

Viologen-mediated Reductive Dehalogenation of α -Halogeno Ketones

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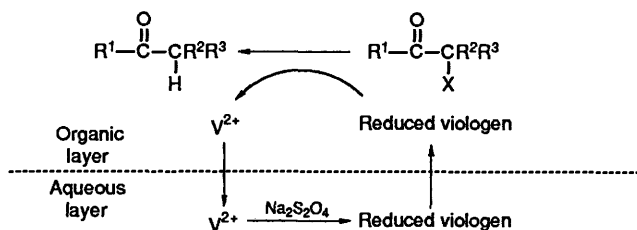
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Various α -halogeno ketones undergo reductive dehalogenation to the corresponding ketones almost quantitatively with sodium dithionite using viologen as an electron-transfer catalyst in organic solvent-water two-phase systems.

Viologens (1,1'-dialkyl-4,4'-bipyridinium, V^{2+}) are known to produce the cation radicals ($V^{+\cdot}$) and quinoids (V) forms by one- and two-electron reduction, respectively. The reduced forms are easily reoxidized to V^{2+} . Viologens have received much attention as herbicides¹ and as electron relays in photochemical solar energy conversion into hydrogen.² Recently, reactions have been studied using V^{2+} as an electron-transfer catalyst (ETC) for the reduction of organic compounds. It was reported that various vicinal dibromides,³ azobenzene,⁴ aromatic aldehydes and ketones,⁵ and acrylonitrile⁶ could be reduced effectively in the presence of V^{2+} as ETC. The use of viologens as electron-carriers in enzyme-catalysed reactions has also been investigated.^{3c,7}

A number of methods have been developed to accomplish the reductive dehalogenation of α -halogeno ketones.⁸ We describe here a novel reductive dehalogenation of some α -halogeno ketones by sodium dithionite ($\text{Na}_2\text{S}_2\text{O}_4$) in two-phase systems using viologens as electron-mediators (see Scheme).



Scheme. Cyclic pathway for the viologen-mediated dehalogenation of α -halogeno ketones by sodium dithionite.

Addition of aqueous sodium dithionite to a mixture of an α -halogeno ketone and viologen in an organic solvent-water two-phase system under a nitrogen atmosphere resulted in an instantaneous blue coloration in the aqueous phase, which is due to the one-electron reduction product of viologen, $V^{+\cdot}$. When the mixture was stirred, the blue radical cation was extracted into the organic phase. A reversal in the solubility of the oxidized (V^{2+}) and reduced ($V^{+\cdot}$) forms of viologens between aqueous and organic phases makes them useful ETCs in the reduction of organic substances in two-phase systems.³

Reductive dehalogenation of α -halogeno ketones with sodium dithionite proceeded smoothly in the presence of catalytic amounts of viologens in two-phase systems. The results with octyl viologen (OcV^{2+}) in a toluene-water system are summarized in the Table. In the absence of viologens, the reaction either scarcely proceeded or the reduction yields were low (Table). These results clearly suggest that OcV^{2+} mediates the dehalogenation process. Since the molar ratio of the viologen to α -halogeno ketones was much less than the stoichiometric value, 2, the active reductant in the dehalogen-

ation was recycled in the process. The cycle number of the viologen was as large as 150 (entry (1c)).

The use of methyl viologen (MV^{2+}) in place of OcV^{2+} made no significant change in the yield of the dehalogenation. However, the yield dropped considerably when benzyl viologen (BnV^{2+}) was employed. For example, the reduction yield for (3) after the reaction mixture had been stirred for 1.5 h at 35 °C with the molar ratio of viologen to (3) of 0.1 was >90% with MV^{2+} and OcV^{2+} , while it was only 34% with BnV^{2+} under the same conditions. This can be ascribed to the lower oxidation potential of $\text{BnV}^{+\cdot}$ compared with that for the corresponding radicals of the aliphatic viologens.⁹

The dehalogenation reactions of the α -halogeno ketones by sodium dithionite with octyl viologen was also tried in diethyl ether-water, ethyl acetate-water, dichloromethane-water two-phase systems, as well as a homogeneous methanol-water (3:1) medium. The difference in organic layer in the two-phase systems did not afford a significant change in the reduction yield. However, use of the methanol-water medium lowered the yield; for example, the reduction yield for (3) dropped to 70–80% from >90% under the aforementioned reaction conditions.

The active reductant for α -halogeno ketones could be either the radical cation $V^{+\cdot}$ or the two-electron reduction product V which is formed by the disproportionation reaction of $V^{+\cdot}$ ($2V^{+\cdot} \rightarrow V + V^{2+}$) in the organic layer.^{3a-c} The spectroscopic studies on the $\text{OcV}^{+\cdot}$ in different two-phase systems showed that the disproportionation constant (K_d) depends strongly on the organic phases: the reported K_d values are >10 in toluene, 1.5 in diethyl ether, and 0.3 in ethyl acetate.^{3b} Although there is strong evidence that the two-electron reduction product V is the active species in the viologen-mediated reduction of vicinal dibromides^{3a-c} and aldehydes and ketones,⁵ the weak dependence of the reduction yield of the α -halogeno ketones on the organic phases observed in this study suggests the possibility that the active species for the dehalogenation of the α -halogeno ketones is the radical cation $V^{+\cdot}$.¹⁰ This view is supported by the similarity of the reduction yield with methyl viologen and octyl viologen, and the moderate yield obtained in methanol-water as the medium.

In conclusion, the present study demonstrates the reductive dehalogenation of α -halogeno ketones by sodium dithionite using viologens as an electron-transfer catalyst in two-phase systems. We consider the present procedure can be a mild and inexpensive alternative route for the reduction of α -halogeno ketones. Further studies on the details of the reaction mechanism and utilization of this technology in the reduction of other types of organic compounds are underway.

Experimental

Materials.—Octyl and benzyl viologens were prepared by treating 4,4'-bipyridine (Aldrich) with a 2–3 fold excess of octyl or benzyl bromide at 85–90 °C without solvent for 3 h. The

Table. Reductive dehalogenation of α -halogeno ketones to the corresponding ketones by sodium dithionite using octyl viologen as an electron carrier in toluene-water two-phase systems.^a

Entry	Substrate ^b	OcV ²⁺ / Subs.	Yield (%) ^{c,d}
(1)a	2-Bromoacetophenone	>0.03	>98 (64) ^d
b		0.02	89
c		0.01	78
d		0.00	17
(2)a	2-Chloroacetophenone	0.1	93
b		0.00	15
(3)a	2-Bromo-4'-methylacetophenone	0.1	>98
b		0.05	95 (67) ^d
c		0.02	38
(4)	2,4'-Dibromoacetophenone	0.1	>98
(5)a	2-Bromo-4'-methoxyacetophenone	0.1	>98
b		0.05	>95 (72) ^d
(6)	2-Chloro-2-phenylacetophenone	0.1	>98
(7)	2-Bromoisobutyrophenone	0.1	96
(8)	2-Bromo-2'-acetophenone	0.1	>98
(9)	(+)-3-Bromocamphor	0.1	50

^a Reaction time was 3 h at 35 °C. ^b For compounds (3)–(8), no appreciable dehalogenation was observed in the absence of the viologen. ^c From the ¹H NMR or GLC analysis. ^d Numbers in parentheses are the isolated yields.

solidified reaction mixture was triturated with CH₂Cl₂, filtered, and recrystallized from ethanol. Yields were almost quantitative and their NMR spectra were consistent with their structures. Methyl viologen and α -halogeno ketones were purchased from Aldrich.

Typical Procedures for Dehalogenations.—An aqueous solution (5 ml) containing K₂CO₃ (3 mmol) and Na₂S₂O₄ (4 mmol) was added dropwise to a mixture of α -halogeno ketone (2 mmol) and viologen (0.2 mmol) in toluene (30 ml)–water (10 ml) under a nitrogen atmosphere. Stirring was continued for 3 h at 35 °C after which the aqueous layer was extracted with CH₂Cl₂ (2 × 30 ml). The combined organic layers were dried, concentrated, and analysed by ¹H NMR, for (1)–(8), or GLC, for (9). Control experiments were carried out in the same manner, but without viologens. For isolated yields, the reactions were carried out with 8 mmol of substrates, 0.4 mmol of octyl viologen, 6 mmol of K₂CO₃, and 16 mmol of Na₂S₂O₄ in toluene (50 ml)–water (20 ml). After work-up, the products were purified by Kugelrohr distillation. The b.p. and spectral

data for the products were consistent with the structural assignments.

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