Effect of Pressure on Two Cyclodextrin-Promoted Ester Hydrolyses

W. J. le Noble,*[1a] S. Srivastava,[1a] R. Breslow,*[1b] and G. Trainor[1b]

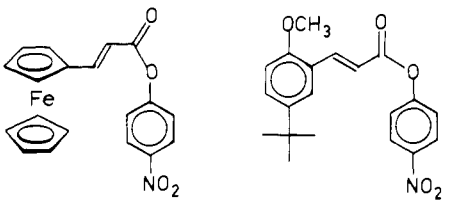
Contribution from the Chemistry Departments, State University of New York, Stony Brook, New York 11794, and Columbia University, New York, New York 10027.
Received September 21, 1982

Abstract: Measurements are reported of the effect of pressure on the rate of transacylation of *p*-nitrophenyl (*E*)-β-ferrocenylacrylate (**1**) and of *p*-nitrophenyl 2-methoxy-5-*tert*-butyl-(*E*)-cinnamate (**2**) in 50/50 aqueous ethylene glycol at 30 °C and at a controlled pH in the presence of β-cyclodextrin (**3**). For **1**, the observed rate constants of the reactions with cyclodextrin and with solvent at several pressures up to 180 MPa are analyzed by means of Eadie plots to give the volume change involved in the complexation step and the activation volume of the rate-controlling step (the latter is corrected for the pressure-induced pH changes): they are −15 and +1.0 cm^3/mol, respectively. The activation volume for the simple solvolysis reaction is −12.8 cm^3/mol. The results with cyclodextrin suggest that the substrate fits tightly in the complex, but that partial withdrawal is required to bring about release of *p*-nitrophenoxide. Thus, **1** is not yet the best possible substrate for **3** as an enzyme model. For **2**, an overall activation volume of about +20 cm^3/mol is found at the highest concentrations of **3**. The ln *k* vs. pressure curves show a minimum below 100 MPa, indicating that the catalysis of **3** can virtually be squeezed out of operation. While it is thus clear that the fit for **2** is much poorer than for **1**, solubility limitations ruled out any attempt at further dissection by means of Eadie plots. The insights derived from the volume profiles are consistent with the conclusions reached earlier from the analysis of rates and models.

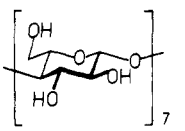
This article describes the confluence of two lines of research that have been pursued in our laboratories for several years. In one of these, we have explored the limits of the ability of cyclodextrins to serve as enzyme models. Thus, we have found that in those instances in which space-filling models suggest the exceptionally precise fitting of the transition state for reaction of a substrate ester molecule in the cavity of a cyclodextrin, its presence can lead to impressive accelerations in the rate of transacylation of the ester. Rate enhancements at saturation close to 10^8 times those of simple solvolysis reactions under the same conditions have been observed;[2] these exceed by many orders of magnitude the rate effects that cyclodextrins have long been known to have on many organic reactions conducted in aqueous solutions.[3]

In other work, we have learned that fruitful insights concerning chemical reactions can be gained from knowledge of their volume profiles.[4] Volume changes from the initial to transition and final states can be deduced from pressure effects on the rate and equilibrium constants, respectively; alternatively, densitometric and dilatometric measurements have also played a role. These changes in volume are a reflection of changes in bonding and in solvation; thus, the volume profile of a reaction is often found to be helpful in illuminating its structure profile as well.

These summaries suggest that a study of the effect of pressure on reactions subject to cyclodextrin promotion might provide insights otherwise not easily available. It appeared that reactions involving the interactions of such large host molecules as cyclodextrins and appropriate guest species might well be characterized by large volume effects and, accordingly, by unusual pressure sensitivities. We report here such a study for the transacylation of two esters, *p*-nitrophenyl (*E*)-β-ferrocenylacrylate (**1**) and *p*-nitrophenyl 2-methoxy-5-*tert*-butyl-(*E*)-cinnamate (**2**), in the presence of β-cyclodextrin (**3**). We take note in passing that a few early reports involving the combined uses of cyclodextrins and high pressure have already appeared;[5] although these studies have turned up information of interest, they did not in any way overlap with the work reported here.



1 **2**



3

Results and Discussion

The basic approach consisted, as in the previous work at atmospheric pressure,[6] of measuring the pseudo-first-order hydrolysis rate constant (k_{obsd}) for *p*-nitrophenoxide ion formation as a function of cyclodextrin concentration. The results, when viewed together with the solvolysis rate of uncomplexed substrate (k_{un}) in the context of an Eadie plot,[7] yield an intercept and slope that in turn reveal the rate constant (k_{com}) of the controlling step (i.e.,

(1) (a) At Stony Brook; (b) at Columbia.

(2) For a recent example, see: Trainor, G. L.; Breslow, R. *J. Am. Chem. Soc.* **1981**, *103*, 154.

(3) For recent reviews, see: Bender, M. L.; Komiyama, M. "Cyclodextrin Chemistry"; Springer-Verlag: New York, 1977. Saenger, W. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 344. Tabushi, I. *Acc. Chem. Res.* **1982**, *15*, 66. Breslow, R. *Science (Washington, D.C.)* **1982**, *218*, 532.

(4) For recent reviews, see: Isaacs, N. S. "Liquid Phase High Pressure Chemistry"; Wiley: New York, 1981. Kelm, H. "High Pressure Chemistry"; D. Reidel: Hingham, MA, 1978.

(5) (a) Torgerson, P. M.; Drickamer, H. G.; Weber, G. *Biochemistry* **1979**, *18*, 3079, this paper reports pressure effects on the emission spectra of two fluorescent probes in the presence of poly-β-cyclodextrin. (b) Turro, N. J.; Okubo, T.; Weed, G. C. *Photochem. Photobiol.* **1982**, *35*, 325, this article reports enhanced intramolecular excimer formation of 1,3-bichromophoric propanes by cyclodextrin complexation under pressure. (c) Taniguchi, Y.; Makimoto, S.; Suzuki, K. *J. Phys. Chem.* **1981**, *85*, 3469, these authors report the effect of pressure on the rate of base-promoted hydrolysis of α-naphthyl and *p*-nitrophenyl acetate in the presence of α-, β-, and γ-cyclodextrin. The *alcohol* moiety is complexed in these reactions. (d) Hoiland, H; Hald, L. H.; Kwammen, O. J. *J. Solution Chem.* **1981**, *10*, 775, the authors report that the volume changes observed upon complexation of several small anions in cyclodextrins suggest that they are not dehydrated at any stage. (e) Turro, N. J.; Okubo, T.; Chung, C. *J. Am. Chem. Soc.* **1982**, *104*, 3954, in this paper, the authors describe the reconnaissance of cyclodextrin cavities by complexation of a fluorescent probe under pressure.

(6) Breslow, R.; Czarniecki, M. F.; Emert, J.; Hamaguchi, H. *J. Am. Chem. Soc.* **1980**, *102*, 762.

(7) Eadie, G. S. *J. Biochem.* **1942**, *146*, 85.

0002-7863/83/1505-2745$01.50/0

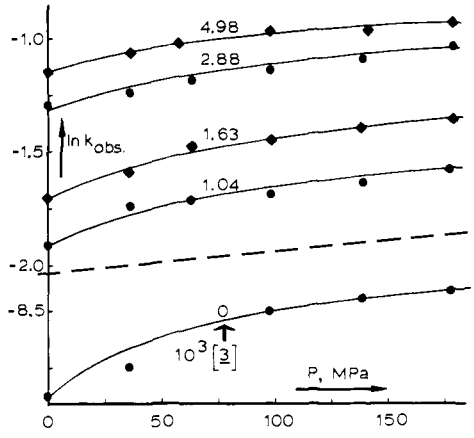


Figure 1. Effect of pressure on both k_{obsd} and k_{un} for **1**. Some of the data have been omitted for clarity.

that of the complexed ester itself) and the complex dissociation equilibrium constant (K_d), respectively.

Initial scouting experiments turned up the problem that the aqueous medium employed earlier could not be used under high pressure since Me_2SO component crystallized even well below 100 MPa (≈1000 atm). A 50/50 (v/v) mixture of water and ethylene glycol was subsequently used. Its quality as a medium for enhancement of hydrolysis is less outstanding than that of aqueous Me_2SO: the acceleration at atmospheric pressure was found to be only about 3500 as opposed to 360000 in the latter.[8] However, as a medium for our study of the volume profile, the mixture was satisfactory.

Knowledge of the pH of the system is obviously required to measure the rate constants. Two questions arise: one of these concerns the meaning and measurement of pH in this mixed solvent system, and the other is related to the effect of pressure on pH. Concerning the first of these questions, we observed that dissolution of identical quantities of the phosphate buffer salt in equal volumes of water and 50/50 aqueous ethylene glycol gives rise to solutions whose pH readings differ by 1.20 (with water giving the higher one). This statement applies to the entire "pH" range applied in this work. Thus, the subsequent addition of identical quantities of base to both solutions produced the same increases in pH reading. We conclude that whatever the significance of the reading in the mixed solvent system, relative pH readings in this medium lead to the correct ratios of H^+ concentration—our only concern here. The effect of pressure on the pH of the phosphate buffer used can be calculated from the first two ionization volumes of phosphoric acid or from the partial molar volumes of mono- and diphosphate salts, but none of this information is available for the mixed solvent used. We therefore proceeded by measuring the densities of solutions of potassium hydroxide, monophosphate, and diphosphate. The results, treated as described in the experimental section, gave −1.8 cm³/mol as the reaction volume for the process

$$HPO_4^{2-} + H_2O \rightleftarrows H_2PO_4^- OH^- \qquad (1)$$

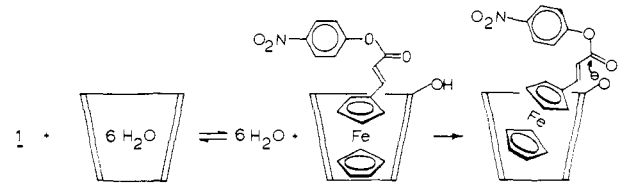
This small value means that the pressure effect on the pH of the system will require only a minor correction on the rate results discussed below.

A casual inspection of the overall rates observed under pressure reveals that there is no special or unusual gross effect; that is, both the cyclodextrin reaction at low pH and the solvolysis reaction in extremely basic medium are accelerated to about the same extent (see Figure 1). However, a more detailed insight emerges when the data are analyzed by means of Eadie plots at various pressures to give, separately, the dissociation constant K_D and the rate of the transacylation step at saturation. Good correlations were obtained; the results are given in Table I.

Table I. Effect of Pressure on K_d and k_{com} of **1**

P, MPa	k_{com}, s⁻¹	K_d, mM	r
0.1	0.47	2.33	0.97
36.1	0.46	1.71	0.98
63.9	0.48	1.71	0.98
98.6	0.49	1.55	0.99
140.0	0.51	1.69	0.99
180.0	0.52	1.61	0.98

Scheme I



The prequilibrium volume change for complexing of **1** with **3** is −14.7 ± 1 cm³/mol. This is a remarkable result. Thus, the capacity of the cyclodextrin cavity is of the order of 125 cm³/mol, enough to hold six or seven water molecules. The fact that replacing them by a single ferrocene-containing molecule leads to a considerable *reduction* of the overall volume is testimony to the tight fit of this substance in the cavity: volume changes in aqueous media upon complexation of neutral molecules are known in only a few cases,[5a,b] but in those instances they vary from zero to extremely positive.[5] Given the precise fit, the immediate reason for the volume decrease is presumably that water in the cavity is less extensively hydrogen bonded than in the bulk solvent. Since H-bond formation is generally credited with a volume reduction of 4 cm³/mol,[9] three or four such bonds are evidently broken when each cyclodextrin molecule is filled.

The activation volume of the solvolysis reaction was found to be −12.8 ± 1 cm³/mol. This is in good accord with other reports of base-mediated ester hydrolysis under pressure in mixed solvents;[10] these reports have been interpreted as evidence for the volume-reducing effect of the newly forming C–O bond in the tetrahedral intermediate. By contrast, the Eadie plots show that the complex in the cyclodextrin reaction releases *p*-nitrophenoxide with an activation volume (corrected for the pH effect described earlier) of +1.0 cm³/mol. Since the acylation mechanisms are surely the same, there must now be another factor operating on the complex that is associated with expansion. We believe that the reaction with the peripheral hydroxyls of **3** requires a partial withdrawal of the ferrocene moiety from the cavity. Since this is part of an activation rather than an equilibrium step, it is not necessary that water reenter the cavity as the ferrocene "leans out". The evacuation of the cavity, based on the previously mentioned capacity of 125 cm³/mol, amounts to about 10% of that space. The argument is graphically demonstrated in Scheme I. It is another way of saying that the transition state for transacylation is less highly bound than the initial state. Evidently, the need to form the new bond imposes an additional constraint upon the structure of the complex. This conclusion supports the idea[2] that further rate enhancements may yet be possible, if substrates can be designed in which the transition states are bound *more* strongly than the initial states.

The second example, involving a similar study with **2**, was undertaken with the objective of supporting the conclusion reached for **1**; it had already been shown[6] that the transition state for reaction of **2** with β-cyclodextrin induced partial withdrawal from the cavity. However, an unexpected result was encountered: at low pressures, the overall reaction was retarded by low pressures,

(8) This type of solvent effect had been noticed before; see: Siegel, B.; Breslow, R. *J. Am. Chem. Soc.* **1975**, *97*, 6869. We have since observed that Me_2SO is unusually sensitive to solvent sorting by Menger's probe (F. M. Menger and T. D. Singh, *J. Org. Chem.*, **1980**, *45*, 183; W. J. le Noble and E. Gebicka, unpublished work).

(9) Fishman, E.; Drickamer, H. G. *J. Chem. Phys.*, **1956**, *24*, 548. For an extensive listing of volume changes in chemical reactions and for references to earlier surveys, see: Asano, T.; le Noble, W. J. *Chem. Rev.* **1978**, *78*, 407.

(10) Tonnet, M. L.; Whalley, E. *Can. J. Chem.* **1975**, *53*, 3414.

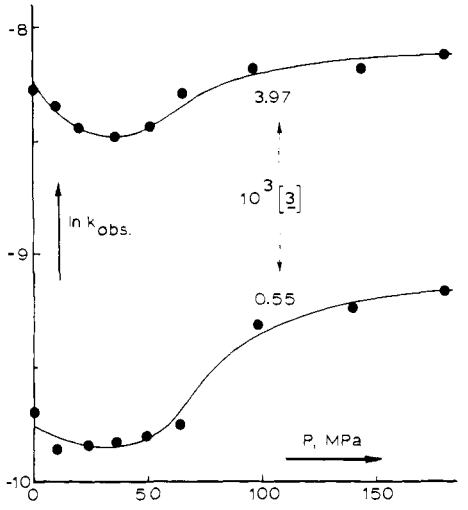


Figure 2. Raw data for the rate of transacylation of **2** in the presence of **3** (intermediate concentrations omitted for clarity).

as expected if such withdrawal occurs, but the deceleration levels off, and the rate reaches a minimum and is enhanced again at higher pressures. This same minimum was observed at all concentrations of **3** used; it comes at the lowest pressures at low concentration of **3** and gradually moves to higher pressure with increasing amounts of **3** present (see Figure 2). The possible occurrence of such curves was foreseen about 15 years ago,[11] but it has not been encountered clearly until now. It means that the reaction has two pathways available: a fast one that is retarded by pressure, and a slow one that is accelerated by it and eventually overtakes the fast path. In the present case, these two branches are obviously the reaction with cyclodextrin and simple solvolysis reactions, respectively. This observation provides an unusual bit of support for the proposition often heard at high-pressure congresses to the effect that one can have much more confidence in activation volumes than in the other activation parameters. Indeed, we can recall no instance in which the activation energy and entropy of a reaction alone revealed the operation of competing mechanisms before it was known on other grounds.

At atmospheric pressure and high concentration of **3**, the cyclodextrin reaction predominates and one can essentially ignore the solvolysis contribution; thus, at 4 mM **3**, $\Delta V^{\ddagger} = +21$ cm^3/mol. We were not able to dissect our data into equilibrium and activation parts. Even at modest pressures, the solvolysis fraction becomes substantial enough that it needs to be determined with good precision in order to help produce convincingly linear Eadie plots. This goal proved to be unattainable: in the absence of **3**, the solubility of ester **2** is far too low to permit rate measurements, as mixing of the stock solutions led to immediate turbidity.[12] At least 0.4 mM **3** was required to keep the solution homogeneous, and at that concentration the minimum is already clearly observable.

While we are thus prevented from obtaining an accurate reading of the rate of the solvolysis reaction, the similarity of the structures of **1** and **2** and that of the high-pressure branch of the overall reaction of **2** with that of the solvolysis reaction of **1** leave little doubt that the activation volume $\Delta V^{\ddagger}_{un}$ for **2** at atmospheric pressure must also be about −10 to −15 cm^3/mol. The main difference between **1** and **2** is clearly in the cyclodextrin reactions. The transition state for reaction of ester **2** evidently does not fit as well in the cyclodextrin cavity; whether the ester itself fits much better in the equilibrium complex remains problematic.

We add a final word regarding the value of the information uncovered. Pressure has been used as a variable in a number of enzyme mechanism studies, and volume changes have been reported in some cases.[13] To date, however, no firm conclusions have been drawn from this knowledge. The difficulty has been that with molecules that large, relatively innocent conformational changes could have large volume effects, for example, by exposing a more hydrophilic surface to the medium. Thus, the *dissociation* of *E. coli* ribosomes is known[14] to be *promoted* by pressure. This floppiness could mask the volume profile, which makes it likely that high-pressure studies with real enzymes will remain of marginal value for some time to come. On the other hand, the use of a rigid model such as **3** permits a much more credible connection to be made between experimental variables and hypothesis.

Experimental Section

Materials and Apparatus. Compounds **1**–**3** were obtained and purified as described previously.[6] The solvents used were reagent grade or Spectrograde. The electrolytes used to prepare the buffers were ACS grade. The equipment employed included a Cary 14 spectrophotometer with thermostated sample compartment, an American Instrument screw press and high-pressure window vessel, optical cells as described previously,[15] a Heise gauge reading to 200 MPa, a Sodev Model 02-D tuning fork densimeter capable of determining densities to 0.00002 g/cm^3 and equipped with programmable circulating thermostat, counter timer and digital printer, and a Beckmann research pH meter with a Duramark pencil combination electrode. The densimeter was calibrated with pure liquids ranging in density from those of *n*-hexane to carbon tetrachloride, and the pH meter was calibrated at 30 °C with two standard solutions (Micro Essential Laboratory) chosen to be one unit apart and to straddle the pH to be measured. Readings were reproducible to better than 0.01 pH unit.

Volume of Mixing. Mixing of 500 mL of water and 500 mL of ethylene glycol in a 1-L volumetric flask at 30 °C was observed to cause a contraction of 11 mL; hence the partial volume of water in this mixture is taken as 494.5/27.8 = 17.80 cm^3/mol. All solutions referred to below are understood to be in this mixed solvent unless otherwise stated.

Partial Volumes of Electrolytes. Densities of solutions of KH_2PO_4, K_2HPO_4, and KOH were determined at 30 °C, and the apparent molar volumes were calculated and extrapolated to infinite dilution as recommended by Millero.[16] Duplicate determinations yielded 48.30 ± 0.01, 43.36 ± 0.18, and 11.04 ± 0.30 cm^3/mol, respectively. Thus, the reaction volume for the buffer equilibrium (eq 1) equals 48.30 + 11.04 − 43.36 − 17.80 = −1.8 cm^3/mol.

Kinetic Measurements. Preliminary experiments showed a half-life of 8–15 min to be convenient; faster reactions made it difficult to charge the cell, assemble the vessel, and achieve constant pressure and temperature sufficiently rapidly, and slower ones led to erratic, small drifts in final absorption. The desired rates were obtained by control of the pH. The buffered cyclodextrin solutions are prepared as follows. A 0.01 M stock solution of KH_2PO_4 (100 mL) is treated with 0.1 M KOH (0.1 mL) so as to give a pH reading of 7.4–8.0; the exact value is chosen so as to give a convenient rate, as noted. A sample of **3** (75–800 mg) is dissolved in part of this solution; warming to 50 °C is necessary to bring about complete dissolution. The rest of the buffer solution is then added, the mixture is thermostated to 30 °C, and the pH is rechecked. In an actual run a stock solution of **1** or **2** in acetonitrile is metered (100 μL) by syringe into a 10-mL volumetric flask and diluted to the mark with the buffered cyclodextrin solution. Part of this is used to charge the optical cell, which is then inserted into the prethermostated window vessel; the latter is assembled, mounted in the spectrophotometer, and pressurized. The entire operation requires about 20 min. After an additional 10 min has elapsed, the optical density at 410 nm is recorded for 8–12 half-lives. The rest of the solution meanwhile serves to measure the pH and to verify that there is no significant drift in it. The pressure during all runs was constant to ±1 MPa or better, and the temperature to ±0.02 °C. For each ester, 5 to 6 concentrations of **3** ranging from 0.5 to 5 mM were

(11) (a) le Noble, W. J. *Prog. Phys. Org. Chem.* **1967**, *5*, 207. (b) Kohnstam, G. *Prog. React. Kinet.* **1970**, *5*, 335. For one possible example, see: Tiltscher, H.; Lohmüller, R. *Z. Naturforsch.,B* **1976**, *31B*, 277.

(12) The reason that solubility problems did not hamper measurements of the solvolysis rate of **1** is that the slow rate in that case permitted the use of unbuffered basic solutions. The buffer seemed to salt **2** out of solution.

(13) Morild, E. *Adv. Protein Chem.* **1981**, *34*, 93. Heremans, K. "High Pressure Science and Technology"; Timmerhaus, K. D.; Barber, M. S., Eds.; Plenum: New York, 1979; Vol. I, p 699. Neuman, R. C.; Owen, D.; Lockyer, G. D. *J. Am. Chem. Soc.* **1976**, *98*, 2982. See also ref 9.

(14) Wishnia, A.; Flaig, B.; Lin, F. L. "High Pressure Science and Technology"; Timmerhaus, K. D., Barber, M. S., Eds.; Plenum: New York, 1979; Vol. I, p 714.

(15) le Noble, W. J.; Das, A. R. *J. Phys. Chem.* **1970**, *74*, 3429. le Noble, W. J.; Schlott, R. *Rev. Sci. Instrum.* **1976**, *47*, 770.

(16) Surdo, A. L.; Bernstrom, K.; Jonsson, C. A.; Millero, F. J. *J. Phys. Chem.* **1979**, *83*, 1255.

employed, and each solution was studied at 5 to 9 pressures ranging from 0 to 180 MPa. For the solvolysis reaction of **1**, 0.01 M solutions of KOH were used instead of the buffers; it was verified that the slight differences in ionic strength between these solutions had no effect.

Calculations. All observed rate constants are based on the first two half-lives, with 15–20 points of regular time intervals being read directly from the recording. The first-order expressions fit in all cases with correlation constants of at least 0.999. The constants found are converted to those for a pH of 10 for **1** and of 8 for **2**. The data for **1** at each pressure are then used to construct Eadie plots based on $k_{obsd} - k_{un} = -K_d \times (k_{obsd} - k_{un})/[3] + (k_{conn} - k_{un})$. Since (as can be seen from Figure 1) there were small variations in the pressure at which the various concentrations of **3** were run, the k_{obsd} values used are those resulting from intrapolations. The pressure dependences of k_{com} and K_d are assessed by means of least-square fits of $\ln k = a + bp + cp^2$, giving ΔV^*_{com} and ΔV_d from $\Delta V^{(*)} = -bRT$; finally ΔV^*_{com} is corrected for the volume change (-1.8 cm^3/mol) caused by the pressure-induced shift in the buffer equilibrium.

Acknowledgment. This work was supported by the N.S.F at Stony Brook and the N.I.H. at Columbia. G.T. expresses appreciation for his N.I.H. postdoctoral fellowship.

Registry No. 1, 85116-52-5; **2**, 73213-41-9; **3**, 7585-39-9.

New Aspects of the Telluroxide Elimination. A Facile Elimination of *sec*-Alkyl Phenyl Telluroxide Leading to Olefins, Allylic Alcohols, and Allylic Ethers

Sakae Uemura* and Shin-ichi Fukuzawa

Contribution from the Institute for Chemical Research, Kyoto University, Uji, Kyoto 611, Japan. *Received September 28, 1982*

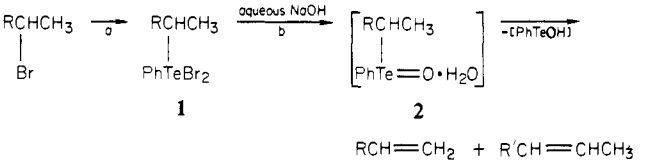
Abstract: The utility of the telluroxide for olefin synthesis, a reaction which previously appeared to be of little value, is described. Treatment of *sec*-alkylphenyltellurium dibromides, except for the cyclohexyl system, with aqueous NaOH at room temperature affords olefins, allylic alcohols, and/or allylic ethers in high yields presumably via the formation of *sec*-alkyl phenyl telluroxides and their facile telluroxide elimination. As to the formation of linear olefins, more preference for elimination toward the less substituted carbon was observed than the selenoxide and sulfoxide eliminations. In the cyclododecyl case only *trans*-cyclododecene was formed as an olefin component in a sharp contrast to the selenoxide elimination that affords a 1:1 mixture of cis and trans isomers. On the contrary, in the *n*-alkyl and cyclohexyl cases the corresponding telluroxides are stable compounds that afford similar elimination products including vinylic ethers only by neat pyrolysis at temperatures above 200 °C.

In contrast to the well-known selenoxide elimination leading to double-bond formation,[1] little is known on the telluroxide elimination.[2] On this subject only two reports have so far appeared to our knowledge. Original work has been done by Sharpless et al.,[3] who reported the formation of mixtures of olefins and/or alcohols by *tert*-butyl hydroperoxide oxidation of several tellurides in benzene without isolation of the telluroxides. Recently, Cava et al.[4] clarified that *n*-dodecyl 4-methoxyphenyl telluroxide is stable and its decomposition to 1-dodecene and the corresponding telluride occurs only in refluxing CCl_4 or toluene for a longer time. We have found that it is not necessarily the case for all telluroxides and, in fact, *sec*-alkyl phenyl telluroxides decompose readily to afford olefins, allylic alcohols, and allylic ethers in high yields under very mild conditions. In this paper we would like to report on the utility of the telluroxide for olefin and allylic compound syntheses, a reaction which previously appeared to be of little value.

Results and Discussion

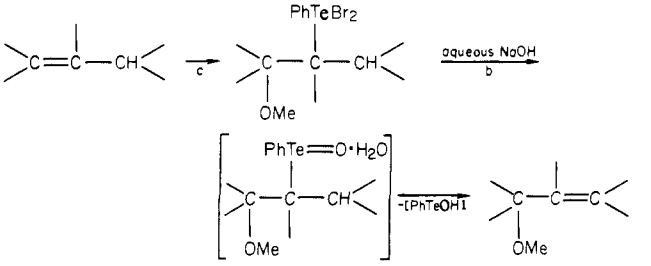
When we tried to prepare *sec*-octyl phenyl telluroxide (or its hydrate) (**2**, R = *n*-C_6H_{13}) by treating the corresponding stable dibromide (**1**, R = *n*-C_6H_{13}) with aqueous NaOH at room temperature,[5] the expected compound could not be isolated and instead a mixture of 1-octene and *trans*- and *cis*-2-octenes was obtained in a yield of 80% together with small amounts of 2-octanol and 2-octanone (Scheme I, Table I).[6] Similar facile telluroxide elimination was also observed to give the corresponding olefins in a yield of over 70% by starting from 2-dodecyl, 2-tetradecyl, cycloheptyl, cyclooctyl, and cyclododecyl bromides, small amounts of the corresponding alcohol and ketone being detected in all cases.[7]

Scheme I



conditions: a, $(PhTe)_2/NaBH_4/EtOH$ (reflux for 1-5 h) and Br_2/CCl_4 (0 °C); b, aqueous 0.5 N NaOH (20-25 °C for **1**-3 h)

Scheme II



condition: c, $(PhTe)_2/Br_2$ or $PhTeBr_3$ in MeOH (reflux for 1-2 h)

(1) For a review, see: (a) Reich, H. J. "Oxidation in Organic Chemistry, Part C"; Trahanovsky, W.; Ed.; Academic Press: New York, 1978; pp 1–130. (b) Clive, D. L. J. *Tetrahedron* **1978**, *34*, 1049. (c) Reich, H. J. *Acc. Chem. Res.* **1979**, *12*, 22.

(2) Uemura, S. *Kagaku (Kyoto)* **1981**, *36*, 381.

(3) Sharpless, K. B.; Gordon, K. M.; Lauer, R. F.; Patrick, D. W.; Singer, S. P.; Young, M. W. *Chem. Scr.* **1975**, *8A*, 9.

(4) Lee, H.; Cava, M. P. *J. Chem. Soc., Chem. Commun.* **1981**, 277.

(5) Detty, M. J. *J. Org. Chem.* **1980**, *45*, 274. The method is known to be the best one for the preparation of the telluroxide that is not contaminated by the corresponding tellurone.

(6) An eliminated phenyltellurenic acid (PhTeOH) was detected partly as diphenyl ditelluride that is probably formed by the following disproportionation and oxidation reactions (see Experimental Section).

$$2PhTeOH \rightarrow PhTeOOH + PhTeH$$

$$2PhTeH \xrightarrow{[O]} (PhTe)_2 + H_2O$$

0002-7863/83/1505-2748$01.50/0