Reactions between Nitrile Oxides and Carbenium Ions: Synthesis of Benzoxazines, Oximes, and Amides through Intramolecular *ortho* or *ipso* Attack

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Reactions between nitrile oxides and benzylic carbocations are described. Different results were obtained when the carbocations were generated from the corresponding chlorides with different Lewis acids, with addition products such as benzoxazines, oximes, and amides being produced. Primary, secondary, and tertiary carbocations showed different reactivities. The product ratios strongly depended on the substituents on the aromatic ring of the benzylic carbocations. Evidence for the proposed mechanism is reported.

Introduction

Nitrile oxides are widely used as dipoles in cycloaddition reactions for the synthesis of various heterocyclic rings.[1] As the carbon atom of the dipole is quite electrophilic, many 1,3-addition reactions have also been performed.[2,3] Nitrile oxides can react with various nucleophiles, such as amines, alkoxides, azides, and alcohols,[2] but as a matter of fact the attack of the dipole's carbon atom at another carbon atom is less easy, and the few reported examples are reactions between nitrile oxides and strong nucleophiles such as carbanions or cyanides.[2] In order to promote reactions between nitrile oxides and less reactive carbon nucleophiles, we became involved in the study of the reactivity of nitrile oxides towards Lewis acids.[4] We had previously found that, in the presence of gaseous BF_3, nitrile oxides gave complexes in which the electrophilicity of the carbon atom was so enhanced that it could react with aromatic systems, stereoselectively yielding aryl oximes, or with tetrasubstituted alkenes to give cycloaddition products.[5] We therefore decided to examine the reactivity of nitrile oxides towards particular Lewis acids such as carbocations, and we now wish to report here that this dipole reacted with benzylic carbocations to provide addition products via an intermediate that underwent intramolecular attack. Although reactions between benzhydryl carbocations and alkenes have been studied in detail,[6] this is to the best of our knowledge the first example of reactions between carbocations and dipoles.

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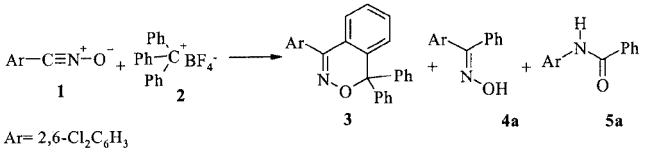
Results

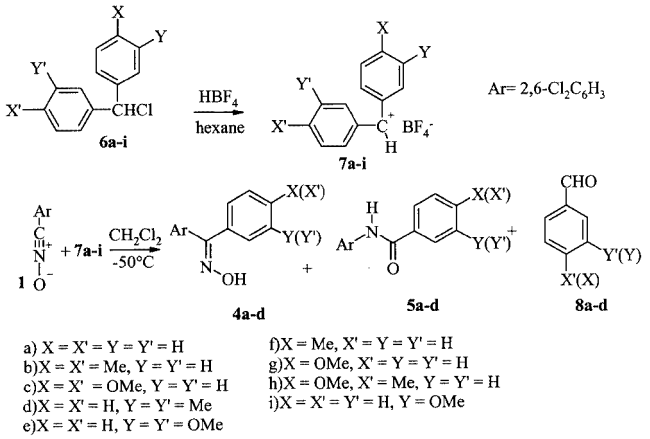
We started our study with a stable nitrile oxide − 2,6-dichlorobenzonitrile oxide (**1**) − and trityl tetrafluoroborate (**2**). The reaction between **1** and **2** gave benzoxazine **3** (20%), the cleavage products oxime **4a** (40%) and amide **5a** (20%), and also benzophenone (Scheme 1).



Scheme 1. Reaction between **1** and trityl tetrafluoroborate

We then extended this reaction to unstable secondary carbocations. Carbenium ions were generated from the corresponding benzhydryl chlorides **6a**−**i** in the presence of HBF_4[7] or of other Lewis acids such as BCl_3,[8] $SbCl_5$,[9] and gaseous BF_3. Reactions between **1** and **7a**−**i**, generated with tetrafluoroboric acid, gave only oximes **4a**−**d**, amides **5a**−**d**, and aldehydes **8a**−**d**, and not the expected benzoxazine **3** (Scheme 2). The yields of **4** and **5** are given in Table 1.

Tetrafluoroborate **7a**, prepared from benzhydryl chloride (**6a**), gave 2,6-dichlorobenzophenone oxime (**4a**), *N*-arylbenzamide **5a**, and benzaldehyde (**8a**) (Entry 1). Bis(*p*-phenyl)-substituted carbocations **7b** and **7c** (Entries 2 and 3) gave the *p*-phenyl-substituted oximes **4b** and **4c**, the *p*-phenyl-substituted benzamides **5b** and **5c**, and the *p*-phenyl-substituted aldehydes **8b** and **8c**, respectively. The bis(*m*-methyl)benzhydryl-substituted salt **7d** (Entry 4) gave *m*-methyl-substituted oxime **4d**, amide **5d**, and aldehyde **8d**. When the phenyl group of the salt was strongly activated by a methoxy group in *meta* position (Entries 5 and 9), the



Scheme 2. Reactions between **1** and benzhydryl chlorides **6a**−**i** in the presence of HBF_4

Table 1. Reactions between **1** and carbocations **7a**−**i**

Entry	Carbocation	Yield (%)[a]	Yield (%)[a]
1	**7a**	**4a** (34)	**5a** (10)
2	**7b**	**4b** (45)	**5b** (13)
3	**7c**	**4c** (59)	**5c** (21)
4	**7d**	**4d** (49)	**5d** (10)
5	**7e**	unchanged **1** and tar recovered	
6	**7f**	**4a** (18) + **4b** (23)	**5a** (5) + **5b** (11)
7	**7g**	**4c** (54)	**5c** (18)
8	**7h**	**4c** (56)	**5c** (15)
9	**7i**	unchanged **1** and tar recovered	

[a] Yields given are those obtained after purification by column chromatography.

carbocation underwent polymerization under these reaction conditions, and no reaction with **1** was observed. When the two aromatic rings of the carbocations were differently substituted (Entries 6−8), their reactions would have been expected to give mixtures of the possible oximes, amides, and aldehydes as the carbocations underwent carbon−carbon cleavage. Only in one case − that of *p*-methylbenzhydryl cation **7f** (Entry 6) − did the reaction afford both possible oximes **4a** and **4b**, amides **5a** and **5b**, and aldehydes **8a** and **8b**. In each of the other two cases (Entries 7 and 8), only one oxime, one amide, and one aldehyde were isolated.

The amides **5** had not been formed through in situ rearrangement of oximes **4**, as we found that the oximes did not give the corresponding amides under the same reaction conditions (and reaction times). We also found that the ratio between oximes and amides was strongly dependent on the amount of HBF_4 used in the reaction. When a large excess of the acid was used, it was possible essentially to obtain only amides (Table 2).

It was possible to obtain oximes instead, by Beckmann rearrangement, by use of PCl_5. Stereoisomerically pure oximes were found to have been formed in all these reactions, the hydroxy group always being on the side opposite to the nitrile oxide's aromatic substituent.

Table 2. Reaction between **7a** and **1** in the presence of HBF_4

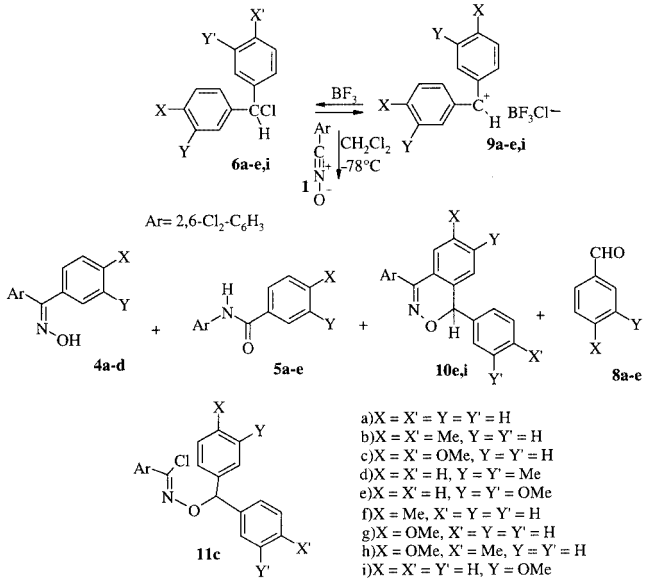
Equiv. of HBF_4	Yield of **4a** (%)	Yield of **5a** (%)
1	35	10
5	15	35
10	traces	50

All these results showed that nitrile oxide reacted with carbocations in good overall yields, and that the intermediate underwent C−C cleavage under these reaction conditions.

The nature of the Lewis acid used to generate the carbocations proved to be very important. BCl_3 and $SbCl_5$, generally used in carbocation reactions, had to be discarded, as the use of their corresponding tetrachloroborates[8] and hexachloroantimonates[9] was unsuccessful and gave no reaction with **1**.

When the carbocation was generated by means of another Lewis acid, such as gaseous boron trifluoride, it was possible to isolate benzoxazine, the addition product in which no bond cleavage had occurred.

Carbocations were therefore prepared by bubbling BF_3 into a solution of the chlorides at −78 °C. As in the case of tetrachloroborate, the salt **9** probably existed in equilibrium with the chloride **6**[8] and its treatment with nitrile oxide **1** gave − besides the oximes **4**, amides **5**, and aldehydes **8** − the benzoxazines **10** and oximate **11** (Scheme 3); yields are given in Table 3.



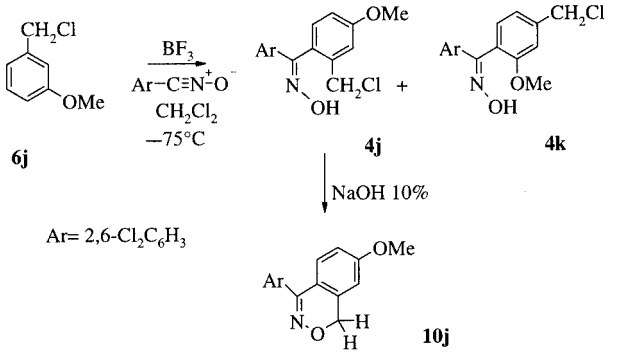
Scheme 3. Reactions between **1** and benzhydryl chlorides **6a**−**e** and **6i** in the presence of BF_3

Benzhydryl chloride (**6a**), chlorobis(*p*-methylphenyl)-methane (**6b**), and chlorobis(*m*-methylphenyl)methane (**6d**) again gave mixture of oximes, amides, and aldehydes (Entries 1, 2, and 4). Under these reaction conditions, however, polymerization of *m*-phenyl-substituted carbocations was

Table 3. Reaction between **1** and **6a−e** and **6i** in the presence of BF_3

Entry	Chloride	*T* [°C]	Yield (%)[a]	Yield (%)[a]	Yield (%)[a]	Yield (%)[a]
1	**6a**	−78	**4a** (3)	**5a** (60)		
2	**6b**	−78	**4b** (15)	**5b** (45)		
3	**6c**	−78	**4c** (10)	**5c** (10)		**11c** (40)
4	**6d**	−78	**4d** (21)	**5d** (41)		
5	**6e**	−78		**5e** (traces)	**10e** (33)	
6	**6e**	+25		**5e** (12)	**10e** (40)	
7	**6i**	−78		**5a** (20) + **5e** (12)	**10i** (30)	
8	**6i**	+25		**5a** (15) + **5e** (15)	**10i** (40)	

[a] Yields given are those obtained after purification by column chromatography.



Scheme 4. Reaction between **1** and primary benzylic chloride **6j** in the presence of BF_3

reduced. Benzoxazines **10e** and **10i** were obtained together with amides **5e** and/or **5a** on treatment of activated *m*-methoxy-substituted chlorides **6e** and **6i** with **1** (Entries 5−8). The corresponding oximes were not isolated. The *p*-methoxyphenyl-substituted chloride **6c** gave the open-chain product **11c**, together with oxime **4c**, amide **5c**, and aldehyde **8c** (Entry 3). Product **11c** could originate from a reaction between **1** and the chloride **6c**, as analogous reactions have been reported.[10] We found, however, that **1** and **6c** did not react in the same reaction time as used above. Reaction did take place in one week, though, affording **11c**.

In all these reactions, the yields of amides were almost always greater than those of oximes; excess BF_3 favored formation of amides more than excess HBF_4.

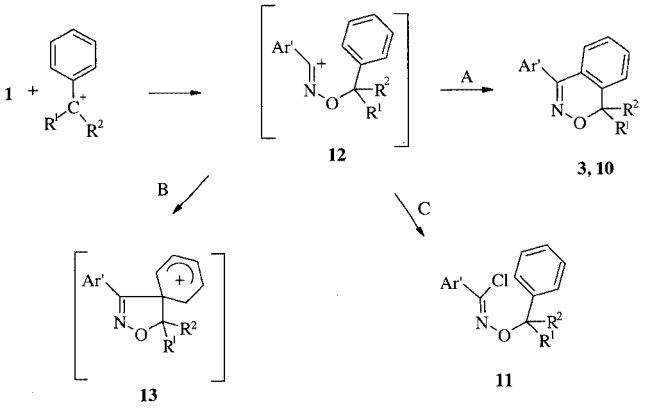
The yields of the benzoxazines **10e** and **10i** were slightly influenced by temperature, and increased to 40% in both cases (Entries 6 and 8) if the reaction was carried out at room temperature.

Treatment with triphenylmethyl chloride at −75 °C in the presence of BF_3 gave benzoxazine **3** (30%), oxime **4a** (10%), and amide **5a** (31%), together with benzophenone. As reported above, the use of stable tetrafluoroborate **2** gave different results.

Treatment with a primary chloride such as **6j** in the presence of BF_3 produced quite different results; a mixture of oximes **4j** and **4k** (4:1) was obtained after 6 h at −75 °C, **4j** undergoing cyclisation to benzoxazine **10j** on treatment with NaOH (Scheme 4). Partial cyclization also occurred during chromatography on silica gel. When the reaction was performed at room temperature, the ratio between the two oximes was almost 1:1.

Discussion

On the basis of the products obtained from the reactions between tertiary and secondary halides and **1**, we suggest that the mechanism involved the initial attack of the carbocation at the oxygen atom of the nitrile oxide, giving intermediate **12** (Scheme 5). Carbocation **12**, in turn, would be able to undergo intramolecular electrophilic substitution and could give rise to different products. The attack could occur at the *ortho* position of the aromatic ring, in which case the benzoxazine **10** or **3** would be formed (pathway A), or at the *ipso* position with formation of the intermediate **13** (pathway B). The intermediate **12** could also undergo chloride attack to form open-chain products **11** (pathway C).

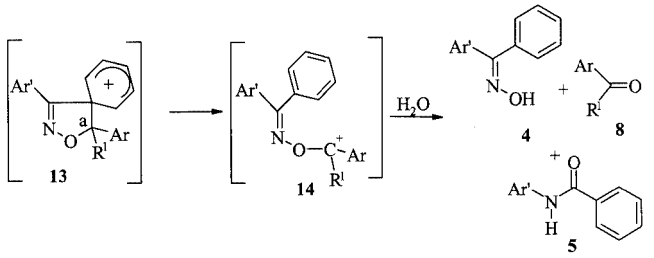


Scheme 5. Proposed mechanism for the reaction between **1** and tertiary and secondary carbocations

Formation of oximes, amides, and aldehydes (or ketones) was clearly due to intermediate **13**. On cleavage of the α bond (Scheme 6) the spiro intermediate **13** would give rise to intermediate **14**, which could in turn hydrolyze to oxime **4** and aldehyde or ketone. All amides obtained were *N*-(2,6-dichlorophenyl)-substituted, and so there must have been a Beckmann-type migration, and so formation of the amides from open-chain derivative **11** can hence be ruled out. As amides **5** would not be formed by Beckmann rearrangement of oximes **4**, they may have originated by rearrangement from either intermediate **13** or **14** and subsequent hydrolysis.

For both pathway A and pathway B, if two different substituted aromatic rings were present in the carbocation, the *ipso* or *ortho* attack should occur only or mainly on the ring with the activated positions (see Table 1, Entries 6−8).

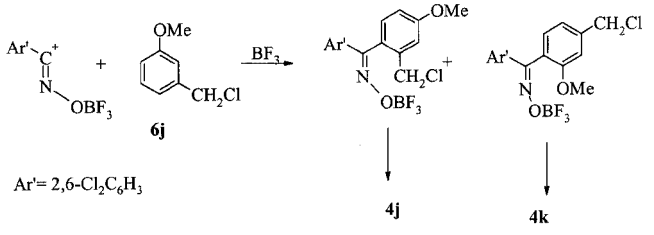
It therefore seems clear that the formation of oxime, amide, and aldehyde was due to preference for the *ipso* attack over the *ortho* one.



Scheme 6. Proposed mechanism for the formation of oximes and amides from intermediate **13**

Oximes and/or amides were always obtained in these reactions, and so the *ipso* attack must always have taken place, even when the position was not activated. The alternative *ortho* attack occurred only if this position of the aromatic ring was strongly activated, as in **6e** and **6i**.[11] It was noteworthy that, in the case of tertiary carbocation **2**, although the *ortho* position was not activated, *ortho* attack occurred and benzoxazine **3a** was formed. The influence of aromatic substituents, the reversibility of addition, and the formation of benzylic carbocation **14** all have to be considered to explain the marked preference for the *ipso* position in these intramolecular electrophilic substitutions.

In the case of primary carbocations, the formation of the two isomeric oximes and the absence of benzoxazine in the reaction medium, make us believe that the reaction mechanism was actually different and that the attack occurred at the carbon atom of the nitrile oxide complex formed in the reaction media (Scheme 7).



Scheme 7. Proposed mechanism for the reaction between **1** and primary benzylic chlorides

At low temperatures, reaction took place in 6 h and was under kinetic control: the main product was **4j**. At room temperature, in contrast (reaction occurred instantaneously), the reaction was under thermodynamic control and the **4j/4k** ratio was almost 1.

Conclusions

Reactions between a 1,3-dipole, such as a nitrile oxide, and benzylic carbocations are discussed. The carbocations reacted with nitrile oxides acting both as reagent and as Lewis acid promoting the addition. The interaction of the carbocation, the Lewis acid, with the negative part of the zwitterion enhanced the dipole electrophilicity and promoted an intramolecular Friedel–Crafts-type attack, resulting in the formation of cyclic products.

In this way, depending on the substituents on the aromatic ring of the carbocation, formal [3+3] or [3+2] cycloadditions occurred. When the *ortho* position was activated, [3+3] cycloaddition took place and benzoxazines were obtained. When, in contrast, the *ipso* position was activated, [3+2] cycloaddition took place, and carbocations of 2-oxa-3-azaspiro[4.5]deca-3,6,9-trienes were produced as unstable intermediates. These intermediates give oximes and amides through cleavage of a carbon–carbon bond.

As far as we know, this is the first example of a reaction between 1,3-dipoles and a carbocation, but as it should not be the only one, this work may open new routes for the formation of heterocyclic rings from zwitterions.

Experimental Section

General: NMR spectra were recorded with a Bruker 250 MHz spectrometer with TMS as internal standard. Mass spectra were performed with a Finnigan TSQ 70 instrument. Melting points are uncorrected. Chromatographic separations were performed on Merck 60 Kieselgel. The stereochemistries of the oximes were determined by Beckmann rearrangement with PCl_5. Alcohols used in the synthesis of benzydryl chlorides **6** were prepared, when commercially not available, from the corresponding aldehydes and aryl bromides by Grignard reactions. Yields given are those obtained after purification by column chromatography; in almost all these reactions, small quantities of nitrile oxide and nitrile oxide dimer (furoxan) were found; yields of aldehydes are not reported as these were always eluted as mixtures with nitrile oxide or nitrile oxide dimer. In some reactions, ^1H NMR monitoring of the mixture showed that the quantity of aldehyde formed was, as would be expected, similar to those of oxime and amide.

Preparation of Benzhydryl Chlorides 6b–i: Benzhydryl chlorides **6b–i** were prepared by bubbling gaseous HCl into a cooled (−10 °C) solution of the corresponding alcohols (0.0164 mol) in dry CH_2Cl_2 (40 mL) in the presence of $CaCl_2$ (4 g). At the end of the reaction, the solvent was removed and the crude chlorides were either crystallized or distilled. Yields were quantitative.

Reaction between 2,6-Dichlorobenzonitrile Oxide (1) and Trityl Fluoroborate (2): Trityl fluoroborate (**2**) (1.00 g, 3.00 mmol) was dissolved in CH_2Cl_2 (100 mL), and compound **1** (0.57 g, 3.0 mmol) was added to this solution. The mixture was stirred at room temperature overnight. The mixture was washed with H_2O, a 10% solution of NH_4Cl, and again with H_2O. It was dried, and the solvent was removed. Column chromatography gave 4-(2,6-dichlorophenyl)-1,1-diphenyl-1*H*-2,3-benzoxazine (**3**, 0.26 g, 20%), (*E*)-2,6-dichlorobenzophenone oxime (**4a**,[4a] 0.32 g, 40%), and 2,6-dichlorobenzanilide (**5a**, 0.16 g, 20%).

Compound 3: White solid (cyclohexane), m.p. 109–110 °C. ^1H NMR (250 MHz, $CDCl_3$, ppm): δ = 7.08–7.62 (m, 12 H), 7.78 (m, 5 H). EI MS: *m/z* (%) = 429 (4) [M^+], 394 (10), 326 (15), 243 (100), 187 (20). $C_{26}H_{17}Cl_2NO$ (430.3): calcd. C 72.57, H 3.98, N 3.25; found C 72.52, H 4.03, N 3.16.

General Procedure for the Treatment of 1 with Chlorides 6a–i in the Presence of HBF_4: Benzhydryl chlorides **6a–i** were dissolved in a two-necked flask in dry *n*-hexane (30 mL) under a stream of nitrogen. The solution was cooled to −50 °C, and a 54% solution of HBF_4 (1 mol-equiv.) in diethyl ether was added. After the precipitation of a red solid, nitrogen was bubbled through the mixture to

remove the solvent, and a solution of **1** in dry CH_2Cl_2 (30 mL), cooled to −50 °C, was added. After a few hours, the mixture was washed with a 10% solution of NH_4Cl and water, and dried. The solvent was removed. Products were separated by column chromatography [eluent from *n*-hexane/ethyl acetate (95:5) to pure ethyl acetate].

Reaction between 6a and 1: Treatment of **6a** (0.46 g, 2.3 mmol) with **1** (0.43 g, 2.3 mmol) in the presence of HBF_4 (0.32 mL) afforded, after workup and purification, (*E*)-2,6-dichlorobenzophenone oxime (**4a**, 0.21 g, 34%) and 2,6-dichlorobenzanilide (**5a**, 0.06 g, 10%).

Reaction between 6b and 1: Treatment of **6b** (0.50 g, 2.2 mmol) with **1** (0.41 g, 2.2 mmol) in the presence of HBF_4 (0.30 mL) afforded, after workup and purification, (*E*)-2,6-dichloro-4′-methylbenzophenone oxime (**4b**, 0.28 g, 45%) and 2′,6′-dichloro-4-methylbenzanilide (**5b**, 0.08 g, 13%).

Compound 4b:[4b] White solid (ethanol/water), m.p. 148−150 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 2.35 (s, 3 H), 7.18 (dt, *J* = 2 and 9 Hz, 2 H), 7.20−7.30 (m, 3 H), 7.60 (dt, *J* = 2 and 9 Hz, 2 H), 8.48 (br. s, 1 H). EI MS: *m*/*z* (%) = 281 (64) [M^+ + 2], 280 (21), 279 (100) [M^+], 262 (27), 244 (27).

Compound 5b: White solid (ethanol/water), m.p. 170−171 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 2.43 (s, 3 H), 7.18 (dd, *J* = 8 and 9 Hz, 1 H), 7.29 (d, *J* = 8 Hz, 2 H), 7.39 (d, *J* = 8 Hz, 2 H), 7.68 (br. s, 1 H), 7.86 (d, *J* = 8 Hz, 2 H). EI MS: *m*/*z* (%) = 279 (2) [M^+], 244 (24), 119 (100). $C_{14}H_{11}Cl_2NO$ (280.2): calcd. C 60.02, H 3.96, N 5.00; found C 59.97, H 4.05, N 4.82.

Reaction between 6c and 1: Treatment of **6c** (0.50 g, 1.9 mmol) with **1** (0.36 g, 1.9 mmol) in the presence of HBF_4 (0.26 mL) afforded, after workup and purification, (*E*)-2,6-dichloro-4′-methoxybenzophenone oxime (**4c**,[4a] 0.33 g, 59%) and 2′,6′-dichloro-4-methoxybenzanilide (**5c**,[4a] 0.12 g, 21%).

Reaction between 3d and 1: Treatment of **6d** (0.50 g, 2.2 mmol) with **1** (0.41 g, 2.2 mmol) in the presence of HBF_4 (0.30 mL) afforded, after workup and purification, (*E*)-2,6-dichloro-3′-methylbenzophenone oxime (**4d**, 0.30 g, 49%) and 2′,6′-dichloro-3-methylbenzanilide (**5d**, 0.06 g, 10%).

Compound 4d: White solid (ethanol/water), m.p. 142−144 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 2.34 (s, 3 H), 7.10−7.50 (m, 7 H), 8.35 (br. s, 1 H). EI MS: *m*/*z* (%) = 279 (16) [M^+], 262 (25), 244 (57), 91 (100). $C_{14}H_{11}Cl_2NO$ (280.2): calcd. C 60.02, H 3.96, N 5.00; found C 59.95, H 4.09, N 4.87.

Compound 5d: White solid (ethanol/water), m.p. 168−169 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 2.45 (s, 3 H), 7.20 (dd, *J* = 8 and 9 Hz, 1 H), 7.36−7.46 (m, 4 H), 7.66 (br. s, 1 H), 7.70−7.82 (m, 2 H). EI MS: *m*/*z* (%) = 279 (2) [M^+], 244 (37), 119 (100). $C_{14}H_{11}Cl_2NO$ (280.2): calcd. C 60.02, H 3.96, N 5.00; found C 60.01, H 3.99, N 4.94.

Reaction between 6f and 1: Treatment of **6f** (0.50 g, 2.3 mmol) with **1** (0.44 g, 2.3 mmol) in the presence of HBF_4 (0.32 mL) afforded, after workup and purification, 0.11 g (18%) of (*E*)-2,6-dichlorobenzophenone oxime (**4a**), (*E*)-2,6-dichloro-4′-methylbenzophenone oxime (**4b**, 0.15 g, 23%), 2,6-dichlorobenzanilide (**5a**, 0.03 g, 5%), and 2′,6′-dichloro-4-methylbenzanilide (**5b**, 0.07 g, 11%).

Reaction between 6g and 1: Treatment of **6g** (0.50 g, 2.2 mmol) with **1** (0.41 g, 2.2 mmol) in the presence of HBF_4 (0.30 mL) afforded, after workup and purification, (*E*)-2,6-dichloro-4′-methoxybenzophenone oxime (**4c**, 0.35 g, 54%) and 2′,6′-dichloro-4-methoxybenzanilide (**5c**, 0.12 g, 18%).

Reaction between 6h and 1: Treatment of **6h** (0.50 g, 2.0 mmol) and **1** (0.38 g, 2.0 mmol) in the presence of HBF_4 (0.28 mL) afforded, after workup and purification, (*E*)-2,6-dichloro-4′-methoxybenzophenone oxime (**4c**, 0.33 g, 56%) and 2′,6′-dichloro-4-methoxybenzanilide (**5c**, 0.09 g, 15%).

Reaction between 6a and 1 in the Presence of BF_3: BF_3 gas was bubbled into a solution of **6a** (0.44 g, 2.2 mmol) in 50 mL of dry CH_2Cl_2 at −78 °C. A solution of **1** (0.41 g, 2.2 mmol) in dry CH_2Cl_2 (20 mL), cooled to −78 °C, was added under a stream of nitrogen. After 4 h, the mixture was treated with H_2O, a 10% solution of NH_4Cl, and again with H_2O, and dried. The solvent was removed. Column chromatography afforded (*E*)-2,6-dichlorobenzophenone oxime (**4a**, 0.02 g, 3%) and 2′,6′-dichlorobenzanilide (**5a**, 0.35 g, 60%).

Reaction between 6b and 1 in the Presence of BF_3: BF_3 gas was bubbled into a solution of **6b** (0.50 g, 2.2 mmol) in dry CH_2Cl_2 (50 mL) at −78 °C. A solution of **1** (0.41 g, 2.2 mmol) in dry CH_2Cl_2 (20 mL), cooled to −78 °C, was added under a stream of nitrogen. After 4 h, the mixture was treated with H_2O, a 10% solution of NH_4Cl, and again with H_2O, and dried. The solvent was removed. Column chromatography afforded (*E*)-2,6-dichloro-4′-methylbenzophenone oxime (**4b**, 0.09 g, 15%) and 2′,6′-dichloro-4-methylbenzanilide (**5b**, 0.28 g, 45%).

Reaction between 6c and 1 in the Presence of BF_3: BF_3 gas was bubbled into a solution of **6c** (0.60 g, 2.3 mmol) in dry CH_2Cl_2 (50 mL) at −78 °C. A solution of **1** (0.43 g, 2.3 mmol) of dry CH_2Cl_2 (20 mL), cooled to −78 °C, was added under a stream of nitrogen. After 4 h, the mixture was treated with H_2O, a 10% solution of NH_4Cl, and again with H_2O, and dried. The solvent was removed. Column chromatography afforded *N*-[bis(4-methoxyphenyl)methoxy]-2,6-dichlorobenzenecarboximidoyl chloride (**11c**, 0.41 g, 40%), (*E*)-2,6-dichloro-4′-methoxybenzophenone oxime (**4c**, 0.07 g, 10%), and 2′,6′-dichloro-4-methoxybenzanilide (**5c**, 0.07 g, 10%).

Compound 11c: White solid (*n*-hexane), m.p. 94−95 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 3.80 (s, 6 H), 6.34 (s, 1 H), 6.88 (m, 4 H), 7.30 (m, 7 H). ^{13}C NMR ($CDCl_3$, ppm): δ = 55.2, 87.4, 113.7, 128.0, 128.7, 131.4, 132.3, 132.4, 132.7, 135.4, 159.2. MS: *m*/*z* (%) = 449 (1) [M^+], 228 (48), 227 (100). $C_{22}H_{18}Cl_3NO_3$ (450.7): calcd. C 58.62, H 4.03, N 3.11; found C 58.51, H 3.91, N 2.97.

Reaction between 6d and 1 in the Presence of BF_3: BF_3 gas was bubbled into a solution of **6d** (0.50 g, 2.2 mmol) in dry CH_2Cl_2 (50 mL) at −78 °C. A solution of **1** (0.41 g, 2.2 mmol) in dry CH_2Cl_2 (20 mL), cooled to −78 °C, was added under a stream of nitrogen. After 4 h, the mixture was treated with H_2O, a 10% solution of NH_4Cl, and again with H_2O, and dried. The solvent was removed. Column chromatography afforded (*E*)-2,6-dichloro-3′-methylbenzophenone oxime (**4d**, 0.13 g, 21%) and 2′,6′-dichloro-3-methyl-benzanilide (**5d**, 0.25 g, 41%).

Reaction between 6e and 1 in the Presence of BF_3. Procedure a: BF_3 gas was bubbled into a solution of **6e** (0.53 g, 2.0 mmol) in dry CH_2Cl_2 (100 mL) at −78 °C. A solution of **1** (0.38 g, 2.0 mmol) in dry CH_2Cl_2 (20 mL), cooled to −78 °C, was added under a stream of nitrogen. After 6 h the mixture was washed with water, a 10% solution of NH_4Cl, and again with H_2O, and dried. The solvent was removed. Column chromatography afforded 4-(2,6-dichlorophenyl)-7-methoxy-1-(3-methoxyphenyl)-1*H*-2,3-benzoxazine (**10e**, 0.27 g, 33%) and traces of 2′,6′-dichloro-3-methoxybenzanilide (**5e**). **Procedure b:** BF_3 gas was bubbled into a solution of **6e** (0.53 g, 2.0 mmol) and **1** (0.38 g, 2.0 mmol) in dry CH_2Cl_2 (100 mL) at

room temperature. Reaction was instantaneous and afforded, after purification, 4-(2,6-dichlorophenyl)-7-methoxy-1-(3-methoxyphenyl)-2,3-benzoxazine (**10e**, 0.33 g, 40%) and 2′,6′-dichloro-3-methoxybenzanilide (**5e**, 0.07 g, 12%).

Compound 10e: Oil. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 3.76 (s, 3 H), 3.82 (s, 3 H), 6.12 (s, 1 H), 6.49 (s, 1 H), 6.81 (m, 2 H), 6.94 (m, 1 H), 7.05 (m, 2 H), 7.20−7.50 (m, 4 H). EI MS: *m*/*z* (%) = 415 (70) [M + 2], 413 (100) [M^+], 379 (65), 347 (60), 227 (84).

Compound 5e: White solid (ethanol/water), m.p. 188−189 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 3.88 (s, 3 H), 7.06−7.30 (m, 2 H), 7.35−7.56 (m, 5 H), 7.63 (br. s, 1 H). EI MS: *m*/*z* (%) = 295 (10) [M^+], 260 (100), 135 (100). $C_{14}H_{11}Cl_2NO_2$ (296.2): calcd. C 56.78, H 3.74, N 4.73, Cl 23.94; found C 56.96, H 3.95, N 4.51.

Reaction between 6i and 1 in the Presence of BF_3. Procedure a: BF_3 gas was bubbled into a solution of **3i** (0.47 g, 2.0 mmol) in dry CH_2Cl_2 (100 mL) at −78 °C. A solution of **1** (0.38 g, 2.0 mmol) in dry CH_2Cl_2 (20 mL), cooled to −78 °C, was added under a stream of nitrogen. After 4 h and the usual workup, the reaction afforded 4-(2,6-dichlorophenyl)-7-methoxy-1-phenyl-1*H*-2,3-benzoxazine (**10i**, 0.23 g, 30%), 2′,6′-dichloro-3-methoxybenzanilide (**5e**, 0.07 g, 12%), and 2′,6′-dichlorobenzanilide (**5a**, 0.12 g, 20%). **Procedure b:** BF_3 gas was bubbled at room temperature into a solution of **6i** (0.47 g, 2.0 mmol) and **1** (0.38 g, 2.0 mmol) in dry CH_2Cl_2 (100 mL). Reaction was instantaneous and afforded, after workup and purification, 4-(2,6-dichlorophenyl)-7-methoxy-1-phenyl-2,3-benzoxazine (**10i**, 0.31 g, 40%), 2′,6′-dichloro-3-methoxybenzanilide (**5e**, 0.09 g, 15%), and 2′,6-dichlorobenzanilide (**5a**, 0.09 g, 15%).

Compound 10i: White solid (ethyl acetate), m.p. 108−110 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 3.77 (s, 3 H), 6.15 (s, 1 H), 6.47 (s, 1 H), 6.81 (m, 2 H), 7.25−7.55 (m, 8 H). ^{13}C NMR ($CDCl_3$, ppm): δ = 55.4, 78.5, 111.2, 113.3, 115.2, 126.0, 128.0, 128.1, 128.3, 128.5, 128.7, 130.8, 131.5, 135.6, 135.7, 136.2, 137.2, 156.4, 162.8. EI MS: *m*/*z* (%) = 385 (48) [M + 2], 383 (69) [M^+], 348 (100), 317 (28), 239 (59), 197 (85). $C_{21}H_{15}Cl_2NO_2$ (384.3): calcd. C 65.64, H 3.93, N 3.65; found C 65.40, H 3.84, N 3.29.

Reaction between Triphenylmethyl Chloride and 1 in the Presence of BF_3: BF_3 gas was bubbled into a solution of triphenylmethyl chloride (0.61 g, 2.2 mmol) in dry CH_2Cl_2 (50 mL) at −78 °C. A solution of **1** (0.41 g, 2.2 mmol) in dry CH_2Cl_2 (20 mL), cooled to −78 °C, was added under a stream of nitrogen. After 6 h, the mixture was treated with H_2O, a 10% solution of NH_4Cl, and again with H_2O, and dried. The solvent was removed. Column chromatography afforded 4-(2,6-dichlorophenyl)-1,1-diphenyl-2,3-benzoxazine (**3**, 0.28 g, 30%), (*E*)-2,6-dichlorobenzophenone oxime (**4a**, 0.06 g, 10%) and 2′,6′-dichlorobenzanilide (**5a**, 0.18 g, 31%).

Reaction between 3-Methoxybenzyl Chloride (6j) and 1 in the Presence of BF_3. Procedure A: BF_3 gas was bubbled into a solution of **6j** (0.50 g, 3.2 mmol) in dry CH_2Cl_2 (50 mL) at −70 °C. A cooled solution of **1** (0.60 g, 3.2 mmol) in dry CH_2Cl_2 (20 mL), cooled to −78 °C, was added under a stream of nitrogen. After 8 h, a mixture of oximes **4j** and **4k** was obtained. The mixture, after workup and column chromatography on silica gel, gave a mixture of **4j**, **4k**, and **10j** in variable ratio. When the crude mixture was washed with a 10% solution of NaOH, the mixture gave after column chromatography 4-(2,6-dichlorophenyl)-7-methoxy-1*H*-2,3-benzoxazine (**10j**, 0.60 g, 61%) and the oxime **4k** (0.10 g, 9%). **Procedure B:** BF_3 gas was bubbled at room temperature into a solution of **6j** (0.50 g, 3.2 mmol) and **1** (0.60 g, 3.2 mmol) in dry CH_2Cl_2 (50 mL). The reaction was instantaneous, and ^{1}H NMR examination of the mixture showed that oximes **4j** and **4k** were present in a ratio of 45:55. The mixture was treated with NaOH and gave a mixture of 4-(2,6-dichlorophenyl)-7-methoxy-1*H*-2,3-benzoxazine (**10j**, 0.35 g, 35%) and oxime **4k** (0.44 g, 40%).

Compound 4j: White solid (*n*-hexane), m.p. 143−146 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 3.85 (s, 3 H), 4.78 (s, 2 H), 6.80 (dd, *J* = 3 and 9 Hz, 1 H), 7.03 (d, *J* = 9 Hz, 1 H), 7.20−7.40 (m, 4 H), 7.88 (br. s, 1 H). EI MS: *m*/*z* (%) = 343 (3) [M^+], 326 (30), 307 (100), 272 (60). $C_{12}H_{12}Cl_3NO_2$ (344.6): calcd. C 52.28, H 3.51, N 4.06; found C 52.45, H 3.73, N 3.82.

Compound 4k: White solid (*n*-hexane), m.p. 184−185 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 3.78 (s, 3 H), 4.57 (s, 2 H), 6.98 (m, 2 H), 7.17−7.35 (m, 3 H), 7.49 (d, *J* = 8 Hz, 1 H), 8.50 (br. s, 1 H). EI MS: *m*/*z* (%) = 343 (2) [M^+], 326 (50), 308 (80), 252 (35), 91 (100). $C_{12}H_{12}Cl_3NO_2$ (344.6): calcd. C 52.28, H 3.51, N 4.06; found C 52.28, H 3.88, N 4.37.

Compound 10j: White-purple solid (ethyl acetate), m.p. 108−110 °C. ^{1}H NMR (250 MHz, $CDCl_3$, ppm): δ = 3.84 (s, 3 H), 5.12 (s, 2 H), 6.78 (m, 3 H), 7.30−7.48 (m, 3 H). EI MS: *m*/*z* (%) = 309 (60) [M + 2], 307 (100) [M^+], 276 (70), 272 (65). $C_{15}H_{11}Cl_2NO_2$ (308.2): calcd. C 58.46, H 3.60, N 4.55, Cl 23.01; found C 58.57, H 3.88, N 4.37.

Reaction between 6c and 1: Chloride **6c** (0.25 g, 9.5 mmol) and **1** (0.18 g, 9.5 mmol) were dissolved in 30 mL of dry CH_2Cl_2. After a week, column chromatography afforded **11c** (0.17 g, 40%).

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