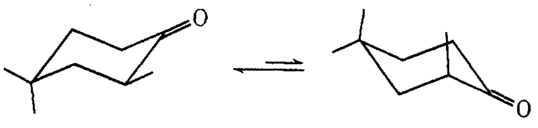
give rise to the trans alcohol,[1,2] a very simple experiment is possible that clarifies the origin of the cis alcohol. 2,4,4-Trimethylcyclohexanone (4) serves as a model for conforma-



4e 4a

tion **1e** of 2-methylcyclohexanone, conformation **4a** being virtually forbidden by virtue of the 1,3-diaxial interaction of the methyl groups. Thus the stereochemical product ratio from reduction of **4** represents to a good approximation that from the *equatorial conformation of 2-methylcyclohexanone* (**1e**), and a deviation from this of the observed product ratio of 2-methylcyclohexanone (**1**) is a measure of the contribution of the axial conformation (**1a**).

2,4,4-Trimethylcyclohexanone[3] is obtainable by ketone transposition of isophorone,[4,5] the penultimate intermediate providing an authentic sample of *trans*-2,4,4-trimethylcyclohexanol. Reduction of 2-methylcyclohexanone and 2,4,4-trimethylcyclohexanone under identical conditions by sodium borohydride gave 31 and 18%, respectively, of the cis isomer.

Regarding the rate of formation of the trans alcohol from 2-methylcyclohexanone as a single term E_A (that from conformation **1e**), but the rate of formation of the cis alcohol as the sum of two terms E_E and A_A arising from the conformations with equatorial and axial methyl groups respectively, the stereochemical product ratio (cis:trans) can be written as

$$(A_A + E_E)/E_A = 31.69$$

Similarly, for reduction of 2,4,4-trimethylcyclohexanone[6]

$$E_E/E_A = 18/82$$

From these equations it follows that $A_A = 1.05E_E$ or, expressing A_A and E_E as percentages of the total reaction leading to *cis*-2-methylcyclohexanol, 51% of this product arises from axial attack on **1a** while 49% of the product is derived by equatorial attack on the more stable conformation **1e.** This result is in sharp contrast with formation of *trans*-2-methylcyclohexanol, which is derived almost exclusively from **1e.**[1]

Conclusions

While some doubt must exist on the exactitude of the above figures (see ref 6), it appears that the *less* stable conformation of 2-alkylcyclohexanones plays at least a substantial role in the reduction to the cis alcohol. Any rationalization of stereochemical product ratio arising from reduction of these ketones should be consistent with this fact.

Experimental Section

2,4,4-Trimethylcyclohexanone (4) was prepared by oxidation[5] of *trans*-2,4,4-trimethylcyclohexanol, which was obtained by reduction and hydroboration of isophorone:[4] bp 191° [lit.[3] bp 191°]; $n^{21}D$ 1.4485 (lit. $n^{20}D$ 1.4493[3]); 2,4-dinitrophenylhydrazone mp 149–150° (lit.[9] mp 151.5° [2]). Ir and NMR spectra were in accord with published data.[9]

Reduction Procedures. Reductions were carried to completion in 2-propanol at 25° with a twofold molar excess of sodium borohydride as previously described.[1,10] GLC analyses were performed both on a Perkin-Elmer 990 gas chromatograph using a 50-ft S.C.O.T. TCEP column and on a Hewlett-Packard F & M Scientific 402 high efficiency gas chromatograph using a dual-packed column of Carbowax and TCEP, which gave base line separation of diastereomeric alcohols and ketone.[11] Both chromatographs were attached to an Infotronics CRS-208 electronic integrator for peak area determination. Reductions were performed in quadruplicate, and product ratios, which were determined both mechanically and electronically, were found to be reproducible within ±1%.

Registry No.—**1,** 583-60-8; **2,** 7443-52-9; **3,** 7443-70-1; **4,** 2230-70-8; 4 2,4-dinitrophenylhydrazone, 2522-10-3; *trans*-2,4,4-trimethylcyclohexanol, 2518-25-4; sodium borohydride, 16940-66-2.

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Effects of α Substitution on the Rate of Chloromercuriolactonization of Esters of γ,δ-Unsaturated Acids[1]

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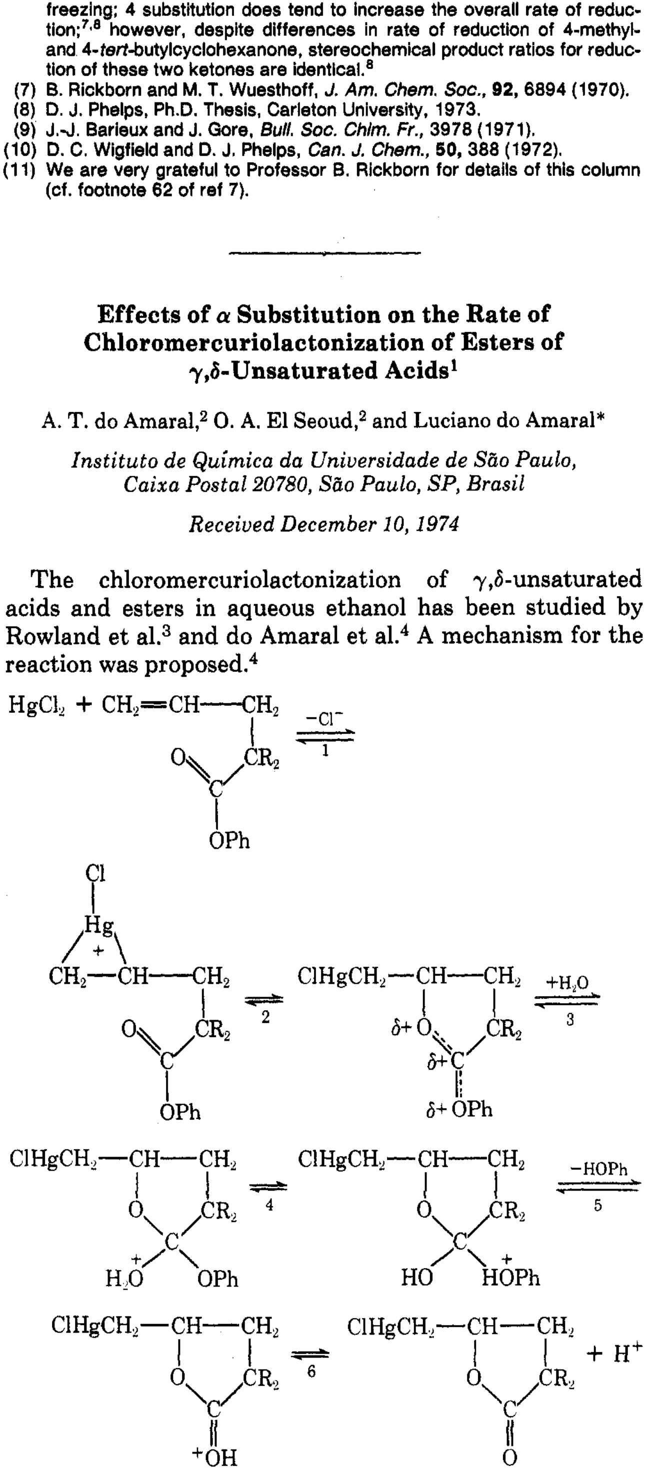
The chloromercuriolactonization of γ,δ-unsaturated acids and esters in aqueous ethanol has been studied by Rowland et al.[3] and do Amaral et al.[4] A mechanism for the reaction was proposed.[4]



Recently do Amaral and Melo studied the effect caused by substituents in the α position of the γ,δ-unsaturated acids on the rate of iodolactonization.[5]

In the present work, a kinetic investigation was undertaken in order to obtain rate information pertinent to the chloromercuriolactonization of esters of γ,δ-unsaturated acids referring specifically to effects caused by substituents on the α position of the esters.

Experimental Section

Materials. 4-Pentenoic acid was obtained from the Chemical Procurement Laboratories; 2-phenyl-2-pentenoic acid and 2,2-diphenyl-4-pentenoic acid were synthesized according to known procedures.[4] Phenyl allylacetate (I), phenyl allylphenylacetate (II), and phenyl allyldiphenylacetate (III) were prepared according to known procedures.[4] All other chemicals were reagent grade and were used without further purification.

Product Analysis. The products of the reaction of the esters with mercuric chloride were prepared according to known procedures,[4] and identified as δ-chloromercuri-γ-lactones:[4] from ester I, mp 81–82° (lit.[3,4] mp 81–82°); from ester II, mp 173° (lit.[4] mp 172.5–173.5°); from ester III, mp 203–204° (lit.[4] mp 203–204°).

Kinetic Measurements were carried out spectrophotometrically with the aid of a Zeiss PMQ II spectrophotometer equipped with a cell holder through which water from a thermostated bath was continuously circulated. The required reaction temperature was measured inside the cell with an accuracy of ±0.05°. Reagent solutions were prepared in 50% aqueous ethanol (v/v) and had the following concentrations: ester solution, 4.0×10^{-4} *M;* mercuric chloride, 3.0×10^{-1} *M;* and sodium perchlorate, 1.0 *M*. Kinetic runs were carried out as follows. All reagents, except the ester solution, were pipetted into a reaction tube, mixed, and left in the water bath for 30 min for thermal equilibration. An ionic strength of 0.10 was obtained by addition of calculated volumes of sodium perchlorate solution. At zero time, a measured quantity of the ester solution was added to the mixture, which was then shaken and transferred rapidly to the reaction cell. The reaction kinetics were monitored by following the appearance of the liberated phenol at the appropriate wavelength until a constant reading was reached. In all cases a sufficient excess of mercuric chloride was used to ensure pseudo-first-order kinetic behavior. Observed first-order rate constants, k_{obsd}, were evaluated from plots of log ($\text{OD}_\infty - \text{OD}_t$) against time and the expression $k_{\text{obsd}} = 0.693/t_{1/2}$, and expressed in min^{-1}. Second-order rate constants, k_2, were determined by dividing k_{obsd} by the mercuric chloride concentration, and expressed in M^{-1} min^{-1}.

Results and Discussion

Rate measurements have indicated that the reaction of esters of γ,δ-unsaturated acids and mercuric chloride to yield chloromercuriolactones is second order, first order in both ester and mercuric chloride.[4]

Rate constants for the reaction of phenyl allylacetate (I), phenyl allylphenylacetate (II), and phenyl allyldiphenylacetate (III) with mercuric chloride in aqueous ethanol were measured at three temperatures. Results are presented in Table I. From Table I it can be seen that α-phenyl groups increase the rate of the reaction at the three temperatures studied. This increase is more pronounced for ester III than for ester II. This observation is in accordance with the Thorpe–Ingold considerations about the effects exerted by substituents on the ease of ring formation.[6]

Table I
Second-Order Rate Constants Multiplied by 10^3, Expressed in M^{-1} min^{-1}, for the Reaction of Phenyl Allylacetate (I), Phenyl Allylphenylacetate (II), and Phenyl Allyldiphenylacetate (III) with Mercuric Chloride in Ethanol–Water (50% v/v) and Ionic Strength 0.10

Ester	25°	35°	45°
I	1.4	3.6	8.3
II[a]	6.3	15.8	35
III	120	200	350

[a] From ref 4.

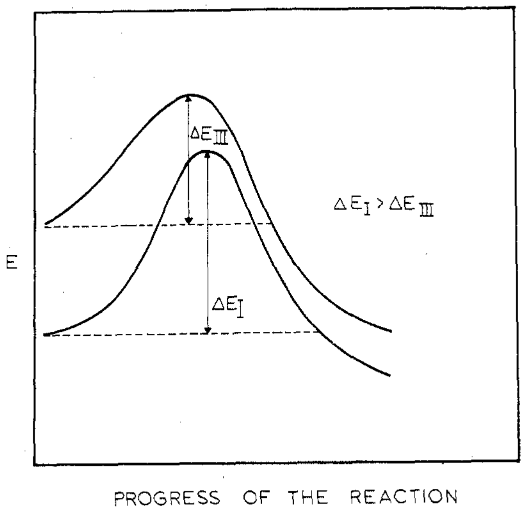


Figure 1. Potential energy profile for step 5 of the reaction path for the reactions of phenyl allylacetate (I) and phenyl allyldiphenylacetate (III) with mercuric chloride.

Arrhenius plots of log k_2 vs $1/T$ for the reaction of esters I, II, and III with mercuric chloride gave reasonably straight lines from which the activation energy, E_a, was determined by least-squares analysis (Table II). The enthalpy of activation, $\Delta S^\ddagger$, was calculated from the formula given by Schaleger and Long.[7] The activation parameters are shown in Table II. One notices from Table II that the values of entropy of activation become more negative with increasing degree of substitution at the α position of the ester substrate, and the values of the enthalpy of activation decrease in the same order.

Table II
Activation Parameters for the Reaction of Esters I, II, and III with Mercuric Chloride in Ethanol–Water (50% v/v) and Ionic Strength 0.10

Ester	E_a, kcal mol^{-1}	$\Delta H^\ddagger$, kcal mol^{-1}	$\Delta S^\ddagger$, eu	$\Delta G^\ddagger$, kcal mol^{-1}
I	18.0	17.4	−21.9	23.9
II	15.5	14.9	−27.3[a]	23.0[a]
III	10.4	9.8	−38.5	21.3

[a] Calculated from data in ref 4.

These results can be discussed in terms of the effect of the α-phenyl groups on the free energy of activation, $\Delta G^\ddagger$. The polar effect of the α-phenyl groups will be small because they are not directly attached to the carbonyl group. On the basis of a purely polar effect, one would expect a slight decrease in the rate going from ester III to ester I owing to the small electron-attracting properties of the phenyl group relative to hydrogen. We are left, therefore, with the possibility that these groups increase the reaction rate predominantly through a steric effect; that is, the more bulky the groups attached to the α carbon atom, the greater the reaction rate.

We have previously proposed that step 5, in which the phenol departs, is the rate-determining step for chloromercuriolactonization.[4] in the ground state for this reaction the conformational strain that results from the nearly eclipsed groups on the α and central carbon atom is greater in ester III than in ester I. In the transition state, the phenol molecule starts to depart, and the central carbon–oxygen bond begins to acquire more sp^2 character.[8] As a result of this $sp^3 \rightarrow sp^2$ change,[9] bonds will spread out and there will be a relief from the eclipsing strain mentioned above.[10] The magnitude of such relief will depend on its original value in the ground state and is, of course, much greater for ester III than for ester I. In summary, this represents a higher initial energy and a lower energy difference, ΔE_a, between the ground and transition states of ester III than of ester I. Figure 1 illustrates this concept. The reported $\Delta S^\ddagger$ values, assuming constant contributions from the solvent, are also in accordance with the diagram given. $\Delta S^\ddagger$ changes from −38.5 to −21.9 eu in going from ester III to ester I. This means that the transition state of ester III is more ordered in relation to its ground state than in the case of ester I.

The increasing values of ΔE_a (or $\Delta H^\ddagger$) in going from ester III to ester I mean that in the former the transition state is reached earlier, and consequently is less sensitive to temperature variation. This conclusion can also be reached by a consideration of the much greater steric crowding present in the former ester's transitions state (vide supra).

Registry No.—I, 51231-09-5; II, 51231-03-9; III, 51231-12-0; mercuric chloride, 7487-94-7.

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(10) There will also be an angle strain on passing from the 109° of the sp^3 state to the 120° of the sp^2 state. Such strain will work against the sp^3-sp^2 change. Since such changes take place easily in the cyclopentane series, angular strain can be of minor importance as compared to conformational strain.

Reactions of Dichlorine Heptoxide and of Hypohalites with Alkyl Iodides[1]

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Stable aromatic polyvalent iodine compounds[2] are obtained from iodides with oxidizing reagents such as chlorine,[2] peracetic acid,[3] or dinitrogen pentoxide.[4] However, for aliphatic iodides, stable halogen adducts have been reported only with electron-withdrawing substituents such as fluorine[5,6,7] or sulfone.[8,9] Methyl iodide dichloride decomposes at −30° to give methyl chloride,[10] and similar reactions of alkyl iodides with peracetic acid[11] and with chlorine[12] have been studied kinetically at higher temperatures. The preparation of trifluoromethyl perchlorate from trifluoromethyl iodide and chlorine perchlorate has recently been reported.[13] The present work deals with reactions of alkyl iodides with dichlorine heptoxide and with hypohalites.

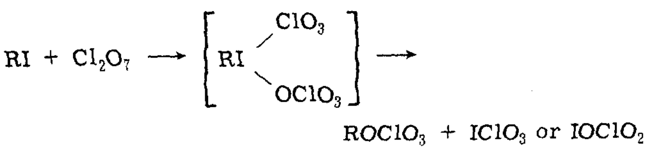
Ethyl iodide reacted rapidly at 0° with dichlorine heptoxide in carbon tetrachloride to give a white precipitate identified as iodine pentoxide. The composition of the soluble products was determined by NMR using a quantitative internal standard, and for a given reactant mixture the reproducibility of yields was 5–10%. With equimolar amounts of the reagents, or with an excess of dichlorine heptoxide, the products soluble in carbon tetrachloride were ethyl perchlorate (63% yield based on ethyl iodide), ethyl acetate (22%), and small amounts of diethyl ether (0–3%). With a 2:1 molar ratio of ethyl iodide to dichlorine heptoxide, the ethyl iodide was consumed completely to give ethyl perchlorate (33%), ethyl acetate (13%), and diethyl ether (21%). When a higher ratio of ethyl iodide to dichlorine heptoxide was used the additional ethyl iodide remained unreacted, and the same product mixture was obtained.

Since the above yields are all based on ethyl iodide consumed, almost the same total quantity of perchlorate is produced from 2 mol of ethyl iodide as from 1 mol. If the products of the experiment using 1 mol of ethyl iodide per mole of Cl_2O_7 are subtracted from the products of the 2-mol experiment, the second mole is seen to yield about 40% diethyl ether, 3% ethyl perchlorate, and 4% ethyl acetate. These results suggest that the equimolar reaction gives a by-product, not detectable by NMR, that converts additional ethyl iodide to ether.

In the reaction of methyl iodide with dichlorine heptoxide similar products were obtained with the exception of the ester, presumably because of the greater oxidation resistance of the methyl group. Equimolar amounts of the reagents gave methyl perchlorate (45%) and dimethyl ether (12%), whereas a 2:1 ratio of methyl iodide to dichlorine heptoxide gave methyl perchlorate (24%) and dimethyl ether (26%). Thus, the first mole of methyl iodide gives predominantly perchlorate, and the second, ether.

In the above experiments the entire amount of ethyl iodide was added rapidly to the dichlorine heptoxide solution. To assess the stability of the implicated ether-forming intermediate, a series of experiments was carried out in which equimolar amounts of ethyl iodide and dichlorine heptoxide were reacted, the solutions were filtered, and after varying time intervals, a second mole of ethyl iodide was added. When this time interval was 15 min, 85% of the second mole was consumed; when the interval was 1 hr, 50% was consumed; and when it was 3 hr none of the added ethyl iodide was consumed.

Thus, the initial reaction of ethyl iodide with dichlorine heptoxide gives a compound, not visible by NMR, that reacts further with ethyl iodide at a rate slower than the initial reaction to give ether. Simple stoichiometry for the reaction of molar amounts of ethyl iodide and dichlorine heptoxide to form ethyl perchlorate would give perchloryl iodide or its isomer. Several paths can be envisioned for the



reaction of inorganic intermediates of this type with ethyl iodide. Displacement of iodine, possibly via a trivalent intermediate, could take place as follows. Reaction of these or