

Selectivity towards hydrodehalogenation and dehalo-coupling in the reduction of trichloromethyl derivatives with iron(II) chloride

Ugo Folli, Francesca Goldoni, Dario Iarossi, Silvia Sbardellati and Ferdinando Taddei

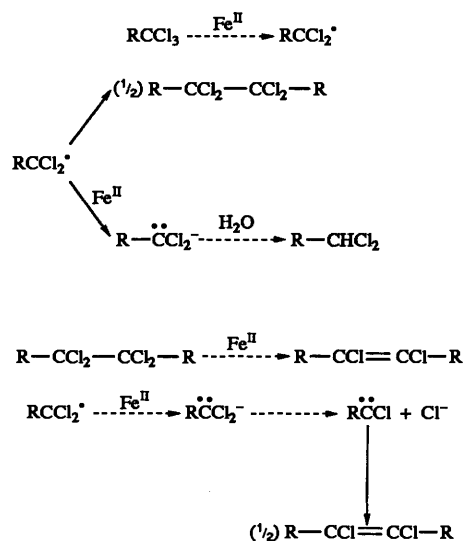
Dipartimento di Chimica, Università, Via Campi 183, 41100 Modena, Italy

The reductive electron transfer (ET) induced on a series of RCCl_3 derivatives by iron(II) chloride has been studied. The main reaction products are the homocoupling dimer, $\text{RCCl}_2\text{-CCl}_2\text{R}$, and the H/Cl substitution derivative, RCHCl_2 , and the majority of the compounds examined exhibit a highly selective tendency to form just one of these products. As a general rule, the RCHCl_2 compound is the main product when the R group contains substituents which make further reduction of the radical to the carbanion easier and behave as ligands towards the iron(II) ion. In the other cases, the dimer $\text{RCCl}_2\text{-CCl}_2\text{R}$ is the main product. A few exceptions are found, and these are discussed in view of the possible effects of the R moiety on the different possible routes for the reaction products. The presence of unsaturated derivatives, RCCl=CClR (*E/Z* mixture), was observed in the case of the reactions where the homocoupling product was also obtained and is ascribed, on the basis of experimental evidence, to a dehalogenation mechanism of the dimer $\text{RCCl}_2\text{-CCl}_2\text{R}$ assisted by the iron(II) ion.

The reductive electron transfer (ET) on alkyl halides is a dissociative process¹⁻⁴ and, regardless of its concerted or stepwise nature,⁵ leads to a halide anion and to a radical. The products originating from the reaction of Fe^{II} salts with haloalkanes⁶⁻¹¹ have been characterized. One of the most commonly studied systems is benzotrifluoride, which exhibits a fairly high reactivity at room temperature and, in boiling acetonitrile (MeCN), is transformed¹⁰ in high yields into the homocoupling product of the intermediate radical, *i.e.* tetrachlorodiphenylethane. When the same solvent is used with an excess of a stronger reducing species,¹⁰ *e.g.* LiFeCl_3 , a mixture of the two isomeric dichlorostilbenes is obtained, with the (*Z*)-isomer in higher yield. When the reaction is carried out⁹ in DMSO with $\text{FeCl}_2\cdot 4\text{H}_2\text{O}$, tetrachlorodiphenylethane is the only product detected at temperatures below 60 °C, whereas the unsaturated derivatives are formed at higher temperatures. At higher temperatures and with a stronger reducing species a similar effect is observed^{7,10,12} as regards the relative amounts of the saturated coupling products and of the unsaturated derivatives, even when the reaction is carried out on dichlorodiphenylmethane and on dichlorophenylmethane.

While the presence of reaction products containing hydrogen, *e.g.* RCHCl_2 , has never been observed in the reactions carried out with iron(II) salts on benzotrifluoride, the presence of chloroform among the products has been reported⁶ in the case of carbon tetrachloride. For this molecule, the unsaturated compound, tetrachloroethylene, which is formed by reacting CCl_4 with FeCl_2 in MeCN, was assumed⁶ to be generated through a dichlorocarbene intermediate, released by the trichloromethyl radical after further reduction by the metal ion. The hypothesis of the presence of the carbene intermediate was supported⁶ by reactions characteristic of this species.

The reaction of trichloromethyl derivatives RCCl_3 with a reducing species like Fe^{II} , according to a reaction mechanism which was discussed in a previous paper¹³ has been summarized in Scheme 1. The inner-sphere electron transfer process is also suggested by the oxidation potential of Fe^{II} in MeCN which is about +1.1 V (SCE),¹⁴ and makes an outer sphere ET too slow. Three kinds of molecules can be expected to be generated as main reaction products: the coupling product $\text{RCCl}_2\text{-CCl}_2\text{R}$, the product from H/Cl substitution, RCHCl_2 , and the unsaturated (*E/Z*)-isomers RCCl=CClR .



Scheme 1 Proposed reaction steps occurring in the transformation of RCCl_3 compounds induced by $\text{FeCl}_2\cdot 4\text{H}_2\text{O}$ in anaerobic conditions

The yield of the different derivatives depends¹³ on the molar ratio substrate- Fe^{II} and the temperature, but the most striking determining factor seems to be the chemical nature of R.

In the present paper we report an experimental investigation regarding the influence of the nature of the R group on the products and on the selectivity that the reaction assumes, depending on the choice of group.

Experimental

Compounds

The trichloromethyl derivatives 1-12, reported in Scheme 2, were either commercial products or were synthesized according to known procedures.

Warning: benzotrifluoride and its derivatives are strongly suspected of having carcinogenic properties.

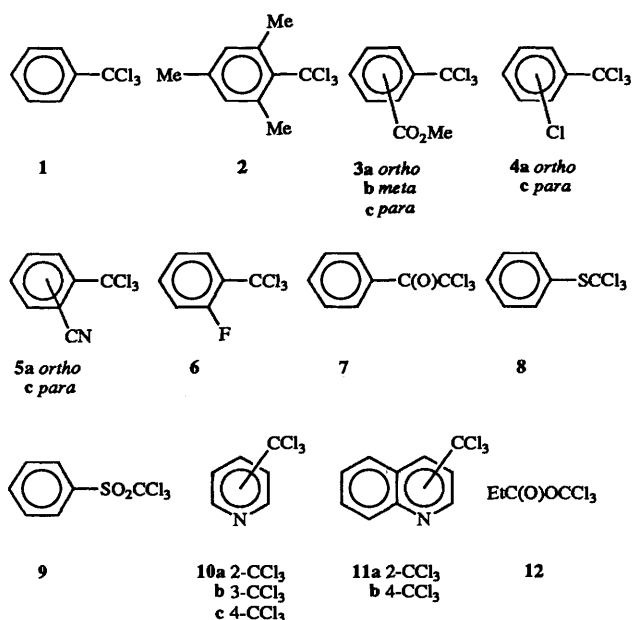
General reaction procedures

The reactions were carried out in MeCN, in which both the organic substrates and iron(II) chloride are sufficiently soluble.

Table 1 Reaction conditions^a and identified products in the reductive dehalogenation induced by FeCl₂·4H₂O on the trihalides RCCl₃

Compound	R	[Substrate]:[FeCl ₂ ·4H ₂ O]	T/°C	t/h	Product [Yield (%)]
1	Ph	1:2	25	7	RCCl ₂ -CCl ₂ R (93)
			80	2.5	RCCl ₂ -CCl ₂ R (74), RCO ₂ H (8)
2	2,4,6-Me ₃ C ₆ H ₂	1:1	25	24	RCCl ₂ -CCl ₂ R (> 70)
3a	2-MeCO ₂ C ₆ H ₄ ^b	1:2	25	7	RCCl ₂ -CCl ₂ R (77)
3b	3-MeCO ₂ C ₆ H ₄	1:2	25	7	RCCl ₂ -CCl ₂ R (82)
3c	4-MeCO ₂ C ₆ H ₄	1:2	25	7	RCCl ₂ -CCl ₂ R (95)
4a	2-ClC ₆ H ₄	1:2	25	7	RCCl ₂ -CCl ₂ R (38), RCCl=CClR (39, Z/E = 1.3)
4c	4-ClC ₆ H ₄	1:2	25	7	RCCl ₂ -CCl ₂ R (80)
5a	2-CNC ₆ H ₄	1:2	25	7	RCCl ₂ -CCl ₂ R (64)
5b	4-CNC ₆ H ₄	1:2	25	7	RCCl ₂ -CCl ₂ R (91)
6	2-FC ₆ H ₄	1:2	25	7	RCCl ₂ -CCl ₂ R (57)
			80	7	RCCl ₂ -CCl ₂ R (51), RCCl=CClR (39, isomer ratio = 2) ^c
7	PhC(O) ^d	1:2	25	48	RCHCl ₂ (52)
			82	23	RCHCl ₂ (32)
8	PhS	1:2	25	7	RCHCl ₂ (26), RCHO (31), RCH ₂ Cl (~2)
9	PhSO ₂	1:2	25	7	No product
10a	2-Pyridyl	1:2	25	30	RCHCl ₂ (60)
			82	30	RCHCl ₂ (82)
10b	3-Pyridyl ^e	1:2	25	30	RCCl ₂ -CCl ₂ R (82)
10c	4-Pyridyl	1:2	25	30	RCHCl ₂ (71)
11a	2-Quinolyl	1:1	25	7	RCHCl ₂ (14), RCCl ₂ -CCl ₂ R (5)
			25	7	RCHCl ₂ (41), RCCl ₂ -CCl ₂ R (9)
			25	7	RCHCl ₂ (44), RCCl ₂ -CCl ₂ R (8)
11b	4-Quinolyl	1:2	25	7	RCHCl ₂ (52)
12	EtOC(O) ^f	1:2	25	48	RCHCl ₂ (28), RCCl ₂ -CCl ₂ R (19)
					RCCl=CClR (6, E/Z = 94/6)

^a Where not otherwise specified an initial concentration of 0.038 mol dm⁻³ for RCl₃ was employed. ^b Initial concentration 0.11 mol dm⁻³. ^c The relative amount of the Z and E isomers was not assigned. ^d Initial concentration 0.085 mol dm⁻³. ^e Initial concentration 0.248 mol dm⁻³. ^f Initial concentration 0.093 mol dm⁻³.

**Scheme 2** Organic substrates RCl₃ employed in the present work

We used MeCN (Aldrich, HPLC grade) freshly distilled from P₂O₅ and stored over molecular sieves (Merck 0.5 nm), and also commercial FeCl₂·4H₂O, both compounds being kept in an argon atmosphere. The solvent was dried in order to introduce a constant amount of water, namely that of the hydrated iron salt, into the reaction medium. The reduction potential of the iron(II) ion in fact depends on the amount of water present in solution.¹³ The reaction vessel, containing the iron salt and the organic substrate in separate ampoules, was vacuum-degassed and flushed with argon free of oxygen. The

solvent was stirred into the mixture in order to start the reaction. After a period of time the reaction was stopped by letting air enter the reaction vessel and water was added to the mixture. After extraction with chloroform, the organic solution was washed with water, dried and then made up with chloroform to a known final volume. This solution was then analysed by GLC and HPLC techniques (the latter being employed for thermally-unstable compounds); GLC was carried out with a Hewlett-Packard 5890 instrument fitted with a phenylsilicone column HP5 (phase 5%) and HPLC with a Hewlett-Packard 1090 unit fitted with a RP-18 (25 cm) column. The eluent was MeCN-H₂O, the amount of the two components being optimized for each reaction mixture. Detection of the components was based on the UV absorption at 230 and 255 nm. A Hewlett-Packard 5989A spectrometer was employed for GLC-MS and HPLC-MS measurements.

Quantitative determinations of the amounts of reaction products, were carried out on standard solutions made up with reagents and final products, the latter being isolated and characterized or independently synthesized.

Results and discussion

The results of the reactions of the compounds reported in Scheme 2 are set out in Table 1: yields of the compounds have been determined by the techniques described in the Experimental part and differences to 100 are given by the starting material recovered. The results reported in Table 1 show that the compounds employed in the reaction with FeCl₂·4H₂O can be divided into three main groups on the basis of the compounds they yield: the homocoupling compound, RCCl₂-CCl₂R, almost exclusively—compounds 1–6, 10b; the H/Cl substitution compound, RCHCl₂, almost exclusively—compounds 7–9, 10a, 10c, 11b; a mixture of the RCCl₂-CCl₂R and RCHCl₂—compounds 11a and 12. Since the reaction should proceed through an ET reduction step with the

formation of an intermediate RCCl_2^{\cdot} radical, we assume, at the present stage of the discussion, that the unsaturated compounds are not obtained from reactions directly involving this radical.

Previously, we reported¹³ that the homocoupling of radicals competes with the formation of a carbanion coordinated with the ferric ion, a proton being transferred to this carbanion from a water molecule which is most likely to be present already in the coordination shell of the metal atom. Further reduction of the radicals depends on their reduction potentials, since the reducing agent, $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$, is kept constant, and to the best of our knowledge the reduction potentials of the RCCl_2^{\cdot} radicals are not known. Reduction potentials have been reported^{15,16} for benzyl radicals with substituents in the ring and electron-withdrawing substituents make reductions of these radicals easier: the reduction potentials of substituted benzyl radicals give a linear Hammett plot with σ^- . This correlation holds for substituted cumyl and diphenylmethyl radicals as well.¹⁶ The existence of this correlation for benzyl radicals has been taken as an indication¹⁵ that their reduction potentials are dominated by carbanion stability, and the same probably applies to RCCl_2^{\cdot} radicals. Thus, the molecules containing carbanion-stabilizing groups in the R moiety are likely to be involved in H/Cl substitution which yields RCHCl_2 , as is the case of compounds 7–9, 10a, 10c and 11b. In these molecules groups are present which are good carbanion stabilizers: it is in fact generally accepted that stabilization of α -carbanions by R groups should follow the order¹⁷ $\text{NO}_2 > \text{COPh} > \text{CO}_2\text{Me} > \text{SO}_2\text{Ph} > 4\text{-C}_5\text{H}_4\text{N} > 2\text{-C}_5\text{H}_4\text{N} > 3\text{-C}_5\text{H}_4\text{N} > \text{Ph}$. The ability of SR groups to stabilize α -carbanions has also been demonstrated¹⁸ and discussed.¹⁹ When groups with a lower α -carbanion stabilizing ability are involved, the activation energy required for homocoupling and H/Cl substitution respectively, can be virtually identical, as occurs with compounds 11a and 12. In these cases, the increase in the molar ratio iron(II)–substrate seems to promote H/Cl substitution as was observed experimentally for compound 11a.

A peculiarity is observed in the respective behaviour of quinoline and pyridine derivatives, a certain amount of the coupling product being formed when the reaction centre CCl_3 is in position 2 of quinoline, derivative 11a, but not in the corresponding pyridine derivative 10a. However, this can be explained, for it is known²⁰ that, (i) alkyl groups in positions 2 and 4 of pyridine are more reactive to base-catalysed deprotonation than those bonded to a benzene ring, and (ii) in the quinoline system deprotonation of the methyl groups present in different positions occurs²⁰ in the order $4 > 2 > 3$. The presence of a small amount of coupling product in the case of compound 11a but not of 10a would thus depend on the slightly lower stability of the α -carbanion in the quinoline system and/or on the impaired ability of quinoline to bind to the Fe^{II} ion when the CCl_3 group is in position 2.

Another point worthy of comment is the behaviour of the compounds containing S and SO_2 groups, namely compounds 8 and 9. Both PhS and PhSO_2 are expected^{17,18} to stabilize α -carbanions, yet the latter should have a stronger effect. The acidity of the protonated carbons α to these groups support^{17a,18} this order. The results for the reactions carried out on derivatives 8 and 9 show that both those compounds give the H/Cl substitution compound, yet the reaction is much slower for the compound containing the SO_2 group. The explanation for this behaviour should perhaps be found in the fact that the radical anion $\text{RCCl}_3^{\cdot-}$ formed in the ET process on compound 9 is more stable than in the other case (its stepwise, as opposed to its concerted, nature should be enhanced), and the breaking of the C–Cl bond requires a higher activation energy. The electron should in fact be largely delocalized in the SO_2 group, as occurs²¹ for the RSO_2^{\cdot} radical.

A final point to be tackled in the discussion of the experi-

mental results reported here is that concerning the formation of the unsaturated derivatives $\text{RCCI}=\text{CCIR}$. These can, in principle, be formed through different routes; two of the most likely being: (i) homocoupling of two radicals and dehalogenation of the dimeric product assisted by iron(II) ions; (ii) associative interaction of a radical RCCl_2^{\cdot} with an iron(II) ion via an ET step, elimination of Cl^- ion and carbenic coupling. In derivative 6 the formation of unsaturated dimers is observed only at high temperature and when the $\text{RCCl}_2\text{--CCl}_2\text{R}$ derivative is warmed in the presence of iron(II) chloride a mixture of unsaturated compounds with the same E/Z ratio as in the reaction with RCCl_3 is obtained. For compounds 4a and 12 the amount of unsaturated derivatives increases as the temperature rises. The dimeric $\text{RCCl}_2\text{--CCl}_2\text{R}$ compounds do not react in the absence of $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ nor does isomerization occur when the Z isomer (verified¹³ for compound 12) of $\text{RCCI}=\text{CCIR}$ is warmed with $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ in boiling MeCN. Furthermore, unsaturated derivatives are not observed when the main reaction compound is RCHCl_2 : in this case the carbene-like species should be easily formed from the carbanion following route (ii). Chlorine elimination from $\text{PhC}(\text{Cl}_2)\text{C}(\text{Cl}_2)\text{Ph}$ in the presence of LiFeCl_3 at high temperature with the formation of unsaturated dichlorostilbenes [the (Z)-isomer being more abundant] has also been observed previously.^{9,10} In the formation of the unsaturated derivatives, $\text{RCCI}=\text{CCIR}$, route (i) seems to be preferred and these compounds should not originate directly from reactions of the RCCl_2^{\cdot} radicals: nevertheless, the mechanism underlying this process, which requires the participation of iron(II) ions, is not at present completely understood.

Acknowledgements

Financial support from the Italian *Ministero per l'Università e per la Ricerca Scientifica e Tecnologica* (MURST) is gratefully acknowledged.

References

- 1 L. Ebersson and M. Ekström, *Acta Chem. Scand., Ser. B*, 1988, **42**, 101, 113; L. Ebersson, M. Ekström, T. Lund and H. Lund, *Acta Chem. Scand., Ser. B*, 1989, **43**, 101.
- 2 B. V. Timokhin, *Russ. Chem. Rev.*, 1990, **59**, 193.
- 3 J. M. Saveant, *J. Am. Chem. Soc.*, 1987, **109**, 6788.
- 4 R. Benassi, F. Bernardi, A. Bottoni, M. A. Robb and F. Taddei, *Chem. Phys. Lett.*, 1989, **161**, 79.
- 5 J. Bertran, I. Gallardo, M. Moreno and J. M. Saveant, *J. Am. Chem. Soc.*, 1992, **114**, 6892, 9576.
- 6 M. Asscher and D. Vofsi, *J. Chem. Soc. B*, 1968, 947.
- 7 K. Onuma, J. Yamashita and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, 1970, **43**, 836.
- 8 T. A. Cooper and T. Takeshita, *J. Org. Chem.*, 1971, **36**, 3517.
- 9 T. Shirafuji, Y. Yamamoto and H. Nozaki, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 1994.
- 10 K. Onuma, J. Yamashita and H. Hashimoto, *Bull. Chem. Soc. Jpn.*, 1973, **46**, 333.
- 11 L. Wilputte-Steinert, *Transition Met. Chem.*, 1978, **3**, 172.
- 12 J. M. Khurana, G. C. Maikap and S. Mehta, *Synthesis*, 1990, 731.
- 13 A. Cornia, U. Folli, S. Sbardellati and F. Taddei, *J. Chem. Soc., Perkin Trans. 2*, 1993, 1847.
- 14 I. M. Kolthoff and J. F. Coetzee, *J. Am. Chem. Soc.*, 1957, **79**, 1852.
- 15 A. Sim, D. Griller and D. D. Wayner, *J. Am. Chem. Soc.*, 1989, **111**, 754.
- 16 A. Sim, P. H. Milne, D. Griller and D. D. Wayner, *J. Am. Chem. Soc.*, 1990, **112**, 6635.
- 17 (a) F. G. Bordwell, J. E. Bares, J. E. Bartmess, G. E. Drucker, J. Gerhold, G. J. McCollum, M. Van Der Puy, N. R. Vanier and W. S. Matthews, *J. Org. Chem.*, 1977, **42**, 326; (b) F. G. Bordwell, W. S. Matthews and N. R. Vanier, *J. Am. Chem. Soc.*, 1975, **97**, 442; (c) S. Bradamante and G. Pagani, *J. Chem. Soc., Perkin Trans. 2*, 1986, 1047.
- 18 J. F. Arens, M. Fröling and A. Fröling, *Recl. Trav. Chim. Pays-Bas*,

- 1959, **78**, 663; J. Hine, *Physical Organic Chemistry*, McGraw-Hill, New York, 1962, p. 201; H. Hogeveen, G. Maccagnani, F. Montanari and F. Taddei, *Boll. Sci. Fac. Chim. Ind. Bologna*, 1963, **XXI**, 259.
- 19 F. Bernardi, A. Bottoni, A. Venturini and A. Mangini, *J. Am. Chem. Soc.*, 1986, **108**, 8171.
- 20 B. C. Uff, in *Comprehensive Heterocyclic Chemistry*, ed. A. J. Boulton and A. McKillop, vol. 2, part 2A, Pergamon Press, Oxford, 1984.
- 21 R. S. Boyd, A. Gupta, R. F. Langler, S. P. Lowrie and J. A. Pincock, *Can. J. Chem.*, 1980, **58**, 331.

Paper 4/06537I

Received 25th October 1994

Accepted 5th January 1995