Stereochemical Control of Anodic Cyanomethoxylation

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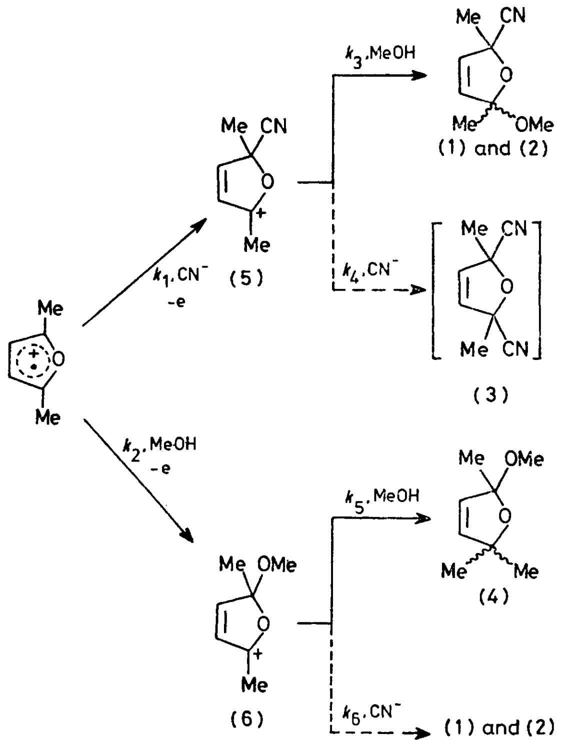
Summary A platinum electrode controls the stereochemistry of the anodic mixed 1,4-addition of cyano- and methoxy-groups to 2,5-dimethylfuran; the isomer ratio of the products varies significantly with the type of aromatic additive as well as the initial concentration of the substrate, the *cis*:*trans* ratio changing from 2·89:1 to 1·46:1.

STUDIES of anodic oxidations in methanolic solutions containing cyanide ion should provide information on the probable location of the reaction of anodically generated cationic species.[1–3] The question as to whether these reactive intermediates are transformed into products while still adsorbed on the electrode or after desorption into solution is still not resolved.[4,5] A study of the stereoisomeric products in anodic 1,4-additions to the furan ring should offer an instructive approach to this problem, because in this reaction the two stereoisomeric products appear to be formed under conditions of kinetic control.[1,3,6] The isomeric products are formed in typical *ECEC* sequences,[1] and the cation radical mechanism in the Scheme readily explains all our previous experimental observations on the reaction. The cation radical of 2,5-dimethylfuran and the cations (**5**) and (**6**) react competitively with CN^- ion and the solvent methanol (or the MeO^- ion as a result of the equilibrium between CN^- and MeO^-). Since the rate constants k_3 = *ca.* k_5 and k_4 = *ca.* k_6 the fact that (**3**) was absent from the product mixture suggests that the cation (**5**) is a key intermediate in forming the isomeric products (**1**) and (**2**).



Scheme

If the cyanomethoxylation proceeded *via* the cationic species (**5**) which was adsorbed a different *cis–trans* isomer ratio in the products would be obtained than would be the case if the ratio of isomers were controlled solely by their relative thermodynamic stabilities; if the final nucleophilic attack occurred in the bulk solution, the observed isomer ratio would be similar to the isomer composition for the homogeneous equilibrium. This communication describes the effect of changing the concentration of the substrate and the influence of aromatic additives on the *cis–trans* isomer ratio of the oxidative addition products and a proposal concerning the probable location where the nucleophilic reaction takes place.

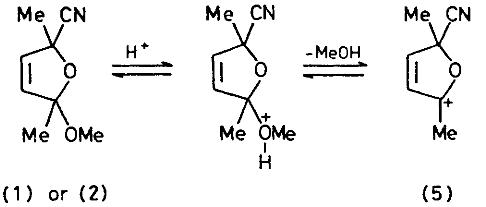
The Table summarizes the results of the anodic cyanomethoxylation of 2,5-dimethylfuran conducted at 25·0 °C. Each isomer ratio reported is the average of two or more runs. Individual isomer ratios were reproducible to 2—3%. The data listed in the Table clearly show that the ratio of the *cis* (**1**) to the *trans* (**2**) isomers of 2-cyano-5-methoxy-2,5-dimethyldihydrofuran decreased with increasing concentration of 2,5-dimethylfuran. Comparative experiments were also carried out in the presence of aromatic molecules. Significantly, 1,4-dimethoxybenzene and pyridine both caused greater changes in the *cis*:*trans* ratio than aromatic hydrocarbons such as t-butylbenzene, naphthalene, or pentamethylbenzene. 2,5-Dimethylfuran itself gave almost the same isomer ratio as was observed in the presence of an equimolar amount of the above-mentioned aromatic hydrocarbons. The dependence observed of the isomer ratio on the concentration of the substrate itself or of additives is characteristic of adsorption processes. It is therefore possible to determine the relative adsorptivity of the aromatic molecules from the change in the ratio of the isomers of the products of anodic cyanomethoxylation of 2,5-dimethylfuran. Our results suggest the following order of adsorptivity of aromatic compounds in methanolic solution: pyridine > anisole ≃ naphthalene > 2,5-dimethylfuran > pentamethylbenzene > t-butylbenzene.

Table. Isomer ratio of the products of cyanomethoxylation of 2,5-dimethylfuran, at a platinum electrode unless otherwise stated, under various conditions.[a]

Conc./M of 2,5-dimethylfuran	Additive	(**1**) : (**2**)
0·01	None	2·89 : 1
0·05	”	2·75 : 1
0·20	”	2·51 : 1
0·40	”	2·39 : 1
0·80	”	2·14 : 1
1·60	”	2·15 : 1
3·20	”	1·98 : 1
0·20	0·20M Bu^tPh	2·51 : 1
”	0·20M C_6HMe_5	2·45 : 1
”	0·20M Naphthalene	2·36 : 1
”	0·20M Anisole	2·36 : 1
”	0·05M Pyridine	2·12 : 1
”	0·10M Pyridine	1·94 : 1
”	0·20M Pyridine	1·86 : 1
”	0·40M Pyridine	1·68 : 1
”	0·05M $C_6H_4(OMe)_2$-1,4	1·46 : 1
0·20 [b]	None	1·57 : 1

[a] Results at 1·30 V. E_p = 1·30 V, sweep rate 100 mV s^{-1}. SCE reference. Initial concentration of NaCN 0·4M. Isomeric compositions were determined by analytical g.l.c. (PEG 6000).
[b] Vitreous carbon electrode.

If final nucleophilic attack occurs in the homogeneous phase, the observed isomer ratio would be consistent with the isomer ratio for homogeneous equilibrium. To obtain a value for the equilibrium isomer composition, *cis–trans* isomerization was carried out in methanol in the presence of 1% trifluoroacetic acid at 25·0 °C. [Acid-catalysed interconversion of (**1**) and (**2**) proceeds *via* the intermediate (**5**), equation (1).] The equilibrium was reached within 1 h. The equilibrium value for the ratio (**1**) : (**2**) is **1·42 : 1**.



(1)

(1) or (2) (5)

A high *cis*:*trans* ratio in the anodic reaction compared with the equilibrium value suggests that addition of the nucleophile, especially the final chemical step, is sterically controlled by the electrode.

Electrochemical oxidations were also performed at a vitreous carbon anode to compare the role of anode materials With this anode the isomer ratio approaches the equilibrium mixture.

The abnormally strong influence of 1,4-dimethoxybenzene compared with anisole is intriguing. An exchange electron-transfer reaction[7] may explain the results, because 1,4-dimethoxybenzene is oxidized at the potential of the experiment (E_p 1·1 V *vs.* SCE[2]). Electron transfer from solution-phase 2,5-dimethylfuran to the initially generated cation radical of 1,4-dimethoxybenzene would result in the cation radical of 2,5-dimethylfuran which would lead to the equilibrium ratio of isomeric products.

A final comment on the differences between the results presented here and previous results is relevant. In earlier reports the reaction was performed at higher concentrations of the substrate for preparative purposes, and so the presence of slight stereochemical effects in the electrode processes was overlooked as an experimental error. The present paper describes a careful evaluation of the isomeric product ratio using various initial concentrations of the substrate and concurrently a precise value of the homogeneous equilibrium isomer composition. Some of the discrepancies between the figures given here and those obtained before could be due to the slightly different experimental conditions.

In conclusion, reactions of cyanide and/or methoxide ion with cationic species from 2,5-dimethylfuran occur on or near the electrode (*i.e.*, in the double layer) and are sterically controlled by the electrode and/or the double layer.

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