

## Reactions of Schiff Bases with Superoxide Ion in Acetonitrile

Katsuyoshi SHIBATA,\* Yoshiyuki SAITO, Katsuyoshi URANO, and Masaki MATSUI  
 Department of Industrial Chemistry, Faculty of Engineering, Gifu University, Yanagido, Gifu 501-11  
 (Received April 2, 1986)

**Synopsis.** The reactions of Schiff bases such as *N*-benzylideneanilines with superoxide ion in acetonitrile under mild conditions gave the cyanomethyl adducts, 3-arylamino-3-arylpropionitriles, as the main products in relatively good yields. In the case of *N*-(4-nitrobenzylidene)aniline, the adduct was further oxidized to  $\beta$ -anilino-4-nitrocinnamitrile. No oxidative products such as amides were obtained except in the reactions of *N*-(4-chloro- and 4-nitrobenzylidene)aniline.

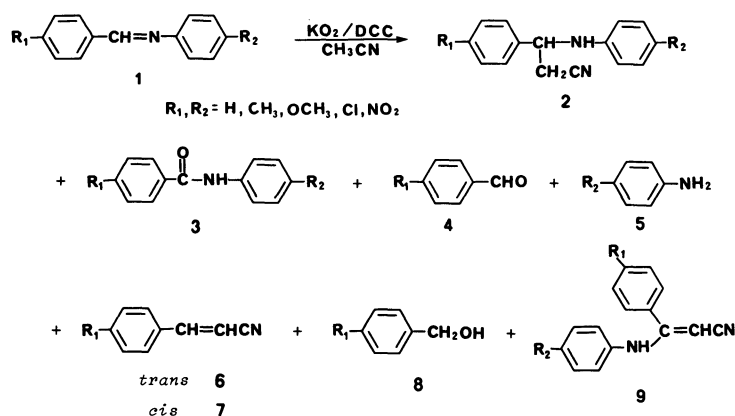
Although superoxide ion reacted with many organic compounds as oxidant, reductant, nucleophile, base, or radical,<sup>1)</sup> there have been only a few reports on carbon–nitrogen double-bonds with superoxide ion. These reports have been on the oxidations of iminium fluorosulfates and nitrones to the corresponding amide and hydroxamic acids respectively;<sup>2)</sup> the reaction of hydrazine to azine,<sup>3)</sup> and the reactions of oximes to *O,O'*-methylenebis(oxime)s in the presence of Pd(II) and dichloromethane.<sup>4)</sup>

We found that *N*-benzylideneanilines (**1**) with a C=N bond reacted with superoxide ion and acetonitrile in the presence of dicyclohexano-18-crown-6(DCC), resulting in the formation of 3-anilino-3-

phenylpropionitriles (**2**) as the main product. This paper will describe the reactions of the various Schiff bases with superoxide ion in acetonitrile.

### Results and Discussion

Substituted *N*-benzylideneanilines (**1**) and DCC were dissolved in dry acetonitrile, after the addition of powdered KO<sub>2</sub>, the mixture was stirred for 1 h under an argon atmosphere at room temperature. Then the solution was treated with water to decompose the unreacted KO<sub>2</sub>, and extracted with ether. The results are summarized in Scheme 1 and Table 1. Cyanomethyl adducts (**2a–d**, **2f–i**) to the C=N bond of **1** were obtained as the main products in 32–71% yields. In addition, benzaldehydes (**4**), anilines (**5**), *trans*- and *cis*-cinnamitriles (**6** and **7**), and benzyl alcohols (**8**) were obtained in low yields. In these cases of R<sub>1</sub>=Cl and NO<sub>2</sub> (**1d** and **1e**), the **3d** and **3e** amides, derived from the oxidation of the C=N bond with superoxide ion, were obtained in about 15% yields. No 3-anilino-3-(4-nitrophenyl)propionitrile (**2e**) was afforded from 4-nitrobenzylideneaniline (**1e**). It can be assumed that **2e** was further dehydrogenated by superoxide ion to form



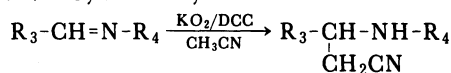
Scheme 1.

Table 1. Reactions of *N*-Benzylideneanilines (**1a–i**) with Superoxide Ion in Acetonitrile (room temp, 1 h)

	Substituent		Conv %	Yield <sup>a)</sup> /%								
	R <sub>1</sub>	R <sub>2</sub>		2	3	4	5	6	7	8	9	
<b>1a</b>	H	H	84	71	—	Trace	8	2	Trace	2	—	
<b>1b</b>	Me	H	47	55	—	6	13	6	Trace	—	—	
<b>1c</b>	MeO	H	54	68	—	Trace	11	2	2	—	—	
<b>1d</b>	Cl	H	41	58	17	16	17	Trace	—	Trace	—	
<b>1e</b>	NO <sub>2</sub>	H	53	—	16	2	6	—	—	—	31	
<b>1f</b>	H	Me	30	54	—	Trace	10	3	Trace	Trace	—	
<b>1g</b>	H	MeO	32	72	—	3	16	6	Trace	Trace	—	
<b>1h</b>	H	Cl	100	32	—	—	42	8	Trace	—	—	
<b>1i</b>	H	NO <sub>2</sub>	100	48	—	Trace	34	15	3	—	—	

a) Yields were determined by GLC analysis and based on converted substrates.

Table 2. Cyanomethylations of Various Schiff Bases



	Substituent		Time h	Temp °C	Conv %	Adduct	Yield <sup>a)</sup> %
	R <sub>3</sub>	R <sub>4</sub>					
<b>10</b>	Cyclohexyl	Ph	1	60	43	<b>11</b>	12
<b>12</b>	Ph	Cyclohexyl	20	60	12	—	—
<b>13</b>	Ph	1-Naphthyl	1	rt	94	<b>14</b>	34
<b>15</b>	Ph	2-Naphthyl	1	rt	97	<b>16</b>	48
<b>17</b>	1-Naphthyl	Ph	1	rt	95	<b>18</b>	90
<b>19</b>	2-Naphthyl	Ph	1	rt	95	<b>20</b>	73
<b>21</b>	1-Naphthyl	1-Naphthyl	1	rt	98	<b>22</b>	41

a) GLC analysis.

Table 3. Melting Points and Analytical Data of 3-Arylamino-3-arylpropionitriles (**2a—d**, **2f—i**) and  $\beta$ -Anilino-4-nitrocinnamionitrile (**9e**)

Compd No.	Mp $\theta_m/^\circ\text{C}$	IR(KBr) cm <sup>-1</sup>	MS <i>m/z</i> (M <sup>+</sup> )	<sup>1</sup> H NMR $\delta$ (CDCl <sub>3</sub> ) ppm	Found(Calcd)/%		
					C	H	N
<b>2a</b>	81.5—82.5 (lit. <sup>7</sup> 80—82)	3350 2275	222	2.89 (2H, dd, <i>J</i> =5.9, 1.8 Hz, CH <sub>2</sub> ), 4.20 (1H, br s, NH), 4.76 (1H, t, <i>J</i> =6.0 Hz, CH)			
<b>2b</b>	70—71	3320 2260	236	2.34 (3H, s, CH <sub>3</sub> ), 2.89 (2H, dd, <i>J</i> =6.0, 0.9 Hz, CH <sub>2</sub> ), 4.18 (1H, s, NH), 4.71—4.75 (1H, m, CH), <sup>a)</sup> 6.6—7.3 (9H, m, Ar)	81.57 (81.32)	6.90 6.83	11.74 11.85
<b>2c</b>	108.5—109	3350 2250	252	2.84 (2H, d, <i>J</i> =6.2 Hz, CH <sub>2</sub> ), 3.78 (3H, s, OCH <sub>3</sub> ), 4.18 (1H, s, NH), 4.70 (1H, t, <i>J</i> =7.3 Hz, CH), 6.6—7.3 (9H, m, Ar)	76.01 (76.16)	6.27 6.39	11.34 11.15
<b>2d</b>	109—110	3380 2250	256	2.87 (2H, dd, <i>J</i> =5.9, 2.9 Hz, CH <sub>2</sub> ), 4.18 (1H, br s, NH), 4.73 (1H, t, <i>J</i> =5.9 Hz, CH), 6.6—7.4 (9H, m, Ar)	70.02 (70.17)	4.99 5.10	10.77 10.91
<b>2f</b>	64.5—65	3360 2240	236	2.21 (3H, s, CH <sub>2</sub> ), 2.88 (2H, dd, <i>J</i> =6.0, 1.7 Hz, CH <sub>2</sub> ), 4.07 (1H, br s, NH), 4.73 (1H, t, <i>J</i> =6.0 Hz, CH), 6.5—7.4 (9H, m, Ar)	81.49 (81.32)	6.97 6.83	11.69 11.85
<b>2g</b>	111—112	3370 2240	252	2.84 (2H, dd, <i>J</i> =6.2, 2.2 Hz, CH <sub>2</sub> ), 3.70 (3H, s, CH <sub>3</sub> O), 4.66 (1H, t, <i>J</i> =6.2 Hz, CH), 6.5—7.4 (9H, m, Ar)	76.37 (76.16)	6.46 6.39	11.02 11.15
<b>2h</b>	54—56	3370 2250	256	2.89 (2H, dd, <i>J</i> =7.3, 6.2 Hz, CH <sub>2</sub> ), 4.25 (1H, br s, NH), 4.72 (1H, t, <i>J</i> =5.9 Hz, CH), 6.5—7.4 (9H, m, Ar)	70.08 (70.17)	5.02 5.10	10.99 10.91
<b>2i</b>	109—110	3360 2260	267	2.97 (2H, dd, <i>J</i> =6.6, 5.9 Hz, CH <sub>2</sub> ), 4.8—4.95 (1H, m, CH), 5.28 (1H, br s, NH), 6.5—8.0 (9H, m, Ar)	67.21 (67.40)	4.79 4.90	15.87 15.72
<b>9e</b>	145—146	3270 2200	265	4.79 (1H, s, CH), 6.02 (1H, br s, NH), 7.2—8.4 (9H, m, Ar)	67.80 (67.95)	4.12 4.18	15.97 15.85

a) This signal was varied from m to t by the addition of D<sub>2</sub>O.

the olefin **9e**. Compound **1** might be decomposed to **4** and **5** by base (O<sub>2</sub><sup>-</sup> or HO<sub>2</sub><sup>-</sup>). Compound **4a** reacts with superoxide ion in acetonitrile to yield **6a—8a**.<sup>5</sup> We also observed the formations of **6a—8a** under the same conditions as the reaction of **1a**.

Shrader has obtained **2a** in a 54% yield by photo-ring-opening reaction of 1,5-diphenyl-2-pyrazoline under 22 h irradiation.<sup>6</sup> On the other hand, the method using superoxide ion, (**2a**) has given a better yield (71%) in a shorter reaction time (1 h).

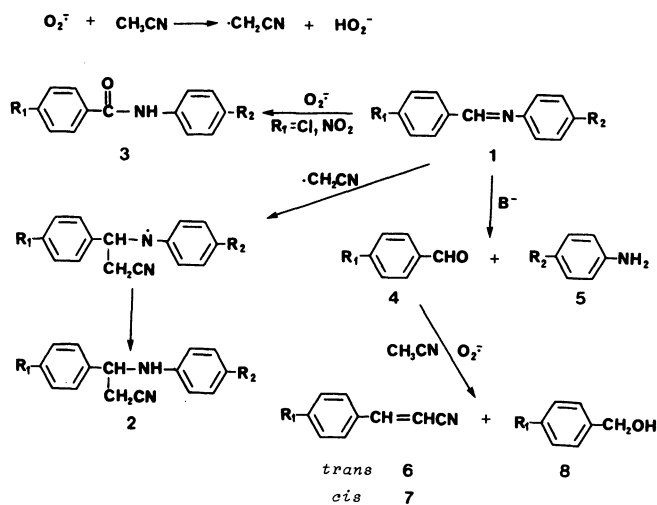
Similar reactions were carried out with cyclohexyl-, 1-naphthyl-, and 2-naphthyl-substituted compounds instead of the phenyl group of **1**. The results are summarized in Table 2. When *N*-(hexahydrobenzylidene)aniline (**10**) reacted with superoxide ion for 1 h at 60°C, the cyanomethyl adduct (**11**) was obtained

in a 12% yield; however, no cyanomethyl adduct was afforded from *N*-benzylidenecyclohexylamine (**12**) even 20 h at 60°C. In the cyanomethylations of naphthyl-substituted Schiff bases, no difference in reactivity was observed between 1-naphthyl- and 2-naphthyl-substituted Schiff bases. *N*-Naphthyl-substituted Schiff bases (**13**, **15**, **21**) gave cyanomethyl adducts (**14**, **16**, **22**) in lower yields than C-substituted ones (**17**, **19**). The physical properties of cyanomethyl adducts are summarized in Tables 3 and 4.

On the basis of the results mentioned above, the formation of **2** is explained by Scheme 2. In the reaction of **1**, superoxide ion abstracts the hydrogen atom from acetonitrile, thus giving cyanomethyl radical. This cyanomethyl radical attacks the carbon of the C=N bond and gives cyanomethyl adducts (**2**) via radical

Table 4. Melting Points and Analytical Data of 3-Anilino-3-cyclohexylpropionitrile (11) and 3-Aryl-3-(arylamino)propionitriles (14, 16, 18, 20, 22)

Compd No.	Mp $\theta_m/^\circ\text{C}$	IR(KBr) $\text{cm}^{-1}$	MS $m/z(\text{M}^+)$	$^1\text{H NMR } \delta(\text{CDCl}_3)$ ppm	Found(Calcd)/%		
					C	H	N
11	62—62.5	3340 2210	228	1.0—2.0 (11H, m, $\text{C}_6\text{H}_{11}$ ), 2.64 (2H, dd, $J=11.9, 4.9$ Hz, $\text{CH}_2$ ), 3.4—3.55 (1H, m, CH), 3.64 (1H, br s, NH), 6.6—7.3 (5H, m, Ar)	79.08 (79.25)	8.22 8.43	12.39 12.32
14	113.5—114	3405 2260	272	3.03 (2H, d, $J=6.2$ Hz, $\text{CH}_2$ ), 4.83 (1H, br s, NH), 4.95 (1H, t, $J=6.0$ Hz, CH), 6.5—8.0 (12H, m, Ar)	83.91 (83.79)	5.98 5.92	10.18 10.29
16	125.5—126	3440 2260	272	2.97 (2H, d, $J=5.9$ Hz, $\text{CH}_2$ ), 4.52 (1H, br s, NH), 4.90 (1H, t, $J=6.0$ Hz, CH), 6.7—7.7 (12H, m, Ar)	83.72 (83.79)	5.79 5.92	10.27 10.29
18	114—114.5	3380 2260	272	3.08 (2H, ddd, $J=51.3, 16.9, 5.9$ Hz, $\text{CH}_2$ ), 4.37 (1H, s, NH), 5.57 (1H, t, $J=5.9$ Hz, CH), 6.6—8.0 (12H, m, Ar)	83.88 (83.79)	5.82 5.92	10.32 10.29
20	134—134.5	3415 2245	272	2.99 (2H, dd, $J=5.9, 3.3$ Hz, $\text{CH}_2$ ), 4.31 (1H, s, NH), 4.93 (1H, t, $J=6.0$ Hz, CH), 6.6—7.9 (12H, m, Ar)	83.62 (83.79)	5.74 5.92	10.41 10.29
22	149.5—150.5	3360 2240	322	3.32 (2H, dd, $J=28.6, 5.9$ Hz, $\text{CH}_2$ ), 5.05 (1H, br s, NH), 5.77 (1H, t, $J=5.9$ Hz, CH), 6.4—8.1 (14H, m, Ar)	87.58 (87.54)	4.77 4.90	7.72 7.56



intermediates. Oae et al. have reported that diaryl sulfide reacted with superoxide ion in acetonitrile to yield bis(arylthio)acetonitrile as the main product; its formation mechanism might be via the cyanomethyl radical.<sup>7)</sup> When  $\text{R}_1=\text{NO}_2$  and Cl, the electron density of the carbon of the  $\text{C}=\text{N}$  bond is decreased, and **3** are obtained by the nucleophilic attack of superoxide ion. In the case of  $\text{R}_1=\text{NO}_2$ , the resulting adduct is further oxidized to **9e**. On the other hand, **1** are decomposed to **4** and **5** by bases, and **4** further reacts with acetonitrile and superoxide ion to yield **6—8**.

### Experimental

Melting points are uncorrected. NMR spectra were measured by the use of a JEOL GX-270 Spectrometer in a  $\text{CDCl}_3$  solution; the chemical shifts were expressed in units from the internal  $\text{Me}_4\text{Si}$ . Mass spectra were measured by means

of a Hitachi M-52 Spectrometer (20 eV). IR spectra were recorded over KBr disks with a JASCO A-302 Spectrometer. Gas chromatography was performed on a Shimadzu 4C-PF Gas chromatograph (2% OV-1 or 5% FFAP).

**Materials.** *N*-Benzylideneanilines (**1**) and the various Schiff bases were prepared from the corresponding aldehydes and amines. The resulting Schiff bases were recrystallized from ethanol. Potassium superoxide (Alfa) was crushed and pulverized in a dry atmosphere. The acetonitrile was purified by distillation in the presence of  $\text{P}_2\text{O}_5$  and stored Molecular Sieves (3A, 1/16). Dicyclohexano-18-crown-6 (Tokyo Kasei) was used as received.

**General Procedure.** *N*-Benzylideneaniline (**1a**) (300 mg, 1.65 mmol) and DCC (300 mg, 0.81 mmol) were dissolved in dry acetonitrile (50  $\text{cm}^3$ ). After powdered  $\text{KO}_2$  (500 mg, 7.04 mmol) has been added to the solution, the mixture was stirred under an argon atmosphere. After 1 h, water (50  $\text{cm}^3$ ) was slowly added to decompose the residual  $\text{KO}_2$ . The mixture was extracted with ether in the presence of NaCl. The ether layer was dried over  $\text{MgSO}_4$  and evaporated (rotary). The extract was separated by thin-layer chromatography (Merck, Silica Gel 60 PF<sub>254</sub>; hexane:dichloromethane=1:2).

### References

- 1) a) E. Lee-Ruff, *Chem. Soc. Rev.*, **6**, 195 (1977); b) D. T. Sawyer, *Acc. Chem. Res.*, **14**, 393 (1981); c) A. A. Frimer, *Superoxide Dismutase*, **2**, 83 (1982).
- 2) A. Picot, P. Milliet, M. Cherest, and X. Lushinchi, *Tetrahedron Lett.*, **18**, 3811 (1977).
- 3) C. I. Chern and J. S. Filippo, Jr., *J. Org. Chem.*, **42**, 178 (1978).
- 4) T. Hosokawa, T. Ohta, Y. Okamoto, and S. Murahashi, *Tetrahedron Lett.*, **21**, 1259 (1980).
- 5) M. J. Gibian, D. T. Sawyer, T. Ungermann, R. Tangpoonpholvivat, and M. M. Morrison, *J. Am. Chem. Soc.*, **101**, 640 (1979).
- 6) L. Schreder, *Tetrahedron Lett.*, **12**, 2977 (1971).
- 7) S. Oae, T. Takata, and Y. H. Kim, *Bull. Chem. Soc. Jpn.*, **54**, 2712 (1981).