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Electron Impact Induced Fragmentation of Aromatic N-Alkoxy-imines I. Ring Closure in $(M–CH_2O)^{+\bullet}$ Ions by Intramolecular Aromatic Substitution#

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Summary. N-Butoxy- and N-propoxy-imines derived from *o*-, *m*-, and *p*-substituted benzaldehydes (X = F, Cl, Br, I) decompose upon electron impact to the respective aldoximes by loss of C_nH_{2n} and competitively *via* 1,5-distonic radical cations by loss of CH_2O to 1,3-distonic ions which eliminate $H^\bullet$ and/or a halogen atom in the course of homolytic aromatic substitution, giving rise to cyclic $(M–CH_2O–H^\bullet)^+$ or $(M–CH_2O–X^\bullet)^+$ ions.

Keywords. N-Alkoxybenzaldimines; Electron impact ionization; Distonic ions; Ring closure; Homolytic aromatic substitution.

Elektronenstoßinduzierte Fragmentierung aromatischer N-Alkoxy-imine, 1. Mitt. Ringschluß von $(M–CH_2O)^{+\bullet}$-Ionen durch intramolekulare aromatische Substitution

Zusammenfassung. N-Butoxy- und N-Propoxy-imine aus *o*-, *m*-, und *p*-substituierten Benzaldehyden (X = F, Cl, Br, I) zersetzen sich unter Elektronenbeschuß durch Verlust von C_nH_{2n} zu den entsprechenden Aldoximen. In einer Konkurrenzreaktion entstehen über 1,5-distonische Radikalkationen durch Abspaltung von CH_2O 1,3-distonische Ionen, die im Verlauf einer homolytischen aromatischen Substitution $H^\bullet$ und/oder ein Halogenatom eliminieren, wodurch cyclische $(M–CH_2O–H^\bullet)^+$-oder $(M–CH_2O–X^\bullet)^+$-Ionen gebildet werden.

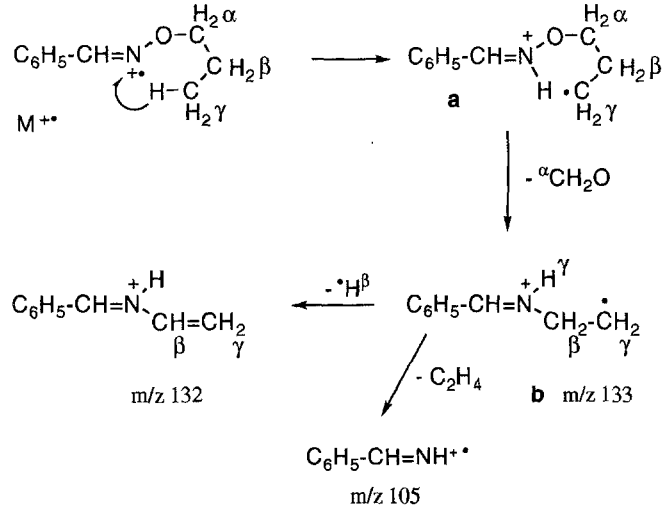
Introduction

Alkoxy-imine (oxime ether) increments frequently occur in drugs, *e.g.* fluvoxamine [2], cephalosporines [3], macrolide antibiotics [4], and antidepressiva [5] as well as in insecticides [6]. Moreover, they are used as synthons [7] and for identification and purification of thermolabile carbonyl compounds [8]. Whereas there is a wealth of papers dealing with various aspects of the MS behaviour of aliphatic and aromatic N-methoxy-imines [9], less information is published in the case of homologous N-alkoxy-imines.

Dedicated with warm regards to Prof. Dr. *D. Seebach*, Zürich, on the occasion of his 60th birthday

In 1971, *Cooks* and *Varvoglis* [10] reported on a series of alkoxy-imines with varying length of the alkyl chain (C_1–C_3) derived *inter alia* from benzaldehyde, substituted benzaldehydes, and benzophenone. The *n*-propyl ethers turned out to be unique in undergoing CH_2O elimination from the molecular ions, followed by loss of a hydrogen atom or ethene. A mechanistic interpretation is given by initial migration of a γ-H atom to nitrogen generating a 1,5-distonic ion **a** which decomposes in the course of a 4-centered rearrangement to the 1,3-distonic ion **b** (Scheme 1).

We found that elimination of CH_2O is not restricted to *n*-propoxy-imines; it is a common feature of oxime ethers with alkyl chains longer than C_2H_5 [1]. This study is concerned with the behaviour of alkoxy-imines of halogenated benzaldehydes upon ionization by electron impact and with the reactivity of the $(M–CH_2O)^{+\bullet}$ ions **b**.

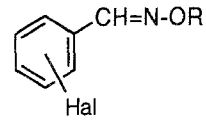


Scheme 1

Results and Discussion

A series of *n*-propoxy-, *n*-butoxy-, and (3-methyl)butoxy-imines of halogenated benzaldehydes were synthesized and examined at 70/12 eV and by MIMS (B/E = const. linked scans; first field free region: 1st FFR) of their molecular and $(M–CH_2O)^{+\bullet}$ ions.

In order to explain the general features of fragmentation, the 70 and 12 eV mass spectra of **10** and the B/E linked scan spectra of its molecular ion are shortly discussed (Fig. 1). At high ionization energies, two important primary fragment ions and their decomposition products predominate. 1) Loss of CH_2O from $M^{+\bullet}$ at $m/z = 211/213$ triggered by 1,5-H-migration from Cγ to N gives rise to the ions at



R^1= *n*-C_3H_7; R^2= *n*-C_4H_9; R^3= CH_2-CH_2-$CH(CH_3)_2$

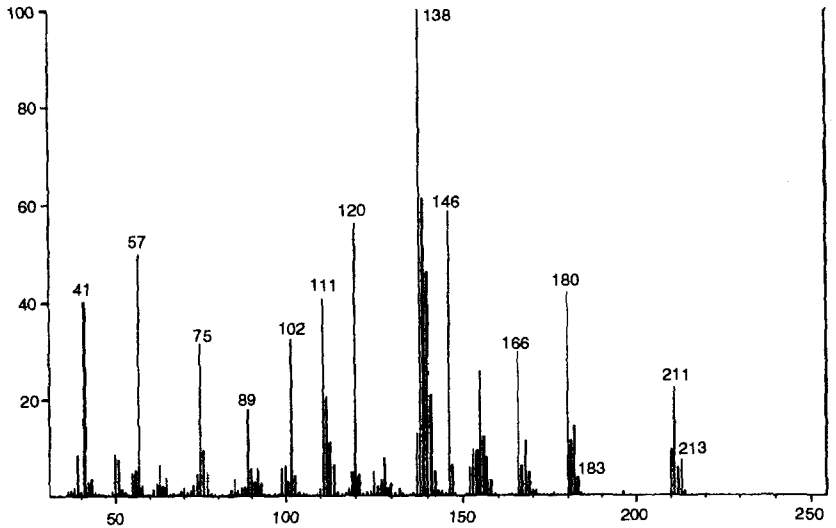
Cmpd.	Hal	R	Cmpd.	Hal	R
1	*o*-F	R^1	**14**	*m*-Br	R^2
2	*o*-Cl	R^1	**15**	*p*-Br	R^2
3	*m*-Cl	R^1	**16**	*o*-I	R^2
4	*p*-Cl	R^1	**17**	*o*-F	R^3
5	*o*-Br	R^1	**18**	*o*-Cl	R^3
6	*o*-I	R^1	**19**	*o*-Br	R^3
7	*o*-F	R^2	**20**	*o*-I	R3
8	*m*-F	R^2	**21**	*o,o'*-Cl_2	R^1
9	*p*-F	R^2			
10	*o*-Cl	R^2		C_6Y_5-CX=N-O-C_4H_9	
11	*m*-Cl	R^2	**22**	X=H Y=D	
12	*p*-Cl	R^2	**23**	X=D Y=H	
13	*o*-Br	R^2	**24**	C_6H_5-CH=N-O-C_4D_9	

Table 1. Selected data from the EIMS (70 / 12 eV; sum of $^{35+37}Cl$ / $^{79+81}Br$) and MIMS ($M^{+\bullet}$, ^{35}Cl/^{79}Br; B/E linked scans) of **1**, **2**, **5**, and **6** (% rel. int (% TIC); ^{13}C corr.)

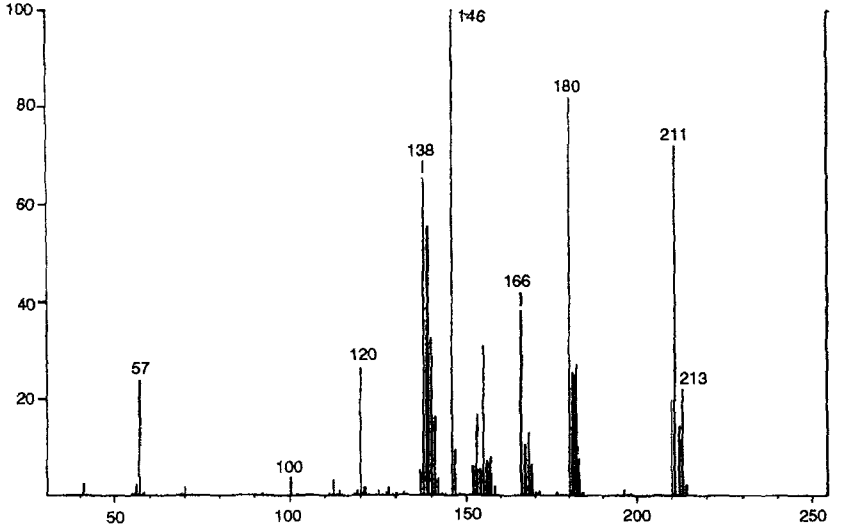
	$(M-CH_2O)^{+\bullet}$	$(M-CH_2O-H^{\bullet})^{+}$	$(M-CH_2O-X^{\bullet})^{+}$	$(M-C_3H_6)^{+\bullet}$	$(M-C_3H_6-X^{\bullet})^{+}$
1 70 eV	17 (1.9)	40 (4.5)	5 (0.5)	41 (4.7)	14 (1.6)
12 eV	26 (8.9)	50 (17.1)	5 (1.0)	24 (8.3)	1 (0.3)
MIMS	100 (69.5)	22 (15.0)	<1 (0.4)	1 (0.5)	–
2 70 eV	14 (1.3)	36 (3.2)	19 (1.6)	53 (4.6)	100 (8.8)
12 eV	10 (3.6)	21 (8.0)	9 (3.2)	14 (5.1)	12 (4.5)
MIMS	100 (56.8)	18 (10.4)	8 (4.7)	2 (1.0)	–
5 70 eV	5 (0.6)	23 (2.8)	16 (1.9)	17 (2.0)	100 (12.1)
12 eV	12 (3.0)	28 (7.0)	12 (3.2)	15 (3.8)	23 (5.9)
MIMS	100 (58.7)	11 (6.3)	2 (1.1)	3 (1.9)	–
6 70 eV	4 (0.6)	34 (4.9)	8 (1.2)	14 (2.0)	48 (6.9)
12 eV	2 (1.2)	21 (10.2)	5 (2.5)	6 (3.0)	15 (7.3)
MIMS	38 (18.7)	100 (49.0)	2 (0.9)	8 (4.0)	1 (0.3)

m/z = 181/183 which subsequently eliminate a H atom (*m/z* = 180/182), C_2H_4 (*m/z*= 153/155), or a methyl radical (*m/z* = 166/168) in accordance with Scheme 1 [10][1]. In addition, a strong ion at *m/z* = 146 comes up, corresponding with loss of the *o*-Cl atom from the $(M-CH_2O)^{+\bullet}$ ion.

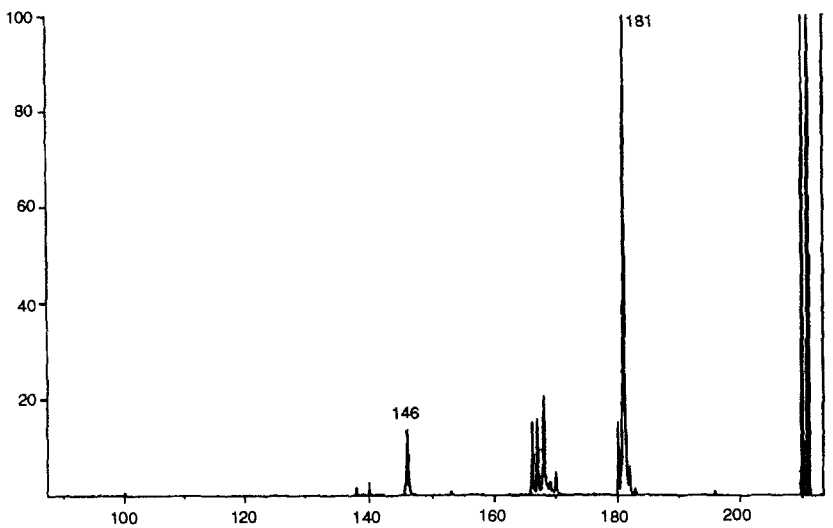
[1] The loss of $^{\bullet}CH_3$ indicates a rearrangement within ion **b** or its analogues, which will be discussed in a forthcoming paper



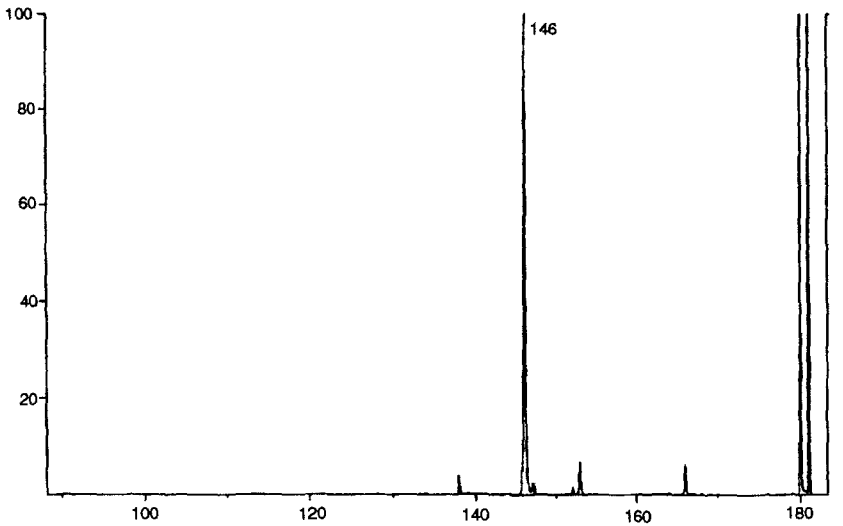
EIMS (70 eV) of **10**



EIMS (12 eV) of **10**



MIMS (B/E) of **10** ($M^{+\bullet}$; ^{35}Cl)



MIMS (B/E) of $(M\text{-}CH_2O)^{+\bullet}$ of **10** (^{35}Cl)

Fig. 1. Mass spectra of **10**

2) Elimination of C_4H_8 from $M^{+\bullet}$ affords ions at $m/z = 155/157$ which decompose by the same routes as the molecular ions of *o*-chlorobenzaldoxime, *e.g.* loss of oxygen ($m/z = 139/141$), $^{\bullet}OH$ ($m/z = 138/140$), or $Cl^{\bullet}$ ($m/z = 120$) [10]. Lowering the ionization energy (12 eV) causes the oxime ion and its daughter ions to decrease, whereas the $(M–CH_2O)^{+\bullet}$ ion and its product ions gain intensity, the ion at $m/z = 146$ being the base peak.

Metastable molecular ions of **10** (1st FFR; B/E) lose (in competition to $H^{\bullet}$ elimination) preferably CH_2O and thereupon $Cl^{\bullet}$. The oxime ion, however, is totally suppressed. This fact supports the postulation of a 1,5-Hγ-migration to N (Scheme 1) since a six-membered transition state expectedly is more favorable than a tight four-centered one as in the case of a 1,3-H-shift from C_β to oxygen, yielding the oxime ions [10].

The unexpected loss of a chlorine atom from the $(M–CH_2O)^{+\bullet}$ ions in the case of **10** prompted us to examine further halogenated oxime ethers (F, Cl, Br, I) with respect to type and to different length of the alkyl chain.

Table 2. Selected data from the EIMS (70/12 eV; sum of $^{35+37}Cl/^{79+81}Br$) and MIMS ($M^{+\bullet}$, $^{35}Cl/^{79}Br$; B/E linked scans) of **7**, **10**, **13**, and **16** (% rel. int (% TIC); ^{13}C corr.)

	$(M–CH_2O)^{+\bullet}$	$(M–CH_2O–H^{\bullet})^{+}$	$(M–CH_2O–X^{\bullet})^{+}$	$(M–C_4H_8)^{+\bullet}$	$(M–C_4H_8–X^{\bullet})^{+}$
7 70 eV	23 (2.6)	73 (8.1)	10 (1.1)	17 (1.9)	9 (1.0)
12 eV	37 (7.8)	100 (21.1)	0.2 (0.03)	17 (3.6)	2 (0.4)
MIMS	100 (64.1)	4 (3.0)	–	–	–
10 70 eV	15 (1.5)	56 (5.4)	58 (5.6)	33 (3.2)	56 (5.4)
12 eV	33 (4.2)	109 (13.9)	100 (12.8)	39 (5.0)	26 (3.4)
MIMS	92 (27.3)	14 (4.4)	13 (4.1)	–	–
13 70 eV	19 (1.1)	75 (4.9)	64 (4.1)	18 (1.2)	81 (5.2)
12 eV	37 (4.4)	108 (14.0)	100 (12.1)	16 (1.9)	25 (3.1)
MIMS	33 (19.0)	5 (2.5)	0.6 (0.3)	–	–
16 70 eV	7 (0.6)	52 (3.9)	63 (4.7)	23 (1.7)	52 (3.9)
12 eV	12 (3.1)	58 (11.5)	54 (10.8)	22 (4.5)	9 (1.9)
MIMS	33 (19.6)	7 (0.4)	0.7 (0.4)	–	–

Table 3. Selected data from the EIMS (70/12 eV; sum of $^{35+37}Cl/^{79+81}Br$) and MIMS ($M^{+\bullet}$, $^{35}Cl/^{79}Br$; B/E linked scans) of **10–12** (% rel. int (% TIC); ^{13}C corr.)

	$(M–CH_2O)^{+\bullet}$	$(M–CH_2O–H^{\bullet})^{+}$	$(M–CH_2O–Cl^{\bullet})^{+}$	$(M–C_4H_8)^{+\bullet}$	$(M–C_4H_8–Cl^{\bullet})^{+}$
10 70 eV	15 (1.5)	56 (5.4)	58 (5.6)	33 (3.2)	56 (5.4)
o 12 eV	33 (4.2)	109 (13.9)	100 (12.8)	39 (5.0)	26 (3.4)
MIMS	92 (27.3)	14 (4.4)	13 (4.1)	–	–
11 70 eV	31 (7.0)	117 (9.4)	31 (2.5)	29 (2.3)	17 (1.4)
m 12 eV	50 (8.2)	133 (21.8)	34 (5.5)	19 (3.1)	2 (0.3)
MIMS	35 (20.6)	3 (3.5)	1 (0.5)	–	–
12 70 eV	16 (1.3)	102 (8.3)	40 (3.3)	60 (4.8)	3 (0.25)
p 12 eV	18 (3.2)	110 (19.4)	38 (6.7)	27 (4.7)	0.3 (0.04)
MIMS	48 (18.2)	46 (17.2)	11 (4.1)	–	–

In Tables 1 and 2, the relative intensities and the percentage of the total ion current (TIC) of $(M–CH_2O)^{+\bullet}$ and $(M–C_nH_{2n})^{+\bullet}$ ions and their daughter ions resulting from loss of H$^\bullet$ and Cl$^\bullet$ of the propoxy-imines **1**, **2**, **5**, **6** and butoxy-imines **7**, **10**, **13**, and **16**, are listed. In most cases there is a strong discrimination of the oxime $(M–C_nH_{2n})^{+\bullet}$ and $(M–C_nH_{2n}–Cl^\bullet)^+$ ions against $(M–CH_2O)^{+\bullet}$ and $(M–CH_2O–Cl^\bullet/H^\bullet)^+$ ions when lowering the internal energy of the resp. molecular ions. From all $(M–CH_2O)^{+\bullet}$ ions the halogen atoms are lost. However, there is no straightforward trend with respect to the dissociation energies of the C-halogen bond or the nature of the alkyl group. The major reaction of $(M–CH_2O)^{+\bullet}$ ions is H$^\bullet$ elimination.

Furthermore, the data in Table 3 show that loss of halogen is not limited to the *ortho* position. $(M–CH_2O)^{+\bullet}$ ions of *meta*- and *para*-isomers **11** and **12**, too, eliminate a chlorine atom, though to a smaller amount (*o*:*m*:*p* = 1.0:0.4:0.6 at 70 eV). In the case of **10**, loss of Cl$^\bullet$ from $(M–CH_2O)^{+\bullet}$ is of the same magnitude as that of H$^\bullet$; in the case of **11** and **12**, however, H$^\bullet$ elimination exceeds that of Cl$^\bullet$.

Additional information was obtained from the spectra (B/E linked scans) of metastable $(M–CH_2O)^{+\bullet}$ ions decomposing in the 1st FFR. The results are compiled in Tables 4–6.

Table 4. MIMS of $(M–CH_2O)^{+\bullet}$ ions (B/E linked scans; $^{35}Cl/^{79}Br$) of propoxy-imines **1–6**, **21** (% rel. [int. % TIC])

Ion cmpd.	ΔH$^\bullet$	$\Delta H_3C^\bullet$	ΔHal$^\bullet$	ΔC_2H_4	Δ 29 u
1	100 (90.3)	1 (0.9)	6 (5.4)	0.6 (0.5)	3 (2.7)
2	100 (73.8)	0.5 (0.4)	23 (17.3)	0.5 (0.4)	11 (7.9)
3	100 (87.2)	0.6 (0.5)	8 (6.6)	0.6 (0.5)	6 (5.0)
4	100 (89.7)	0.6 (0.5)	9 (8.0)	0.6 (0.5)	11 (10.2)
5	100 (66.8)	1 (0.9)	13 (8.5)	3 (2.1)	32 (21.7)
6	100 (96.2)	0.2 (0.2)	2 (1.9)	0.3 (0.3)	1.5 (4.4)
21	–	–	100 (72.4)	1 (0.9)	37 (26.7)

Table 5. MIMS of $(M–CH_2O)^{+\bullet}$ ions (B/E linked scans; $^{35}Cl/^{79}Br$) of butoxy-imines **7–15** (% rel. int. [% TIC])

Ion cmpd.	ΔH$^\bullet$	$\Delta H_3C^\bullet$	ΔHal$^\bullet$	Δ C_2H_4	Δ 29 u	Δ 43 u
7	100 (85.1)	6 (4.9)	5 (3.8)	1 (1.1)	6 (4.6)	0.6 (0.5)
8	100 (87.3)	4 (3.9)	1 (1.1)	0.6 (0.5)	8 (6.6)	0.6 (0.5)
9	100 (89.8)	4 (3.4)	0.6 (0.6)	2 (1.7)	4 (3.4)	1 (1.1)
10	100 (61.5)	3 (1.9)	53 (32.7)	4 (2.3)	0.6 (0.4)	2 (1.2)
11	100 (54.0)	1 (1.1)	3 (3.2)	–	1 (1.1)	0.5 (0.6)
12	100 (73.5)	6 (4.2)	21 (15.8)	0.6 (0.5)	7 (5.1)	1 (0.9)
13	100 (52.4)	10 (5.1)	61 (32.0)	11 (5.9)	2 (0.8)	7 (3.2)
14	100 (95.8)	0.5 (0.5)	3 (2.8)	–	1 (0.9)	–
15	100 (81.9)	4 (3.2)	16 (12.8)	0.5 (0.3)	3 (2.2)	–

Table 6. MIMS of $(M–CH_2O)^{+\bullet}$ ions (B/E linked scans; $^{35}Cl/^{79}Br$) of 3-methylbutoxy-imines **17–20** (% rel. int. [%TIC])

Ion cmpd.	$\Delta H^\bullet$	$\Delta H_3C^\bullet$	$\Delta Hal^\bullet$	Δ 29 u	Δ 42 u	Δ 55 u	Δ 57 u
17	100 (76.7)	13 (9.7)	3 (2.4)	5 (3.9)	1 (1.0)	6 (4.9)	2 (1.4)
18	100 (57.0)	3 (1.5)	69 (39.6)	0.6 (0.4)	0.6 (0.4)	1 (0.7)	0.6 (0.4)
19	100 (82.8)	1 (1.1)	14 (14.0)	0.6 (0.5)	–	1 (1.1)	0.6 (0.5)
20	100 (94.0)	1 (1.1)	0.6 (0.6)	0.6 (0.6)	–	3 (3.1)	0.6 (0.6)

Propoxy-imines **1–6** (Table 4)

The dominating reaction of $(M–CH_2O)^{+\bullet}$ is the loss of $H^\bullet$. The *ortho* substituted $(M–CH_2O)^{+\bullet}$ ions lose the halogen atoms in the order Cl (**2**) > Br (**5**) > F (**1**) > I (**6**). In the case of the three positional isomers **2**, **3**, and **4**, loss of *o*-$Cl^\bullet$ gives rise to $(M–CH_2O–Cl^\bullet)^+$ ions of much greater abundance than loss of *m*-$Cl^\bullet$ or *p*-$Cl^\bullet$.

Butoxy-imines **7–15** (Table 5)

$H^\bullet$-loss from $(M–CH_2O)^{+\bullet}$ ions is again the main reaction. $(M–CH_2O)^{+\bullet}$ ions decrease in intensity from *ortho* to *para* isomer (**7–9**). $(M–CH_2O–Cl^\bullet)^+$ and $(M–CH_2O–Br^\bullet)^+$ ions show an irregularity in as much as those from the *para* isomers **12** and **15** carry a higher percentage of the total ion current than the *meta* isomers **11** and **14**. The values of the analogous isomeric ions **10/13**, **11/14**, and **12/15**, however, are of the same magnitude.

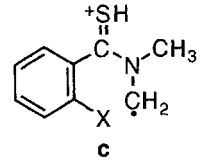
(3-Methylbutoxy)-imines **16–19** (Table 6)

There is a sharp decrease in intensity of the $(M–CH_2O–Cl^\bullet)^+$ ions: Cl (**17**) > Br (**18**) > I (**19**) (39 to 0.6% TIC) to the profit of $H^\bullet$ elimination (57 to 94% TIC).

In summary, the halogen substituents are lost from all positions of the phenyl ring with considerable preference of the *ortho* positions. There is no obvious relationship between the intensities of $(M–CH_2O–Hal^\bullet)^+$ ions and the C-Hal bond strength which decreases from C_6H_5-F to C_6H_5-I (F: 5.4 eV, Cl: 4.1 eV, Br: 3.5 eV, I: 2.8 eV [11]), since the elimination of iodine gives rise to very weak signals only. Loss of a H atom from $(M–CH_2O)^{+\bullet}$ ions is pronounced in all cases, as well at 70 and 12 eV as from metastable ions. This $H^\bullet$ may come from the side chain or from the aromatic group: $(M–CH_2O)^{+\bullet}$ ions from the oxime ether **22** (C_6D_5) lose 90% $D^\bullet$ and 10% $H^\bullet$, those from **23** exclusively $H^\bullet$ (*i.e.* the methine H is retained as already stated by *Cooks* [10]), and $(M–CH_2O)^{+\bullet}$ from **24** (C_4D_9) expels 98% $H^\bullet$ and 2% $D^\bullet$. Without considering possible kinetic isotope effects it can be concluded that maximally 10% of the hydrogen is lost from the alkyl group as shown in Scheme 1. Moreover, $H^\bullet$ elimination is totally suppressed in the case of *o,o'*-dichlorobenzaldoxime ether **21**, the $(M–CH_2O)^{+\bullet}$ ion of which loses solely $Cl^\bullet$ (Table 4).

From these results we conclude that the elimination of H$^\bullet$ and halogen atoms from the phenyl group comes to pass in the course of a cyclization process *via* reactive intermediates which arise by intramolecular aromatic substitution. Reactions of this type frequently occur in radical cations and are well documented [12, 13]. In the case of the most extensively studied and best understood examples the reaction sequence starts from the molecular ions by addition of a hetero atom to the *ortho* position of the aromatic ring with consecutive elimination of the *ortho* substituent (*e.g.* H$^\bullet$, Hal$^\bullet$) or after isomerization by a series of 1,2 H shifts with loss of the *meta* and *para* substituents [13, 14].

The distonic fragment ion **b** (Scheme 1) or its alkyl homologues contain an isolated primary (**1–6**, **21**), secondary (**7–16**, **24**), or tertiary (**17–20**) C radical which can attack the aromatic ring at the *ortho* positions. Aromatic substitution by C radicals is well known in solution and gas phase chemistry [15]. The rearranged molecular ions of N,N-dimethylthiobenzamide and its *ortho* substituted derivatives (CH_3, Hal), for instance, lose H$^\bullet$ and the *ortho* substituent (Hal$^\bullet$), the key intermediate being the distonic ion **c** with the radical site localized at the C atom of the former N-CH_3 increment [16]. The molecular ions of the three isomeric chlorophenyl-butadienes [17] cyclize to $C_{10}H_8$ (naphthalene) by loss of Cl$^\bullet$ from every position, followed by H$^\bullet$ elimination.



c

The $(M–CH_2O)^{+\bullet}$ ions (*e.g.* **b** in Scheme 1) eliminate Hal$^\bullet$ preferentially from the *ortho* position; *meta* and *para* substituents are lost to a lesser extent. In the case of the three chloro isomers **2**, **3**, and **4** the resulting $(M–CH_2O–Cl^\bullet)^+$ ions give virtually identical collisional activation (CA) mass spectra [18] (1st FFR, B/E linked scans, He, Fig. 2) which is good evidence that these ions have an identical structure (or that there is produced an identical mixture of structures). So we propose a course of reaction as shown in Scheme 2:

The isolated C radical can attack at *both ortho* positions of the phenyl group; a new C–C bond is formed, and the cyclization product (*e.g.* o_1 and o_2) is stabilized by elimination of the former *o*-substituent *o*-*X*$^\bullet$ or H$^\bullet$. As the positive charge and the radical electron reside in the same delocalized orbital of the bicyclic addition products, hydrogen migration around the former phenyl ring by 1,2 H shifts can take place [13]. In this way, reactive intermediates with *X* and *H* at the *meta* (m_1, m_2) or *para* positions come up which can lose *X*$^\bullet$ or H$^\bullet$. The high intensities of the $(M–CH_2O–H^\bullet)^+$ ions can be explained by the regioselectivity of the C radicals [19] as they obviously prefer addition at the unsubstituted *ortho* position, in particular, if *X* is voluminous (*e.g.* iodine) and/or in the case of the bulky *tert.* radicals.

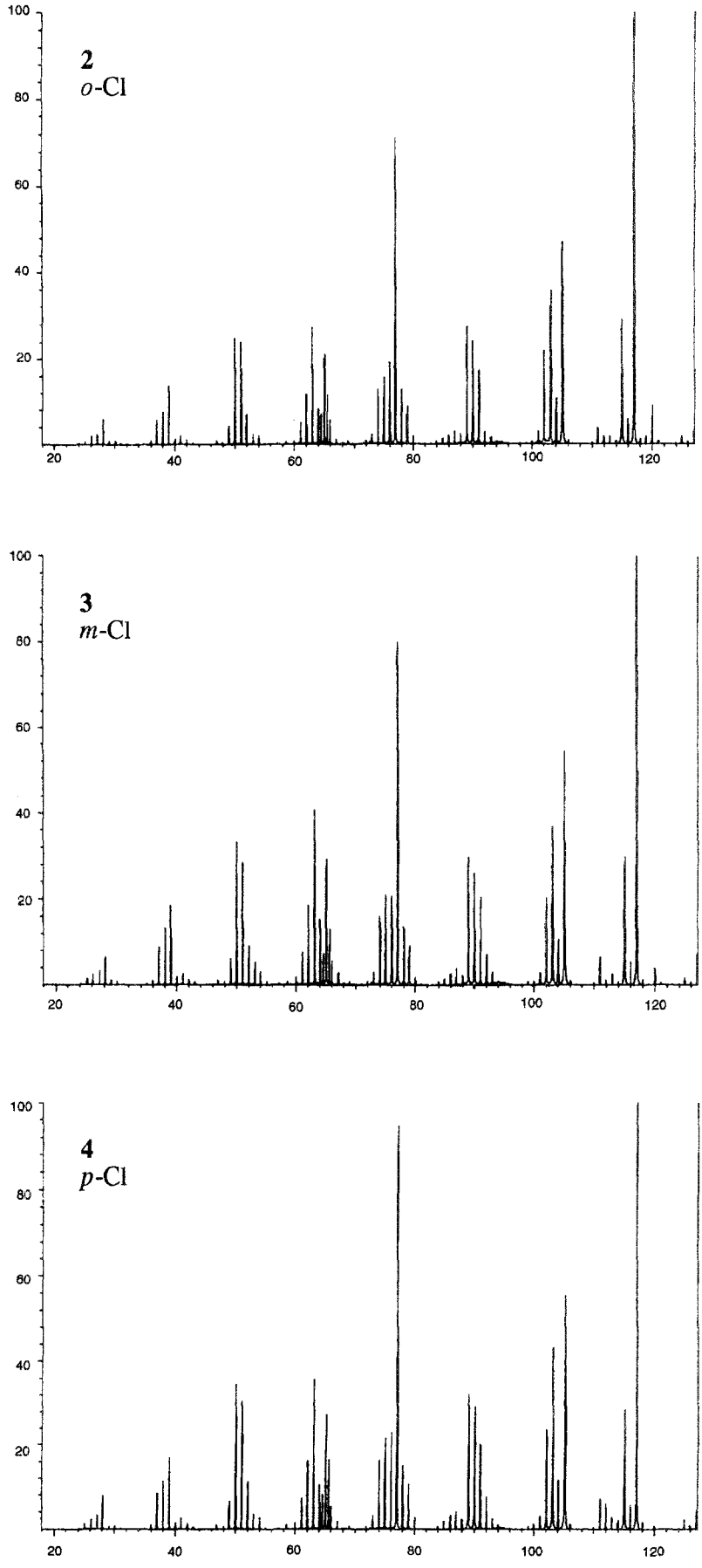
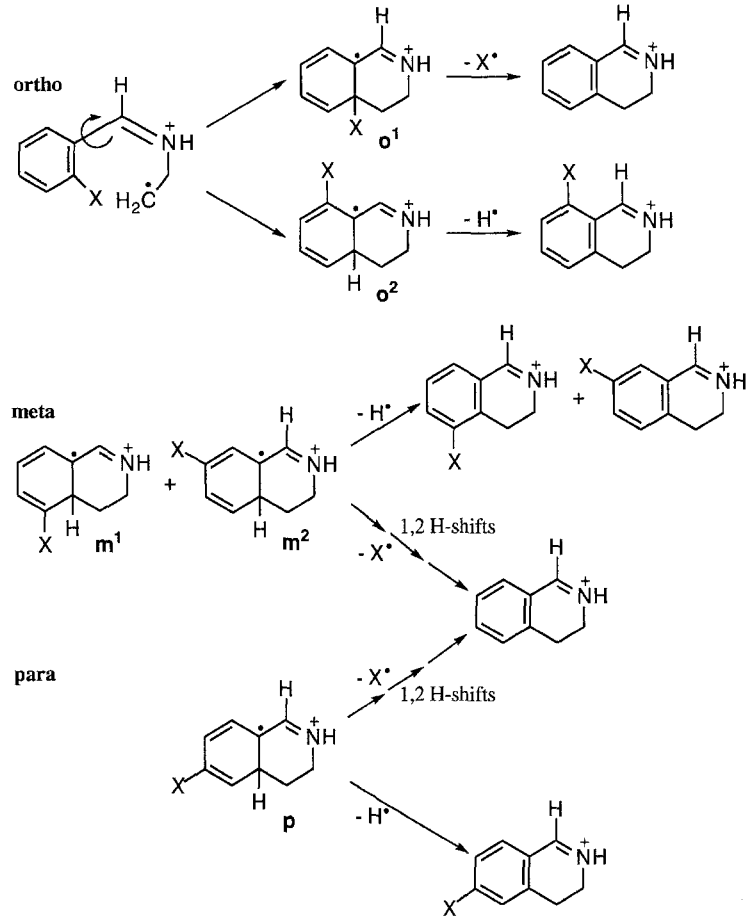


Fig. 2. CA-MS (B/E, 1st FFR; He) of $(M–CH_2O–Cl^{\bullet})^+$-ions from *o*- (**2**), *m*- (**3**), and *p*- (**4**) chloro-N-propoxybenzaldimines



Scheme 2

Experimental

Melting points: Büchi SMP 20, uncorrected. IR spectra: Nicolet 510 FT-IR. Data acquisition: Apple Macintosh II ci. ^{1}H NMR spectra: Varian EM 390 (90 MHz), *TMS* as int. standard, solvent: $CDCl_3$ with 1% *TMS*. MS: EIMS (70; 12 eV), MIMS, CA-MS (He, accumulated data from 100 individual scans) MAT 95. TLC: Merck 5554 (DC-Al sheets, silica 60 F_{254}). GC: HP 5890 II, carrier gas: He, detector: FID, column: OV 101 50 m × 0.32 mm × 0.3 µm. Elementary analyses: Mikroanalytisches Labor, University of Regensburg. All compounds are colorless oily liquids, if not otherwise stated.

D_9-n-Iodobutane

D_9-*n*-Butanol (Aldrich) was reacted with red phosphorus and I_2 [20].

Benzaldehydes
D_5-Benzaldehyde

Reaction of D_5-bromobenzene with metallic Li in dry ether [21, 22] affords D_5-phenyllithium which reacts with dimethyl formamide [23] affording D_5-benzaldehyde.

α-D-Benzaldehyde

Reduction of benzoyl chloride with $LiAlD_4$ in ether produces α,α-D_2-benzyl alcohol which was oxidized with pyridinium chromate [24] in ether.

Benzaldehyde oximes

These oximes were prepared according to a general procedure [25], reacting the benzaldehydes with hydroxylamine hydrochloride/sodium acetate in 70% ethanol.

N-Alkoxybenzaldimines

The title compounds were synthesized following known protocols:

a) alkylation of the benzaldoxime sodium salts [26, 27] by treatment of the oximes (0.05 mol) with alkyl bromides or iodides (0.053 mol) in ethanolic solution of NaOEt (from 1.15 g (0.05 g atom) Na metal in 100 ml of EtOH) under reflux.

b) Iodo-benzaldoximes were converted into their silver salts by dissolving the oximes (0.02 mol) and 0.84 g (0.021 mol) NaOH in 20 ml of water. Then 3.6 g (0.021 mol) $AgNO_3$ are added. The precipitate is washed with water and dried, mixed with 50 ml of ether and 0.04 mol of alkyl iodide, and stirred overnight under exclusion of light [25].

The purity of the oxime ethers was checked by GC.

N-(n-Propoxy)-2-fluorobenzaldimine (**1**)

Yield: 60%; b.p.: 98°C; IR (film): 3078 (CH), 3045 (CH), 2968 (CH), 2939 (CH), 2879 (CH) cm^{-1}; ^1H NMR: $\delta = 8.30$ (s, 1H, CH=N), 8.10–6.75 (m, 4H, arom), 4.15 (t, 2H, $J = 7.5$ Hz, CH_2-CH_2-CH_3), 1.75 (sext, 2H, $J = 7.5$ Hz, CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{10}H_{12}FNO$ (181.2); calcd.: C 66.3, H 6.68, N 7.7; found: C 66.1, H 6.93, N 7.7.

N-(n-Propoxy)-2-chlorobenzaldimine (**2**)

Yield: 53%; $b.p._{20-25}$: 96–104°C; IR: 3072 (CH), 2968 (CH), 2937 (CH), 2879 (CH) cm^{-1}; ^1H NMR: $\delta = 8.45$ (s, 1H, CH=N), 8.05–6.95 (m, 4H arom), 4.15 (t, 2H, $J = 7.5$ Hz, CH_2-CH_2-CH_3), 1.75 (sext, 2H, $J = 7.5$ Hz, CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{10}H_{12}ClNO$ (197.7); calcd.: C 60.8, H 6.12, N 7.1; found: C 60.8, H 5.99, N 7.2.

N-(n-Propoxy)-3-chlorobenzaldimine (**3**)

Yield: 54%; $b.p._{0.04}$: 63–65°C; IR: 3066 (CH), 2970 (CH), 2879 (CH) cm^{-1}; ^1H NMR: $\delta = 7.98$ (s, 1H, CH=N), 7.65–7.10 (m, 4H arom), 4.12 (t, 2H, $J = 7.5$ Hz, CH_2-C_2H_5), 1.75 (sext, 2H, $J = 7.5$ Hz, CH_2-CH_2-CH_3), 0.98 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3); $C_{10}H_{12}ClNO$ (197.7); calcd.: C 60.8, H 6.12, N 7.1; found: C 60.6, H 6.01, N 7.1.

N-(n-Propoxy)-4-chlorobenzaldimine (**4**)

Yield: 63%; $b.p._{0.05}$: 65–67°C; IR: 3033 (CH), 2968 (CH), 2879 (CH) cm^{-1}; ^1H NMR: $\delta = 7.98$ (s, 1H, CH=N), 7.60–7.05 (m, 4H arom), 4.10 (t, 2H, $J = 7.5$ Hz, CH_2-C_2H_5), 1.73 (sext, 2H, $J = 7.5$ Hz, CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{10}H_{12}ClNO$ (197.7); calcd.: C 60.8, H 6.12, N 7.1; found: C 60.8, H 6.12, N 7.3.

N-(n-Propoxy)-2-bromobenzaldimine (**5**)

Yield: 62%; b.p.$_{7.0-8.0}$: 143–145°C; IR: 3068 (CH), 2966 (CH), 2937 (CH), 2877 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.45$ (s, 1H, CH=N), 8.00–6.95 (m, 4H arom), 4.15 (t, 2H, $J = 7.5$ Hz, $CH_2C_2H_5$), 1.75 (sext, 4H, $J = 7.5$ Hz, CH_2-CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{10}H_{12}BrNO$ (242.1); calcd.: C 49.6, H 5.00, N 5.8; found: C 49.6, H 4.74, N 6.0.

N-(n-Propoxy)-2-iodobenzaldimine (**6**)

Yield: 43%; slightly yellow liquid; b.p.$_{0.01}$: 86–87°C; IR: 3064 (CH), 2966 (CH), 2935 (CH), 2872 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.40$ (s, 1H, CH=N), 7.95–6.90 (m, 4H arom), 4.15 (t, 2H, $J = 7.5$ Hz, CH_2-C_2H_5), 1.75 (sext, 2H, $J = 7.5$ Hz, CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{10}H_{12}INO$ (289.1); calcd.: C 41.5, H 4.18, N 4.8; found: C 41.8, H 4.22, N 5.0.

N-(n-Butoxy)-2-fluorobenzaldimine (**7**)

Yield: 31%; b.p.$_{0.01}$: 50–51°C; IR: 2962 (CH), 2875 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.35$ (s, 1H, CH=N), 8.00–6.90 (m, 4H arom), 4.25 (t, 2H, $J = 7.5$ Hz, O-CH_2-CH_2), 1.95–1.20 (m, 4H, CH_2-CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}FNO$ (195.2); calcd.: C 67.7, H 7.23, N 7.2: found: C 67.3, H 7.29, N 7.3.

N-(n-Butoxy)-3-fluorobenzaldimine (**8**)

Yield: 50%; b.p.$_{0.1}$: 61–62°C; IR: 3074 (CH), 3043 (CH), 2962 (CH), 2875 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.05$ (s, 1H, CH=N), 7.55–6.90 (m, 4H arom), 4.20 (t, 2H, $J = 7.5$ Hz, O-CH_2-CH_2), 1.95–1.20 (m, 4H, O-CH_2-$(CH_2)_2$-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}FNO$ (195.2); calcd.: C 67.7, H 7.23, N 7.2; found: C 67.5, H 6.89, N 7.3.

N-(n-Butoxy)-4-fluorobenzaldimine (**9**)

Yield: 41%; b.p.$_{0.1}$: 65–66°C; IR: 3045 (CH), 2962 (CH), 2875 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.05$ (s, 1H, CH=N), 7.75–6.85 (m, 4H arom), 4.15 (t, 2H, $J = 7.5$ Hz, O-CH_2-CH_2), 1.90–1.15 (m, 4H, CH_2 $(CH_2)_2CH_3$), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}FNO$ (195.2); calcd.: C 67.7, H 7.23, N 7.2; found: C 67.7, H 7.23, N 7.3.

N-(n-Butoxy)-2-chlorobenzaldimine (**10**)

Yield: 68%; b.p.$_{0.01}$: 75–76°C; IR: 3070 (CH), 2962 (CH), 2875 (CH) cm^{-1}; ^{1}H NMR $\delta = 8.50$ (s, 1H, CH=N), 8.00–7.05 (m; 4H arom), 4.20 (t, 2H, $J = 7.5$ Hz, CH_2-C_3H_7(n)), 1.95–1.20 (m, 4H, CH_2-CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}ClNO$ (211.7); calcd.: C 62.4, H 6.67, N 6.6; found: C 62.0, H 6.60, N 6.7.

N-(n-Butoxy)-3-chlorobenzaldimine (**11**)

Yield: 54%; b.p.$_{0.03}$: 80–81°C; IR: 3066 (CH), 2960 (CH), 2875 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.00$ (s, 1H, CH=N), 7.70–7.05 (m, 4H arom), 4.20 (t, 2H, $J = 7.5$ Hz, CH_2-C_3H_7(n)), 1.90–1.20 (m, 4H CH_2-CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}ClNO$ (211.7); calcd.: C 62.4, H 6.67, N 6.6; found C 62.1, H 6.65, N 6.7.

N-(n-Butoxy)-4-chlorobenzaldimine (**12**)

Yield: 55%; b.p.$_{0.03}$: 79–80°C, IR: 3033 (CH), 2962 (CH), 2875 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.05$ (s, 1H, CH=N), 7.65–7.15 (m, 4H arom), 4.20 (t, 2H, $J = 7.5$ Hz, CH_2-$C_3H_7(n)$), 1.90–1.15 (m, 4H, CH_2-CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}ClNO$ (211.7); calcd.: C 62.4, H 6.67, N 6.6; found C 62.2, H 6.75, N 6.7.

N-(n-Butoxy)-2-bromobenzaldimine (**13**)

Yield: 63%; b.p.$_{0.02}$: 87–88°C; IR: 3068 (CH), 2960 (CH), 2875 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.50$ (s, 1H, CH=N), 8.00–7.05 (m, 4H arom), 4.20 (t, 2H, $J = 7.5$ Hz, CH_2-$C_3H_7(n)$), 1.95–1.20 (m, 4H, CH_2-CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}BrNO$ (256.1); calcd.: C 51.6, H 5.51, N 5.5; found: C 51.5, H 5.59, N 5.7.

N-(n-Butoxy)-3-bromobenzaldimine (**14**)

Yield: 57%; b.p.$_{0.01}$: 90–91°C; IR: 3064 (CH), 2956 (CH), 2870 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.00$ (s, 1H, CH=N), 7.90–7.60 (m, 5H arom), 4.20 (t, 2H, $J = 7.5$ Hz, O-CH_2-CH_2), 2.10–1.20 (m, 4H, O-CH_2-CH_2-CH_2), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}BrNO$ (256.1); calcd.: C 51.6, H 5.51, N 5.5; found: C 51.5, H 5.38, N 5.6.

N-(n-Butoxy)-4-bromobenzaldimine (**15**)

Yield: 48%; b.p.$_{0.01}$: 87–88°C; IR: 2960 (CH), 2935 (CH), 2873 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.00$ (s, 1H, CH=N), 7.45 (s, 4H arom), 4.15 (t, 2H, $J = 7.5$ Hz, O-CH_2-CH_2), 2.00–1.15 (m, 4H, O-CH_2-CH_2-CH_2), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}BrNo$ (256.1); calcd.: C 51.6, H 5.51, N 5.5; found: C 51.6, H 5.53, N 5.6.

N-(n-Butoxy)-2-iodobenzaldimine (**16**)

Yield: 41%; slightly yellow liquid; b.p.$_{0.02}$: 95–97°C; IR: 3064 (CH), 2960 (CH), 2873 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.30$ (s, 1H, CH=N), 8.15–6.80 (m, 4H arom), 4.20 (t, 2H, $J = 7.5$ Hz, CH_2-C_3H_7), 1.95–1.10 (m, 4H, CH_2-CH_2-CH_2-CH_3), 0.95 (t, 3H, $J = 7.5$ Hz, CH_2-CH_3) ppm; $C_{11}H_{14}INO$ (303.1); calcd.: C 43.6, H 4.66, N 4.6; found: C 43.4, H 4.38, N 4.8.

N-(3-Methylbutoxy)-2-fluorobenzaldimine (**17**)

Yield: 45%; b.p.$_{0.01}$: 64–65°C; IR: 3078 (CH), 3045 (CH), 2962 (CH) cm^{-1}; ^{1}H NMR: $\delta = 8.35$ (s, 1H, CH=N) , 8.00–6.90 (m, 4H arom), 4.25 (t, 2H, $J = 7.5$ Hz, O-CH_2-CH_2), 2.05–1.45 (m, 3H, CH_2-$CH(CH_3)_2$), 0.95 (d, 6H, $J = 7.5$ Hz, $CH(CH_3)_2$) ppm; $C_{12}H_{16}FNO$ (209.3); calcd.: C 68.9, H 7.71, N 6.7; found: C 69.1, H 7.68, N 6.9.

N-(3-Methylbutoxy)-2-chlorobenzaldimine (**18**)

Yield: 64%; b.p.$_{0.01}$: 84–85°C; IR: 3070 (CH), 3014 (CH), 2960 (CH), 2873 (CH) cm^{-1}; ^{1}H NMR: δ =8.48 (s, 1H, CH=N), 8.05–7.00 (m, 4H arom), 4.20 (t, 2H, $J = 7.5$ Hz, CH_2-CH_2-$CH(CH_3)_2$), 2.05–1.35 (m, 3H, CH_2-CH_2-$CH(CH_3)_2$), 0.95 (d, 6H, $J = 7.5$ Hz, $CH(CH_3)_2$) ppm; $C_{12}H_{16}ClNO$ (225.7); calcd.: C 63.9, H 7.15, N 6.2; found: C 64.0, H 7.18, N 6.3.

N-(3-Methylbutoxy)-2-bromobenzaldimine (**19**)

Yield: 59%; b.p.$_{0.01}$: 83–84°C; IR: 3068 (CH), 2958 (CH) cm^{-1}; ^{1}H NMR: δ = 8.45 (s, 1H, CH=N), 8.00–6.95 (m, 4H arom), 4.20 (t, 2H, J = 7.5 Hz, C*H*$_2$-CH$_2$-CH(CH$_3$)$_2$), 2.10–1.40 (m, 3H, CH$_2$-C*H*$_2$-C*H*(CH$_3$)$_2$), 0.95 (d, 6H, J = 7.5 Hz, CH(C*H*$_3$)$_2$) ppm; $C_{12}H_{16}BrNO$ (270.2); calcd.: C 53.4, H 5.97, N 5.2; found: C 53.5, H 6.06, N 5.4.

N-(3-Methylbutyoxy)-2-iodobenzaldimine (**20**)

Yield: 57%; slightly yellow liquid; b.p.$_{0.04}$: 106–107°C; IR: 3064 (CH), 2958 (CH), 2871 (CH) cm^{-1}; ^{1}H NMR: δ = 8.35 (s, 1H, CH=N), 8.15–6.85 (m, 4H arom), 4.22 (t, 2H, J = 7.5 Hz, C*H*$_2$-CH$_2$-CH(CH$_3$)$_2$), 2.00–1.30 (m, 3H, CH$_2$-C*H*$_2$-C*H*(CH$_3$)$_2$), 0.98 (d, 6H, J = 7.5 Hz, CH(C*H*$_3$)$_2$) ppm; $C_{12}H_{16}INO$ (317.2); calcd.: C 45.4, H 5.09, N 4.4; found: C 45.2, H 5.05, N 4.6.

N-(n-Propoxy)-2,6-dichlorobenzaldimine (**21**)

Yield: 35%; b.p.$_{2.0}$: 138°C; IR: 3080 (CH), 2968 (CH), 2879 (CH) cm^{-1}; ^{1}H NMR: δ = 8.28 (s, 1H, CH=N), 7.45–6.85 (m, 3H arom), 4.15 (t, 2H, J = 7.5 Hz, C*H*$_2$-C$_2$H$_5$), 1.75 (sext, 2H, J = 7.5 Hz, CH$_2$-C*H*$_2$-CH$_3$), 0.95 (t, 3H, J = 7.5 Hz, CH$_2$-C*H*$_3$) ppm; $C_{10}H_{11}Cl_2NO$ (232.1); calcd.: C 51.7, H 4.78, N 6.0; found: C 51.8, H 4.76, N 6.4.

N-(n-Butoxy)-D$_5$-benzaldimine (**22**)

Yield: 40%; b.p.$_{0.02}$: 58–59°C; IR: 2960 (CH), 2875 (CH), 2283 (CD) cm^{-1}; ^{1}H NMR: δ = 8.10 (s, 1H, CH=N), 4.20 (t, 2H, J = 7.5 Hz, C*H*$_2$-C$_3$H$_7$(n)), 1.90–1.25 (m, 4H, CH$_2$-C*H*$_2$-C*H*$_2$-CH$_3$), 1.00 (t, 3H, J = 7.5 Hz, CH$_2$-C*H*$_3$).

N-(n-Butoxy)-α-D-benzaldimine (**23**)

Yield: 35%; b.p.: see **22**; IR: 3064 (CH), 3027 (CH), 2960 (CH), 2875 (CH), 2219 (CD) cm^{-1}; ^{1}H NMR: δ = 7.75–7.15 (m, 5H arom), 4.15 (t, 2H, J = 7.5 Hz, C*H*$_2$-CH$_2$-C$_2$H$_5$), 1.90–1.20 (m, 4H, CH$_2$-C*H*$_2$-C*H*$_2$-CH$_3$), 0.92 (t, 3H, J = 7.5 Hz, CH$_2$-C*H*$_3$).

N-(D$_9$-n-Butoxy)-benzaldimine (**24**)

0.5 g (0.0026 mol) D$_9$-*n*-iodobutane; 0.315 g (0.0026 mol) benzaldoxime; yield; 58% b.p.: see **22**; IR: 3083, 3064, 3029, 2988 (CH), 2217, 2108 (CD) cm^{-1}; ^{1}H NMR: δ = 8.10 (s, 1H, CH=N), 7.75–7.20 (m, 5H arom) ppm; EI-MS (70 eV): *m/z* (%) = 186 (27; M^{+}·), 154 (22: [M–32]$^{+}$·), 153 (100; [M–33]$^{+}$), 105 (59; C$_7$H$_5$DN^{+}), 77 (41; C$_6$H$_5^{+}$).

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