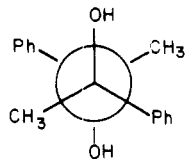
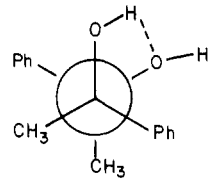
observed; this ratio has been explained[2,12] as that due to conformational control via interspecies hydrogen bonding at the time of combination.



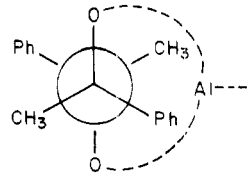
A
(all like groups opposed, major route to meso)



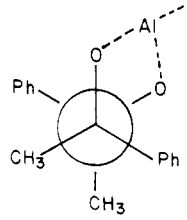
B
(phenyl groups opposed, a major route to *dl*)

In aprotic media, the formation of II would be minimal, and the "dimerization", presumably intramolecularly from I, would predominate.

Reasoning similar to that proposed for the ketyl radical dimerization would be invoked to explain *dl* predominance, i.e.,



A'
(major route to meso)



B'
(phenyl groups opposed, a major route to *dl*)

Some combination of oxygen–aluminum bond distances and/or bond strengths would increase the utilization of pathway B′ relative to B and increase the preference for the *dl* product.

Another aspect of the problem deserves comment. Utilization of the *components* of an aluminum alkoxide in a protic medium is associated with the production of pinacol while a preformed alkoxide (Merwein–Pondorf–Verley reaction) is employed to produce simple carbinol. A comparison of the two pathways, using the alcohol/alkoxide preferred in MPV reactions (2-PrOH), would permit the observation of whether the readily interacting alcohol and aluminum together produce any alkoxide in situ which, if formed, should give rise to some simple carbinol. No carbinol was observed under such circumstances (entry 5 in Table I). The preformed alkoxide studies gave only carbinol (entry 18, 2-PrOH) or a neglible reaction (EtOH).

Experimental Section

The procedures employed by Newman[6] and by Schriebmann[1] were adapted as follows (variation in amounts and times will be found in Table I [13,14]). The acetophenone (Eastman Reagent), aluminum foil (Baker purified, 18 in.^{2} × 0.001 in., ~0.75 g cut in small squares), solvent (simple or 1:1 with alcohol), and 0.1 g of $HgCl_2$ were added to a flask in that order. The reaction mixture was cooled and hydrolyzed with a 0.5 M HCl/ice slurry, after the appropriate reflux. The organic layer was separated, the aqueous layer was thoroughly extracted with the common solvent, and the combined organic layers were washed successively with 0.5 M HCl, 5% $NaHCO_3$, and saturated NaCl and dried over $MgSO_4$. The dried material was concentrated to the complete removal of solvent, and the residue was weighed (material balance) and dissolved in $CDCl_3$. Yields and diastereomeric ratios were determined by NMR.[15]

The preformed aluminum alkoxide studies differed only in the replacement of the components of aluminum amalgam with the preformed reagent; e.g., 4.1 g of freshly distilled aluminum 2-propoxide,[16] 0.122 g of acetophenone, 10 mL of 2-propanol, and 10 mL of benzene refluxed 4 h produced a nearly quantitative yield of methylphenylcarbinol and no pinacol.

Registry No. Acetophenone, 98-86-2; α-methylbenzyl alcohol, 98-85-1; *dl*-2,3-diphenyl-2,3-butanediol, 22985-90-6; *meso*-2,3-diphenyl-2,3-butanediol, 4217-65-6.

(11) E. Hayon and M. Simic, *Acc. Chem. Res.*, 7, 114 (1974).
(12) While the arguments are somewhat lengthy and have been provided in detail elsewhere,[2] it might be helpful to note that simple dimerization of any such radicals (or radical anions) would be expected to produce a predominance of the meso form as argued from the viewpoint that only when all like groups are opposed do we have a minimum of nonbonded interactions. Accordingly, some other influence(s) must be controlling.
(13) J. H. Stocker and D. H. Kern, *J. Org. Chem.*, 31, 3755 (1966).
(14) J. H. Stocker and R. M. Jenevein, *J. Org. Chem.*, 33, 294 (1968).
(15) J. H. Stocker, D. H. Kern, and R. M. Jenevein, *J. Org. Chem.*, 33, 412 (1968).
(16) Preformed according to T. Bersin, "Newer Methods of Preparative Organic Chemistry", Interscience, New York, 1948, p 132.

Conformational Analysis of *cis*- and *trans*-2,6-Diphenyl-5,6-dihydro-2*H*-thiopyran

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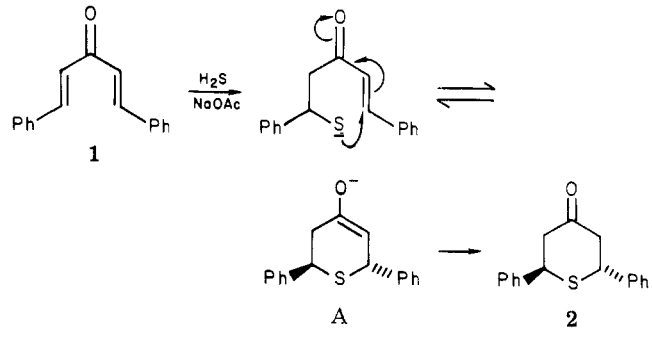
Received April 5, 1979

Not much is known of the conformation of 4-heterosubstituted cyclohexene rings.[1] Such a ring has been invoked as a conformational model, however, to explain the preferential formation of the less stable trans isomer of 2,6-diphenyltetrahydro-1-thiopyran-4-one (2) from reaction of dibenzylideneacetone (1) and sodium acetate in 90% aqueous ethanol saturated with hydrogen sulfide.[2]



1 A 2

The proposed reaction mechanism required that both the trans and cis intermediate enols prefer a boat conformation. The trans isomer of the intermediate enolate A, having both phenyl groups equatorial, was expected to be more stable than the cis isomer, having one phenyl axial and the other equatorial. With the assumption that the transition state for the formation of the enolate A is similar to A, the conformational differences accounted for the preferential formation of the trans isomer.

(1) Conformational studies were reported recently on some simple 5,6-dihydro-2*H*-pyran systems: O. Achmatowicz, Jr., M. Chmielewski, J. Jurczak, and L. Kozerski, *Rocz. Chem.*, 48, 481 (1974); O. Achmatowicz, Jr., M. Chmielewski, J. Jurczak, L. Kozerski, and A. Zamojski, *Org. Magn. Reson.*, 4, 537 (1972); O. Achmatowicz, Jr., A. Ejchart, J. Jurczak, L. Kozerski, J. S. Pyrek, and A. Zamojski, *Rocz. Chem.*, 46, 903 (1972); O. Achmatowicz, Jr., J. Jurczak, A. Konowal, and A. Zamojski, *Org. Magn. Reson.*, 2, 55 (1970).
(2) C. A. R. Baxter and D. A. Whiting, *J. Chem. Soc. C*, 1174 (1978).

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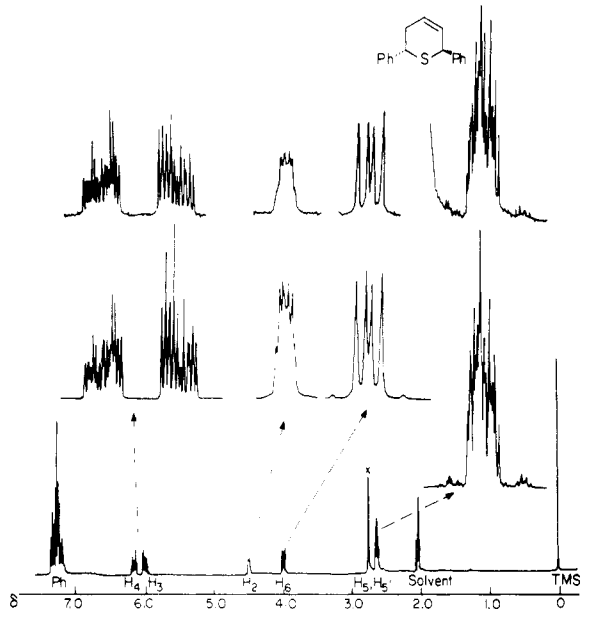
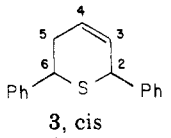


Figure 1. Observed and calculated spectra for *trans*-2,6-diphenyl-5,6-dihydro-2*H*-thiopyran in acetone-d_6. Expanded portions of the spectra are shown at the top with calculated spectra underneath. Intensity anomalies in the calculated spectra occur largely because of a small number of computer points used by the program for display.

Half-boat conformations would be surprising, however, since the boat conformation of cyclohexene is believed not to be a local-minimum-energy form.[3] Instead it probably serves as the transition state for the interconversion of the two half-chairs. As we had samples of both *cis*- and *trans*-2,6-diphenyl-5,6-dihydro-2*H*-thiopyran (**3** and **4**),[4] we decided to undertake a high-field proton NMR analysis of the coupling constants to shed light on the conformations of the two compounds.



3, cis
4, trans

Experimental Section

The synthesis of the compounds has been described.[4] The NMR samples were about 1% w/v concentration and were degassed with several freeze–thaw cycles before being sealed. Traces of tetramethylsilane were added to give reference NMR signals.

All NMR spectra were obtained at 270 MHz on a Bruker WH-270 spectrometer in the Fourier transform mode with quadrature detection. Spectral widths of 2400 Hz in 32K of memory gave a computer resolution of 0.15 Hz/channel. Normally, 100 free-induction decays were averaged, with a pulse separation of 6.9 s. The resulting averaged free-induction decays were Fourier transformed without exponential weighting to give line widths of about 0.6 Hz. Approximately 70° "flip angles" were used for excitation. The probe temperature was about 30 °C for most spectra. At low temperature, the error in temperature measurement is less than 5 °C.

Spectral analysis was done in the first stages with the Nicolet program ITRCAL on the Nicolet 1180 computer of the spectrometer. Final calculations were made with the iterative program LAOCOON III[5] so that we could take advantage of the error analysis routine.

(3) (a) N. L. Allinger and J. T. Sprague, *J. Am. Chem. Soc.*, **94**, 5734 (1972); (b) R. Bucourt, *Top. Stereochem.*, **8**, 159 (1974).
(4) C. H. Chen, G. A. Reynolds, N. Zumbulyadis, and J. A. Van Allan, *J. Heterocycl. Chem.*, **15**, 289 (1978).
(5) Quantum Chemistry Program Exchange, Department of Chemistry, Room 204, Indiana University, Bloomington, IN 47401, Program III.

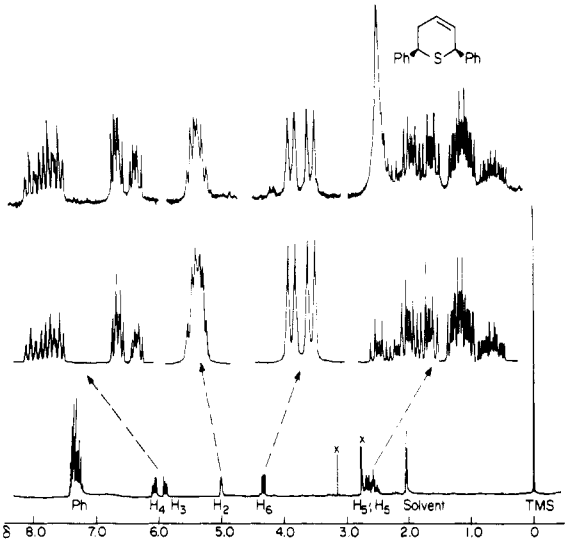


Figure 2. Observed and calculated spectra for *cis*-2,6-diphenyl-5,6-dihydro-2*H*-thiopyran. See Figure 1 for details.

Table I. Calculated Chemical Shifts and Coupling Constants (Hz) for *cis*- and *trans*-2,6-Diphenyl-5,6-dihydro-2*H*-thiopyran in Acetone-d_6

parameter	cis (3)	trans (4)
ν_2	1354.82 (δ 5.02)	1223.581 (δ 4.53)
ν_3	1598.47 (δ 5.92)	1631.28 (δ 6.04)
ν_4	1644.14 (δ 6.09)	1672.65 (δ 6.20)
ν_5	692.47 (δ 2.56)	722.07 (δ 2.67)
$\nu_{5'}$	729.37 (δ 2.70)	712.64 (δ 2.64)
ν_6	1169.82 (δ 4.33)	1085.24 (δ 4.02)
J_{23}	2.03	5.00
J_{24}	−2.46	−1.93
J_{25}	2.68	1.26
$J_{25'}$	4.02	2.55
J_{26}	0.00[a]	0.00[a]
J_{34}	10.79	10.76
J_{35}	−1.74	−2.04
$J_{35'}$	−2.71	−2.37
J_{36}	0.00[a]	0.00[a]
J_{45}	6.07	5.56
$J_{45'}$	2.35	2.71
J_{46}	−0.48	−0.31
$J_{55'}$	−17.70	−17.83
J_{56}	3.59	4.06
$J_{5'6}$	11.51	10.24

[a] Assumed.

For the final calculations the simulation was done in parts. In the first part only the C-4 proton resonances were assigned, and all of the nonzero parameters except J_{46} were allowed to vary. In this way the very small J_{46} values were not distorted by the fact that they were not resolved in the C-6 proton region of the spectrum. The final least-squares fit for both spectra was 0.13 Hz. The observed spectra compared with those calculated are shown in Figures 1 and 2.

Results

The results of the spectral analysis are given in Table I. For the trans isomer (**4**) the chemical shifts of the C-5 and the C-5′ protons are very similar. As a result, coupling constants involving these protons do not correspond to any observed splittings in the spectrum. For example, when deuteriochloroform was tried as a solvent, the C-6 proton resonance gave only a sharp triplet for which the observed splittings are averages of the actual coupling constants.[6] With a solvent such as acetone-d_6, the chemical shifts of the C-5 and C-5′ protons differed enough that the coupling

(6) R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, **39**, 216 (1961).

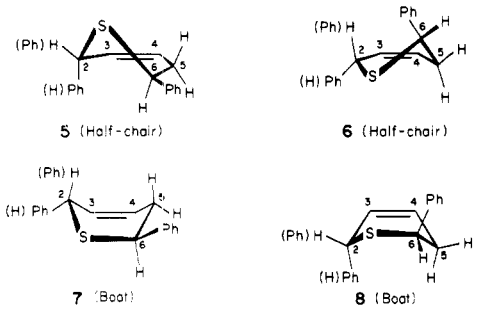


Figure 3. Possible conformations for *cis*- and *trans*-2,6-diphenyl-5,6-dihydro-2*H*-thiopyran.

constants could be determined by computer analysis.

The signs of coupling constants in Table I were checked by spectral calculations with different sign combinations and by spin-tickling experiments. No other sign combination (other than a complete reversal of all signs) was consistent with the experimental results. Calculated errors in the coupling constants based on the LAOCOON III program were all less than 0.03 Hz. Because of possible effects of such things as assignment of overlapping lines to a single frequency and underestimation of errors by the program, we believe that more realistic confidence limits are ±0.1 Hz. Such conservative error limits are certainly adequate for the present purposes.

At about −70 °C the spectra were less well resolved because of increases in line widths. Nevertheless, a satisfactory fit of the spectrum of the cis isomer (**3**) in acetone-d_6 was found with chemical shifts which were within 12 Hz of the room-temperature values. Coupling constants differed by less than 0.1 Hz except for $J_{55'}$, $J_{5'6}$, and $J_{35'}$ for which −17.82, 11.68, and 2.56 Hz were found. For the trans isomer (**4**) ν_2 and ν_4 changed to 1249.6 and 1685.7 Hz and ν_5 and $\nu_{5'}$ became 718.9 and 712.7 Hz while other chemical shifts changed by less than 5 Hz. The more similar chemical shifts for ν_5 and $\nu_{5'}$ with the reduced resolution at low temperature made spectral simulation difficult. The sum of $J_{5'6}$ and J_{56} increased to 14.7 Hz, however, possibly as a result of a slight increase in $\nu_{5'6}$. Other couplings did not appear to be different from the room-temperature values except $J_{55'}$ which went to −18.2 Hz.

Discussion

For analysis we consider only the four possible conformations shown in Figure 3 (and their mirror images) for each of the compounds. Nevertheless, boat conformations are not thought to lie at an energy minimum for cyclohexene compounds[3] and are unlikely possibilities for ground-state conformations. We assume that each compound exists almost exclusively in a single conformation. The small changes in coupling constants with temperature for the cis isomer justify such an assumption, but we cannot rule out the presence of small amounts of minor conformations for the trans conformation. The consistency of the final analysis suggests that we make only minor errors by assuming there is only a single conformation, however.

We will consider each of the coupling constants for the two compounds in order, using for the analysis the correlations of dihedral-angle effects on long-range couplings which have been worked out by Barfield and co-workers.[7] The main differences in J values for the two compounds occur only for the couplings to the C-2 proton. We will assume then that the conformations of the two compounds are similar except around the C-2 end of the molecule.

Cis Isomer. We note immediately that by the Karplus relation J_{56} and $J_{5'6}$ should be almost equal in conformations **6** and **8**, contrary to observation. Thus, we rule out **6** and **8** and need only differentiate between **5** and **7**. This can be done in terms of the dihedral-angle dependence which has been predicted for homoallylic couplings. The observed value of $J_{25'}$ is close to the predicted maximum[7] for homoallylic couplings, indicating that the dihedral angles between the double bond and the C_2H bond and the C_4–C_5 bond and the $C_{5'}H$ bond are both close to 90°. Such angles can be achieved only in **5**.

The other coupling constants lead to further refinements in the structure of **3**. On a Dreiding model the dihedral angles between C_4H, C_5H, and $C_{5'}H$ would appear to be almost equal, and yet the coupling constants J_{45} and $J_{45'}$ are significantly different. Since a Karplus-type relation should hold,[8] we propose that the ring is flattened, with the axial C-5′ proton being tilted into the ring. Such a distortion helps relieve some of the steric interaction between the axial C-6 proton and the axial C-2 proton. We hesitate to give definite values for the dihedral angles resulting from this distortion but suggest that the dihedral angle between C_4H and $C_{5'}H$ approaches 90° and that between C_4H and C_5H approaches 30°, accounting for the different observed coupling constants.[7] Ring flattening is consistent with J_{45} being greater than $J_{45'}$ and with J_{35} being more negative than $J_{35'}$. Assignment of the C-5′ proton to the axial position is in accord with all of the coupling constants. The dihedral angles involving the double bond which are suggested require J_{23} to be similar to J_{45}, as observed.

Trans Isomer. The analysis of those couplings not involving the C-2 proton is similar to that for the cis isomer. Thus, we rule out conformations **6** and **8** very quickly on the basis of J_{56} and $J_{5'6}$. We can also rule out **7**, because the homoallylic coupling should be large for that conformation, on the order of that seen for the cis isomer. Once again the half-chair **5** appears to be the predominant conformation, although the possible increase in $J_{5'6}$ at −70 °C may indicate the presence of a small amount of **6** at room temperature.

Following arguments similar to those used for the cis isomer, we would expect J_{23} to be close to J_{45} and J_{24} to be close to J_{35}, as is the case. We also observe that if both **3** and **4** exist in conformation **5**, $J_{25'}$ of **3** should be close to $J_{25'}$ of **4**, as we do find. We also find J_{23} of **3** to be less than J_{23} of **4**, as it should be.

Chemical Shifts. In many respects chemical shifts are not as useful for conformational analysis as are coupling constants. The differences in chemical shifts between **3** and **4** are, nevertheless, consistent with conformation **5**. The largest differences (greater than 0.15 ppm) are for the C-2 and C-6 protons. The difference for the C-2 site is understandable since this is the position where the change in stereochemistry occurs. We note, though, that the axial proton in the cis isomer (**3**) absorbs at higher frequency than does the equatorial proton in the trans isomer (**4**). This order is opposite that usually seen for cyclohexane derivatives. The shielding effects of the double bond and the C–S bond undoubtedly play a role here. Indeed, a reversed order of chemical shifts has also been observed

(7) (a) M. Barfield and B. Chakrabarti, *Chem. Rev.*, **69**, 757 (1969); (b) M. Barfield and S. Sternhell, *J. Am. Chem. Soc.*, **94**, 1905 (1972); (c) M. Barfield, A. M. Dean, C. J. Fallick, R. J. Spear, S. Sternhell, and P. W. Westerman, *ibid.*, **97**, 1482 (1975).

(8) S. Sternhell, *Q. Rev., Chem. Soc.*, **23**, 236 (1969).

(9) J. S. A. Brunskill, A. De, and D. L. Ewing, *J. Chem. Soc., Perkin Trans. 1*, 629 (1978).

for saturated six-membered-ring heterocycles containing sulfur.[10]

The C-6 proton is located directly in front of the phenyl ring in the trans compound and thus should be shielded by it. In the cis isomer the phenyl ring at the C-2 position is placed further away. Thus it is quite reasonable for the C-6 proton of **4** to absorb at considerably lower frequency than the C-6 proton of **3**.

Conclusions

Our evidence is consistent with the major conformation for each isomer being the half-chair **5**. Of course, there may be small amounts of the minor conformation **6** in equilibrium with **5**, especially for the trans isomer (**4**). We do not feel, however, that an accurate estimate of the equilibrium constants based on the Karplus relations is reasonable at this time. Our data indicate that half-chair conformations rather than boat conformations are most probable for other 4,5-dihydro-2*H*-thiopyrans.

We may partially explain why conformation **5** is favored for the trans compound (**4**) in terms of the $A^{(1,2)}$ effect.[11] For conformation **6** there would be an unfavorable interaction between the phenyl group at position 2 and the double bond proton on C-3 which is removed in conformation **5**. In both conformations there is an unfavorable C-1, C-3 interaction of a phenyl group and a proton across the ring. For the cis compound (**3**) the unfavorable $A^{(1,2)}$ interaction between the C-2 phenyl and the C-3 proton in **5** is counterbalanced by the C-1, C-3 interaction between the phenyl groups which would exist in **7**.

Our data indicate that one cannot invoke a boat conformation to predict a higher stability for the trans isomer (**4**) than for the cis isomer (**3**). The relative stability of the two compounds may not even be an accurate indicator for the relative stabilities of the transition states involved in the reaction of **1**. Direct chemical equilibration of **3** and **4** would be interesting, but no reaction occurred with sodium methoxide in refluxing methanol even after 3 days.

Registry No. **3**, 67139-94-0; **4**, 67139-93-9.

(10) S. A. Khan, J. B. Lambert, O. Hernandez, and F. A. Carey, *J. Am. Chem. Soc.*, **97**, 1468 (1975); J. B. Lambert and J. E. Goldstein, *ibid.*, **99**, 5689 (1977).
(11) F. Johnson, *Chem. Rev.*, **68**, 375 (1968).

Specific and Selective Site Reactions in Alkanoate Derivatives. 1. Factors Affecting ω-1 Chlorinations by *N*-Chloroamines[1]

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Received October 13, 1978

Minisci et al.[3] reported the first *intermolecular* variation of the Hoffman–Loeffler–Freytag (HLF) reaction for chlorination of methyl esters of short-chain fatty acids (C_4–C_7) with *N*-chlorodialkylamines. Mainly monochlorinated esters were formed which were functionalized preferentially at the penultimate (ω-1) position[3] (72–92%). These results were interpreted on the basis of a charge repulsion between the amino cation radical generated in the presence of a catalyst and the protonated carboxylic acid group of the substrate as shown in eq 1.[4] Subsequent

$$CH_3CH_2(CH_2)_xC(=\overset{+}{O}H)OR' + R_2\overset{+}{N}H\cdot \rightarrow CH_3\dot{C}H(CH_2)_xC(=\overset{+}{O}H)OR' + R_2\overset{+}{N}H_2 \quad (1)$$

investigations have determined the kinetics of the reaction,[5] enlarged the scope of the substrates derivatized,[6] and examined the effect of medium acidity[4-6] and the steric structure of the *N*-chloroamines[7,8] on the reaction's selectivity. In view of the need in fatty acid chemistry for reactions that permit selective targeting of substituents in saturated chains, we have chosen the intermolecular HLF chlorinations for a systematic examination of its parameters and a determination of its utility when applied to longer chain fatty acids.

Table I. Variation of Substrate Chain Length

substrate[a]	% convrsn[b]	% selectivity for end positions ω	ω-1	ω-2
hexanoate	98	15	82	3
octanoate	90	7	73	15
decanoate	80	4	55	20
dodecanoate	70	3	43	16
tetradecanoate	65	3	27	11
hexadecanoate	55	2	20	8
octadecanoate	40	1	14	5

[a] Methyl esters, 2 M in H_2SO_4 (97%), 1:1 amine/ester, 10% Fe^{2+}. [b] Determined by GLC.

Results and Discussion

We chose methyl decanoate as the model chain for study since ω-1 selectivity was appreciable for this chain length and all of the isomeric chloro products were fully resolvable by capillary GLC. In some instances, other acids, amides, and esters were employed to derive additional details. The factors evaluated were the medium acidity,[9] the ratio of *N*-haloamine to substrate,[9] the initiator concentration,[9] the substrate concentration,[10] the functionality of the substrate,[10] chain length, and *N*-chloroamine structure.

Our results on the first three factors above generally agree with those of previous investigators.[9] However, the substrate concentration, a factor not examined by others, is a crucial parameter, since we found that it affects conversion,[10] selectivity,[10] and the nature of the product. In fact, the nature of the product is altered at low substrate concentrations; for example, in the chlorination of methyl octanoate (1 M), the resultant chloro products isomerize by migration of chlorine, leading to subsequent formation of γ- and δ-lactones. These lactones have not previously

(1) Presented in part at the 11th Middle Atlantic Regional Meeting of the American Chemical Society, April, 1977.
(2) Agricultural Research, Science and Education Administration, U.S. Department of Agriculture.
(3) F. Minisci, R. Galli, A. Galli, and R. Bernardi, *Tetrahedron Lett.*, 2207 (1967).
(4) F. Minisci, *Synthesis*, 1 (1973).
(5) J. Spanswick and K. V. Ingold, *Can. J. Chem.*, **48**, 5461 (1970).
(6) N. C. Deno, W. E. Billups, R. Fishbein, C. Pierson, R. Whalen, and J. C. Wyckoff, *J. Am. Chem. Soc.*, **93**, 438 (1971).
(7) R. Bernardi, R. Galli, and F. Minisci, *J. Chem. Soc. B*, 324 (1968).
(8) N. C. Deno, R. Fishbein, and J. Wyckoff, *J. Am. Chem. Soc.*, **93**, 2065 (1971).
(9) Data for medium acidity, ratio of *N*-haloamines to substrate, and initiator concentration are available as supplementary material in Table III.
(10) Data for the substrate concentrations and end-group functionalities are available as supplementary material in Table IV.

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