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

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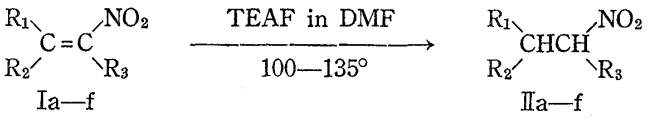
Selective reduction of carbon-carbon double bond conjugated with nitro group has been demonstrated with a number of examples by the use of the TEAF reagent (triethylamine–formic acid azeotrope) in N,N-dimethylformamide. In addition, formic acid reduction of carbon-carbon double bond conjugated with both 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 hydrogenation[4] and reduction with complex metal hydrides such as sodium borohydride,[5] lithium borohydride[6] 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 reagent[7]) in N,N-dimethylformamide (DMF) at 100—135°. The results of reduction of a number of nitrostyrenes are



Ia—f IIa—f

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).
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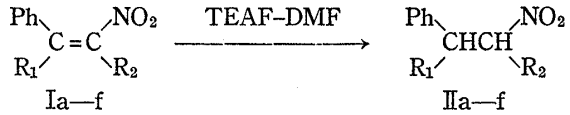
6) H. Shechter, D.E. Ley, and E.B. Roberson, Jr., *J. Am. Chem. Soc.*, **78**, 4984 (1956).
7) K. Narita and M. Sekiya, *Chem. Pharm. Bull.* (Tokyo), **25**, 135 (1977).

Table I. Formic Acid Reduction[a] of β-Nitrostyrenes



Ia—f IIa—f

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_2H_5	115—120	14.0	83.5
Id	H	CH_2Ph	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 HCO_2H), 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.

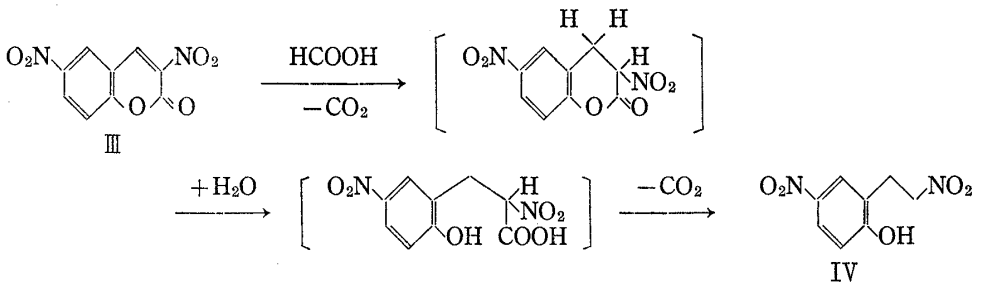


Chart 2

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

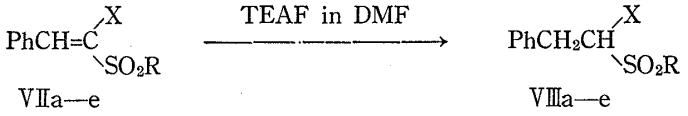
Chart 3

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; $NO_2>CN>SO_2C_6H_5>COC_6H_5$. 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, carbony

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

and ethoxycarbonyl are not so efficient that carbon-carbon double bonds effective for the reduction have been recognized to be conjugated doubly with them at one side of the olefinic carbons.

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-

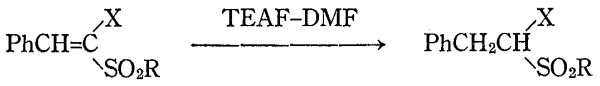


VIIa—e VIIIa—e

Chart 4

sulfonylstyrene was inert to the reduction even at 150°, whereas styrenes conjugated with both sulfonyl and other electron-withdrawing group underwent the reduction to give the corresponding reduction products. β,β-Bis-(phenylsulfonyl)styrene was reduced to 1-phenylthio-1-phenylsulfonyl-2-phenylethane, where one of the phenylsulfonyl grouping was reduced to phenylthio grouping.

Table II. Formic Acid Reduction of α,β-Unsaturated Sulfonyl Compounds



VIIa—e VIIIa—e

Compd. No.	R	X	React. temp.[b] (°C)	React. time (hr)	Yield[c] (%)
VIIa	Ph	CO_2Et	110—113	2.0	71.7
VIIb	Ph	$COCH_3$	60—65	3.0	90.3
VIIc	Ph	COPh	118—120	4.0	71.9
VIId	CH_3	COPh	125—130	3.5	81.6
VIIe	Ph	$CONH_2$	130—135	5.0	17.3

a) Substrate: 0.02 mol, TEAF: 5.2 g (0.06 mol as HCO_2H), DMF: 40 ml.
b) Temperature effecting considerable evolution of carbon dioxide.
c) Based on the product isolated.

Experimental[9]

Conjugated Nitroalkenes——Compounds, Ia—d, were prepared by condensation of the corresponding nitroalkanes and benzaldehyde in acetic acid using ammonium acetate as catalyst. Compounds, Ie and If, were prepared by nitration of stilbene and 1,1-diphenylethylene, respectively, with acetyl nitrate. Compounds, III and IV, and 2,4-dinitrostilbene were prepared according to the method described in the literatures cited. Ia: Yellow needles (EtOH), mp 57—58° (lit.[10] mp 58—59°); Ib: Yellow needles (EtOH), mp 64° (lit.[10] mp 64—65°); Ic: Yellow oil, bp 95—102° (0.05 mmHg); Id: Yellow crystals (MeOH), mp 57° (lit.[11] mp 58°); Ie: Yellow needles (hexane), mp 71—72° (lit.[12] mp 72—73°); If: Yellow prisms (ligroin-benzene), mp 85—87° (lit.[13] mp 88—88.5°); III: Yellow plates, (AcOH), mp 178—180° (lit.[14] mp 180—181°); V: Yellow needles

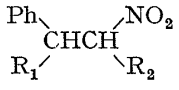
9) All melting points and boiling points are uncorrected. Infrared (IR) spectra were recorded on a Hitachi EPI-G2 spectrophotometer. Nuclear magnetic resonance (NMR) spectra were taken with a Hitachi R-24 spectrophotometer (at 60 MHz). Chemical shift values are given in δ (ppm) relative to tetramethylsilane as an internal standard. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, sx=sextuplet, m=multiplet.
10) C.B. Gairaud and G.R. Lappin, *J. Org. Chem.*, **18**, 1 (1953).
11) T. Severin, D. Scheel, and P. Adhikary, *Chem. Ber.*, **102**, 2966 (1969).
12) F.G. Bordwell and E.W. Garbisch, Jr., *J. Org. Chem.*, **27**, 2322 (1962).
13) G. Wittig and W. Gaub, *Chem. Ber.*, **80**, 363 (1947).
14) A. Clayton, *J. Chem. Soc.* (London), **97**, 1397 (1910).

(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 CO_2 was introduced in order to check evolution of CO_2 by saturated $Ba(OH)_2$ solution. After CO_2 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. $MgSO_4$. 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 CO_2 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. $MgSO_4$. 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 ν_{max}^{KBr} cm^{-1}: 3250 (OH), 1550

Table III. Physical and Analytical Data of the Reduction Products



IIb—f

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	$C_9H_{11}NO_2$	65.44 (65.01	6.71 6.52	8.48 8.32)
IIc	H	C_2H_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_2Ph	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–, J=6.0 Hz), 2.72—3.44 (m, 2H, CH_2<, J=7.0 Hz), 4.40—4.48 (sx, 1H, –CH<, J=7.0 Hz), 7.18 (s, 5H, C_6H_5)
IIc	1545	0.98 (t, 3H, CH_3CH_2–, J=8.0 Hz), 1.52—2.30 (m, 2H, CH_3CH_2<), 2.80—3.50 (m, 2H, CH_2<), 4.42—4.88 (m, 1H, –CH<), 7.27 (s, 5H, C_6H_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<, J=6.0, 9.0 Hz), 7.35 (s, 5H, C_6H_5), 7.15 (s, 5H, C_6H_5)
IIf	1550	4.77 (q, 1H, –CH<, J=7.0, 9.0 Hz), 5.23 (d, 2H, CH_2<, J=7.0 Hz), 7.20 (s, 10H, two C_6H_5)

a) IIb—f were measured in $CDCl_3$.

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.

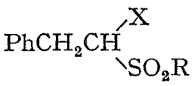
16) K.R. Hargreaves and A. Mcgookin, *J. Soc. Chem. Ind.* (London), **69**, 186 (1950).

and 1520 (NO_2). NMR (in DMSO-d_6) δ: 3.30 (t, 2H, $-C\underline{H}_2CH_2NO_2$, J=7.0 Hz), 4.30 (t, 2H, $-CH_2C\underline{H}_2NO_2$, 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)cinnamonitrile (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 CO_2 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. $MgSO_4$. 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 $C_{15}H_{12}N_2O_2$: C, 71.41; H, 4.80; N, 11.11. Found: C, 71.62; H, 4.82; N, 11.05. IR ν_{max}^{KBr} cm^{-1}: 2230 (CN), 1520 and 1340 (NO_2). NMR (in $CDCl_3$) δ: 3.20 (d, 2H, $-CH_2-$, J=7.0 Hz), 4.14 (t, 1H, $-CH\langle$, J=7.0 Hz), 6.89—7.33 (m, 5H, C_6H_5), 7.70 (AA′XX′ q, 4H, p-$NO_2C_6H_4$, J_{AX}=48 Hz, $J_{A'X}$=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



VIIIa—e

Compd. No.	R	X	Appearance (Recryst. solvent)	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N
VIIIa	Ph	CO_2Et	Prisms (EtOH)	97—98	$C_{17}H_{18}SO_4 \cdot 1/2H_2O$	62.40 (62.59	5.81 5.53	
VIIIb	Ph	$COCH_3$	Plates (EtOH)	97—99	$C_{16}H_{16}SO_3$	66.66 (66.80	5.59 5.55)	
VIIIc	Ph	COPh	Needles (MeOH)	137.5—138	$C_{21}H_{18}SO_3$	71.99 (71.90	5.59 5.22)	
VIIId	CH_3	COPh	Needles (MeOH)	137—138	$C_{16}H_{16}SO_3$	66.66 (66.40	5.59 5.58)	
VIIIe	Ph	$CONH_2$	Prisms (AcOH)	199—200	$C_{15}H_{15}NSO_3$	62.28 (61.88	5.23 5.21	4.84 5.03)

Compd. No.	IR ν_{max} (cm^{-1})	NMR (δ)[a]
VIIIa	1730 (CO), 1290, 1130 (SO_2)	0.96 (t, 3H, CH_3-, J=7.0 Hz), 3.28 (d, 2H, $-CH_2CH-$, J=10.0 Hz), 3.78—4.33 (m, 3H, $-CH\langle$ and $CH_3C\underline{H}_2O-$), 7.19 (s, 5H, C_6H_5), 7.53—8.00 (m, 5H, $C_6H_5SO_2-$)
VIIIb	1750 (CO), 1300, 1140 (SO_2)	2.16 (s, 3H, CH_3-), 3.17 (d, 1H, $\rangle C\langle^{H_a}_{\underline{H}_b}$, J=9.0 Hz), 3.21 (d, 1H, $\rangle C\langle^{H_a}_{\underline{H}_b}$ J=6.0 Hz), 4.55 (q, 1H $-CH\langle$, J=6.0, 9.0 Hz), 6.95—7.35 (m, 5H, C_6H_5), 7.50—8.00 (m, 5H, $C_6H_5SO_2-$)
VIIIc	1665 (CO), 1305, 1150 (SO_2)	3.36 (d, 2H, $CH_2\langle$, J=7.0 Hz), 6.06 (t, 1H, $-CH\langle$, J=7.0 Hz), 7.14 (s, 5H, C_6H_5), 7.36—7.96 (m, 10H, C_6H_5CO and $C_6H_5SO_2$)
VIIId	1670 (CO), 1310, 1130 (SO_2)	3.02 (s, 3H, CH_3-), 3.56 (d, 2H, $CH_2\langle$, J=7.0 Hz), 5.12 (t, 1H, $-CH\langle$, J=7.0 Hz), 7.16 (s, 5H, C_6H_5), 7.30—7.85 (m, 5H, C_6H_5CO)
VIIIe	3400, 3300, 3250 3200 (NH_2) 1705, 1675 (CO), 1298, 1130 (SO_2)	3.14 (d, 2H, $-C\underline{H}_2CH\langle$, J=8.0 Hz), 4.42 (t, 1H, $-CH_2C\underline{H}-$, J=8.0 Hz) 7.22 (s, 5H, C_6H_5), 7.52—8.08 (m, 7H, $C_6H_5SO_2$ and NH_2)

a) VIIIc and VIIIe were measured in DMSO-d_6, and others were in $CDCl_3$.

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, $-CH_2C\underline{H}_3$, $J=7.0$ Hz), 4.22 (q, 2H, $-C\underline{H}_2CH_3$, $J=7.0$ Hz), 7.42 (s, 5H, C_6H_5), 7.52—7.99 (m, 6H, $C_6H_5SO_2-$ and $-CH=$); 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 $C_{16}H_{14}O_3S$: 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 sammarized 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 ν_{max}^{KBr} cm^{-1}: 1305 and 1135 (SO_2). NMR (in $CDCl_3$) δ: 3.28—4.35 (m, 3H, $-C\underline{H}_2C\underline{H}=$), 7.11—7.45 (m, 15H, aromatic protons). *Anal.* Calcd. for $C_{20}H_{18}O_2S_2$: 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.

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