One-component One-pot Multi-annulation by Anodic Oxidation of Aryl Substituted Ketene Imines (Vinylideneamines)

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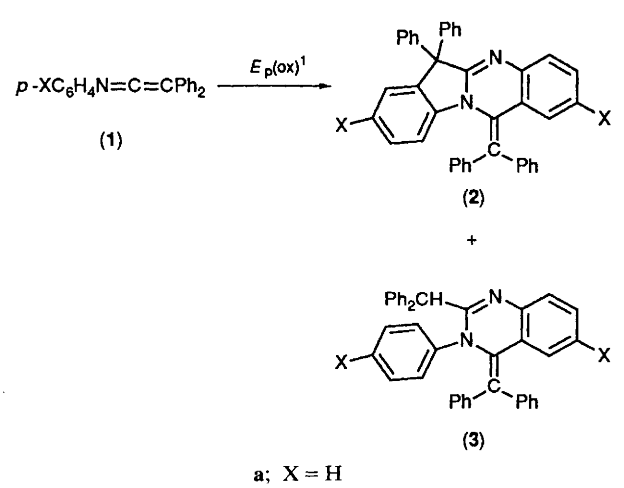
The one-pot one-component unique electrochemical synthesis of tetra- and bi-heterocycles by anodic oxidation of aryl-substituted ketene imines is described; the *X*-ray crystal structure of one of the heterocyclic products is presented.

Heterocumulenes have become increasingly useful in the synthesis of heterocycles by condensation with polar multiple bonds and dipolar systems.[1] Thermal and photochemical cycloadditions of ketene imines with appropriate reagents have led to the formation of four-, five-, and six-membered rings. Furthermore, ketene imines tend to dimerize upon thermolysis to yield the four-membered ring azetidines.[2] Recently, we have shown that electrochemical oxidation of other heterocumulenes, such as alkyl isothiocyanates, in either acetonitrile[3] or dichloromethane,[4] leads indeed to the formation of heterocycles. However, these were exclusively five-membered ring derivatives. Interestingly, the introduction of aromatic substituents instead of alkyl groups (*e.g.*, PhNCO, β-naphthyl-NCO, or PhNCS)[3] leads to the formation of polymers, or cleavage products (*e.g.*, benzophenone from $Ph_2C{=}C{=}O$).[5]

In the present work we report a unique high-yield poly-annulation process of ketene imines. This seemingly complex process involves one-pot one-component electrosynthesis of tetracyclic heterocycles *via* anodic oxidation of aryl-substituted ketene imines in dichloromethane.

Four ketene imines (**1a**—**d**) of the type $Ph_2C{=}C{=}N{-}(C_6H_4X\text{-}p)$ were synthesized by a known procedure[6] and investigated by means of both cyclic voltammetry and controlled-potential electrolysis. Each substrate was found to exhibit two irreversible oxidation waves, the first in the region of 0.9—1.1 V and the second at 1.5—2.0 V (*vs.* Ag/AgCl reference electrode). Preparative oxidation of each compound was carried out at the first oxidation wave. In a typical experiment (**1c**) (1 mmol) was dissolved in CH_2Cl_2–0.1 M Et_4NBF_4 (50 ml) contained in a three-compartment 'H-type' cell and was oxidized at a Pt anode. Dry conditions were employed; the solvent was distilled from CaH_2 and stored over 4 Å molecular sieves; the electrolyte was dried *in vacuo* at 120 °C for ~30 h. An electrolysis was run under a nitrogen atmosphere (passed through V^{2+}–Zn/Hg oxygen trap and dry molecular sieves) and terminated after all starting material



a; X = H
b; X = Me
c; X = OMe
d; X = Br

Scheme 1

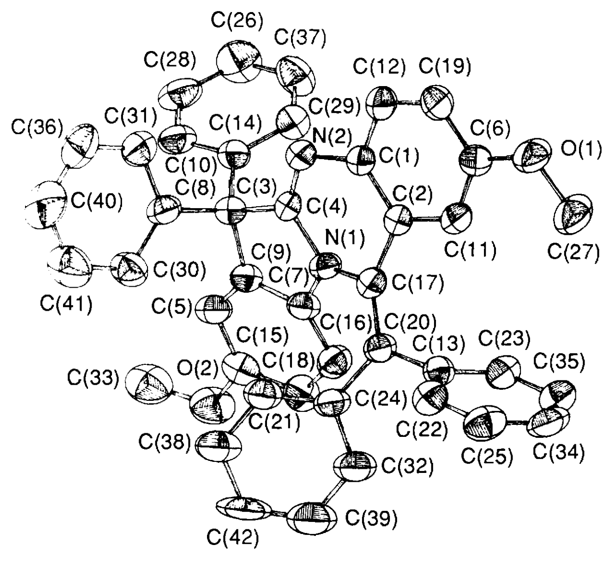


Figure 1. ORTEP drawing of the *X*-ray crystal structure of (**2c**).

had been consumed (checked by TLC sampling). The ~40 mA initial current dropped to ~2 mA at the end of the electrolysis. The work-up involved extraction of the electrolyte into water (3 × 150 ml), separation of the organic phase, drying over $MgSO_4$, filtering, and evaporation of the solvent. The solid product mixture was redissolved in the minimum volume of dichloromethane and separated chromatographically on a silica gel plate with the aid of a 2:3 (v/v) mixture of CH_2Cl_2–light petroleum (b.p. 40—60 °C) as eluant. Three product types were isolated from each ketene imine and the major ones [(from (**1a**)—(**1c**)] were found to be tetracycles (actually cyclic dimers) of type (**2**). The results are illustrated in Scheme 1 and summarized in Table 1.

The heterocyclic products of type (**2**) and (**3**) were fully characterized by spectroscopic means† and crystallographic measurements. It is virtually impossible to identify them, especially the type (**2**) products, without *X*-ray structure analysis. An ORTEP drawing of the structure of (**2c**), is shown in Figure 1.‡

The formation of products (**2a**—**d**) could be described by an oversimplified mechanistic scheme, involving an initial removal of an electron from the HOMO of the ketene imine, followed by dimerization between two initially electrogenerated cation radicals (an EC mechanism), or between a cation radical and neutral molecule of substrate, to yield the final product of type (**2**), *via* an ECE type mechanism. Either of these two mechanisms would require 1 F/mol of electricity. However, it seems that the mechanism is more complicated, because the coulometry affords only values between 0.41 and 0.48 F/mol (Table 1) for the formation of about 70% of (**2**). Further mechanistic studies, identification of other products, and investigation of other ketene imines may shed light on this problem.

Table 1. Redox potentials (*E*/V)[a] of (**1a**—**d**) and isolated yields of products[b] from anodic oxidation.

	$E_p(ox)^1$	$E_p(ox)^2$	Products (% yield)		F/mol[c]
(**1a**)	1.07	1.87	(**2a**) (70)	(**3a**) (3)	0.42
(**1b**)	1.04	1.75	(**2b**) (67)	(**3b**) (2)	0.41
(**1c**)	0.98	1.50	(**2c**) (71)	(**3c**) (3)	0.45
(**1d**)	1.14	2.0	(**2d**) (12)	(**3d**) (36)	0.48

[a] At 50 mV/s, between 0 and +2 V, *vs.* Ag/AgCl reference electrode. [b] The corresponding amides, (p-XC_6H_4)NHCOCHPh$_2$, were formed in 5—10% yield and compared with known compounds.[6] [c] These coulometric values were obtained after all starting material had been consumed.

Electrochemical oxidation of the products (**3**) did not give (**2**), showing that (**3**) is not a precursor of (**2**).

It is noteworthy that chemical oxidation of ketene imines, especially aryl-substituted examples, has been studied with various oxidizing agents: oxygen,[8] peroxy acids,[9] ozone,[10] and *N*-oxides.[11] In general, the oxidation of ketene imines of type (**1**) leads to the exclusive formation of cleavage products, *e.g.*, Ph_2CO, ArNC, and ArNCO. It follows therefore, that the unique one-component tetra-annulation *via* three bonds formation observed in this study, is an exclusive electrochemical process. Such a process has not been observed either by thermal or photochemical cycloadditions, or by chemical oxidations of ketene imines.

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† ^1H and ^{13}C NMR, MS, IR, and UV-VIS data for all products will be reported in full elsewhere.

‡ *Crystal data* for dimer (**2c**): monoclinic, space group $P2_1/a$, a = 17.468(9), b = 16.529(9), c = 11.951(7) Å, β = 65.92(4)°, V = 3150(1) Å^3, $F(000)$ = 1260, Z = 4, D_c = 1.26 g cm^{-3}. Of 4046 measured reflections, 2656 with $F > 4\sigma(F)$ were considered. The structure was solved by direct methods. Least squares refinement with anisotropic thermal parameters for non-hydrogen atoms converged at R = 0.059. No absorption or extinction corrections were applied. All calculations were carried out with two versions of SHELX.[7] Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

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