On the Mechanism of the Pyrolytic Elimination Reaction of Acetates[1]

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The mechanism generally accepted for the pyrolysis of acetates to alkenes is a one-step gas-phase reaction with a cyclic transition state. The isomer ratios observed in the alkene products are generally inconsistent with the mechanism, but are consistent with a surface-catalyzed reaction. While true gas-phase reactions appear to have been observed in kinetic experiments, we believe that the experimental conditions employed in most cases where isomer ratios in the products have been reported, which are the conditions commonly used for preparative work, result in a surface-catalyzed reaction.

The pyrolysis of a carboxylic ester to yield an alkene and a carboxylic acid has been known for more than 100 years. Other esters, such as xanthates, undergo a similar reaction. These pyrolyses have been of interest for synthetic purposes, and also from a mechanistic point of view. Extensive review articles have been published concerning them.[2,3]

The most common method of pyrolyzing an ester is referred to as the *gas-phase* method. In this method, the ester is added dropwise to a heated glass tube (200–600 °C) and the products and unreacted ester are swept through the tube by a steady stream of an inert gas. The heated tube is often filled with helices or glass wool. While this procedure is the most common one, various modifications are also used. If the ester is a high-boiling compound, the ester may be pyrolyzed in the liquid phase by simply heating below its boiling point.[2] A number of variations of the methods described above are used. For example, a liquid phase pyrolysis can be carried out on a low-boiling ester using a sealed ampule.[4] Gas phase pyrolyses are also conducted in static reactors.

The generally accepted mechanism for these pyrolyses has one step, with a cyclic transition state as shown.[2,3]
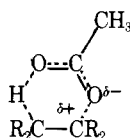
Assuming this transition state to be correct, the correlation of reaction rates with Hammett substituent constants[3,5] indicates that there is a significant amount of charge separation in the breaking of the C–O bond, and none in breaking of the C–H bond. The reaction is generally believed to be concerted, because products that might be produced by a carbonium ion mechanism are not usually found. Thus, free carbonium ions of the kind generated during a solvolysis reaction do not occur here. Since the elimination is predominantly cis and a free carbonium ion intermediate is not formed, it has been assumed that the transition state is cyclic.[2,3]

Sixma[6] found that at lower temperatures the pyrolysis of esters showed first-order kinetics only when the surfaces of the reactor were deactivated. Sixma's product isomer ratios are in good agreement with other data from pyrolyses run over undeactivated surfaces, which seems to indicate that the amount of reaction caused by active surfaces is small compared with the amount of normal reaction.

Smith and co-workers[5,7] have also found that first-order kinetics and no change in rate with change in the surface/volume ratios were obtained only when the surface of their stainless steel reactor was deactivated. They do not indicate that they believe the mechanism of the reaction occurring under those conditions to be completely different from that observed by other workers, who did not deactivate their surfaces, so apparently it is believed that the amount of reaction caused by active surfaces is normally small.

Original Objectives. When this research project was undertaken, it seemed well established that the gas-phase mechanism was in all cases the predominant reaction pathway. It has been known for a long time that more trans alkene than cis alkene is formed when a secondary alcohol is pyrolyzed. As shown in the representative examples in Table I, the experimental cis/trans ratios agree to within experimental error with the ratios predicted by the equation $k_{rel} = \exp(-\Delta H / RT)$, where k_{rel} = cis/trans ratio and $\Delta H^\circ = H^\circ_{cis} - H^\circ_{trans}$, and H° = the heat of formation of the compound. If the gas-phase mechanism were correct, this relationship is consistent with a transition state which looks either like the alkene produced or like the eclipsed ester, because there are approximately the same eclipsed interactions present in the eclipsed ester as there are in the alkene.

It has been proposed[2] that the transition state has a geometry like the staggered, ground-state ester. We do not believe that such a transition state is consistent with the cis/trans ratios in Table I—especially the small cis/trans ratio found for 2,2-dimethyl-3-hexene.

If the gas-phase mechanism were correct, we should be able to use a relationship similar to that found useful in prediction of the cis/trans ratio to predict the 1-alkene/2-alkene ratios found when esters of the type $CH_3CR_1(OCOCH_3)CHR_2R_3$ are pyrolyzed.

The number of experimental enthalpy differences available for alkenes are too few to test the prediction of isomer ratios by this method. Fortunately, experimental enthalpies are not the only ones available. In recent years molecular mechanics calculations have been developed and refined for use in calculating such quantities.[11] These calculations have found use in structural and thermodynamic studies. More recently there calculations have been applied to the study of chemical reactions.[12]

Table II compares some experimental 1-alkene/2-alkene ratios obtained by pyrolysis, corrected for statistical effects (k_1^H/k_2^H) with the corresponding energy differences. As one can readily see, there is no correlation between k_1^H/k_2^H and the relative stabilities of the alkenes. The data were cast in the form

$$RT \ln (k_1^H/k_2^H) = \Delta G_{sub} + C \Delta E$$

where ΔG_{sub} accounts for differences in the relative stability of the alkenes due to changes in the amount of substitution in going from the 1-alkene to the 2-alkene, and C is a proportionality constant to take into account that the transition state is not exactly like the alkene in geometry. A least-squares analysis gave a value of C that was small and negative. The correlation coefficient for this value of C was low. This means that if there was in fact a relationship between the relative energies of the alkenes and the isomer ratios, there is a small tendency for the less stable isomer to be preferred. As expected, an analysis of the data assuming that the geometry of

Table I. The Cis/Trans Ratios of Some Pyrolysis Products

Compd	Exptl[a] cis/trans	Calcd[b] cis/trans
2-Butene	0.54[8]	0.47
2-Pentene	0.67[9]	0.52
2-Hexene	0.49[9]	(0.75) 0.67
3-Hexene	0.47[9]	(0.29) 0.51
2,2-Dimethyl-3-hexene	0.08[9]	0.04

[a] Obtained by direct measurement on pyrolysis products. [b] Calculated from the heats of formation (ref 10).

the transition state is like that of the eclipsed ester gave no better results.

Proposed Mechanism. The data in Table II cannot be explained by the generally accepted mechanism. An alternative mechanism which will account for these facts involves a three-step surface reaction. The steps are as follows. (1) In a rapid equilibrium step the compound is adsorbed with the ester group on the surface. (2) In a second step the ester C–O bond is broken to form a carbonium ion. This carbonium ion is stabilized by the surface, and in so far as possible, the ion adopts a conformation which allows maximum contact between the surface and the ion. In the pyrolysis of at least some esters, this step appears to be reversible. (3) In the rate-determining step, the carbonium ion loses a β hydrogen to form the alkene. These steps may be more or less concerted, and the degree of concertedness may vary with the compound.

Discussion

There is a large amount of data in the literature on the pyrolysis of esters. Any reaction mechanism proposed for the reaction must be consistent with *all* of these data. Tables III–VII are samples of the data available. The observations about the pyrolysis of esters which are consistent with the gas phase mechanism are as follows. (1) As shown in Table V, the loss of a cis β hydrogen is much preferred to the loss of a trans β hydrogen. (2) Rearrangement products are rare. (3) When both the cis and the trans alkene can be formed by the loss of a cis β hydrogen, the cis/trans ratio is about what would be expected on the basis of the relative stabilities of the alkenes. (4) The deuterium isotope effect, shown in Table VII, shows that the β hydrogen is lost in the slow step of the reaction. (5) The more acidic the acid produced, or the more stable the carbonium ion that would result from alkyl–oxygen cleavage, the faster the reaction.[20] The change in rate shown in Table VI and in ref 20 with increased ability of the acid or hydrocarbon portion of the ester to stabilize a charge has been rationalized[3] as being consistent with the gas-phase mechanism
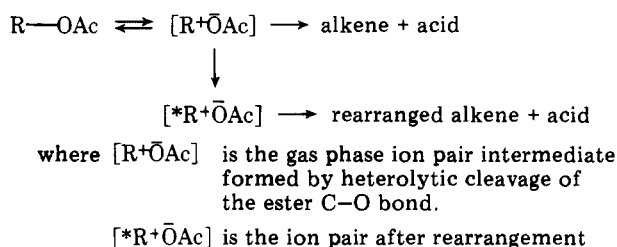
by saying that there is increased charge separation in going from the ester to the transition state.

In addition to the five observations which can be accounted for by the gas-phase mechanism, there are four additional "anomalies" that a reaction mechanism should be able to account for. They are: (6) How are the rearrangement products in Table IV formed? The esters prolyzed in Table IV are different from most esters in that if a carbonium ion forms on the carbon bonded to the ester, it will be stabilized by neighboring group participation, or it is an ion hypothesized to be nonclassical. The gas-phase mechanism does not explain why the presence of neighboring group participation causes rearrangement products to be formed. (7) In the pyrolysis of 3-methyl-2-pentyl[6] acetate the cis/trans ratio is 2/1, while a ratio of 1/1 would be anticipated. If only cis eliminations occur, then *cis*-3-methyl-2-pentene is formed from *threo*-3-methyl-2-pentyl acetate and *trans*-3-methyl-2-pentene is formed from *erythro*-3-methyl-2-pentyl acetate. This means that the 1-alkene/2-alkene ratio for the threo isomer is half that of the erythro isomer. Why is the 1-alkene/2-alkene ratio for two compounds as similar as *erythro*- and *threo*-3-methyl-2-pentyl acetate so different, when there is in general so little difference between the $k_1{}^H/k_2{}^H$ ratios of the quite different compounds in Table II?

(8) The pyrolysis of *trans*-1,2-dimethylcyclopentyl acetate gives almost no exocyclic alkene, while the pyrolysis of *cis*-1,2-dimethylcyclopentyl acetate gives 20–30% exocyclic alkene.[8] Since the trans acetate has ½ the number of cis β ring hydrogens as the cis acetate, one would expect about 50% more of the exocyclic alkene in the pyrolysis of the trans acetate, not 90–100% less.

(9) Why is the $k_1{}^H/k_2{}^H$ ratio for the compounds in Table II so similar—except for 4,4-dimethyl-2-pentyl acetate?

Ion Pair Mechanism. The mechanism described in the introduction is not the only mechanism that has been proposed for the pyrolysis of esters. The ion pair mechanism, shown schematically below, was proposed to account for the

$$R\text{—}OAc \rightleftharpoons [R^+\bar{O}Ac] \longrightarrow alkene + acid$$
$$\downarrow$$
$$[*R^+\bar{O}Ac] \longrightarrow rearranged\ alkene + acid$$

where $[R^+\bar{O}Ac]$ is the gas phase ion pair intermediate formed by heterolytic cleavage of the ester C–O bond.

$[*R^+\bar{O}Ac]$ is the ion pair after rearrangement

charge effects discussed in observation 5 above, and the rearrangement products shown in Table IV.[4,6,25]

Our objections to this mechanism are: (1) It is no better at

Table II. Isomer Ratio Compared with Energy Differences

Registry no.	Alcohol (as acetate)	Exptl 1-alkene/2-alkene ratio	$k_1{}^H/k_2{}^{Ha}$	$RT \ln (k_1{}^H/k_2{}^H)$ $T = 450\ °C$	$\Delta E,{}^b$ kcal/mol	Ref[c]
	2-Butanol	0.94	0.62	−0.43	0.24	6
626-38-0	2-Pentanol	0.92	0.61	−0.70	0.80	
34860-03-2	3-Methyl-2-pentanol	2.0	0.68	−0.55	1.30	
	4-Methyl-2-pentanol	0.85	0.57	−0.81	0.85	14
60388-83-2	4,4-Dimethyl-2-pentanol	0.31	0.21	−2.2	0.80	
	2-Methyl-2-butanol	1.6	0.53	−0.90	0.20	14
34859-98-2	2-Methyl-2-pentanol	2.1	0.69	−0.52	0.52	
34856-44-5	2,4-Dimethyl-2-pentanol	1.6	0.54	−0.90	1.60	
27540-75-6	2,4,4-Trimethyl-2-pentanol	2.85[d]	0.85	−0.15	4.15	

[a] 1-Alkene/2-alkene ratio, adjusted to account for the relative numbers of β hydrogens. [b] Energy of the 2-alkene minus the energy of the 1-alkene, calculated using the force field in ref 13. For the kind of number being calculated here, average errors of the order of 0.4 kcal/mol may be expected. [c] If no reference is given, the results are from the present work. [d] The products isomerized rapidly.

Table III. Pyrolysis Products of Some Esters

Ester	Products and yields			Note
OCCH₃	49%	32%	19%	a
OCCH₃	48%	37%	15%	b
OCCH₃	70%	10%	20%	c
OCCH₃	46%	54%		d
OCCH₃	24%	59%	17%	b
OCCH₃	21%	9%		e
	65%	5%		
OCCH₃	20–30%	40–50%	25–30%	f
OCCH₃	1–4%	5–10%	89–95%	f

a Reference 6. *b* This work. *c* Reference 6. The percentages actually reported in ref 6 are 3-methyl-1-pentene, 70%; cis-3-methyl-2-pentene, 10%; and trans-3-methyl-2-pentene, 20%. We have reversed the percentages for the cis and trans isomers because in the early 1960's the American Petroleum Institute reversed the designation of the isomers. We believe that the old designations were used in ref 6. *d* Reference 14. *e* Reference 9. *f* Reference 8.

explaining observations 7–9 than the generally accepted mechanism is. (2) One would expect many esters to rearrange, not just esters in which the carbonium ion is stabilized by neighboring group participation. (3) The ion pair mechanism does not readily explain why the loss of a cis β hydrogen is much preferred to the loss of a trans β hydrogen. (4) The term ion pair intermediate means that an energy barrier separates the ion pair from the ester and the alkene. There is no reason to believe that an energy barrier would separate the ion pair from the ester. The gas-phase cleavage of a bond is generally taken to be a monatonic function with energy increasing with increased distance between the atoms forming the bond.

Explanation of Experimental Observations by Proposed Mechanism. The number preceding each explanation (below) refers to the correspondingly numbered observation above.

(1) The almost exclusive loss of cis β hydrogens is explained by the fact that it is the surface or the acid counterion lying on the surface that pulls off the hydrogens. The ester is adsorbed on the surface with the ester group down. Only hydrogens cis to the ester will be in contact with the surface.

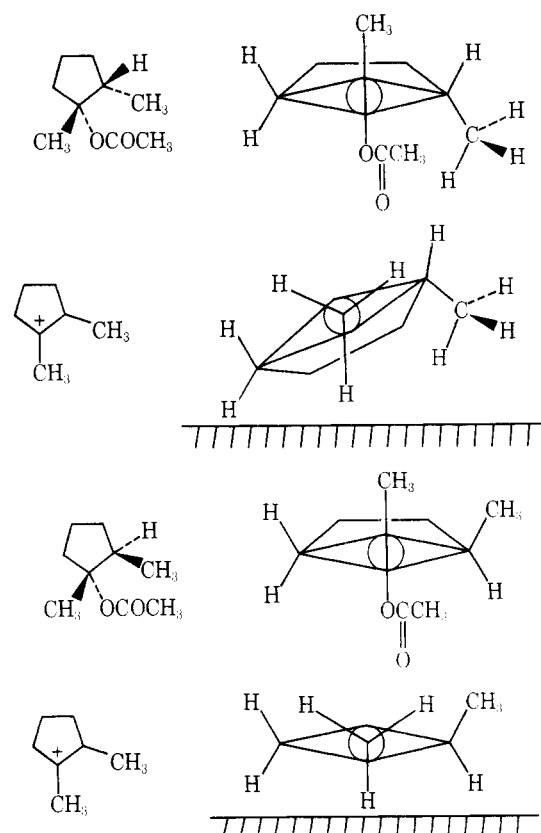(2) Carbonium ions in solution readily rearrange. One might

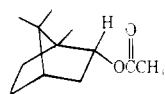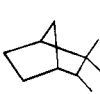**Figure 1.** 1,2-Dimethylcyclopentane carbonium ions adsorbed on a surface.
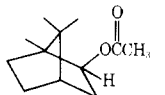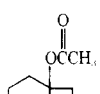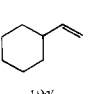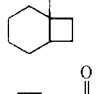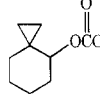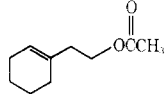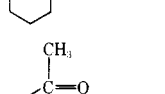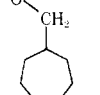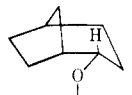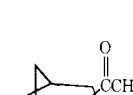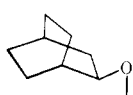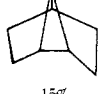
expect that the carbonium ion intermediate here should also readily rearrange. However, a carbonium ion stabilized by interactions with a solid surface is in a quite different environment than the same ion in solution. A solvent is highly mobile and it can stabilize the ion no matter how the charge moves during the course of a rearrangement. An ion on a surface is stabilized by an immobile "active" site and/or by the similarly immobile acid counterion. If the charge on such an ion were to move it would become a "free" and therefore unstabilized ion. This means that an ion on a surface, compared with the same ion in solution, would be very reluctant to rearrange.

(3) Trans alkenes are formed in preference to cis alkenes because it is energetically favored for the ester and carbonium ion to have as close a contact with the surface as possible.[26] Closest contact is possible only if the molecule is in a planar conformation—that is to say, the molecule must have either an anti-coplanar or an eclipsed coplanar conformation. The eclipsed conformation leads to the cis alkene, while the anti conformation leads to the trans alkene. Since the anti conformation is lower in energy than the eclipsed conformation, more of the ester will be absorbed in the anti than in the eclipsed conformation.

(4) We believe that the loss of the β hydrogen is the rate-determining step of the reaction, so the proposed mechanism is consistent with with deuterium isotope effects shown in Table VII.

(5) Our mechanism is consistent with the data in Table VI and related facts,[20] which show that the more acidic the parent acid of the ester, and/or the more stable a carbonium ion formed, the faster the reaction rate. Since the total activation energy is the sum of the energy required to form the carbonium ion plus the activation energy for the removal of the β hydrogen, the more stable the carbonium ion is, the faster the overall reaction will be (other things being equal).

Table IV. Pyrolysis of Some Esters That Give Rearrangement Products

Ester	Products and yields				Temp, °C	Ref
(bicyclic acetate structure)	61%	23%	14%		345	15
(bicyclic acetate structure)	20%	32%	48%		345	15
(spiro acetate structure)	80%	7%	0%	12%	240	16
	9%	50%	21%	19%	480	16
(cyclopropyl acetate structure)	95%	4%	0%	1%	320	16
(cyclohexenyl ethyl acetate structure)	26%	0%	0%	74%	330	16
	14%	0%	0%	85%	440	16
(cycloheptenyl methallyl ester structure) → 350 °C	27%	4%	5%		350	4
	7%	32%	10%	15%		

(6) The rearrangement products in Table IV are produced from carbonium ions that are stabilized by neighboring group participation or by the formation of a 2-norbornyl or cyclopropylcarbinyl cation. Despite the exceptionally rapid skeletal rearrangements of the 2-norbornyl and cyclopropylcarbinyl cations in solution, the origin of the nonclassical carbonium hypothesis, the interactions of the ions with the surface have slowed the rate of skeletal rearrangement sufficiently that even at the elevated temperatures at which the pyrolyses are run, a distinctly nonequilibrium distribution of products is obtained.

Thus we can conclude that the carbonium ion stabilization by the surface is highly effective in reducing the rate of rearrangement, but not 100% so. Only ions with a high propensity for rearrangement manage to do so.

(7) As explained above, the cis/trans ratio in the pyrolysis of 3-methyl-2-pentyl acetate is the result of the 1-alkene/2-alkene ratio of the *threo*-3-methyl-2-pentyl acetate being half that of *erythro*-3-methyl-2-pentyl acetate. This difference is readily explained if one examines the two possible conformations each ester can adopt when it is absorbed on the surface. In conformation A both the erythro and threo isomers have the 3-methyl and the 3-ethyl on the surface; the 3-hydrogen is held off the surface. Conformation A leads to 1-alkene only because the 3 hydrogen is not on the surface. Conformation B of the threo isomer has the 3 ethyl and 3 hydrogen on the surface; the 3 methyl is held off the surface. Conformation B of the erythro isomer has the 3 methyl and 3 hydrogen on the surface; the 3 ethyl is held off the surface. Since it is energetically more favorable to have the larger 3
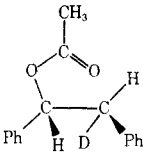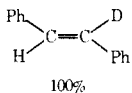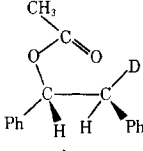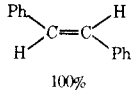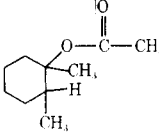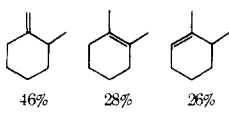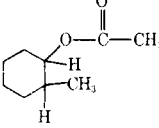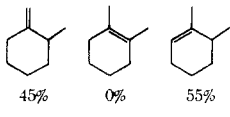
ethyl on the surface than to have the 3 methyl on the surface, conformation B of the erythro is less stable than conformation B of the threo isomer, and the A/B ratio of the threo will be lower as a result. Since conformation B leads to both 1-alkene and 2-alkene, the lower A/B ratio of the threo isomer means its 1-alkene/2-alkene ratio will be lower, in agreement with what is observed.

(8) Table III shows that the pyrolysis of *trans*-1,2-dimethylcyclopentyl acetate gives almost no exocyclic alkene, while the pyrolysis of *cis*-1,2-dimethylcyclopentyl acetate gives 30–35% exocyclic alkene. As shown in Figure 1, when the methyl groups are cis, the carbonium ion has the 1-methyl on the surface and as a result one of its hydrogens can be removed by the surface to form the exocyclic alkene. When the methyls are trans, the 2-methyl is on the surface. This causes the 1-methyl to be held off the surface and as a result the surface is unable to remove a methyl hydrogen and form the exocyclic alkene.

(9) The generally small differences in the $k_1{}^H/k_2{}^H$ ratios in Table II are the result of the fact that generally both the 1-alkene and the 2-alkene can be formed from both of the two planar conformations of the carbonium ion. As a result, any differences in the energies of the two planar conformations will not affect the $k_1{}^H/k_2{}^H$ ratio. Usually the change in steric interactions in going from the carbonium ion to an alkene adsorbed on the surface is small so the change in geometry in going from carbonium ion to alkene generally has no effect on the ratios either.

Esters with *tert*-butyl groups γ to the ester (i.e., 4,4-dimethyl-2-pentyl acetate and 5,5-dimethyl-3-hexyl acetate)

Table V. Preference for Elimination of Cis β Hydrogen

Ester	Products	Ref
erythro	100%	17
threo	100%	17
	46% 28% 26%	8
	45% 0% 55%	8

Table VI. Relative Rates of Pyrolysis of Acetates

Ester	Rel rate	Ref
$C_2H_5OCOCH_3$	1.0	18
$i\text{-}C_3H_7OCOCH_3$	19.0	18
$t\text{-}C_4H_9OCOCH_3$	1170.0	19

Table VII. Deuterium Isotope Effects

Ester	K_H/K_D	Temp, °C	Note
Ethyl-$1,1,2,2$-d_4 acetate	2.0	500	a
Ethyl-$1,1,2,2,2$-d_5 acetate	2.1	400	b
dl-erythro-2-Butyl acetate	1.7	400	c
1-Methylcyclohexyl-$2,2,6,6$-d_4 acetate	1.9	400	d

[a] Reference 22. [b] Reference 23. [c] Reference 21. [d] Reference 24.

are exceptions to the general rule, that the change in the steric energy is small in going from carbonium ion to alkene. In the planar ion there is a very severe steric interaction between the α hydrogen and a γ *tert*-butyl group. When a double bond forms between the ester carbon and a γ *tert*-butyl group (e.g., when $(CH_3)_3CCH=CHR$ rather than $(CH_3)_3CCH_2CH=CHR$ is formed) the angle between the ester carbon and the γ *tert*-butyl group changes from approximately tetrahedral (109.5°) to trigonal (120°). The increase in the bond angle reduces the severity of the interaction between the α hydrogen and the γ *tert*-butyl group. This is the cause of the seemingly anomolous $k_1{}^H/k_2{}^H$ ratio for the pyrolysis of 4,4-dimethyl-2-pentyl acetate, and the reason that the 2-alkene/3-alkene ratio in the pyrolysis of 5,5-dimethyl-3-hexyl acetate is so much less than 1/1. Note that the severity of the interaction between the α hydrogen and the γ *tert*-butyl group is caused by the requirement that the ion be planar. As shown in Table II, the steric energy difference in 4,4-dimethyl-1-pentene and 4,4-dimethyl-2-pentene *after* they have left the surface and are able to adopt the most favorable geometries is no different from similar alkenes in Table II.

True Gas Phase Ester Pyrolysis. We believe that the only conditions which have been demonstrated to give a true gas-phase reaction are those used by Smith[5,7] and by Maccoll.[27] They have shown that when a stainless steel reactor is deactivated by carbonizing the surfaces, and air is excluded from the apparatus, there is not change in rate with change in the surface/volume ratio. Only small amounts of air reactivated the carbonized surface, so we assume that workers who carbonized the surfaces of their apparatus, but did not discuss excluding air from the apparatus, were in fact observing a surface reaction.

Recently Taylor[28] observed that some of the esters he pyrolyzed were undergoing a surface reaction, despite the fact the reactions were first order and that he believed that the remainder of the esters pyrolyzed were true gas-phase reactions. Since the conditions used in his study were almost identical with those used by Smith[5,7] and co-workers (where they observed no change in rate with change in the surface to volume ratio), it is unclear what conditions are necessary to ensure that the reaction takes place in the gas phase. It is

possible that these conditions vary from one ester to another.

It appears that glass might be so active as to be impossible to deactivate. Thies and Shick[4] were able to deactivate their glass apparatus to the extent that the rate decreased by a factor of 100, but they were able to obtain an unrearranged product only when the pyrolysis was conducted in the liquid phase and at a much higher temperature. Sixma[6] obtained first-order kinetics when the glass apparatus was coated with silicone oil. We believe that Sixma was still observing a surface reaction. As discussed above, the 1-alkene/2-alkene ratio observed by Sixma[6] in the pyrolysis of 3-methyl-2-pentyl acetate is consistent with the surface mechanism but not with the cyclic mechanism, and first-order kinetics are not inconsistent with a surface reaction.

The ability of surfaces to catalyze the pyrolysis of esters is probably related to the separation of charge that occurs in going to the transition state. It is unclear to us why, in a transition state located in between an ester and an alkene, the carbon bonded to the ester should show increased positive charge and not a decrease in the positive charge, but it is clear that charge separation requires energy, especially in the gas phase. A polar surface, like glass, would be expected to stabilize the charge separation, and thus decrease the activation energy for the reaction. A carbonized surface is nonpolar and therefore inactive, but after such a surface has reacted with air it becomes polar and catalytically active.

Reactions Similar to Carboxylic Ester Pyrolyses. There are a variety of other thermolytic reactions which also produce alkenes. Among these are the pyrolyses of xanthates, alkyl halides, and vinyl ethers. Each of these reactions is believed to have a unimolecular gas-phsse reaction pathway, and each is considered to be so similar to ester pyrolyses that they have been included with the latter in the same review articles.[2,3] We have not looked in detail at any of these reactions, but, like carboxylic ester pyrolyses, it is known that under some conditions surfaces influence these reactions.[3] Surface catalysis in these reactions is generally believed to result from the surface being a source of free radicals. In the light of the foregoing discussion, surface catalysis by a nonradical mechanism—namely stabilization of charge separation in the transition state—could be important.

Experimental Section

A mixture of the alcohol, acetic anhydride, and pyridine in a 3:5:1 ratio was placed in a flask fitted with a reflux condenser and a drying tube. After the flask was heated on a steam bath overnight, the reaction mixture was washed successively with approximately five times its volume of each of the following solutions: (1) saturated NaCl–NaHCO$_3$ solution, (2) 10% HCl in saturated NaCl solution, and (3) saturated NaCl–NaHCO$_3$ solution. The ester was then dried over molecular sieves for several days and an IR was taken to confirm the conversion of the alcohol to ester.

Pyrolysis Procedure. The ester was dropped onto an electrically heated column packed with Pyrex helecies at a rate of about 1–2 drops every 5 s. The column was heated to 450 ± 5 °C and the column was flushed with N$_2$ at a rate estimated to be 0.5 ml/s. The receiver at the bottom of the column was kept in a dry ice–acetone bath.

Analysis of the Pyrolysis Products. The pyrolysis products were analyzed on a Varian Aerograph Model 700 (commonly known as an Autoprep) equipped with a thermal conductivity detector. To separate the isomers, a 15 or 30 ft × 0.25 in. i.d. column packed with a saturated AgNO$_3$–ethylene glycol solution on Chromosorb W (40–60 mesh) was used. The ratio of absorbent to AgNO$_3$ solution was 2:1. The column temperature was about 35 °C. A flow rate of approximately 60 ml/min of He was generally used. The column decomposed rapidly (1 week) when left at room temperature, and was kept in a freezer when not in use.

The peaks were identified by simultaneous injection into the VPC of a mixture of the pyrolysis product mixture and a sample of the olefin in question. To determine the relative amounts of the isomeric olefins in the mixture, the VPC trace of the product mixture was Xeroxed and the peaks were cut and weighed.

Registry No.—1-Pentene, 109-67-1; *trans*-2-pentene, 646-04-8; *cis*-2-pentene, 627-20-3; 3-methyl-1-pentene, 760-20-3; *trans*-3-methyl-2-pentene, 616-12-6; *cis*-3-methyl-2-pentene, 922-62-3; 4,4-dimethyl-1-pentene, 762-62-9; *trans*-4,4-dimethyl-2-pentene, 690-08-4; *cis*-4,4-dimethyl-2-pentene, 762-63-0; 2-methyl-1-pentene, 763-29-1; 2-methyl-2-pentene, 625-27-4; 2,4-dimethyl-1-pentene, 2213-32-3; 2,4-dimethyl-2-pentene, 625-65-0; 2,4,4-trimethyl-1-pentene, 107-39-1; 2,4,4-trimethyl-2-pentene, 107-40-4.

References and Notes

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Carbamate Analogues of Oligonucleotides

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Some dinucleoside phosphate and trinucleoside diphosphate analogues that possess internucleoside carbamate bonds (–OCONH–) are described. These compounds are prepared in good yields under mild conditions by reaction of a nucleoside 3′-*O*-*p*-nitrophenyl carbonate intermediate with a 5′-aminonucleoside. The internucleoside carbamate linkage is stable and does not hydrolyze in acidic or basic solution or in solutions containing snake venom or spleen phosphodiesterase.

We describe in this paper the synthesis and chemical properties of oligonucleotide analogues containing 3′–5′ carbamate linkges between nucleoside units.[1] These compounds were prepared as models to explore the synthesis and stability of oligonucleotides with such linkages. Our interest in this class of compounds was stimulated by the prospect that the stepwise chemical synthesis of such analogues might be readily achieved and that these unique analogues might have important biochemical properties such as template activity, resistance to enzyme-catalyzed degradation, interferon induction, or phosphodiesterase inhibition. The carbamate linked analogues were particularly interesting since Baker and

co-workers, working with isolated enzyme systems, found evidence for the simulation of phosphate by the *O*-carbamate in a derivative of 6-mercaptopurine.[2] However, these same workers were unable to detect such simulation with several other nucleoside carbamates.[3] Various oligonucleotide analogues containing such linkages as phosphonate,[4] thiophosphate,[5] phosphoramidate,[6] carboxymethyl,[7] and carbonate[8,9] have been reported in the literature and several of these have been found to have interesting biochemical activity.

The general synthetic approach for the formation of the carbamate linkage was modeled after the active ester method of polypeptide synthesis and Baker's method of nucleoside