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Externally sensitized mesolytic fragmentations in dithiane–ketone adducts

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Abstract—The apparent activation enthalpies, $\Delta H^{\neq}$, for externally sensitized mesolytic fragmentations in benzophenone–dithiane adducts were obtained in variable temperature photolyses and compared with DFT activation barriers calculated for β-scission in the corresponding oxygen-centered radicals. The results of these experimental and theoretical studies further support the mechanism in which deprotonation of the hydroxy-group, in the transient cation radical, is coupled with intramolecular electron transfer furnishing the O-centered radical, which subsequently fragments. The quantum yields of fragmentation increase for higher alkyl substituted dithiane adducts.

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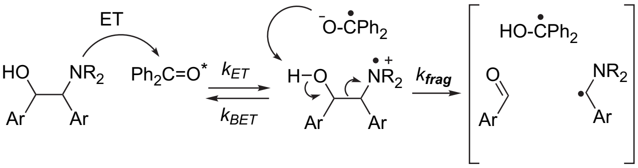
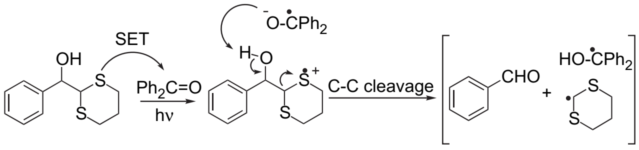
1. Introduction

Heteroatom-centered cation radicals, C_β–C_α–$X^{\bullet+}$, which are readily generated by photoinduced electron transfer (ET), are subject to mesolytic fragmentation. It is well known that removal of one electron from the heteroatom's lone pair in the ground state significantly reduces the bond order of the geminal bonds, which either increases the acidity of the alpha-proton (H–C_α) or causes the C_α–C_β bond to cleave. In our previous work we utilized this increased acidity of the alpha-proton and developed an efficient electrochemical deprotection for carboxylates in general, and amino acids in particular, based on esters of hydroxymethyldithiane.[1] In this paper we will focus primarily on photoinduced C–C bond fragmentations in adducts of dithianes with ketones.

ET-induced fragmentations in vicinal amino alcohols and diols have been extensively studied.[2] The accepted mechanistic rationale includes photoinduced electron transfer to an ET-sensitizer, e.g., benzophenone, followed by a mesolytic cleavage of the generated cation radical, assisted by the benzophenone anion radical deprotonating the vicinal hydroxy group. It was noted that the C–C bond cleavage step is reminiscent of the Grob fragmentation in closed shell systems.[3]



One of the early examples by Whitten and Ci involved thioindigo-sensitized fragmentation in the *threo-* and *erythro*-2-morpholino-1,2-diphenylethanol.[3a] Assuming that the only temperature-dependent process in the reaction of the geminate ion radical pair is k_{frag}, they determined the Arrhenius activation energy for the *threo-* and *erythro* diastereomers to be 4.9 and 2.8 kcal/mol, respectively. This demonstrates a strong conformational dependence of the cleavage and shows that the activation barrier is very low.



Similar reactions of sulfido-alcohols are also known. For example, Gravel et al. utilized the C–C cleavage in β-phenylthioalkanols as a synthetic method for indirect cleavage of olefins[4] and also in carbohydrate synthesis.[5] Some time ago we found that dithianes are particularly suitable for this chemistry: their adducts are readily synthesized and they cleave efficiently upon photoinduced fragmentation. The mechanism of cleavage in dithiane adducts was investigated by utilizing classical physical organic methods such as the Hammett substituent effect, the kinetic isotope effect,[6] and laser flash photolysis studies.[7] Our initial mechanistic findings were in keeping with the universally recognized 'Grob-like' mechanism, until we tested the photoinduced fragmentation in the *tert*-butyl derivative **A**, which in addition to the expected pivalaldehyde **B** ('normal' cleavage) produced dithiane-2-carboxaldehyde **C** as a major product in 1:6.2 ratio.[8] It became clear that the quasi-Grob electron

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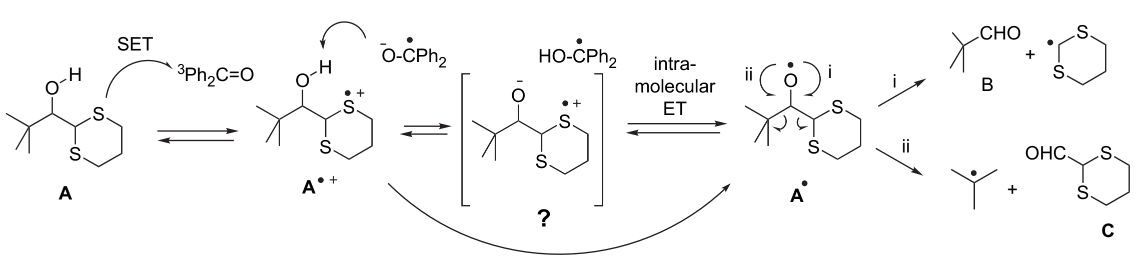
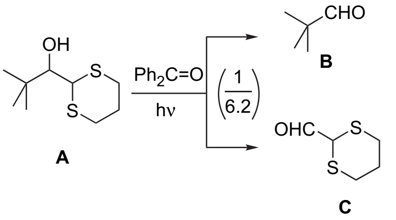
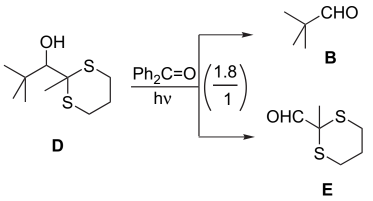


Scheme 1.

pushing rationale needed refinement because adduct **A** was primarily cleaving the wrong bond.



Further experimental and computational investigation suggested that deprotonation of the hydroxy group in the initially generated cation radical does not result in the formation of a charge separated 'Grob-like' precursor $^{-}$O–C–C–S$^{+\bullet}$–R, but rather produces a neutral oxygen-centered radical (or a species behaving as one) via intramolecular electron transfer. The O-centered radical undergoes subsequent fragmentation in either direction and the partitioning correlates with stability of the produced radicals, Scheme 1.[9] When methyldithiane derivative **D** was used in place of **A**, the ratio of **B**:**C**=1:6.2 was inverted to become **B**:**E**=1.8:1, all in keeping with relative stability of *tert*-butyl, dithian-2-yl, and 2-methyldithian-2-yl radicals. We also compared the results of the fragmentation in methylene chloride and acetonitrile, which constitutes almost an order of magnitude difference in the dielectric constant, and did not see any difference in the partitioning within experimental error. All these results seem to indicate that the charge separated species does not exist, or at best it is in fast equilibrium with the alkoxy radical (Scheme 1).

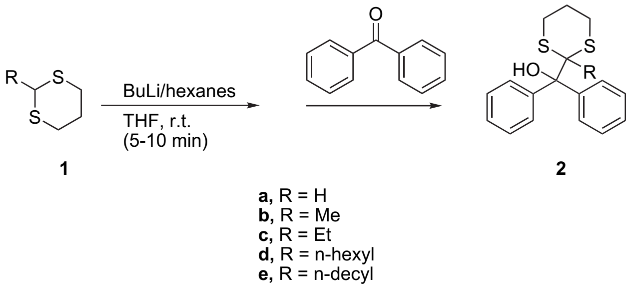


The case of *tert*-butyl derivatives, such as **A** and **D**, is unique in a sense that it allowed us to discover this new channel in the mechanism of fragmentation simply by product analysis. For dithiane adducts of aromatic aldehydes and ketones the barrier for the aryl radical departure is prohibitively high, i.e., it is the dithiane radical, which is *always* departing. Therefore, it is much more difficult to ascertain whether or not the original Grob-like mechanism for cleavage competes with the anomalous O-centered radical mechanism (or either one of them is operating exclusively) in the case of aromatic adducts. Because of the presence of sulfur it is synthetically challenging, if not impossible, to generate the O-radical $\mathbf{A}^{\bullet}$ from an alternative precursor, for example, a peroxide, and study the effect of substituents on the rate of its degradation.

In this paper we report our experimental and computational study of the mechanism of photoinduced cleavage in adducts of 2-alkyl substituted dithianes with benzophenone, which is intended to further refine the mechanism of fragmentation. Benzophenone-sensitized mesolytic fragmentations, in adducts of the sensitizer itself, result in generation of more benzophenone and, as such, constitute its amplification. Hence, our particular interest in this system, which we plan to utilize in various photochemical applications.

2. Results and discussion

Benzophenone adducts **2a**–**e** of unsubstituted (**1a**), 2-methyl- (**1b**), 2-ethyl- (**1c**), 2-hexyl (**1d**), and 2-decyl (**1e**) dithiane were synthesized according to a modified Corey–Seebach procedure[10] (Scheme 2) and their photoinduced fragmentation was studied over a temperature range from −40 to +40 °C in acetonitrile upon benzophenone sensitization. The driving force for the oxidative electron transfer from the dithiane moiety to the triplet state of benzophenone in acetonitrile is rather large: the one electron reduction potential of triplet benzophenone is −1.68 V (vs SCE in acetonitrile),[11] whereas various 2-substituted dithianes oxidize in the range of +0.73 to +1.18 V in the same solvent.[12] During the course of a laser flash photolysis study[7] we found that the rate of initial electron transfer quenching of triplet benzophenone with dithiane–benzophenone adduct in dry acetonitrile was near the diffusion limit, $8.4\pm0.7\times10^{8}\ M^{-1}\,s^{-1}$. In 10% aqueous acetonitrile the quenching rate was even higher, $1.31\pm0.06\times10^{9}\ M^{-1}\,s^{-1}$. In the present study we have determined the dependence of the quantum efficiency of fragmentation on temperature and compared the experimental (apparent) activation enthalpy with the calculated activation barrier for the β-scission in the corresponding



Scheme 2.

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