ELECTROCHEMICAL CROSS-COUPLING OF ORGANIC HALIDES : TRICHLOROMETHYLATION AND RELATED SYNTHESIS OF GEM-DICHLORO COMPOUNDS

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Abstract : The cross-coupling of activated alkyl halides with carbon tetrachloride or substituted trichloromethanes can be obtained electrochemically in good yield in an undivided cell with a sacrificial anode.

Direct trihalomethylation (eq 1, R'=X=halogen) and related reactions (eq 1, R'=X)

$$R-X + R'CX_3 \longrightarrow R-CX_2 - R' + 2X$$
 (1)

are of constant current interest¹ because of the potential synthetic as well as biological value of the product. Of pertaining importance today are the trifluoromethyl bearing compounds². No general way for direct trichloromethylation has been described so far; all the known methods are of restricted applicability for i) α -chloromethyl anions are very unstable and rapidly give carbenes³; ii) the corresponding organometallic species with Mg or Li are not easy to prepare and decompose above - 65° C and -73° C respectively ^{4,5}.

We have already reported⁶ that the electroreduction of CCl₄ at room temperature in presence of a sacrificial anode gives CCl_3 which efficiently adds to carbonyl bonds of aldehydes and ketones.

This note, whose content has been patented⁷, describes the use of this very simple procedure to the trichlomethylation of alkyl halides (eq 1, X = Cl, Br ; R' = Cl). Similarly gem-dichlorocompounds were obtained by electrochemical cross-coupling of alkyl halides and substituted trichloromethanes (eq 1, X = Cl, Br ; R' = C₆H₅, CH₃, CO₂CH₃).

The electrolyses were conducted in an undivided cell with a sacrificial anode of zinc (R' = Cl, C₆H₅, CO₂CH₃) or magnesium (R' = CH₃, CF₃) and a cathode of stainless steel. The reported runs (table 1) have been performed at room temperature under argon in a 1:1 mixture of tetramethyl urea (TMU) - tetrahydrofurane (THF) as solvent, at constant current, with an ammonium salt as supporting electrolyte⁸.

The nature of the metal used as anode was chosen according to the reduction potential of $R'CC1_3$. Zinc is preferably used, when compatible, to prevent further reduction of the product. THF-TMU mixture was found to be the solvent of choice as we noted that yields were identical with hexamethyl- phosphoramide (HMPA) in place of TMU, and lower in N,N-dimethyl-formamide or in N-methylpyrrolidone.

The reaction can be schematically described as follows :

$$M \longrightarrow M^{n+} + ne$$
 (2)

at the cathode :

at the anode :

$$R'CC1_3 + 2e \longrightarrow R'CC1_2 + C1^{-1}$$
(3)

 $R'CC1_2^- + RX \longrightarrow RCC1_2R' + X^-$ (4)

The efficiency of the process is clearly related to the presence of the ions M^{n+} produced by oxidation of the anode (eq 2) for very few amounts of cross-coupling product were formed in a diaphragm cell in the absence of metallic ions, though details of the mechanism are not well understood so far.

! ! entry !	! ! R'CC1 ₃ ! (40 mmol) !	PX RX (20 mmo1)	l l anode l	RCC1 ₂ R [']	i yield ^b %	! ! ! other product !	yield ^b %
1	cc14	PhCH ₂ Br	Zn	PhCH ₂ CC1 ₃	70	! ! !	·
2	CC14	CH3CHC10C02Et	l "	CH3CH(CC13)0C02Et	60	1	
l 3	cc14	BrCH ₂ CO ₂ Me	! • !	CT3CCH2C02Ne	30	C1 ₂ C=CHC0 ₂ Me	45
4	1 cc14	CH ₃ (CH ₂) ₈ CH ₂ Br		CH3(CH2)8CH2CC13	40		
5	PhCC13	PhCH ₂ Br	! . !	PhCH2CC12Ph	65		
6	PhCC13	CH2=CHCH2Br	! •	CH2=CHCH2CC12Ph	10	PhCC1=CHCH=CH2	55
7	PhCC13	BrCH ₂ CO ₂ Me		PhCCT2CH2CO2Me	66	PhCC1=CHC02Me	10
8	CC13C02Me	PhCH ₂ Br	•	PhCH ₂ CC1 ₂ CO ₂ Me	65		
9	CF3CC13	PhCH ₂ Br	Mg	PhCH2CC12CF3	32	1	!
10	сн _з сст _з	CH3CHC10C02Et		CH3CH(CC12CH3)0C02Et	50		

Table 1. Electrochemical cross-coupling of organic halides^a.

^aAll new products gave satisfactory elemental analysis.

^bIsolated yield relative to RX.

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- 8. Typical procedure : In a cylindrical undivided cell of 40 ml, fitted with a Zn-rod as anode and a stainless steel grid as cathode, are introduced 35 ml of a 1:1 THF-TMU mixture as solvent,NBu₄BF₄ (0.17 g, 0.5 mmol) and NBu₄I (0.18 g, 0.5 mmol) as supporting electrolyte, CCl₄ (4 ml, 40 mmol) and PhCH₂Br (2.4 ml, 20 mmol). Three mol electron are passed per mol PhCH₂Br at constant current with density of 2 A/dm², under argon, at room temperature. Work-up followed by flash silica gel column chromatography gives 2,2,2-trichloroethylbenzene in 70 % yield.

(Received in France 14 January 1988)