

Bis(pentafluorophenyl) disulfide as a hydrogen abstractor and an electron acceptor from the resulting radical intermediate

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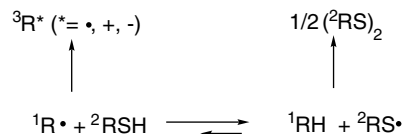
Abstract—The pentafluorobenzenethiyl radical is an efficient hydrogen abstractor from an activated methylene or methine group and bis(pentafluorophenyl) disulfide is an efficient electron acceptor from the resulting radical intermediate. Thus benzyl-OTBS ether was easily converted into the corresponding pinacol, and 2-phenyl-1,3-dioxanes are converted into the monobenzoates of diols.

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The hydrogen transfer between a thiol and a carbon radical is reversible and the equilibrium is shifted more to the thiyl radical (Scheme 1).¹ In biological system, nucleic acids and proteins are often damaged by other toxic species generating the free radicals of these biomolecules. The damage, however, is repaired by the thiol of another biomolecule such as glutathione and the cysteine residue of proteins.² This repair process is based on the favorable equilibrium of the hydrogen transfer from sulfur to carbon (Scheme 1, $^1R\cdot$ = ‘damaged biomolecule’).³ On the other hand, the chemical transformation of an organic molecule (1RH) by a thiyl radical ($^2RS\cdot$) involves the unfavorable hydrogen transfer from carbon to sulfur.

This unfavorable hydrogen abstraction by the thiyl radical becomes more efficient upon removal of the carbon radical. Furthermore, the rate of hydrogen transfer is affected by the polarity factor of both the hydrogen donor and acceptor.⁴ Thiyl radicals are electrophilic and alkyl radicals are nucleophilic based on the polarity concept of free radical.^{4b}

The pentafluorobenzenethiyl (PFBT) radical must be strongly electrophilic with a low reduction potential and



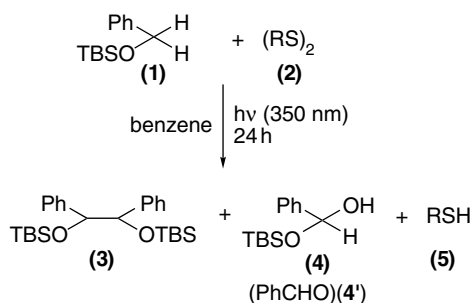
Scheme 1.

this property must stimulate the hydrogen transfer from an alkyl group to the thiyl radical. Schaefer III et al. described in recent paper⁵ that “perfluorinated aromatics will be very effective electron acceptor and may be useful in the invention of new materials and new reactions”. An alkyl radical has a rather low oxidation potential and the perfluorinated aromatics have a positive electron affinity in contrast to the negative electron affinity for common aromatics.⁵ Furthermore, the disulfides containing electronegative substituents have a rather low reduction potential compared to dialkyl disulfides.⁶ Thus bis(pentafluorophenyl) disulfide (BPFDD) must be an efficient electron acceptor from a carbon radical to produce a carbo-cation. These situations prompted us to test the hydrogen abstraction of benzyl-OTBS ether ($\text{PhCH}_2\text{O-SiMe}_2\text{Bu}$) (**1**) by thiyl radicals including the PFBT radical and the results are shown in Scheme 2 and Table 1.

The photolyses of dimethyl and bis(2-phenylethyl) disulfides in the presence of 2 mol equivalents of benzyl-TBS ether (**1**) gave pinacol **3** as a mixture of diastereomers⁷ but diphenyl disulfide produced no product (Scheme 2 and Table 1).⁸ On the other hand, the

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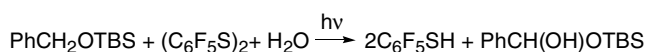
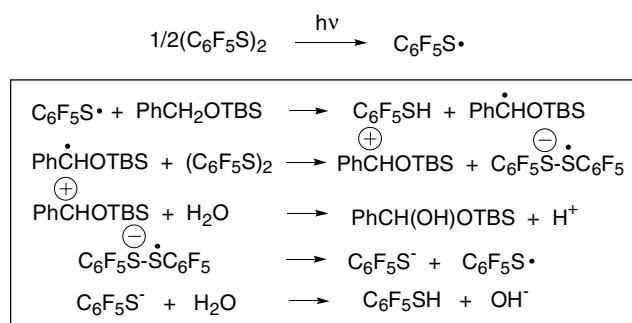
Scheme 2.

Table 1. Photolyses of disulfides (2) in the presence of benzyl-OTBS ether

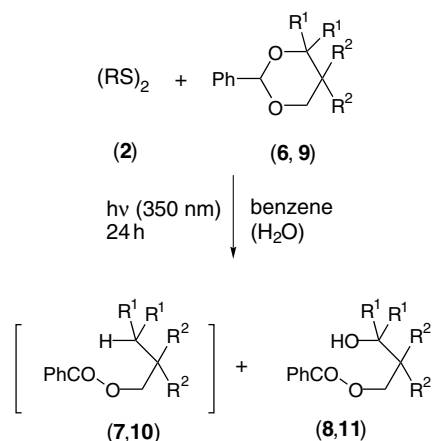
Disulfide (2)	Product yield (%)	
	3	4+4'
(MeS) ₂	62.6	0.0
(PhCH ₂ CH ₂ S) ₂	46.5	0.0
(PhS) ₂	0.0	0.0
(C ₆ F ₅ S) ₂	5.9	44.2

photolysis of BPFD gave mostly benzaldehyde (4') and its congener 4⁹ together with a small amount of pinacol 3. The former (4') must be derived from the latter (4) under the reaction conditions and the work up procedure. Diphenyl disulfide showed no reactivity most probably due to the unfavorable equilibrium (Scheme 1) as reported by Fujisawa et al.⁷ The equilibrium is overweighed the right side due to the low S–H bond energy. The reaction scheme for the reaction with BPFD is summarized in Scheme 3. The reaction is triggered by the thiyl radical generated by photolysis of the disulfide and the following chain process produces the oxidation product. However, this chain reaction must be inefficient due to the rapid annihilation of the thiyl radical by disulfide formation.

Next, 2-phenyl-5,5-dimethyl-1,3-dioxane (6)¹⁰ was subjected to a reaction with the thiyl radicals.⁸ The thiyl radicals from disulfides 2 gave only the benzoate ester



Scheme 3.



6,7,8 : R¹=H, R²=Me 9,10,11 : R¹=Me, R²=H

Scheme 4.

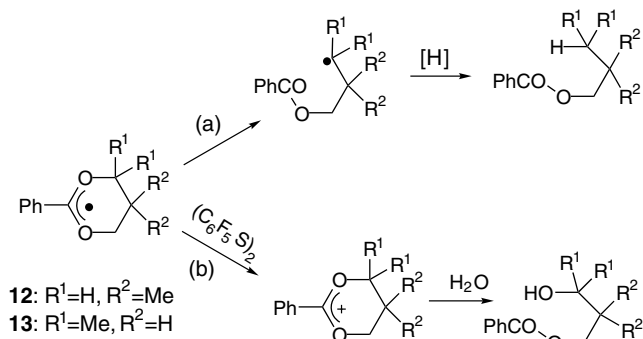
Table 2. Photolyses of disulfides (2) in the presence of 1-phenyl-1,3-dioxane

Disulfide (2)	Substrate	Irradiation time (h)	Product yield (%)	
(MeS) ₂	6	24	7 (trace)	8 (70.1)
(PhS) ₂	6	24	7 (0.0)	8 (12.5)
(C ₆ F ₅ S) ₂	6	3	7 (0.0)	8 (64.5)
(MeS) ₂	9	24	10 (93.5)	11 (4.1)
(PhS) ₂	9	24	10 (4.1)	11 (5.4)
(C ₆ F ₅ S) ₂	9	3	10 (3.5)	11 (36.0)

8, 11 an oxidation product, without the formation of an ester 7, the isomerization product (Scheme 4 and Table 2). When 2-phenyl-4,4-dimethyl-1,3-dioxane (9)¹² was used as the substrate,⁸ both the isomerization product 10¹¹ and the oxidation product 11¹¹ were obtained (Table 2). A similar mechanism must be operating as in the case of the benzyl-TBS ether, but the intermediate carbon radical seems to be more easily oxidized.

To understand the origin of oxygen in the product 8, the reactions were conducted under different conditions. The reaction solution was thoroughly degassed by repeated thaw–freeze cycling under vacuum but no distinct change was observed in the results. On the other hand, the addition of a small amount of water to the reaction solution increased the formation rate of the product 8. These results indicate that the hydroxyl groups in the products 8 and 11 are derived from the moisture in the reaction solution and not from the dissolved oxygen.

In general, the reactions are clean and the reaction solutions contain the products, the thiols from the disulfide, and the intact starting materials. Small amount of diphenyl sulfide was formed by direct photolysis of the disulfide. All the reactions were stopped before complete consumption of the starting materials for the evaluation of the relative reactivity, and the



Scheme 5.

product yields can be improved by prolonged irradiation.

Compared to the benzyl-TBS ether radical, the 2-phenyl-1,3-dioxanyl radicals, **12** and **13**, are more susceptible to the electron transfer to the disulfide, which produces the oxidation products **8** and **11** from the substrates **6** and **9**, respectively, even by using dimethyl or diphenyl disulfides. It is noteworthy that 2-phenyl-4,4-dimethyldioxane (**9**) produced an isomerization product in spite of no isomerization product from 2-phenyl-5,5-dimethyldioxane (**6**). This result is accounted for by the competitive process between the skeletal rearrangement (route a) and the electron transfer (route b) of the intermediate radical (Scheme 5). The ring opening of the dioxanyl radical intermediate **13** from **9** is favorable due to the formation of a tertiary radical¹³ and prevails over electron transfer when the electron acceptor is dimethyl disulfide. Diphenyl disulfide is not active both in the initial hydrogen abstraction and also electron transfer, which results in the low yields of products **10** and **11**. The PFBT radical is an efficient hydrogen abstractor and BPDFD is a good electron acceptor that predominantly gives the oxidation product **11**. The electron transfer is considered to take place between the carbon radical and the disulfide since it has been known that no electron transfer occurs between an allyl silyl ether and the PFBT radical¹⁴ derived from the corresponding thiol. However, we cannot eliminate the possible electron transfer between the intermediate carbon radical, **12** and **13**, and the thiyl radical from the present experimental results.

In contrast, the ring cleavage isomerization of the intermediate **12** is slow due to the formation of the less stable primary alkyl radical, and the electron transfer to disulfides prevails to produce the product **8** even with dimethyl disulfide.

As described above, the PFBT radical acts as an efficient hydrogen abstractor due to its electrophilic nature, and BPDFD acts as an oxidizing agent. These reactions of BPDFD are expected to work similarly for the hydroxylation of alkanes activated by the adjacent group such as hydroxyl, ether, or double bond.

Acknowledgements

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- Fujisawa, H.; Hayakawa, Y.; Sasaki, Y.; Mukaiyama, T. *Chem. Lett.* **2001**, *23*, 632–633, Pinacol **3** is a mixture of diastereomers.
- The photolyses were carried out in the following manner. One of the disulfides (0.05 mol/L) and the substrate **1**, **6**, or **9** (0.10 mol/L) in benzene were placed in a Pyrex reaction tube and degassed by bubbling argon while in an ultrasonic bath. The mixture was irradiated by a Rayonet photoreactor equipped with 350 nm lamps. For the quantitative determination of the products, an aliquot of the reaction mixture was subjected to ¹H NMR measurement using an internal standard. For product identification, the condensed residue of the reaction mixture was separated by TLC plate (SiO₂) and GPC (gel permeation chromatography) on JAIGEL-1H eluted by 1,2-dichloroethane.
- The hemiacetal **4** quantitatively gave the benzaldehyde oxime. **4**: ¹H NMR (400 MHz) δ -0.08 (3H, s), -0.04 (3H, s), 0.84 (9H, s), 6.17 (1H, s), 7.26–7.31 (3H, m), 7.34–7.36 (2H, m).
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- Products **8**, **10**, and **11**, colorless oils, were identified by comparison to the authentic samples prepared from benzoyl chloride and the corresponding diols. **8**: ¹H NMR (400 MHz) δ 1.02 (6H, s), 2.33 (1H, br s, OH), 3.39 (2H, s), 4.19 (2H, s), 7.45 (2H, dd, *J* = 7.4 and 5.1), 7.58 (1H, tt, *J* = 7.4 and 1.5), 8.04 (2H, dd, *J* = 5.1 and 1.5). **10**: ¹H NMR (400 MHz) δ 0.98 (6H, d, *J* = 6.8), 1.45 (2H, q, *J* = 6.8), 1.80 (1H, nonet, *J* = 6.8), 4.35 (2H, t, *J* = 6.8), 7.42 (2H, dd, *J* = 7.6 and 7.4), 7.55 (1H, t, *J* = 7.4), 8.04 (2H, d, *J* = 7.6). **11**: ¹H NMR (400 MHz) δ 1.32 (6H, s), 1.96 (2H, t, *J* = 6.8), 4.25 (2H, t, *J* = 6.8), 7.44 (2H, t, *J* = 7.5), 7.55 (1H, t, *J* = 7.5), 8.04 (2H, d, *J* = 7.5).
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