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A NEW, HIGHLY SELECTIVE, TYPE OF RADICAL CHLORINATION

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IT has been recently (1) claimed that the facile intermolecular hydrogen abstraction is not a reaction characteristic of protonated amino radicals obtained from N-chloroamines. This statement is rather surprising, since the intramolecular hydrogen abstraction (2) (Hoffman-Loeffler reaction) is a very easy process. In our opinion, the problem is connected with the selectivity towards different substrates and positions and not with the possibility of reaction.

Actually we have found that saturated hydrocarbon chains are quite easily chlorinated by N-chlorodimethylamine in acidic medium. The results, expressed as per cent isomers, for the methyl esters of butanoic, pentanoic, hexanoie and heptanoic acids, are summarized in Table 1 .

TABLE 1

CH_3OOC	CH_2	CH_2	CH_3
	—	86.4	13.6

CH_3OOC	CH_2	CH_2	CH_2	CH_3
	—	15.7	77	7.3

CH_3OOC	CH_2	CH_2	CH_2	CH_2	CH_3
	—	4.7	13.5	78	3.9

CH_3OOC	CH_2	CH_2	CH_2	CH_2	CH_2	CH_3
	traces	1	4.6	19.8	71.9	2.7

The experimental conditions are the same for all cases: powdered ferrous sulphate

(0.05 mol) is added to a stirred solution of the N-chlorodimethylamine(0.1 mol) and the ester(0.12 mol) in conc. sulphuric acid/ acetic acid (85:15). The reaction is very rapid and exothermic, but the temperature is not allowed to rise above 40°C by external cooling. The isomer distribution was determined by gaschromatographic analysis.

The reaction mechanism is essentially the same as for the Hoffman-Loeffler reaction (2) with the only difference that an intermolecular hydrogen abstraction takes place.

$$(CH_3)_2\overset{+}{N}HCl + Fe^{++} \longrightarrow (CH_3)_2\overset{+}{\underset{\cdot}{N}}H + FeCl^{++}$$

$$R—H + (CH_3)_2\overset{+}{\underset{\cdot}{N}}H \longrightarrow R\cdot + (CH_3)_2\overset{+}{N}H_2$$

$$R\cdot + (CH_3)_2\overset{+}{N}HCl \longrightarrow R—Cl + (CH_3)_2\overset{+}{\underset{\cdot}{N}}H$$

We rule out an alternative mechanism, involving chlorine atoms, as suggested in the case of radical bromination by N-bromosuccinimide (3) :

$$R—H + Cl\cdot \longrightarrow R\cdot + HCl$$

$$R\cdot + Cl_2 \longrightarrow R—Cl + Cl\cdot$$

$$(CH_3)_2\overset{+}{N}HCl + HCl \longrightarrow (CH_3)_2\overset{+}{N}H_2 + Cl_2$$

In fact, under our reaction conditions, the N-chloroamine does not oxidize the hydrogen chloride appreciabily and the selectivity is much higher than with chlorine atoms(4). This selectivity is toohigh to be caused by the different reaction conditions, but can be mainly explained by two factors:the greater sensitivity of the protonated amino radicaltowards the inductive effects of the substituent, which is operative even in the ε position, and the different reactivity of the methylene and methyl groups. We think that the strong electrophilic character of the protonated amino radical is responsible for this behaviour and this view is supported also by the unusually high selectivity observed in the homolytic aromatic amination by N-chloroamines under the same conditions (5). Furthermore in this last reaction the selectivity increases by using cuprous instead of ferrous salt (6) and decreases with increasing amount of acetic acid (in mixture with sulphuric acid) (7) :the same trend, even if less marked, is observed for the radical chlorination of methyl caproate, as shown by the results summarized in Table 2 .

The easy availability of N-chlorodimethylamine (8), the very simple experimental conditions, the highly selective attack with other chlorinating agents, make this new type of radical chlorination interesting also from a synthetic point of view. These features are also characteristic of other reactions of amino radicals (with olefinic (1,9) and aromatic compounds (5)), which thus again prove to be one of the most versatile reacting species.

TABLE 2

	CH_3OOC—CH_2	—CH_2	—CH_2	—CH_2	—CH_3
H_2SO_4 , Fe^{++}	—	0.7	6.3	87.3	5.7
H_2SO_4 85% , CH_3COOH 15%, Fe^{++}	—	4.7	13.5	78	3.9
H_2SO_4 , Cu^+	—	0.3	4.7	89.4	5.6
H_2SO_4 85% , CH_3COOH 15% , Cu^+	—	2.2	9.2	84.5	4.1

REFERENCES

1. R.S.Neale. Tetrahedron Letters 483 (1966).
2. R.S.Neale and M.R.Walsh. J.Am.Chem.Soc. 87 1255 (1965)and references quoted therein.
3. C.Walling,A.L.Rieger and D.D.Tanner. J.Am.Chem.Soc. 85 3129 (1963) and references quoted therein.
4. H.Singh and J.M.Tedder. J.Chem.Soc. B 605 (1966).
5. F.Minisci,R.Galli,M.Cecere and V.Trabucchi. Chimica e Industria 48 716,1147,1324(1966).
6. F.Minisci,A.Galli,R.Galli and R.Bernardi. Ibid. in press.
7. F.Minisci,R.Galli,A.Galli and R.Bernardi. Ibid. 49 252 (1967).
8. F.Minisci,R.Bernardi,V.Trabucchi and L.Grippa. Ibid. 48 484 (1966).
9. F.Minisci,R.Galli and M.Cecere. Tetrahedron Letters 3163 (1966).