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New Free-Radical Chain Processes Involving Substitution of Vinyl and Aryl Chlorides by Alkanes, Alkenes, Esters and Ethers.

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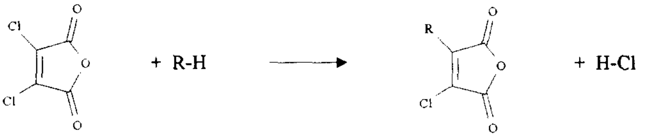
Abstract. New free-radical substitutions of vinyl and aryl chlorides by alkanes, alkenes, ethers and esters are described. The free-radical chains are rationalized on the basis of the known kinetics of the elementary steps involved. Copyright © 1996 Published by Elsevier Science Ltd

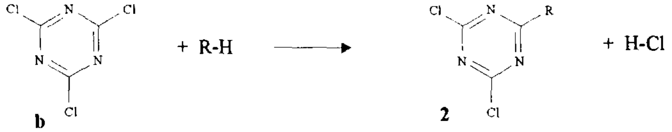
The kinetics of free-radical reactions is gaining an increasing importance for the development of new syntheses, because the rate constants of the elementary steps are only rarely macroscopically affected by the reaction medium. The quantitative kinetic data determined beforehand by the most sophisticated methodologies (flash photolysis, pulse radiolysis etc.) can be utilized with good reliability in quite different conditions for new synthetic strategies.

Taking advantage of the knowledge of the relative reactivities, we have developed new free-radical reactions involving substitution of chlorine atoms on vinyl and aryl chlorides by alkanes, alkenes, ethers and esters (eqs. 1-5)



a 1

(1)



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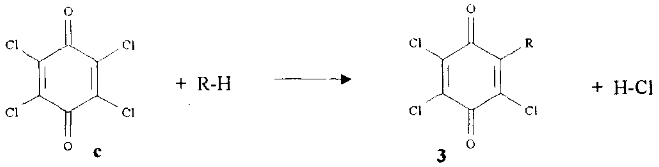
(2)



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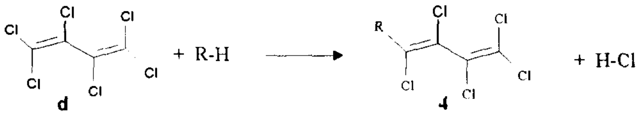
(3)



d 4

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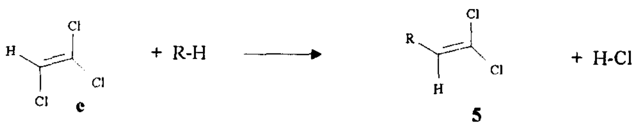
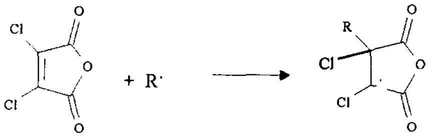


(5)

RH = Cyclohexane (**A**), 2,3-dimethylbutane (**B**), toluene (**C**), cyclohexene (**D**), dioxane (**E**), isopropylacetate (**F**), anisole (**G**)

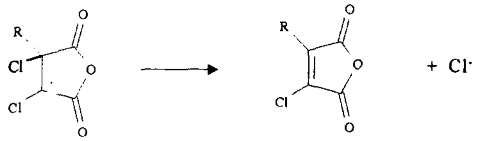
These substitutions appear to be quite unusual in the traditional picture of organic synthesis, also considering that they are carried out under mild conditions. However, the results are well rationalized if we consider the reactivity of the involved elementary steps:

i) the high reactivity of nucleophilic carbon-centered radicals towards electron-deficient unsaturated compounds (alkenes[1,2], quinones[1,3], heteroaromatic bases[1,4]); rate constants in the range 10^4 - 10^8 M^{-1} s^{-1} have been evaluated[1-4] for these reactions (i.e. reaction 6)



(6)

ii) The high rate of fragmentation of β-chloroalkyl radicals ($>10^6$ s^{-1})[5] (eq.7)



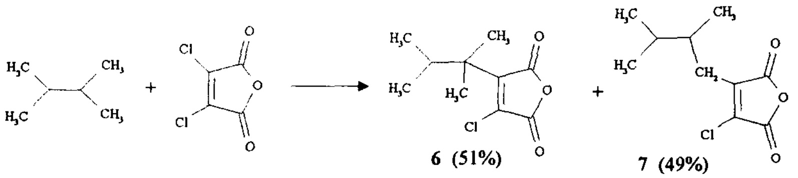
(7)

iii) the high rate of hydrogen abstraction from C-H bonds by chlorine atom ($>10^8$ M^{-1} s^{-1}) (eq.8)

$$R\text{-}H + Cl^{\cdot} \longrightarrow R^{\cdot} + HCl \qquad (8)$$

Eqs. 6, 7 and 8 are the elementary steps of the free-radical chains. Thus a free-radical initiator, also at low temperature, is sufficient to initiate the radical chains and to achieve conversions of synthetic interest. The conversions reported in the Table can be increased by increasing the amount of the initiator. We have utilized benzoyl peroxide at 80°C, t-butylperbenzoate at 110°C and t-butyl peroxalate at 40°C as initiators.

The main limitation of these new chain processes is related to the low regio- and chemoselectivity of the chlorine atom reactions. The regioselectivity is obviously irrelevant with reagents characterized by only one kind of reactive C-H bond (cyclohexane, dioxane, toluene, anisole, etc.). When both tertiary and primary C-H bonds are present, the selectivity is rather low: with 2,3-dimethylbutane and dichloromaleic anhydride the two substitution products **6** and **7** were obtained in almost equal amounts (eq.9)



(9)

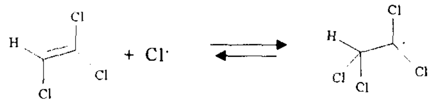
The reactivity of the C^3-H bond appears to be about 6 times higher than that of the C^1-H bond, considering the statistical correction. We have taken advantage of one of the few macroscopic solvent effects in free-radical reactions to increase the selectivity of reaction (9). Thus, carrying out reaction (9) in benzene solution, **7** and **6** were obtained respectively in 86% and 14% yield: that is, the C^3-H bond results 37 times more reactive than the C^1-H bond, in agreement with the Russell[6] solvent effect in the chlorination of alkanes. To obtain a good chemoselectivity it is important to use an excess of alkane, alkene ether or ester in order to prevent further attack of chlorine atoms to the reaction products.

By using 1,1,2-trichloroethylene as solvent in the presence of cyclohexane, the chlorine atom, in addition to hydrogen abstraction from cyclohexane (eq.8), adds to the double bond (eq.10), leading to hexachlorobutene **8** according to eq.11, in a chain process

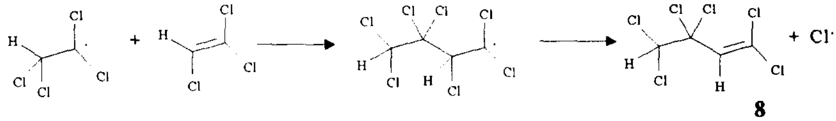
Table. Homolytic substitution of Vinyl and Aryl Chlorides[1]

Chloride	RH	T°C	Reaction time	Conv. (%)[2]	Reaction Products	Yields (%)[3]
a	A	80	3	100	**1**	72
a	B	40	5	20	**6** (51%), **7** (49%)	81
a[4]	B	40	5	15	**6** (86%), **7** (14%)	89
a	C	110	2	80	**1**	60
a[4]	D	40	5	57	**9** (34%), **10** (66%)	71
a[4]	E	80	3	79	**1**	45
a	F	80	2	66	R = $MeCOCH(Me)CH_2$- (16%) R = $MeCOC(Me)_2CH_2$- (84%)	52
a[4]	G	80	5	50	**1**	43
b	A	80	24	23	**2**	74
c[4]	A	80	24	40	**3**	66
c	C	110	24	37	**3**	71
c[4]	D	80	24	33	**11** (47%), **12** (53%)	62
d	A	80	24	26	**4**	78
e[5]	A	80	3	15	**5**	35

1) 10 mmol of chloride, 1 mmol of initiator (t-butyl peroxalate at 40°C, benzoyl peroxide at 80°C or t-butyl perbenzoate at 110°C), 10 mmol of $CaCO_3$ in 20 mL of R-H were heated for the time reported in the Table. The reaction products were analyzed by GLC-MS and NMR; 2) based on the chloride; 3) based on the converted chloride; 4) 10 mL of benzene and 5 mL of R-H were utilized as solvent; 5) trichloroethylene (10 mL) (**e**) and cyclohexane (5 mL) have been utilized both in large excess, with only 0.2 g of benzoylperoxide as initiator; hexachlorobutene **8** was formed in 44% yield (based on reacted **e**); in the absence of cyclohexane, **8** was obtained in 78% yields.



(10)



(11)

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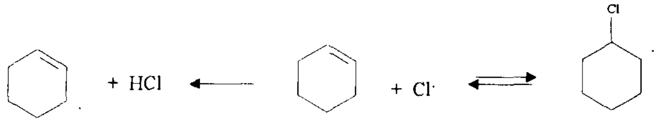
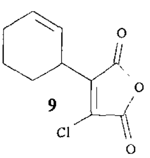
The behaviour of simple alkenes with dichloromaleic anhydride (**a**) or with chloranil (**c**) is similar for some aspects: chlorine atom can abstract hydrogen atoms (mainly from allylic C-H) or add to the unsaturated bond (eq.12)



(12)

Both intermediate radicals substitute the vinylic chlorine atom, giving derivative **9**, two isomers (1:4 ratio) of **10**, **11** and two isomers (1:3 ratio) of **12**.



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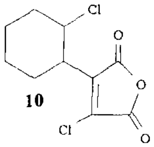

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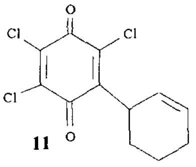

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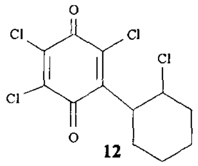

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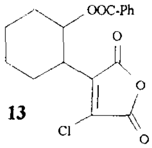
These results suggest that the addition of β-chloroalkyl radicals to **a** and **e** must be rather fast, considering their high rate of fragmentation ($>10^6$ s^{-1})[5].

By using benzoyl peroxide as the initiator, compound **13** is formed as by-product, generated by the addition of benzoyloxy radical to the double bond[7] and further substitution of the vinyl chloride.



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