acid structure or (b) that the lactone ring exists in a distorted conformation.[5] The possibility of a hydroxy acid structure is ruled out from its ir spectrum wherein there is no absorption for the CO_2H group. Further work is in progress toward elucidation of the conformation of the lactone ring.



1, R = H
12, R = CH_3



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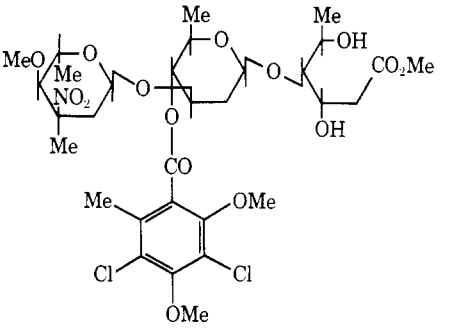

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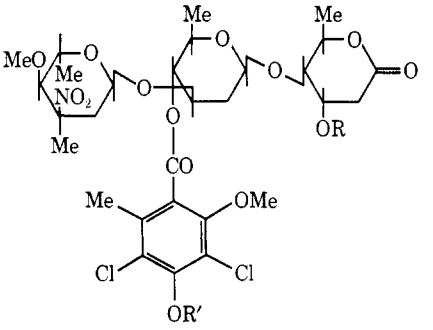


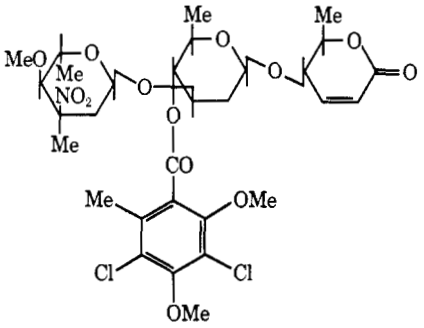
4, R = H; R′ = Me
4a, R = R′ = H
5, R = $COCH_3$; R′ = Me

The absolute stereochemistry of the sugar lactone part of **4** was established in the following way. Compound **4** on heating with acetic anhydride and pyridine yielded an anhydro compound **6**: $C_{30}H_{39}NCl_2O_{15}$ (M^+ 751); mp 174–175°; λ_{max} 287 (1008) and 208 nm (46,066); no hydroxyl absorption in the infrared. The nmr spectrum of **6** was consistent with the assigned structure and showed the presence of two vinyl hydrogens at δ 5.86 (q, 1 H, J = 1.8 and 10 Hz, H_2) and 6.9 (q, 1 H, J = 2 and 10 Hz, H_3). In circular dichroism compound **6** showed a negative Cotton effect, $[\theta]_{250}$ $-40{,}900$, suggesting *R* configuration at C_5.[6] The

(4) A. K. Ganguly, O. Z. Sarre, and S. Szmulewicz, *Chem. Commun.*, 746 (1971).

(5) R. C. Sheppard and S. Turner, *ibid.*, 77 (1968); F. I. Carroll and J. T. Blackwell, *Tetrahedron Lett.*, 4173 (1970); R. N. Johnson and N. V. Riggs, *ibid.*, 5119 (1967).

(6) R. Bucourt, M. Legrand, M. Vignan, J. Tessier, and V. Delaroff, *C. R. Acad. Sci.*, **257**, 2679 (1963); D. Arigoni, W. Von Daehne, W. O. Godtfredsen, A. Melera, and S. Vangedal, *Experentia*, **20**, 344 (1964).

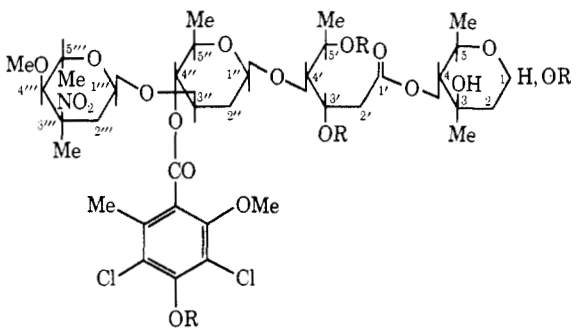


6

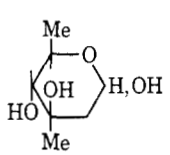
methyl ether of everninonitrose (**12**) in CD also showed a negative Cotton effect, $[\theta]_{244}$ −1600.

Mass spectra of **3** and **4** were completely consistent with the assigned structures. Principal ion compositions and their probable origins are summarized in Scheme I.

The linkage of **4a** to **2** in everheptose is established by deducing the structure of **7**, another hydrolysis product of everninomicin D. Compound **7** is an amorphous solid, $C_{36}H_{53}O_{18}NCl_2 \cdot 1.5H_2O$, $[\alpha]D$ −44.9°, and forms an amorphous tetraacetate **8**, $C_{44}H_{61}O_{22}NCl_2$, $[\alpha]D$ −40.0°. When a solution of **7** in tetrahydrofuran was treated with an ethereal solution of diazomethane, it underwent smooth cleavage to **4** and evermicose[7] (**9**).



7, R = H
8, R = $COCH_3$



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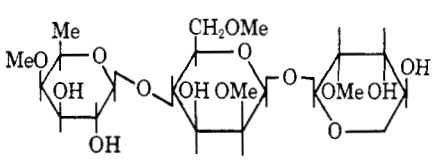

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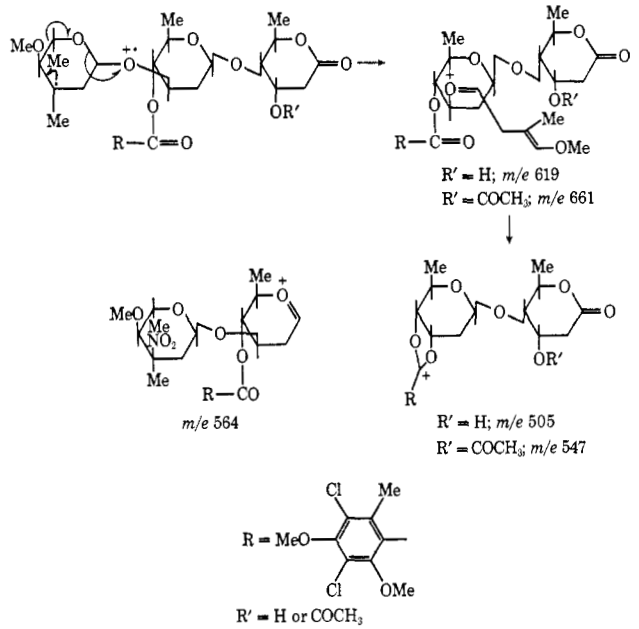
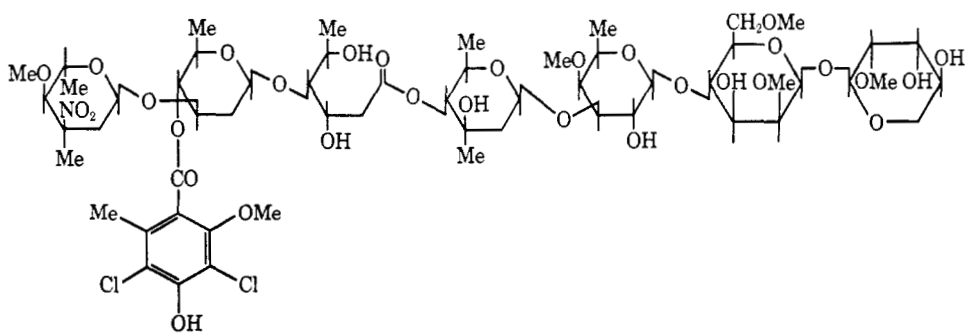
Scheme I



(O_2N + Me), three acetate methyl groups at 2.0, 2.04, and 2.1, an aromatic methyl and an aromatic acetate methyl group at 2.39, one aliphatic methoxyl group at 3.60, and an aromatic methoxyl group at 3.90. Besides the above signals the nmr spectrum also showed the presence of $H_{1''}$ (δ 4.58, 1 H, q, J = 2.5 and 8.5 Hz), H_4 (δ 4.7, 1 H, d, J = 10 Hz), $H_{4''}$ (δ 4.9, 1 H, t, J = 9 Hz), $H_{3'}$, $H_{5'}$ (δ 5.09, 4.93, 2 H), $H_{3'}$ (δ 5.03, 1 H, m), H_1 (δ 5.27, 1 H, q, J = 3.5 and 8.5 Hz). Irradiation of H_5 (δ 3.59) made both H_4 (δ 4.7) and C_5 methyl (δ 1.2) doublets into singlets. The above facts confirm the structure of **8** in all its details. The mass spectrum of **8** was also consistent with the assigned structure.

The elucidation of the structure of compound **7** establishes the linkage of evermicose **9** to compound **4a** and, as we already know the linkage of evermicose **9** to evertriose[8] (**10**) in evertetrose (**2**), it follows that everheptose has to be represented by structure **11**.

Although we are not entirely clear as to the mechanism of the cleavage of everheptose **11** and **7** in methanol solution using diazomethane, it appears that the presence of free phenolic hydroxyl groups in **11** and **7** contributes toward the stability of the above molecules (perhaps by hydrogen bonding keeping the



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The nmr spectrum of **8** shows the presence of four methyl doublets at δ 0.9, 1.2, 1.28, and 1.4, two aliphatic methyl singlets at 1.37 (HO + CH_3) and 1.68 molecule in a particular conformation). Once the phenolic hydroxyl groups are methylated the cleavage could occur simply by ester interchange with methanol.

(7) A. K. Ganguly and O. Z. Sarre, *Chem. Commun.*, 1149 (1969).

(8) A. K. Ganguly and O. Z. Sarre, *ibid.*, 911 (1970).

Alternatively, when methanol is excluded and the methylation carried out in THF solution using diazomethane, everheptose (**11**) is cleaved to **4** and **2**. It is not unlikely that diazomethane besides methylating the phenolic hydroxyl group causes (a) the opening of the ester linkage (which is probably enhanced by the hydrogen bonding with the β-hydroxyl group in the intermediate) and (b) cyclization to the δ-lactone **4** through anion formation.[9]

Acknowledgment. We wish to express our thanks to Sir Derek Barton and Professor J. Meinwald for many stimulating discussions.

(9) Satisfactory elementary analyses were obtained for all new compounds; ir spectra were recorded in chloroform solution; optical rotations were measured in chloroform solution; nmr spectra were taken at 100 MHz in $CDCl_3$ with internal TMS standard. All the coupling constant values were obtained using spin–spin decoupling experiments. The mass spectral assignments were based on high resolution mass spectrometry.

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Hydrogen Abstraction by Thiyl Radicals

Sir:

Data are available on the selectivity and polar character of most common free radicals,[1] but the thiyl radical, a ubiquitous species in organic chemistry[2] and radiation biology,[3] is a notable exception. Hydrogen abstraction by thiyl radicals from organic substrates (eq 1) is well documented.[2a,d,4] However, a quantitative study of this reaction has not been published, although work by Walling and Rabinowitz[4] and by van Zwet and Kooyman[5,6] has provided important semiquantitative data. Kellogg, in a recent review,[2a] has stated that it will be difficult to obtain quantitative data on reaction 1 because of its reversibility.

$$RS\cdot + QH \xrightarrow{k_H} RSH + Q\cdot \qquad (1)$$

A method for the quantitative study of eq 1 is presented here; the method was conceived in order to take advantage of the very reversibility of eq 1 which has hindered previous studies. The key of this method is to utilize tritium-labeled thiol (RSH*) as a solvent; in this milieu, Q· radicals generated in eq 1 abstract hydrogen from RSH* to re-form the substrate QH* which is now tritium labeled (eq 2). The level of

$$Q\cdot + RSH^* \longrightarrow QH^* + RS\cdot \qquad (2)$$

radioactivity in the recovered QH* can be related to the specific rate constant for eq 1. Tritium isotope effects are involved in the calculation, but they can be evaluated independently.[7,8] Because there are no data in the literature with which to test our method, we have developed two kinetic schemes for the determination of relative values of k_H (eq 1).

Table I gives data on the cyclohexanethiyl radical.

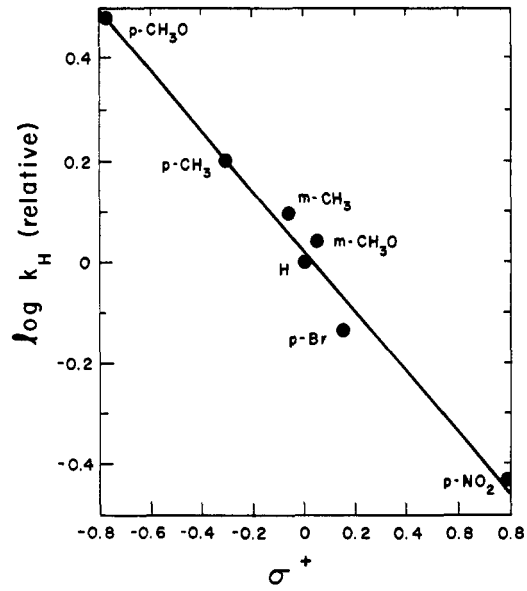

Figure 1. A plot of relative values of k_H (eq 1) *vs.* Hammett σ^+ constants.

Table I. Relative Rate Constants per Reactive Hydrogen for Hydrogen Abstraction by the Cyclohexanethiyl Radical at 80° [a]

Hydrogen donor	n[b]	Relative k_H[c] Scheme I	Scheme II
Anisole	3	≪0.032	
m-Xylene	6	0.043	0.048
Mesitylene	9	0.057	
p-Xylene	6	0.066	
p-Nitroethylbenzene	2	0.37	
p-Bromoethylbenzene	2	0.73	
Ethylbenzene	2	(1.0)	(1.0)
m-Ethylanisole	2	1.1	
m-Ethyltoluene	2	1.25[d]	
p-Ethyltoluene	2	1.6[d]	
p-Ethylanisole	2	3.0	
Diphenylmethane	2	1.5	
Cumene	1	6.3	6.6
p-Cymene	1	8.8	

[a] These data have *not* been corrected for the ratio of isotope effects.[7,13] [b] Number of reactive hydrogens assumed. [c] Reproducibility suggests these data are accurate to ±5%. [d] k_H applies to secondary benzylic position.

A Hammett plot[9] of the data for substituted ethylbenzenes at 80° gives an excellent correlation using σ^+ with

(1) (a) W. A. Pryor, "Free Radicals," McGraw-Hill, New York, N. Y., 1966, Chapter 12; (b) W. A. Pryor, D. Fuller, and J. P. Stanley, *J. Amer. Chem. Soc.*, **94**, 1632 (1972); (c) R. S. Davidson, *Quart. Rev., Chem. Soc.*, **21**, 249 (1967); (d) A. F. Trotman-Dickenson, *Advan. Free-Radical Chem.*, **1**, 1 (1965); (e) C. Walling, "Free Radicals in Solution," Wiley, New York, N. Y., 1957; (f) J. A. Howard and K. U. Ingold, *Can. J. Chem.*, **41**, 1744 (1963).

(2) (a) R. M. Kellogg, "Methods in Free-Radical Chemistry," Vol. II, E. S. Huyser, Ed., Marcel Dekker, New York, N. Y., 1969, p 101; (b) K. Griesbaum, *Angew. Chem., Int. Ed. Engl.*, **9**, 273 (1970); (c) S. G. Cohen, "Organosulfur Chemistry," M. J. Janssen, Ed., Interscience, New York, N. Y., 1967; (d) U. Schmidt, *Angew. Chem., Int. Ed. Engl.*, **3**, 602 (1964).

(3) (a) "Radiation Damage and Sulphydryl Compounds," International Atomic Energy Agency, Vienna, 1969; (b) K. I. Altman, G. B. Gerber, and S. Okada, "Radiation Biochemistry," Vol. I, Academic Press, New York, N. Y., 1970; (c) S. Colowick, *et al.*, Ed., "Glutathione," Academic Press, New York, N. Y., 1954.

(4) G. Walling and R. Rabinowitz, *J. Amer. Chem. Soc.*, **81**, 1137 (1959).

(5) H. van Zwet and E. C. Kooyman, *Recl. Trav. Chim. Pays-Bas*, **87**, 48 (1968).

(6) H. van Zwet and E. C. Kooyman, *ibid.*, **86**, 1143 (1967).

(7) W. A. Pryor and K. G. Kneipp, *J. Amer. Chem. Soc.*, **93**, 5584 (1971).

(8) E. S. Lewis and M. M. Butler, *Chem. Commun.*, 941 (1971).

(9) Substituent constants taken from J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963.