

# Computer Simulation of Intramolecular Hydrogen Abstraction in the Photochemistry of *p*-Benzophenonecarboxylate Esters

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**Abstract:** This paper is concerned with a Monte Carlo treatment of remote oxidation in long hydrocarbon chains attached to a benzophenone moiety. The model considered is that of a hydrocarbon chain embedded in a tetrahedral lattice. The attached hydrogens are explicitly included in the calculation but the energy difference between trans and gauche states of the hydrocarbon chain is neglected. The theoretical problem is basically that of calculating a ring close probability and we present a new Monte Carlo variance reduction scheme which concentrates the sampling on those chain conformations which lead to ring closure. We discuss the influence on the results of such factors as the size of the benzophenone moiety and the geometry of attachment of the hydrocarbon chain, and we compare the predictions of the model with experimental results of Breslow and coworkers.

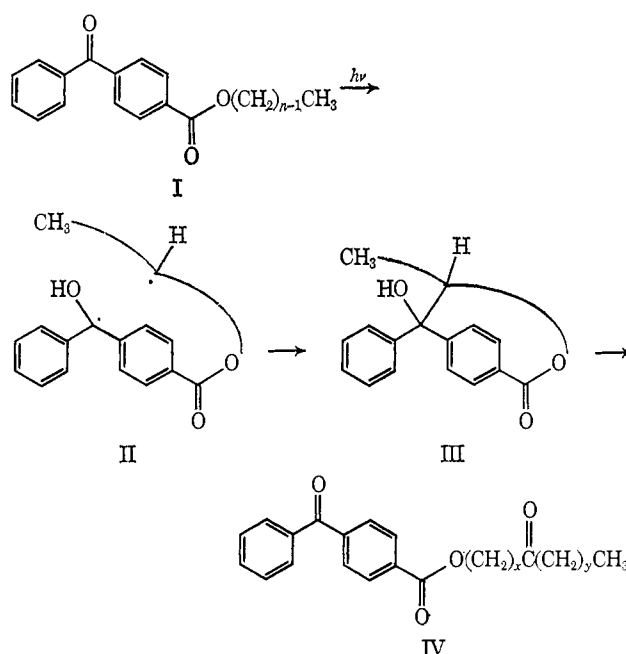
One of the most difficult and challenging problems in synthetic organic chemistry is presented in the conversion of stearic acid to oleic acid. This reaction, which is carried out with ease by certain aerobic bacteria,<sup>1</sup> not only involves breaking a 94 kcal/mol C-H bond, but occurs with positional specificity among chemically equivalent methylenes. Our concern in this paper is to examine ways in which the conformational preferences of a hydrocarbon chain may contribute, in the hands of an organic chemist, to site selectivity in its oxidation reactions.

The first real approach to this problem was presented several years ago by Breslow<sup>2,3</sup> in his remote oxidation experiments. He approached this problem by attaching a functional group to the molecule to be attacked, in such a way that only relatively few sites could be reached by the functional group. The reaction is intramolecular and the specificity is introduced by inserting a rigid region between the functional group and the region of the molecule to be attacked. Substituted benzophenones were employed as the remote functional group, and the first experiments used long chain alcohols as the covalently attached substrates.<sup>2</sup>

The benzophenone moiety is excited photochemically. In its triplet state, it abstracts a hydrogen atom from the chain. Among the products of the diradical produced is the coupling product III. This is transformed chemically in several steps to the desired product IV, which has had a CH<sub>2</sub> oxidized to a carbonyl. Only certain methylene groups can come sufficiently close to the carbonyl oxygen atom for them to be attacked. For instance, in a 16-carbon chain reaction only occurs between carbons 9 and 15 with carbon 14 being particularly susceptible to reaction.<sup>2</sup> The specificity could presumably be varied by attaching the chain at the meta instead of the para position.

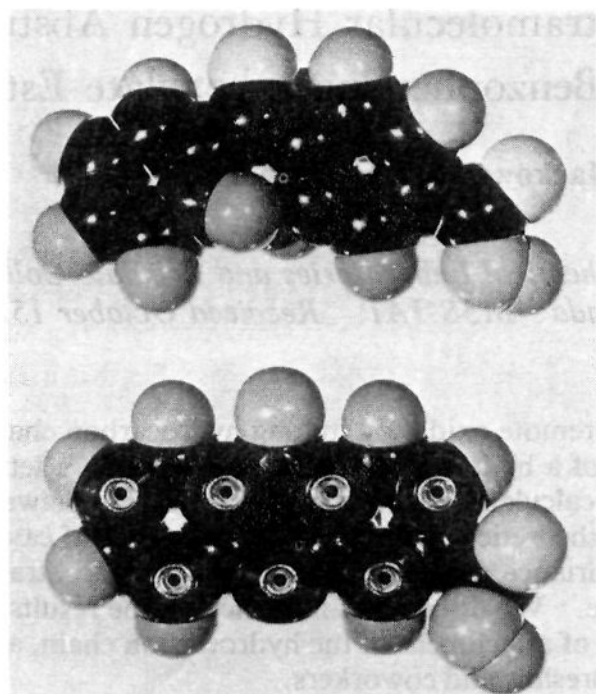
Variation in site selectivity with a change in the distance separating the functional group from the point of attachment of the substrate has been observed by

- (1) K. Bloch, *Accounts Chem. Res.*, **2**, 193 (1969).
- (2) R. Breslow and M. Winnik, *J. Amer. Chem. Soc.*, **91**, 3083 (1969).
- (3) (a) R. Breslow, S. Baldwin, T. Flechtner, P. Kalicky, S. Liu, and W. Washburn, *J. Amer. Chem. Soc.*, **95**, 3251 (1973); (b) R. Breslow, J. A. Dale, P. Kalicky, S. Y. Liu, and W. N. Washburn, *ibid.*, **94**, 3276 (1972); (c) R. Breslow and P. Kalicky, *ibid.*, **93**, 3540, (1971); (d) R. Breslow and P. C. Scholl, *ibid.*, **93**, 2331 (1971); (e) R. Breslow and S. W. Baldwin, *ibid.*, **92**, 732 (1970).



Breslow in his studies of steroid substrates.<sup>3</sup> These substrates are rigid and offer the further simplifying feature of presenting relatively few oxidizable sites. Breslow has pointed out that good predictions can be made for the sites of hydrogen abstraction from steroid substrates by careful examination of molecular models.<sup>3a</sup> With hydrocarbon chain substrates, one is not so fortunate. Our calculations examine the conformational contributions of the hydrocarbon chain to the distribution of oxidation sites in IV in the hope that a more thorough knowledge of chain conformational behavior will lead to useful site-selective syntheses in these systems.

The aim of this work is to understand the role played by the conformational flexibility of the hydrocarbon chain in determining the degree of specificity of the oxidation of the methylene groups by the carbonyl oxygen in I. We make the assumption that the probability of oxidation of a methylene group is proportional to the probability that that methylene group is in the neighborhood of the carbonyl oxygen. Thus we are interested in calculating the relative probabilities that



**Figure 1.** Space filling models: (a) benzophenone-4-carboxylate; (b) its simulated model for tetrahedral lattice based calculations. See the text for details.

the various methylene groups are in a particular region of space. The problem is similar to that of calculating ring closure probabilities, and it is well known that the functional dependence of ring closure probabilities depends on whether or not the excluded volume effect is included in the calculation.<sup>4-7</sup> Sisido,<sup>8</sup> in a theoretical study of intramolecular reaction between two functional groups connected by a polymethylene chain, has shown that neglect of excluded volume leads to poor agreement with experimental results. We therefore wish to take cognisance of the excluded volume effect, and this has lead us, for computational simplicity, to examine a model in which the hydrocarbon chains are confined to a tetrahedral lattice. We include the methylene hydrogens by considering the polymethylene chain as a lattice walk with second neighbor exclusions.

There have been several previous calculations of cyclization probabilities for similar systems including an exact enumeration study of hydrocarbons up to and including decane by Smith and Mortensen,<sup>9</sup> a Monte Carlo study by Fluendy,<sup>10</sup> and the previously mentioned work of Sisido.<sup>8</sup> None of these calculations, however, can account for the bulk of the benzophenone group, which should exert a major effect on the observed chemistry and calculated cyclization probabilities.

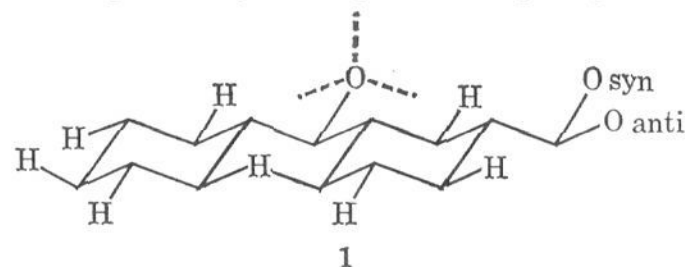
Monte Carlo methods have also been used recently by Morawetz<sup>11</sup> to simulate a conceptually similar problem: the distribution of intramolecular catalysis rates for ester hydrolysis with increasing distance between the ester and remote (catalytic) functional group.

### The Model

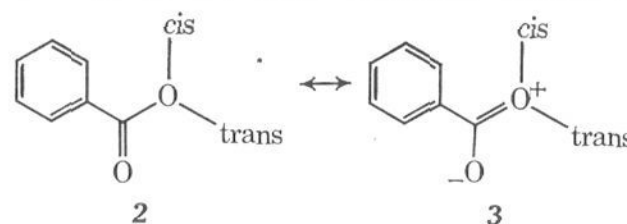
Benzophenone-4-carboxylate is modeled in the lattice

- (4) C. Domb, *Proc. Cambridge Phil. Soc.*, **50**, 586 (1954).  
 (5) J. L. Martin, M. F. Sykes, and F. T. Hioe, *J. Chem. Phys.*, **46**, 3478 (1967).  
 (6) R. E. Trueman and S. G. Whittington, *Proc. Phys. Soc., London (Gen.)*, **5**, 1664 (1972).  
 (7) A. Guttman and M. F. Sykes, *Proc. Phys. Soc., London (Solid State Phys.)*, **6**, 945 (1973).  
 (8) M. Sisido, *Macromolecules*, **4**, 737 (1971).  
 (9) R. P. Smith and E. M. Mortensen, *J. Chem. Phys.*, **35**, 714 (1961).  
 (10) M. A. D. Fluendy, *Trans. Faraday Soc.*, **59**, 1681 (1963).  
 (11) N. Goodman and H. Morawetz, *J. Polym. Sci., Part C*, **31**, 177 (1970); *J. Polym. Sci., A-2*, **9**, 1657 (1971).

as dicyclohexyl ketone with both rings in the chair form, and the ketone and 4-carboxyl functions are set coplanar with the rings. Only the equatorial hydrogens are in-



cluded, and we let the chair form simulate the  $\pi$ -cloud thickness of the aromatic rings. The models in Figure 1 show that this simulation is quite reasonable. We assume that the ester function in I is coplanar with the ring, with the syn and anti forms of the ester equally populated. We choose to begin all chains in the trans conformation about the ester C-O single bond. This choice is made routinely in conformational calculations of polyesters.<sup>12</sup> It stems from resonance contribution (cf. 2 and 3) to the ester stability, which, while not



nearly as important as amide resonance, provides a rotational barrier to interconversion of cis and trans forms. Steric interactions make the cis form higher in energy than the trans, and an energy difference of 2.0 kcal/mol would allow only 3% of the total chains from that conformation. The cis conformation of *N*-methylbenzamide, a useful model for I, cannot be detected by pmr in solution.<sup>13</sup>

Chains are grown stepwise from either the syn or anti oxygens to a length of 30 carbons. The first step is specified in the trans (or, if desired, cis or perpendicular) direction. The particulars of the calculation are specified in the following section. A "hit" is defined as occupation of the first neighbor or second neighbor lattice sites of the ketone oxygen by a hydrogen from a chain CH<sub>2</sub> group. The former are called "inner hits" and are counted separately from "outer hits." The estimated number of hits by the *i*th CH<sub>2</sub> in a chain of length *n* is taken as proportional to the probability of that CH<sub>2</sub> occupying the reactive volume of the ketone carbonyl. In agreement with experimental evidence,<sup>2</sup> hits at the terminal methyl groups are not counted.

No bias is included in these calculations for the known preference for the trans conformations of the chain.<sup>14</sup> Our decision to set  $E_{\text{trans}} = E_{\text{gauche}}$  was dictated by technological and financial limitations. The results of these calculations are applicable strictly only in the high-temperature limit, and this aggravates attempts at comparison to solution experiments. The tetrahedral lattice introduces the artifact that all bonds including C-H bonds become 1.54 Å long. Abberations which might result from this assumption are minimized, fortunately, since the attendant assumption of hard sphere potentials has an offsetting effect.<sup>8,9</sup>

- (12) D. A. Brandt, A. E. Tonelli, and P. J. Flory, *Macromolecules*, **2**, 228 (1969).  
 (13) H. Kessler, *Angew. Chem., Int. Ed. Engl.*, **9**, 219 (1970); W. E. Stewart and T. H. Siddall, *Chem. Rev.*, **70**, 517 (1970).  
 (14) J. March, "Advanced Organic Chemistry: Reactions, Mechanisms, and Structure," McGraw-Hill, New York, N. Y., 1968, p 104.

## Monte Carlo Methods

The Monte Carlo technique which has been used in these calculations is a variant of that described by Rosenbluth and Rosenbluth.<sup>15</sup> Their method is an attractive one although, since their original paper, it has seldom been used. The ideal is to circumvent the attrition problem present in all "walk growing" Monte Carlo methods by using a type of importance sampling.

In the simplest approach the walk is grown by adding steps, chosen with equal probability from the appropriate set of lattice vectors and, if an intersection occurs (*i.e.*, since we are including hydrogen atoms, if the walk is two steps from a point already visited), the walk is discarded. This leads to a very high attrition especially if first or second neighbors are excluded. Rosenbluth and Rosenbluth mitigated the attrition by only allowing the addition of steps which would not lead to an immediate intersection.

Suppose that, for the  $i$ th walk generated in the sample, at the  $j$ th step there are  $a_{ij}$  steps which might be added which do not lead to an immediate intersection. The step to be added is chosen with equal probability ( $1/a_{ij}$ ) from among these  $a_{ij}$  possible steps. Occasionally  $a_{ij}$  will be zero which corresponds to the walk being "trapped" but this will be rare in three dimensions. When the walk is either completed or trapped it is assigned a weight

$$W_i^n = \sum_{j=1}^n a_{ij} \quad (1)$$

so that a "trapped" walk has zero weight. The total number ( $C_n$ ) of allowed walks of  $n$  steps can then be estimated as

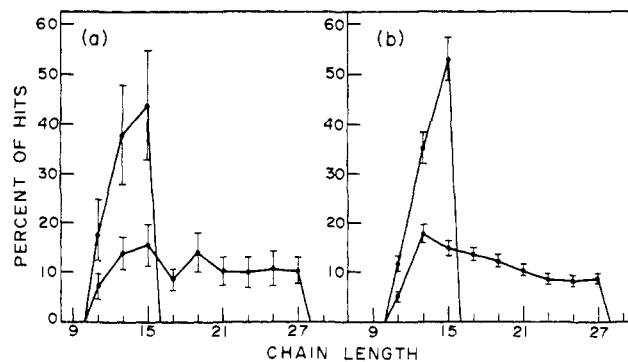
$$\hat{C}_n = (1/N) \sum_{i=1}^N W_i^n \quad (2)$$

where  $N$  is the sample size.

In this work we are interested in estimating the population of a subclass of allowed walks, *i.e.*, those which have the  $k$ th methylene group within a given distance of a reactive oxygen atom. We could use the above technique by assigning a walk zero weight unless the walk is a member of this subclass. However, this is inefficient in that a good deal of time would be spent in examining walks which never reach the reactive region. The efficiency can be improved considerably by using a second importance sampling technique. The idea is to artificially increase the number of walks in the sample which can lead to reaction and to remove the resulting bias by suitable reweighting. It is convenient to think of sampling under an attractive pseudopotential centered at the reactive oxygen, so that steps which bring the walk closer to this oxygen are chosen with higher probability. Consider the addition of the  $j$ th step to the  $i$ th walk in the sample. Suppose that the  $m$ th direction would result in the walk (after  $j$  steps) being a distance  $r_m$  from the reactive oxygen. Then the probability of the  $m$ th direction being chosen would be

$$p_m = f(r_m) / \sum_{k=1}^{a_{ij}} f(r_k) \quad (3)$$

(15) (a) M. N. Rosenbluth and A. W. Rosenbluth, *J. Chem. Phys.*, **23**, 356 (1955); (b) F. L. McCrackin, *J. Res. Nat. Bur. Stand., Sect. B*, **76**, 193 (1972); (c) F. L. McCrackin, J. Mazur, and C. M. Guttman, *Macromolecules*, **6**, 859 (1973); (d) J. Mazur, C. M. Guttman, and F. L. McCrackin, *ibid.*, **6**, 872 (1973).



**Figure 2.** Effects of pseudopotential on the estimated distribution of hits for 16- and 28-carbon chains: (a) no pseudopotential,  $\alpha = 1.0$ ; (b) pseudopotential parameter,  $\alpha = 0.70$ . 30,000 chains are sampled for each, for I in the trans-syn conformation. Inner hits. Error bars represent one standard deviation.

where  $f(r)$  can have any suitable form. The function chosen in this work was

$$f(r) = \alpha \alpha^r \quad (4)$$

If the  $m$ th step is chosen the weight associated with that step would be

$$a_{ij}^* = 1/p_m \quad (5)$$

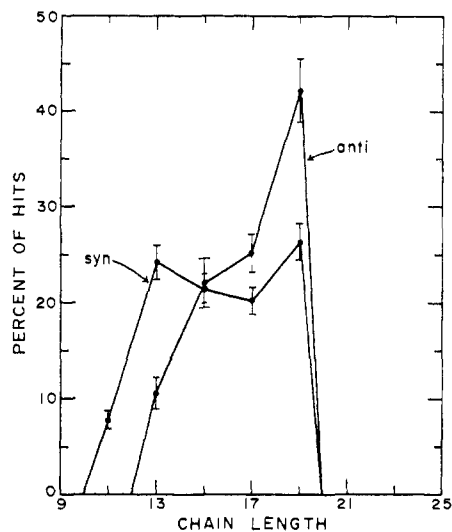
and eq 1 and 2 would be unchanged except that  $a_{ij}$  would be replaced by  $a_{ij}^*$ .

## Results and Discussion

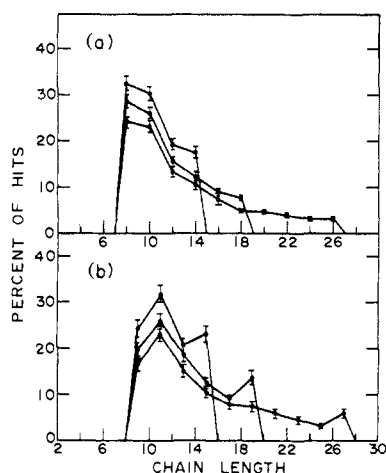
These calculations represent the limits of our current financial resources. As such it is interesting to evaluate the effectiveness of the pseudopotential, which is novel with this report, as an importance sampling procedure. Figure 2 presents the estimated relative number of hits for 16- and 28-carbon chains. For each calculation, 30,000 chains are sampled for I in the trans-syn conformation. In Figure 2a, no pseudopotential importance sampling is used; in Figure 2b, the pseudopotential parameter ( $\alpha$ ) in eq 4 is set equal to 0.70. The error bars represent 1 standard deviation. We estimate that it would require a fourfold larger sample size to generate the data in Figure 2b without recourse to the pseudopotential importance sampling. One can, in principle, use stronger values for the pseudopotential ( $\alpha < 0.70$ ). We have used values of  $\alpha$  as low as 0.65. Below this value serious distortions occur in the estimates. These are thought to occur when entire regions of space remain unsampled, and our method for removing the pseudopotential bias breaks down.

Figure 3 presents the distribution of hits in the 20-carbon ester of I for both the syn and anti rotamers. Rather pronounced differences in the two distributions are seen. The syn conformation leads to many more hits at the lower carbon numbers accessible to the ketone oxygen, while the anti conformation leads to hits concentrated near the end of the chain. The chains in the syn conformation have a somewhat higher probability of reaching the reactive oxygen. This is accounted for in Figure 5b, which presents the normalized weighted sum of the hit estimates for both rotamers.

Figure 4 presents the distribution of hits in 16-, 20-, and 28-carbon esters of I with the ester in the cis conformation. The top graph presents the distribution of



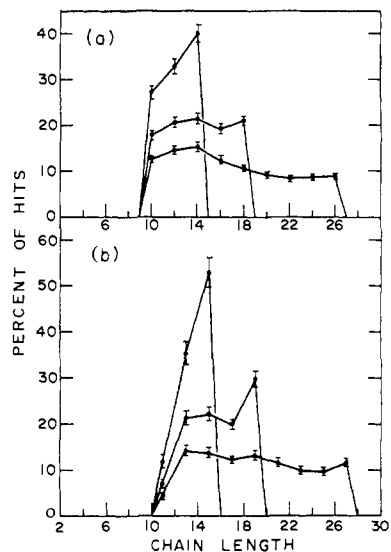
**Figure 3.** Effect of syn and anti rotamers on the estimated distribution of inner hits for I in the trans conformation: syn, 90,000 chains; anti, 60,000 chains sampled.



**Figure 4.** Effect of chain length on the estimated distribution of hits in I for the cis conformation: (a) hits at the outer lattice sites; (b) hits at the inner lattice sites; 60,000 chains were sampled.

hits at the outer lattice sites; the lower graph presents the distribution at the inner lattice sites. While we have assumed the cis conformation unimportant in our subsequent comparison of calculated hits with Breslow's experimental data, these data are important in understanding the predictions of the model. Hits occurring at low carbon numbers are most important in this conformation. The maximum sites of attack are carbons 8-11, with the hits tapering off at larger carbon number. The curves in Figure 4 represent a normalized weighted average of hits from chains begun in the cis-syn and cis-anti conformations. Since the absolute estimates of hits is larger for cis than for trans chains, these estimates can assume chemical importance at high temperature or in reactions in the mass spectrometer.<sup>16</sup>

The results of our calculations for 16-, 20-, and 28-carbon chains grown from the trans conformation are presented in Figure 5. The data are presented as the



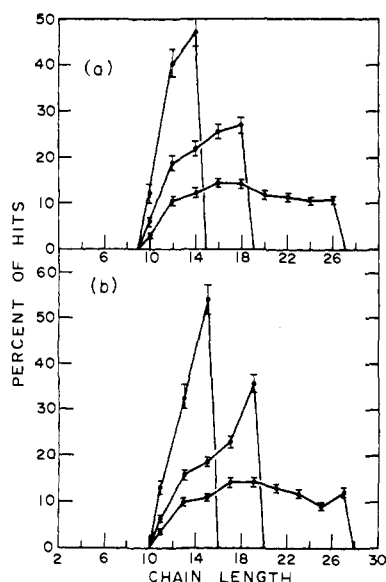
**Figure 5.** Effect of chain length on the estimated distribution of hits for I in the trans conformation: (a) hits at the outer lattice sites; (b) hits at the inner three lattice sites; 150,000 chains were sampled.

normalized per cent of hits at each carbon and are thus relative values. In this way, we hope that distortions of the physical situation introduced by the crudeness of our model will be minimized. In Figure 5b hits only at odd-carbon numbers are obtained, since only even-membered rings are accessible on a tetrahedral lattice. Hits at even carbon numbers may be obtained by examining occupancy by a  $\text{CH}_2$  hydrogen of the second tier of (outer) lattice sites around the ketone oxygen (Figure 5a). This allows us to examine the hydrogen abstraction phenomenon for a larger reactive radius. Strictly speaking, these two distances are 1.54 and 2.51 Å from the ketone oxygen, and the latter is probably too large for reaction to occur in real molecules.<sup>17</sup> Within the context of our model, which relies on hard-sphere potentials, it is more useful to think of a hit at an inner lattice site as an approach of a  $\text{CH}_2$  to within the distance of the product O-H bond length. Hits at the outer sites then represent reaction at about 1.6 times this distance.

There are eight outer sites and three inner lattice sites which surround the reactive oxygen in our model. It is not surprising that any given chain length suffers two to three times as many hits in the outer tier of lattice sites (at even carbon numbers) than in the inner sites. The distribution of hits, however, within the chain is not very different. In Figure 5, (a) and (b) compare the distribution of hits at outer and inner sites, respectively, for 16-, 20-, and 28-carbon chains. The outer sites (a) show relatively more hits at the lower number carbons and slightly fewer at the higher number carbons. An end-of-chain effect seen in the 20-carbon ester is less pronounced in the hits at the outer lattice sites. For the longer chains ( $n \geq 20$ ), the maximum number of hits occurs at  $\text{C}_{14}$  at the outer sites and at  $\text{C}_{13} \sim \text{C}_{15}$  at the inner sites. In both sets of data, the bulk of the benzophenone prevents the first nine

(16) See, for example, S. Meyerson, I. Puskas, and E. K. Fields, *Chem. Ind. (London)*, 1845 (1968); *J. Amer. Chem. Soc.*, **95**, 6056 (1973); J. Cable and C. Djerassi, *ibid.*, **93**, 3905 (1971); M. A. Winnik, C. K. Lee, and P. T. Y. Kwong, *ibid.*, **96**, 2901 (1974).

(17) The maximum distance over which hydrogen abstraction can occur in the related McLafferty rearrangement of steroidal ketones in the mass spectrometer is 1.8 Å: H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Organic Compounds," Holden-Day, San Francisco, Calif., 1967, p 157.



**Figure 6.** Effect of chain length on the estimated distribution of hits for I in the trans conformation. Hit sites are limited to those coplanar with the benzophenone, simulating the location of the nonbonding electrons on the ketone oxygen: (a) outer hits; (b) inner hits; 60,000 chains were sampled.

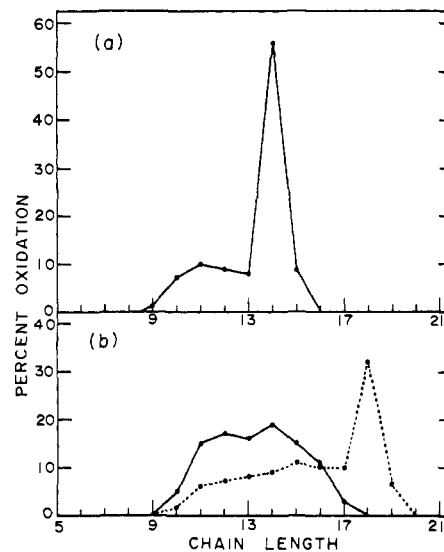
methylenes of the chain from reaching the ketone oxygen.

The distribution of hits within the chain is broad. Little selectivity is seen in the 28-carbon esters. Little synthetic utility would be predicted for such long chains if the conditions of our model apply to solution photochemistry. We should keep in mind that the assumption we made, that the trans and gauche conformations have equal energy, is not correct; these calculations should apply only in the high temperature limit. Higher temperatures do broaden the experimentally observed distribution of reactive sites (*vide infra*).

In the calculations for shorter chains, hits concentrate near the end of the chain. For 11- and 12-carbon chains, one could conclude that site specificity would be high enough for synthetic utility, since the benzophenone bulk prevents attack at the first nine carbons.

**Directional Dependence of Hydrogen Abstraction.** We have examined the directional dependence of hydrogen abstraction in I by counting hits only at those lattice sites coplanar with the benzophenone. These sites simulate the location of the nonbonding electron pairs of the ketone oxygen. These data are plotted in Figure 6. Very small differences are seen between these data and the data in Figure 5.

**End-of-Chain Effects.** An end-of-chain effect is responsible for the large fraction of hits at C<sub>14</sub> and C<sub>15</sub> in the 16-carbon chains, and C<sub>18</sub> and C<sub>19</sub> in the 20-carbon chain. This end effect is an unexpected outcome of these calculations. Its magnitude depends upon chain length, syn or anti conformation of the ester function (Figure 3), and whether the ester is in the cis or trans conformation about its C–O single bond (Figures 4 and 5). This conformational dependence most likely reflects the distance of the first carbon of the chain from the ketone oxygen. Calculations applied to esters of *p*-carboxybenzaldehyde (substituting H for Ph in I) show smaller end effects. The physics of this end effect are not well understood. Its magnitude is



**Figure 7.** Per cent reaction at various carbon sites along the hydrocarbon chain in the photochemical reaction of I in dilute solution in carbon tetrachloride: (a) 16-carbon chain, 23°C; (b) 20-carbon chain at 23°C (solid line), 60–65°C (dotted line). Data were taken from ref 2 and 18.

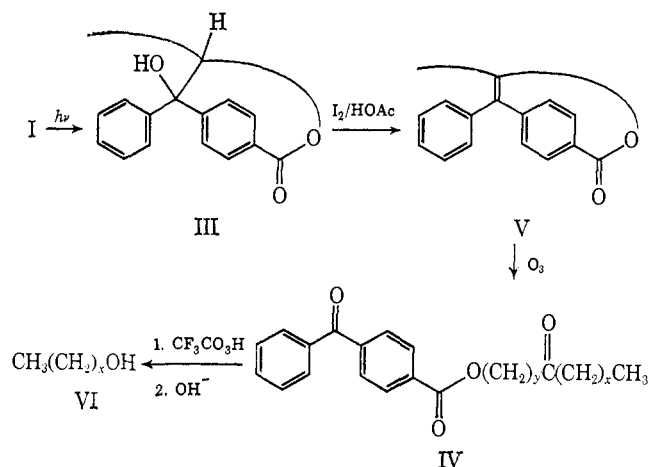
very much a function of the bulk of the benzophenone, and of the remote phenyl ring in particular. A similar effect, although of uncertain magnitude (*vide infra*), has been observed in the solution chemistry (Figure 7). We predict that it will be correspondingly less important in the photochemistry of long chain acetophenone derivatives than in long chain benzophenone derivatives.

We can, of course, calculate the hit distribution for the hypothetical "molecule" containing only the reactive oxygen and the carboxylate at which the chains are attached; these arranged with the same spatial distribution as for the previous calculations. This excludes minimal volume from the chain. We have carried out this calculation and observe a somewhat smaller end effect. In these calculations chains can pass through the space which the benzophenone rings would occupy. Hits occur at carbons 8 and 9, respectively, at the outer and inner sites. The distribution of hits is clearly perturbed from that in Figure 3, indicating that excluded volume effects are important in these calculations. The degree of perturbation here is not sufficient, however, to warrant a more detailed investigation with our crude model.

**Comparison with Experimental Results.** Figure 7 presents the experimental data of Breslow and Winnik<sup>2,18</sup> which these calculations were intended to simulate. Their data require some comment. Two assumptions were made in the correlation of product analysis with the original sites of hydrogen abstraction. The first (see Scheme I) was that the presence of a ketone at the *i*th carbon in IV indicated hydrogen abstraction from C<sub>*i*</sub>H<sub>2</sub> in the photolysis of I. A second assumption was that the distribution of oxidation sites in IV reflects the distribution of hydrogen abstraction sites in I. Since III and V were well characterized, the first assumption is valid. The second assumption would be valid if the chemical yield of IV approached quantitative; however, III represented only 25–40% of the

(18) M. A. Winnik, Ph.D. Thesis, Columbia University, 1969.

Scheme I



photoproduct.<sup>18</sup> The remaining material, as yet uncharacterized, seemed to be due to coupling of the intermediate diradical into either of the benzene rings. Since this process might vary among the various alkyl radicals, we must keep in mind that the curves in Figure 7 reflect this bias.

Another problem with these data is the absolute magnitude of per cent reaction at the antepenultimate carbon. Formation of a ketone at this position was detected as ethanol in the analytical approach.<sup>18</sup> Two corrections were in order for the raw data. One stemmed from a bias against ethyl migration in the Baeyer-Villiger reaction;<sup>19</sup> the other, from experimental difficulties in extracting ethanol from an aqueous solution containing the other alcohols. Only the former correction was applied. Uncertainty in the latter factor means that the absolute value of the per cent oxidation of  $C_{n-2}H_2$  should be treated with caution. The magnitude of the per cent oxidation at the penultimate carbon is the most accurately known and this value supports the increase in oxidation of the furthestmost carbons in the 20-carbon ester at 60–65° in carbon tetrachloride.

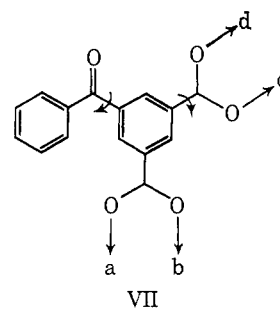
We must be extremely cautious at this time in comparing our calculated distribution of hits with the experimental results in Figure 7. The paucity of experimental data, uncertainties in that data, and the absence of detailed studies of the effects of temperature on the hydrocarbon chains in these molecules aggravate the comparison. We are attempting to introduce a temperature parameter into our computer program which will allow us to set  $E_{trans} \neq E_{gauche}$ . This will mitigate matters considerably. With these cautionary remarks in mind, some comparisons are still valid.

If the end effects seen in the experimental results are exaggerated, the correspondence between the calculated results and the experimental results for the 16-carbon ester at 23°, and especially for the 20-carbon ester at 60–65°, is encouraging. For the 16-carbon ester, the maximum at  $C_{14}$  is predicted by the outer-hit data. The even greater fraction of hits at  $C_{15}$  at the inner lattice sites might reflect the limitations of lattice calculations or the temperature difference between experiment

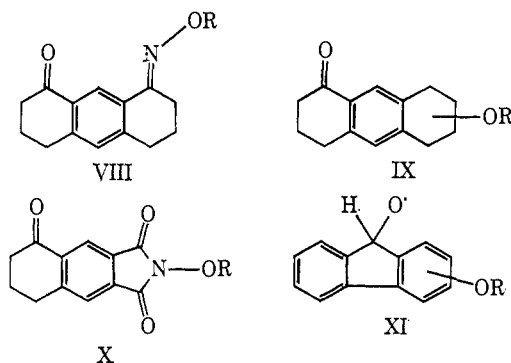
(19) M. A. Winnik and V. Stoute, *Can. J. Chem.*, **51**, 2788 (1973).

and calculation. For the 20-carbon ester at 60–65°, one maximum at  $C_{15}$  is correctly predicted. The end-of-chain effect here is seen both in the calculations and in the high-temperature photolysis.

The data in Figures 5 and 6 are the sum of hit estimates for both the syn and anti rotamers of the carboxyl group. In Figure 2 one sees that this relatively minor change in  $C_1$ -ketone oxygen distance has a major effect on the distribution of hits in a 20-carbon chain. This rotational flexibility in the reactive head group is synthetically disadvantageous. The *m*-benzophenone-carboxylate esters VII are probably useless for site-specific synthesis with flexible chains. The four different rotamers would lead to four different sets of



hit distributions from chains originating at a, b, c, and d. Selectivity here would be expected, of course, for penultimate oxidation of chains too short to reach the reactive function, except from position d. More useful synthetically would be reactants such as the oxime ester VIII, the ether IX, the imide X, and an even wider variety of alkoxy radical derivatives such as XI. One



of our aims is to refine our program so that one, contemplating carrying out this kind of chemistry, might, for \$25–50 computing time, determine the site of maximal reaction, and the expected distribution of products.

Breslow has discussed the importance of substrate conformational rigidity in obtaining high site specificity in his steroid oxidations.<sup>3</sup> Reactant conformational rigidity is probably more important. The site specificity of the desaturase enzyme system which converts stearic acid to oleic acid must take advantage of this principle.

**Acknowledgment.** We wish to thank Research Corporation and The National Research Council of Canada for financial support.