

Note

Electrochemical nuclear acetamidation of aromatic compounds at the platinum anode

Laxmi Kant Sharma, Sanjeev Kumar, Pragati Yadav
& R K P Singh*

Electrochemical Laboratory of Green Synthesis, Department of
Chemistry, University of Allahabad, Allahabad 211 002, India

E-mail: rkp.singh@rediffmail.com

Received 19 September 2007; accepted (revised) 9 April 2008

The electrochemical nuclear acetamidation of aromatic compounds ethylbenzoate, acetophenone, benzoic acid and benzene have been carried out at platinum anode under the process of nuclear oxidation. The removal of electrons from the aromatic π -electron system is achieved by the electrochemical oxidation. The electrolysis is carried out at the constant anode potential in an electrolytic cell assembly containing reaction mixture and electrodes. The products 4-acetamidoethylbenzoate, 4-acetamidoacetophenone, 4-acetamidobenzoic acid and *N*-phenylacetamide formed during the electrolysis are reported here.

Keywords: Electrochemical oxidation, controlled potential electrolysis, platinum electrode, solvent extraction, green chemistry

The result of the studies on the nuclear acetamidation of aromatic compounds *viz* ethylbenzoate, acetophenone, benzoic acid and benzene is reported in the present communication. The reaction is an important example of nuclear oxidation of aromatic compounds which is not easily possible by the conventional chemical synthetic methods. Singh and co-workers^{1,2} have studied some anodic processes. The nuclear acetamidation is a substitution of acetamido group on benzene nucleus through the nuclear oxidation pathway. Therefore, the reaction is a result of oxidative nuclear aromatic substitution. To achieve this, all the electrolysis were carried out at constant potential by using a conventional three electrode cell assembly with platinum working as well as counter electrodes and saturated calomel electrode as reference electrode.

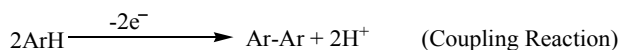
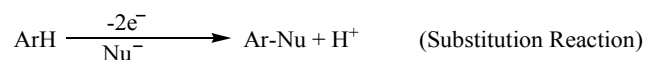
Results and Discussion

The nuclear acetamidation of aromatic compounds does not require any specific reagent, catalyst or acid and base. It takes place through formation of free radicals in solution. Good reviews are available for

the free radical reactions³⁻⁶. Electrode processes in the realm of organic reactions are superior⁷ to conventional organic processes with some modifications such as an anode and a cathode, whose potential can be controlled at will, which can act as oxidant and reductant for a substrate.

Electrochemical reactions have attracted much attention due to several advantages such as rapid reaction rates and higher yield of pure products with non-polluting nature of the reactant^{7,8}.

The removal of electrons from aromatic π -electron systems may be achieved by electrochemical oxidation and the resulting aromatic cation radical or other aromatic cationic species undergoes a variety of reactions⁸ such as aromatic substitution⁹⁻¹² and coupling.



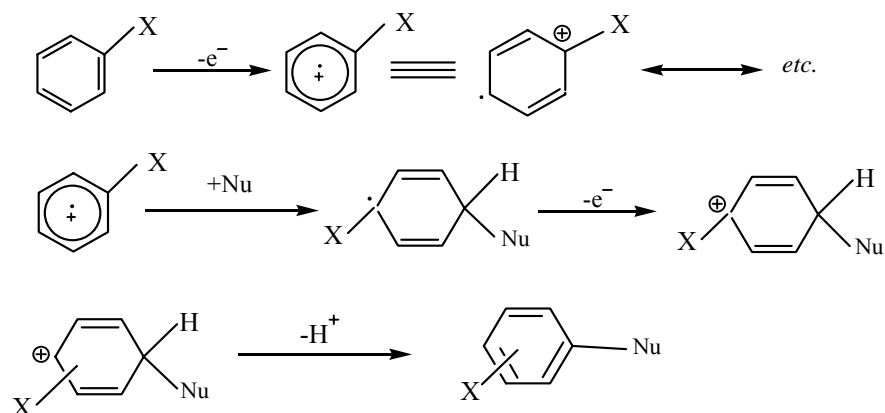
Nuclear aromatic acetamidation have been achieved by the anodic oxidation of aromatic compounds in the presence of acetonitrile.

The mechanism of nuclear aromatic substitution have been given^{13,14} in **Scheme I**.

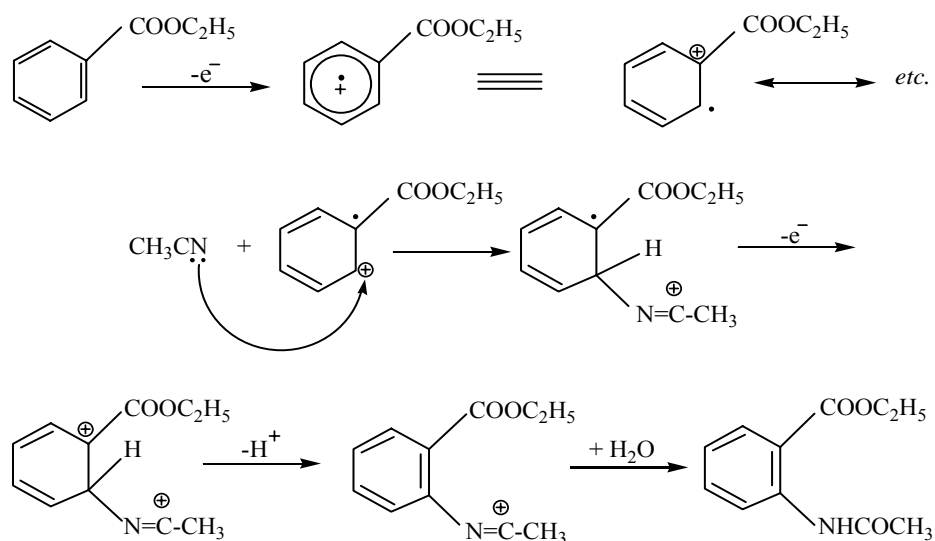
Therefore, the proposed mechanism for the nuclear acetamidation will be as shown in **Scheme II**.

An important point of this electrochemical study is to identify which component of this reaction solution is actually undergoing electron transfer. In fact, all nuclear aromatic substitutions were thought to involve an attack on the hydrocarbon by an electrochemically generated reagent. The voltammetric data shows that the primary electrochemical step in the nuclear aromatic substitution is the oxidation of the hydrocarbon^{13,14}, since the benzene ring is easily oxidized relative to the substituting group. However, it is not necessary for all anodic reactions to be initiated by oxidation of the aromatic substrate.

Now, it is generally accepted that nearly all oxidations of aromatic hydrocarbons involves removal of one electron from the hydrocarbon to afford a radical cation. The structure of the radical cation and the environment in which it is generated are factors which both influence its subsequent



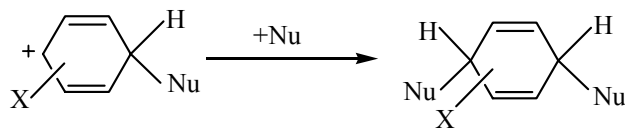
Scheme I



Scheme II

reactions. It would be expected for the nuclear aromatic substitution and addition to be most favoured in the presence of strong nucleophiles and when the ring is not highly alkylated. This is due to the less stable benzylic type carbocation stabilized by hyperconjugation, *i.e.*, the alkyl substituents enhance the stability of benzylic carbocation or radical formed at the initial stage, where the attacking centre becomes alkylated.

Now, the nucleophile is another reactant which can attack the ring to afford a cationic intermediate which most commonly loses a proton after a second electron transfer to regenerate the aromatic ring and afford a nuclear aromatic substitution product. But in special cases it may suffer attack by a second molecule of the nucleophile to afford an addition product.



The factors determining either of the two alternatives – whether the nuclear aromatic substitution or addition is actually chosen – are not yet fully clear but it appears that the nuclear substitution path is always preferred. It appears reasonable, since the loss of the proton restores the aromatic stability and, therefore, has a low activation energy, which is observed only in case of simple benzenoid hydrocarbon systems¹⁵.

In this particular system, the reaction takes place at the RT in a potential difference range of between 1.80V to 2.80V, but the specific potential for the

reaction from various observations is found to be approximately 2.5V vs Hg/Hg²⁺. A total of 0.5-3.0 F mol⁻¹ electricity was passed for the electrolysis which is very small in comparison to the energy input used for other conventional methods.

Experimental Section

The reaction mixture contained 25 mL of 0.1 M solution of starting material using acetonitrile as a solvent and 25 mL of the 0.1 M aqueous solution of KCl, which was used as supporting electrolyte^{16,17}. In this reaction, acetonitrile was the solvent as well as the nucleophile for the substitution reaction.

All the compounds, ethylbenzoate, acetophenone, benzoic acid, benzene, acetonitrile, mercury, KCl and chloroform were of AnalaR grade. Water used for the experiments was double distilled.

The electrolysis were carried out at constant potential difference in a four necked bottle which was designed in the laboratory. For this constant potential electrolysis, a conventional three electrode cell assembly was used along with platinum^{18,19} (flattened sheet of dimension 1.0 cm × 0.5 cm) as working as well as counter electrode and saturated calomel electrode (SCE) as reference electrode.

All the electrolysis experiments were carried out at their corresponding oxidation potentials and were completed in 3 hr. After 3 hr no oxidation product was seen to diffuse in the bulk. All the products were solid and coloured and entirely different from the starting compound.

The observations recorded in these reactions are depicted in **Table I**.

The product was extracted from the reaction mixture into chloroform layer by simple solvent extraction method after diluting the reaction solution with double distilled water. The two immiscible layers were shaken in separatory funnel and allowed to settle. After some time the chloroform layer containing desired product separated out and was removed.

Analysis of the product

All the products were analyzed by chemical methods as well as by spectral studies. As per the mechanism, following products were obtained in the electrolysis leading to nuclear oxidation (**Scheme III**).

It is expected that both *ortho* and *para* products would be formed. However, *ortho* product is stabilized by intramolecular hydrogen bonding and hence is the major product. The *ortho* product was purified by chromatography.

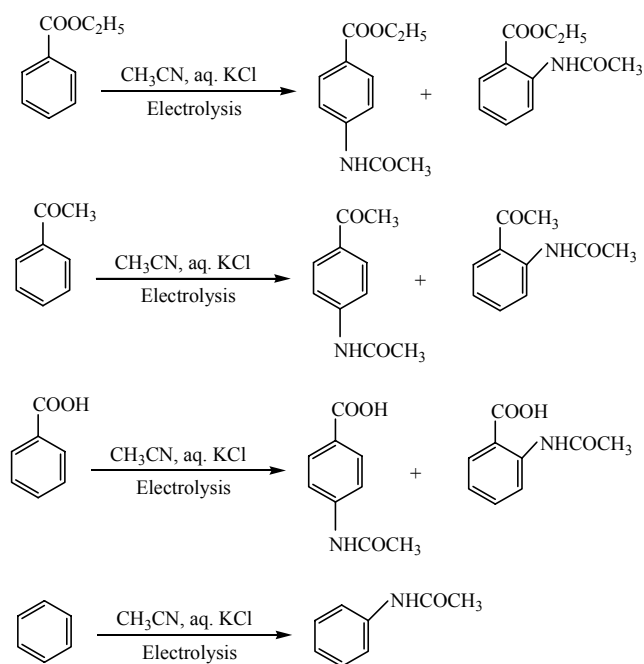
On examining the ratio of *ortho* to *para* products it was found that the major products in all the three series are *ortho* which are stabilized by intramolecular hydrogen bonding. These products were purified by preparative chromatography (C₆H₁₄:C₆H₆, 4:6, v/v). The *o/p* ratio in each case was found to be ≈ 9:1.

Spectral characterization data

4-Acetamidoethylacetate, 2-Acetamido ethylacetate: C₁₁H₁₃NO₃, Mol.wt. 207; IR (KBr): 3320 (NH), 1730 (carbonyl), 735-860 cm⁻¹ (*o*, *p*-disubstituted benzene); ¹H NMR (CDCl₃): δ 1.30 (t, 3H, *J* = 7.0 Hz, methyl-CH₂CH₃), 4.20 (q, 2H, *J* = 7.0 Hz,

Table I — Current-potential data of electrolysis as recorded by potential-cum-galvanostat

Time	Current in mA			
	Ethyl benzoate	Acetophenone	Benzoic acid	Benzene
3 hr	19.47	26.70	22.00	23.10
	19.33	26.50	21.95	23.00
	19.32	26.48	21.80	22.88
	19.30	26.40	21.80	22.75
	18.85	26.30	21.70	22.60
	18.85	26.00	21.55	22.50
	18.75	25.75	21.50	22.38
	17.86	25.62	21.40	22.25
	17.56	25.40	21.25	22.15
	17.55	25.15	21.05	22.00
	17.50	24.82	20.90	21.95
	17.50	24.50	20.83	21.80
	17.36	24.30	20.65	21.63
	17.25	24.00	20.50	21.50
	Applied Potential	2.50 V	2.50 V	2.51 V
Yield	>90%	>80%	>85%	>90%



Scheme III

methylene), 6.94-6.99 (dd, 4H, $J = 2.6$ and 5.6 Hz, Ar-H), 3.39 (s, 3H, methyl-COCH₃); ¹³C NMR (CDCl₃): δ 129.1 (Ar-CH), 134.7 (Ar-C), 61.7 (methylene), 161.0 (carboxylic), 13.3, 50 (methyl-CH₂CH₃, COCH₃), 20.0 (carbonyl).

4-Acetamidoacetophenone, 2-Acetamidoacetophenone: C₁₀H₁₁NO₂, Mol. wt. 177; IR (KBr): 3320 (NH), 1730 (carbonyl), 735-860 cm⁻¹ (*o*, *p*-disubstituted benzene); ¹H NMR (CDCl₃): δ 2.35 (s, 3H, methyl-COCH₃), 6.94-6.99 (dd, 4H, $J = 2.6$ and 5.6 Hz, Ar-H), 3.39 (s, 3H, methyl-NHCOCH₃); ¹³C NMR (CDCl₃): δ 129.1 (Ar-CH), 134.7 (Ar-C), 20.9, 199.5 (carbonyl-COCH₃, NHCOCH₃), 27.6, 50 (methyl-COCH₃, NHCOCH₃).

4-Acetamidobenzoic acid, 2-acetamidobenzoic acid: C₉H₉NO₃, Mol. wt. 179; IR (KBr): 3320 (NH), 1730 (carbonyl), 735-860 cm⁻¹ (*o*, *p*-disubstituted benzene); ¹H NMR (CDCl₃): δ 6.94-6.99 (dd, 4H, $J = 2.6$ and 5.6 Hz, Ar-H), 11.0 (s, 1H, hydroxy, exchangeable with D₂O), 3.39 (s, 3H, methyl); ¹³C NMR (CDCl₃): δ 129.1 (Ar-CH), 134.7 (Ar-C), 173.1 (carboxylic), 20.9 (carbonyl), 50 (methyl).

N-Phenylacetamide: C₈H₉NO, Mol. wt. 135; IR (KBr): 3320 (NH), 1730 (Carbonyl), 690-770 cm⁻¹ (monosubstituted benzene); ¹H NMR (CDCl₃): δ 6.94-6.99 (dd, 4H, $J = 2.6$ and 5.6 Hz, Ar-H), 3.39 (s, 3H, methyl); ¹³C NMR (CDCl₃): δ 129.1 (Ar-CH), 134.7 (Ar-C), 20.9 (carbonyl), 50 (methyl).

Conclusion

It is obvious from the above studies that the electrochemical nuclear acetamidation as an example of nuclear substitution in aromatic compounds provides a good method for nuclear aromatic oxidation which is not so easy to achieve by chemical methods. In the present electrolytic method, electrolysis was carried out at RT and no hazardous chemicals were used. Hence the method is eco-friendly and a contribution to green chemistry.

Acknowledgement

The author thanks the Sophisticated Analytical Instrumentation Facility (SAIF), a division of CDRI (Central Drug Research Institute), Lucknow for recording the spectra and the Head, Department of Chemistry, University of Allahabad for providing necessary facilities. The author also thanks the UGC for providing financial assistance.

References

- 1 Yadav K L, Kumar A, Kumar S & Singh R K P, *Transactions of the SAEST*, 40, **2005**, 106.
- 2 Kumar S, Kumar A & Singh R K P, *Proc Nat Acad Sci India*, 75A IV, **2005**, 233.
- 3 Yadav S R, Goyal P, Sharma A & Sharma I K, *J Indian Chem Soc*, 79, **2002**, 695.
- 4 Weedon B C L, *Advanced Organic Chemistry*, 1, **1960**, 01.
- 5 Vijh A K & Conway B E, *Chem Rev*, 67, **1967**, 623.
- 6 *Organic Electrochemistry* edited by Baizer M M and Lund H, 2nd edn. (Marcel Dekker, New York), **1970**, 132.
- 7 Mann C K & Barnes K K, in *Electrochemical Reactions in Non-aqueous Systems*, (Marcel Dekker, New York), **1970**, 132.
- 8 Fry A J, in *Synthetic Organic Electrochemistry*, 2nd edn. (Wiley Interscience Publication), **1989**, 73.
- 9 Bockmain G & Fritz H P, *Electrochim Acta*, 21, **1976**, 1099.
- 10 Evans D A, Tanis S P & Hart D J, *J Am Chem Soc*, 103, **1981**, 5813.
- 11 Johnson R W, Bendnarski M D, O' Leary B F & Grower E R, *Tetrahedron Lett*, 22, **1981**, 3751.
- 12 Achord J M & Hussey C L, *J Electrochem Soc*, 128, **1981**, 2556.
- 13 Linstead R P, Shephord B R & Weedon B C L, *J Chem Soc*, **1952**, 3624.
- 14 Leung M, Herz J & Salzberg H W, *J Org Chem*, 30, **1965**, 310.
- 15 Barba F, Guirado A & Barba I, *J Org Chem*, 49, **1984**, 3022.
- 16 Yadav K L, Kumar S, Kumar A & Singh R K P, *J Indian Chem Soc*, 81, **2004**, 595.
- 17 Kumar S & Singh R K P, *J Indian Chem Soc*, 82, **2005**, 934.
- 18 Kumar S, Sharma L K & Singh R K P, *J Indian Chem Soc*, 83, **2006**, 1160.
- 19 Kumar S, Yadav P & Singh R K P, *Transactions of the SAEST*, 41, **2006**, 05.