Chemistry of superacids
35.* $NO_2Cl—3MX_n$ systems: superelectrophilic aprotic nitrating agents for deactivated aromatics

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Superelectrophilic nitration of deactivated aromatics with $NO_2Cl—3MX_n$ complexes in aprotic nonpolar solvents such as CH_2Cl_2 makes it possible to obtain the corresponding nitro derivatives in good to almost quantitative yields under mild conditions.

Key words: nitryl chloride—MX_n (M = Al, Ti, Sb)/CH_2Cl_2 system, deactivated arenes; electrophilic nitration.

Electrophilic aromatic nitration is one of the most studied organic reactions. It can also be carried out under typical Friedel—Crafts type conditions[2,3] by treatment with nitryl chloride (NO_2Cl) and Lewis acid catalysts, such as $AlCl_3$.

$$ArH + NO_2Cl \longrightarrow RNO_2 + HCl$$

Use of nitryl chloride with equimolar or less Lewis acids (MX_n) in Friedel—Crafts nitration results in only modest yields of nitration of deactivated arenes. Benzotrifluoride gives only 32% of the nitro product, and *p*-dichlorobenzene is nitrated with difficulty.[4,5] Even lower yields were obtained in the nitration of more strongly deactivated arenes. More soluble $NO_2Cl—MX_n$ complexes with weaker Lewis acids, such as $TiCl_4$, were preferentially used for the nitration of arenes with NO_2Cl. This indicates that the solubility rather than the Lewis acid strength is most significant for the nitrating systems studied.

We now present the results of electrophilic nitration of deactivated arenes (including strongly deactivated ones) with $NO_2Cl—3MX_n$ complexes in aprotic nonpolar solvents such as CH_2Cl_2 under mild conditions, greatly extending the scope for the Friedel—Crafts electrophilic nitration by such complexes. Related $RCOX—2MX_n$ complexes were found by Vol'pin *et al.* as superelectrophilic acylating reagents and catalysts for low-temperature alkane transformations.[6] Related Brõnsted acid activation of a variety of other electrophiles has been much investigated recently.[7] The present work extends Lewis acid activation to nitration.

Results and Discussion

Results of nitration of deactivated arenes with $NO_2Cl—3MX_n$ complexes (Scheme 1) are summarized in Table 1. It was found that $NO_2Cl—3MX_n$ complexes (MX_n = $SbCl_5$, $AlCl_3$) in CH_2Cl_2 solution show high nitrating ability towards a series of strongly deactivated arenes such as benzotrifluoride, nitrotoluene, various polyhalogenated arenes, aroyl derivatives of the type RC_6H_4COX (R = H, Me; X = Me, OEt, NH_2, Cl, CF_3), and even an extremely deactivated compound, *m*-$(CF_3)_2C_6H_4$. Nitration of these compounds was usually carried out at close to ambient temperatures (0 to 20 °C) and short reaction times (10—180 min). Yields of nitrated derivatives were generally good or frequently close to quantitative.

Reactive or moderately deactivated arenes (benzene, halobenzenes) are quantitatively nitrated at −78 °C within a few minutes. Competitive nitration of a benzene—toluene mixture (1 : 1) with a tenfold excess of the substrate relative to the $NO_2Cl—3SbCl_5$ complex showed no selectivity. This indicates that the nitrating species involved are very reactive.[3] The linear nitronium ion, $O=N^+=O$, has no vacant atomic orbital on the nitrogen atom (similarly to the ammonium ion NH_4^+), and thus its reaction with an arene has to occur by polarization of the N=O bond. In contrast to reactive π-donor electron-rich aromatics, deactivated arenes are poor electron donors and are unable to induce such polarization. The nitronium ion must thus be activated in the same way as in strong acid solutions, *i.e.*, by protolytic solvation.[8] In the limiting case, *viz.*, in Brõnsted superacids, the protonitronium dication (NO_2H^{2+}) may be the *de facto* electrophile,[8] especially with respect to

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* For part 34, see Ref. 1.

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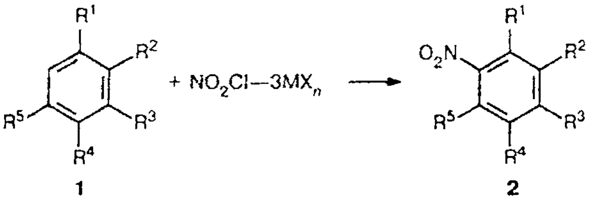
Scheme 1

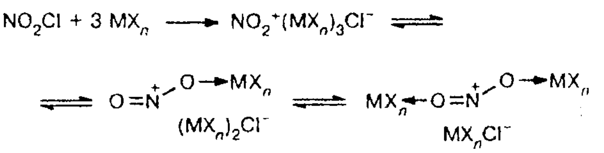


1	2	R^1	R^2	R^3	R^4	R^5
a	a	H	CF_3	H	H	H
a	b	CF_3	H	H	H	H
a	c	H	CF_3	H	H	H
a	d	H	H	CF_3	H	H
b	e	Cl	H	H	Cl	H
c	f	H	NO_2	Me	H	H
c	g	Me	NO_2	H	H	H
d	h	F	H	F	H	F
e	i	Cl	Cl	Cl	Cl	Cl
f	j	F	F	F	H	F
g	k	COOEt	H	H	H	H
g	l	H	COOEt	H	H	H
g	m	H	H	COOEt	H	H
h	n	$CONH_2$	H	H	H	H
h	o	H	$CONH_2$	H	H	H
i	p	COMe	H	H	H	H
i	q	H	COMe	H	H	H
j	r	COOEt	H	H	H	H
j	s	H	COOEt	H	H	H
k	t	$COCF_3$	H	H	H	H
k	u	H	$COCF_3$	H	H	H
l	v	H	CCl_3	H	CCl_3	H

σ-donors such as alkanes.[9] The possibility of the formation of a highly reactive superelectrophilic dication, NO_2H^{2+}, has been demonstrated by *ab initio* quantum-mechanical calculations[10a] and by ^{17}O NMR spectroscopy.[10b] This dication has also been observed in the gas phase by mass spectrometry.[11]

It is now suggested that similar activation of the nitronium is also possible by coordination of the lone pairs of one or both O atoms by suitable Lewis acids MX_n (Scheme 2).

Scheme 2



$$\mathrm{NO_2Cl} + 3\,\mathrm{MX}_n \longrightarrow \mathrm{NO_2}^{+}(\mathrm{MX}_n)_3\mathrm{Cl}^{-} \rightleftharpoons \underset{(\mathrm{MX}_n)_2\mathrm{Cl}^-}{\mathrm{O{=}\overset{+}{N}{-}O{\rightarrow}MX}_n} \rightleftharpoons \underset{\mathrm{MX}_n\mathrm{Cl}^-}{\mathrm{MX}_n{\leftarrow}\mathrm{O{=}\overset{+}{N}{-}O{\rightarrow}MX}_n}$$

The activity of $NO_2Cl—3MX_n$ systems in nitration increases with increase in Lewis acidity and affinity for oxygen, *i.e.*, the use of $SbCl_5$ and particularly $AlCl_3$ results in much more reactive nitrating systems than $NO_2Cl—3TiCl_4$, in spite of the higher solubility of the latter in CH_2Cl_2. For example, $NO_2Cl—3TiCl_4$ was not able to satisfactorily nitrate *p*-dichlorobenzene. Benzotrifluoride reacted with the $NO_2Cl—3TiCl_4$ system accompanied by a considerable degree of F—Cl exchange of the CF_3 group giving *m*-$NO_2C_6H_4CCl_3$ as the major product (see Table 1).

Greatly enhanced nitrating ability was exhibited by the $NO_2Cl—3SbCl_5$ system, although its solubility in CH_2Cl_2 is limited (generally an emulsion or a suspension was obtained). However, the system sucessfully nitrated a wide range of deactivated arenes (see Table 1). Polyhalobenzenes, as well as benzotrifluoride, were nitrated under mild conditions in good to excellent yields. It is interesting to note that no F—Cl exchange in benzotrifluoride was observed in the presence of the $NO_2Cl—3SbCl_5$ system. On the other hand, nitration of 1,2,3,5-tetrafluorobenzene was accompanied by F—Cl exchange in the aromatic ring. This nucleophilic addition—elimination evidently occurs in the highly activated 2,3,4,6-tetrafluoronitrobenzene product. Exchange was absent in the case of 1,3,5-trifluorobenzene. Pentafluorobenzene was not nitrated with the $NO_2Cl—3SbCl_5$ system, even when a large excess of the reagent was used.

The $NO_2Cl—3SbCl_5$ nitrating system was also found most suitable for the nitration of aroyl derivatives (see Table 1). The $NO_2Cl—3AlCl_3$ system is even less soluble but more reactive than $NO_2Cl—3SbCl_5$. Its activity can be demonstrated by quantitative data on the nitration of pentachlorobenzene with the $NO_2Cl—3AlCl_3$ system (although pentafluorobenzene was not nitrated with this system).

It is significant to note that both the $NO_2Cl—3SbCl_5$ and $NO_2Cl—3AlCl_3$ systems are relatively unstable and demonstrate better nitrating ability at lower temperatures (0 to 20 °C). They were preferentially used at ambient temperatures. At higher temperatures, side products of arene chlorination are formed in larger amounts (see Table 1).

Nitration of acetophenone with $NO_2Cl—3SbCl_5$ is particularly interesting since an unusual isomer distribution is observed. The amount of *o*-nitroacetophenone formed (see Table 1) is independent of reaction conditions and is always nearly equal to that of the corresponding *m*-isomer. Most probably, a donor-acceptor interaction of the electrophilic nitrating agent with the carbonyl oxygen atom is involved. In the case of α,α,α-trifluoroacetophenone, however, the *meta* product is predominant.

Experimental

All arenes were obtained from Aldrich and were used without additional purification. Methylene dichloride was dried over CaH_2 and distilled under dry nitrogen. Antimony

Table 1. Nitration of arenes with the $NO_2Cl-3MX_n$ system

Arene	MX_n	Molar ratio arene : NO_2Cl	*T* /°C	Time /min	Products (ratio)	Yield (%)[a]
1a	$TiCl_4$	0.50 : 1.0	20	180	**2a**	9 [b]
1a	$SbCl_5$	0.50 : 1.0	20	15	**2b, 2c, 2d** (0.5 : 94 : 5.0)	97 [c]
1b	$SbCl_5$	0.50 : 1.0	20	15	**2e**	96 [d]
1c	$SbCl_5$	0.50 : 1.0	20	60	**2f, 2g** (69 : 31)	100
1d	$SbCl_5$	0.33 : 1.0	0	40	**2h**	100
1e	$SbCl_5$	0.50 : 1.0	20	60	**2i**	22 [e]
1e	$SbCl_5$	0.50 : 1.0	20	1000	**2i**	23 [f]
1e	$SbCl_5$	0.10 : 1.0	0	90	**2i**	50
1f	$SbCl_5$	0.50 : 1.0	20	10	**2j**	26 [g]
1f	$SbCl_5$	0.50 : 1.0	0	50	**2j**	74 [h]
1g	$SbCl_5$	0.50 : 1.0	20	180	**2k, 2l, 2m** (22 : 76 : 2)	52 [i]
1g	$SbCl_5$	0.33 : 1.0	0	40	**2k, 2l** (12 : 88)	100
1h	$SbCl_5$	0.33 : 1.0	0	40	**2n, 2o** (12 : 88)	100
1i	$SbCl_5$	0.33 : 1.0	0	60	**2p, 2q** (45 : 55)	61
1i	$SbCl_5$	0.33 : 1.0	0	180	**2p, 2q** (45 : 55)	72
1i	$SbCl_5$	0.25 : 1.0	−20	60	**2p, 2q** (42 : 58)	36
1i	$SbCl_5$	0.33 : 1.0	20	60	**2p, 2q** (47 : 53)	27 [j]
1j	$SbCl_5$	0.33 : 1.0	0	90	**2r, 2s** (14 : 86)	40 [k]
1k	$SbCl_5$	0.33 : 1.0	0	120	**2t, 2u** (21 : 79)	100
1l	$AlCl_3$	0.33 : 1.0	0	120	**2v**	48
1e	$AlCl_3$	0.33 : 1.0	0	120	**2i**	100
1i	$AlCl_3$	0.33 : 1.0	0	120	**2p, 2q** (6 : 94)	70 [j]

[a] GLC data.

[b] 3-Chlorotoluene was formed as a side product (yield 55%).

[c] Monochlorinated trifluoromethylnitrobenzene was formed as a side product (yield 3%).

[d] 1,2,4-Trichlorobenzene was formed as a side product (yield 4%).

[e] Hexachlorobenzene was formed as a side product (yield 2%).

[f] Hexachlorobenzene was formed as a side product (yield 16%).

[g] Chlorotrifluorobenzene resulting from nucleophilic substitution of the F atom in the arene was formed as a side product (yield 10%).

[h] Chlorotrifluorobenzene was formed as a side product (yield 26%).

[i] Ethyl chlorobenzoate was formed as a side product (yield 13%, isomer ratio 1 : 5).

[j] Methyl chlorobenzoate was formed as a side product (yield 2%).

[k] Ethyl chlorobenzoate was formed as a side product after hydrolysis and esterification with ethanol (yield 3%).

pentachloride and titanium tetrachloride were were available from Aldrich as 1 *M* solutions in CH_2Cl_2. Anhydrous $AlCl_3$ was purchased from EM Science Inc. Nitryl chloride was prepared according to a method reported in the literature[5,12] by treatment of anhydrous HNO_3 with chlorosulfonic acid (HSO_3Cl, Johnson Matthey), which was distilled before use. Fuming nitric acid and oleum (30%) were available from Fischer Scientific Co. Nitryl chloride was used as a 0.5 *M* solution in dry CH_2Cl_2 and was stored in a refrigerator in a dry nitrogen atmosphere.

GLC analyses were performed on a Varian 3400 chromatograph using a quartz capillary column with DB-1 as the stationary phase. Chromato-mass-spectrometric (GC-MS) analyses were carried out on a Hewlett—Packard 5971 instrument with a mass selective detector coupled to a Hewlett—Packard 5980 gas chromatograph. Identification of products was based on comparison of their mass spectra with those of authentic samples. NMR spectra were recorded on a Varian VXR 200 spectrometer in $CDCl_3$ solutions with $SiMe_4$ as an internal standard.

Nitration with the $NO_2Cl{-}3SbCl_5$ system (typical procedure). A 1 *M* solution of $SbCl_5$ (3 mmol) was placed under dry nitrogen into a three-necked flask equipped with a magnetic stirrer, and the solution was cooled to −78 °C. An NO_2Cl solution (0.5 *M*, 2 mL) was added next; a light yellow precipitate formed. After stirring for 5—10 min, a calculated amount of an arene dissolved in 2 mL of CH_2Cl_2 was added in one portion, and the reaction mixture was brought to 0 °C (or 20 °C) and vigorously stirred for a period of time indicated in Table 1. The mixture was quenched with ice water (50 mL) and thoroughly extracted with CH_2Cl_2 (3×20 mL). The combined organic extracts were washed with 5% aqueous $NaHCO_3$ (2×20 mL) and dried with $MgSO_4$. The products were analyzed by GLC and GC-MS with internal standards. The extract was concentrated, and the nitration products were purified by distillation or recrystallization.

Nitration with $NO_2Cl{-}3AlCl_3$ is carried out in a different way, as $AlCl_3$ is added as a powder.

Nitration with the $NO_2Cl{-}3AlCl_3$ system (typical procedure). An NO_2Cl solution in CH_2Cl_2 (0.5 *M*, 1.33 mL, 0.66 mmol) was added at −78 °C to a vigorously stirred suspension of $AlCl_3$ (0.26 g, 2 mmol) in CH_2Cl_2 (2 mL). After stirring for 5—10 min, a solution of pentachlorobenzene (0.055 g, 0.22 mmol) in CH_2Cl_2 (2 mL) was added. The mixture was warmed to 0 °C and stirred for 2 h. Ordinary work-up gave nitropentachlorobenzene in quantitative yield (GLC data). The product was purified by recrystallization.

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