# Electro-organic Reactions. Part 18.† The Competition between Cleavage at Aryl–Oxygen and at Tetrazol-5-yl–Oxygen Bonds in the Cathodic Reduction of Aryl Tetrazolyl Ethers

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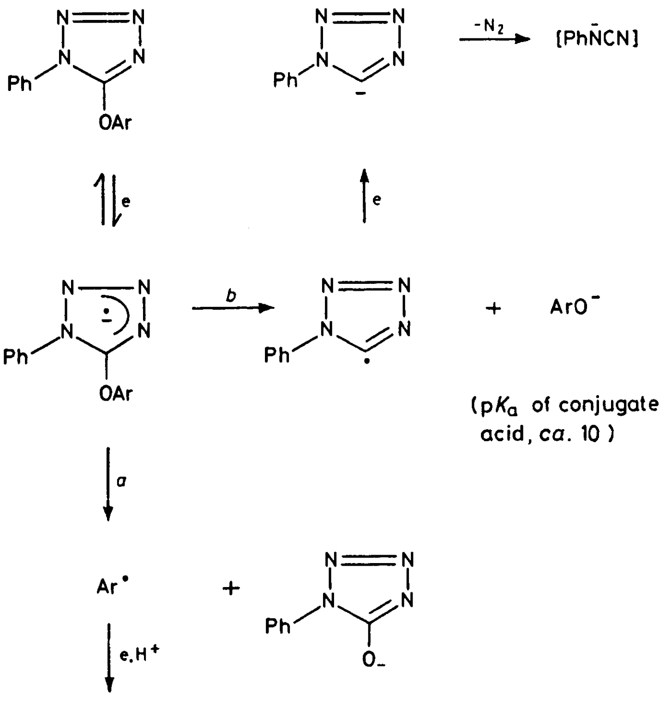
5-Aryloxy-1-phenyltetrazoles are cleaved cathodically in a 2 F $mol^{-1}$ process. Initial electron transfer is to the tetrazole ring and the compounds cleave predominantly at the tetrazolyl–oxygen bond. An exception is 5-(*p*-cyanophenoxy)-1-phenyltetrazole which undergoes 1 F $mol^{-1}$ cleavage to 1-phenyltetrazolone and benzonitrile. Competitive electrolysis of pairs of the tetrazolyl ethers, differently substituted in the aryloxy-ring, allows an estimation of relative rates of cleavage. These rates are found to be roughly related to the p$K_a$ values of the corresponding phenols.

DEOXYGENATION reactions are important in organic synthesis. Several examples of cathodic hydrogenolysis fall into this category, *e.g.* from allylic and benzylic positions acetate (and other carboxylates) may be cleaved cathodically.[1] From less activated positions tosylates,[2] methanesulphonates,[3] and oxalates[4] are easily removed cathodically. Shono and his co-workers[5] have shown that by a suitable choice of leaving group, *i.e.* diethyl phosphate, aryl–oxygen bonds may be cleaved electrochemically and the method is useful for the removal of phenolic hydroxy-groups. The conventional chemical method for the cleavage of phenolic hydroxy-groups involves conversion into tetrazol-5-yl ethers followed by catalytic hydrogenation; either molecular hydrogen[6] or a hydrogen-atom donor[7] may be used in the presence of a metal catalyst.



SCHEME 1

In principle the cathodic cleavage of tetrazol-5-yl ethers should be achievable (Scheme 1). The simple expectation, based on the p$K_a$ values of the conjugate acids of the contending leaving groups, is that cleavage of the anion-radical would proceed preferentially to give aryl radical and the anion of 1-phenyltetrazolone (route *a*). The p$K_a$ in aqueous solution of 5-hydroxy-1-phenyltetrazole[8] is 5.53 whereas that of phenol is *ca.* 10, *i.e.* the tetrazolone anion is much more highly stabilised than phenolate anion. The use of aprotic solvent [*e.g.* *NN*-dimethylformamide (DMF)] is unlikely completely to obscure this large difference.

We herein report on experiments which test the above premise. Contrary to expectation cleavage is predominantly to give phenolate anions and this result, unpromising for applications to synthesis, allows a comparison by competitive electrolysis[9] of the relative leaving group abilities of substituted phenolate anions.

## RESULTS AND DISCUSSION

*Voltammetry and Coulometry.*—The tetrazolyl ethers formed from a variety of phenols reduce at roughly similar potentials (Table 1), *i.e.* at *ca.* −1.90 V (*versus* Ag–AgI). An exception is 5-(*p*-cyanophenoxy)-1-phenyltetrazole which displays on cyclic voltammetry a reduction peak at −1.60 V; it will be seen later that the behaviour of this compound is exceptional in other ways also.

In each case irreversible reduction is found with in some cases one and in some cases two reduction peaks. In the voltammetric experiments reduction is diffusion controlled; the voltammetry of the 2-methoxyphenyl and 4-chlorophenyl ethers was examined in detail and linear plots of $i_p$ *versus* (scan rate)$^{\frac{1}{2}}$ were obtained for scan rates up to 30 V $s^{-1}$. In these, typical, cases reduction was totally irreversible at up to 100 V $s^{-1}$.

Coulometry at controlled potential showed that the aryl tetrazolyl ethers are reduced in a 2 F $mol^{-1}$ process with the notable exception of the 4-cyanophenyl ether which consumes 1 F $mol^{-1}$.

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† Part 17, ref. 14.

*Controlled Potential Electrolyses.*—Contrary to expectations based on the relative basicities of alternative leaving groups (Scheme 1) the tetrazol-5-yl ethers are cathodically cleaved, in the presence of proton donor, predominantly to yield the phenol. Yields are variable and in some cases products of the alternative mode of cleavage are found (Table 2). Cleavage to phenol should be accompanied by the formation of an equivalent amount of 1-phenyltetrazole. In fact relatively small amounts of the tetrazole (*ca.* 10%) accompanied phenol formation.

TABLE 1

Cyclic voltammetric [a] reduction potentials for aryl 1-phenyltetrazol-5-yl ethers

| Aryl group | $-E_p$/V *versus* Ag–AgI |
|---|---|
| Biphenyl-4-yl (1) | 1.75, 1.85 |
| 2-Naphthyl (2) | 1.75, 1.85 |
| *o*-Methoxyphenyl (3) | 1.95 [b] |
| *p*-Methoxyphenyl (4) | 1.85 |
| *p*-Cyanophenyl (5) | 1.60, 2.00 |
| Phenyl (6) | 1.90 |
| *p*-Chlorophenyl (7) | 1.75, 1.90<br>(2.44) [c] |
| 3,5-Dimethoxyphenyl (8) | 1.75, 1.85 |
| 2,6-Dimethoxyphenyl (9) | 1.85 |
| 2,6-Dimethylphenyl (10) | 1.90 |
| 2,4-Dimethylphenyl (11) | 2.00 |
| 3,4,5-Trimethoxyphenyl (12) | 1.75, 1.90 |
| 3,5-Di-isopropylphenyl (13) | 1.95 |

[a] DMF–$H_2O$ (5% v/v), $Et_4NBr$ (0.1M); Hg-coated Pt bead cathode; scan rate in the range 0.35—0.45 V $s^{-1}$. [b] DMF–$Bu_4NI$ (0.1M), 0.1 V $s^{-1}$. [c] DMF–$Bu_4NI$ (0.1M), 0.3 V $s^{-1}$, V *versus* saturated calomel electrode.

TABLE 2

Preparative-scale electrolysis [a] of aryl 1-phenyltetrazol-5-yl ethers

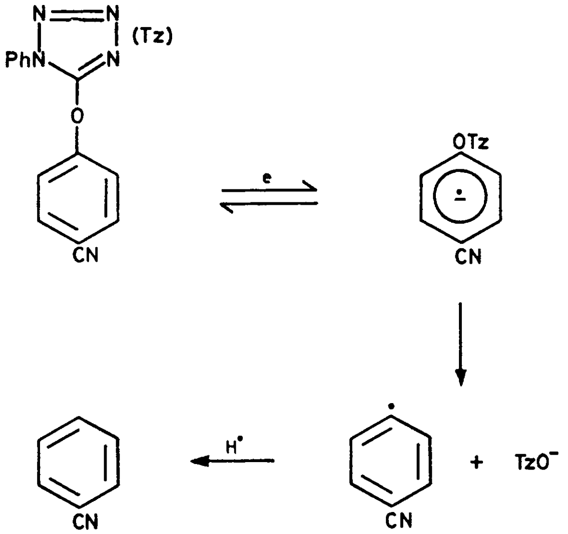
| Aryl ether | ArOH (%) [b] | ArH (%) [b] |
|---|---|---|
| (1) | 80 [b,c] | 9 [b,c] |
| (2) | 75 | 5 |
| (4) | 30 | 30 |
| (5) | | 53 [c,d] |
| (6) | 37 | |
| (7) | 70 | |
| (8) | 45 | |
| (9) | 10 | |
| (10) | 95 | |
| (11) | 47 | |
| (12) | 40 | |
| (13) | 70 | |

[a] DMF–$H_2O$ (5% v/v), $Et_4NBr$ (0.1M); Hg pool cathode; electrolysis at first reduction potential to 2 F $mol^{-1}$. [b] G.l.c. analysis. [c] Isolated yield. [d] 1 F $mol^{-1}$ consumed.

All but one of the ethers studied cleaves according to route *b* of Scheme 1; the similarity of reduction potentials supports the suggestion that initial electron transfer is to the tetrazole moiety. In cyclic voltammetry 1-phenyltetrazole gives reduction at $E_p$ −1.80 V which further supports the hypothesis. The failure to isolate a high yield of 1-phenyltetrazole from preparative electrolyses is not surprising. The tetrazole anion is well known to be unstable and readily to lose nitrogen. This was found for the treatment of 1-phenyltetrazole with sodium hydroxide [10] and for the reaction between 5-chloro-1-phenyltetrazole and butyl-lithium.[11] 1-Phenyltetrazol-5-yl-lithium has been prepared [12] but it decomposes rapidly at >203 K.

Two-electron electrochemical cleavage of 5-chloro-1-phenyltetrazole would also be expected to yield the 1-phenyltetrazolyl anion; we found that controlled potential electrolysis, in aqueous DMF, gave clean 2 F $mol^{-1}$ reduction at −1.60 V but, again, only *ca.* 10% of 1-phenyltetrazole was isolated.

The cleavage pattern apparently changes when initial electron transfer is to the 5-aryloxy-moiety. Cleavage of 5-(*p*-cyanophenoxy)-1-phenyltetrazole is a 1 F $mol^{-1}$ process and it occurs at −1.60 V, *i.e.* at less than the potential required for reduction of the 1-phenyltetrazole system. This behaviour is well rationalised by Scheme 2.



SCHEME 2

An implication of these results is that the direction of cleavage is determined by which part of the molecule accepts the electron, *i.e.* addition to the tetrazole ring is followed by loss of phenoxide whereas addition to the aryl ring is followed by loss of 1-phenyltetrazolone anion. It is not obvious why this should be.

*Relative Leaving Group Abilities of Substituted Phenoxide Ions.*—Recently, relative leaving group abilities in elimination reactions have been the subject of much study.[13] No obvious correlation has been found between the abilities of various groups to depart from, say, a carbanion and such parameters as the basicity or nucleophilicity of the leaving group or with bond strengths or polarisability. We have developed for cathodic cleavage reactions a method of competitive electrolysis [9,14] which allows comparison of leaving group abilities. For comparison of rates of cleavage of groups at the benzylic position of *p*-methoxycarbonylbenzyl derivatives a qualitative ordering [14] of leaving ability is $Et_3N > Ph_3P \gg RCO_2^-$. The p$K_a$ values of the conjugate acids are, respectively, 10.8, *ca.* 2.6, and *ca.* 4.5, *i.e.* even gross differences in leaving group ability cannot easily be explained in terms of basicity.

Within a given series, the carboxylates, there is a very rough correlation[9] with the p$K_a$ of the corresponding acid.

As shown above simple consideration of basicities cannot account for the observed direction of cleavage of the tetrazol-5-yl ethers; it is generally the more basic group (phenoxide) which leaves from the anion-radical.

TABLE 3

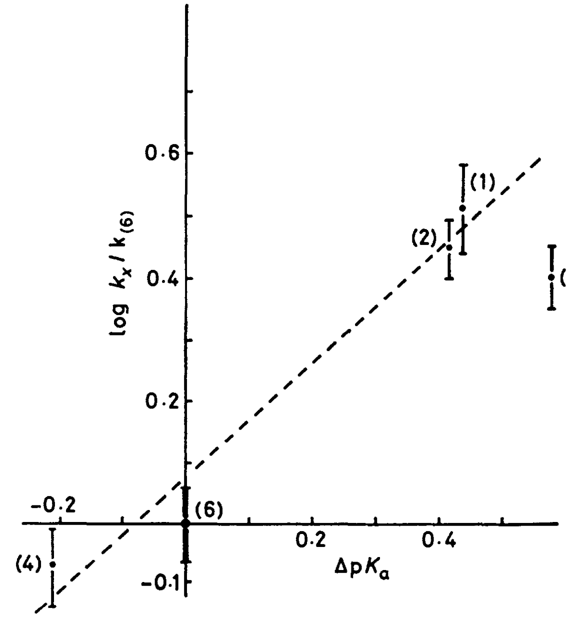
Relative rates of cleavage by competitive electrolysis[a]

| Competing substrates $(x + y)$ | Phenols (%) % from $(x)$ : % from $(y)$ | Current yield (%) | $k_x/k_y$ | $(k_x/k_y)$ av. |
|---|---|---|---|---|
| (1) + (7) | 30 : 23 | 76 | 1.30 | |
| (1) + (6) | 46 : 18 | 91 | 2.56 | 3.26 ± 0.54 |
| (1) + (6) | 55 : 15 | 100 | 3.67 | |
| (1) + (6) | (55 : 14)[b] | 99 | 3.93 | |
| | | | (2.89)[c] | |
| (2) + (7) | (30[d] : 28)[b] | 83 | 1.07 | |
| (4) + (6) | 31 : 36 | 96 | 0.86 | |
| (7) + (6) | 49 : 22 | 101 | 2.23 | 2.52 ± 0.30 |
| | | | (2.82)[c] | |
| (2) + (6) | 54 : 17 | 101 | 3.18 | 2.80 ± 0.28 |
| (2) + (6) | (54[d] : 19)[b] | 104 | 2.84 | |
| | | | (2.38)[c] | |

[a] At −1.75 V (*versus* Ag–AgI). [b] At −1.90 V. [c] Calculated from ratios involving other pairs. [d] Includes allowance for yield of naphthalene; for competitive electrolyses involving (1) only traces of biphenyl were formed.

Competitive electrolysis of pairs of tetrazolyl ethers, differently substituted in the phenolic ring, should allow an estimation of relative rates of cleavage and indicate whether such rates may be related to the stability of the leaving phenoxide ion. The major criteria for application of the competition method[9] are that reduction is diffusion controlled and that the competing pair reduce at similar potentials and by the same mechanism. As in previous applications of this method[9,14] the preparative scale competitive electrolyses are carried out at somewhat below the limiting current, *i.e.* at a point where electron transfer between substrate and electrode is reversible. It is also probable that rapid electron transfer between the two radical-anions provides an additional mechanism for equilibration of the low stationary concentrations of radical-anions. The reversible reduction potentials of the competing substrates are likely to be closely similar because the structures of the electrophores are identical and the substituent effect of the leaving groups will be small. In these circumstances it is our contention that the major factor governing the relative rate of consumption of the substrates is the relative rate of cleavage of the radical-anions. The argument is similar to that deployed by Curtin and Hammett[15] for the reactions of conformationally mobile systems. These criteria are well met for cathodic cleavage of tetrazol-5-yl ethers.

Controlled potential electrolyses of equimolar mixtures of pairs of tetrazol-5-yl ethers were performed; electrolysis was continued to 0.7 F mol$^{-1}$, based on the combined starting materials, and the crude electrolysis mixture was analysed by g.l.c. The coulombic yield of each phenol was calculated and from several experiments results were accepted only from those which gave a combined current efficiency in excess of 75%. Most were in the region of >95%. As a cross check on relative rates calculated from these results some ratios were calculated indirectly by overlap with other competition experiments. The results are given in Table 3; the precision of the experiments is not great and the relative rates are judged accurate to ±15%. These error limits are assumed in the Figure, from which it is evident that, with the exception of the data for the *p*-chlorophenyl ether, a rough correlation between p$K_a$ and leaving group ability exists. The relative rates are, within the considerable experimental error, independent of potential. The results from tetrazolyl ether cleavage are therefore in line with those from other cathodic cleavage reactions, *i.e.* only within a closely related series of leaving groups is the leaving ability roughly and inversely related to basicity.



Relationship between rates of cleavage (relative to that for 5-phenoxy-1-phenyltetrazole) and Δp$K_a$ of the corresponding phenols

A possible reason for the rate of loss of *p*-chlorophenoxide ion being apparently slower than expected is that in a competing reaction chloride ion is lost. This would have the effect, in these experiments, of increasing the yield of phenol relative to *p*-chlorophenol, thereby lowering the measured relative rate. The loss of chlorine has been well established for cleavage of 5-(*p*-chlorophenoxy)-1-phenyltetrazole by catalytic hydrogenation.[6] For cathodic cleavage, however, it seems that chloride is not cleaved from the benzene ring; 4-chlorophenol is formed in high yield and furthermore chloride was not detected in the products of electrolysis of the *p*-chlorophenyl derivative carried out in DMF–$H_2O$ (5% v/v) with $Bu_4NClO_4$ (0.1M) at −2.5 V (*versus* s.c.e.).

## EXPERIMENTAL

Methods for the purification of solvents and the preparation of electrolytes have been described in previous papers in this series as has the electrochemical apparatus used for controlled potential electrolysis, cyclic voltammetry, and controlled potential coulometry. Cyclic voltammograms obtained at fast scan rates were stored and re-plotted using a Hi-Tek signal averager, model AA512.

1-Phenyltetrazol-5-yl ethers were prepared by Musliner and Gates' method.[6] Satisfactory m.p.s and spectroscopic data were obtained for known compounds; compounds not previously reported are included in Table 4 together with supporting physical and analytical data. An authentic sample of 1-phenyltetrazolone was obtained by hydrolysis of 5-phenoxy-1-phenyltetrazole in aqueous sodium hydroxide (1M).

TABLE 4

5-(Aryloxy)-1-phenyltetrazoles

| Compound | M.p. (°C) | Percentage composition. Found (calc.) C | H | N |
|---|---|---|---|---|
| (5) | 120—122 | 63.6<br>(63.85) | 3.4<br>(3.45) | 26.65<br>(26.6) |
| (8) | 90—93 | 60.2<br>(60.4) | 5.0<br>(4.7) | 19.15<br>(18.8) |
| (9) | 117—121 | 59.9<br>(60.4) | 4.7<br>(4.7) | 19.2<br>(18.8) |
| (10) | 124—125 | 67.25<br>(67.65) | 5.25<br>(5.25) | 21.0<br>(21.05) |
| (11) | 61—64 | 67.4<br>(67.65) | 5.5<br>(5.25) | 20.95<br>(21.05) |
| (12) | 117—118 | 58.4<br>(58.54) | 4.8<br>(4.9) | 17.05<br>(17.05) |
| (13) | 47—49 | 70.75<br>(70.8) | 6.95<br>(6.85) | 17.55<br>(17.4) |

*Controlled Potential Electrolysis and Product Analysis.*—Typically, electrolysis of the tetrazol-5-yl ether (0.001 mol) was carried out in DMF–$H_2O$ (5% v/v)–$Et_4NBr$ (0.1M) in a conventional H-cell (catholyte volume 50 cm$^3$) at a mercury pool cathode. Initial current densities were of the order of 0.007 A cm$^{-2}$ which dropped after 2 F mol$^{-2}$ to *ca.* 0.000 6 A cm$^{-2}$.

The electrolyte was poured into water (200 cm$^3$), the solution made alkaline (NaOH) and the hydrocarbon product extracted with ether. The phenolic product was isolated from the aqueous phase after acidification.

A portion of the neutralised electrolyte was also analysed by temperature-programmed g.l.c. (Hewlett–Packard 5830A with a methylated silicone column [OV101]). The use of internal standards and a knowledge of appropriate response factors enabled yields of both hydrocarbon and phenolic products to be calculated.

*Competitive Electrolyses.*—Electrolysis followed by g.l.c. analysis was carried out as described above except that a 1 : 1 mixture of two tetrazolyl ethers (0.005 mol of each) was used.

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