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ELECTROCHEMICALLY INDUCED $S_{RN}1$ AROMATIC NUCLEOPHILIC SUBSTITUTION. MONOANIONS OF β -DICARBONYL AND β -CYANOCARBONYL COMPOUNDS AS NUCLEOPHILES.

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Summary: *Monoanions deriving from β-dicarbonyl or β-cyanocarbonyl compounds can be used as nucleophiles in electrochemically induced $S_{RN}1$ aromatic nucleophilic substitution with different substrates including cyano or benzoyl substituted aromatic halides and 2 - chloroquinoline.*

Electrochemical inducement, at the potential of the first wave of ArX , of $S_{RN}1$ [1] aromatic nucleophilic substitution of aryl or heteroaryl halides is based on the following reaction scheme :

$$
\begin{array}{lrcl}
(1) & \mathrm{ArX} + 1e & \rightleftharpoons & \mathrm{ArX}^{\bullet -} \\
(2) & \mathrm{ArX}^{\bullet -} & \rightarrow & \mathrm{Ar}^{\bullet} + \mathrm{X}^{-} \\
(3) & \mathrm{Ar}^{\bullet} + \mathrm{Nu}^{-} & \rightarrow & \mathrm{ArNu}^{\bullet -} \\
(4) & \mathrm{ArNu}^{\bullet -} - 1e & \rightleftharpoons & \mathrm{ArNu} \\
(5)\ \text{or} & \mathrm{ArNu}^{\bullet -} + \mathrm{ArX} & \rightleftharpoons & \mathrm{ArNu} + \mathrm{ArX}^{\bullet -} \\
\hline
(6) & \mathrm{ArX} + \mathrm{Nu}^{-} & \rightarrow & \mathrm{ArNu} + \mathrm{X}^{-}
\end{array}
$$

As can be seen from the overall equation (6) no electrons are consumed when this mechanism is operative. Various nucleophiles can be used in these reactions [2,3] but monoanions of β-dicarbonyl compounds were reported not to react under photostimulation with phenyl [4] or quinolyl [5] radicals, although the 1,3 -dianions of β -diketones reacted quite well through the terminal carbanion site [4,6]. Later on Beugelmans and coll. described the photostimulated reactions of monoanions of β-dicarbonyl compounds with cyano-substituted aryl compounds [7].

We have found that the reaction of β-dicarbonyl and β-cyanocarbonyl anions with aryl halides can be induced electrochemically, that cyclic voltammetry ofers an easy prediction of the reactivity and that the reaction of these nucleophiles is not restricted to cyanoaryl radicals.

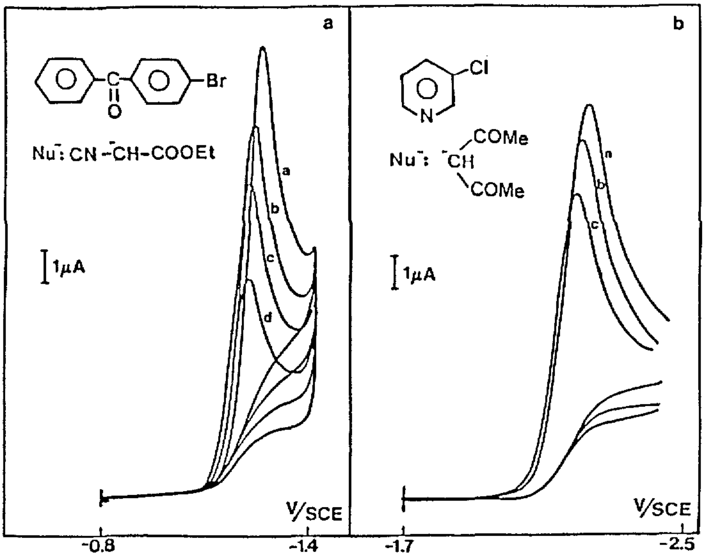


Figure A. a) [4-bromobenzophenonc] = 3.4.10 $^{-3}$ M, NBu$_4$ BF$_4$ 0.1 M in DMSO : [Nu$^-$] = 0 ; b) [Nu$^-$] : 2.8 10^{-2} M, c) [Nu$^-$] : 5.2 10^{-2} M, d) [Nu$^-$] = 0.10 M . B - a) [3-chloropyridine] = 2.1 10^{-3}M, NEt$_4$ClO$_4$ 0.1,M in DMSO, [Nu$^-$] = 0 ; b) [Nu$^-$] = 2.5 10^{-2}M ; c) [Nu$^-$] = 5.0 10^{-2}M Scan rate : 0.2 Vs^{-1}

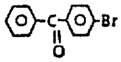
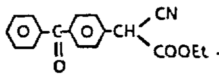
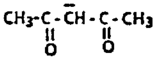
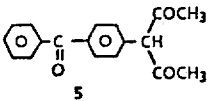
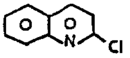
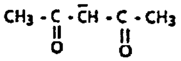
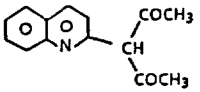
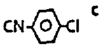
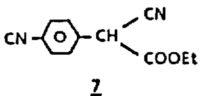
Expt	Substrate	Nucleophile	Solvent	Substituted product	Yield	F/Mole
1	 1 C = 3.85 10^{-2} M	CN-$\bar{C}$H-COOEt 1 M	DMF 100 ml	 4	80% a	0,57
2			DMSO 100 ml		94 % a	0,36
3		 $CH_3-\underset{O}{\overset{\parallel}{C}}-\bar{C}H-\underset{O}{\overset{\parallel}{C}}-CH_3$ 0.5 M	DMSO 50 ml	 5	51 % b	0,84
4	 2 C = 9.23 10^{-2} M	 $CH_3-\underset{O}{\overset{\parallel}{C}}-\bar{C}H-\underset{O}{\overset{\parallel}{C}}-CH_3$ 0.5 M	DMSO 50 ml	 6	12 % b	1.9
5	 c 3 C = 8.5 10^{-2} M	CN-$\bar{C}$H-COOEt 0.24 M	liq NH$_3$ 80 ml	 7	48 % a	1.2

Table. Preparative electrolyses

a) determined by HPLC b) recrystallized yield c) in the presence of a mediator : 4,4'-bipyridine c = 2.5 10^{-2} M

Occurence of the reaction can be tested by cyclic voltammetry : since in the electrocatalysis process no electrons are consumed, the height of the cyclic voltammetry peak of the substrate should decrease upon addition of the nucleophile[2]. This peak of the substrate eventually disappears when the electrocatalytic process prevails over the aryl radical consuming side reaction (electron and H-atom transfer[2]). This is clearly observed on the Figure in the case of 4-bromobenzophenone and tetrametylammonium ethylcyanoacetate and in the case of 3-chloropyridine and teramethylammonium acetylacetonate. The results of preparative electrolyses carried out at the potential of the first wave of the substrate are reported in the table. Electrons were transferred either directly by the electrode (expts 1-4) or through a mediator which shuttles the electrons from the electrode to the substrate in solution (redox catalysis) [2,8] . The last column shows that the consumption of electrons is always lower than the 2 F/mole required for the reduction of the aromatic halide and that the better the yield of substituted product, the lower the number of Faraday consumed. The remaining product, besides some unelectrolyzed starting material, is the dehalogenated substrate obtained by hydrogen atom transfer to the aromatic radical or through further reduction and protonation (for example in experiment 3 the yield of benzophenone was 32% and 1% of 4-bromobenzophenone remained unelectrolyzed). These side reactions are responsible for the observed consumption of electricity.

These experiments show that monoanions of β-dicarbonyl compounds are reasonably good nucleophiles, they can react under electrochemically induced $S_{RN}1$ conditions not only with strongly activated substrates as 4-chlorobenzonitrile but even with much less reactive substrates such as 2-chloroquinoline.

Electrochemically induced $S_{RN}1$ reaction offers a new route to the arylation of β-dicarbonyl compounds[7] in addition to already known methods : Ulman reaction [9,10] catalysis by nickel or palladium [11] , SnAr [12] or aryne substitution [13], reaction via cyclopentadienyliron complexes [14] .

Experimental

The electrochemical procedures for cyclic voltammetry and electrolysis have already been described [2a, 2b] . The solutions were analysed by HPLC on a 15 cm, 5 μ , C18 column eluted with CH_2Cl_2-heptane mixtures.

Ethyl [4-benzoyl phenyl] cyanoacetate **4**[15]. The 100ml of electrolyzed solution are poured into 250ml HCl 6N and extracted with methylene chloride. The organic layer is washed with water , dried and evaporated. The residual oil is chromatographed on a silica column (CH_2Cl_2 75, Heptane 25) to give a bright yellow oil . NMR ($CDCl_3$, TMS) : δ = 1,30 (t,3H), δ =4,30 (q, 2H), δ = 4,82 (s,1H), δ= 7,2-8 (m,9H). Mass m/e : 293 (19), 249 (7.5), 221 (87,5), 192 (37.5), 144 (85), 105 (93), 77(100). IR (neat) 2233,1747,1610,1505 cm^{-1}.

3-(4-Benzoyl phenyl)- 2,4-pentanedione **5** . Beige crystals m.p 131°C (methanol) ,NMR ($CDCl_3$, TMS) : δ = 1.93 (s, 6H), δ= 7,2-8 (m, 9H). Mass m/e : 280(100), 265 (72), 238 (20) , 220(11), 149 (21),, 105 (93), 77(55). IR (Nujol) 1662, 1655, 1610, 1600, 1470 cm^{-1} .

3(2-Quinolyl)- 2,4-pentanedione 6 . Yellow crystals m.p. 160° C (dec) (ether pentane) NMR;($CDCl_3$,TMS) $\delta=2.07$(m,6H), $\delta=6-8.8$ (m,6H), Mass (C.I., NH_3) : 228(M+H+), IR (Nujol) 1675, 1605 cm^{-1}.

Ethyl (4-cyanophenyl) cyanoacetate 7. The liquid ammonia solution is neutralized with ammonium chloride and evaporated, the remaining solid is taken up with CH_2Cl_2. The concentrated organic layer is chromatographed on silica (CH_2Cl_2 90, MeOH 10) to give a colourless oil, NMR ($CDDCl_3$, TMS) : δ = 1.20 (t, 3H), δ = 4,25 (d, 2H), δ = 4,85 (s,1H), δ = 7,5-7,9 (m,4H). Mass m/e : 215 (7), 170 (6), 143(35), 142(100), 97(35) . IR (neat) : 2254, 2233,1751, 1747, 1610, 1505 cm^{-1}.

References

1- J.F. Bunnett, Acc. Chem. Res. 11, 413 (1978).

2- a) J. Pinson and J.M. Savéant, J. Am. Chem. Soc. **100**, 1506 (1978) b) C. Amatore, J. Chaussard, J. Pinson, J.M. Savéant and A. Thiébault, J. Am. Chem. Soc. **101**, 6012 (1979). c) J.M. Savéant, Acc. Chem. Res. **13**, 323, (1980). d) C. Amatore, M.A. Oturan, J. Pinson, J.M. Savéant and A. Thiébault, J. Am. Chem. Soc. **106**, 6318 (1984). e) C. Amatore, M.A. Oturan, J. Pinson, J.M. Savéant and A. Thiébault, J. Am. Chem. Soc. **107**, 3451 (1985). f) N. Alam, C. Amatore, C. Combellas, J. Pinson, J.M. Savéant, A. Thiébault and J.N. Verpeaux, J. Org. Chem. **53**, 1496, (1988).

3-R.A Rossi and R.H. Rossi, Aromatic Substitution by the $S_{RN}1$ mechanism, ACS Monograph 178, Am. Chem. Soc. (1983).

4- J.F. Bunnett and J.C. Sundberg, J. Org. Chem. 41, 1702 (1976).

5- J. Hay and J.F. Wolfe, J. Am. Chem. Soc. **97**, 3702 (1975).

6- J.F. Wolfe, J.C. Greene and T. Hudlicky, J. Org. Chem. **37**, 3199 (1972).

7- R. Beugelmans, M. Bois Choussy and B. Boudet, Tetrahedron, **38**, 3479 (1982).

8- J.E. Swartz and T.E. Stenzel, J. Am. Chem. Soc. **106**, 2520 (1984).

9- A. Bruggink and A. McKillop, Tetrahedron, **31**, 2607 (1975).

10- K. Seto, S. Takahashi and T. Tahara, J. Chem. Soc. Chem. Comm. 122, (1985).

11- a) A.A. Millard and M.W. Rathke, J. Am. Chem. Soc., **99**, 4833 (1977).
b) J.F. Fauvarque and A. Jutand, J. Organomet. Chem. **177**, 273 (1979)

12- J. Bourdais and C. Germain, Tetrahedron Letters, 195, (1970).

13- W.W. Leake and R. Levine, J. Am. Chem. Chem. Soc., **81**, 1627, (1959).

14- A.S. Abd El Aziz, C.C. Lee, A. Piorko and R.G. Sutherland, Synthetic Communications, ,**18**, 291, (1988).

15- Obtained as a sodium salt : D. Farge, C. Jeanmart, N.M. Messer, C. Moutonnier, (Société des Usines Chimiques Rhône-Poulenc), Patent Fr 1,516, 775.

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