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Electronic, Steric and Acid-Base Effects on the Anodic Oxidation of Aryl-Substituted Ketene Imines

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Abstract: Aryl-substituted ketene imines (**1a-1i**) have been studied both in dichloromethane and acetonitrile by cyclic voltammetry. In addition to the multi-annulated heterocycles products of type **2-4** previously obtained by ketene imines **1a-1d**, the anodic oxidation of ketene imines containing electron-withdrawing substituents and electron-donating substituents at the *ortho* position, affords also monocyclic dimers of type **5** (from **1e-1f**) and of type **6** (from **1h-1i**). The results are discussed in terms of both electronic and steric effects.

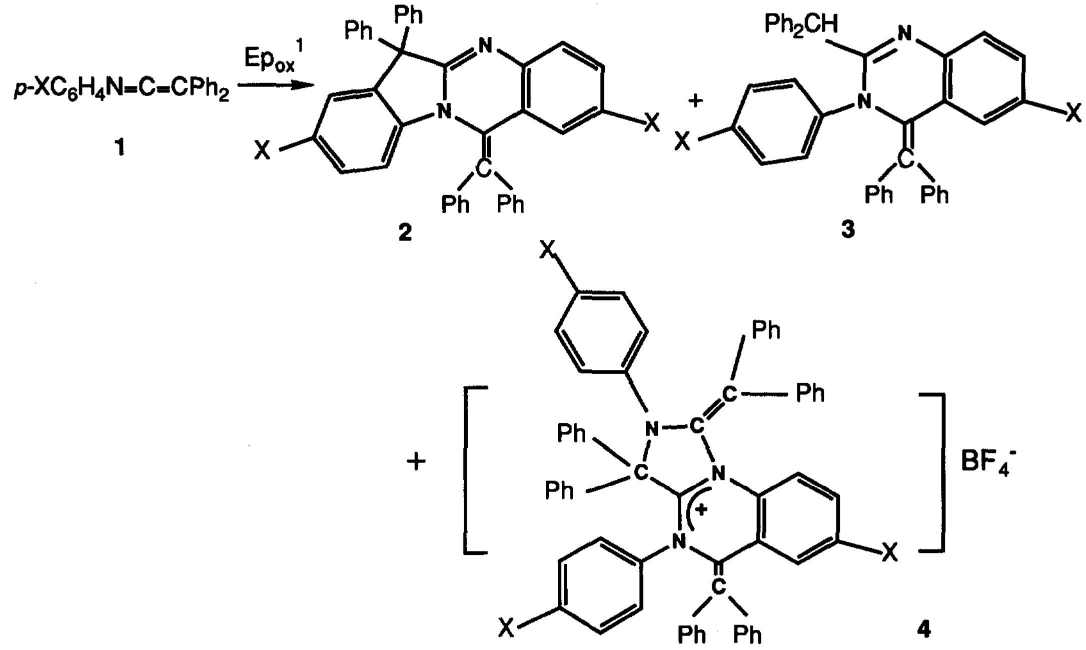
INTRODUCTION

Ketene-imines have become increasingly useful in the synthesis of heterocycles by condensation with polar multiple bonds and dipolar systems [1]. We have previously reported [2] the one-pot formation of polyheterocycles by anodic oxidation of aryl-substituted ketene-imines containing electron-donating substituents at the *para* position to the nitrogen: $Ph_2C{=}C{=}N\text{-}(p\text{-}C_6H_4X)$ (**1a**, X=H; **1b**, X=Me; **1c**, X=OMe; **1d**, X=Br). A unique multi-annulation electrochemical process takes place, from which a variety of heterocyclic products is obtained (**2-4**, Scheme 1) Whereas the bicyclic product of type **3** contains only a dihydroquinazoline moiety, the tetracyclic one (**2**) involves two fused moieties of dihydroquinazoline and indole, forming indoloquinazoline derivatives. The latter are not naturally occuring compounds, but each of the individual moieties in the fused system is found in alkaloids and biologically active drugs [3]. The syntheses of products **2** and **4** are not known. However, the multi-step syntheses of isomeric derivatives of **2** have been described [4].

Although we found that each ketene imine derivative yields products of type **2-4** (Scheme 1), there was a pronounced difference among them; ketene imines **1a-1c** produce **2**, **3** and **4** in similar yields, 67-71%, 2-3%

and 15-18%, respectively, without a noticeable substituent effect. On the other hand, the brominated ketene imine **1d**, affords the same spectrum of products but with different preferences: 12%, 36% and 29%, respectively, for **2**, **3** and **4**.

Scheme 1



In light of the above observations, the present work describes the effect of both electronic and steric effects by investigating the anodic oxidation of ketene imines containing electron-withdrawing substituents at different positions (*p*- NO_2 (**1e**), *m*- NO_2 (**1f**), *p*- CN (**1g**)), and electron-donating substituents at the *ortho* position (*o*- Me (**1h**) and *o*- OMe (**1i**)), respectively. The results are compared with our former findings of electron-rich *para* aryl-substituted ketene-imines (**1a**-**1d**). Furthermore, since the previously suggested [2] mechanisms for the formation of the heterocycles **2**-**4** involve release of protons, anodic oxidation of representative ketene-imines has been carried out in the presence of a base as proton capture. Under such conditions, different type of products, other than **2**-**4**, are obtained.

RESULTS AND DISCUSSION

Cyclic voltammetry

Cyclic voltammetry of ketene-imines **1a**-**1i** has been studied both in dichloromethane and acetonitrile (Table 1). In the former solvent, all ketene imines studied, except for **1e**-**1g**, exhibit two irreversible oxidation waves, whereas **1e**-**1g** exhibit only one. However, in acetonitrile, which has a wider potential 'window', all ketene-imines show at least two irreversible oxidation waves, among which **1a**, **1c**-**1d** and **1h**-**1i** afford a third irreversible one. It is noteworthy, that all oxidation waves, in either media, remain irreversible even upon increasing sweep rate from 50mV/s to 1000mV/s. Examination of the first oxidation potential values ($\mathrm{Ep_{ox}}^1$) obtained in dichloromethane indicates that they are only moderately affected by the substituents. The effect is even smaller in the more polar solvent, acetonitrile. The change of $\mathrm{Ep_{ox}}^1$ as a function of Hammett σ constants [5] (Figure 1a) affords a shallow slope of 0.161 and correlation coefficient of R=0.962±0.073. (A plot against σ^+ yields even worse correlation, with R=0.850). Since the two double bonds in the cumulenic system are perpendicular to each other, the above observation strongly suggests that: (a) the interaction between the lone-pair of the nitrogen and the π–orbital of the C=C bond is small, and (b) the initial electrochemical oxidation takes place primarily at the C=C site rather than at the C=N or aryl site. This suggestion is supported [6-8] by chemical and spectroscopic results which have indicated that out of the three resonance forms of ketene-imines, the second one (II), in which the negative charge is located at the external carbon, prevails:

Table 1. Cyclic Voltammetric Data for Ketene Imines **1a** -**1i**[a]

Ketene imine (substituent)	$\mathrm{Ep_{ox}}^1$ (V)[b]	$\mathrm{Ep_{ox}}^2$ (V)[b]
1a (H)	1.07 (0.94)	1.87 (1.89; 2.30)
1b (p-Me)	1.04 (0.94)	1.75 (1.72; 2.20)
1c (p-OMe)	0.96 (0.93)	1.45 (1.47; 1.77)
1d (p-Br)	1.14 (1.03)	2.0 (1.90; 2.35)
1e (p-NO_2)	1.25 (1.09)	[c] (2.25)
1f (m-NO_2)	1.23 (1.06)	[c] (2.15)
1g (p-CN)	1.15 (1.09)	[c] (2.18)
1h (o-Me)	0.97 (0.94)	1.85 (1.89; 2.27)
1i (o-OMe)	0.90 (0.90)	1.63 (1.62; 1.95[d])

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[a] [1]=5 mM; 0.1M tetrabutylammonium perchlorate in CH_2Cl_2. All potentials are recorded at Pt vs Ag/AgCl reference electrode. Scan rate: 50 mV/s.

[b] Values in parantheses represent results in CH_3CN-0.1M Et_4NBF_4.

[c] No second oxidation wave is found in CH_2Cl_2.

[d] An ill-defined wave.

$$\underset{\text{I}}{\mathrm{C{=}C{=}N}} \longleftrightarrow \underset{\text{II}}{\overset{-}{\mathrm{C}}\text{-}\overset{+}{\mathrm{C}}{=}\mathrm{N}} \longleftrightarrow \underset{\text{III}}{\mathrm{C}{=}\overset{+}{\mathrm{C}}\text{-}\overset{-}{\mathrm{N}}}$$

Upon examining the second column in Table 1, one could detect a stronger dependence of the second oxidation peak potentials ($\mathrm{Ep_{ox}}^2$) with the nature of the substituent and its position on the ring. This implies that the π–system of the aryl group is involved in the second oxidation step. Indeed, a Hammett plot [5] (Figure 1b) of $\mathrm{Ep_{ox}}^2$ against σ^+ gives a larger slope of 0.479, with correlation coefficient of R=0.996±0.180).

The third oxidation wave, which has been observed in acetonitrile and only for ketene-imines containing electron-donating substituents, could be attributed to the oxidation of the aryl moieties in these derivatives.

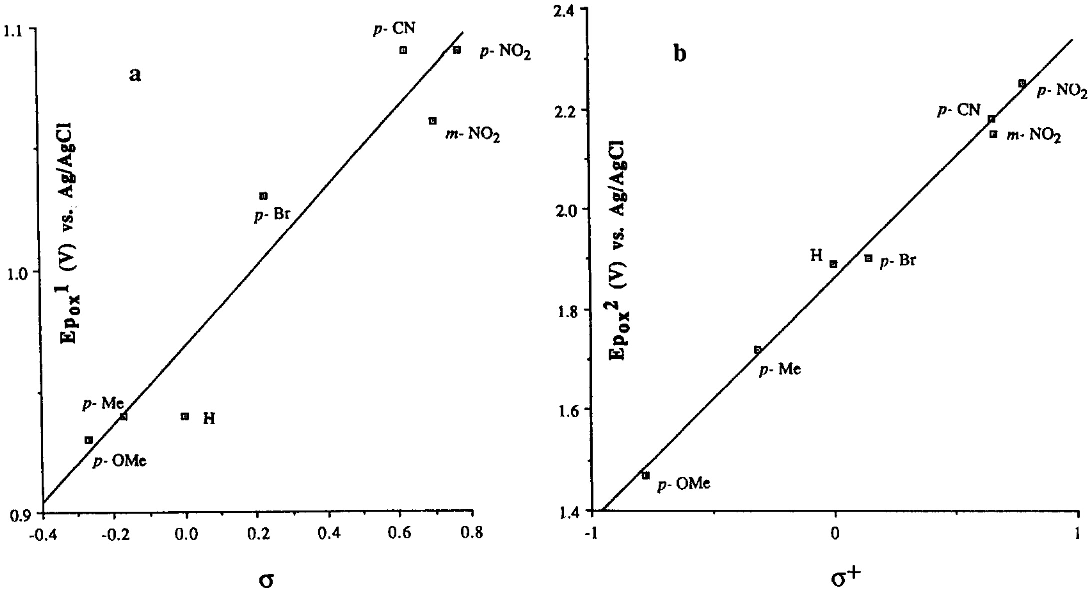


Figure 1. Hammett correlations for anodic peak potentials of ketene-imines **1a-1i** (in acetonitrile); a) Ep_{ox}^1 vs. σ constants; b) Ep_{ox}^2 vs. σ^+ constants

The cathodic region (0 to -2V) for the reduction of ketene-imines **1a-1i** in dichloromethane, has been examined too, and no reduction waves were found for ketene-imines with electron-donating substituents (**1a-1d** and **1h-1i**). However, when an electron-withdrawing group is present, reduction waves are detected. Each of **1e** and **1f** exhibits three irreversible reduction waves at -1.1, -1.5, -1.65V and at -1.05, -1.26, -1.65V, respectively. Upon comparison with the reduction potentials of *m*- and *p*- nitroanilines [9], it is likely that the corresponding first two waves in **1e** and **1f** correspond to the reduction of the nitro group, and the third one to the reduction of the cumulenic functionality. This assumption is supported by the observation that **1g**, which contains a cyano group and is known not to be reduced under these conditions, shows only one irreversible reduction wave at -1.78V, attributed to the reduction of the cumulenic grouping.

Anodic oxidation of 1e-1i

The results from anodic oxidation of electron-rich ketene imines **1a-1d** have been reported previously [2]. It seems logical to compare them with the outcome from **1e-1i**, in order to examine both steric and electronic effects on the nature and yield of products. The results are summarized in Table 2.

Table 2. Chemical yields of products from anodic oxidation of 1e -1i[a] at their first Ep_{ox}^{1} (V)

Ketene-imine	2(%)	3(%)	4(%)	5(%)	6(%)	amide(%)[b]	F/mol[c]
1e	5	40	-	7	-	10	0.38
1f	-	39	-	13	-	18	0.37
1g	t	20	8	t	-	8	0.28[d]
1h	45	-	-	-	16	14	0.57
1i	19	-	12	t	21	16	0.55

[a] Ketene-imine concentration: 33-35mM in CH_2Cl_2-0.1M Et_4NBF_4. The solvent was distilled from CaH_2 and the solvent-electrolye solution was stored over molecular sieves (4Å) before electrolysis. Trace amounts (t) were detected by mass spectra.

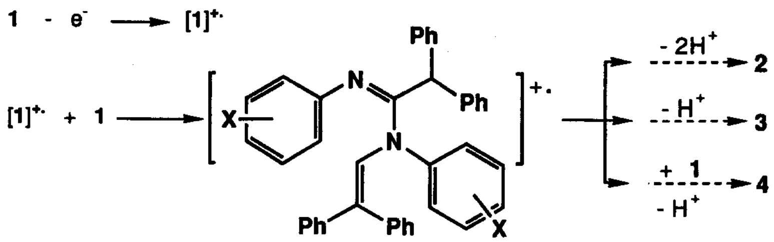
[b] The corresponding amides, (p-XC_6H_4)$NHCOCHPh_2$, were compared with known compounds.[16] Mass spectra and elemental analysis for all products were satisfactory.

[c] These coulometric values refer to "moles of 1 andwere obtained after all starting material was consumed.

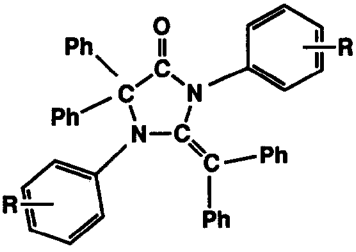
[d] Electrolysis did not go to completion because anode is coated with insoluble non-conducting black material. About 17% of unreacted ketene-imine left.

Previously we have discussed [2] the various electrochemically induced cyclization processes for the formation of products of type 2-4 and proposed the involvement of benzylic and vinylic cations. The initial electrochemical oxidation of **1** to generate the corresponding cation-radical, followed by intermolecular coupling with a neutral molecule of **1** and subsequent cyclization reactions, has been suggested [2] on the basis of the observed coulometry of ~0.5 F/mol of **1**, as is described in Scheme 2.

Scheme 2



All cyclization processes for generating products **2-4** involve at least one attack at the *ortho* position of the aryl ring. Obviously, if positively charged intermediates are involed, then electron-withdrawing substituents (as in **1e-1g**), or for sterically hindered derivatives with substituents at the *ortho* position (as in **1h-1i**), should inhibit such processes. Therefore, it is not surprising that products of type **2** and **4**, whose formation requires *more than one* electrophilic attack at the aryl groups, are obtained in lower yields from these particular ketene-imines (**1e-1i**, in Table 2). Evidently, the outcome from ketene-imines with electron-withdrawing groups (**1e-1g**) indicates that the major product from these derivatives is the bicyclic dimer of type **3**, which involves only one electrophilic attack. The tetracyclic dimer of type **2** is observed in a noticeable amount (5%) only in the case of **1e**, while the tricyclic trimer salt of type **4** was isolated (8%) only from **1g**. Surprisingly, both nitro-substituted ketene imines (**1e** and **1f**) afford exclusively a new type of monocyclic dimer, diazolidone **5**, in 7 and 13% yield, respectively. It is noteworthy, that this type of product has not been detected previously in any of the former ketene imines studied. Whereas the actual synthesis of **5** is unknown, that of its derivatives have been published [10]. Also, oxidation of **5** could lead to derivatives of naturally occuring hydantoin and allantoin, which are used as drugs, herbicides and fungicides[10].



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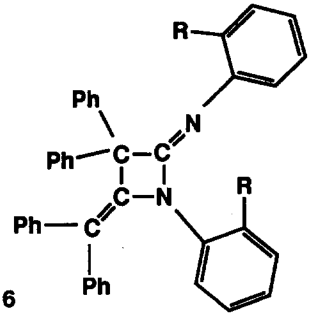

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In order to study steric effects on the cyclization processes, two ketene-imines (**1h** and **1i**), possessing substituents at one of the *ortho* positions to the nitrogen, were prepared and investigated electrochemically. Table 2 shows that they both form the tetracyclic dimer of type **2** in 45% and 19% yields, respectively, but not as efficiently as the ketene-imines with the same substituents at the *para* position (~70% of **2**, [2]). The less efficient cyclization in **1h** and **1i** could be attributed to steric effects, because one of the *ortho* positions is blocked by a methyl and methoxy group, respectively. None of them yielded the bicyclic dimer of type **3**, whereas the tricyclic salt was isolated only from **1i** in 12% yield. Interestingly, unlike the corresponding *para* substituted isomers (**1b** and **1c**), the *ortho* ones produce new cyclic dimers which consist of one four-memebered ring heterocycle, iminoazetidine **6**. This type of products is useful precursor for β-lactams and its dione derivatives which have antibacterial and anti-inflammatory activities, respectively [11].

Spectral data (IR, UV-VIS, ^{1}H- and ^{13}C-NMR, MS and combustion analysis whenever appropriate) for all products obtained from **1e**-**1i** are summarized in Table 3. The characteristic features of products of type **2**-**4** have been discussed earlier [2]. It is noteworthy that the ^{1}H-NMR of **4i** shows an upfield absorption (2.64 *ppm*) for one of its methoxy groups. This is probably due to the shielding effect exerted by one of the neighboring phenyl rings. Furthermore, the typical C=N stretching frequency (1602-1609 cm^{-1}) in products of type **3** disappears in **3e** and **3f**, for not so obvious reasons. Products of type **5** have a typical carbonyl absorption in the IR (1735-1745 cm^{-1}); in their mass spectra, they all afford a molecular ion (M$^+$) as the base peak. The ^{1}H- and ^{13}C-NMR spectra are less informative due to their complexity. The structure of **5e** has been determined by a single crystal X-ray diffraction [12-14]. ORTEP and stereo drawings of **5e** are shown in Figure 2.

Product **6h** affords a molecular ion as the base peak in its mass spectrum. Interestingly, it shows two characteristic absorptions in the IR, at 1644 and 1736 cm^{-1}. While the former absorption could be attributed to

Table 3. Spectral data of products

Product[a]	IR (KBr) ν (cm^{-1})	UV (CH_2Cl_2) λ_{max} nm(ε)	^{1}H-NMR(δ_{ppm}) ($CDCl_3$/TMS)	^{13}C-NMR(δ_{ppm}) ($CDCl_3$/TMS)	(MS)[b] m/z (%)
2e	1604 (C=N) 1339; 1530 (NO_2)	370 (13125) 285 (sh, 19895) 231 (sh, 36198)	6.93-7.50 (m, 20H) 7.80-8.00 (m, 5H) 8.23 (dd, 1H, J=10,2.5 Hz)		CI: 627 (MH^+, 100) EI: 626 (M^+, 100) 596(18), 401 (90), 446 (2),
2h	1644 (C=N)	350 (19237) 294 (sh, 15847)	2.32 (s, 3H), 2.46 (s, 3H) 6.62-7.55 (m, 24H) 7.98 (d, 2H, J=7.5Hz)	18.20, 19.53 ($2CH_3$), 61.43 (Ph_2C-Ar), 165.23 (N-C=N) the rest: 122.53-146.70	EI: 564 (M^+, 15), 279 (20), 167 (18), 77 (30), 56 (100)
2i	1643 (C=N)	355 (15492) 310 (sh, 12788) 260 (sh, 34029)	3.66 (s, 3H), 3.82 (s, 3H) 6.20-7.49 (m, 24H) 7.89 (d, 2H, J=6.6 Hz)	54.93, 57.69 (OCH_3), 62.10 (Ph_2C-Ar), 165.08 (N-C=N) the rest: 109.03-153.92	CI: 597 (MH^+, 100) EI: 596 (M^+, 100) 429 (7), 298 (2), 165 (2)
3e	1347, 1542 (NO_2)	398 (13964) 284 (sh, 25720)	4.99 (s, 1H) 6.59-7.33 (m, 23H) 7.47 (d, 1H,J=2.3Hz) 7.78 (d, 2H,J=8.9Hz) 7.94 (dd, 1H,J=8.82, 2.2 Hz)	54.02 (Ph_2CH-) 160.32 (N-C=N) the rest: 109.01-148.11	EI: 628 (M^+, 25), 450 (7), 167 (100)
3f	1350, 1530 (NO_2)	400 (1641) 300 (sh, 18452)	5.12 (1H), 6.57-7.48 (m, 26H) 7.97 (dd, 1H,J=4.8, 1.8 Hz)	54.47 (Ph_2CH-) 160.28 (N-C=N) the rest: 103.42-147.80	EI: 628 (M^+, 10), 535 (5), 386 (6), 310 (10), 256 (100), 167 (30)
3g	2228 (C≡N) 1602 (C=N)	338 (8206) 250 (sh, 16147)	5.03 (s, 1H) 6.64-7.38 (m, 27H)	54.85 (Ph_2CH-) 160.94 (N-C=N) the rest: 108.33-147.54	CI: 589 M^+, 100) EI: 588 M^+, 100), 421(6), 267 (30), 167 (52)
4g	2224 (C≡N) 1638 (C=N)	420 (4535) 235 (low)	4.90-5.10 (m, 1H) 5.57-5.65 (m, 1H) 6.00-7.50 (m, 39H)		DCI: 589(3), 452(48), 396 (50),391(82), 295 258(69),219 (65)(100)

Table 3 (cont.)

4i	1637(C=N) 1048	460 (3430) 234 (low)	2.64 (s, 1H) 3.34 (s, 1H) 3.96 (s, 1H) 5.15 (d, 1H,J=7.5Hz) 6.00-7.50 (m, 40H)	FAB: 897(MH+,8),598(12) DEI: 598(14),448(18), 29 (30),254(56),212(40) 182 (36), 149 (20) 105(100)
5c	1735 (C=O)		3.43 (s, 3H)3.57 (s, 3H), 6.07 (d, 2H,J=8.7 Hz)6.45 (d, 2H,J=8.7 Hz)6.55 (d, 2H, J=9.0 Hz)6.74-7.01 (m, 12H) 7.18-7.36 (m, 4H)7.39-7.41 (m, 6H)	Cl: 615 (MH+, 100) El: 614 (M+, 100), 299 (34), 287 (11), 272 (11), 254 (33), 210 (17), 195 (1), 181 (1), 165 (27)
5e[c]	1745 (C=O) 1616 (C=C)		6.88-7.45 (m, 26H) 7.87 (d, 2H,J=9.1 Hz)	Cl: 645 (MH+, 100) El: 644 (M+, 100),314(13), 330 (1), 301 (1)
5f	1737 (C=O) 1616 (C=N)		6.5-8.0 (m)	Cl: 645 (MH+, 17) El: 644 (M+, 29), 450(10), 330(3),314(51),301(4), 194(17),166(24)165(100
6h	1736 (C=O) 1644 (C=N)		1.46 (s, 3H) 2.22 (s, 3H) 6.26 (d, 2H, J=5.9 Hz) 6.57 (d, 4H, J=6.0 Hz) 6.26-7.00 (m, 10H) 7.14-7.16 (m, 10H)	DEI: 566 (M+, 20), 344 (100), 283 (42), 222 (35)

[a] Elementary analyses (C,H,N) for all products were satisfactory.

[b] Cl=chemical ionization; El:=electron impact; DEI=direct probe; FAB=fast atom bombardment with Xe or Ar.

[c] Structure was determined by X-ray analysis.

the C=N bond, the origin of the latter is not clear. A similar observation has been reported by Barker and coworkers [15] for an iminoazetidine containing a methyl instead of aryl group (1630 and 1745 cm^{-1}). The mass spectrum of **6h** shows a molecular ion with m/z=566(20%) and other fragments typical for the iminoazetidine ring. The two methyl groups appear in the ^{1}H-nmr spectrum as two singlets, at 1.46 and 2.22 ppm.

The mass spectrum of product **6i** shows a weak molecular ion signal at m/z=598(2%), in addition to other two major fragments with m/z=182(72%) (benzophenone, confirmed by GCMS) and m/e=448(55%). Actually, these two 'fragments' could be attributed to products obtained by a decomposition of, e.g., dioxethane intermediate (Scheme 3) which was previously formed by a reaction of **6i** with oxygen. This may imply that **6i**,

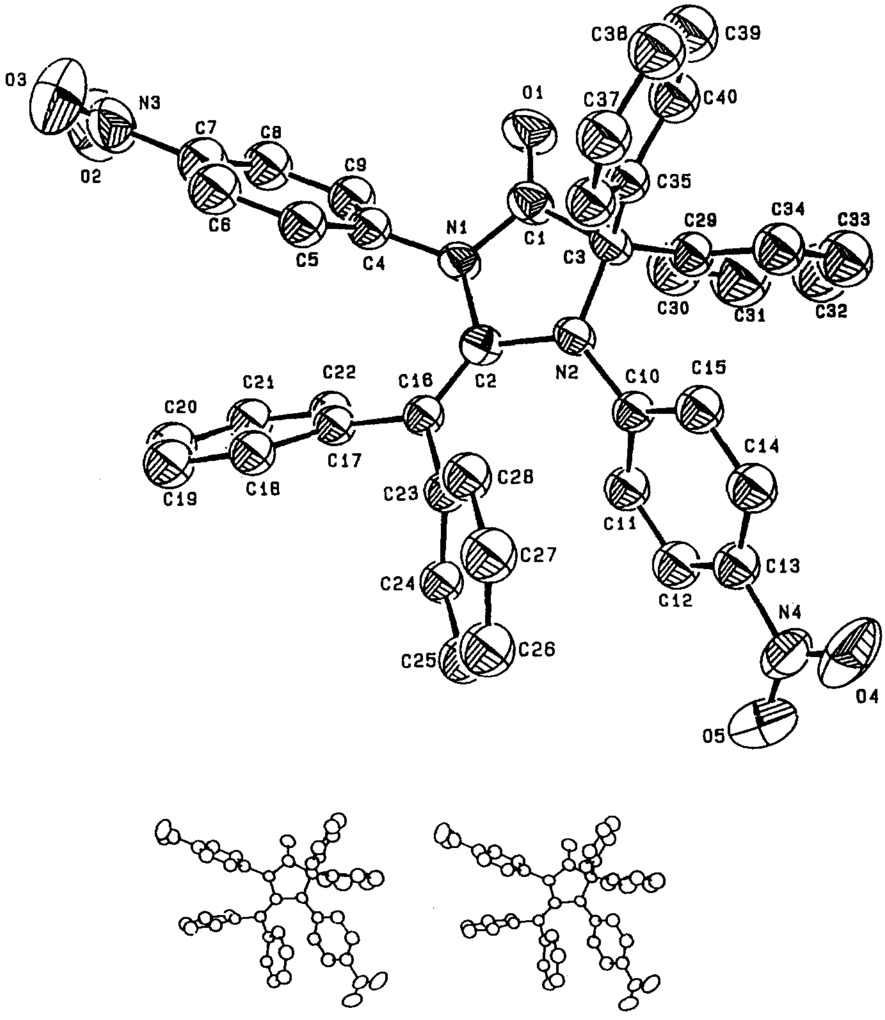
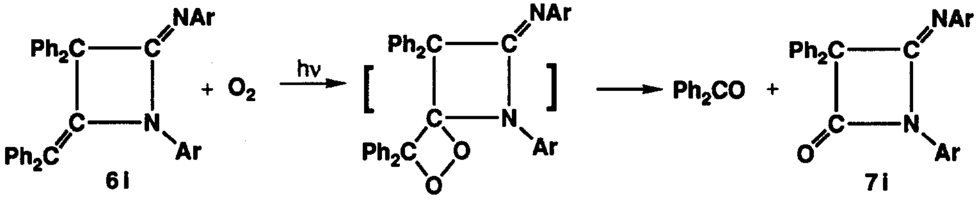


Figure 2. ORTEP and STEREO views of **5e**

Scheme 3



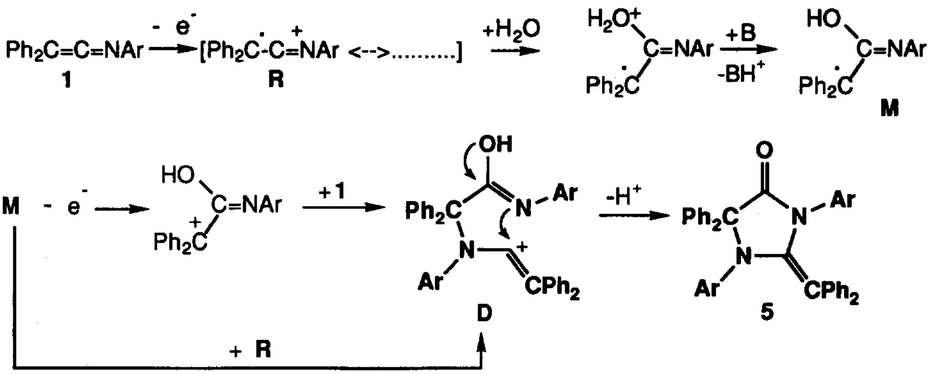
unlike **6h**, is less stable and mostly undergoes air decomposition (reaction with oxygen) prior to its injection to the mass spectrometer. In the IR, the product mixture does not show an absorption higher than 1700 cm^{-1} (as in **6h**) but exhibits two carbonylic ones at 1660 cm^{-1} and 1680 cm^{-1}, corresponding to benzophenone and presumably **7i**, respectively. It is noteworthy that the reaction of double bonds with singlet oxygen to give a dioxetane intermediate, which usually cleaves to aldehydes or ketones, is well established [16].

MECHANISM

The independence of the first oxidation peak potential (Ep_{ox}^1) of **1** with the nature of the substituent, as revealed by cyclic voltammetric data and Hammett plot (Figure 1a), indicates that initial electrochemical oxidation takes place primarily at the C=C site rather than at the C=N or aryl site. Also, the irreversibility of Ep_{ox}^1 shows that the cation-radical of **1** undergoes fast follow-up chemical reaction. However, the dependence of the second oxidation peak potential (Ep_{ox}^2) with the nature of the substituent (Figure 1b) implies that the π–system of the aryl group is involved in the second oxidation step. These observations support the various mechanistic schemes proposed for the formation of products of type **2-4**. All the previously suggested cyclization routes (Scheme 2) involve deprotonation processes. In order to study the effect of the released protons on the nature of products formed, we have undertaken an investigation of the anodic oxidation of ketene-imines in the presence of proton ccaptures, namely bases.

An addition of pyridine to the electrolysis mixture containing a ketene-imine, results in a strong adsorption of the pyridine at the anode surface, or its immediate reaction with a positively charged intermediate of ketene imine, to cause passivation of the anode surface (platinum or glassy carbon) by forming an insulating and insoluble film. Consequently, no current could be transferred through the solution to allow electrolysis. Therefore, pyridine was substituted with 2,6-lutidine, in which the two methyl groups mask the lone pair of the nitrogen atom, inhibiting both a reaction with positively charged species, as well adsorption at the anode surface. Furthermore, the presence of base (in excess) which captures released protons, eliminates any previously suggested [2] protonation processes. As an example, the anodic oxidation of ketene imine **1c** under these conditions yields 21% of the corresponding diazolidone, **5c** (among other unidentified products, and ~10% of unreacted **1c**). No amide, **2c**, **3c** or **4c** has been detected. The formation of type **5** products could be rationalized according to Scheme 4, after initial electrochemical step, followed by a reaction with water (a contaminant in, e.g., the highly hygroscopic electrolyte used):

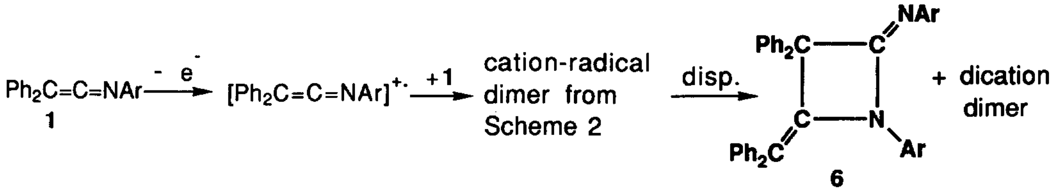
Scheme 4



The observation that products of type **5** are obtained only from the two nitro-substituted ketene imines and not from the the cyano derivative is somewhat puzzling. One possible explanation is based on a former observation [17] that BF_4^- is highly solvated by water molecules and tends to concentrate in the vicinity of the anode surface. Therefore, the nitro group which is more polar than the cyano group, has a lesser 'chance' to diffuse away from the polar electrode surface before immediately reacting with water molecules (which are brought to the surface by solvated BF_4^- ions).

The last two entries in Table 2 relate to two ketene imines with electron-releasing substituents at the *ortho* position. Interestingly, in addition to the formation of **2** and **4** in mild yields, both **1h** and **1i** produce new monocyclic products, iminoazetidines of type **6**. The latter are known to be formed chemically by direct thermolysis of ketene imines [1]. Hoever, their chemical formation under the acidic electrochemical conditions cannot be ruled out. Our attempts to obtain them by treating **1** with acid under aprotic conditions, have been unsuccessful. Consequently, they could be formed electrochemically by initial formation of ketene imine cation-radical, followed by consecutive chemical reactions (Scheme 5).

Scheme 5



Finally, a comparison between the last two entries in Table 2 shows two major differences: (a) the tetracyclic dimer **2h** is formed in a higher yield (45%) than **2i** (16%), and (b) a product of type **4** is obtained only from **1i**. These two findings could be partially explained, by the greater steric effect and stronger inductive effect exerted by the methoxy group in **1i** than that of the methyl group in **1h**. The more bulky methoxy group inhibits a free rotation along the Ar-N axis in the electrogenerated intermediates, and therefore deactivates intramolecular electrophilic attack at the *ortho* position of the aryl group to form **2**. Under such restrictions, a preferred pathway, in which intermolecular electrophilic reaction (with a third molecule of ketene-imine) to form the type **4** organic salt, takes place. Indeed, the corresponding **4i** is formed at the expense of **2i** (last entry in Table 2), whereas no **4h** is observed from the oxidation of **1h**.

CONCLUSION

Cyclic voltammetery data of aryl-substituted ketene imines mostly afford two irreversible oxidation waves. The first anodic peak potential was found to be almost independent of the nature of the substituent (bad correlation with Hammett constants). This implies that the first electrochemical oxidation step takes place at the $Ph_2C=C$ rather than at the C=NAr moiety. However, the second anodic peak potential varies linearly with Hammett constants, indicating that the second electrochemical step is strongly affected by the aryl group.

Previous results from anodic oxidation of electron-rich substituted ketene imines afforded a unique electrochemical process, from which multi-annulated heterocyclic products (**2**-**4**) are formed in one pot synthesis. The current work indicates that electron-poor substituted ketene imines produce, in addition to products of type **2**-**4**, also five-membered ring heterocycles of type **5**. However, unlike other ketene imines studied, the anodic oxidation of sterically hindered ones leads to the formation of four-membered ring heterocycles of type **6**, among other products. It is noteworthy, that products of type **2** and **4** are new heterocycles, and those of **3**, **5** and **6** are derivatives of biologically active naturally occuring compounds.

EXPERIMENTAL SECTION

Materials

Tetraethylammonium tetrafluoroborate ($TEABF_4$, supporting electrolyte) was purchased from Aldrich (>99%) and used after vacuum drying (~2mmHg) at 120°C for ~30h. Commercially available Ag/AgCl (from Bioanalytical Systems) was used as reference electrode. HPLC grade CH_2Cl_2 (distilled from CaH_2) was used for preparative electrolyses.

Ketene-imines **1h**-**1i** and **1e**-**1g** were prepared according to known procedures [18] The former were made by dehydrating their corresponding amides with P_2O_5 in dry pyridine. The latter were made by preparing α–chloroimadoylchlorides from the corresponding amides and PCl_5 in toluene, followed by a reaction with copper powder. In a typical experiment for the preparation of **1e**, a mixture of 0.056 moles of diphenic acid and 7.5mL of freshly distilled thionyl chloride, in a 100mL round-bottom flask, was refluxed for two hours. After vacuum distillation of the remaining thionyl chloride, the viscous residue was dissolved in diethyl ether and slowly added to a stirred solution (100mL) of 0.056 moles of *para*-nitroaniline in ether. The white precipitate (accompished overnight) was filtered and washed with 100mL HCl 0.5M, to remove unreacted amine, followed by recrystallization from ethyl acetate. The corresponding amide was obtained in 60-80% yield. A magnetically stirred solution containing 0.0095 moles amide and 0.019 moles of PCl_5 in 50mL dry toluene was refluxed for ~5 hr. The cold mixture washed by 3x150mL water to remove phosphoroxychloride. The solvent toluene was distilled and the solid residue was dissolved in 30-40mL diethyl ether and left open to air. After few days, 1.83g of white shiny crystals of the corresponding α–chloroimadoylchloride was precipitated (m.p.=121-122°C). The latter was refluxed with 2g Cu powder in 50mL toluene for overnight. Then it was cooled to room temperature, and filtered. The solid was washed with 50mL toluene and filtered again. The solvents were evaporated from the combined filtrates. The solid residue was dissolved in 50mL diethyl ether, and then precipitated by adding 100mL petroleum ether (40-60). After cooling overnight in a refrigirator, 0.6g (40%) of red crystals of **1e** are formed (mp=86.5°C; lit.[14b] 85-87°C).

Spectral Instruments

For spectral measurements, the following instruments have been used: Nicolet 5ZDX: FT-IR spectrometer; Perkin-Elmer Lambda 5 UV-VIS spectrometer; Brukner WP200SY NMR spectrometer, and Finnigan 4020 Quadrapole or V.G. Model 7035 mass spectrometers.

Electrochemistry

For electrochemical measurements, a Princeton Applied Research (PAR) potentiostat Model 173, a PAR Universal Programmer Model 175 and Yokogawa XY-recorder Model 3036, were employed. A glass cylinder closed at one end, containing 1-5mM substrate in 5-10mL solution was used for cyclic voltammetry, employing Pt button (3×10^{-3} cm^2) working electrode, surrounded by Pt net cylinder auxiliary electrode. All potentials were measured vs. Ag/AgCl reference electrode. An 'H' type three-compartment cell equipped with medium glass frit as a membrane was used for preparative electrolysis. A polished silver wire quasi-reference electrode, immersed in a glass cylinder with fine glass frit at its end and containing electrolyte solution, was used in these experiments. Typically, the anodic compartment contains 0.3-1 mmol of ketene-imine dissolved in 30mL of CH_2Cl_2-0.1M Et_4NBF_4. The mixture was stored over molecular sieves (4Å) which was previously heated to 150°C under vacuum for ~30h. All experiments were performed under nitrogen atmosphere free of oxygen (V^{2+}/Zn-Hg trap) and free of moisture (dry molecular sieves trap). Electrolyses were terminated when no ketene-imine was detected by TLC. The workup involved stripping of the solvent followed by water addition and extraction into diethyl ether (in which $TEABF_4$ electrolyte is insoluble). After phase separation, drying over $MgSO_4$ and filtration, the solution was concentrated and column separated by Chromatotron (Harrison) Model 7924T, using 2mm thick silica gel (PF-254 with $CaSO_4$, from Merck) round plates. Products were separated by gradual elution with 80/20 PE/CH_2Cl_2 to pure CH_2Cl_2.

Supplementary Material Available

ORTEP and crystallographic procedures for **5e**; spectra of **5f** (6 pages). This material is contained in many libraries on microfische, immediately follows this article in microfilm version of the Journal and can be ordered from the ACS; see any current masthead page for ordering information.

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12. Crystal data for the monocyclic dimer **5e**: $C_{40}H_{28}N_4O_5{\cdot}CH_2Cl_2$, MW=729.6, monoclinic, space group $P2_1/c$, a=10.862(2), b=15.497(2), c=21.521(4) Å; β=95.65(2)°; V=3605.0(8) $Å^3$; Z=4; D_c=1.34 gm^{-3}; μ(CuKα), cm^{-1} =19.32; Number of unique reflections=4102;Number of reflections with $I \geq 3\sigma(I)$=3197; R=0.099. Data were measured on an ENTRAF- NONIUS CAD-4 automatic diffractometer. CuKα (λ=1.54178 Å) radiation with graphite crystal monochromator in incident beam was used. The standard CAD-4 centering, indexing, and data collection programs were used. The unit cell parameters were determined by a least- squares fit of 24 accurately centered reflections within limits $22 \leq \theta \leq 26°$. Intensity data were collected using the θ-2θ technique to a maximum of 2θ of 110°.
13. The atomic positions, thermal parameters, bond lengths and bond angles appear in the supplementary material.
14. All non-hydrogen atoms were found by using SHELX-86 direct method analysis, Sheldrick, G. M. Crystallographic Computing Packages, Universities of Cambridge and Gotingen, Press, pp. 175-189 (1985). All crystallographic computing was done on a CYBER 855 computer at the Hebrew University of Jerusalem, using SHELX 1977 structure determination package.
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