Viologen-mediated Reductive Desulfonylation of α-Nitro Sulfones by Sodium Dithionite

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Reductive desulfonylation of α-nitro sulfones to give the corresponding nitro compounds was carried out conveniently with sodium dithionite, by using octylviologen as an electron-transfer catalyst in organic solvent–water two-phase systems. Sulfones which do not have an α-nitro group are not desulfonylated. A reaction scheme involving a nitroalkyl radical has been proposed.

Viologens (1,1'-dialkyl-4,4'-bipyridiniums, V^{2+}) undergo two consecutive one-electron reduction processes to the respective cationic radical ($V^{•+}$) and quinoid (V) forms. The reduced forms are easily reoxidized to V^{2+}. They have attracted attention as herbicides[1] and electron mediators in photochemical conversion of light energy into hydrogen.[2] More recently, viologens have been utilized as an electron-transfer catalyst (ETC) for the reduction of various organic compounds.[3-8] It was reported that nitroalkenes,[3] 1,2-dibromides,[4] activated carbonyl compounds,[5] azobenzene,[6] acrylonitrile,[7] and α-halogeno ketones[8] could be reduced effectively in the presence of viologen as an ETC. In a previous paper,[8] we showed that various α-halogeno ketones undergo reductive dehalogenation to the corresponding ketones almost quantitatively with sodium dithionite using viologen as an ETC in organic solvent–water two-phase systems. This finding prompted us to undertake a study on the viologen-mediated reduction of other classes of organic compounds in the hope of providing a convenient and practical route for reductive transformation of synthetic intermediates.

α-Nitro sulfones are potentially useful synthetic intermediates. Arylsulfonylnitromethanes and secondary α-nitro sulfones bear highly acidic proton(s) and therefore can undergo the typical carbanion reactions such as C-alkylation[9] and Michael addition.[10] The benzenesulfonyl group of α-nitro sulfones may be replaced by a variety of nucleophiles[11] or a hydrogen atom.[9,12-14] Several reagents including sodium hydrogen telluride,[12] 1-benzyl-1,4-dihydronicotinamide,[9,13] and 1,3-dimethyl-2-phenylbenzimidazoline,[14] have been employed to replace the sulfonyl group by a hydrogen atom. However, these methods either have a very limited scope[12] or involve use of a large excess of reagents[9,13] or non-routine reaction condition (sealed-tube reaction).[14]
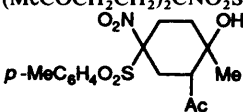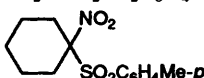
In this paper we show that reductive desulfonylation of various α-nitro sulfones can be conveniently achieved in good yields with sodium dithionite in the presence of octylviologen (OcV^{2+}) as an ETC in organic solvent–water two-phase systems.

Results and Discussion

α-Nitro sulfones used in this study were made by one of three routes: alkylation of (phenylsulfonyl)nitromethane,[9] Michael-type addition reactions of (phenylsulfonyl)nitromethane to methyl vinyl ketone,[10]† and sulfonylation of α-halogeno nitro compounds[15] (see Experimental section for details).
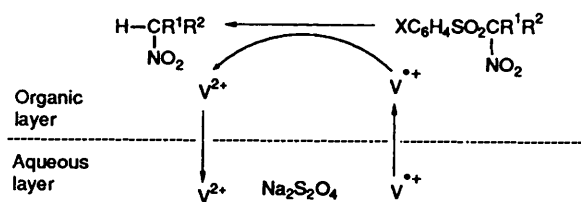
The reductive desulfonylation of various α-nitro sulfones was

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† The reaction of (phenylsulfonyl)nitromethane and methyl vinyl ketone using a catalytic amount of triethylamine in tetrahydrofuran (THF) gave a mixture of monoadduct **5** and bisadduct **6**. Forced reaction conditions produced the intramolecular aldol condensation product **7**. Zeilstra and Engberts (ref. 10) reported only products **6** and **7**.

Table 1 Reductive desulfonylation of α-nitro sulfones to the corresponding nitro compounds by sodium dithionite using octylviologen as an ETC in dichloromethane–water two-phase systems[a]

Entry	Substrate[b]	Yield (%)[c,d]
1	$PhCH_2CHNO_2SO_2Ph$	>98 (62)[d]
2	$PhCH_2CHNO_2SO_2C_6H_4Me\text{-}p$	>98
3	$Me[CH_2]_7CHNO_2SO_2Ph$	>98 (76)[d]
4	$EtO_2CCH_2CHNO_2SO_2Ph$	60
5	$MeCOCH_2CH_2CHNO_2SO_2Ph$	>98 (68)[d]
6	$(MeCOCH_2CH_2)_2CNO_2SO_2Ph$	>98 (50)[d]
7		>95 (72)[d]
8	$Me_2CNO_2SO_2C_6H_4Me\text{-}p$	65, 10[e]
9		55

[a] Reaction time was 3 h at 35 °C, and the molar ratio of the viologen to the substrate was 1:10. [b] In the absence of the viologen no appreciable desulfonylation was observed except for entry **5** which showed 30% conversion. [c] From the ¹H NMR analysis. [d] Numbers in parentheses are the isolated yields. [e] Yield of $Me_2C(NO_2)CMe_2NO_2$.

performed by sodium dithionite with or without OcV^{2+} in dichloromethane–water two-phase system at 35 °C under nitrogen. The results are summarized in Table 1. Table 1 shows that the desulfonylation of most α-nitro sulfones to the corresponding nitroalkanes proceeds almost quantitatively in the presence of the viologen. In the absence of the viologen, the desulfonylated product was not detected except for entry **5** which showed ~30% conversion based on ¹H NMR analysis. Since the molar ratio of OcV^{2+} to the substrate is 1:10, it is clear that the viologen mediates the reaction and the active reductant produced from the dithionite reduction of the viologen is recycling as shown in Scheme 1.

Scheme 1 Cyclic pathway for the viologen-mediated reductive desulfonylation of α-nitro sulfones by sodium dithionite

Neither the use of methylviologen in place of octylviologen nor the change of organic layer to toluene or ethyl acetate made a significant change in the reduction yield. The blue colour, which is due to the one-electron reduction product ($V^{•+}$) of

viologen, was sustained in the organic phase during the reaction. These accord with the observations made in the reductive dehalogenation of α-halogeno ketones[8] and seem to suggest that the active species for this reaction is the viologen radical cation $V^{\cdot+}$ rather than the quinoid (V) form of the viologen.

The sulfones which do not have an α-nitro group, e.g., benzyl phenyl sulfone, could not be desulfonylated under these experimental conditions. Though the exact mode of the reaction is not clear at this point, the general mechanism shown in Scheme 2 is proposed for the viologen-mediated reduction of α-nitro sulfones by sodium dithionite: the reduction is initiated by a single-electron-transfer from $V^{\cdot+}$ to α-nitro sulfones I, generating the radical anion II. Ejection of the benzenesulfinate anion * from II gives the nitroalkyl radical III, which is further reduced by $V^{\cdot+}$ to produce a carbanion IV. Protonation of the carbanion completes the reduction. The reduction of 2-nitro-2-(p-tolyl-sulfonyl)propane 8 yielded 2,3-dimethyl-2,3-dinitrobutane as a minor product. This seems to support the intermediacy of the radical III.
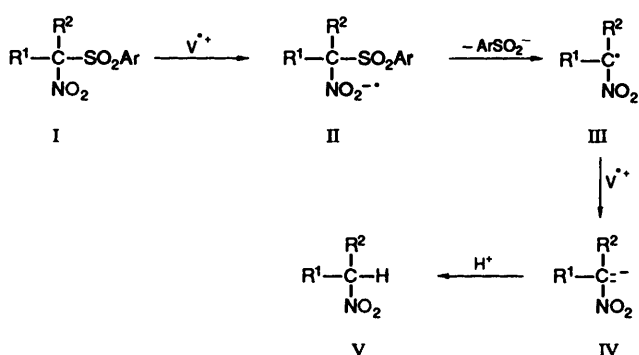
Scheme 2 Proposed mechanism for the viologen-mediated desulfonylation of α-nitro sulfones

In conclusion, α-nitro sulfones are easily desulfonylated by sodium dithionite with octylviologen to give the corresponding nitroalkanes. The mildness of the present desulfonylation is well demonstrated in the reactions of substrates 4–7 where carbonyl groups are not affected. We consider this reaction will broaden versatility of the benzenesulfonyl group as an activating group in organic synthesis. Further studies on the utilization of the viologen as an ETC for the reduction of different types of organic compounds are in progress.

Experimental

NMR spectra were obtained with a Bruker FT NMR Aj 80 spectrometer and melting points were measured with an electrothermal melting point apparatus.

Materials.—Octylviologen was prepared from 4,4′-bipyridine and 1-bromooctane as described previously.[8]

[2-Nitro-2-(phenylsulfonyl)ethyl]benzene 1[9,14] 2-acetyl-1-methyl-4-nitro-4-(p-tolylsulfonyl)cyclohexan-1-ol 7,[10] 2-nitro-2-(p-tolylsulfonyl)propane 8[14,15] and 1-nitro-1-(p-tolylsulfon-yl)cyclohexane 9[14,15] were prepared by the literature procedures. Their m.p.s and spectroscopic data were consistent with the reported values except for the slight differences in the m.p.s of the following compounds: 8, m.p. 111–113 °C (lit.,[15] 109–110 °C; lit.[14] 110–111 °C); 9, m.p. 139–140 °C (lit.,[15] 135–136.5 °C; lit.,[14] 136–137 °C).

Other α-nitro sulfones were prepared in the following way.

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* This is very analogous to many instances that benzenesulfinate anion serves as a leaving group with S_N1-reactive substrates: for recent examples see ref. 16.

[2-*Nitro*-2-(p-*tolylsulfonyl*)*ethyl*]*benzene* 2.—The procedure of Wade[9] was applied. A mixture of α-bromotoluene (4.11 g, 24 mmol) and the sodium salt of (p-tolylsulfonyl)nitromethane[17] (10.4 g, 44 mmol) in dimethyl sulfoxide (DMSO) (20 cm³) was stirred at room temperature under nitrogen for 24 h and then added to ice–water and acidified (pH 1) with 2.4 mol dm⁻³ HCl. The organic products were extracted into dichloromethane. The extract was washed with water adjusted to pH ∼4, and then rapidly washed with 5% aq. NaOH. The separated dichloromethane layer was dried (Na₂SO₄) and concentrated. Column chromatography (silica gel; dichloromethane) followed by recrystallization from 95% ethanol afforded *compound* 2 (3.50 g, 48%), m.p. 107–108 °C; δ_H(CDCl₃) 7.9–7.0 (9 H, m), 5.70 1 H, dd, *J* 10 and 4), 3.7–3.4 (2 H, m) and 2.50 (3 H, s) (Found: C, 59.2; H, 5.0; N, 4.6. $C_{15}H_{15}NO_4S$ requires C, 59.00; H, 4.95; N, 4.59%).

1-*Nitro*-1-(*phenylsulfonyl*)*nonane* 3.—A mixture of 1-iodo-octane (2.13 g, 8.88 mmol) and the sodium salt of (phenyl-sulfonyl)nitromethane (8.1 g, 36.3 mmol) in hexamethylphos-phoric triamide (HMPA) (18 cm³) was stirred at room temperature under nitrogen for 14 h and then worked up as described for compound 2 to afford *compound* 3 (1.0 g, 36%), m.p. 49–51 °C; δ_H(CDCl₃) 8.0–7.5 (5 H, m), 5.49 (1 H, dd, *J* 8 and 6), 2.1–2.4 (2 H, m), 1.5–1.1 (12 H, m) and 0.87 (3 H, skewed t) (Found: C, 57.5; H, 7.5; N, 4.4. $C_{15}H_{23}NO_4S$ requires C, 57.49; H, 7.40; N, 4.47%).

Ethyl 3-*Nitro*-3-(*phenylsulfonyl*)*propionate* 4.—A mixture of ethyl bromoacetate (0.494 g, 2.96 mmol) and the sodium salt of (phenylsulfonyl)nitromethane (2.7 g, 12.1 mmol) in HMPA (6 cm³) was stirred at room temperature under nitrogen for 15 h and then worked up as described for compound 2 to yield *compound* 4 (0.35 g, 41%), m.p. 84–85 °C; δ_H([²H₆]DMSO + CDCl₃) 8.0–7.5 (5 H, m), 6.36 (1 H, dd, *J* 8 and 6), 4.16 (2 H, q, *J* 7), 3.5–3.3 (2 H, m) and 1.25 (3 H, t, *J* 7) (Found: C, 45.9; H, 4.7; N, 4.6. $C_{11}H_{13}NO_6S$ requires C, 45.99; H, 4.56; N, 4.88%).

5-*Nitro*-5-(*phenylsulfonyl*)*pentan*-2-*one* 5 *and* 5-*Nitro*-5-(*phenylsulfonyl*)*nonane*-2,8-*dione* 6.—A solution of (phenyl-sulfonyl)nitromethane (2.0 g, 10 mmol), methyl vinyl ketone (1.42 g, 20 mmol) and triethylamine (0.1 g) in tetrahydrofuran (THF) (5 cm³) was stirred at 0 °C for 1 h and then at room temperature for 23 h. The reaction mixture was added to ice–water. After acidification (pH 1) the mixture was extracted with dichloromethane, and the extract was dried with sodium sulfate and concentrated. Column chromatography [silica gel; hexane–ethyl acetate (6:4)] followed by recrystallization from 95% ethanol afforded *compound* 5 (1.0 g, 37%) and *compound* 6 (1.1 g, 32%) as separate fractions.

Compound 5: m.p. 61–62 °C; δ_H(CDCl₃) 8.0–7.5 (5 H, m), 5.8–5.6 (1 H, m), 2.8–2.3 (4 H, m) and 2.14 (3 H, s) (Found: C, 48.4; H, 4.9; N, 5.0. $C_{11}H_{13}NO_5S$: C, 48.70; H, 4.83; N, 5.16%).

Compound 6: m.p. 100–101 °C; δ_H(CDCl₃) 8.0–7.4 (5 H, m), 3.0–2.3 (8 H, m) and 2.17 (6 H, s) (Found: C, 52.8; H, 5.6; N, 4.1. $C_{15}H_{19}NO_6S$ requires C, 52.78; H, 5.61; N, 4.10%).

Typical Procedures for Desulfonylation.—An aq. solution (5 cm³) containing K₂CO₃ (0.138 g, 1.0 mmol) and Na₂S₂O₄ (0.348 g, 2.0 mmol) was added dropwise to a mixture of α-nitro sulfone (1.0 mmol) and octylviologen (0.1 mmol) in di-chloromethane (30 cm³)–water (5 cm³) under nitrogen. The mixture was stirred for 3 h at 35 °C and worked up as usual.[8] A control experiment was carried out without the viologen. For isolated yields, the reactions were carried out with α-nitro sulfones (4 mmol), the viologen (0.2 mmol), K₂CO₃ (3 mmol) and Na₂S₂O₄ (8 mmol) in CH₂Cl₂ (30 cm³)–water (15 cm³). After work-up, the products were purified by Kugelrohr

distillation or column chromatography. ^{1}H NMR data of the desulfonylated products are the following:

PhCH$_2$CH$_2$NO$_2$ [18] δ_H 7.4–7.1 (5 H, m), 4.59 (2 H, t, J 7) and 3.29 (2 H, t, J 7); C$_9$H$_{19}$NO$_2$ [19] δ_H 4.37 (2 H, t, J 7), 2.2–1.8 (2 H, m), 1.5–1.0 (12 H, m) and 0.87 (3 H, skewed t); EtO$_2$-CCH$_2$CH$_2$NO$_2$ [20] δ_H 4.66 (2 H, t, J 7), 4.16 (2 H, q, J 7), 2.96 (2 H, t, J 7) and 1.25 (3 H, t, J 7); MeCOCH$_2$CH$_2$CH$_2$NO$_2$ [21] δ_H 4.34 (2 H, t, J 7), 2.10 (3 H, s) and 2.7–2.0 (4 H, m); (Me-COCH$_2$CH$_2$)$_2$CHNO$_2$ [22] δ_H 4.53 (1 H, quintet, J 7), 2.15 (6 H, s) and 2.7–2.0 (8 H, m); 2-acetyl-1-methyl-4-nitrocyclohexan-1-ol δ_H 4.7–4.2 (1 H, m), 3.81 (1 H, d, J 2), 2.8–1.3 (7 H, m), 2.27 (3 H, s) and 1.23 (3 H, s).

Analytical data for 2-acetyl-1-methyl-4-nitrocyclohexan-1-ol (m.p. 86–87 °C): (Found: C, 53.7; H, 7.5; N, 6.9. C$_9$H$_{15}$NO$_4$ requires C, 53.72; H, 7.51; N, 6.96%).

Acknowledgements

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