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Electrophilic components in the electrochemical acetoxylation of substituted arenes

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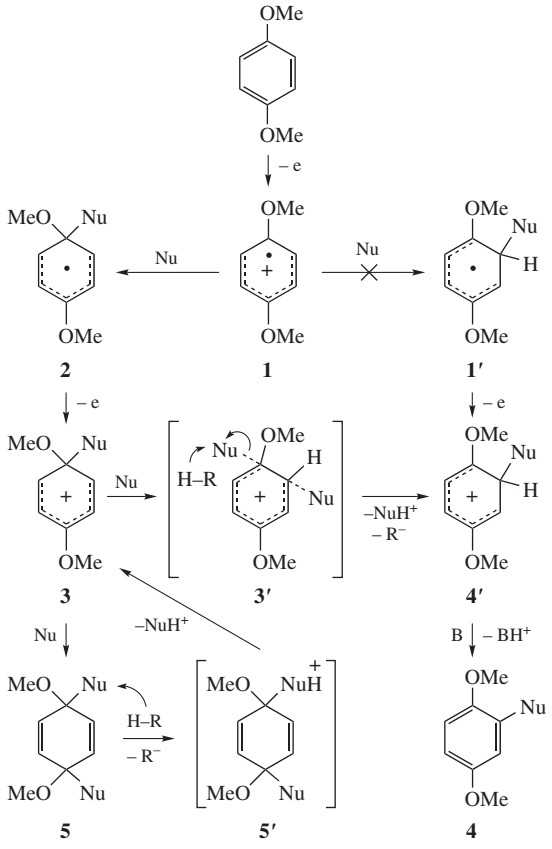
The mechanism of anodic acetoxylation of substituted arenes under conditions of undivided galvanostatic electrolysis in MeCN containing acetate is suggested and an important role of electrophilic components (AcOH or $ZnCl_2$) catalyzing transformation of intermediate *ipso*-acetoxylated polysubstituted arenonium cations to corresponding *ortho*-acetoxylated arenonium cations, which give acetoxylation products after deprotonation, is experimentally proved.

The anodic acetoxylation of 1,4-dimethoxybenzene (DMB) under conditions of undivided galvanostatic electrolysis in MeCN containing an $AcOH/AcO^-$ mixture[1] and a corresponding DMB azolation process[2] proceed (Scheme 1) *via* the *ipso*-attack of radical cation **1** and formation of radical **2**. Then, this radical is oxidized to arenonium cation **3**. The cation, which is a key intermediate of the process, can interact with nucleophiles at both *ortho*- and *ipso*-positions of the aromatic ring leading to corresponding *ortho*-substitution and *ipso*-bisaddition products, **4** and **5**, respectively.†

The N-dimethoxyphenylation of azoles suggests[2] an important role of acidic mixture components. They catalyze the transformation **3** → **4′**, which proceeds *via* a *cine*-substitution mechanism, as well as the transformation **5** → **5′** → **3**, which makes the conversion **3** → **5** reversible. The last stage, in turn, makes possible the continuous transformation of **5** into **4** observed during the electrolysis. However, in the anodic acetoxylation of DMB (in contrast to its azolation), product **5** was not formed and product



Scheme 1

† The ^1H NMR spectra of sample solutions in a $[^2H_6]DMSO–CCl_4$ (1:1, v/v) mixture were recorded on a Bruker AC-300 instrument.

Commercial 1,4-, 1,3-DMB, anisole, $ZnCl_2$, Et_4NOAc, AcOH (98–99% purity, ACROS) and 1,2-DMB (99% purity, Aldrich) were used.

Procedure for the synthesis of 4-methoxyphenyl acetate. A mixture of 9 ml (0.08 mol) of acetic anhydride and 5 g (0.04 mol) of 4-hydroxyanisole was stirred for 5 h at 100–120 °C. After that the excess of anhydride and acetic acid formed were distilled off under vacuum at 50 °C (25–30 Torr) to give 4.5 g (70%) of light gray liquid crystallizing at room temperature. ^1H NMR, δ: 2.24 (s, 3H, OCOMe), 3.78 (s, 3H, MeO), 6.88 (d, 2H, $CH_{arom.}$, J 9.5 Hz), 6.97 (d, 2H, $CH_{arom.}$, J 9.5 Hz). The spectrum corresponds to the published data.[7]

Electrolysis of MeCN/arene/Et_4NOAc/AcOH (or $ZnCl_2$) mixtures. A mixture of 1 mmol of an arene with 1.5 mmol of Et_4NOAc and 1.5 mmol of AcOH or 1.0 mmol of $ZnCl_2$ (did not dissolved completely) was added to 50 ml of MeCN and electrolyzed at a constant current (50 mA) in an undivided cell with Pt electrodes (areas: anode, 37.2 cm^2, cathode, 12.3 cm^2). The supporting electrolyte was Et_4NOAc. After passing 2F of electricity per mole of arene the electrolysis was stopped. Then, the solvent was distilled off on a rotary evaporator at 20–25 °C (25–30 Torr) and the residue was analyzed by ^1H NMR. Yields of electrolysis products were calculated on the basis of two electron conversion of arene *via* comparing integral intensities of well identified singlet protons of the products (OMe and OCOMe protons) and protons of tetraethylammonium cation of the supporting electrolyte (CH_2 and Me groups).

2,5-Dimethoxyphenyl acetate. ^1H NMR, δ: 2.24 (s, 3H, MeCOO), 3.70 and 3.71 (2s, 6H, 2MeO), 6.73 (d, 1H, $CH_{arom.}$, J 2.94 Hz), 6.79 (dd, 1H, $CH_{arom.}$, J_1 2.94 Hz, J_2 9.56 Hz), 7.04 (d, 1H, $CH_{arom.}$, J 9.56 Hz). The spectrum corresponds to the literature data.[1,8]

2,4-Dimethoxyphenyl acetate. ^1H NMR, δ: 2.22 (s, 3H, Me), 3.78, 3.85 (2s, 6H, 2MeO), 6.59 (m, 1H, $CH_{arom.}$), 6.87 (d, 1H, J 8.8 Hz), 7.19 (d, 1H, J 8.8 Hz).

3,4-Dimethoxyphenyl acetate. ^1H NMR, δ: 2.23 (s, 3H, Me), 3.78, 3.79 (2s, 6H, 2MeO), 6.55 (dd, 1H, $CH_{arom.}$, J_1 2.9 Hz, J_2 8.8 Hz), 6.66 (d, 1H, $CH_{arom.}$, J 2.9 Hz), 6.8–6.9 (m, 1H, $CH_{arom.}$).

The spectra of 2,4-dimethoxyphenyl acetate and 3,4-dimethoxyphenyl acetate correspond to the published data.[9]

3-(Acetoxy)-5-methoxyphenyl acetate. ^1H NMR, δ: 2.24, 2.26 (2s, 6H, 2Me), 3.80 (s, 3H, MeO), 6.85 (d, 1H, $CH_{arom.}$, J 2.7 Hz), 6.92–6.99 (m, 1H, $CH_{arom.}$), 7.08 (d, 1H, $CH_{arom.}$, J 8.3 Hz). According to the spectrum a product substituted to *ortho*-position to acetoxy group (not methoxy) is formed.[10]

4 was obtained only when the medium contained AcOH in addition to the AcO^- ion.[1]

It was considered[3] that radical **2** (Nu = AcO^-) is unstable. For this reason, the acetoxylation of DMB in AcOH containing acetate proceeds *via* the stages **1** → **1′** → **4′** → **4** (Scheme 1). However, it is hard to explain from this point of view the influence of AcOH[1] on the effectiveness of acetoxylation. On the other hand, it can be suggested, for example, that intermediate **3** is decomposed faster than its *ipso*-interaction with acetate (but not azolate) ion occurs; therefore, product **5** is not formed (**3** is probably less stable with Nu = AcO^- than with Nu = Az^-). Nevertheless, AcOH, which does not affect the stage of *ipso*-interaction, may assist electrophilically the abstraction of the acetoxy group from intermediate **3′**. As a result, the rearrangement of cation **3** to cation **4′** is catalyzed and its kinetics starts dominating over cation **3** decomposition rate. From this point of view, the acetoxylation mechanism may be described by Scheme 1.

Thus, the suggested acetoxylation mechanism is based on an idea concerning the role of acidic components working as electrophiles and promoting the transformation of cation **3** to cation **4′**. The correctness of this conclusion may be easily confirmed *via* changing AcOH for other electrophiles, for example, Lewis acids. We specially studied the acetoxylation of various substituted arenes in MeCN containing the acetate ion with $ZnCl_2$ additives.

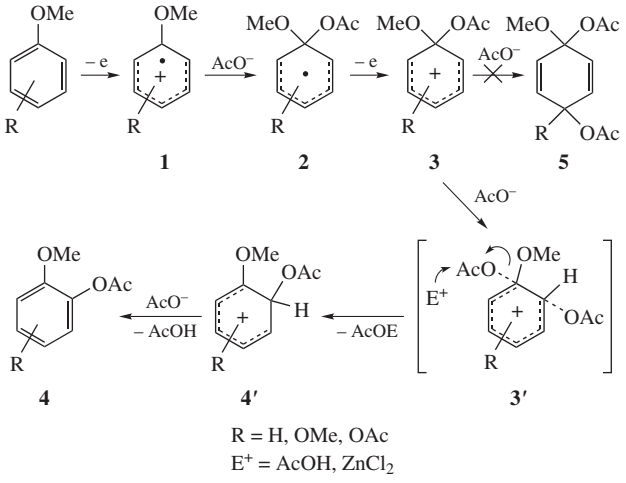
The anodic acetoxylation of substituted arenes leading to *ortho*-substitution products[3,4–6] is usually carried out in AcOH with AcONa additives or in MeCN containing AcOH and its salts (Table 1, runs 1–8). For comparison, the table also contains data on the acetoxylation of the same arenes but in the absence of AcOH, using the MeCN/$ZnCl_2$/Et_4NOAc system (runs 1′–8′).

It is seen in the table (runs 1, 1′, 8, 8′) that the products of DMB acetoxylation did not form in MeCN containing only an acetate salt as a nucleophile. However, the addition of electrophilic species to this system changed the situation dramatically. After the addition of AcOH, DMB acetoxylation product was obtained in 21% yield (run 2) and 4-methoxyphenyl acetate acetoxylation product, in 23% yield (run 7). A change of AcOH for $ZnCl_2$ led to a substantial increase of acetoxylation product yield to 70% in case of DMB (run 2′) and 29% in case of 4-methoxyphenyl acetate. These results are consistent with the instability of corresponding (Nu = AcO^-, Scheme 1) arenonium cations **3** and show that $ZnCl_2$ (taking in account its low concentration in the reaction medium: < 1.0 mol per 1 mol of arene)

Table 1 Yields of *ortho*-acetoxylation products after electrolysis (Pt anode) of arenes in systems containing AcOH salt/AcOH (including data[1,3,6]) or AcOH salt/$ZnCl_2$ mixture.

Run	Arene	Systems containing AcOH salt/AcOH mixture			Run	MeCN containing $ZnCl_2$[a]/Et_4NOAc mixture
		Medium	Nucleophile[b]	Yield[c] (%)		Yield[c] (%)
1	1,4-DMB[1]	MeCN[d]	Et_4NOAc	0	1′	0[d]
2	1,4-DMB[1]	MeCN[e]	Et_4NOAc	21	2′	70
3	1,4-DMB[3]	AcOH	AcONa	68	3′	70
4	1,3-DMB[3]	AcOH	AcONa	3	4′	19
5	1,2-DMB[3]	AcOH	AcONa	9	5′	12
6	Anisole[6]	AcOH	AcONa	27	6′	30
7	4-Methoxyphenyl acetate	MeCN[e]	Et_4NOAc	23	7′	29
8	4-Methoxyphenyl acetate	MeCN[d]	Et_4NOAc	Traces	8′	Traces[d]

[a]Less than 1.0 mol per 1 mol of arene due to low solubility in MeCN. [b]1.5–2.0 mol per 1 mol of arene. [c]On the basis of consumed arene. [d]Without AcOH or $ZnCl_2$ additives. [e]With 1.5 mol AcOH additive per 1 mol of arene.



Scheme 2

is a more effective electrophilic catalyst of the acetoxylation reaction than AcOH.

In general, it follows from the table that, in the anodic acetoxylation of arenes, a change of AcOH for $ZnCl_2$ in all cases leads to an increase of the product yields. These results in conjunction with previous data[1] allow us to describe the mechanism of acetoxylation of arenes using Scheme 2.

The electrophilic components of the medium (E^+ = AcOH, $ZnCl_2$) not only assist the abstraction of the acetoxy group from the *ipso*-position of intermediate **3′** but also make the *ortho*-attack by the AcO^- ion easier due to bond polarization. This makes possible the rearrangement of arenonium cation **3′** into cation **4′**, which undergoes deprotonation leading to final product **4**.

On the other hand, the presence of electrophiles such as AcOH or $ZnCl_2$ does not affect the *ipso*-interaction of cation **3** with the nucleophile (AcO^-). This is the reason why *ipso*-bis-addition products **5** were never observed experimentally (Table 1).

In general, the results allow us to conclude that the anodic acetoxylation of arenes, as well as the anodic N-dimethoxyphenylation of azoles, follows the same mechanism including the formation of arenonium cations **3** as key intermediates (Schemes 1 and 2).

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