ELECTROGENERATED ACID CATALYZED ACYLATION OF ELECTRON-RICH AROMATICS

Norberto Gatti Istituto G.Donegani S.p.a., v. Fauser 4, I-28100 Novara, Italy

<u>Summary</u>: The acylation of electron-rich aromatic compounds was achieved in good yields under very mild conditions using an electrogenerated acid catalyst. $M(ClO_4)_m$ dissolved in an organic anhydride (optionally mixed with a polar aprotic solvent) is useful for the electrochemical transformation in a divided cell.

The most important method for the preparation of aryl ketones is Friedel-Craft acylation^[1]. Usually in this reaction more then one mole of catalyst is required per mole of acylating agent, except for very active substrates where small amount of catalyst are sufficient to carry out the reaction at high temperature^[2]: among catalysts the most common are zinc chloride, iodine and ferric chloride. Mineral acids has also been used in special cases to promote Friedel-Craft reactions^[3]. The acid generated in the proximity of the anode surface during electrolysis was recently recognized as a powerful method for chemical tranformations^[4]. Electrochemistry can provide a methodology to produce a catalytic amount of a particularly reactive acid under very mild conditions.

Here we present the first example of electrogenerated acid (EGA) catalyzed reaction in an organic anhydride giving, under very mild conditions, an electrophilic substitution by the acyl group on an activated aromatic compounds. The acylation of methoxy-substituted aromatic derivatives catalyzed by electrogenerated acids can be achieved at room temperature using the organic anhydride as reaction solvent. With acetic anhydride the acetylicion gave from acceptable to excellent yields (32-95%) in 2-4 hours, with g od selectivities.

In a typical experiment $iClO_4$ (1,5 mmol) was dissolved in a mixture of CH_2Cl_2 (75 ml) and the appropriate anhydride (25 ml)^[5], then the solution was placed in the compartments of a divided cell. The substrate (10 mmol) was dissolved in the anodic compartment and electrolyzed at a platinum anode under constant current until a very small amount of electricity was passed (0.003-0.03 F/mole). After 2-4 hours of stirring at room temperature the product was recovered in good yields.

The following features characterize this reaction: (1) without electrolysis no product was detected and the substrate was recovered unchanged; (2) during the electrolysis dark gray lithium metal was deposited on the cathode; (3) similar results were achieved using a pre-electrolyzed solution^[6]; (4) when the reaction was performed in an undivided cell very little amount of product was recovered even if high quantities of electricity were supplied (0.1 F/mol, 8 hours, yield 12%); (5) the effect of the supporting electrolyte does not depend from the cation of the perchlorate: lithium, magnesium and tetraethyl ammonium salts gave similar results, while no reaction occurred when lithium or tetrabutyl ammonium fluoborate has been used as supporting electrolyte.

The analysis of these experimental results suggests that the reaction was catalyzed by an electrogenerated acid that promoted the production, from the organic anhydride, of the acyl cation ($RC=O^+$), intermediate of the acylation reaction^[7].

The results of the electrochemical acylation are summarized in Table 1. β -alkoxynaphthalenes gave selective acetylation in the α position in very high yields (95%). This reaction is sensitive to the reactivity or bulk of the anhydride: thus when 2-methoxynaphthalene was reacted with propionic and pivalic anhydride, the products were always acylated in position 1 but with decreasing yields. With the use of acetonitrile as reaction solvent, the yield of the acetylation was much lower (30%). 1-Methoxynaphthalene was selectively acetylated to the extent of 90% in position 4.

The procedure has been applied to methoxybenzenes (entries 7-10). Anisole gave an acceptable yield (56%) of p-methoxyacetophenone with the ortho isomer as a minor by-product (para/ortho ratio = 21). More interesting is the comparison of the reactivity of the three isomers of dimethoxybenzene. Among them, veratrole (the ortho isomer) exibits the highest reactivity giving 4-acetyl-1,2-dimethoxybenzene in 84% yield, with very high selectivity. The reactivity diminished from the ortho to the meta and the para isomer.

Anthracene was also acetylated with this procedure giving predominantly 9-acetylanthracene in 62% yield. No reaction at all was detected when naphthalene, 1-chloro and 2-acetoxynaphthalene were tested, even at 50°C (0.05 F/mol).

n.	Substrate ^a	F/mol	Time (h)	Product	Yield ^b Se (%)	lectivity° (%)
1 2	CC OCH3	0.003 ^d 0.006	2 2	OCH3	83 95(30) ^h	92 98
3		0.006 *	2	OCH2CH3	74 ⁱ	94
4		0.040 ^{f,g}	4	OCH3	22	75
5	OCH3	0.006	2	CH3	90	98
6	OCH ₂ CH ₃	0.006	2	O CH3	H ₃ 95	98
7	OCH ³	0.030	3	OCH2	56	78
8	OCH3 OCH3	0.020	2		84	96
9	OCH3	0.020	2	OCH3 OCH3 OCH3	59	84
10	OCH3	0.030	4		32	79
11		0.020	2		62	88

Table	1:	EGA-catalyzed	acylation	of	electron-rich	aromatics
-------	----	---------------	-----------	----	---------------	-----------

Table's notes: a) LiClO₄ (15 mmol) dissolved in 75 ml of CH₂Cl₂ and 25 ml of acetic anhydride; 10 mmol of substrate were dissolved at room temperature in the anodic compartment of a divided cell and electrolyzed on a platinum anode (S. = 10 cm²) at a current density of 1-2 mA/cm², then stirring for 2-4 hours. b) Yields (based on starting material) were determined by g.l.c. using n-tetradecane as internal standard. c) based on reacted substrate. d) solvent: 100 ml of acetic anhydride. e) propionic anhydride as the acylating agent. f) pivalic anhydride as the acylating agent. g) 35 °C. h) solvent: CH₃CN/acetic anhydride (75/25). i) 1-(2methoxynaphtyl)-2-methyl-pentan-1,3-dione as the main by-product.

These results show a promising possibility in the acylation of activated aromatic derivatives under very mild conditions and constitute a new interesting development in the field of electrogenerated acidcatalyzed synthesis.

REFERENCES AND NOTES

- G.Olah, <u>"Friedel-Crafts and related reactions"</u>, vol. 1 p. 91, Interscience, New York(1963)
- (2) D.E.Pearson, C.A.Buehler, <u>Synthesis</u> 533 (1972)
- (3) in Ref. (1) see Vol.3, P.H.Gore, p.11
- (4) K.Uneyama, in <u>Topics of Current Chemistry</u>, Vol. 142, p. 167, Springer Verlag, Berlin Heidelberg (1987)
- (5) The solvents were used as received without further purification.
- (6) 2-Methoxynaphtalene (10 mmol) was allowed to react with the anodic solution for two hours at room temperature.
- (7) a) J.March, in <u>"Advanced Organic Chemistry"</u>, III ed. p.487, Wiley Interscience. b) H.Burton, P.F.G.Praill, <u>J.Chem.Soc.</u> 1203 (1950)

(Received in UK 17 May 1990)

3936