Pergamon

Tetrahedron Vol. 50, No. 25, pp. 7589-7596, 1994

0040-4020/94 $7.00+0.00

0040-4020(94)00382-3

Nitrile Oxide-BF_3 Complex as Electrophilic Moiety towards Aromatic Systems: Stereospecific Synthesis of Oximes

Sergio Auricchio,* Antonella Bini , Eros Pastormerlo, Aldo Ricca and Ada M. Truscello

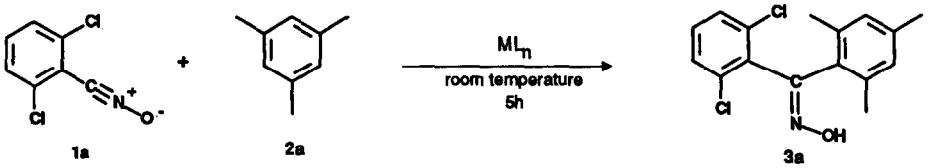
Dipartimento di Chimica, Politecnico di Milano, via Mancinelli 7, 20131 Milano

Abstract: Aromatic Oximes are obtained stereospecifically by action of Nitrile Oxide-BF_3 complexes on Aromatic Compounds.

Introduction

Boron trifluoride catalyses cycloaddition reactions of nitrile oxides with various dipolarophiles yielding many heterocycles which cannot be obtained from the uncatalysed reaction.[1] In the absence of a dipolarophile, the nitrile oxide-BF_3 complex gives various dimers depending on the reaction conditions. In particular, different dimers are obtained if BF_3 etherate (where the Lewis acid is strongly coordinated) or gaseous BF_3 is used.[2]

It is also known that nitrile oxides can react at the carbon atom with strong nucleophiles to give oximes.[3] Recently Kim *et al.* reported that the nitrile oxide-Lewis acid complex can react with aromatic compounds yielding ketoximes.[4] **(Scheme 1)**



1a **2a** **3a**

ML_n = $AlCl_3$, BF_3 etherate, $SnCl_4$, $FeCl_3$.

Scheme 1

The main limitation of the method proposed by Kim *et al.* for the synthesis of oximes is the low reaction rate: 2,6-dichlorobenzonitrile oxide **1a** reacts with mesitylene **2a** in five hours at room temperature to give the oxime **3a**. In these conditions many nitrile oxides dimerises and therefore the synthesis of oximes, using Lewis acids as $AlCl_3$, $SnCl_4$, $FeCl_3$, is limited only to the very stable nitrile oxides; 2,6-dichlorobenzonitrile oxide **1a** was, in fact, the only nitrile oxide used.[4]

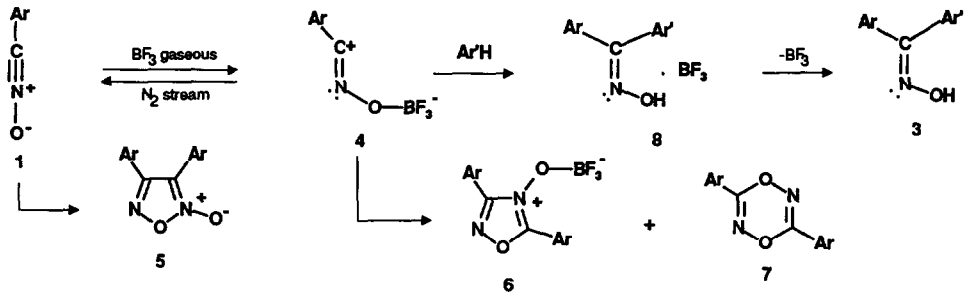
The alternative approach[4] , starting from hydroxymoyl chloride, due to the long reaction time and the temperature used, did not afford the desired oximes, but only the corresponding amides *via* the Beckmann rearrangement.

Recently our group resumed the study on the reactivity of the nitrile oxide-BF_3 complex and obtained the oximes **3** using gaseous BF_3 as Lewis acid.[5]

In consideration of the synthetic utility, we wish to report our efforts in the stereospecific synthesis of aromatic oximes. Up to now, the synthesis of the thermodynamically less stable stereoisomer of oximes was very laborious.[6]

Results and Discussion

Electrophilic aromatic substitution of a relatively non-polar moiety as nitrile oxide[7] was possible by complexation with BF_3, as shown in **Scheme 2**.



Scheme 2

The nitrile oxide-BF_3 complex **4** has been postulated by many authors,[2,4,8] but it was never isolated. We have found the conditions to obtain complex **4**: when gaseous boron trifluoride is bubbled through a solution of nitrile oxide **1** in hexane, a precipitate is formed. Removal of the solvent by decantation gives the complex **4** as a white solid. It is possible to keep unaltered the complex only under BF_3 atmosphere and only for a short time. A stream of inert gas or the exposure to air of the freshly formed complex, reconverts the complex to the starting nitrile oxide **1** with a little amount of furoxan **5**. The storage of the solid complex for one day under BF_3 atmosphere yields a mixture of the dimers **6** and **7**.[2] Addition of an aromatic system to freshly prepared complex **4** yields, in a few minutes, the oxime-BF_3 complex **8**. The oxime-BF_3 complexes have been previously reported,[9] and it is known that their treatment with an aqueous solution of sodium bicarbonate yields oximes **3**.

This procedure is not always the best synthetic method that can be used. Depending on the stability of the nitrile oxide or aromatic system used, it is better to select different experimental conditions.

We report here the four procedures used:

i) gaseous BF_3 is bubbled until saturation through a stirred solution of nitrile oxide in the dry aromatic reagent. After few minutes the excess of BF_3 is eliminated with a stream of N_2.

ii) same as (i) but the aromatic reagent is diluted with *n*-hexane.

iii) a cooled solution of nitrile oxide in *n*-hexane is added with a syringe pump to a BF_3 saturated solution of the aromatic reagent in *n*-hexane.

iv) a cooled solution of nitrile oxide in the aromatic reagent is added with a syringe pump to a BF_3 saturated solution of the aromatic reagent.

In all cases and in spite of the low temperature that it is possible to use, the reactions occur so quickly that only very little amounts of dimers are formed. The low temperature, the high rate and the immediate

quenching of the reaction avoid the Beckmann rearrangement of the oximes. Regardless of the nitrile oxide used, the yields are very good with many aromatic systems and dimers are obtained only with deactivated compounds, such as benzoates or nitrobenzenes. The regioisomeric distribution of oximes **3** was determined by NMR spectra and gaschromatographic analyses. Direct GC analyses of the oximes could not be quantitative and it was performed on the corresponding amides. The results are summarised in Table 1.

It is interesting to note that the formation of oximes is quite stereospecific. Stereoisomers (*E* or *Z*) cannot be determined by analytical methods and the stereochemistry was determined indirectly by identification or characterisation of amides obtained by Beckman transposition. In all cases the lone pair on nitrogen and the approaching aromatic system are *trans*. This stereospecificity agreed with the previously reported reactivity of the nitrile oxides with many other nucleophilic systems.[10]

As a consequence of this stereospecificity, the reaction of very activated nitrile oxides, as mesitonitrile oxide, with aromatic compounds leads principally to amides by the intermediates mesityl aryl ketoximes. The *anti* mesityl oximes obtained are in the appropriate configuration for a Beckman transposition. But, for the same reason, it is possible to synthesise the stereoisomeric pure *syn* mesityl oximes **3a, 3k, 3q** using the appropriate nitrile oxides and mesitylene. This method therefore makes available a useful route for the synthesis of aromatic oximes of known configuration.

Acknowledgements

We gratefully acknowledge the Ministero dell'Università e della Ricerca Scientifica e Tecnologica (MURST) for support. We would also like to thank Mrs. Rosanna Bernardi for help with GC work.

Experimental

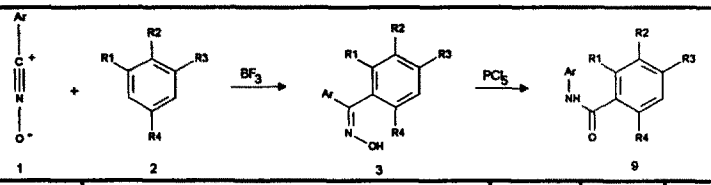
NMR spectra were determined with TMS as internal standard on a Bruker 250 MHz. GC-MS and MS spectra were performed with a Finnigan TSQ 70 instrument operating at ion source temperature of 150°C. The following GC conditions were used: fused-silica capillary column (25 m X 0.2 mm i.d.); the pressure 12 psi; oven temperature programme 220°(1) / 3°/min 270°(22). Chromatographic separations were performed using Merck Kieselgel 60. M.p.s. of oximes **3** were performed on recrystallised products (ethanol/water) and are uncorrected. Amides **9** were obtained from reaction of oximes **3** with PCl_5, *via* Beckmann rearrangement.

(Z)-2',6'-Dichloro-2,4,6-trimethylbenzophenone oxime (3a).

Gaseous BF_3 was bubbled until saturation through a stirred solution of 2,6-dichlorobenzonitrile oxide (**1a**) (188 mg, 1 mmol) and anhydrous mesitylene (**2a**) (2 ml) in *n*-hexane (20 ml). After few minutes the excess of BF_3 was eliminated with a stream of N_2. The precipitate was filtered, dissolved in ethyl acetate, washed with a 2% solution of $NaHCO_3$ and dried over Na_2SO_4. The solvent was removed to give (*Z*)-2',6'-dichloro-2,4,6-trimethylbenzophenone oxime (**3a**) as a white solid (85%).

3a: mp 184-186°C. Anal. Calcd. for $C_{16}H_{15}Cl_2NO$: C, 62.53; H, 4.92; N, 4.56. Found: C, 62.41; H, 4.85; N, 4.51. Mass spectrum: m/z 309 (M+2, 8); 307 (M+, 11); 292 (29); 290 (35); 147 (100); 144 (55); 120 (40); 119 (24); 105 (53). ^1H NMR (DMSO): 11.95 (1H, brs, OH), 7.60-7.30 (3H, m), 6.82 (2H, s), 2.20 (3H, s), 2.08 (3H, s).

Table 1. Reaction of Nitrile Oxide(1a-c)-BF_3 Complexes with Aromatic Compounds(2a-f)



1 2 3 9

1-BF_3 + 2 → 3	Ar	R1	R2	R3	R4	Method	Yield %	Isomer Distribution	Amide
1a + 2a → 3a	2,6-$Cl_2C_6H_3$	CH_3	H	CH_3	CH_3	ii	85		9a
1a + 2b → 3b	2,6-$Cl_2C_6H_3$	H	H	CH_3	H	i	88	64	9b*
1a + 2b → 3c	2,6-$Cl_2C_6H_3$	CH_3	H	H	H	i	88	19	9c*
1a + 2b → 3d	2,6-$Cl_2C_6H_3$	H	CH_3	H	H	i	88	17	9d*
1a + 2c → 3e	2,6-$Cl_2C_6H_3$	H	H	OCH_3	H	ii	92	90	9e
1a + 2c → 3f	2,6-$Cl_2C_6H_3$	OCH_3	H	H	H	ii	92	10	9e
1a + 2d → 3g	2,6-$Cl_2C_6H_3$	CH_3	H	CH_3	H	ii	74		9g
1a + 2e → 3h	2,6-$Cl_2C_6H_3$	H	CH_3	CH_3	H	ii	60	96	9h
1a + 2e → 3i	2,6-$Cl_2C_6H_3$	CH_3	CH_3	H	H	ii	60	4	9h
1a + 2f → 3j	2,6-$Cl_2C_6H_3$	H	H	H	H	i	75		9j
1b + 2a → 3k	2-ClC_6H_4	CH_3	H	CH_3	CH_3	ii	70		9k
1b + 2b → 3l	2-ClC_6H_4	H	H	CH_3	H	i	77	90	9l
1b + 2b → 3m	2-ClC_6H_4	CH_3	H	H	H	i	77	10	9l
1b + 2c → 3n	2-ClC_6H_4	H	H	OCH_3	H	ii	72	90	9n
1b + 2c → 3o	2-ClC_6H_4	OCH_3	H	H	H	ii	72	10	9n
1b + 2f → 3p	2-ClC_6H_4	H	H	H	H	i	80		**
1c + 2a → 3q	C_6H_5	CH_3	H	CH_3	CH_3	iii	50		9q
1c + 2b → 3r	C_6H_5	H	H	CH_3	H	iv	74	80	9r
1c + 2b → 3s	C_6H_5	CH_3	H	H	H	iv	74	20	9s
1c + 2c → 3t	C_6H_5	H	H	OCH_3	H	iii	60	90	9t
1c + 2c → 3u	C_6H_5	OCH_3	H	H	H	iii	60	10	9u
1c + 2f → 3v	C_6H_5	H	H	H	H	iv	72		**

* Attempts to separate amides 9b-d failed.

** Amides 9p and 9v were not prepared because the corresponding oximes were compared with authentic samples.

2',6'-Dichloro-2,4,6-trimethylbenzanilide (9a).

9a: mp 190-191°C. Anal. Calcd. for $C_{16}H_{15}Cl_2NO$: C, 62.53; H, 4.92; N, 4.56. Found: C, 62.49; H, 4.88; N, 4.52. Mass spectrum: m/z 309 (M+2, 2); 307 (M+, 3); 148 (11); 147 (100); 119 (14). ^1H NMR ($CDCl_3$): 7.42 (2H, d, 8 Hz), 7.27-7.16 (2H, m), 6.90 (2H, s), 2.50 (6H, s), 2.32 (3H, s).

Reaction of 2,6-dichlorobenzonitrile oxide with Toluene.

Gaseous BF_3 was bubbled until saturation through a stirred solution of 2,6-dichlorobenzonitrile oxide (**1a**) (188 mg, 1 mmol) in anhydrous toluene (**2b**) (20 ml). After few minutes the excess of BF_3 was eliminated with a stream of N_2. The solvent was removed, the crude was dissolved in ethyl acetate, washed with a 2% solution of $NaHCO_3$ and dried over Na_2SO_4. The organic solvent was removed to give a mixture of the regioisomeric oximes **3b**, **3c**, **3d** as a white solid (88%). The regioisomeric ratio (64:19:17) was determinated by the ^1H NMR spectrum of the mixture. Attempts to isolate the main regioisomeric oxime (**3b**) by recrystallisation failed.

(E)-2,6-Dichloro-4'-methoxybenzophenone oxime (3e).

The same procedure described for compounds **3a** was used. The reagents were 2,6-dichlorobenzonitrile oxide (**1a**) (188 mg, 1 mmol) and anhydrous anisole (**2c**) (2 ml). A mixture of **3e** and (*E*)-2,6-dichloro-2'-methoxybenzophenone oxime (**3f**) was obtained in 92% yield. The regioisomeric ratio (9:1) was determined by ^1H NMR spectrum. The mixture was recrystallised twice to give (*E*)-2,6-dichloro-4'-methoxybenzophenone oxime (**3e**) as a white solid.

3e: mp 170-171°C. Anal. Calcd. for $C_{14}H_{11}Cl_2NO_2$: C, 56.95; H, 3.76; N, 4.75. Found: C, 57.04; H, 3.84; N, 4.82. Mass spectrum: m/z 297 (M+2, 20); 295 (M+, 30); 278 (11); 166 (52); 134 (14); 115 (25); 109 (64); 105(100). ^1H NMR($CDCl_3$):7.68(2H,dd, J=9, 2 Hz), 7.40-7.20(3H, m), 6.89(2H, dt, J= 9, 2 Hz), 3.82(3H,s).

2',6'-dichloro-4-methoxybenzanilide (9e) .

9e: mp 193-194°C. Anal. Calcd. for $C_{14}H_{11}NO_2Cl_2$: C, 56.95; H, 3.76; N, 4.75. Found: C, 57.10; H, 3.74; N, 4.87. Mass spectrum: m/z 295 (M+, 0.6); 260 (19); 135 (100); 107 (12). ^1H NMR ($CDCl_3$): 7.93 (2H, dt, J=9, 2 Hz), 7.54 (1H, brs, OH), 7.43-7.15 (3H, m), 6.98 (2H, dt, J=9, 2 Hz), 3.89 (3H,s).

(Z)-2',6'-Dichloro-2,4-dimethylbenzophenone oxime (3g).

The same procedure described for compounds **3a** was used. The reagents were 2,6-dichlorobenzonitrile oxide (**1a**) (188 mg, 1 mmol) and anhydrous *m*-xylene (**2d**) (2 ml). (*Z*)-2',6'-Dichloro-2,4-dimethylbenzophenone oxime (**3g**) was obtained in 74% yield. The product was slightly impure as confirmed by GC and GC-MS analyses of the corresponding amides, which showed the presence of the regioisomeric amides (4%). The product was recrystallised to give **3g** as a white solid.

3g: mp 153-154°C. Anal. Calcd. for $C_{15}H_{13}Cl_2NO$: C, 61.43; H, 4.47; N, 4.78. Found: C, 61.38; H, 4.40; N, 4.78. Mass spectrum: m/z 295 (M+2, 2); 293 (M+, 4); 278 (2); 276 (4) 258 (9); 133 (100). ^1H NMR ($CDCl_3$): 7.39-7.19 (3H, m), 7.15 (1H, d, J= 8 Hz), 7.10 (1H, brs), 6.93 (1H, dd, J= 2 , 8 Hz,), 2.47 (3H, s), 2.31 (3H, s).

2',6'-Dichloro-2,4-dimethylbenzanilide (9g).

9g: mp 143-144°C. Anal. Calcd. for $C_{15}H_{13}NOCl_2$: C, 61.43; H, 4.47; N, 4.78. Found: C, 61.40; H, 4.38; N, 4.68. Mass spectrum: m/z 293 (M+, 1); 260 (4); 258 (12); 134 (8); 133 (100). ^1H NMR ($CDCl_3$): 7.56 (1H, d, 8 Hz), 7.45-7.15 (4H, m), 7.10 (2H, m), 2.54 (3H, s), 2.37 (3H, s).

(E)-2,6-Dichloro-3',4'-dimethylbenzophenone oxime (3h).

The same procedure described for compounds **3a** was used. The reagents were 2,6-dichlorobenzonitrile oxide (**1a**) (188 mg, 1 mmol) and anhydrous *o*-xylene (**2e**) (2 ml). The crude mixture was chromatographated on silica gel (hexane/ethyl acetate 9/1 as eluent) to give (*E*)-2,6-dichloro-3',4'-dimethylbenzophenone oxime (**3h**) in 60% yield. GC and GC-MS analyses of the corresponding amide, obtained *via* Beckmann rearrangement, showed that the regioisomer **9i** was also present in a 1 : 25 ratio and therefore that (*Z*)-2',6'-Dichloro-2,3-dimethylbenzophenone oxime (**3i**) was also formed in the reaction. The product was recrystallised to give **3h** as a white solid.

3h: mp 173-174°C. Anal. Calcd. for $C_{15}H_{13}Cl_2NO$: C, 61.43; H, 4.47; N, 4.78. Found: C, 61.55; H, 4.52; N, 4.82. Mass spectrum: m/z 295 (M+2, 43), 293 (M+, 60), 278 (16), 276 (23), 258 (23), 122 (16), 107 (22), 106 (100), 105 (22). ^{1}H NMR (DMSO): 11.78 (1H, s, OH), 7.60-7.35 (3H, m), 7.08 (1H, d, 2 Hz), 6.94 (1H, dd, J= 8 , 2 Hz,), 6.83 (1H, d, J= 8 Hz), 2.33 (3H, s), 2.25 (3H, s).

2',6'-Dichloro-3,4-dimethylbenzanilide (9h).

9h: mp 183-184°C. Anal. Calcd. for $C_{15}H_{13}Cl_2NO$: C, 61.43; H, 4.47; N, 4.78. Found: C, 61.60; H, 4.55; N, 4.83. Mass spectrum: m/z 293 (M+, 1); 133 (100). ^{1}H NMR ($CDCl_3$): 7.74 (1H, d, J= 2 Hz), 7.68 (1H, dd, J= 8 , 2 Hz), 7.60 (1H, brs, NH), 7.42-7.15 (4H, m), 2.34 (6H, s).

(E)-2,6-Dichlorobenzophenone oxime (3j).

The same procedure described for compounds **3b** was used. The reagents were 2,6-dichlorobenzonitrile oxide (**1a**) (188 mg, 1 mmol) and anhydrous benzene (**2f**) (20 ml). (*E*)-2,6-dichlorobenzophenone oxime (**3j**) as a white solid (200 mg, 75%) was obtained.

3j: mp 139-141°C. Anal. Calcd. for $C_{13}H_9Cl_2NO$: C, 58.87; H 3.42; N 5.28. Found: C, 58.97; H 3.53; N 5.30. ^{1}H NMR (DMSO): 11.95 (1H, brs, OH), 7.65-7.35 (8H, m). Mass spectrum: m/z 265 (4, M+); 232 (11); 230 (31); 106 (9); 105 (100).

The oxime underwent Beckmann transposition to give the 2,6-dichlorobenzanilide (**9j**)[11] (compared with a pure sample obtained from benzoyl chloride and 2,6-dichloroaniline).

(Z)-2'-Chloro-2,4,6-trimethylbenzophenone oxime (3k).

In the same way as described above, 2-chlorobenzonitrile oxide (**1b**) reacted with mesitylene (**2a**) and BF_3 to give (*Z*)-2'-chloro-2,4,6-trimethylbenzophenone oxime (**3k**) in 70% yield as a white solid.

3k: mp 214-216°C. Anal. Calcd. for $C_{16}H_{16}ClNO$: C, 70.31; H, 5.90; N, 5.13. Found: C, 70.15; H, 5.79; N, 5.07. Mass spectrum: m/z 275 (M+2, 13); 273 (M+, 35); 258 (27); 256 (46); 145 (13); 144 (100); 120 (19). ^{1}H NMR (DMSO): 11.60 (1H, brs, OH), 7.50 (1H, dd, J= 8 , 2 Hz), 7.32 (2H, m), 7.11 (1H, dd, J= 8 , 2 Hz), 6.88 (2H, s), 2.24 (3H, s), 2.02 (3H, s).

2'-Chloro-2,4,6-trimethylbenzanilide (9k).

9k: mp 97-98°C. Anal. Calcd. for $C_{16}H_{16}ClNO$: C, 70.31; H, 5.90; N, 5.13. Found: C, 70.30; H, 5.85; N, 5.10. Mass spectrum: m/z 273 (M+, 9); 148(12); 147 (100); 119 (17). ^{1}H NMR($CDCl_3$): 8.55 (1H, dd, J= 8, 2 Hz), 7.75 (1H, brs, NH), 7.37 (2H, m), 7.10 (1H, td, J= 8 , 2 Hz), 6.91 (2H, s), 2.38 (6H, s), 2.32 (3H, s).

(E)-2-Chloro-4'-methylbenzophenone oxime (3l).

In the same way as described for the reaction of 2,6-dichlorobenzonitrile oxide (**1a**), 2-chlorobenzonitrile oxide (**1b**) (188 mg, 1 mmol) reacted with toluene (**2b**) (20 ml) in the presence of BF_3 to give a white solid. A mixture of **3l** and (*E*)-2-chloro-2'-methylbenzophenone oxime (**3m**) (90:10) in 77% overall yield is shown

by ^1H NMR and confirmed by GC and GC-MS analyses of the amides obtained *via* Beckmann reaction. The solid was recrystallised to afford (*E*)-2-chloro-4'-methylbenzophenone oxime (**3l**).

3l: mp 121-122°C. Anal. Calcd. for $C_{14}H_{12}ClNO$: C, 68.55; H, 4.94; N, 5.71. Found: C, 68.35; H, 4.90; N, 5.68. Mass spectrum: m/z 247 (M+2, 35); 245 (M+, 100); 230 (24); 228 (59); 210 (46); 192 (13); 178 (13); 165 (13). ^1H NMR ($CDCl_3$): 8.78 (1H, brs, OH), 7.48 (2H, dt, J= 8 , 2 Hz), 7.28-7.45 (4H, m), 7.19 (2H, dt, J= 8 , 2 Hz), 2.38 (3H,s).

2'-Chloro-4-methylbenzoanilide (9l).

9l: mp 92-93°C. Anal. Calcd. for $C_{14}H_{12}ClNO$: C, 68.55; H, 4.94; N, 5.71. Found: C, 68.47; H, 4.91; N, 5.70. Mass spectrum: m/z 245 (M+, 2); 210 (4); 119 (100). NMR ($CDCl_3$): 8.58 (1H, dd, J= 8 , 2 Hz), 8.44 (1H, brs, NH), 7.82 (2H, dt, J= 8.5 , 2 Hz), 7.40 (2H, td, J= 8 , 2 Hz), 7.32 (2H, dt, J= 8.5 , 2 Hz), 7.08 (1H, td, J= 8 , 2 Hz), 2.43 (3H, s).

(E)-2-Chloro-4'-methoxybenzophenone oxime (3n).

In the similar way as described for the reaction of 2,6-dichlorobenzonitrile oxide (**1a**), 2-chlorobenzonitrile oxide (**1b**) was allowed to react with anisole (**2c**) and BF_3 to give, after the usual work-up, a white solid (72%). ^1H NMR spectrum and GC-MS analyses of the corresponding amides obtained by Beckmann reaction, showed that the product was a mixture (9 :1) of **3n** and its regioisomer, probably (*E*)-2-chloro-2'-methoxybenzophenone oxime (**3o**). The product was recrystallised to give (*E*)-2-chloro-4'-methoxybenzophenone oxime (**3n**) as a white solid.

3n: mp 124-125°C. Anal. Calcd. for $C_{14}H_{12}ClNO_2$: C, 64.35; H, 4.63; N, 5.36. Found: C, 64.38; H, 4.70; N, 5.36. Mass spectrum: m/z 263 (M+2, 32); 262 (M+1, 13); 261 (M+, 89); 246 (16); 244 (45); 229 (16); 226 (11); 152 (11), 108 (100). ^1H NMR ($CDCl_3$): 8.85 (1H, brs, OH), 7.58 (2H, dt, J = 9 , 2 Hz), 7.5-7.3 (4H, m), 6.89 (2H, dt, J= 9 , 2 Hz), 3.82 (3H, s).

2'-Chloro-4-methoxybenzanilide (9n).

9n: mp 135-136°C. Anal. Calcd. for $C_{14}H_{12}NO_2Cl$: C, 64.35; H, 4.63; N, 5.36. Found: C, 64.22; H, 4.60; N, 5.31. Mass spectrum: m/z 261 (M+, 6); 226 (26); 135 (100). ^1H NMR ($CDCl_3$): 8.56 (1H, dd, J= 8.5 , 2 Hz), 8.39 (1H, brs, NH), 7.89 (2H, dt, J= 9 , 2 Hz) 7.41 (1H, dd, J= 8.5 , 2 Hz), 7.33 (1H, td, J= 8.5 , 2 Hz), 7.07 (1H, td, J= 8.5 , 2 Hz), 7.01 (2H, dt, J= 9 , 2 Hz), 3.89 (3H, s).

Reaction of 2-chlorobenzonitrile oxide with benzene (3p).

In the same way as described for the reaction of 2,6-dichlorobenzonitrile oxide (**1a**), 2-chlorobenzonitrile oxide (**1b**) reacted with benzene (**2b**) in the presence of BF_3 to yield (*E*)-2-chlorobenzophenone oxime (**3p**) as a white solid (80%).[6]

(Z)-2,4,6-Trimethylbenzophenone oxime (3q).

In a similar procedure as described above, reaction of benzonitrile oxide (**1c**) and mesitylene (**2a**) in the presence of BF_3, afforded (*Z*)-2,4,6-trimethylbenzophenone oxime (**3q**) in 50% yield as a white solid.

3q: mp 132-133°C. Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16; N, 5.85. Found: C, 80.12; H, 7.08; N, 5.79. ^1H NMR ($CDCl_3$): 2.11 (s, 6H); 2.34 (s, 3H); 6.97 (s, 2H); 7.31 (m, 3H); 7.48 (m, 2H); 8.32 (s, 1H). 240 (15); 239 (M+, 70); 238 (12); 224 (36); 223 (18); 222 (90); 221 (10); 207 (30); 178 (27); 145 (12); 144 (100); 120 (36). Beckmann reaction of the oxime **3q** gave the corresponding amide **9q**.[12]

Reaction of benzonitrile oxide with toluene.

In the same way as described above, benzonitrile oxide (**1c**) reacted with toluene (**2b**) in the presence of BF_3 to give a mixture of two oximes in 74% yield. NMR spectrum of the oximes and GC analyses of the corresponding amides **9r**[13], **9s**[14] showed that (*Z*)-4-methylbenzophenone oxime (**3r**)[15] and (Z)-2-methylbenzophenone oxime (**3s**)[14] were present in a 8 :2 ratio.

Reaction of benzonitrile oxide with anisole.

A cooled solution of benzonitrile oxide (**1c**) (119 mg, 1 mmol) in n-hexane (50 ml) was added with a syringe pump to a BF_3 saturated solution of anisole (**2c**) (2 ml) in n-hexane (10 ml). After the usual work-up the crude was chromatographated on silica gel using hexane-ethyl acetate 9:1 as eluent to give a mixture of the two oximes in 60% yield. NMR spectrum of the oximes and GC analyses of the corresponding amides **9t**[16], **9u**[17] showed that (*Z*)-4-methoxybenzophenone oxime (**3t**)[18] and (*Z*)-2-methoxybenzophenone oxime (**3u**)[19] were in 9:1 ratio.

Reaction of benzonitrile oxide with benzene (3v).

A cooled solution of benzonitrile oxide (**1c**) (119 mg, 1 mmol) in anhydrous benzene (**2f**) (50 ml) was added with a syringe pump to a BF_3 saturated solution of benzene (10 ml). After 30 minutes the solvent was removed, the crude dissolved in ethyl acetate, washed with a 2% solution of $NaHCO_3$ and dried over sodium sulphate. The solvent was removed and the mixture was chromatographated on silica gel (hexane/ethyl acetate 9/1 as eluent) to give benzophenone oxime (**3v**) in 72% yield which was compared with a pure sample obtained from benzophenone.

References

1. Morrocchi, S.; Ricca, A.; Velo, L. *Tetrahedron Lett.*, **1967**, *4*, 331
2. Morrocchi, S.; Ricca, A.; Selva, A.; Zanarotti, A. *Gazz. Chim. Ital.*, **1968**, *50*, 558
3. Grundmann, C.; Grünanger, P. *The Nitrile Oxides*, Springer-Verlag: Berlin, **1971**; pp. 120-132.
4. Kim, J. N.; Ryu, E. K. *Tetrahedron Lett.*, **1993**, *34*, 3567-3570.
5. Auricchio, S.; Ricca, A.; Pastormerlo, E.; Truscello, A. M. *Proceedings of XXI Convegno Nazionale della Divisione di Chimica Organica*, **1993**, 248.
6. Porter, C. W.; Wilcox, H. B. *J. Am. Chem. Soc.*, **1934**, *56*, 2688.
   Coffer, D. L.; Scheer, B.; Bizzarro, F. T.; Cheung, J. B. *J. Org. Chem.*, **1984**, *49*,296.
7. Grundmann, C.; Grünanger, P. *The Nitrile Oxides*, Springer-Verlag: Berlin, **1971**; pp.140-174.
8. Kanemasa, S.; Tsuruoka, T.; Wada, E. *Tetrahedron Lett.*, **1993**, *34*, 87 and references cited.
9. Hauser, C. R.; Hoffenberg, D. S. *J. Am. Chem. Soc.*, *1955*, *77*, *4885*.
10. Hegarty, A. F. *Acc. Chem. Res.*, **1980**, *13*, 448 and references cited therein.
11. Petyunin, P. A.; Tetynewa, L. A. *Zh. Obshch. Khim.*, **1958**, *28*, 1548.
12. Leuckart, R. *J. Prakt. Chem.*, **1890**, *[2] 41*, 308.
13. Fischli, H. *Chem Ber.* **1879**, *12*, 616.
14. Smith, A. W. *Chem Ber.*, **1891**, *24*, 4047.
15. Hantzsch, A. *Chem Ber.*, **1890**, *23*, 2326.
16. Lossen, W. *A. Ch.*, **1875**, *175*, 293.
17. Haller, A. *Compt. Rend. Acad. Sc.*, **1895**, *121*, 189
18. Hantzsch, A. *Chem Ber.*, **1891**, *24*, 53.
19. Billon, P. *A. Ch.*, **1927**, *7*, 332.

(*Received in UK* 22 *February* 1994; *revised* 22 *April* 1994; *accepted* 29 *April* 1994)