Electrochemical Oxidation of 1-Phenylpyrazolidin-3-ones. Part 1. 4- and 5-Substituted 1-Phenylpyrazolidin-3-ones

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The electrochemical oxidation of 4-methyl-, 5-phenyl-, and 4-hydroxymethyl-4-methyl-1-phenylpyrazolidin-3-one in acetonitrile has been studied. All three systems behave in a manner similar to that of the parent 1-phenylpyrazolidin-3-one, the major reaction pathway involving formation of a 1-phenylpyrazolin-3-one.

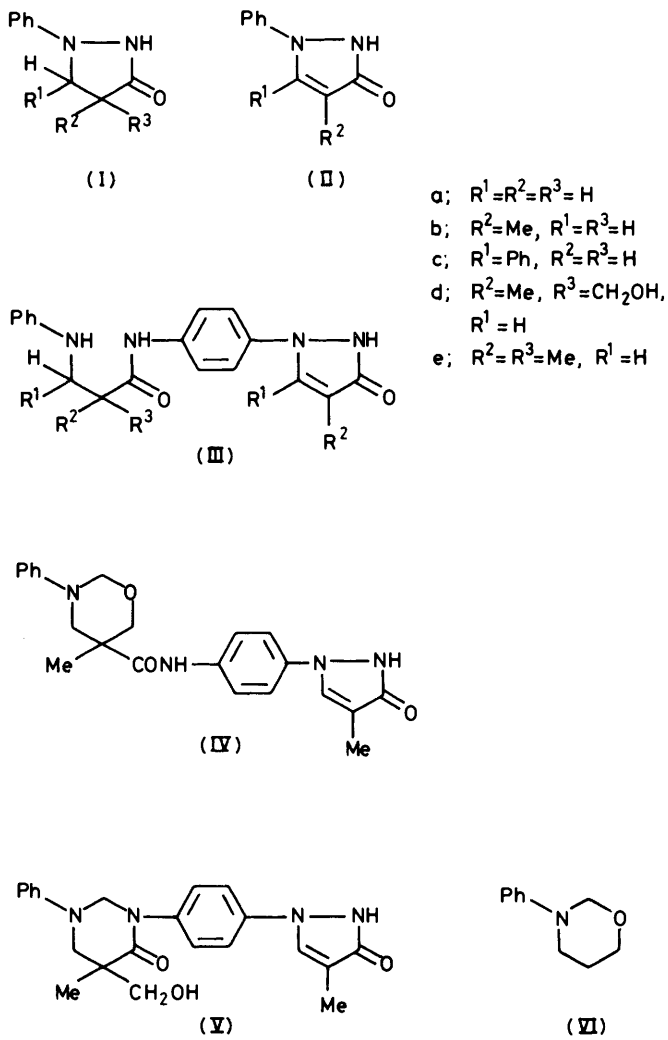
1-Phenylpyrazolidin-3-one and various substituted 1-phenylpyrazolidin-3-ones are used as photographic, superadditive developing agents in aqueous-based developing systems,[1] and as primary developing agents in ' dry ' (non-aqueous) photographic systems.[2] Since the pyrazolidinones function as reducing agents in developing systems, there has been considerable interest in the electrochemical oxidation of these systems both in aqueous alkaline [3] and non-aqueous media.[4] The previous electrochemical studies in non-aqueous media were concerned solely with the behaviour of the parent system, 1-phenylpyrazolidin-3-one (Ia), in Et_4NClO_4–CH_3CN,[4a] and in Et_4NCl–CH_3CN.[4b] The present paper extends these studies to some 4- and 5-substituted 1-phenylpyrazolidin-3-ones (Ib–d).

Results and Discussion

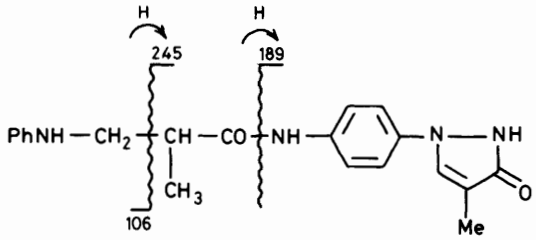
The controlled-potential electro-oxidation of 1-phenylpyrazolidin-3-one (Ia) in acetonitrile containing Et_4NClO_4 as the electrolyte gives two products, 1-phenylpyrazolin-3-one (IIa) (75%) and 3-anilino-*N*-[4-(3-oxopyrazolin-1-yl)phenyl]-propionamide (IIIa) (20%),[3a] but when Et_4NCl is the electrolyte only the pyrazolinone (IIa) is produced.[3b] As reported below, this behaviour appears to be general for 1-phenylpyrazolidin-3-ones (I) which have an R^3 group which is readily eliminated, *viz.* R^3 = H for (Ia—c) and R^3 = CH_2OH for (Id).

4-Methyl-1-phenylpyrazolidin-3-one (Ib).—The electro-oxidation of (Ib) in acetonitrile containing Et_4NBF_4 gave 4-methyl-1-phenylpyrazolin-3-one (IIb) † as the major product and 3-anilino-2-methyl-*N*-[4-(4-methyl-3-oxopyrazolin-1-yl)-phenyl]propionamide (IIIb) as the minor product. When Et_4NCl was the electrolyte, only (IIb) was produced.

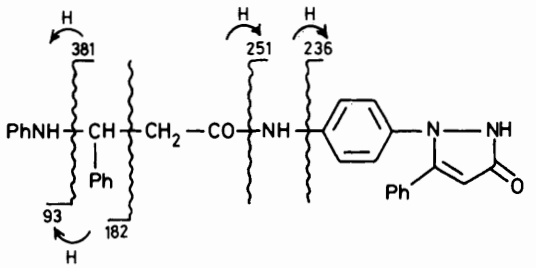
The structure of (IIIb) was assigned by spectroscopic analysis following the method used for (IIIa). A molecular formula of $C_{20}H_{22}N_4O_2$ was indicated by both the elemental analysis and the parent ion in the mass spectrum (*m/e* 350). The 100 MHz ^1H n.m.r. spectrum ([$^2H_6$]DMSO) showed the following main features consistent with structure (IIIb): a monosubstituted benzene ring (δ 6.4—7.2) and a *p*-disubstituted benzene ring (AA'BB' pattern centred at δ 7.59), methyl and olefinic absorptions at δ 1.93 and 7.75, respectively (both singlets), in perfect agreement with the corresponding absorptions for (IIb), a further methyl absorption at δ 1.22, coupled to a saturated methylene proton (*J* 6 Hz) (the methyne and methylene absorptions were obscured by the H_2O absorption in the solvent), and exchangeable proton absorptions at δ 9.67 and 9.45—10.0. The i.r. spectrum (Nujol mull) showed absorbance at 3 430 (NH secondary amide), 3 300 (NH secondary amine), 2 730 (hydrogen-bonded OH, pyrazolin-3-ones exist in the enol form in the crystalline state [5]), and 1 660 cm^{-1} (amide C=O). The fragmentation pattern observed in the mass spectrum paralleled that observed for (IIIa),[4a] with the main peaks occurring at *m/e* 245 (*M* − C_7H_7N), 189 (*M* − $C_{10}H_{11}NO$), and 106 (C_7H_8N) (see Scheme 1).



† Authentic samples of (IIa—c) were prepared by chemical oxidation ($FeCl_3$ or *p*-benzoquinone) of the corresponding (I).



Scheme 1



Scheme 2

^{13}C N.m.r. spectra [a] of (IV), (VI), (IIb), and (Id)

	(IV)	(VI)	(IIb)	(Id)
$-C(CH_3)=$	7.10		7.12	
$-CH=$	103.00		103.51	
$-C(CH_3)=$	126.40		126.59	
Pyrazolinone C=O	161.34		161.63	
$-CONH-$	172.50			176.45
CH_3-C	42.41			47.00
CH_3-C	19.87			19.16
$-CH_2-O$	72.99	67.39		
$-CH_2-N$	55.31	48.15		
$N-CH_2-O$	80.53	80.77		
C_6H_5-N	148.44	148.69		
	129.11	128.96		
	119.66	119.30		
	116.39	117.07		
	or			
	116.59			
$N-C_6H_4-N$	135.95			
	135.07			
	121.35			
	116.39			
	or			
	116.59			

[a] In [$^2H_6$]DMSO; δ p.p.m. from Me_4Si.

1,5-*Diphenylpyrazolidin*-3-*one* (Ic).—The electro-oxidation of (Ic) in acetonitrile containing Et_4NBF_4 gave 1,5-diphenylpyrazolin-3-one (IIc) as the major product, and 3-anilino-3-phenyl-*N*-[4-(5-phenyl-3-oxopyrazolin-1-yl)phenyl]propionamide (IIIc) as the minor product. When Et_4NCl was the electrolyte, only (IIc) was produced.

The structure of (IIIc) was assigned in a manner similar to those of (IIIa and b). Exact mass determination of the parent ion (*m/e* 474) in the mass spectrum gave the molecular formula as $C_{30}H_{26}N_4O_2$. The 100 MHz ^{1}H n.m.r. spectrum ([$^2H_6$]DMSO) was poorly resolved but the 360 MHz spectrum clearly showed the following features consistent with the structure (IIIc): two non-equivalent methylene protons [δ 2.88 and 3.00 (J_{gem} 14.5 Hz)], both coupled to a methyne proton (δ 5.02) with J 6.0 and 7.9 Hz respectively, an olefinic proton [δ 6.00 (s)], and exchangeable proton absorptions at δ 5.96 and 9.84. The aromatic proton absorptions appeared as a multiplet at δ 6.61—7.61. The i.r. spectrum (Nujol mull) showed absorbance at 3 320 NH (secondary amine), 2 580 (hydrogen-bonded OH), and 1 665 cm^{-1} (amide C=O). The fragmentation pattern in the mass spectrum paralleled those observed for (IIIa and b). The principal peaks were at *m/e* 381 ($M - C_6H_7N$), 251 ($M - C_{15}H_{13}NO$), 236 ($M - C_{15}H_{14}N_2O$), 182 (PhNHCHPh), and 93 ($PhNH_2$) (see Scheme 2).

4-*Hydroxymethyl*-4-*methyl*-1-*phenylpyrazolidin*-3-*one* (Id).—The electro-oxidation of (Id) followed a similar course to that observed for (Ia—c), except that the CH_2OH group at C(4) was eliminated instead of H. Thus oxidation in acetonitrile containing Et_4NBF_4 gave 4-methyl-1-phenylpyrazolin-3-one (IIb) as the major product and a 'dimer' as the minor product. When Et_4NCl was the electrolyte only (IIb) was produced.

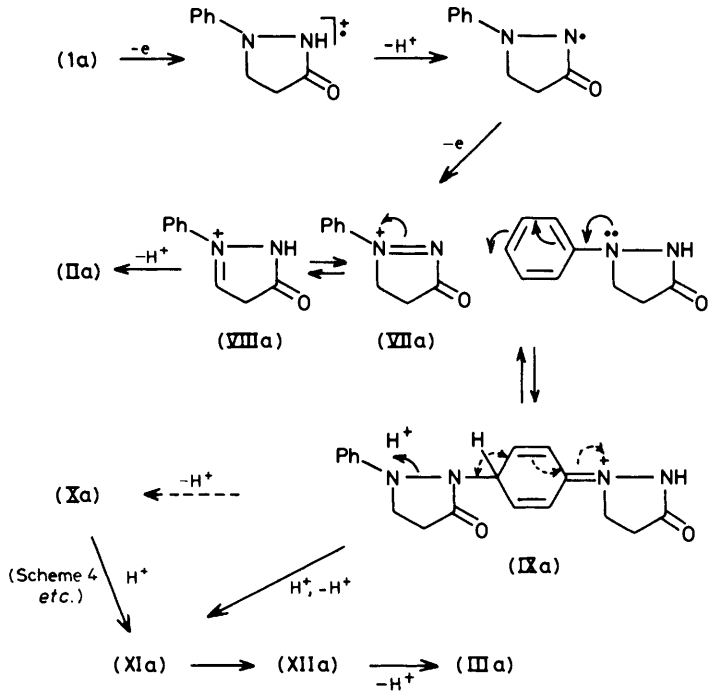
The structure of the 'dimer' was not quite what was expected on the basis of the previous examples, namely (IIId), but appeared to be formed from it by Mannich reaction with the formaldehyde eliminated during the formation of the major product (IIb). On the basis of the spectroscopic and chemical evidence we have assigned the structure as (IV). This is related to (IIId) by the insertion of a methylene group (from HCHO) between the amine nitrogen and the hydroxy oxygen in (IIId).

Elemental analysis and exact mass determination of the parent ion (*m/e* 392) in the mass spectrum of the 'dimer' indicated a molecular formula of $C_{22}H_{24}N_4O_3$. The ^{1}H n.m.r. spectrum ([$^2H_6$]DMSO) showed the following features: four methylene protons, giving characteristic AB doublets of non-equivalent geminal protons, at chemical shifts typical of methylene groups attached to a single heteroatom [δ 3.47, 3.66, 3.92, and 4.22 (J_{gem} 12 and 13 Hz)], a further broad AB system at a chemical shift typical of a methylene group between two heteroatoms [δ 4.82, J_{gem} *ca.* 10 Hz)], an uncoupled methyl group attached to saturated carbon (δ 1.16), a 4-methyl-1-phenylpyrazolin-3-one moiety characterised by singlet methyl (δ 1.90) and olefinic proton (δ 7.90) absorptions [*cf.* (IIIb)], and two exchangeable protons at δ 9.36 and 10.02. The i.r. spectrum (Nujol mull) showed absorbance at 3 340 (NH secondary amide), 2 720, 2 620 (hydrogen-bonded OH), and 1 665 cm^{-1} (amide C=O).

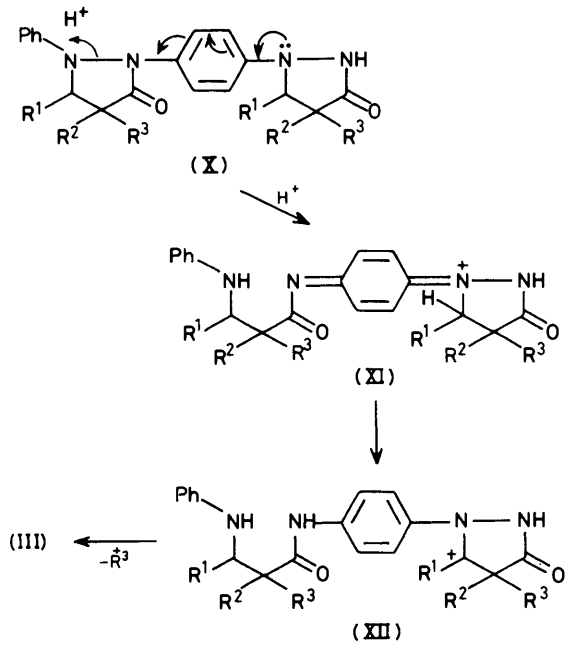
The alternative structure (V), related to (IIId) by the insertion of a methylene group between the amine and amide nitrogen atoms in (IIId), is also reasonably consistent with the above evidence, but the exact correspondence between the methylene proton absorption at δ 4.82 for the 'dimer' and that for C(2) in tetrahydro-3-phenyl-1,3-oxazine (VI), and the excellent correlation between the ^{13}C resonances for the 'dimer' and those of (VI), (IIb), and (Id) (see Table) argues convincingly that (IV) rather than (V) is the correct structure. [The mass spectroscopic fragmentation pattern did not differentiate clearly between the two possible structures (IV) and (V).]

Further support for structure (IV) was obtained by treating 3-anilinopropan-1-ol and *N*-phenyl 3-anilinopropionamide, as models for the various parts of (IIId), with formaldehyde. While the former condensed readily, under conditions very similar to those of the electrolysis, to give (VI), the latter could not be induced to condense even under rather forcing conditions.

Mechanism.—Since an electroanalytical study of the electro-oxidation of 1-phenylpyrazolidin-3-ones will be



Scheme 3



Scheme 4

reported in Part 3,[6] a full discussion of the mechanism of formation of the 1-phenylpyrazolin-3-ones will not be given here. It is sufficient to say that the pyrazolinones are probably formed by elimination of H^+ [for (Ia—c)] or HCHO and H^+ [for (Id)] from the intermediate cation (VIII) [see Scheme 3 for the specific case of (Ia)].

In attempting to rationalise the formation of the ' dimers ' in Et_4NBF_4–CH_3CN it is important to note that the formation of (IIIa) from (Ia) does not commence until the electrolysis is 15% complete,[4a] and that these products are not formed when Et_4NCl is the electrolyte. Both observations suggest that an acidic medium is a prerequisite for the formation of these products; Cl^- acts as a base in acetonitrile (HCl is 99% associated)[7] and the medium is prevented from becoming acidic as the electrolysis proceeds if Et_4NCl is present. On the basis of these and other observations the previous workers proposed[4a] a mechanism which involves the formation and subsequent rearrangement of the dimer (X); Scheme 4 is an adaptation of their mechanism to the more general case considered here.

If this mechanism is correct then there is no reason why those 1-phenylpyrazolidin-3-ones which do not possess a readily eliminated group at C(4), *e.g.* (Ie), should not proceed along the pathway as far as (XII), particularly as the route to the pyrazolinone is blocked. However, electrolysis of two systems of this type under similar conditions gave extremely complex product mixtures [h.p.l.c. analysis indicated >24 products from (Ie), none of which could be isolated and characterised].[8] In view of this, the lack of direct evidence for the formation and subsequent reaction of the intermediate dimers, *e.g.* h.p.l.c. analysis of samples taken during the electrolysis of (Ib) failed to detect any products other than (IIb) and (IIIb), and the fact that dimers of type (III) are only isolated from pyrazolidinones which are readily oxidised to pyrazolinones, we considered other possible, but perhaps less probable, mechanisms for the formation of (III) which involve reaction between (I) and (II) at some intermediate stage in the electrolysis. The formation of (II) thus becomes a prerequisite for the formation of (III).

In order to test this possibility, a mixture of (Ib) and (IIa) was electrolysed in Et_4NBF_4–CH_3CN; this should give a ' crossed dimer ' as well as (IIIb) if ' dimer ' formation is occurring *via* the pyrazolinone. However, h.p.l.c. analysis of the product mixture detected only (IIb), (IIIb), and unchanged (IIa). We therefore conclude that ' dimer ' formation does *not* occur *via* the pyrazolinone (II), and that the pyrazolinone ring in the ' dimer ' is probably formed after the initial dimerisation has occurred, as originally proposed.[4a]

An observation which is pertinent to the above discussion is that the presence of an *N*-methyl group at position 2 in (Ia) causes the reversible cyclic voltammetric peak potential ($E_{p,a}$) to appear at 0.530 V (*versus* Ag–0.1M-$AgNO_3$ in CH_3CN), an anodic shift of 0.28 V, and the oxidation–reduction system to become reversible even at low sweep rates [0.1 V s^{-1}; (Ia) shows reversibility above 2.5 V s^{-1}].[6] This indicates that the chemical reaction following initial electron transfer from (Ia) is loss of H^+ from position 2 to give a radical, and suggests the mechanism shown in Scheme 3 for the formation of the primary ' dimer '. Further oxidation (heterogeneous or homogeneous) of the radical would give the cation (VIIa), which could then electrophilically substitute into the phenyl group of the parent pyrazolidinone and thus lead to (IIIa). The transformation of the primary ' dimer ' (IXa) to (XIa) by either of the routes shown would be acid catalysed. This revised mechanism differs from that originally proposed[4a] in the detailed manner in which the intermediate (XIa) is formed. The cation (VIIa) could also be involved in the formation of the major product (IIa), *via* a deprotonation–protonation isomerisation to the cation (VIIIa). While Scheme 3 is given for the specific case of (Ia), it is assumed that it would be applicable to (Ib—d) also.

Experimental

Chemicals.—The 1-phenylpyrazolidin-3-ones (Ia, b, and d) were supplied by Eastman Kodak Ltd. Compound (Ic) was prepared according to a literature procedure[9] and had m.p. 160—161 °C (lit.,[9] 159 °C). Tetraethylammonium chloride was

supplied as the monohydrate; the anhydrous salt was obtained by storing over P_2O_5 *in vacuo* for 7 days.

Acetonitrile (Fisons SLR grade) was purified by treatment with potassium permanaganate and sodium carbonate, followed by distillation.[10]

Samples of the 1-phenylpyrazolin-3-ones (IIa—c) were prepared by chemical oxidation [iron(III) chloride or *p*-benzoquinone] in water of the corresponding pyrazolidin-3-ones. Compound (IIa) had m.p. 151—153 °C (from water) (lit.,[11] 154 °C), (IIb) had m.p. 207—210 °C (from ethanol) (lit.,[12] 210 °C), and (IIc) had m.p. 256—257 °C (from DMF–methanol) (lit.,[13] 252 °C).

H.p.l.c. analyses were performed using 100 × 5 mm columns packed with Hypersil (5 μm). The eluant was either ethyl acetate (50% water saturated), or ethanol (10—15%)–hexane containing 0.3% water.

Electrolyses.—Preparative controlled-potential electrolyses were performed in a divided cell (two concentric glass cylinders, the inner cylinder being the cathodic compartment and separated by a sintered glass disc at its base from the outer anodic compartment), using a cylindrical platinum wire gauze as the working electrode, a platinum sheet as the secondary electrode, and an Ag–0.1M-$AgNO_3$ in acetonitrile reference electrode.

Electrolysis of 4-*Methyl*-1-*phenylpyrazolidin*-3-*one* (Ib).—(a) Et_4NCl *electrolyte*. Oxidation of (Ib) (1.76 g, 0.01 mol) at +0.3 V in 0.085M-Et_4NCl in acetonitrile (100 ml) was terminated after 1.5 F mol^{-1} had passed. The anodic solution was concentrated to *ca.* 10 ml by rotary evaporation and then poured into water (200 ml). A solid separated which was filtered off, washed with light petroleum (b.p. 40—60 °C), and dried. This was shown by h.p.l.c. to be pure 4-methyl-1-phenylpyrazolin-3-one (IIb). After recrystallisation from ethanol it had m.p. 210—212 °C (lit.,[12] 210 °C); δ (100 MHz; $CDCl_3$) 1.94 (s, CH_3), 7.01—7.75 (m, Ph), and 8.00 (s, =CH); $\nu_{max.}$ (film) 2 620 (w) and 2 720 (w) (H-bonded OH) cm^{-1}; *m/e* 174 (*M*).

(b) Et_4NBF_4 *electrolyte*. Oxidation of (Ib) (0.01 mol) at +0.6 V in 0.1M-Et_4NBF_4 in acetonitrile (100 ml) was terminated after 1.0 F mol^{-1} had passed. The anodic solution was concentrated to *ca.* 30 ml and then poured into water (200 ml). The resulting mixture was neutralised with sodium carbonate and then extracted with ethyl acetate (6 × 25 ml). Distillation of the solvent from the combined extracts gave a red oil, which was dissolved in the minimum amount of hot methanol and poured into water (150 ml). A solid (0.50 g) was precipitated; this was filtered off and dried. Chromatography on silica gel grade III (50 × 2.5 cm) gave two major products, 4-methyl-1-phenylpyrazolin-3-one (IIb) (0.10 g), m.p. 208—210 °C, which was eluted with light petroleum (b.p. 40—60 °C)–ethyl acetate (4 : 1) and 3-*anilino*-2-*methyl*-N-[4-(4-*methyl*-3-*oxopyrazolin*-1-*yl*)*phenyl*]*propionamide* (IIIb) (0.10 g), m.p. 223—226 °C (from methanol–water) (Found: C, 68.75; H, 6.2; N, 16.2. $C_{20}H_{22}N_4O_2$ requires C, 68.55; H, 6.35; N, 16.0%), which was eluted with light petroleum (b.p. 40—60 °C)–ethyl acetate (3 : 2).

A quantitative h.p.l.c. analysis of an electrolysis mixture, terminated after 1.2 F mol^{-1} had passed, indicated that the material yields of (IIb) and (IIIb) were 28 and 19%, respectively (current yields 47 and 16%, respectively).

Electrolysis of 1,5-*Diphenylpyrazolidin*-3-*one* (Ic).—(a) Et_4NCl *electrolyte*. Oxidation of (Ic) (1.18 g, 0.005 mol) at +0.3 V in 0.068M-Et_4NCl in acetonitrile (50 ml) was terminated after 1.5 F mol^{-1} has passed. The anodic solution was evaporated to dryness and the solid residue was recrystallised from ethanol to give 1,5-diphenylpyrazolin-3-one (IIc) (0.71 g, 60% yield, 80% current yield), m.p. 248—250 °C (lit.,[13] 252 °C), δ (60 MHz; [$^2H_6$]DMSO) 6.07 (s, 1 H), and 6.85—7 90 (m, 10 H); $\nu_{max.}$ (Nujol) 2 580 (m, H-bonded OH) cm^{-1}.

(b) Et_4NBF_4 *electrolyte*. Oxidation of (Ic) (0.005 mol) at +0.6 V in 0.1M-Et_4NBF_4 in acetonitrile (50 ml) was terminated after 1.2 F mol^{-1}. The anodic solution was concentrated to *ca.* 5 ml, water (50 ml) was added, and the mixture was extracted with ethyl acetate (6 × 10 ml). After drying ($MgSO_4$), the combined extracts were concentrated and chromatographed on silica gel grade III (50 × 2.5 cm). Elution with light petroleum (b.p. 40—60 °C)–ethyl acetate (7 : 3) gave 1,5-diphenylpyrazolin-3-one (IIc) (0.15 g, 12%), m.p. 248—250 °C. Elution with methanol gave a red tar (0.50 g) which was rechromatographed. Elution with chloroform gave a red oil (0.081 g) which solidified on trituration with ether. The solid (0.050 g, m.p. 141—151 °C), was recrystallised from a mixture of tetrahydrofuran, toluene, and hexane to give 3-*anilino*-3-*phenyl*-N-[4-(5-*phenyl*-3-*oxopyrazolin*-1-*yl*)-*phenyl*]*propionamide* (IIIc) (38 mg) (Found: *m/e* 474.205 408. $C_{30}H_{26}N_4O_2$ requires *M*, 474.205 564).

Electrolysis of 4-*Hydroxymethyl*-4-*methyl*-1-*phenylpyrazolidin*-3-*one* (Id).—(a) Et_4NCl *electrolyte*. Oxidation of (Id) (1.06 g, 0.005 mol) at +0.3 V in 0.086M-Et_4NCl in acetonitrile (50 ml) was terminated after 1.0 F mol^{-1} had passed. A solid was isolated by the usual work-up procedure; this was shown by h.p.l.c. to be pure 4-methyl-1-phenylpyrazolin-3-one (IIb).

(b) Et_4NBF_4 *electrolyte*. Oxidation of (Id) (0.01 mol) at +0.6 V in 0.1M-Et_4NBF_4 in acetonitrile (100 ml) was terminated after 1.4 F mol^{-1}. After concentrating the anodic solution to *ca.* 5 ml, it was poured into water (200 ml). The off-white solid (1.32 g) which separated was filtered off and chromatographed on silica gel grade III (100 × 2.5 cm). Elution with light petroleum (b.p. 40—60 °C)–ethyl acetate (7 : 3) gave 4-methyl-1-phenylpyrazolin-3-one (IIb) (0.30 g, 17%), m.p. 207—209 °C. Elution with light petroleum (b.p. 40—60 °C)–ethyl acetate (2 : 3) gave 1-(5-*methyl*-3-*phenyltetrahydro*-1,3-*oxazin*-5-*yl*)-N-[4-(4-*methyl*-3-*oxopyrazolin*-1-*yl*)*phenyl*]*formamide* (IV) (0.31 g, 16%), m.p. 172—174 °C (Found: *m/e*, 392.183. 964. $C_{22}H_{24}N_4O_3$ requires *M*, 392.184 829).

Electrolysis of 4-*Methyl*-1-*phenylpyrazolidin*-3-*one* (Ib) *in the Presence of* 1-*Phenylpyrazolin*-3-*one* (IIa).—Oxidation of a mixture of (Ib) (0.002 mol) and (IIa) (0.002 mol) at +0.6 V in 0.2M-Et_4NBF_4 in acetonitrile (50 ml) was terminated after 1.42 F mol^{-1} of (Ib) had passed. The product mixture was isolated and chromatographed following the procedure used for the oxidation of (Ib) alone. Elution with light petroleum (b.p. 40—60 °C)–ethyl acetate (4 : 1) gave a solid (0.86 g) which was shown by h.p.l.c. analysis to be a mixture of (IIa and b). Elution with light petroleum (b.p. 40—60 °C)–ethyl acetate (3 : 2) gave (IIIb) (0.10 g), m.p. 225—227 °C. No ' crossed dimer ' was observed.

Attempted Acid-catalysed Reaction of 1-*Phenylpyrazolidin*-3-*one* (Ia) *with* 1-*Phenylpyrazolin*-3-*one* (IIa).—Compound (Ia) (0.006 mol) was added to (IIa) (0.006 mol) in acetonitrile (50 ml), and 2 ml of the solution was removed as a control sample. 60% Aqueous perchloric acid (1.00 g, 0.0062 mol) was added to the remaining solution and further 2 ml samples were removed at 0.5, 5, and 72 h. Rotary evaporation of each sample and examination by ^1H n.m.r. spectroscopy ([$^2H_6$]-DMSO) indicated that no reaction had occurred.

3-*Anilinopropan*-1-*ol*.—3-Chloropropan-1-ol was treated with aniline in water at 140 °C following a published procedure.[14] The resulting 3-anilinopropan-1-ol (10.6 g, 56%) had b.p. 128—135 °C at 1 mmHg; δ (60 MHz; CCl_4) 1.26—1.85 (m, $CH_2CH_2CH_2$), 2.96 (t, *J* 7 Hz, $CH_2CH_2CH_2$), 3.48 (t, *J* 7 Hz, $CH_2CH_2CH_2$), 4.00br (s, OH and NH), and 6.19—7.28 (m, Ph).

N-*Phenyl*-3-*anilinopropionamide*.—Acrylic acid was treated with aniline according to a published procedure.[15] *N*-Phenyl-3-anilinopropionamide (33%) had m.p. 89—91 °C (lit.,[15] 91—93 °C); δ (100 MHz; CD_3CN) 2.58 (t, *J* 6 Hz, CH_2CH_2), 3.41 (t, *J* 6 Hz, CH_2CH_2), 4.37br (s, NH), 6.50—7.66 (m, 2 × Ph), and 8.48br (s, NH); $\nu_{max.}$ (Nujol) 3 380 (w, NH), 3 300 (m, NH), and 1 660 cm^{-1} (s, CONH); *m/e* 240 (*M*) (Found: C, 75.25; H, 6.55; N, 11.85. Calc. for $C_{15}H_{16}N_2O$: C, 75.0; H, 6.65; N, 11.65%).

Tetrahydro-3-*phenyl*-1,3-*oxazine* (VI).[14]—3-Aminopropan-1-ol (4.0 g) was stirred with an excess of 40% aqueous formaldehyde solution during 72 h. The solution was extracted three times with ether, and the combined extracts were concentrated and distilled to give the oxazine (2.8 g, 70%), b.p. 82—85 °C at 0.4 mmHg; δ (60 MHz; [$^2H_6$]DMSO) 1.38—1.85 (m, $CH_2CH_2CH_2$), 3.54 (t, *J* 5 Hz, $CH_2CH_2CH_2$), 3.86 (t, *J* 5 Hz, $CH_2CH_2CH_2$), 4.86br (s, OCH_2N), and 6.63—7.47 (m, Ph).

3-Aminopropan-1-ol (1.0 g) in acetonitrile (25 ml) also reacted with formaldehyde (37% aqueous solution, 40 ml) at 20 °C during 1 h to give the oxazine.

Attempted Reaction of N-*Phenyl*-3-*anilinopropionamide with Formaldehyde*.—*N*-Phenyl-3-anilinopropionamide (2.0 mmol) in acetonitrile (25 ml) had not reacted with formaldehyde (37% aqueous solution, 2.0 mmol) after 24 h at 20 °C. It also failed to react when the formaldehyde was present in excess, and when fluoroboric acid was present.

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