

Facile Deoxygenation of Phenols and Enols Using Sodium Borohydride–Nickel Chloride

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A facile deoxygenation reaction of phenol and 1,3-dicarbonyl compounds was investigated. Phenols, enolizable 1,3-diketones and 3-ketoesters were converted into the toluene-*p*-sulfonates which were reduced by a sodium borohydride–nickel chloride system to give the deoxygenated aromatic compounds, alcohols and esters, respectively.

Sodium borohydride–transition metal salt systems have been used for efficient reduction of various functional groups.^{1–7} In our investigation, the reduction system also reduced aryl and enol toluene-*p*-sulfonates by using nickel chloride as a transition metal. Reduction of aryl sulfonic esters has been known to give deoxygenated products,⁸ however, aryl toluene-*p*-sulfonates cannot be successfully reduced.^{9,10} On the other hand, reduction of enolizable 1,3-dicarbonyl compounds is less selective and generally gives complicated products.¹¹ We report here a mild deoxygenation reaction of phenols, 1,3-diketones and 3-ketoesters *via* aryl or enol toluene-*p*-sulfonates to produce aromatic compounds, monoalcohols and esters, respectively.

Results and Discussion

The deoxygenation of phenols and enolizable 1,3-dicarbonyl compounds were performed by a two-step reaction. Phenols **1–8**, 3-oxoester **25** and 1,3-diones **26–29** were converted into their corresponding toluene-*p*-sulfonates **9–16**, **30** and **31–34** respectively (Tables 1 and 2). Compounds **4**, **6** and **8** gave ditosyl **12**, **14** and tritosyl **16** derivatives respectively. The aryl or enol tosylates were separated by column chromatography and were reduced with NaBH₄ in the presence of NiCl₂·6H₂O in chloroform–methanol (1:1) or in methanol. The reduction of aryl toluene-*p*-sulfonates gave corresponding aromatic hydrocarbons in practically useful yields (93–96%, Table 1). 2-Naphthyl toluene-*p*-sulfonate **9** was reduced to naphthalene **17** by the NaBH₄–NiCl₂ system without the formation of tetralin, which was reported to form by the hydrogenation of compound **9** in the presence of Raney nickel.⁹ In the reduction of compounds **12** and **16**, toluene-*p*-sulfonamide was not reduced. A ketone was converted into an alcohol and aliphatic sp² carbons were also hydrogenated (**21** and **23**).

Table 2 shows the results of the deoxygenation of a 3-oxoester and 1,3-diketones which gave an ester and alcohols in 68–92% yield. Tosyl derivatives of 1,3-diketones were converted into alcohols with 5 equiv. NaBH₄. Reduction of compound **31** with smaller amounts of NaBH₄ (3 equiv.) gave a mixture of 3-phenylcyclohexanol **36** (40%) and 3-phenylcyclohexanone (60%). This suggests that the enol toluene-*p*-sulfonate is reduced faster than the ketone. Tosylation of compound **29** afforded a mixture of products and compound **34** was isolated in 57% yield from compound **29**. Reduction of the mixture gave product **39** and 4-phenylbutan-2-ol in the ratio of 6:4 in 79% total yield.

The effect of catalysts and hydrogen donors was investigated in the reduction of compound **14**. The aryl toluene-*p*-sulfonate **14** was not reduced by NaBH₄ in the absence of NiCl₂·6H₂O. Moreover, the substrate was not reduced by NaBH₄–CuCl₂·2H₂O, NaBH₄–CoCl₂·6H₂O, NaBH₄–FeCl₃·6H₂O, NaBH₄–CrCl₃·6H₂O, NaBH₄–ZnCl₂, NaBH₄–CuCl, nor NaBH₄–

Pd(AcO)₂. Reaction with LiAlH₄ in THF gave a corresponding phenol 3-hydroxyestra-1,3,5(10)-trienyl toluene-*p*-sulfonate. Pd/C was not effective in the reduction with H₂ or NaBH₄. The result suggests that NiCl₂·6H₂O plays an important role in the hydrogenation of aryl and enol toluene-*p*-sulfonates by NaBH₄. The NaBH₄–transition metal salt systems are adapted to the reduction of alkenes and NiCl₂·6H₂O is known to catalyse the hydrogenation less efficiently than CuCl₂·2H₂O or CoCl₂·6H₂O.² In the present study for the reduction of aryl toluene-*p*-sulfonates, the effect of NiCl₂·6H₂O was clearly observed. It is suggested that nickel boride or nickel–BH₄[–] complex, which is formed *in situ*, coordinates with the π-electrons of the olefinic bonds of arenes or enols. By the hydride addition on the activated sp² carbons from uncoordinated BH₄[–], the toluene-*p*-sulfonate anion may be eliminated to form deoxygenated aromatic compounds or esters. Although a difference of susceptibility to hydride addition has been observed between the C=C double bond and ketone moiety in the reduction of 3-oxoenol toluene-*p*-sulfonates, corresponding alcohols were obtained after the complete reaction.

Experimental

NMR spectra were measured at 270 (¹H) and 67.89 MHz (¹³C) in CDCl₃ containing TMS as an internal standard. *J*-Values in Hz. IR and UV spectra were recorded on a JASCO IR-810 infrared spectrometer and a JASCO UVDEC-460 spectrophotometer. M.p.s were determined on a micro hot-stage and are uncorrected. Thin-layer chromatography was carried out on Kieselgel GF₂₅₄(Merck) of 0.25 mm thickness. Wakogel C-200 (Wako) was used for column chromatography.

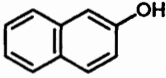
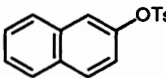
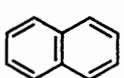
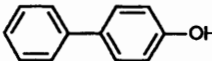
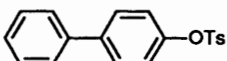
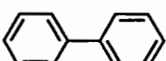
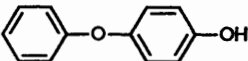
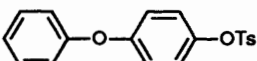
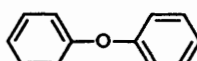
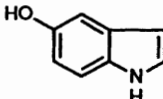
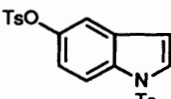
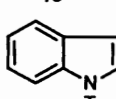
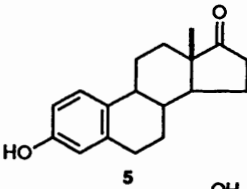
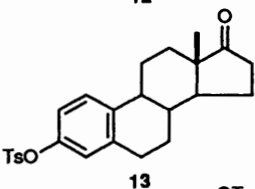
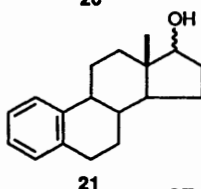
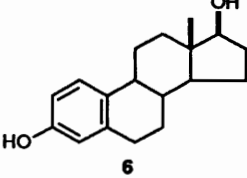
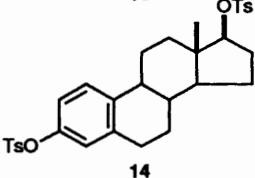
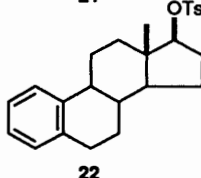
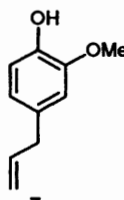
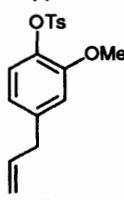
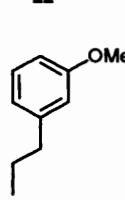
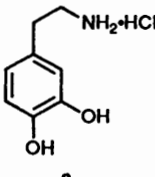
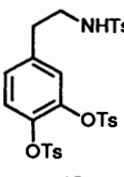
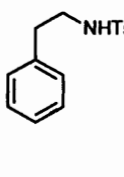
Preparation of Tosyl Derivatives.—Sodium hydride (27 mg, 1.1 mmol) and tosyl chloride (210 mg, 1.1 mmol) were dissolved in 2-naphthol **1** (144 mg, 1 mmol) in dry THF (30 cm³) under Ar and the mixture was kept at room temperature with continuous stirring for 24 h. After addition of brine, the aqueous solution was extracted with AcOEt; the combined organic extracts were washed with NaHCO₃ (10%) and brine. The solution was dried (MgSO₄) and the tosyl derivatives were separated by column chromatography (silica gel, hexane–AcOEt) to yield 2-naphthyl toluene-*p*-sulfonate **9** (285 mg, yield 95.6%).

Compounds **10–13**, **15**, **30** and **34** were prepared similarly.

1-Benzoylprop-1-en-2-yl toluene-*p*-sulfonate **34** was separated from the mixture of tosyl derivatives (yield 57% from 1-benzoylpropan-2-one **29**).

1-Tosylindol-5-yl toluene-*p*-sulfonate **12**; m.p. 149–151 °C; δ_H 2.36 (3 H, s), 2.45 (3 H, s), 6.59 (1 H, dd, *J* 3.7, 0.7), 6.85 (1 H, dd, *J* 8.8, 2.2), 7.22 (1 H, d, *J* 2.2), 7.23 (2 H, d, *J* 8.1), 7.29 (2 H, d, *J*

Table 1 Deoxygenation of phenols *via* the aryl toluene-*p*-sulfonates

Substrate	NaBH ₄ -NiCl ₂	ArOTs	Product	Yield (%) ^a
	20:1			96
	20:1			94
	20:1			94
	20:1			96
	20:1			95
	20:1			93
	20:1			95
	30:1			95

^a Based on ArOTs.

8.1), 7.58 (1 H, d, *J* 3.7), 7.67 (2 H, d, *J* 8.1), 7.73 (2 H, d, *J* 8.1) and 7.84 (1 H, d, *J* 8.8); δ_C 21.58, 21.70, 108.84, 114.11, 11.99, 118.91, 126.81, 127.90, 128.49, 129.75, 129.99, 131.26, 132.28, 133.02, 134.94, 145.33, 145.36 and 145.64; $\nu(\text{KBr})/\text{cm}^{-1}$ 3132, 2925, 1594, 1440, 1368, 1180, 1128 and 1085; $\lambda_{\text{max}}/\text{nm}$ 218 (log ϵ 4.12) and 250 (log ϵ 3.82).

2-Methoxy-4-prop-2-enylphenyl toluene-*p*-sulfonate **15**; oil; δ_H 2.42 (3 H, s), 3.33 (2 H, d, *J* 6.5), 3.52 (3 H, s), 5.05 (1 H, dd, *J* 6.8, 1.9), 5.09 (1 H, d, *J* 1.9), 5.90 (1 H, m), 6.66 (1 H, d, *J* 2.0), 6.68 (1 H, dd, *J* 8.8, 2.0), 7.03 (1 H, d, *J* 8.8), 7.28 (2 H, d, *J* 8.1) and 7.72 (2 H, d, *J* 8.1); δ_C 21.52, 39.85, 55.32, 112.75, 116.25, 120.38, 123.56, 128.45, 129.20, 133.09, 136.56, 140.23, 144.87 and 151.41; $\nu(\text{neat})/\text{cm}^{-1}$ 3055, 2970, 1634, 1595, 1370, 1288, 1260, 1195 and 1175; $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 228 (log ϵ 3.70).

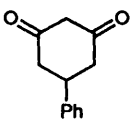
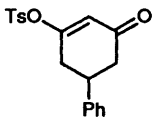
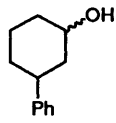
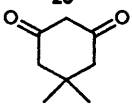
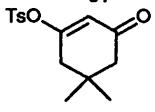
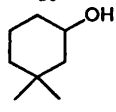
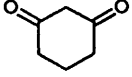
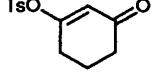
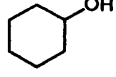
1,2-Bis(ethoxycarbonyl)vinyl toluene-*p*-sulfonate **30**; oil; δ_H

1.23 (6 H, m), 2.47 (3 H, s), 4.18 (4 H, m), 6.17 and 6.71 (1 H, s, *Z* and *E*), 7.39 (2 H, d, *J* 8.1) and 7.82 (2 H, d, *J* 8.1); δ_C 13.54, 13.65, 13.77, 21.53, 21.60, 61.37, 61.55, 62.35, 62.58, 118.85, 120.44, 128.34, 128.49, 129.55, 129.85, 131.76, 133.16, 143.18, 144.86, 145.55, 146.14, 160.15, 160.89, 162.08 and 163.13; $\nu(\text{KBr})/\text{cm}^{-1}$ 3070, 2986, 1730, 1647, 1595, 1472, 1373, 1329 and 1272; $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 225 (log ϵ 4.47).

Compound **34**; m.p. 32–34 °C; δ_H 2.23 (6 H, s), 6.28 (1 H, s), 7.20 (2 H, d, *J* 7.0), 7.35 (2 H, d, *J* 7.0), 7.36 (1 H, m), 7.48 (1 H, t, *J* 7.0), 7.64 (2 H, d, *J* 8.1), 7.69 (2 H, d, *J* 8.1); δ_C 21.32, 21.65, 115.92, 127.88, 128.37, 128.46, 130.20, 131.09, 132.80, 136.84, 145.16, 153.87 and 188.19; $\nu(\text{KBr})/\text{cm}^{-1}$ 3054, 2924, 1672, 1639, 1594, 1386, 1195, 1180, 1135 and 1089; $\lambda_{\text{max}}(\text{EtOH})/\text{nm}$ 243 (log ϵ 4.12) and 308 (log ϵ 4.25).

Estra-1,3,5(10)-triene-3,17-diol **6** (272 mg, 1 mmol), tosyl

Table 2 Deoxygenation of 3-oxoester and 1,3-diketones *via* enol toluene-*p*-sulfonates

Substrate	NaBH ₄ -NiCl ₂	ROTs	Product	Yield (%) ^a	
EtO ₂ CCH=C(ONa)CO ₂ Et		5:0.5	EtO ₂ CCH=C(OTs)CO ₂ Et	(CH ₂ CO ₂ Et) ₂	92
25 		5:1	30 	35 	82
26 		5:1	31 	36 	68
27 		5:1	32 	37 	77
28		5:1	33	38	79
PhCOCH ₂ COCH ₃		5:1	PhCOCH=C(OTs)CH ₃	PhCH(CH ₂) ₂ CH ₃ OH	79
29			34	39	

^a Based on ROTs.

chloride (420 mg, 2.2 equiv.) and 4-dimethylpyridine (250 mg) were dissolved in pyridine (5.0 cm³) and the solution was allowed to stand at room temperature for 2 h. Aqueous HCl (10%; 20 cm³) was poured into the mixture and the solution was extracted with AcOEt and the organic portion washed with brine and dried (MgSO₄). Estra-1,3,5-(10)-triene-3,17-diyl toluene-*p*-sulfonate **14** was isolated by silica gel column chromatography (560 mg, yield 96.5%).

Compounds **8** and **26–28** were similarly treated to yield products **16** and **31–33** respectively.

4-[2-(*p*-Tolyl)sulfonylaminoethyl]-1,2-phenylene bis(toluene-*p*-sulfonate) **16**; m.p. 103–105 °C; δ_H 2.38 (3 H, s), 2.42 (3 H, s), 2.43 (3 H, s), 2.70 (2 H, t, *J* 7.3), 3.10 (2 H, m), 5.30 (1 H, br s), 6.96 (2 H, m), 7.07 (1 H, d, *J* 10.2), 7.27 (6 H, m) and 7.70 (6 H, m); δ_C 21.35, 21.60 (2 C), 34.98, 43.64, 124.12, 124.46, 126.87, 128.13, 128.29, 128.34, 128.42, 128.46, 129.64, 129.70, 129.82, 131.79, 136.51, 138.53, 139.60, 140.89, 143.50, 145.64 and 145.71; ν(KBr)/cm⁻¹ 3260, 3050, 2930, 1592, 1498, 1370, 1300, 1176 and 1080; ν_{max}(EtOH)/nm 228 (log ε 4.40).

3-Oxo-5-phenylcyclohex-1-enyl toluene-*p*-sulfonate **31**; m.p. 49–51 °C; δ_H 2.48 (3 H, s), 2.60 (2 H, m), 2.75 (2 H, m), 3.37 (1 H, m), 5.90 (1 H, s), 7.20 (2 H, d, *J* 8.1), 7.3 (5 H, m) and 7.82 (2 H, d, *J* 8.1); δ_C 21.78, 36.32, 39.09, 43.49, 116.51, 126.60, 127.36, 128.26, 128.91, 130.17, 132.36, 141.53, 146.26, 167.23 and 197.77; ν(KBr)/cm⁻¹ 3064, 2958, 1676, 1635, 1595, 1375, 1193, 1178, 1107 and 1080; λ_{max}(EtOH)/nm 228 (log ε 4.35), 254 (log ε 4.41).

5,5-Dimethyl-3-oxocyclohex-1-enyl toluene-*p*-sulfonate **32**; oil; δ_H 1.03 (6 H, s), 2.19 (2 H, s), 2.35 (2 H, s), 2.47 (3 H, s), 5.80 (1 H, s), 7.38 (2 H, d, *J* 8.1) and 7.81 (2 H, d, *J* 8.1); δ_C 21.53, 27.75, 32.63, 42.18, 50.28, 115.66, 128.02, 129.96, 132.19, 146.02, 166.42 and 198.43; ν(neat)/cm⁻¹ 3060, 2950, 1678, 1630, 1596, 1360, 1190 and 1175; λ_{max}(EtOH)/nm 223 (log ε 3.86), 252 (log ε 3.76).

3-Oxocyclohex-1-enyl toluene-*p*-sulfonate **33**; 101–105 °C; δ_H 1.95 (2 H, m), 2.32 (2 H, m), 2.47 (3 H, s), 2.48 (2 H, m), 5.81 (1 H, s), 7.39 (2 H, d, *J* 8.1) and 7.83 (2 H, d, *J* 8.1); δ_C 20.71, 21.67, 28.50, 36.32, 116.64, 128.13, 130.06, 132.33, 146.13, 168.14 and 198.60; ν(KBr)/cm⁻¹ 1672, 1659, 1622, 1590, 1382, 1193, 1105 and 1080; ν_{max}(EtOH)/nm 228 (log ε 4.41).

*Reduction of Aryl Toluene-*p*-sulfonates by NaBH₄-NiCl₂.*—2-Naphthyl toluene-*p*-sulfonate **9** (150 mg, 0.5 mmol) and NiCl₂·6H₂O (120 mg, 1 equiv.) was dissolved in CHCl₃-MeOH (10 cm³; 1:1) and NaBH₄ (380 mg, 20 equiv.) was added portionwise with ice cooling. The solution immediately became dark with evolution of hydrogen gas. The black precipitates were filtered off and washed with methanol and the filtrate and washings were combined and condensed under reduced pressure. To the residual solution, HCl (10%) and water were added and the solution was extracted with ether; the extract was washed with brine, dried (MgSO₄) and evaporated. Further purification was performed by silica gel column chromatography (hexane-AcOEt) to obtain naphthalene **17** (61.4 mg, 96.0%).

Compounds **9–16** were reduced similarly (except for the amounts of NaBH₄ and NiCl₂·6H₂O used) (see Table 1).

Estra-1,3,5(10)-trien-17-ol **21** (a mixture of 17-α and β isomers, 1:9); δ_H 0.70 and 0.78 (3 H, s, α and β), 1.2–2.5 (13 H, m), 2.87 (2 H, m), 3.73 and 3.81 (1 H, t, *J* 8.1, d, *J* 7.6, β and α), 7.14 (3 H, m) and 7.29 (1 H, d, *J* 5.9); ν(KBr)/cm⁻¹ 3400, 2940, 1480, 1382, 1241, 1135 and 1051.

Estra-1,3,5(10)-trien-17-yl toluene-*p*-sulfonate **22**; m.p. 161–163 °C; δ_H 0.83 (3 H, s), 1.1–2.3 (13 H, m), 2.46 (3 H, s), 2.84 (2 H, m), 4.35 (1 H, t, *J* 7.7), 7.10 (3 H, m), 7.24 (1 H, d, *J* 7.0), 7.34 (2 H, d, *J* 8.0) and 7.80 (2 H, d, *J* 8.0); δ_C 11.75, 23.05, 25.74, 27.03, 27.75, 29.40, 29.74, 36.16, 38.22, 43.29, 44.21, 49.21, 89.84, 125.31, 125.68, 125.73, 127.87 (2 C), 129.04, 129.72 (2 C), 136.50, 139.83, 144.45 and 147.30; ν(KBr)/cm⁻¹ 2920, 1358, 1350, 1194, 1171 and 1095; λ_{max}(EtOH)/nm 220 (log ε 3.96).

*Reduction of Enol Toluene-*p*-sulfonates by NaBH₄-NiCl₂.*—Compound **30** (170 mg, 0.5 mmol) and NiCl₂·6H₂O (60 mg, 0.5 equiv.) was dissolved in MeOH and NaBH₄ (95 mg, 5 equiv.) was added by portions with ice cooling. After the filtration, the washings were combined and condensed under reduced pressure. The residual solution was extracted with ether, dried (MgSO₄) and purified by column chromatography to yield dimethyl succinate **35** (80 mg, yield 92%).

Compounds **31–34** were reduced similarly (1.0 equiv. of NiCl₂·6H₂O was added) to yield compounds **36–39** respec-

tively. Cyclohexanol **38** was isolated by distillation (b.p. 158–162 °C).

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