phenol ($pK_a = 7.15$) and NdEDTA was also investigated. Significant LIS's were observed only for the protons ortho to the ionized hydroxyl group, their intrinsic LIS being 0.68 ppm. Also the complex formed was found to be relatively weak (dissociation constant of 160 ± 40 mM). The comparison between *p*- and *o*-nitrophenol suggests that chelation plays an important role in complex formation for the latter substrate. Both salicylaldehyde and *o*-nitrophenol contain, in addition to the ionizing hydroxyl group, oxygen containing functional groups that are well suited for the formation of a stable six-membered ring upon chelation.

In the case of chelation the complex formed will be devoid of axial symmetry. Moreover, also absent will be the possibility for internal rotation or stereochemical rearrangement of the substrate within the complex, i.e., absent will be the mechanisms leading to effective axial symmetry in many lanthanide shift reagent systems.[5] It is not surprising, therefore, that the internal shift ratios (given in Tables I and II as Δ_i/Δ_4) are different for the three lanthanides investigated. A similar behavior has recently been observed for the Pr^{3+} and Eu^{3+} complexes of the ethyl ester of *N*-acetyl-L-3-nitrotyrosine (ANTE).[6] For the analysis of the LIS's in such systems the complete pseudocontact shift equation (cf., e.g., ref 6 and references therein)

$$\Delta_M = r^{-3}[K_1(3\cos^2\theta - 1) + K_2(\sin^2\theta\cos 2\phi)] \qquad (1)$$

has to be employed. One of the effects of rapid internal rotations or stereochemical rearrangements of the substrate in the complex is to average out the second term of eq 1, in which case the magnitude of the total shift is also reduced. Referring to the LIS values of *o*- and *p*-nitrophenol this effect is clearly revealed. We also note that the shifts induced by the LnEDTA chelates in the spectrum of *o*-nitrophenol are of similar magnitude as those reported for the corresponding aquo lanthanides and another substrate, ANTE, containing the *o*-nitrophenolate group.[6] In other instances, e.g. carboxylates, the LIS by the aquo ions have been found to be much larger than those by the EDTA chelates.[1] It seems that the difference between the carboxylates and the *o*-nitrophenolates arises from the chelating ability of the nitrophenolate moiety, which may prevent the averaging out of a substantial part of the pseudocontact shift.

Contact contributions to the observed LIS's cannot be ruled out altogether. They are likely to increase in the order Pr < Nd < Eu.[7] However, for an accurate separation between contact and pseudocontact contributions data for a larger number of lanthanides are needed. With the data presently available and using the tabulated theoretical estimates of the relative contact and pseudocontact LIS's (cf. ref 7 and references cited therein) one finds that only the LIS of CHO of salicylaldehyde could be largely of contact origin.

Acknowledgments. The technical assistance of Naomi Bauman and helpful discussions with Gabriel A. Elgavish are gratefully acknowledged. This work was supported in part by a grant from the United States-Israel Binational Science Foundation.

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(1) G. A. Elgavish and J. Reuben, *J. Am. Chem. Soc.*, in press.
(2) Cf., e.g., C. Postmus, Jr., L. B. Magnuson, and C. A. Craig, *Inorg. Chem.*, **5**, 1154 (1966).
(3) Spectra were recorded with a Varian T-60 spectrometer operating at the ambient probe temperature of 39 ± 1°. Solutions were made up in D_2O containing ca. 0.1% v/v dioxane, the resonance of which served as internal reference. Substrate concentrations were in the range 75–120 mM. The shift reagents were prepared by mixing equivalent amounts of the lanthanide trichloride and Li_4EDTA. The pH was adjusted to be in the range 8.6–9.3 using either LiOD or DCl.
(4) R. E. Lenkinski and J. Reuben, *J. Magn. Reson.*, **21**, 47 (1976), and references cited therein.
(5) (a) J. M. Briggs, G. P. Moss, E. W. Randall, and K. D. Sales, *J. Chem. Soc., Chem. Commun.*, 1180 (1972); (b) W. DeW. Horrocks, Jr., *J. Am. Chem. Soc.*, **96**, 3022 (1974).
(6) T. D. Marinetti, G. H. Snyder, and B. D. Sykes, *J. Am. Chem. Soc.*, **97**, 6562 (1975).
(7) J. Reuben, *J. Magn. Reson.*, **11**, 103 (1973).

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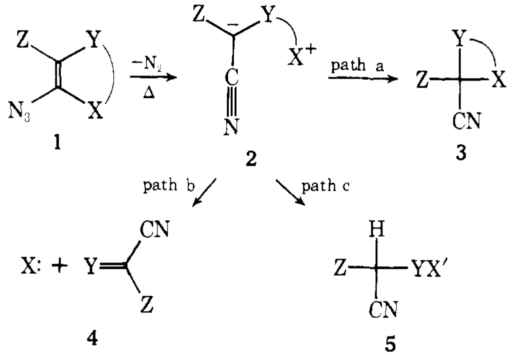
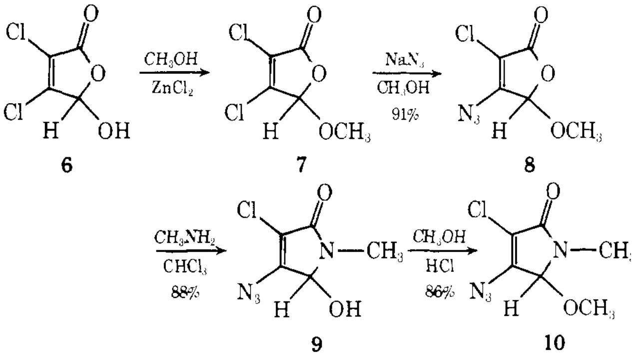
Chlorocyanoketene. A New β-Lactam Synthesis

Sir:

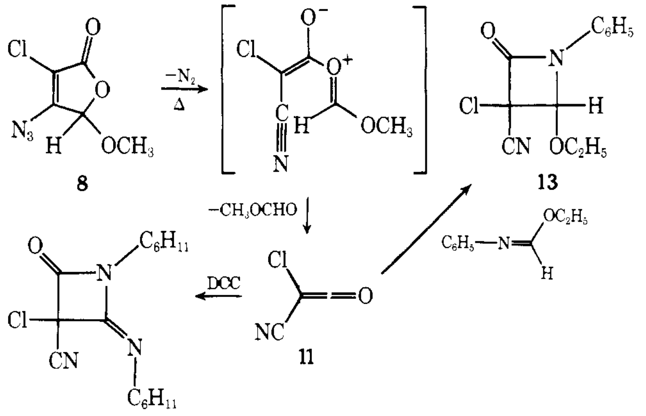
A working mechanistic model for the rearrangements of certain cyclic vinyl azides, which has significant predictive powers for synthetic objectives, can be formally viewed as outlined below. That is, we assume cleavage of **1** to **2** to be facile when X can easily carry a positive charge and Y and/or Z are anion stabilizing substituents. The zwitterionic intermediate, **2**, can then ring close to **3** (path a), cleave to **4** (path b), or, in cases where X carries an acidic proton, collapse to **5** (path c).[1]



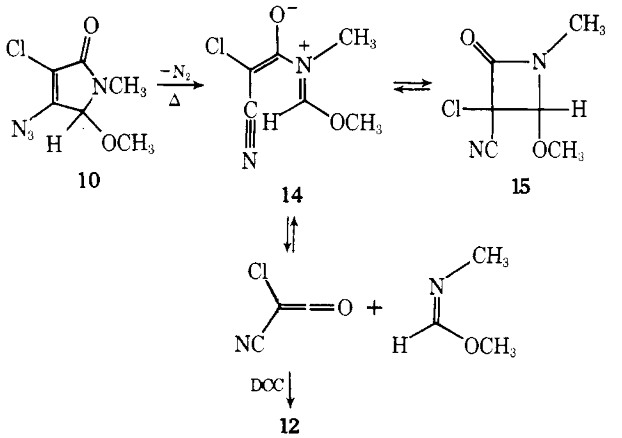
Reported here is the thermal chemistry of some selected heterocyclic β-azidoeneones that undergo rearrangements and fragmentations which are predictable according to the above model. Of particular interest is the observed cleavage of β-azido-α-chloro-γ-methoxy-$\Delta^{\alpha,\beta}$-crotonolactone (**8**)[2] to the previously unknown chlorocyanoketene (**11**) and the ring contraction of 4-azido-3-chloro-1-methyl-5-methoxy-Δ^3-pyrrolinone (**10**) to the β-lactam (**15**). The potential versatility of the cyanoketene and β-lactam syntheses described here is obvious when one considers the general synthetic route to their respective butenolide and pyrrolinone precursors. These were prepared from the commercially available mucochloric acid **6** as outlined below.[3] It is significant to note that a vast chemistry of mucohalic acids has been reported, and that synthetic methodology exists which allows their structural modifications at the α-, β-, and γ-positions.[4] Thus, a detailed study of the synthetic scope and mechanisms of these azide thermolyses is warranted and will appear subsequently. When



a benzene solution containing stoichiometric amounts of the lactone **8** and dicyclohexylcarbodiimide was refluxed for 3 h, the ketene adduct **12** was isolated in 88% yield: mp, 69–70°; ir (Nujol, cm^{-1}) 2230, 1850, 1730; ^{1}H NMR (CDCl$_3$, δ) 3.65 m (1), 1.68 m (10). In an analogous fashion the β-lactam **13** was isolated in 48% yield when the thermolysis of **8** was accomplished in the presence of ethyl *N*-phenylformimidate: mp 66–67°; ir (Nujol, cm^{-1}) 1780; ^{1}H NMR (CDCl$_3$, δ) 1.41 t (3), 3.94 q (2), 5.37 s (1), 7.39 m (5). It is noteworthy that this cycloaddition appears to be stereospecific in that only one diastereomer was detected by ^{1}H NMR analysis of the crude reaction product. However, the stereochemistry of this adduct has not been determined.[5]

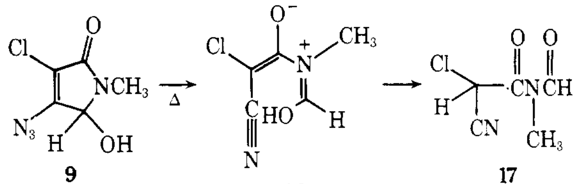


From the above results, it was anticipated that a direct synthesis of β-lactams could be accomplished from the thermolysis of certain 4-azidopyrrolinones. For example, thermolysis of 4-azido-3-chloro-1-methyl-5-methoxy-Δ^3-pyrrolinone (**10**) could give the proposed zwitterion **14** which could ring close directly to the β-lactam **15** (path a). Such zwitterionic intermediates have previously been shown to be the penultimate precursors to β-lactams when ketenes cycloadd to imines.[6] The above ring contraction would be unique in that the dipolar intermediate would be generated from the heterocyclic precursor, **10**, rather than from a direct cycloaddition of chlorocyanoketene to methyl *N*-methylformimidate. Thus, not only a synthetically useful entry into the β-lactam nucleus would result but also a mechanistic question regarding the cycloaddition of chlorocyanoketene to imidates, e.g., **11** → **13**, could be answered. That is, *assuming* that the zwitterion, **14**, is formed upon thermolysis of **10** and that it undergoes electrocyclic ring closure to the β-lactam, **15**, is the zwitterion also in equilibrium with chlorocyanoketene and methyl *N*-methylformimidate? The following results indicate that this is so. When a benzene solution of **10** was refluxed for 15 h and the resulting residue purified by molecular distillation, a 58% isolated yield (>90% by ^{1}H NMR analysis of the crude product) of the β-lactam was realized: oil; ir (neat) 2250, 1800; ^{1}H NMR (CDCl$_3$, δ) 2.92 s (3), 3.66 s (3), 4.84 s (1). Again, only one stereoisomer was detected.[5] When the experiment was repeated in the presence of a stoichiometric amount of dicyclohexylcarbodiimide, the ketene was trapped to give **12** in 17% yield, and no β-lactam, **15**, was detected. The complete absence of **15** was surprising until it was found that it also cleaves to the ketene under the reaction conditions. That is, when a benzene solution of **15** and a stoichiometric amount of dicyclohexylcarbodiimide was refluxed for 8 h, **12** was again detected by ir analysis of the crude reaction mixture. The following mechanistic scheme is therefore in agreement with these results.

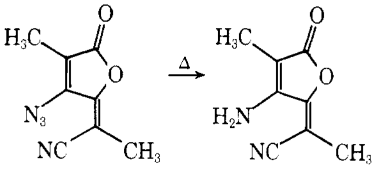


No direct evidence for the existence of the proposed zwitterionic intermediates in the reactions outlined here has yet been obtained. However, additional data which are interpretable in terms of such intermediates and which are also consistent with the XYZ mechanistic model come from the following three experiments:

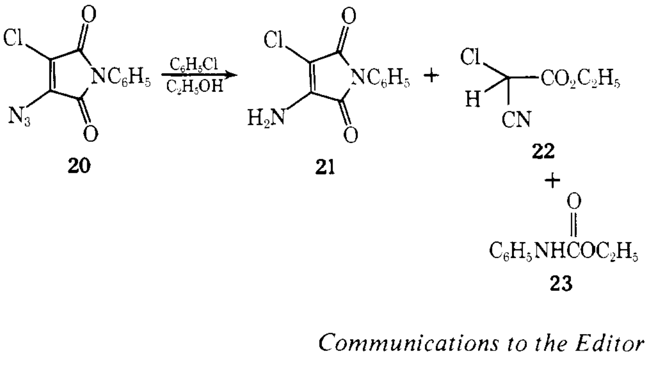
(1) Thermolysis of the azidocarbanolamide, **9**, gives the imide **17** in 26% isolated yield: oil; ir (Nujol, cm^{-1}) 3300, 1720, 1680; ^{1}H NMR (CDCl$_3$, δ) 3.16 s(3), 6.43 s(1), 9.42 s(1). This product can be envisaged as arising from the zwitterion **16** via proton transfer (path c).



(2) Thermolysis of β-azido-γ-alkylidene-Δ$^{\alpha,\beta}$-butenolides would not be expected to give products arising from a zwitterionic intermediate since the γ-alkylidene moiety would not stabilize an incipient positive charge. In fact, when β-azido-γ-cyanoethylidene-α-methyl-Δ$^{\alpha,\beta}$-butenolide (**18**)[7] was pyrolyzed in refluxing toluene for 5 days, only the corresponding β-amino derivative **19**[8] was detected in addition to unreacted starting material. Also, only **19** could be isolated (25%) when the thermolysis was done in refluxing chlorobenzene in the presence of a stoichiometric amount of dicyclohexylcarbodiimide. However, this latter experiment gave a complex mixture of products as evidenced by TLC analysis.



(3) Azido-substituted maleimides would be expected to thermally cleave to cyanoketenes and isocyanates (path b) since the carbonyl adjacent to the azide group would stabilize the positive charge in the zwitterionic intermediate. Thus, when 2-azido-3-chloro-N-phenylmaleimide (**20**)[9] was thermalyzed



(chlorobenzene) in the presence of 5 equiv of ethanol, the ester **22** (22%), carbamate **23** (32%), and 2-amino-3-chloro-N-phenylmaleimide (**21**)[10] (20%) were isolated. The ester and carbamate arise from ethanol addition to the respective cumulenes. The amino compound **21** is of particular note since its formation suggests that a nitrene may precede zwitterion formation and is trapped by hydrogen atom abstraction.

Acknowledgment. The authors wish to thank the National Science Foundation (MPS74-06932) for financial support of this work.

Dedication: This work is dedicated to Professor Harold R. Snyder in honor of his retirement after an illustrious career on the faculty of the University of Illinois, Champaign-Urbana.

References and Notes

(1) We have utilized this simple model to guide our previous work on the thermal chemistry of azidoquinones: H. W. Moore, *Chem. Soc. Rev.*, **2,** 415 (1973).

(2) Combustion analyses and mass spectral properties of all new compounds described here are in agreement with their formulations.

(3) γ-Methoxy-α,β-dichloro-$\Delta^{\alpha,\beta}$-crotonolactone (**7**) is a known compound (V. Zikan, L. Vrba, B. Kakac, and M. Semonsky, *Collect. Czech. Chem. Commun.*, 38, 1091 (1973)). The other compounds in this series, i.e., **8, 9,** and **10,** are new compounds and were identified from their spectral properties and combustion analyses.

(4) See, for example, T. I. Bobrova, S. D. Volodkovish, and S. S. Kukalenko, *Zh. Obsch. Khim.*, **44,** 390 (1974); F. Zanker and F. Reischeneder, German Patent, 2,053,073 (1973), *Chem. Abstr.*, **77,** 75020 (1972); E. Winterfeldt and J. M. Nelke, *Chem. Ber.*, **101,** 3163 (1968); M. Semonsky, N. Kucharczyk, V. Zikan, and V. Jelinek, Czechoslovak Patent, 145,820 (1972), *Chem. Abstr.*, **78,** 159241 (1973); S. Jung, L. Jung, and P. Cordier, *C.R. Acad. Sci. Ser C,* **262,** 1793 (1966); M. Semonsky, E. Rockova, V. Zikan, B. Kakac, and V. Jelinek, *Collect. Czech. Chem. Commun.*, **28,** 377 (1963).

(5) *E*-Stereochemistry of **13** and **15** is assumed. This is based upon the report that chloroketene cycloadds to imines to give primarily the *trans*-3-chloro-2-azetidinones: D. A. Nelson, *Tetrahedron Lett.*, 2543 (1971).

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(7) H. W. Moore, H. R. Shelden, D. W. Deters, and R. J. Wikholm, *J. Am. Chem. Soc.*, **92,** 1675 (1970).

(8) H. W. Moore and H. R. Shelden, *J. Org. Chem.*, **33,** 4019 (1968).

(9) The azide was prepared in 77% yield by treating an acetonitrile solution of 2,3-dichloro-*N*-phenylmaleimide with 1 equiv of sodium azide, mp 113° dec.

(10) This compound was identified from its spectral properties and its independent synthesis by catalytic reduction of **20.**

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Oscillations in Chemical Systems. 15.[1] Deliberate Generation of Trigger Waves of Chemical Reactivity

Sir:

The oxidation of malonic acid by acidic bromate exhibits remarkable behavior when catalyzed by some 1-equivalent redox couples. Belousov[2] first observed homogeneous oscillations with the Ce(III)-Ce(IV) system, and Zhabotinsky[3] observed moving regions of alternating oxidation and reduction of the indicator catalyst ferrous phenanthroline.

Winfree[4,5] has studied the latter system in detail. When the solution is spread in a thin film saturated with air, the indicator may remain almost indefinitely in the reduced form without oxidation. However, this steady state situation is excitable, and reaction at a localized heterogeneous "pacemaker" can create a region of oxidation that then travels outward undamped at constant velocity as a thin band or trigger wave. Winfree[5] reports fascinating spirals and scrolls that can result from perturbation of these bands. Field and Noyes[6] measured band migration rates at different reagent concentrations and elucidated the mechanism of propagation. They also developed a model[7] of how the medium in the steady state could be excited by localized depletion of bromide ion.

The pacemakers observed by Winfree[4,5] were apparently adventitious dust particles, and he had no way to control the initiation of specific bands. Field and Noyes[6] found that nichrome wire could act as a pacemaker broadcasting repetitive pulses at a definite frequency. However, they still had no control over initiating individual pulses of oxidation. We report here a system in which such pulses can be generated at will.

Silver seemed a logical reagent to involve in local depletion of bromide ion, and we found that either a small crystal of silver nitrate or a piece of silver wire acted as an excellent pacemaker and generated successive waves of chemical activity. However, the pacemaking activity of a silver wire electrode could be suppressed by biasing it negative with respect to a platinum electrode in the same solution. The negative bias obviously suppresses the reaction $\mathrm{Ag(s)} + \mathrm{Br^-(aq)} \rightarrow \mathrm{AgBr(s)} + \mathrm{e^-}$.

If such a biased silver electrode is pulsed positive by a square wave lasting a few milliseconds, the oxidizing region that is generated moves outward as a trigger wave. The duration of the pulse necessary to generate such a wave is reduced if the pulse potential is more positive, and it is a fairly reproducible function of reactant concentrations. For the experiments at 25 °C reported here, trigger waves were suppressed by a negative bias of 0.6 V, and square wave pulses were 2.0 V positive.

The critical pulse width necessary to initiate a trigger wave varied between 1 and 7 ms and decreased linearly with increasing concentration of either H_2SO_4 or $NaBrO_3$. Extrapolations suggested the critical pulse width would go to zero either at $[\mathrm{BrO_3^-}] = 0.12$ M, $[\mathrm{H_2SO_4}] = 0.37$ M or at $[\mathrm{BrO_3^-}] = 0.075$ M, $[\mathrm{H_2SO_4}] = 0.60$ M. If $[\mathrm{BrO_3^-}][\mathrm{H_2SO_4}] \geqslant 0.045\ \mathrm{M}^2$, the 0.6-V negative bias apparently can no longer suppress pacemaking activity.

When critical pulse widths were plotted against concentrations of malonic acid, ferrous phenanthroline, or bromomalonic acid, the best lines through the points were horizontal or had slightly positive slopes; these reagents either have no effect on or slightly inhibit trigger wave generation. These results are consistent with our previous conclusions that both the rate of autocatalytic generation of bromous acid[8,9] and the rate of trigger wave propagation[6] depend only upon the product $[\mathrm{H^+}][\mathrm{BrO_3^-}]$ and not upon other concentrations.

Following a pulse of duration t, an ion reacting at an electrode should exhibit an approximately linear concentration gradient for a distance $2(Dt/\pi)^{1/2}$ where D is the diffusion coefficient. We have previously[6] estimated D for $\mathrm{Br^-}$ to be $1.8 \times 10^{-5}\ \mathrm{cm^2\ s^{-1}}$. Then a pulse of 4 ms would influence bromide concentration for a distance of about 3 μm; this distance is comparable to the calculated[6] width of the band front in an advancing trigger wave.

We also measured the voltage drop across a 100 ohm resistance in series with the electrode. The current during the pulse was about 0.6 mA and the electrode area was about 0.016 $\mathrm{cm^2}$. This current is about 10^4 times that sufficient to deplete all of the estimated[6] 4×10^{-7} M bromide ion in the zone of possible influence, and it is obvious that other species contributed to reaction at the electrode.

A trigger wave from a pulsed silver electrode can be directed down a channel in a Teflon waveguide at a rate of the order of millimeters per minute as measured previously.[6] When the wave reaches a platinum electrode, it will generate a response that can be introduced as a signal to an electronic circuit. We therefore have a homogeneous solution that can model a situation very like a nerve axon in that a controlled input at one point can generate a wave of chemical activity that moves unidirectionally at a known rate and delivers a signal to another predetermined point with a predictable delay.

The observations reported here reinforce our previous[6,7,9] mechanistic interpretation of this system. We shall publish a