[Chem. Pharm. Bull.
27(1) 198-203 (1979)]

UDC 547.332.04 : 547.291'233.3.04

Formic Acid Reduction. XXVII.¹⁾ Selective Reduction of Carbon-Carbon Double Bonds conjugated with Nitro and Sulfonyl Groups

KATSUMI NANJO and MINORU SEKIYA

Shizuoka College of Pharmacy²⁾

(Received July 21, 1978)

Selective reduction of carbon-carbon double bond conjugated with nitro group has been demonstrated with a number of examples by the use of the TEAF reagent (triethylamine-formic acid azeotrope) in N,N-dimethylformamide. In addition, formic acid reduction of carbon-carbon double bond conjugated with both sulfonyl and other electron-withdrawing groups has been exemplified by the same manner.

Keywords—formic acid redn; selective redn; formic acid-triethylamine azeotrope; conjugated nitroalkene; nitroalkane; α,β -unsatd. sulfone

In several papers^{1,3)} from this laboratory, it has been shown that the formic acid reduction provides a practical method effective for selective reduction of electron-deficient carbon-carbon double bonds. The formic acid reduction of carbon-carbon double bonds conjugated with carbonyl,^{3a)} cyano,^{1,3b)} nitro^{3b)} and sulfonyl^{3b)} group have been informed previously, but the last two only in our short communication.^{3b)} We, therefore, wish to disclose in detail together with extensive studies.

An attractive route for synthesis of nitroalkanes involves selective reduction of conjugated nitroalkenes, the method for which previously reported includes catalytic hydrogenation⁴⁾ and reduction with complex metal hydrides such as sodium borohydride,⁵⁾ lithium borohydride⁶⁾ and sodium trimethoxyborohydride.⁶⁾ Extensive investigation of formic acid reduction of conjugated alkenes has developed a successful procedure for selective reduction of the carbon-carbon double bonds of conjugated nitroalkenes.

Conjugated nitroalkenes were efficiently reduced to the corresponding nitroalkanes by the use of the formic acid-triethylamine azeotrope (TEAF reagent⁷⁾) in N,N-dimethylformamide (DMF) at 100–135°. The results of reduction of a number of nitrostyrenes are

Chart 1

summarized in Table I. The failure of unsubstituted β -nitrostyrene to undergo the reduction

- 1) Part XXVI: K. Nanjo, K. Suzuki, and M. Sekiya, *Chem. Pharm. Bull.* (Tokyo), **25**, 2396 (1977).
- 2) Location: 2-2-1 Oshika, Shizuoka-shi 422, Japan.
- 3) a) M. Sekiya and C. Yanaihara, *Chem. Pharm. Bull.* (Tokyo), **17**, 747 (1969); M. Sekiya and K. Suzuki, *Chem. Pharm. Bull.* (Tokyo), **18**, 1530 (1970); T. Okukawa, K. Suzuki, and M. Sekiya, *Chem. Pharm. Bull.* (Tokyo), **22**, 448 (1974); K. Suzuki, H. Fukawa, T. Okukawa, and M. Sekiya, *Chem. Pharm. Bull.* (Tokyo), **24**, 607 (1976); b) K. Nanjo, K. Suzuki, and M. Sekiya, *Chemistry Letters*, **1976**, 1169.
- 4) R.E. Harmon, J.L. Parsons, D.W. Cooke, S.K. Gupta, and J. Schoolenberg, *J. Org. Chem.*, **34**, 3684 (1969).
- 5) A. Hassner and C. Heathcock, *J. Org. Chem.*, **29**, 1350 (1964); A.I. Meyers and J.C. Sircar, *J. Org. Chem.*, **32**, 4134 (1968); A. Hassner, J.M. Larkin, and J.E. Dowd, *J. Org. Chem.*, **33**, 1733 (1968).
- 6) H. Shechter, D.E. Ley, and E.B. Roberson, Jr., *J. Am. Chem. Soc.*, **78**, 4984 (1956).
- 7) K. Narita and M. Sekiya, *Chem. Pharm. Bull.* (Tokyo), **25**, 135 (1977).

TABLE I. Formic Acid Reduction^{a)} of β -Nitrostyrenes
$$\begin{array}{c}
 \text{Ph} \\
 \diagup \\
 \text{C}=\text{C} \begin{array}{l} \diagup \text{NO}_2 \\ \diagdown \text{R}_2 \end{array} \\
 \diagdown \text{R}_1 \\
 \text{Ia-f}
 \end{array}
 \xrightarrow{\text{TEAF-DMF}}
 \begin{array}{c}
 \text{Ph} \\
 \diagup \\
 \text{CHCH} \begin{array}{l} \diagup \text{NO}_2 \\ \diagdown \text{R}_2 \end{array} \\
 \diagdown \text{R}_1 \\
 \text{IIa-f}
 \end{array}$$

Compd. No.	R ₁	R ₂	Reaction temp. (°C) ^{b)}	Reaction time (hr)	Yield (%) ^{c)}
Ia	H	H	100—105	4.5	0 ^{d)}
Ib	H	CH ₃	120—122	6.0	70.0
Ic	H	C ₂ H ₅	115—120	14.0	83.5
Id	H	CH ₂ Ph	114—116	4.5	26.5 ^{e)}
Ie	H	Ph	130—135	28.0	59.3
If	Ph	H	130—135	8.0	57.3

a) Substrate: 0.02 mol, TEAF: 5.2 g (0.06 mol as HCO₂H), DMF: 40 ml.

b) Temperature effecting considerable evolution of carbon dioxide.

c) Based on the product isolated.

d) Resulted in polymerization.

e) Starting material was recovered in 63.4% yields.

is attributed to its polymerization. As previously known,⁸⁾ α,β -unsaturated nitroalkenes are susceptible to the base-catalyzed polymerization. The reduction in such basic medium is accompanied by the competing polymerization which, as illustrated in Table I, apparently depends on steric influence of the olefinic substituents.

In extensive studies, 3,6-dinitrocoumarin (III) was reduced at room temperature to give 2-(2-nitroethyl)-4-nitrophenol (IV) in 37% yield. Process of this reaction may involve hydrolysis and successive decarboxylation after the reduction of the 3,4-double bond.

Chart 2

2,4-Dinitrostilbene did not undergo the reduction, whereas α -(*p*-nitrophenyl)cinnamionitrile (V) was reduced at 90—91° to give α -(*p*-nitrophenyl)- β -phenylpropionitrile (VI) in 73% yield.

Chart 3

Nature of electron-withdrawing group, with which carbon-carbon double bond is conjugated, is responsible for reactivity for the formic acid reduction. As reported previously,^{3b)} effect of the electron-withdrawing groups is in the order; NO₂ > CN > SO₂C₆H₅ > COC₆H₅. Carbon-carbon double bonds conjugated with a nitro group can undergo the formic acid reduction, as indicated in the foregoing. However, groups such as cyano, sulfonyl, carbonyl

8) H. Wieland and E. Sakellarios, *Ber.*, **52**, 898 (1919).

Further experiments included an examination of the formic acid reduction of a series of alkenes conjugated with sulfonyl group. Results are summarized in Table II. β -Phenyl-

(EtOH), mp 175—176° (lit.¹⁵) mp 175—176°; 2,4-dinitrostilbene: Yellow prisms (AcOH), mp 137—138° (lit.¹⁶) mp 138°).

Formic Acid Reduction of β -Nitrostyrenes (Ia—f) (Table I) **General Procedure**—A mixture of 0.02 mol of Ia—f and 5.2 g (0.06 mol based on HCOOH) of TEAF in 40 ml of DMF was stirred at appropriate temperature. Dry air free from CO₂ was introduced in order to check evolution of CO₂ by saturated Ba(OH)₂ solution. After CO₂ evolution almost ceased, DMF and excess TEAF were distilled off under reduced pressure. The residue was dissolved in benzene. The benzene solution was washed with water and dried over anhyd. MgSO₄. Evaporation of benzene under reduced pressure gave the crude reduction product. Recrystallization or distillation under reduced pressure gave pure reduction product. In the run with If, the product was purified by passing through a basic alumina column using benzene-ethyl acetate as an eluent. Physical and analytical data of the reduction products are summarized in Table III.

Formic Acid Reduction of 3,6-Dinitrocoumarin (III)—To a solution of 1.4 g (0.006 mol) of III, 1.56 g (0.018 mol based on HCOOH) of TEAF was added at room temperature with stirring. Evolution of CO₂ almost ceased after 2 hr. DMF and excess TEAF were distilled off under reduced pressure. The residual oil was dissolved in benzene and the benzene solution was washed with water and dried over anhyd. MgSO₄. After evaporation of benzene, the resulting oily material was chromatographed on silica gel column using benzene-ethyl acetate=100/1 as an eluent, to give 0.48 g (37%) of IV as yellow powder, mp 133—135°. The structure of this compound was assigned by its IR and NMR spectra. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3250 (OH), 1550

TABLE III. Physical and Analytical Data of the Reduction Products

<div><div><div><div><div>Ph</div><div>CHCH</div><div>NO₂</div></div><div><div>R₁</div><div></div><div>R₂</div></div></div></div><div>IIb—f</div></div>								
Compd. No.	R ₁	R ₂	Appearance (Recryst. solvent)	mp (°C) or bp (°C/mmHg)	Formula	Analysis (%)		
						Calcd. (Found)		
						C	H	N
IIb	H	CH ₃	Liquid	85—95/0.45	C ₉ H ₁₁ NO ₂	65.44 (65.01)	6.71 (6.52)	8.48 (8.32)
IIc	H	C ₂ H ₅	Liquid	85—100/0.3	C ₁₀ H ₁₃ NO ₂	67.02 (67.50)	7.31 (7.30)	7.82 (7.65)
IId	H	CH ₂ Ph	Needles (EtOH)	102.5—103.5	C ₁₅ H ₁₅ NO ₂	74.66 (74.52)	6.27 (6.28)	5.81 (5.83)
IIe	H	Ph	Liquid	120—124/0.04	C ₁₄ H ₁₃ NO ₂	73.99 (74.35)	5.77 (5.75)	6.16 (6.12)
IIf	Ph	H	Prisms (EtOH)	70—71	C ₁₄ H ₁₃ NO ₂	73.99 (74.14)	5.77 (5.88)	6.16 (6.17)

Compd. No.	IR ν_{max} (cm ⁻¹) NO ₂	NMR (δ) ^{a)}
IIb	1540	1.43 (d, 2H, CH ₃ -, <i>J</i> =6.0 Hz), 2.72—3.44 (m, 2H, CH ₂ <, <i>J</i> =7.0 Hz), 4.40—4.48 (sx, 1H, -CH<, <i>J</i> =7.0 Hz), 7.18 (s, 5H, C ₆ H ₅)
IIc	1545	0.98 (t, 3H, CH ₃ CH ₂ -, <i>J</i> =8.0 Hz), 1.52—2.30 (m, 2H, CH ₃ CH ₂ <), 2.80—3.50 (m, 2H, CH ₂ <), 4.42—4.88 (m, 1H, -CH<), 7.27 (s, 5H, C ₆ H ₅)
IId	1550	2.85—3.52 (m, 4H, two CH ₂ <), 4.68—5.18 (m, 1H, -CH<), 7.22 (s, 10H, aromatic protons)
IIe	1550	3.05—4.90 (m, 2H, CH ₂ <), 5.58 (q, 1H, -CH<, <i>J</i> =6.0, 9.0 Hz), 7.35 (s, 5H, C ₆ H ₅), 7.15 (s, 5H, C ₆ H ₅)
IIf	1550	4.77 (q, 1H, -CH<, <i>J</i> =7.0, 9.0 Hz), 5.23 (d, 2H, CH ₂ <, <i>J</i> =7.0 Hz), 7.20 (s, 10H, two C ₆ H ₅)

a) IIb—f were measured in CDCl₃.

- 15) B. Prager, P. Jacobson, P. Schmidt, and D. Stern (eds.), "Beilsteins Handbuch der Organischen Chemie," 4th ed., Vol. 9, Deutschen Chemischen Gesellschaft, 1926, p. 694.
 16) K.R. Hargreaves and A. McGookin, *J. Soc. Chem. Ind.* (London), **69**, 186 (1950).

and 1520 (NO₂). NMR (in DMSO-*d*₆) δ : 3.30 (t, 2H, -CH₂CH₂NO₂, $J=7.0$ Hz), 4.30 (t, 2H, -CH₂CH₂NO₂, $J=7.0$ Hz), 7.00 (d, 1H, aromatic proton, $J=7.0$ Hz), 8.02 (d, 1H, aromatic proton, $J=7.0$ Hz), 8.08 (s, 1H, aromatic proton), 11.40 (broad s, 1H, OH).

Formic Acid Reduction of α -(*p*-Nitrophenyl)cinnamionitrile (V)—A mixture of 2.5 g (0.01 mol) of V and 2.6 g (0.03 mol based on HCOOH) of TEAF in 20 ml of DMF was stirred at 90–91°. Evolution of CO₂ almost ceased after 6 hr. The reaction solution was concentrated under reduced pressure to remove DMF and excess TEAF. The resulting residue was dissolved in benzene and the benzene solution was washed with water and dried over anhyd. MgSO₄. Evaporation of benzene gave the crude reduction product, which was chromatographed on silica gel column using benzene–hexane=5/1 as an eluent to give 1.85 g (72.2%) of VI. Recrystallization from EtOH gave yellow prisms, mp 91–93°. Anal. Calcd. for C₁₅H₁₂N₂O₂: C, 71.41; H, 4.80; N, 11.11. Found: C, 71.62; H, 4.82; N, 11.05. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 2230 (CN), 1520 and 1340 (NO₂). NMR (in CDCl₃) δ : 3.20 (d, 2H, -CH₂-, $J=7.0$ Hz), 4.14 (t, 1H, -CH<, $J=7.0$ Hz), 6.89–7.33 (m, 5H, C₆H₅), 7.70 (AA'XX' q, 4H, *p*-NO₂C₆H₄, $J_{\text{AX}}=48$ Hz, $J_{\text{A'X}}=9.0$ Hz).

α,β -Unsaturated Sulfonyl Compounds—Compounds, VIIa and VIId, were prepared by condensation of the corresponding active methylene compounds and benzaldehyde in benzene or toluene using ammonium

TABLE IV. Physical and Analytical Data of the Reduction Products

$\text{PhCH}_2\text{CH} \begin{array}{l} \nearrow \text{X} \\ \searrow \text{SO}_2\text{R} \end{array}$ VIIa–e						
Compd. No.	R	X	Appearance (Recryst. solvent)	mp (°C)	Formula	Analysis (%)
						Calcd. (Found) C H N
VIIa	Ph	CO ₂ Et	Prisms (EtOH)	97–98	C ₁₇ H ₁₈ SO ₄ ·1/2H ₂ O	62.40 5.81 (62.59 5.53)
VIIb	Ph	COCH ₃	Plates (EtOH)	97–99	C ₁₆ H ₁₆ SO ₃	66.66 5.59 (66.80 5.55)
VIIc	Ph	COPh	Needles (MeOH)	137.5–138	C ₂₁ H ₁₈ SO ₃	71.99 5.59 (71.90 5.22)
VIIId	CH ₃	COPh	Needles (MeOH)	137–138	C ₁₆ H ₁₆ SO ₃	66.66 5.59 (66.40 5.58)
VIIe	Ph	CONH ₂	Prisms (AcOH)	199–200	C ₁₅ H ₁₅ NSO ₃	62.28 5.23 4.84 (61.88 5.21 5.03)

Compd. No.	IR ν_{max} (cm ⁻¹)	NMR (δ) ^{a)}
VIIa	1730 (CO), 1290, 1130 (SO ₂)	0.96 (t, 3H, CH ₃ -, $J=7.0$ Hz), 3.28 (d, 2H, -CH ₂ CH-, $J=10.0$ Hz), 3.78–4.33 (m, 3H, -CH< and CH ₃ CH ₂ O-), 7.19 (s, 5H, C ₆ H ₅), 7.53–8.00 (m, 5H, C ₆ H ₅ SO ₂ -)
VIIb	1750 (CO), 1300, 1140 (SO ₂)	2.16 (s, 3H, CH ₃ -), 3.17 (d, 1H, >C< $\begin{smallmatrix} \text{H}_a \\ \text{H}_b \end{smallmatrix}$, $J=9.0$ Hz), 3.21 (d, 1H, >C< $\begin{smallmatrix} \text{H}_a \\ \text{H}_b \end{smallmatrix}$, $J=6.0$ Hz), 4.55 (q, 1H -CH<, $J=6.0, 9.0$ Hz), 6.95–7.35 (m, 5H, C ₆ H ₅), 7.50–8.00 (m, 5H, C ₆ H ₅ SO ₂ -)
VIIc	1665 (CO), 1305, 1150 (SO ₂)	3.36 (d, 2H, CH ₂ <, $J=7.0$ Hz), 6.06 (t, 1H, -CH<, $J=7.0$ Hz), 7.14 (s, 5H, C ₆ H ₅), 7.36–7.96 (m, 10H, C ₆ H ₅ CO and C ₆ H ₅ SO ₂)
VIIId	1670 (CO), 1310, 1130 (SO ₂)	3.02 (s, 3H, CH ₃ -), 3.56 (d, 2H, CH ₂ <, $J=7.0$ Hz), 5.12 (t, 1H, -CH<, $J=7.0$ Hz), 7.16 (s, 5H, C ₆ H ₅), 7.30–7.85 (m, 5H, C ₆ H ₅ CO)
VIIe	3400, 3300, 3250 3200 (NH ₂) 1705, 1675 (CO), 1298, 1130 (SO ₂)	3.14 (d, 2H, -CH ₂ CH<, $J=8.0$ Hz), 4.42 (t, 1H, -CH ₂ CH-, $J=8.0$ Hz), 7.22 (s, 5H, C ₆ H ₅), 7.52–8.08 (m, 7H, C ₆ H ₅ SO ₂ and NH ₂)

a) VIIc and VIIe were measured in DMSO-*d*₆, and others were in CDCl₃.

acetate-acetic acid or piperidine-acetic acid as catalyst. VIIb, VIIc, VIIE, β,β -bis(phenylsulfonyl)styrene and β -phenylsulfonylstyrene were prepared according to the method reported in the literature cited below. VIIa: Liquid, NMR (in CDCl_3) δ : 1.16 (t, 3H, $-\text{CH}_2\text{CH}_3$, $J=7.0$ Hz), 4.22 (q, 2H, $-\text{CH}_2\text{CH}_3$, $J=7.0$ Hz), 7.42 (s, 5H, C_6H_5), 7.52—7.99 (m, 6H, $\text{C}_6\text{H}_5\text{SO}_2-$ and $-\text{CH}=\text{}$); VIIb: Needles (EtOH), mp 101—101.5° (lit.¹⁷) mp 90°; VIIc: Plates (EtOH), mp 134—136.5° (lit.¹⁸) mp 137—138°; VIId: Needles (AcOH), mp 133—136°. *Anal.* Calcd. for $\text{C}_{16}\text{H}_{14}\text{O}_3\text{S}$: C, 67.12; H, 4.93. Found: C, 67.32; H, 4.72; VIIE: Colorless powder (EtOH), mp 185—186° (lit.¹⁷) mp 192°; β,β -Bis(phenylsulfonyl)styrene: Slender prisms (EtOH), mp 171—173° (lit.¹⁹) mp 176°; β -Phenylsulfonylstyrene: Needles (iso- Pr_2O), mp 72—73° (lit.²⁰) mp 75—76°.

Formic Acid Reduction of α,β -Unsaturated Sulfonyl Compounds (VIIa—e) (Table II) General Procedure—A mixture of 0.02 mol of VIIa—e and 5.2 g (0.06 mol based on HCOOH) of TEAF in 40 ml of DMF was stirred at appropriate temperature (Table II). After CO_2 evolution almost ceased, DMF and excess TEAF were distilled off under reduced pressure. The resulting residue was dissolved in benzene or ethyl acetate and washed with water. The solution was dried over anhyd. MgSO_4 . Evaporation of the solvent under reduced pressure gave the crude reduction product. Recrystallization or chromatography on silica gel column gave pure reduction product. Physical and analytical data of the reduction products are summarized in Table IV.

Formic Acid Reduction of β,β -Bis(phenylsulfonyl)styrene—A mixture of 0.77 g (0.002 mol) of β,β -bis(phenylsulfonyl)styrene and 0.52 g (0.006 mol based on HCOOH) of TEAF in 4 ml of DMF was stirred at 135—140°. Evolution of CO_2 almost ceased after 2.5 hr. The reaction solution was concentrated under reduced pressure to remove DMF and excess TEAF. The resulting residue was dissolved in benzene and the benzene solution was washed with water and dried over anhyd. MgSO_4 . Evaporation of benzene gave crude reduction product, which was chromatographed on silica gel column using benzene-ethyl acetate=10/1 as an eluent to give 0.15 g (18.8%) of 1-phenylsulfonyl-1-phenylthio-2-phenylethane. Recrystallization from EtOH gave colorless needles, mp 113—115°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1305 and 1135 (SO_2). NMR (in CDCl_3) δ : 3.28—4.35 (m, 3H, $-\text{CH}_2\text{CH}=\text{}$), 7.11—7.45 (m, 15H, aromatic protons). *Anal.* Calcd. for $\text{C}_{20}\text{H}_{18}\text{O}_2\text{S}_2$: C, 67.79; H, 5.12. Found: C, 67.70; H, 5.11.

Acknowledgement We wish to thank Mr. K. Narita and the other members of the Analysis Center of this college for microanalyses.

17) G. Beck and D. Gunther, *Chem. Ber.*, **106**, 2758 (1973).

18) M. Balasubramanian and V. Baliah, *J. Indian Chem. Soc.*, **32**, 493 (1955) [*C.A.* **50**, 10042f (1955)].

19) H. Stetter and B. Riberi, *Monatsh. Chem.*, **103**, 1262 (1972).

20) M. Asscher and D. Vofsi, *J. Chem. Soc.*, **1964**, 4962.