Studies on Electrolytic Substitution Reactions. XVII.* Selective Nuclear Acetoxylation of Alkylaromatic Compounds

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Anodic nuclear monoacetoxylation of alkylaromatics (p-xylene, isodurene, mesitylene, durene) can be achieved with high selectivity with respect to the side-chain acetate by carrying out the electrolysis in the presence of Pd on carbon in a nondivided cell. This arrangement utilizes cathodically generated hydrogen to effect cleavage of the benzylic acetate as it is formed, thus continuously regenerating the substrate. The nuclear acetate which is resistant toward hydrogenolysis accumulates in the reaction mixture.

It has long been known[1,2] that nuclear anodic acetoxylation of aromatic compounds takes place only in the presence of acetate ion in the electrolyte. While it is then relatively simple to achieve complete selectivity for side-chain (α) acetoxylation of alkylaromatics by using a supporting electrolyte with a non-nucleophilic anion,[3] it is not possible to direct acetoxylation exclusively to ring positions even in the presence of high acetate ion concentrations. In connection with a study on the anodic oxidation of isodurene[4] we found a simple way to increase the nuclear/α isomer ratio drastically, namely to have Pd/C catalyst present in the electrolyte solution during the run (non-divided cell). The cathodically generated hydrogen is then used to regenerate substrate from any benzylic acetate formed, resulting in an enrichment of the nuclear isomer. We now report a study on the scope and limitations of this approach to achieve more selective electrochemical processes.

RESULTS

Small scale experiments

p-Xylene. The effects of a few variables were studied for this substrate because of the simplicity of the system: Only two monoacetoxy derivatives are possible, one derived from nuclear and one from side-chain attack. The effect of substrate concentration (exp. 1–3), anodic current density (exps. 1, 4, 5), temperature (exps. 2, 6, 7), amount of catalyst (exps. 2, 8, 9), cathodic to anodic area ratio (exps. 4, 10) and charge passed per mol of substrate (exps. 4, 11–13) is reported in Table 1. A comparative experiment (exp. 14), run approximately under the same conditions as exp. 4, albeit in the absence of catalyst, it also reported in Table 1. From these data it is apparent that in all experiments with catalyst present the X_N value [= 100 × (nuclear acetate yield) /(total yield of monoacetates)] increases significantly and so does the material yield based on the reacted amount of substrate, except at high temperature (exp. 7).

It can be seen by comparison of exps. 4 and 14 that adding 10 % of catalyst to the cell contents almost completely eliminates the formation of p-methylbenzyl acetate, bringing the material yield based on reacted p-xylene of 2,5-dimethylphenyl acetate from 30 to 75 % and the X_N value from 40 to 98 %. Current yields do not improve much, which shows that the two isomeric acetates are formed at the anode in the same ratio both in the presence and in the absence of catalyst, in keeping with the proposed hydrogenolysis mechanism (eqn. 1). It is
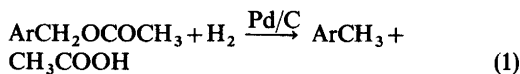
$$ArCH_2OCOCH_3 + H_2 \xrightarrow{Pd/C} ArCH_3 + CH_3COOH \qquad (1)$$

Table 1. Nuclear acetoxylation of *p*-xylene in HOAc/KOAc (0.4 M) in the presence of Pd (10 %)/C.

Exp. No.	Mmol of *p*-xylene	Catalyst/mg mmol^{-1} (*p*-xylene)	Current density/ mA cm^{-2} Anodic	Cathodic	Temp./°C	Charge passed/ F mol^{-1}	Yield/%^{a} Current	Material^c	X_N^b/%
1	2.11	11.4	20	8.5	18	2	19	69	97
2	5.15	10.3	20	8.5	18	2	18	70	98
3	9.46	10.4	20	8.5	18	2	14	68	98
4	1.96	12.2	10	4.3	18	2	19	75	98
5	2.09	10.5	50	21.3	18	2	14	70	98
6	5.16	10.5	20	8.5	50	2	15	61	98
7	5.08	10.8	20	8.5	80	2	7	28	63
8	4.97	4.4	20	8.5	18	2	18	67	93
9	5.09	2.0	20	8.5	18	2	18	49	69
10	2.21	10.8	10	42.5	18	2	19	78	98
11	2.09	12.0	10	4.3	18	4	15	68	97
12	2.06	11.2	10	4.3	18	6	12	62	92
13	2.04	11.3	10	4.3	18	8	9.5	56	86
14	2.02	0	10	4.3	18	2	16	30	40

^{a} 2,5-Dimethylphenyl acetate. ^{b} 100 × (yield of 2,5-dimethylphenyl acetate)/(total yield of monoacetates). ^{c} Based on unrecovered *p*-xylene.

worthwhile noting that reaction (1) is exactly the reverse of the overall cell reaction for the benzylic acetate formation, and therefore only species already present in solution are generated, *i.e.* acetic acid and the hydrocarbon.

To take advantage of the regeneration of the substrate, it is conceivable to run the electrolyses beyond the theoretical value of 2 F mol^{-1}. This is shown by exps. 11 – 13. Of course these experiments show low current yields, in agreement with the above reasoning.

Isodurene, mesitylene, and durene. The conditions established in exp. 11 of Table 1 were then applied to isodurene, mesitylene and durene (see Table 2).

To take account of the widely differing initial nuclear/α isomer ratios the amount of catalyst or its Pd content was adjusted in each case (small amount for mesitylene, larger for isodurene and durene). Again in we see that runs performed in the presence of Pd/C result in significantly increased X_N values. Even durene, which normally is a limiting case of almost exclusive benzylic substitution, can be converted to a product mixture containing 92 % of the nuclear acetate by this method. Again this result is brought about at the expense of a low current yield which is an inherent disadvantage of the method.

Table 2. Nuclear acetoxylation of isodurene, mesitylene and durene in HOAc/KAc (0.4 M) in the presence of Pd (10 %)/C (for isodurene and durene) or Pd (5 %)/C (for mesitylene).

Substrate (Exp. no.)	Substrate/ mmol	Catalyst/mg mmol of substrate	Yield/%^{a} Current	Material^c	X_N^b/%
Isodurene (15)	2.13	0	15	17	22
Isodurene (16)	2.00	26.3	22	71	91
Mesitylene (17)	1.92	0	35	61	93
Mesitylene (18)	1.98	12.6	40	79	100
Durene (19)	4.06	0	4.8	5.6	7
Durene (20)	4.07	39.8	6.5	45	· 92

^{a} Nuclear acetate. ^{b} 100 × (yield of nuclear acetate)/(total yield of monoacetates). ^{c} Based on unrecovered substrate.

Preparative experiments

p-*Xylene and isodurene.* On a scale of *ca.* 0.1 mol, *p*-xylene gave a 51 % yield (based on reacted amount of *p*-xylene) of distilled 2,5-dimethylphenyl acetate, whereas isodurene gave 49 % of distilled 2,3,4,6-tetramethylphenyl acetate. This shows that although the selectivity within the monoacetate fraction has changed to a very high extent, the tendency of nuclear anodic acetoxylation to be accompanied by side-reactions leading to less volatile products has not been influenced.

Concluding, it has been shown that nuclear anodic acetoxylation of alkylaromatics can be achieved with high selectivity if a Pd/C catalyst is added to the electrolyte, thus providing a means of continuously cleaving any benzylic acetate formed by cathodically generated hydrogen. The method is very simple to use on a laboratory scale; on a larger scale we have done preliminary work to show that several possibilities exist to make more efficient use of the catalyst, such as having a fixed bed of catalyst in a flow system, a bed of the catalyst as a three-dimensional cathode, or a catalyst-coated cathode. The method should in principle be applicable to all reaction types where one or several products can revert to starting material by a reasonably fast catalytic hydrogenation reaction.

EXPERIMENTAL

Instrumentation. Small scale electrolyses were carried out using an AMEL Model 552 instrument as a galvanostat. For preparative experiments a Hewlett Packard 6439B power supply was used in the constant current mode.

GLC analyses were performed on a Perkin Elmer 3920 gas chromatograph equipped with a digital integrator and FFAP 3 % on Gaschrom Q 100/120 mesh column (temperature program 70/220 °C at 8 °C min^{-1}).

Efficient agitation (which is essential to obtain the reported results) was provided by powerful magnetic stirrers (AMEL stirrer for small scale experiments and CENCO pyro-mag for preparative ones) and proper selection of the magnetic bar.

Materials. Acetic acid (Carlo Erba RPE or Rudi Pont reag. grade) was crystallized twice before use. Potassium acetate (Carlo Erba RPE) was dried under isodurene) were reagent grade commercial camples used as received. Technical grade isodurene (EGA-Chemie 85 %) was purified by means of a sulfonation-desulfonation method[5] in order to remove durene.[4]

The Pd on carbon catalyst were freshly purchased Engelhard samples. Old samples were found to be less active.

Small scale electrolyses. A 20 ml water jacketed, flat-bottom cell (i.d. 20 mm) was used with magnetic stirring; no cell divider was used. The anode (Ø 8 mm × 40 mm) was a graphite cylinder (Le Carbone Lorraine "Ellor" quality, 8.5 cm^2 area *) held in place at the centre of the cell by means of PTFE spacers crossing it. In order to obtain reproducible and comparable results, a new anode was used for each experiment. This is not however strictly necessary because, although some catalysts stick to graphite pores, used electrodes can be easily cleaned ** and used many times with reasonable reproducibility. The cathode was a bent Pt foil (20 cm^2 area unless otherwise stated).

In a typical experiment with catalyst, weighted amounts of Pd/C and the appropriate substrate were introduced in the cell and 10 ml of supporting electrolyte (0.4 M CH_3COOK in CH_3COOH) was added; the selected constant current was then applied to the stirred slurry. At the end of the experiment, after washing the electrodes with acetic acid, a weighted amount of a suitable compound was added as an internal GLC standard. Isodurene was used as the standard for *p*-xylene and mesitylene electrolyses while hexamethylbenzene was used as the standard for durene and isodurene electrolyses. GLC correction factors were calculated for all substrates, benzylic acetates and nuclear acetates involved using authentic samples, which were also used to check the identity of products by MS. Work-up was performed on a filtered sample by adding water and extracting twice with ether. After washing with saturated $NaHCO_3$ solution and drying with $MgSO_4$ the solution was analyzed by GLC as described above.

Preparative experiments. Various water jacketed 500 ml cells of different internal diameter were used, in combination with various anode sizes and stirring methods, *i.e.*, magnetic and motor stirrers or rotating anode, in general resulting in poorer yields of nuclear acetate and lower X_N values compared to the small scale experiments.

The best results were obtained with a very tall cell (i.d. 46 mm) featuring short reaction times, good agitation (without a vortex) and good cooling by means of tap water.

The anode (140 cm^2 area) was a Ø 20 mm × 225 mm graphite cylinder of the same quality used for small scale experiments and held in place in a similar

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*Geometric area immersed in the solution.

**Ultrasonic cleaning in water and then in acetone is suggested, but simple washing in these media and mechanical cleaning is also satisfactory.

manner.* The cathode was a 316 stainless steel foil (280 cm² area). The electrolyte was typically made up from 390 ml of 0.6 M CH₃COOK in CH₃COOH solution, 10 ml of substrate and catalyst as required. At the current used (1.4 A) the cell voltage was about 17 V and the temperature 17 − 18 °C.

At the end of the electrolysis the contents of the cell (including acetic acid used to wash the cell and the electrodes) were filtered under vacuum. One volume of dichloromethane and one volume of water were added in a 2 l separatory funnel; the aqueous phase was extracted once more with one volume of dichloromethane. The combined organic phases were washed with saturated NaHCO₃ solution, dried over MgSO₄ and filtered under vacuum. After distilling off dichloromethane at atmospheric pressure, the solution was transferred to a micro-distillation apparatus where the product was obtained by distillation at reduced pressure. From p-xylene was isolated 3.4 g (51 %) of pure 2,5-dimethylphenyl acetate at 55 − 56 °C/0.7 mm Hg (recovered unreacted p-xylene 4.3 g: residue of less volatile material 1.8 g) and from isodurene 2.5 g (49 %) of 2,3,4,6-tetramethylphenyl acetate at 95 − 105 °C/ 0.6 mm Hg (recovered unreacted isodurene 5.3 g; residue 1.5 g).

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*New electrodes were used; see footnote under Experimental, Small scale electrolyses.