Reactions of Schiff Bases with Superoxide Ion in Acetonitrile

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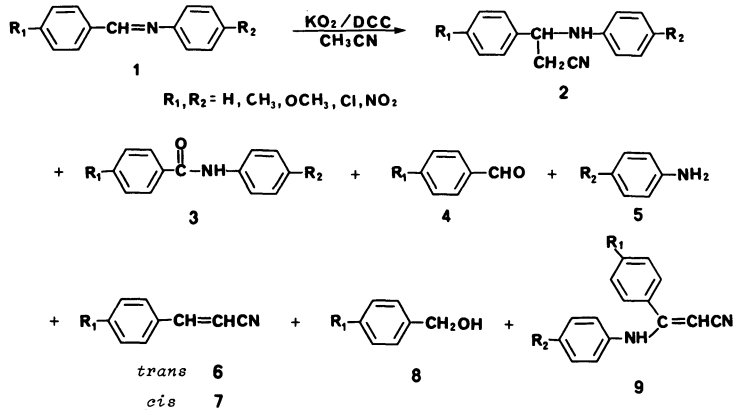
Synopsis. The reactions of Schiff bases such as *N*-benzylideneanilines with superoxide ion in acetonitrile under mild conditions gave the cyanomethyl adducts, 3-arylamino-3-arylpropionitriles, as the main products in relatively good yields. In the case of *N*-(4-nitrobenzylidene)aniline, the adduct was further oxidized to β-anilino-4-nitrocinnamonitrile. 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,[1] 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;[2] the reaction of hydrazine to azine,[3] and the reactions of oximes to *O,O'*-methylenebis(oxime)s in the presence of Pd(II) and dichloromethane.[4]

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_2, 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_2, 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*-cinnamonitriles (**6** and **7**), and benzyl alcohols (**8**) were obtained in low yields. In these cases of R_1=Cl and NO_2 (**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[a]/%							
	R_1	R_2	%	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
1a	H	H	84	71	—	Trace	8	2	Trace	2	—
1b	Me	H	47	55	—	6	13	6	Trace	—	—
1c	MeO	H	54	68	—	Trace	11	2	2	—	—
1d	Cl	H	41	58	17	16	17	Trace	—	Trace	—
1e	NO_2	H	53	—	16	2	6	—	—	—	31
1f	H	Me	30	54	—	Trace	10	3	Trace	Trace	—
1g	H	MeO	32	72	—	3	16	6	Trace	Trace	—
1h	H	Cl	100	32	—	—	42	8	Trace	—	—
1i	H	NO_2	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

$$R_3\text{-}CH{=}N\text{-}R_4 \xrightarrow[CH_3CN]{KO_2/DCC} R_3\text{-}\underset{\displaystyle CH_2CN}{\underset{|}{CH}}\text{-}NH\text{-}R_4$$

	Substituent		Time	Temp	Conv	Adduct	Yield[a]
	R_3	R_4	h	°C	%		%
10	Cyclohexyl	Ph	1	60	43	**11**	12
12	Ph	Cyclohexyl	20	60	12	—	—
13	Ph	1-Naphthyl	1	rt	94	**14**	34
15	Ph	2-Naphthyl	1	rt	97	**16**	48
17	1-Naphthyl	Ph	1	rt	95	**18**	90
19	2-Naphthyl	Ph	1	rt	95	**20**	73
21	1-Naphthyl	1-Naphthyl	1	rt	98	**22**	41

a) GLC analysis.

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

Compd No.	Mp	IR(KBr)	MS	^{1}H NMR δ($CDCl_3$)	Found(Calcd)/%		
	θ_m/°C	cm^{-1}	$m/z(M^+)$	ppm	C	H	N
2a	81.5—82.5 (lit,[7] 80—82)	3350 2275	222	2.89 (2H, dd, J=5.9, 1.8 Hz, CH_2), 4.20 (1H, br s, NH), 4.76 (1H, t, J=6.0 Hz, CH)			
2b	70—71	3320 2260	236	2.34 (3H, s, CH_3), 2.89 (2H, dd, J=6.0, 0.9 Hz, CH_2), 4.18 (1H, s, NH), 4.71—4.75 (1H, m, CH),[a] 6.6—7.3 (9H, m, Ar)	81.57 (81.32	6.90 6.83	11.74 11.85)
2c	108.5—109	3350 2250	252	2.84 (2H, d, J=6.2 Hz, CH_2), 3.78 (3H, s, OCH_3), 4.18 (1H, s, NH), 4.70 (1H, t, J=7.3 Hz, CH), 6.6—7.3 (9H, m, Ar)	76.01 (76.16	6.27 6.39	11.34 11.15)
2d	109—110	3380 2250	256	2.87 (2H, dd, J=5.9, 2.9 Hz, CH_2), 4.18 (1H, br s, NH), 4.73 (1H, t, J=5.9 Hz, CH), 6.6—7.4 (9H, m, Ar)	70.02 (70.17	4.99 5.10	10.77 10.91)
2f	64.5—65	3360 2240	236	2.21 (3H, s, CH_2), 2.88 (2H, dd, J=6.0, 1.7 Hz, CH_2), 4.07 (1H, br s, NH), 4.73 (1H, t, J=6.0 Hz, CH), 6.5—7.4 (9H, m, Ar)	81.49 (81.32	6.97 6.83	11.69 11.85)
2g	111—112	3370 2240	252	2.84 (2H, dd, J=6.2, 2.2Hz, (CH_2), 3.70 (3H, s, CH_3O), 4.66 (1H, t, J=6.2 Hz, CH), 6.5—7.4 (9H, m, Ar)	76.37 (76.16	6.46 6.39	11.02 11.15)
2h	54—56	3370 2250	256	2.89 (2H, dd, J=7.3, 6.2 Hz, CH_2), 4.25 (1H, br s, NH), 4.72 (1H, t, J=5.9 Hz, CH), 6.5—7.4 (9H, m, Ar)	70.08 (70.17	5.02 5.10	10.99 10.91)
2i	109—110	3360 2260	267	2.97 (2H, dd, J=6.6, 5.9 Hz, CH_2), 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)
9e	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_2O.

the olefin **9e**. Compound **1** might be decomposed to **4** and **5** by base (O_2^- or HO_2^-). Compound **4a** reacts with superoxide ion in acetonitrile to yield **6a—8a**.[5] We also observed the formations of **6a—8a** under the same conditions as the reaction of **1a**.

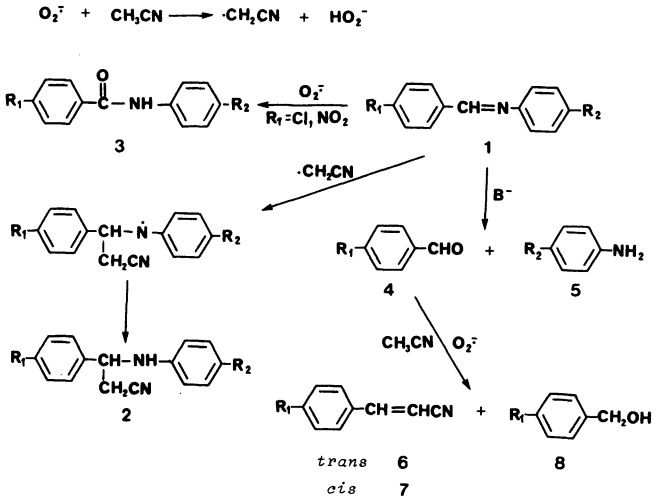
Shrader has obtained **2a** in a 54% yield by photo-ring-opening reaction of 1,5-diphenyl-2-pyrazoline under 22 h irradiation.[6] On the other hand, the method using superoxide ion, (**2a**) has given a better yield (71%) in a shorter reaction time (1 h).

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	IR(KBr)	MS	^{1}H NMR δ($CDCl_3$)	Found(Calcd)/%		
	θ_m/°C	cm^{-1}	$m/z(M^+)$	ppm	C	H	N
11	62—62.5	3340 2210	228	1.0—2.0 (11H, m, C_6H_{11}), 2.64 (2H, dd, J= 11.9, 4.9 Hz, 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, 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, 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, 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, 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, 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)



Scheme 2.

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.[7] When R_1=NO_2 and Cl, the electron density of the carbon of the C=N bond is decreased, and **3** are obtained by the nucleophilic attack of superoxide ion. In the case of R_1=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 $CDCl_3$ solution; the chemical shifts were expressed in units from the internal Me_4Si. 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. Pottasium superoxide (Alfa) was crushed and pulverized in a dry atmosphere. The acetonitrile was purified by distillation in the presence of P_2O_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 cm^3). After powdered 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 cm^3) was slowely added to decompose the residual KO_2. The mixture was extracted with ether in the presence of NaCl. The ether layer was dried over $MgSO_4$ and evaporated (rotary). The extract was separated by thin-layer chromatography (Merck, Silica Gel 60 PF_{254}; hexane:dichloromethane=1:2).

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