

Electrochemical Synthesis of Heterocyclic Compounds: X¹. Anodic Synthesis of *s*-Triazolo [3,4-*a*]pyridinium Salt Derivatives

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A novel way of preparing *s*-triazolo[3,4-*a*] pyridinium salts by anodic oxidation of aryl hydrazones of 2-acetylpyridine, 2-benzoylpyridine and 2-formylpyridine is described. Controlled potential electrolysis was carried out in CH₃CN-Et₄NX media using a Pt-electrode and a divided cell.

The products were obtained in high yield (79—91%) and purity. It has been shown that the conformation of the starting hydrazone does not affect the yield of products and *s*-triazolo [3,4-*a*]pyridinium salts differing in anions can be prepared merely by using a supporting electrolyte carrying the desired anion (ClO₄⁻, TsO⁻, BF₄⁻).

In contrast to numerous systematic studies published on the anodic oxidation of organic compounds containing nitrogen² only few reports have appeared pertaining to hydrazone derivatives³⁻⁷.

In a previous short communication⁸, we described a new route to 1-phenyl-3-methyl-1*H*-1,2,3-triazolo[3,4-*a*] pyridinium perchlorate by anodic oxidation of phenylhydrazone of 2-acetylpyridine. In order to test the general applicability of this reaction, we have now investigated the anodic oxidation of a series of structurally different hydrazone derivatives.

As a result, we can report a new convenient synthesis of several *s*-triazolo [3,4-*a*] pyridinium salts (1b-11b) by electrochemical oxidation of hydrazone derivatives (1a-11a). (see Table).

All oxidations, except 6a→6b and 7→7b, proceeded smoothly at the Pt-gauze anode (3 × 5 cm) without inhibition of the electrode, using controlled-potential electrolysis. In the reactions 6a→6b and 7a→7b, a graphite anode (1.5 × 5 cm) was used. All hydrazones showed two waves in acetonitrile-tetraethylammonium solutions. The first wave can be attributed to oxidation of the parent molecule and the second presumably to hydrazone protonated by the protons liberated along the first wave. Cyclic voltammograms of all hydrazones investigated exhibit irreversible waves in the range of sweep rates from 0.02 to 80 Vs⁻¹. Coulometry at the applied potential showed that the overall electrode reaction was a two-electron oxidation in all cases examined. The preparative electrolysis gave yields of *s*-triazolo [3,4-*a*] pyridinium salt derivat-

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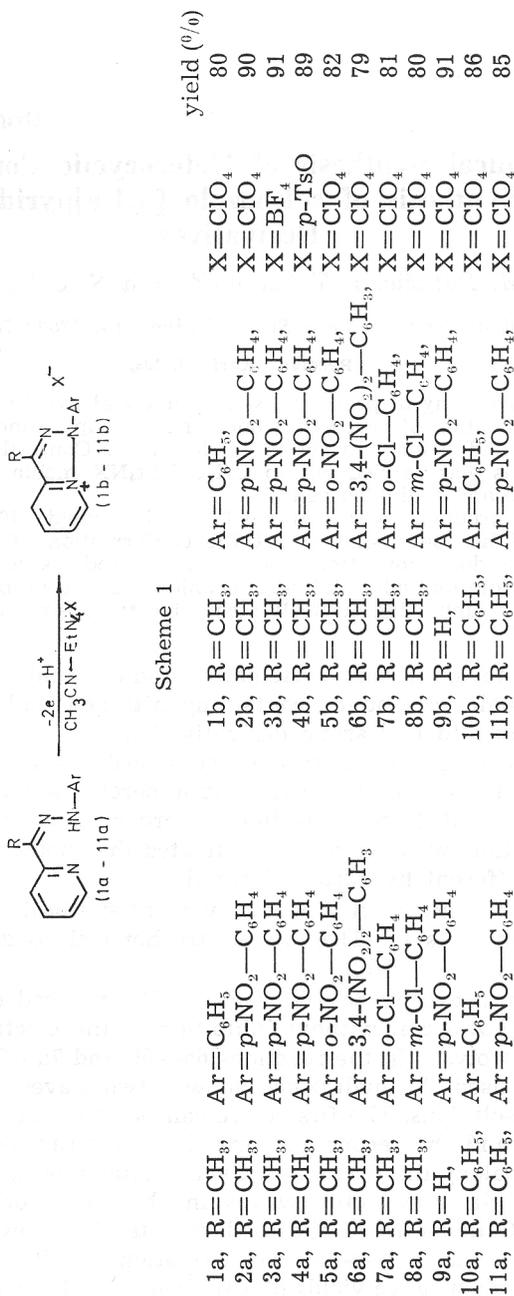


TABLE I
 Conditions and Results of the Electrochemical Cyclisations

Conversion	RDE vol-tammetry ^a results (V vs. SCE)	Applied potential (V vs. SCE)	n-value ^b	Yield of product (%)	M. p. (solvent) (°C)	Molecular formula or lit. m. p.	Anal.		Calc'd	
							%C	%H	%H	%N
1a→1b	0.70 1.05	1.4	2.0	80	240—242 (EtOH)	240—246 ^c lit. 8				
2a→2b	1.10 1.59	1.5	1.9	90	197—200 (EtOH)	C ₁₃ H ₁₁ ClN ₄ O ₆ ^d (354.6)	44.03 43.91	3.10 3.30	15.80 14.91	
3a→3b	1.10 1.50	1.65	2.1	91	228—230 (EtOH)	C ₁₃ H ₁₁ F ₄ N ₄ O ₂ B ^e (341.9)	45.66 45.37	3.21 3.19	16.47 16.48	
4a→4b	1.05 1.50	1.5	2.2	89	258—260 (EtOH)	C ₂₀ H ₁₈ N ₄ O ₅ S ^f (426.3)	56.34 56.52	4.22 4.20	13.14 13.13	
5a→5b	1.12 1.50	1.35	1.95	82	182—190 (EtOH)	C ₁₃ H ₁₁ ClN ₄ O ₆ ^g (354.6)	44.03 44.05	3.10 3.02	15.80 15.51	
6a→6b	1.26 1.55	1.55	1.8	79	240—242 (CH ₃ CN-ether)	C ₁₃ H ₁₀ ClN ₅ O ₈ ^h (399.6)	39.07 38.65	2.50 2.79	17.53 17.30	
7a→7b	0.90 1.32	1.55	2.1	81	244—246 (CH ₃ CN-ether)	C ₁₃ H ₁₁ Cl ₂ N ₃ O ₄ ⁱ (344.1)	45.37 45.81	3.19 3.05	12.21 12.20	
8a→8b	1.0 1.25	1.45	1.9	80	222—224 (CH ₃ CN)	C ₁₃ H ₁₁ Cl ₂ N ₃ O ₄ ^j (344.1)	45.32 45.70	3.19 3.20	12.21 12.25	
9a→9b	1.05 1.50	1.55	2.1	91	278—280 (CH ₃ CN)	C ₁₂ H ₉ ClN ₄ O ₆ ^k (340.6)	42.23 42.40	2.64 2.85	16.45 16.01	
10a→10b	0.90 1.10 0.94 1.15	1.2	2.2—2.4	80—86	217—219 (DMSO—CH ₃ COOEt)	C ₁₈ H ₁₄ ClN ₃ O ₄ ^l (371.6)	58.17 58.20	3.76 3.71	11.30 11.52	
11a→11b	0.90 1.1	1.3	2.2	85	251—253 (DMSO—CH ₃ COOEt)	C ₁₈ H ₁₃ ClN ₄ O ₆ ^m (416.6)	51.89 51.94	3.12 2.89	13.44 13.52	

- ^a Pt-electrode; substrate concentration 10^{-3} mol/dm³; 0.1 M Et₄NClO₄ in acetonitrile; 1500 r.p.m.
^b Determined by coulometry at controlled potential.
^c IR (KBr): $\nu_{\max} = 2095, 1640, 1600, 1490, 1430, 1410, 1085, 760, 630$ cm⁻¹.
¹H-NMR (DMSO-d₆): $\delta = 2.4$ (s, 3H, CH₃); 7.0–8.9 (m, 9H_{arom.}) ppm.
^d IR (KBr): $\nu_{\max} = 3100, 1595, 1565, 1530, 1490, 1100, 855, 625$ cm⁻¹.
¹H-NMR (DMSO-d₆): $\delta = 2.4$ (s, 3H, CH₃); 7.5–8.9 (m, 8H_{arom.}) ppm.
^e IR (KBr): $\nu_{\max} = 3100, 1600, 1570, 1570, 1500, 1090, 855, 630$ cm⁻¹.
¹H-NMR (DMSO-d₆): $\delta = 2.45$ (s, 3H, CH₃); 7.5–8.8 (m, 8H_{arom.}) ppm.
^f IR (KBr): $\nu_{\max} = 3100, 1600, 1575, 1550, 1505, 1330, 1265, 1170, 855, 830, 695$ cm⁻¹.
^g IR (KBr): $\nu_{\max} = 3080, 1605, 1535, 1440, 1350, 1095, 800, 770, 755, 625$ cm⁻¹.
^h IR (KBr): $\nu_{\max} = 3100, 1610, 1570, 1550, 1500, 1335, 1100, 840, 780, 625$ cm⁻¹.
ⁱ IR (KBr): $\nu_{\max} = 3100, 1620, 1595, 1450, 1100, 760, 745, 625$ cm⁻¹.
¹H-NMR (DMSO-d₆): $\delta = 2.45$ (s, 3H, CH₃); 7.0–8.9 (m, 8H_{arom.}) ppm.
^j IR (KBr): $\nu_{\max} = 3100, 1600, 1560, 1530, 1395, 1245, 1095, 850, 800, 775, 630$ cm⁻¹.
¹H-NMR (DMSO-d₆): $\delta = 2.38$ (s, 3H, CH₃); 7.0–8.8 (m, 8H_{arom.}) ppm.
^k IR (KBr): $\nu_{\max} = 3100, 1610, 1600, 1560, 1500, 1455, 1335, 1285, 1100, 815, 755, 625$ cm⁻¹.
¹H-NMR (DMSO-d₆): $\delta = 7.3$ –9.0 (m, 9H_{arom.}) ppm.
^l IR (KBr): $\nu_{\max} = 3100, 1625, 1590, 1490, 1445, 1430, 1300, 1100, 790, 700, 625$ cm⁻¹.
¹H-NMR (DMSO-d₆): $\delta = 7.4$ –9.4 (m, 14H_{arom.}) ppm.
^m IR (KBr): $\nu_{\max} = 3100, 1600, 1530, 1550, 1450, 1325, 1100, 850, 785, 760$ cm⁻¹.
¹H-NMR (DMSO-d₆): $\delta = 7.6$ –9.6 (m, 13H_{arom.}) ppm.

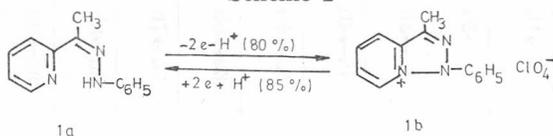
ives ranging from 79 to 91%. The same products were obtained when the electrolysis was carried out in the presence of pyridine at the applied potential of the plateau of the first wave, but some filming of the electrode occurred during the electrolysis.

R. Kuhn and W. Münzing have published the synthesis of *s*-triazolo [3,4-*a*]pyridinium salts by oxidation of phenylhydrazones of 2-acetyl and 2-benzoylpyridine with lead tetraacetate⁹. Synthesis of the products was performed in 29 to 44% yield, but the generality of their method was limited by the following factors: (i) it was not possible to obtain the cyclic product by oxidation of phenylhydrazone of 2-formylpyridine (R=H); (ii) the phenylhydrazone must have adequate stereochemical configuration, e. g. only *cis*-hydrazone gave the cyclised product; (iii) using higher concentrations of the phenylhydrazone derivatives gives rise to intermolecular dehydrogenated products.

The electrochemical oxidative cyclisation is superior to chemical oxidation with lead tetraacetate⁹ in the following ways: (i) the products are obtained in high yield (79–91%) and purity; (ii) pyridinium salts widely differing in anions can be prepared merely by using a supporting electrolyte carrying the desired anion (ClO₄⁻, TsO⁻, BF₄⁻), (iii) it seems that the conformation of the substrate does not affect the yield of product. We have oxidized separately *cis* and *trans* forms of compound 10a, which we have separated according to the published procedure by R. Kuhn and W. Münzing⁹. In both cases we have obtained the same product 10b in 80% (starting from *cis* 10a) and 86% (starting from *trans* 10a) yield; (iv) it is possible to get the products by oxidation of *p*-nitrophenylhydrazone, 9a, of 2-formylpyridine (when R=H).

Compound 1b may be reconverted to 1a by electrochemical reduction (Ep of 1b = -0.8 V vs SCE) at a Pt cathode and also by reduction with ascorbic acid.

Scheme 2



EXPERIMENTAL

Melting points are uncorrected. The IR were taken on a Perkin-Elmer M-377 spectrophotometer in KBr pellets, the NMR spectra were recorded on a Perkin-Elmer R 12 B instrument. Hydrazones were prepared according to the procedure of Kauffmann and Fischer¹⁰ from corresponding arylhydrazines and 2-acetyl-pyridine, 2-benzopyridine or 2-formylpyridine. The apparatus and cells for voltammetry, coulometry and preparative electrolysis have been described earlier⁶. Acetonitrile was purified by refluxing over potassium permanganate for 1h, followed by distillation over P₂O₅.

Anodic Oxidation of Hydrazones (1a-11a), General Procedure

The hydrazone (0.1—1.0 g) is added to the anodic compartment of the cell filled with a 0.1 molar solution of tetraethylammonium perchlorate in acetonitrile (100 ml). The potential is maintained at a fixed value (see Table) by means of an Amel model 551 potentiostat, with initial currents of 150—90 mA. Electrolysis is usually discontinued when the current drops to 5—20 mA which generally requires 0.5—2h. Products (1b—11b) were isolated according to the following methods:

Method A (1b-5b, 8b, 10b, 11b), After electrolysis at controlled potential acetonitrile is evaporated to a volume of ~ 10 ml and ~ 150 ml of water added. The precipitated cyclisation product is isolated by filtration and recrystallised from an appropriate solvent (see Table).

Method B (6b, 7b, 9b) After electrolysis acetonitrile is evaporated to a volume of ~ 10 ml and ~ 150 ml of benzene added. The precipitated mixture of the cyclisation product and supporting electrolyte is filtered of and put into 150 ml of water. The undissolved cyclisation product is isolated by filtration and recrystallised from an appropriate solvent (see Table).

Electrochemical reduction of 1-phenyl-3-methyl-1H-1,2,3-triazolo [3,4-a] pyridinium perchlorate (1b→1a)

Compound 1b (100 mg) was added to the cathodic compartment of the cell filled with a 0.1 molar solution of tetraethylammonium perchlorate in acetonitrile. The potential of the Pt-gauze cathode was maintained at -0.9 V vs. SCE with an initial current of cca 80 mA. Electrolysis was discontinued when the current dropped to cca. 5 mA which took 45 minutes. The electrolysis was carried out under nitrogen atmosphere. The acetonitrile was evaporated to a volume of 10 ml and water (100 ml) added. The precipitated product 1a was recrystallised from ethanol: yield: 58 mg (85%).

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SAŽETAK

Elektrokemijska sinteza heterocikličkih spojeva X. Anodna sinteza s-triazolo [3,4-a]piridinijevih soli*M. Batušić, I. Tabaković i S. Crljenak*

Opisan je novi metod priprave s-triazolo [3,4-a]piridinijevih soli anodnom oksidacijom arilhidrazona 2-acetilpiridina, 2-benzoilpiridina i 2-formilpiridina. Elektrolize kod kontroliranog potencijala izvršene su u ćeliji sa dijafragmom, Pt-anodom i u mediju $\text{CH}_3\text{CN-Et}_4\text{NX}$. Dobiveni su produkti u velikom iskorištenju (79—91%) i sa visokim stupnjem čistoće. Pokazalo se da konformacija polaznog hidrazona ne utječe na iskorištenje produkta a upotrebom osnovnih elektrolita Et_4NX ($\text{X}=\text{ClO}_4$, TsO^- , BF_4^-) mogu se dobiti piridinijeve soli koje imaju različite anione.

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