

Reactions of 4-Nitroquinoline 1-Oxide with Aluminum Chloride

V. P. Andreev and Ya. P. Nizhnik

Petrozavodsk State University, pr. Lenina 33, Petrozavodsk, 185640 Russia
e-mail: andreev@mainpgu.karelia.ru

Received September 3, 1999

Abstract—4-Nitroquinoline 1-oxide reacts with aluminum chloride to give 4-chloroquinoline 1-oxide. Aluminum chloride with 4-nitroquinoline 1-oxide forms a molecular complex in which it acts as electron acceptor and effective nucleophilic reagent (a source of chloride ions).

Halogenated pyridine and quinoline *N*-oxides are key intermediate products in the synthesis of functionally substituted heteroaromatic compounds; they are usually prepared from the corresponding nitro compounds under severe conditions: by prolonged boiling in concentrated aqueous solutions of HCl and HBr or by the action of acid halides and phosphinoyl halides [1].

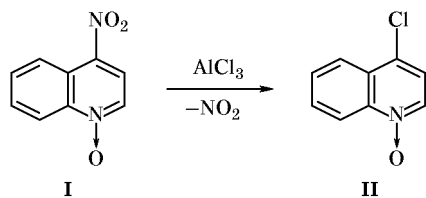
We showed in [2] that passing of gaseous hydrogen chloride or hydrogen bromide through a saturated solution of 4-nitroquinoline 1-oxide (**I**) in chloroform over a period of 15–30 min leads to quantitative replacement of the nitro group by halogen. The mild conditions of this reaction are explained by protonation of the *N*-oxide oxygen atom and increased nucleophilicity of halide ions due to their weak solvation by aprotic solvent.

In continuation of studies in this line, we tried to activate the nitro group in heteroaromatic *N*-oxides for nucleophilic substitution with the aid of anhydrous aluminum chloride. The latter is known to form molecular complexes with *N*-oxides [3], in which the heteroring should exhibit enhanced electrophilicity toward weak nucleophilic reagents. However, AlCl₃ was found to act not only as powerful ν -acceptor but also as effective nucleophilic reagent being a source

of chloride ions. According to the HPLC data, heating of equimolar amounts of 4-nitroquinoline 1-oxide (**I**) and AlCl₃ in acetonitrile for 15 min at 65°C or keeping of the reactant mixture for 24 h at room temperature leads to formation of 4-chloroquinoline 1-oxide (**II**) in quantitative yield.

Addition of an equimolar amount of benzyltriethylammonium chloride (see table, runs nos. 12 and 14) almost does not affect the reaction rate, indicating that under these conditions anhydrous AlCl₃ is at least equally efficient source of chloride ions.

Unlike AlCl₃, such halogen-containing Lewis acids as SbF₃, BF₃, ZnCl₂, and CuCl₂ turned out to be either poor halide ion sources (BF₃) or poor electron acceptors (ZnCl₂ and CuCl₂) or both (SbF₃). Even the use of AlCl₃·6H₂O ensures faster replacement of the nitro group. The reaction was considerably accelerated by preliminary addition to *N*-oxide **I** of boron trifluoride (runs nos. 15 and 16) which is a stronger electron acceptor than anhydrous aluminum chloride (cf. runs nos. 7 and 14). By contrast, the presence of protogenic species capable for specific interactions inhibits the process. This pattern is observed, e.g., in going from acetonitrile to methanol (runs nos. 1 and 2), from AlCl₃ to AlCl₃·6H₂O (runs nos. 1 and 15, 16 and 17, 21 and 22), from BF₃ to CF₃COOH or HClO₄ (runs nos. 6 and 19, 20, 16 and 18). The same effect is observed with the use of hydrogen chloride. The reaction with gaseous HCl in chloroform is complete in 15 min at room temperature; in acetonitrile containing hydrochloric acid it requires 24 h (run no. 24) or 30 min at 65°C (run no. 23); and in 36% hydrochloric acid, despite greater concentration of HCl, the reaction takes 1 h at 100°C.



Substitution of the nitro group in 4-quinoline 1-oxide by chlorine^a

Run no.	Components	Temperature, °C	Yield of 4-chloroquinoline 1-oxide (II), %					
			30 min	60 min	120 min	180 min	240 min	
1	AlCl ₃	65	>99	(5 min – 70%, 15 min – 98%)				
2	AlCl ₃ (methanol)	65		37	48	57	65	
3	ZnCl ₂	65					<1	
4	CuCl ₂	54		2	5	7	10	
5	BF ₃	65		(8 ch – 18%)				
6	[Et ₃ NCH ₂ Ph] ⁺ Cl ⁻ -BF ₃	65	>99					
7	[Et ₃ NCH ₂ Ph] ⁺ Cl ⁻ -BF ₃	20	80	99				
8	SbF ₃	20					0	
9	[Et ₃ NCH ₂ Ph] ⁺ Cl ⁻ -SbF ₃	20			3			
10	[Et ₃ NCH ₂ Ph] ⁺ Cl ⁻ -ZnCl ₂	20		(24 h – 0%)				
11	AlCl ₃ ^b	20		45	55	60	65	
12	AlCl ₃ ^c	20		10 h – 80%, 23	14 h – 88%, 40	19 h – 90%, 47	56	
13	AlCl ₃ ^d	20		10 h – 86%, 1	14 h – 96%, 5	19 h – 98%, 8	12	
14	[Et ₃ NCH ₂ Ph] ⁺ Cl ⁻ -AlCl ₃	20			(19 h – 45%)			
15	AlCl ₃ -H ₂ O	65		25	(24 h – 99%)			
16	AlCl ₃ -H ₂ O-BF ₃ ^d	65	51	<1	20	31	56	
17	AlCl ₃ -BF ₃ ^d	65		(10 h – 83%, 16 h – 86%)				
18	AlCl ₃ -H ₂ O-CF ₃ COOH	65		>99	(5 min – 64%, 15 min – 90%)			
19	[Et ₃ NCH ₂ Ph] ⁺ Cl ⁻ -CF ₃ COOH	65	70	12	45	83	>99	
20	[Et ₃ NCH ₂ Ph] ⁺ Cl ⁻ -HClO ₄	65	65	80	90	93	95	
21	AlCl ₃ -H ₂ O-[Et ₃ NCH ₂ Ph] ⁺ Cl ⁻	65		<1	7			
22	AlCl ₃ ^d -(NC) ₂ C=C(NC) ₂	65			82			
23	Concd. hydrochloric acid	65	>99					
24	Concd. hydrochloric acid	20	50	65	(24 h – >99%)			
25	Concd. hydrochloric acid	100		>99	(15 min – 65%)			

^a In a typical experiment, the reaction mixture contained 0.3 ml of anhydrous acetonitrile (except for runs nos. 2 and 25), 0.1 mmol of 4-nitroquinoline 1-oxide (I), 0.1 mmol of nucleophile, and 0.02 ml of a solution of boron trifluoride-ether complex, concentrated solutions of trifluoroacetic, perchloric, or hydrochloric acid or 0.1 mmol of solid SbF₃, AlCl₃, ZnCl₂, or CuCl₂ as electron acceptor.

^b Molar ratio *N*-oxide (I)-AlCl₃ 2:1.

^c Molar ratio *N*-oxide (I)-AlCl₃ 1:1.

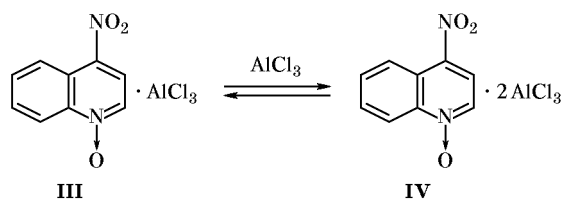
^d Molar ratio *N*-oxide (I)-AlCl₃ 1:2.

^e Boron trifluoride or tetracyanoethylene was added to the reaction mixture before addition of AlCl₃.

We have also found that changing the ratio *N*-oxide I-AlCl₃ from 2:1 to 1:2 slows the reaction down. Obviously, in this case the fraction of complex IV relative to III should increase. Complex IV is characterized by greater deficit of electron density on the aluminum atom (sextet of electrons) due to competition between two AlCl₃ molecules; therefore, generation of nucleophilic species (chloride ion) from complex III is more favorable. Similar adducts of

quinoline *N*-oxides [4] and their styryl derivatives with [5] with BF₃ were isolated in the pure state.

Presumably, nucleophilic substitution of the nitro group in *N*-oxide by the action of AlCl₃ or hydrogen halides (HCl, HBr) involves formation of a molecular complex of I with Lewis or Brønsted-Lowry acid, liberation of halide ion, and attack by the latter on the aromatic ring. It should be noted that proton is such a strong electron acceptor that 4-nitroquinoline



1-oxide hydrochloride cannot be isolated in the pure state (by analogy with the I–AlCl₃ complex) because of very fast replacement of the nitro group by chlorine. On the other hand, the complex of I with BF₃ is fairly stable (complex formation involves the nitro group [4]). Complex formation of other *N*-oxides with HCl and BF₃ occurs at the oxygen atom of the *N*-oxide group, except for 4-(4-dimethylaminostyryl)quinoline *N*-oxide and 4-(4-dimethylaminostyryl)pyridine *N*-oxide which take up the second BF₃ molecule or proton at the amino group.

Apart from *n*-donors, typical *v*-acceptors are also capable of forming π, v -complexes. For example, AlCl₃ and GaCl₃ [6], as well as HCl [7], form complexes with aromatic hydrocarbons, SbHlg₃ forms a complex with weakly basic diphenylamine [8], and soft transition metal cations (mercury, silver, platinum, etc.) give complexes with unsaturated and aromatic hydrocarbons [9].

Dissolution of aromatic hydrocarbons in liquid hydrogen fluoride is accompanied by formation of σ, v -complexes. This process is favored by the presence of boron trifluoride or other Lewis acids. The latter also promote complex formation with hydrogen chloride [7]. It is believed that most bimolecular nucleophilic substitution reactions in the aromatic series involve association processes (formation of σ -complexes [7]).

We plan to examine in more detail the mechanism of nucleophilic substitution in the aromatic series in the presence of *v*-acceptors, specifically as concerns formation of π, v -, *n, v*-, and σ, v -complexes at different stages of the process.

EXPERIMENTAL

The electron spectra were recorded on a Specord UV-Vis instrument in chloroform. The IR spectra were measured on a Specord M-80 spectrometer in KBr. The ¹H NMR spectra were obtained on a Bruker-300 spectrometer using CDCl₃ as solvent and TMS as internal reference.

4-Chloroquinoline 1-oxide (II). *a.* A mixture of 0.19 g of *N*-oxide I and 0.067 g of anhydrous AlCl₃

in 3 ml of dry acetonitrile was heated for 15 min at 65°C. The progress of the reaction was monitored by TLC and HPLC [2]. The solvent was distilled off, and the solid residue was treated with 2 ml of a saturated aqueous solution of NaCO₃ and with chloroform (3 × 2 ml), and the chloroform extract was dried over MgSO₄. The solvent was removed under reduced pressure to obtain 0.145 g (81%) of compound II with mp 132–134°C (mp 133–133.5°C [10]). Its UV, IR, and ¹H NMR spectral data coincided with those of a sample prepared by the procedure reported in [1]. Found, %: C 59.65, 59.95; H 3.43, 3.77; N 7.71, 7.52. C₉H₆ClNO. Calculated, %: C 60.19; H 3.37; N 7.80. 4-Chloroquinoline 1-oxide hydrochloride was obtained as described in [2]; its melting point (151–152°C) and UV spectrum coincided with the data given in [2].

b. A mixture of 0.380 g of *N*-oxide I and 0.134 g of anhydrous AlCl₃ in 6 ml of dry acetonitrile was kept for 24 h at room temperature. The product was isolated as described above in *a.* Yield 0.301 g (84%).

REFERENCES

- Ochiai, E., *Aromatic Amine Oxides*, Amsterdam: Elsevier, 1967.
- Andreev, V.P., Kalistratova, E.G., and Ryzhakov, A.V., *Khim. Geterotsikl. Soedin.*, 1996, no. 4, pp. 516–518.
- Masaguer, F., Sanche, I., and Casas, J.S., *Acta Cient. Compostelana*, 1972, vol. 9, nos. 3–4, pp. 181–184.
- Andreev, V.P. and Ryzhakov, A.V., *Khim. Geterotsikl. Soedin.*, 1994, no. 8, pp. 1087–1092.
- Andreev, V.P., Batotsyrenova, E.G., Ryzhakov, A.V., and Rodina, L.L., *Khim. Geterotsikl. Soedin.*, 1998, no. 8, pp. 1093–1102.
- Gur'yanova, E.N., Gol'dshtein, I.P., and Romm, I.P., *Donorno-aktseptornaya svyaz'* (The Donor–Acceptor Bond), Moscow: Khimiya, 1973, pp. 323, 330.
- Dneprovskii, A.S. and Temnikova, T.I., *Teoreticheskie osnovy organicheskoi khimii* (Theoretical Foundations of Organic Chemistry), Leningrad: Khimiya, 1991, pp. 379, 418.
- Buslaev, Yu.A. and Davidovich, R.L., *Koord. Khim.*, 1989, vol. 15, no. 11, pp. 1444–1445.
- Becker, H., *Einführung in die Elektronentheorie organisch-chemischer Reaktionen*, Berlin: Wissenschaften, 1974, 3rd ed. Translated under the title *Vvedenie v elektronnyuyu teoriyu organicheskikh reaktcii*, Moscow: Mir, 1977, pp. 439–440.
- Ochiai, E., *J. Org. Chem.*, 1953, vol. 18, no. 3, pp. 534–551.