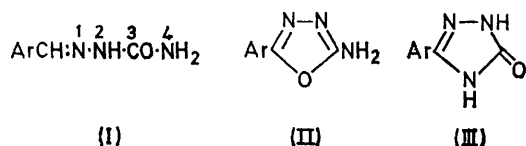


Anodic Oxidation of Organic Nitrogen Compounds. Part I. Cyclization of 1-Arylmethylenesemicarbazides

By Ole Hammerich and Vernon D. Parker,* Department of General and Organic Chemistry, The H. C. Ørsted Institute, University of Copenhagen, Universitetsparken 5, DK-2100 Copenhagen, Denmark

The anodic oxidation of a number of 1-arylmethylenesemicarbazides (I) has been examined in acetonitrile-acetic acid containing sulphuric acid. The reactions were very sensitive to the concentration of water; under ordinary conditions the oxadiazole being formed in high yield, while stringent exclusion of water by introducing acetic anhydride into the solvent system resulted in the formation of the corresponding triazolinones. Rapid-sweep cyclic voltammetry showed that the cyclizations are extremely rapid. The ease of oxidation of the compounds (I) was sensitive to the *para*-substituent in the aryl group, electron-donating groups facilitating oxidation in the expected manner.

CYCLIZATION of 1-arylmethylenesemicarbazides (I) has been achieved in several instances during bromination to yield either oxadiazoles (II) or triazolinones (III).^{1,2}



The latter have also been produced by oxidation by iron(III) chloride³ and the oxadiazoles by oxidation by lead tetra-acetate⁴ of 1-arylmethylenesemicarbazides. Pathways to compounds (II) and (III) have been discussed in a recent communication.⁵ In this paper we report the anodic oxidation of several 1-arylmethylenesemicarbazides which offers a new preparation of oxadiazoles (II) and triazolinones (III).

EXPERIMENTAL

The apparatus used for voltammetry was a multipurpose controlled potential unit designed and constructed in the laboratory of Professor W. White at the University of Kansas. The preparative experiments were carried out at constant current, using a modified Danica-Elektronik power supply type TPS Id. The technique of constant current coulometry and macro-scale electrolysis has been described earlier.⁶ All reactions were carried out at a platinum gauze electrode and potential measurements were made relative to the saturated calomel electrode.

Semicarbazides, oxadiazoles, and triazolinones were all prepared by standard literature procedures and the structures were verified by mass, i.r., and ¹H n.m.r. spectral analysis. The ¹H n.m.r. spectra were especially useful in distinguishing between oxadiazoles and triazolinones. In [²H₆]dimethyl sulphoxide, signals for the amino-protons of the oxadiazoles appears at δ ca. 7.1 p.p.m. and those for the imino-proton of the triazolinones appears at δ ca. 11.5 p.p.m. †

2-Amino-5-*p*-methoxyphenyl-1,3,4-oxadiazole.—1-(*p*-Methoxybenzylidene) semicarbazide (Id) (0.97 g, 5 mmol) was dissolved in a solution of acetic acid (47.5 ml) and sulphuric acid (2.5 ml). Constant-current electrolysis was carried

† This observation was made by Dr. U. Svanholm of this laboratory.

‡ The electrochemical yield of this reaction is ca. 100%. No attempt was made to optimize the work-up procedure.

¹ M. S. Gibson, *Tetrahedron*, 1962, **18**, 1377.

² F. Maggio, G. Werber, and G. Lombardo, *Ann. Chim. Italy*, 1960, **50**, 491.

out at 200 mA until 2.0 Faraday mol⁻¹ had passed. The solution was concentrated on a rotary evaporator to ca. 20 ml and then poured into saturated aqueous sodium carbonate (200 ml). The oxadiazole (85%) precipitated out of solution.

3-*p*-Methoxyphenyl- Δ^2 -1,2,4-triazolin-5-one.—1-(*p*-Methoxybenzylidene)semicarbazide (Id) (0.77 g, 4 mmol) was dissolved in a solution of acetic acid (42.5 ml), acetic anhydride (5.0 ml), and sulphuric acid (2.5 ml). Constant-current electrolysis was carried out at 200 mA for 1 h. The mixture was extracted with dichloromethane (3 \times 50 ml). The extracts were washed several times with concentrated sodium carbonate solution and then several more times with water. After drying (MgSO₄), the solvent was removed under reduced pressure leaving the triazolinone (45%). ‡

The other semicarbazides were oxidized similarly.

RESULTS

Voltammetric and coulometric data for the anodic oxidation of several arylmethylenesemicarbazides appear in the Table. The ease of oxidation was found to be

Voltammetric and coulometric data for oxidation of arylmethylenesemicarbazides (I)

Compound	Ar	σ_p^+	$E_p^{a,b}$	$E_p^{a,c}$
(Ia)	<i>p</i> -ClC ₆ H ₄	+0.11	1.50	1.56
(Ib)	Ph	0	1.46	1.54
(Ic)	<i>p</i> -MeC ₆ H ₄	-0.31	1.37	1.41
(Id)	<i>p</i> -MeO·C ₆ H ₄	-0.78	1.28	1.24
(Ie)	<i>p</i> -Me ₂ N·C ₆ H ₄	-1.7	0.93	<i>d</i>

^a Volts *versus* the standard calomel electrode. ^b Oxidation at a platinum electrode in acetonitrile-acetic acid (4 : 1) containing sodium perchlorate (0.1M) at a voltage sweep rate of 150 mV s⁻¹. ^c Oxidation at a platinum electrode in acetic acid-sulphuric acid (95 : 5) at a voltage sweep rate of 150 mV s⁻¹. ^d The compound is protonated in this solvent system and does not give a well-defined wave.

markedly dependent on the nature of the *para*-substituent in the aryl group. The value of the oxidation peak potential decreased steadily in changing from electron-withdrawing to the highly electron-donating *p*-dimethylamino-group in a manner consistent with the value of σ_p^+ for the *para*-substituent.⁷ The peak currents, on the other hand, were very similar, corresponding to transfer

³ E. Hoggarth, *J. Chem. Soc.*, 1949, 1918.

⁴ T. M. Lambe, R. N. Butler, and F. L. Scott, *Chem. and Ind.*, 1971, 996.

⁵ F. L. Scott, T. M. Lambe, and R. N. Butler, *Tetrahedron Letters*, 1971, 2669.

⁶ V. D. Parker, *Acta Chem. Scand.*, 1970, **24**, 2768.

⁷ H. Van Bekkum, B. E. Verkade, and B. M. Wepster, *Rec. trav. chim.*, 1959, **78**, 821.

of two electrons for all compounds. Coulometric n values for all compounds were very close to 2.

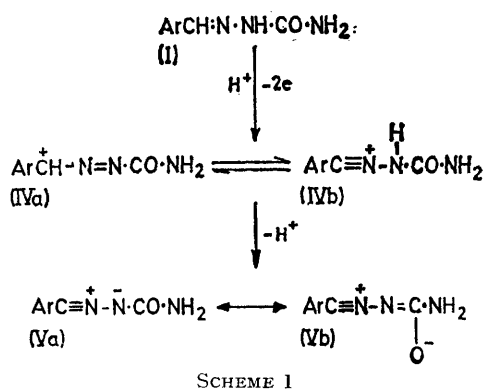
The voltammetry for (Id) is typical for compounds (Ia—d). In acetic acid-sulphuric acid (95:5), the peak voltammogram showed an oxidation peak at +1.24 V along with two additional peaks at +1.50 and +1.92 V. In acetic acid-acetic anhydride-sulphuric acid (85:10:5), however, the first peak was observed at +1.41 V and two other peaks at +1.71 and +1.89 V. The corresponding oxadiazole showed peaks in the first solvent system corresponding to the second two peaks while the authentic triazolinone in the latter system gave peaks again at +1.71 and +1.89 V. At much higher voltage sweep rates (150 V s⁻¹), there was no disappearance of the peaks due to either the oxadiazole or the triazolinone, indicating that these products are formed in very rapid reactions following electron transfer. This is also borne out by the fact that cyclic voltammetry failed to show any reduction peaks due to primary electrode products.

The voltammetry of (Ie) was exceptional. In acetonitrile-acetic acid (4:1), a single 2e-oxidation peak was observed at +0.93 V and on the cathodic sweep, a corresponding 2e-reduction peak was observed at +0.77 V. The ratio of anodic to cathodic peak currents was very close to 1 indicating that the initial oxidation product is stable during the time scale of cyclic voltammetry. The 2-methyl derivative, *p*-Me₂N·C₆H₄·C=N·NMe·CO·NH₂, gave very different results. In this case, a reversible 1e-oxidation peak was observed at +0.8 V in the same solvent system.

The products obtained from the anodic oxidation of (Ia—d) were as expected. When acetic anhydride was not included in the reaction medium in order to reduce the water content, the product was always the oxadiazole. The same reactions carried out in the presence of acetic anhydride produced only the triazolinones. We did not observe mixtures of products under either set of conditions. Difficulty was encountered during attempts to purify products from the *p*-dimethylamino-compound (Ie), however spectral data from the impure products indicate that the same type of products are produced depending on the conditions.

DISCUSSION

Two-electron oxidation of an arylmethylenesemicarbazide (I) would be expected to generate a cation (IV) capable of undergoing internal attack by either oxygen

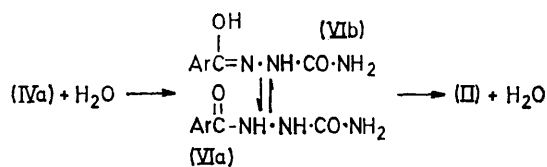


SCHEME 1

or nitrogen to yield the oxadiazole (II) or the triazolinone (III), respectively (see Scheme 1). Deprotonation of

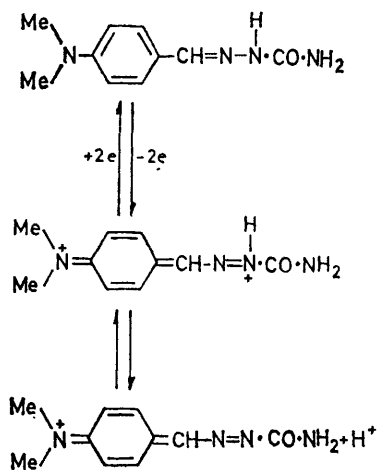
(IV) could occur giving rise to the formation of the dipolar ion (V). Contribution of structure (Vb) should enhance cyclization through oxygen and formation of oxadiazole (II) as has been postulated by Scott and co-workers.⁵ However, under acidic conditions formation of the dipolar ion (V) would be depressed and the reactive intermediate would be expected to be (IV). Attack by nitrogen would be expected to be favoured in view of the greater tendency of nitrogen to stabilize a positive charge in the transition state. Furthermore, alkylation of semicarbazones gives *N*- rather than *O*-alkylated products, which shows that the terminal nitrogen is indeed the most nucleophilic site in the semicarbazone molecule.

An alternative pathway, which might be expected to favour the formation of the *O*-cyclized product is attack on (IVa) by water to give the aroylsemicarbazide (VI) (see Scheme 2). Cyclization of the enolic form (VIb) could conceivably generate the oxadiazole (II).



SCHEME 2

Under our conditions oxadiazoles were the observed products, unless water was kept at a very low concentration by introducing acetic anhydride in the solvent system. Since we worked under strongly acidic conditions, the effect of water cannot be that of a base acting on the cation (IV) to generate the dipolar ion (V). Thus, the mechanism proposed by Scott⁵ to account



SCHEME 3

for oxadiazole formation appears to be somewhat dubious. The suggestion that, when the 2-methyl compound was subjected to conditions under which the parent compound produced oxadiazole, the formation of triazolinones was support of their mechanism is

equally dubious since the 2-methyl compound is structurally incapable of forming an oxadiazole. The role of low concentrations of water in diverting the product from 100% triazolinone to 100% oxadiazole could be due to nucleophilic attack as in Scheme 2.

The fact that the oxidation potentials of the arylmethylenesemicarbazides give a very nearly linear relationship to the σ_p^+ constants shows that the ability of the *para*-substituents to stabilize the positive charge of the initial oxidation product is an important feature in the oxidation. Cyclic voltammetry provided direct evidence for cation (IV) when the substrate was (Ie). The nearly reversible two-electron oxidation most likely corresponds to the reactions in Scheme 3. This is sup-

ported by the fact that the 2-methyl derivative of (Ie), which cannot deprotonate to give a mono-cation, undergoes one-electron oxidation. Of course our data does not establish the sequence of electron and proton loss in going from the semicarbazides to the cations (IV).

In conclusion, the anodic oxidation of arylmethylenesemicarbazides provides a convenient preparative route to either oxadiazoles or triazolinones depending on the conditions selected for the reaction. The role of small amounts of water in precluding the formation of triazolinones remains unsettled although the possible role as a base to produce the dipolar ion (V) can be ruled out.

[2/388 Received, 21st February, 1972]