A Dipyridoimidazolium Salt from Phenylchlorocarbene and 2,2′-Bipyridyl: Synthesis, Reaction Mechanism, and Effect of Rotamerism

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Keywords: Carbenes / Ylides / Cyclization / Intermediates / Solvent effects / Time-resolved spectroscopy

Phenylchlorocarbene, generated by photolysis or thermolysis of the phenylchlorodiazirine, reacts with 2,2′-bipyridyl to give, in alkane solvents, the 6-phenyldipyrido[1,2-*c*:2′,1′-*e*]imidazolium chloride. We investigated the mechanism of the reaction by flash photolysis. Like the mechanism of formation of 3-phenylindolizine from phenylchlorocarbene + 2-vinylpyridine, the process involves generation of the carbene, formation of a pyridinium ylide, and cyclization of the *syn* rotamer of this ylide, with the two N atoms of the bipyridyl in a *syn* relationship. The cyclization product then eliminates Cl^- to give a stable aromatic cation. We observed and identified all the intermediate species and measured the rate constants for the successive elementary reactions. This enabled us to define experimental conditions under which the reaction is nearly quantitative (the chemical yield of isolated product is $>90\,\%$). By contrast, use of a polar solvent such as dichloromethane yields a mixture of the products resulting from the cyclization of both the *syn*- and the *anti*-bipyridylium ylide rotamers. Semiempirical calculations qualitatively account for the effect of solvent polarity on the relative rates of cyclization of the *syn*- and *anti*-bipyridylium ylide rotamers and thus on the nature of the products. These calculations predict that, in the presence of *o*-phenanthroline, a model for the *syn* bipyridyl rotamer, phenylchlorocarbene should not give the expected diazacyclopentaphenanthrene, in agreement with the experiment findings.

Introduction

The reaction of a singlet chlorocarbene with 2-vinylpyridine (**2-VP**) is an innovative method for synthesis of indolizines.[1] The reaction occurs by cyclization of a 2-vinylpyridinium ylide, followed by the elimination of HCl, and two rotamers of the intermediate ylide have been distinguished by their spectroscopic and kinetic properties, although they yield the same final product.[2] Extending this reaction to systems in which the vinyl moiety of **2-VP** is exchanged for an aromatic ring would open the way to the synthesis of large polycyclic aza-aromatic derivatives. Because the aromaticity of the aryl ring would be destroyed by the cyclization of the ylide, this step of the reaction mechanism may well be impossible. In addition, if this aryl ring is unsymmetrical with respect to the pyridine–aromatic bond, two different products, each corresponding to one ylide rotamer, may be formed. For instance, in the case of 2,2′-bipyridyl (**bipy**), we must consider two forms of rotamerism: **1** ↔ **2** and **α** ↔ **β**, corresponding to rotations around the pyridyl–pyridyl and the $>N^+–C^-<$ bonds, respectively, as shown in Scheme 1. Cyclization of the ylide rotamer **1** would give the product **P1**, which cannot eliminate HCl, whereas the cyclization product of rotamer **2**, **P2**, may eliminate HCl to give the 5-phenylpyrido[2,3-*a*]indolizine **M2**. By contrast, with 1,10-phenanthroline (***o*-phen**) and 2-phenylpyridine (**ph-py**), **1** ↔ **2** rotamerism does not exist and the only possible cyclization product is the equivalent of **P1** in the case of ***o*-phen** and **P2** in the case of **ph-py**.

Here we report a study of the reaction of **PCC** with **bipy**, which demonstrates that the synthesis of indolizines by cyclization of pyridinium ylides may, in some cases at least, be extended to the synthesis of larger aza-aromatic compounds and that, depending on the solvent polarity, the result of the reaction is the cyclization either of only one or of both of the intermediate ylide rotamers (Scheme 2).

Results

Continuous Irradiation Measurements

Under continuous irradiation of a solution of **PCD** (0.02 M) + **bipy** (0.1 M) in hexane at 366 nm, a fine yellow precipitate appears immediately. The diffusion due to this precipitate rapidly prevents any significant spectroscopic measurement. We separated this precipitate from the solution by decantation, washed with hexane to eliminate the unreacted starting products, and then dissolved it in meth-

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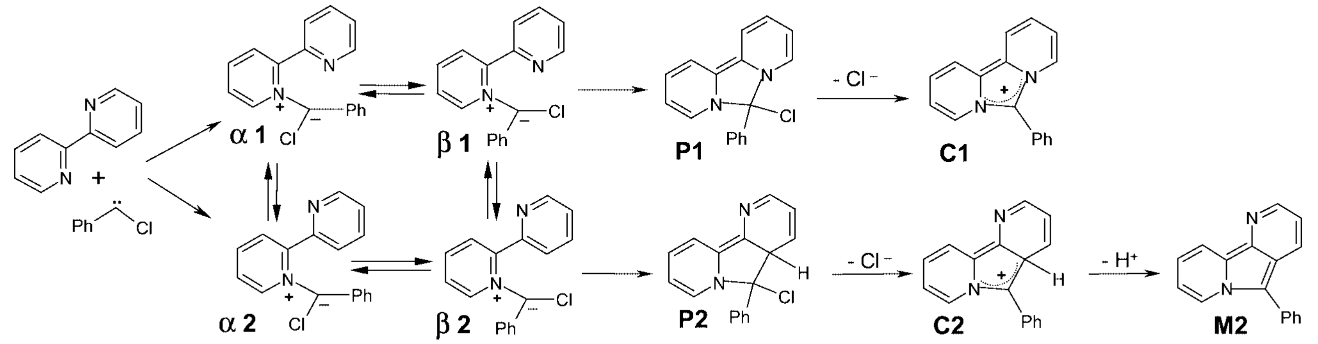
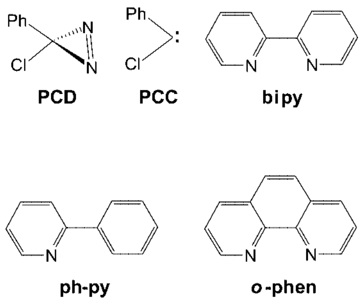


Scheme 1.



Scheme 2.

anol, or dichloromethane, or water to obtain a clear pale yellow solution. We irradiated the same mixture of **PCD** and **bipy** in CH_2Cl_2, in which the erstwhile precipitate is soluble. The evolution of the absorption spectrum as a function of the irradiation time is shown in Figure 1. As a result of the tail of absorption, which extends up to 550 nm, the solution turns to orange and then to deep red instead of the expected pale yellow color, suggesting that the reaction is not as clean as in alkanes.

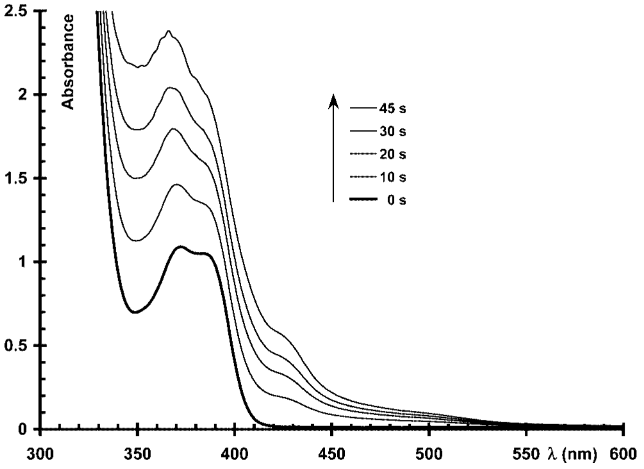


Figure 1. Evolution of the absorption spectrum of a solution of **PCD** (≈ 4.7 mM) + **bipy** (50 mM) in CH_2Cl_2 as a function of the time of irradiation at 366 nm.

Photolyses of **PCD** in the presence of **ph-py** and of ***o*-phen**, the two compounds used as models for the two **bipy** rotamers, gave quite different results. With **ph-py**, a red precipitate appeared after a few seconds of irradiation in isooctane, whereas a solution in CH_2Cl_2 remained clear but rapidly turned to a deep red color, with a long tail of absorption extending up to 650 nm.

By contrast, on photolysis of **PCD** + ***o*-phen** (0.1 M) in CH_2Cl_2 (***o*-phen** is nearly insoluble in alkanes), the evolution of the absorption spectrum in the 340–400 nm region was the same as in the absence of ***o*-phen**: the absorption spectrum progressively changed from that of diazirine into that of azine.

Preparative

The yellow precipitate obtained by photolysis of **PCD** + **bipy** in alkanes was identified as the 6-phenyldipyrido[1,2-*c*:2′,1′-*e*]imidazolium chloride (**C1**) on the following grounds: *i)* its ionic character, indicated by its complete insolubility in alkanes, *ii)* its UV/Vis absorption spectrum, shown in Figure 2, which perfectly matches the spectroscopic data provided by Sasse and Calder,[3] *iii)* the UV/Vis absorption spectrum of the dication obtained in 60% sulfuric acid, also in agreement with the Sasse and Calder data as shown in Figure 2, *iv)* its ^1H NMR spectrum,[4] and *v)* its X-ray crystallographic structure (Figure 3).[5]

This product can easily be prepared in gram amounts by thermolysis of **PCD** in an alkane in the presence of an excess of **bipy.** For instance, we added portionwise[6] a **PCD** solution[7] (0.1 M, 16 mL) to boiling isooctane (55 mL) containing **bipy** (0.2 M, 1.8 g), heated the mixture at reflux for a 5 hour period, separated the precipitate by decantation, washed it with hexane (10 mL portions) to eliminate the unreacted **bipy** until the hexane did not show the characteristic absorption bands of **bipy** at 236 and 281 nm, and then dried the precipitate under vacuum. This gave us a yellow-tan precipitate (454 mg), corresponding to a yield around 98% if it is assumed that this solid is the hemihydrate reported by Sasse and Calder.[3] The absorption spectrum of a MeOH solution of this crude product and that of the pale yellow crystals obtained after recrystallisation from chloroform are the same,[8] indicating that the crude product was pretty pure, so that the indicated yield is really the chemical yield of the reaction.

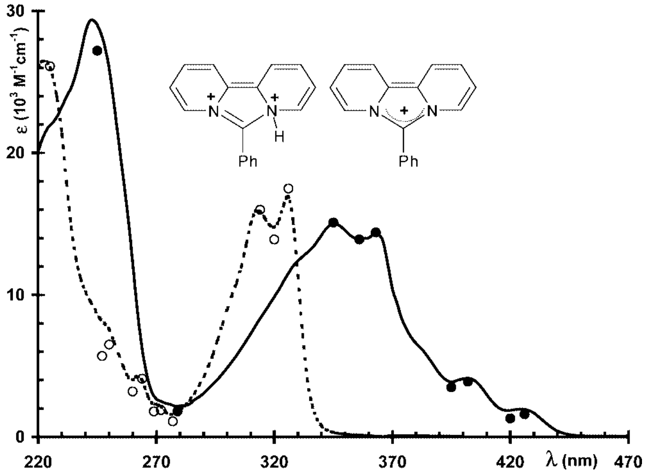


Figure 2. UV/Vis absorption spectrum of the product in MeOH (full line) and in 60% sulfuric acid (dashed line). Closed and open circles are from the Calder and Sasse data (λ_{max}, λ_{min}, ε values) for the cation and dication shown as inserts.

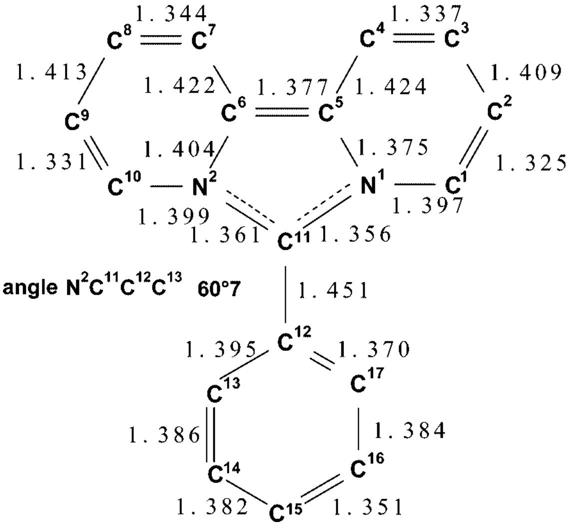


Figure 3. Structure of **C1** as determined by X ray crystallography. The N^1–C^5 and N^1–C^{11} bonds are shorter than N^2–C^6 and N^2–C^{11}, respectively. This asymmetry is induced by the fact that, in the crystal, the Cl^- anion, which lies ≈ 3.6 Å below the dipyridoimidazole cycle and approximately under N^1, is closer to N^1 (≈ 3.7 Å) than to N^2 (≈ 4.5 Å).

Flash Photolysis Measurements

In the absence of added reactant, the absorption of phenylchlorocarbene (**PCC**) in the 280–350 nm region decays by the sum of an efficient second order process yielding a stilbene and several pseudo-first order processes corresponding to reactions of the carbene with the diazirine, the solvent, and oxygen.[9] Under our experimental conditions the resulting decay time is a few µs.

In isooctane, the addition of 1 or 2 mM of **bipy** does not significantly change the decay kinetics of **PCC** measured at 330 nm. No growth of an ylide absorption can be observed in the 450–600 nm region.

With larger amounts of **bipy** (10–100 mM), measurements at 330 nm are no longer possible, because of the strong absorption of **bipy**, but we can observe a transient species absorbing in the 400–700 nm region (see Figure 4). This species is easily identified as the bipyridinium ylide on the basis of its absorption spectrum, given in Figure 5, and of its kinetics of formation. It grows according to first order kinetics with a rise time of τ_{gr}, independently of the observation wavelength and inversely proportionally to [**bipy**], as expected from the expression $k_{gr} = 1/\tau_{gr} = k_0 + k_{yl}$ [**bipy**], where k_0 is the "decay time" of the carbene in the absence of **bipy** and k_{yl} the rate constant for ylide formation. From the plot of $1/\tau_{gr}$ vs. [**bipy**] for [**bipy**] in the 0–0.1 M range, the value of formation, k_{yl}, in isooctane is found to be 2.25×10^7 M^{-1} s^{-1}.[10]

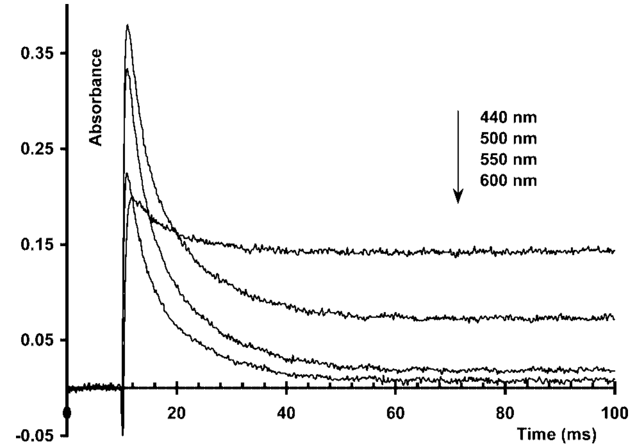


Figure 4. Transient absorption changes, recorded at a 10 ms div^{-1} sweep rate, after excitation of a solution of **PCD** (10 mM) and **bipy** (50 mM) in isooctane with a millisecond flash of light.

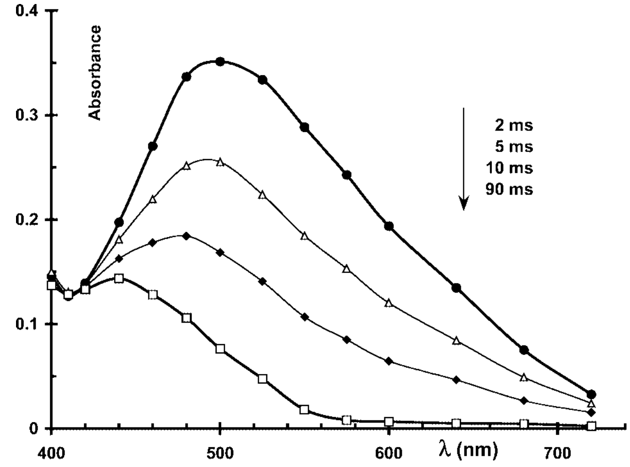


Figure 5. Time-resolved spectra over the 10–100 ms period, reconstructed from traces such as those shown in Figure 4.

The ylide decays with a lifetime of around 10 ms in isooctane at 25 °C. This lifetime depends on temperature, ranging from 3.6 ms at 52 °C to 25 ms at 10 °C, and a plot of ln (1/τ) vs. 1/T, shown in Figure 6, gives the following Arrhenius parameters: E_a = 8.3 kcal mol^{-1} and A = 8.9×10^7 s^{-1}.

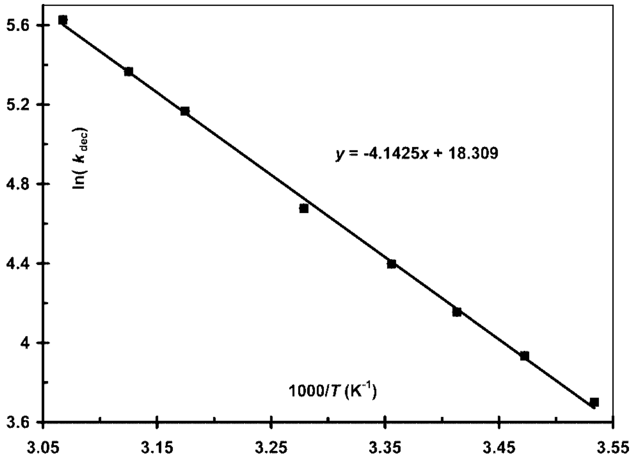


Figure 6. Arrhenius plot for the decay of the ylide.

After the complete disappearance of the ylide absorption, the absorbance of the solution does not return to zero. The amplitude of the remaining absorption depends on the observation wavelength: it is small at 600 nm, noticeable at 500 nm, and quite large at 440 nm, a wavelength dependence expected for the effect of diffusion by a fine precipitate. However, this amplitude fails to increase any longer in the 400–440 nm wavelength range, so the absorption spectrum recorded 90 ms after excitation (see Figure 5) is clearly not due to the effect of diffusion but must be related to a chemical species with a long (or infinite) lifetime. This chemical species cannot be the final product, which does not absorb above 450 nm, nor a by-product, since the reaction is quantitative. It must be the product of the cyclization, **P1**, the calculated absorption spectrum of which consists, in the visible, of a single band with a maximum at 465 nm. The **P1** species decays with a lifetime of a few seconds, difficult to measure because of the diffusion due to the precipitation of final product **C1**. The aggregation of this precipitate from the molecular size to the few microns size extends over 2–3 minutes. During this time, the absorption of the solution due to the diffusion slowly increases to a larger extent in the blue than in the red. However, during the first 4–5 seconds after excitation and in the 420–520 nm range, a small decrease in the absorption occurs following the initial jump of the absorbance, as shown in Figure 7.

The curves representing the growth of the absorbance due to diffusion measured at various wavelengths are similar in shape and differ only by their amplitude: $A_{\mathrm{diff}}^{700} = f(\mathrm{t})$, measured at 700 nm, multiplied by 2, fits the curve $A_{\mathrm{diff}}^{600} = f(\mathrm{t})$, measured at 600 nm, quite well. Similarly, the curves obtained by multiplying $A_{\mathrm{diff}}^{600} = f(\mathrm{t})$ by 2.47 and 6.1 fit the late part (t > 7 s) of the curves A^{500} and A^{440}, which are the sum of A_{diff} and $A_{(\mathrm{P1})}$. Therefore, the absorption curves of **P1** at 440 and 500 nm, $A_{(\mathrm{P1})} = f(\mathrm{t})$, were obtained as the differences $A^{440} - 6.1 \times A_{\mathrm{diff}}^{600}$ and $A^{500} - 2.47 \times A_{\mathrm{diff}}^{600}$ and then plotted on a ln scale in Figure 8. This gives straight lines yielding similar values for the lifetime of **P1** in isooctane at 22 °C: 1.71 and 1.74 s.

In CH_2Cl_2, the behavior of the system is similar, but with some noticeable differences:

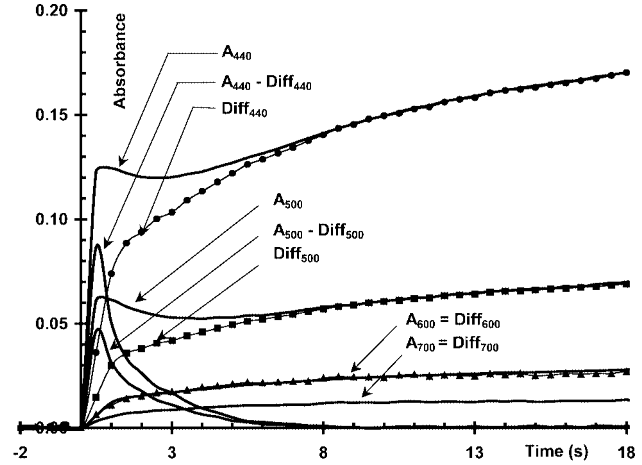


Figure 7. Evolution of the absorbance at 440, 500, 600, and 700 nm for a solution of **PCD** (10 mM) and **bipy** (50 mM) in isooctane excited by a millisecond flash of light. Measurements made every 0.5 s with a HP 8452A spectrophotometer in kinetic mode.

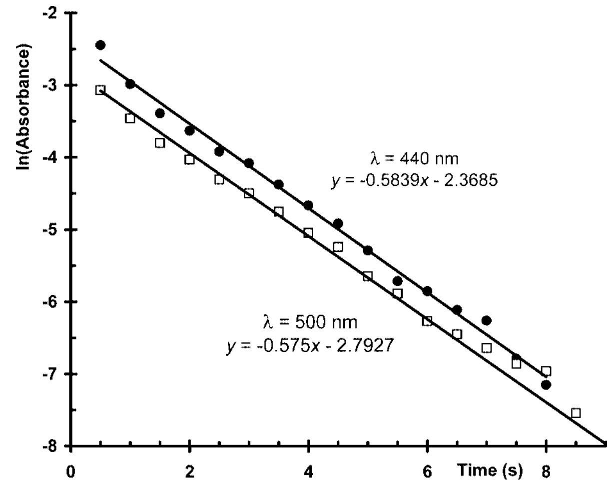


Figure 8. Kinetic analysis of the decay of the absorption of **P1** at 440 and 500 nm over the 1–9 second period of time. The absorption of **P1** as a function of time is obtained as indicated in Figure 7.

a) The lifetime of the ylide, 0.8 ms at 21 °C, measured from flash photolysis traces shown in Figure 9, is about 10 times shorter than in isooctane. As in isooctane, the transient absorbance does not return to zero after completion of the ylide decay.

b) The absorption spectrum of the ylide, shown in Figure 10, is broader and its maximum is red-shifted by about 40 nm.

c) The value of the rate constant for ylide formation, obtained from the plot of $1/\tau_{gr}$ vs. [**bipy**] ($7.7 \times 10^6\ \mathrm{M}^{-1}\,\mathrm{s}^{-1}$ at 25 °C), is three times lower than it is in isooctane.

d) The flash photolysis traces on a 200 ms timescale (see Figure 11) indicate that a part of this remaining absorption corresponds to a species decaying with a 20 ms lifetime (see Figure 12) and with an absorption spectrum in the 400–500 nm region (maximum around 440 nm) similar to that of the **P1** species observed in isooctane, which, however, has a much longer lifetime of 1.7 seconds. This strong effect of

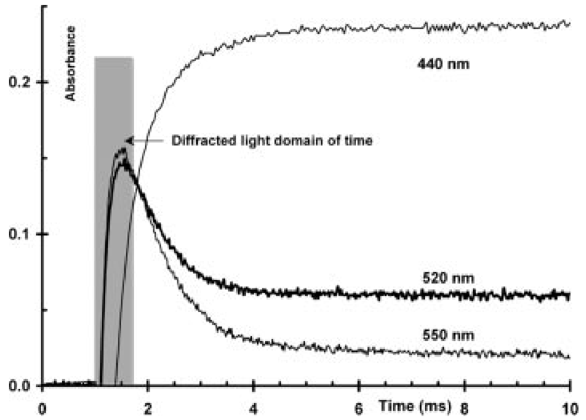


Figure 9. Transient absorption changes, recorded at a 1 ms/div sweep rate, after excitation by a millisecond long flash of light, of a solution of **PCD** (15 mM) and **bipy** (50 mM) in CH_2Cl_2.

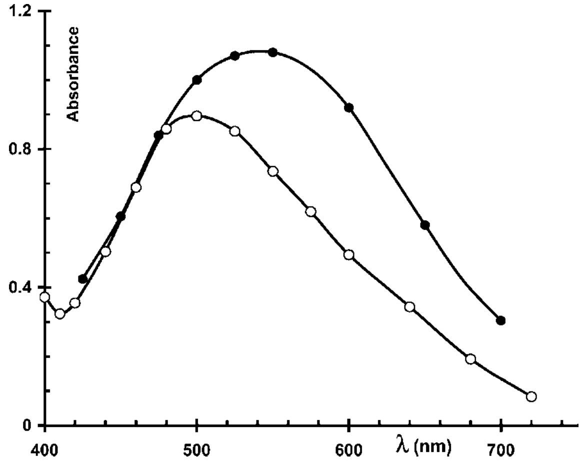


Figure 10. Absorption spectra of the ylide in CH_2Cl_2 (closed circles) and in isooctane (open circles). The latter is taken from Figure 5.

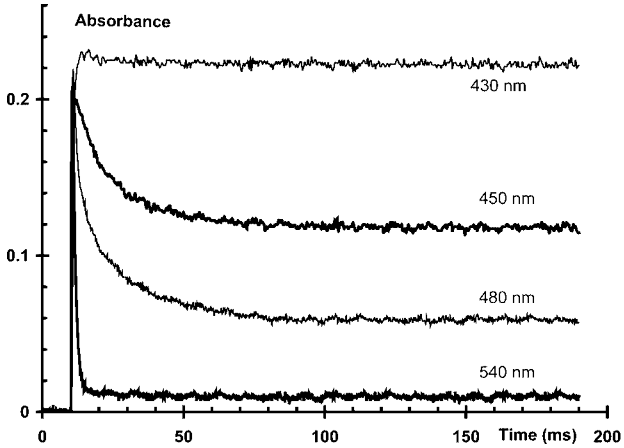


Figure 11. Transient absorption changes, recorded at a 20 ms/div sweep rate, after excitation by a millisecond long flash of light, of a solution of **PCD** (15 mM) and **bipy** (50 mM) in CH_2Cl_2.

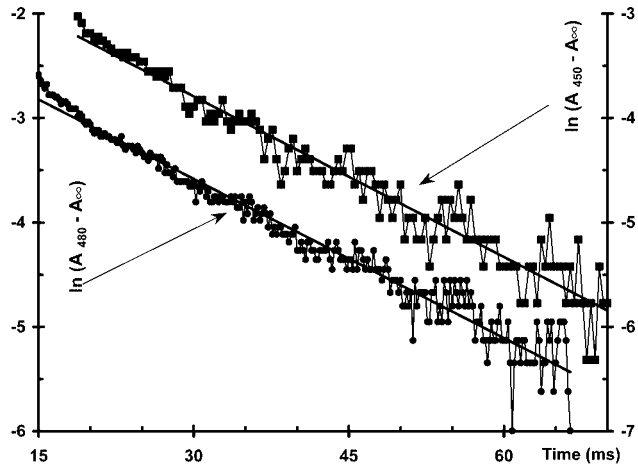


Figure 12. Kinetic analysis of the decay of the absorption at 450 and 480 nm.

the polarity of the solvent on the lifetime of the product(s) of cyclization **P**, which is determined by the rate of Cl^- elimination, is easily explained by the solvation of the Cl^- and **C** ions.

The absorption remaining after 200 ms is stable, over several minutes at least. The final absorption spectrum of the solution can be reproduced as the sum of the spectra of the remaining reactants and of the cation **C1** plus a broad absorption responsible for the long "tail" extending over the 450–600 nm region.

This last component, which also appears in the spectra recorded under continuous irradiation (see Figure 1), is most certainly related to products derived from the cyclization of the rotamer **Y2** of the ylide, because a similar absorption spectrum of the product(s) formed is observed when **bipy** is exchanged for **ph-py**. These products are **P2**, the cation **C2** after elimination of Cl^-, and possibly the molecule **M2** (5-phenylpyrido[2,3-a]indolizine) resulting from the elimination of HCl. Of these three compounds, only **C2** has an absorption band in this part of the visible spectrum. The calculated absorption spectrum of **C2**, shown in Figure 13, shows a band with a maximum at 500 nm. Because **C2** is a polyenic cation, its absorption spectrum is quite different from that of **C1**, which is an aromatic cation.

The ionic character of the colored product was confirmed as follows. The black solid residue remaining after thermolysis of a **PCD** + **bipy** solution in 1,2-dichloroethane and evaporation of the polar solvent was washed with hexane. The resulting hexane solution contained only the **bipy** in excess and traces of azine, but no colored product.

We repeated the washing with hexane until the complete removal of **bipy**; we then dried the black residue, dissolved it in CH_2Cl_2, and subjected it to chromatography (silica gel column, CH_2Cl_2 + 10% MeOH eluent). This first gave the **C1** cation, and some colored product(s) were then extracted when the MeOH fraction of the eluent was boosted to 50%. The UV/Vis absorption spectrum of the colored fractions of this chromatography showed no structure, indicating that the initial colored product did not survive the procedure.

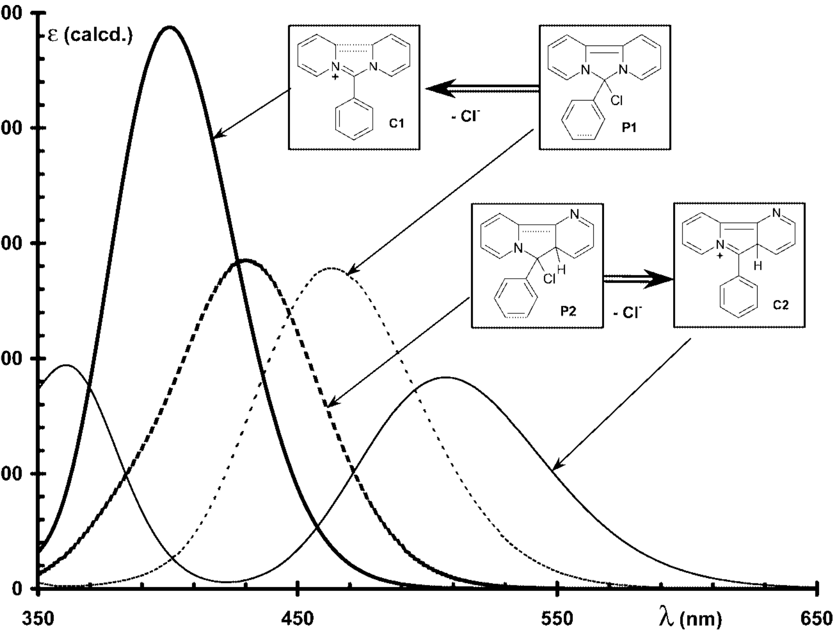


Figure 13. Absorption spectra for **P1**, **P2**, **C1**, and **C2** calculated by ZINDO after optimization of the geometries by MOPAC with PM3 parameters.

Discussion

Synthetic Aspects

For synthetic purposes it is advantageous to conduct the reaction by thermolysis in an alkane, in which the product **C1** precipitates. It is thereby protected against possible secondary reactions and is easily separated from the remaining reactants. Thermolysis (90 °C for 8 hours) of a deaerated isooctane solution containing a low concentration of diazirine (5 mM) to minimize the formation of azine and a large excess of **bipy** (0.1 M) to maximize the yield of ylide formation gave **C1** with a 90% chemical yield (respective to the initial amount of diazirine). Let's recall that the synthesis of **C1** from **bipy** and benzylidene chloride described by Calder and Sasse[3] gave, after a two-week process, an 8% yield, reaching 44% after an additional three weeks.

Mechanism, Kinetics, and Reactivity

From a mechanistic point of view, this experiment demonstrates that the cyclization of pyridinium ylides is still possible when the double bond in the β position of the ylide center is part of an aromatic ring. The mechanism is fully established because all the intermediate species (carbene, ylide, and cyclized product) can be observed, whereas in the (**PCC + 2-VP**) system the cyclized product could not be observed because the elimination of HCl is faster than the cyclization of the ylide.

Some differences between the systems (**PCC + 2-VP**) and (**PCC + bipy**) deserve mention. The rate of ylide formation in isooctane is slower with **bipy** (2.25×10^{7} M^{-1} s^{-1}) than with **2-VP** (7×10^{7} M^{-1} s^{-1})[1] or pyridine (3.3×10^{8} M^{-1} s^{-1}).[11] The apparent relationship between the size of the *ortho* substituent on the pyridine and the decrease of the k_{yl} value suggests that this could be related to some steric hindrance at the level of the transition state. This steric factor is probably not responsible for the variations of the k_{yl} values because, as shown below, the rotation of the pyridyl units around the C^{2}–$C^{2'}$ bond of **bipy** is nearly free, so that distortion of the bipyridine unit needed to reach the transition state must be easy. A more plausible explanation is a change in the availability of the lone pair at nitrogen, a property related to the pK_a values: 5.25 for the pyridine,[12] 4.98 for **2-VP**,[13] and 4.33 ± 0.10 for **bipy**.[14,15] The lower the pK_a value, the less available is the nitrogen lone pair, and the lower is the value of k_{yl}.

By contrast, in the case of ***o*-phen** (pK_a = 5.2;[15] about the same as for pyridine), the lack of ylide formation is probably due to steric effects and not to the availability of the nitrogen lone pair. The calculated enthalpy of the formation of ***o*-phen** increases rapidly with the N–C–C–N dihedral angle. A geometry with $\alpha = 40°$, compatible with a carbene approaching one of the N atoms at a 1.9–2 Å distance without too much steric repulsion by the rest of the molecule, is destabilized by 6.4 kcal mol^{-1}. This would slow down the rate of ylide formation by five orders of magnitude, so that the ylide formation could not compete with the other reaction pathways of the carbene, such as azine formation and reaction with the solvent.

At room temperature, the cyclization of the **bipy** ylide is about 1000 times slower than that of the **2-VP** ylide.[16] This not due to a higher activation energy (the measured value of E_a for the cyclization of the **bipy** ylide, 8.3 kcal mol^{-1}, is even lower than that for the **2-VP** ylide, 12 kcal mol^{-1}), but to a much lower frequency factor, $A \approx 10^{8}$ s^{-1}, which is about four orders of magnitude smaller than in the case of the **2-VP** ylide. This is indicative of a much tighter transition state in the case of the **bipy** ylide and may be also related to the fact that, due to the respective masses of the phenyl, pyridyl, and vinyl moieties, the number of rotational states frozen by the cyclization is much larger in the case of the **bipy** and **ph-py** ylides than in the case of the **2–VP** ylide.[17]

Rotamerism in Alkanes

In isooctane, the only product of the ylide cyclization corresponds to a *syn* geometry of the bipyridyl moiety, whereas it is known that the most stable rotamer of the free **bipy** has an *anti* geometry. The enthalpy of formation calculated with MOPAC with PM3 parameters, ΔH_f, is 2 kcal mol^{-1} lower for the *anti* rotamer of **bipy** than for the *syn* rotamer. By contrast, for the protonated **bipy** and the α and β type ylides, the ΔH_f values of the *syn* rotamers are lower than those of the *anti* rotamers by 4.6, 6.2, and 3 kcal mol^{-1}, respectively. In all cases the rotation around the C2–C2′ bond of **bipy** is nearly free, the ΔH_f values calculated for the orthogonal geometry being between those of the *syn* and *anti* rotamers or, in the case of the β-type ylide, slightly lower (see Table 1).

Therefore, the equilibration between the various ylide geometries is much faster than the cyclization reaction and the nature of the final product, **P1** or **P2**, is determined not by the predominance of one or the other of the ylide structures but by the relative energies of the transition states **TS1** and **TS2** on the pathway to the **P1** and **P2** (assuming that the frequency factors for cyclization to **P1** and **P2** are similar).

We calculated the energetics of the cyclization reaction by the following procedure. The enthalpy of formation of the cyclized product was obtained after optimization of the geometry by molecular mechanics (MM3) followed by MOPAC with PM3 parameters. The enthalpy of formation was then recalculated with the length of the bond formed by the cyclization process locked on progressively increasing values, all the rest of the system being allowed to be optimized. The resulting reaction pathways for the cyclization of the **bipy**-ylide rotamers to **P1** and **P2** are shown in Figure 14, where the calculated values of ΔH_f are plotted vs. the length of the bond formed during the cyclization process. The figure also shows the results of similar calculations for the cyclization of the ***o*-phen** and **2-VP** ylides, regarded as models for the cyclization to **P1** (formation of a second C–N bond) and to **P2** (formation of a C–C bond).

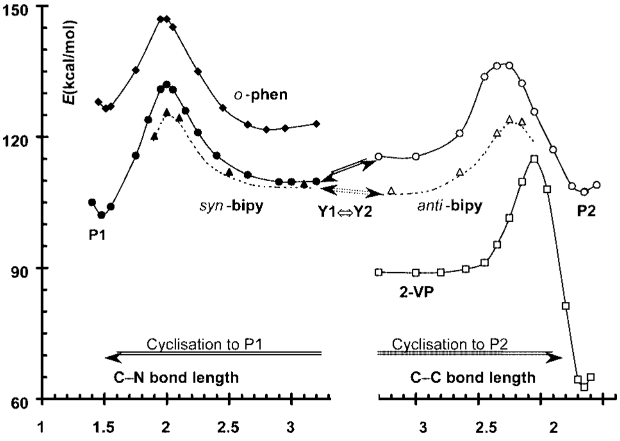


Figure 14. Reaction pathways calculated for the cyclization of the ylides **PCC + 2-VP**, ***o*-phen** and **bipy** (*syn* and *anti*). Full lines: in a nonpolar solvent; dashed lines: cyclization of the *syn* and *anti* **bipy** ylides in a polar solvent, simulated with the COSMO model.

The main conclusions of these calculations are the following:

a) The cyclization is exothermic by 26 kcal mol^{-1} for the **2-VP** ylide and by 8 kcal mol^{-1} for the **bipy** ylide, but it would be endothermic by 5 kcal mol^{-1} for the ***o*-phen** ylide (if it were formed) because the C^5=C^6 bridge hinders the decreases in the N^1–C–C and C–C–N^{10} angles needed to closing the five-membered ring.

b) The calculated activation energies, $E_{a(cycl}$, for cyclization of the **ph-py** and *syn*-**bipy** ylides – 13.7 and 22.5 kcal mol^{-1}, respectively – are lower than for the **2-VP** ylide (26 kcal mol^{-1}). These values, compared with experimental data (5, 8.3 and 12 kcal mol^{-1}), appear overestimated (this is a common occurrence with semiempirical methods) but their relative ordering reflects that of the measured values.

c) The ylide rotamer **Y2** is about 6 kcal mol^{-1} higher in energy than rotamer **Y1**, which should therefore represent more than 99% of the mixture of ylide rotamers.

d) The transition state **TS2** is about 4.5 kcal mol^{-1} higher than **TS1** for the cyclization to **P1**, which should be nearly the only product formed, in agreement with experimental observations.

Rotamerism in Polar Solvents

In a polar solvent, the reaction produces two products: the cation **C1** and a red product that could not be isolated but which we tentatively assigned as the cation **C2** because

Table 1. Increase in the enthalpy of formation calculated with MOPAC (PM3) as a function of changes in θ, the N–C–C–N dihedral angle of the bipyridyl moiety, with respect to the most stable conformation.

ΔH_f [kcal mol^{-1}]	bipy	bipy-H$^+$	Ylide α	Ylide β	*o*-Phenanthroline
syn (0° < θ < 45°)	2	0	0	0.5	ΔH_f = 1.5 for θ = 20°
Perpend. (θ = 90°)	0.8	4.1	4	0	ΔH_f = 3.6 for θ = 30°
anti (150° < θ <180°)	0	4.6	6.2	3.5	ΔH_f = 6.4 for θ = 40°

of: *i)* its ionic character, *ii)* its absorption spectrum, and *iii)* the same type of product being obtained when the **bipy** reactant is changed to **ph-py**. Thus it seems that, in a polar solvent, both the *syn* and *anti* ylide rotamers undergo the cyclization reaction. In order to test this conclusion, the energetics of the cyclization reaction were recalculated with the effects of a polar solvent being taking into account with the COSMO model.[18] The main results of these calculations (see Figure 14) are listed below.

a) The value of $E_{a(cycl)}$ for the **bipy** ylide decreases from 22.5 kcal mol^{-1} in a nonpolar solvent to 16.3 kcal mol^{-1} in a polar solvent, so the cyclization should be faster in CH_2Cl_2 than in an alkane. This agrees with the fact that the ylide lifetime in CH_2Cl_2 is 10 times shorter than it is in isooctane. Again, the quantitative agreement is poor (a 6 kcal mol^{-1} decrease in $E_{a(cycl)}$ should increase k_{cycl} by a factor of 2×10^4), but the trend is correct.

b) In a polar solvent, the ylide rotamers **Y1** and **Y2** are close in energy (109.3 and 107.8 kcal mol^{-1}, respectively), so the observed ylide should be a mixture of both species with **Y2** as major component, whereas it was shown above that, in alkanes, **Y1** should represent more than 99% of the mixture of ylide rotamers. The calculated absorption spectra of **Y1** and **Y2** are different such that the UV/Vis absorption of a mixture should be broader by 50 nm, and its maximum red-shifted by 30 nm with respect to the absorption spectrum of **Y1** alone (see Figure 15). This agrees with the experimental results, shown in Figure 10.

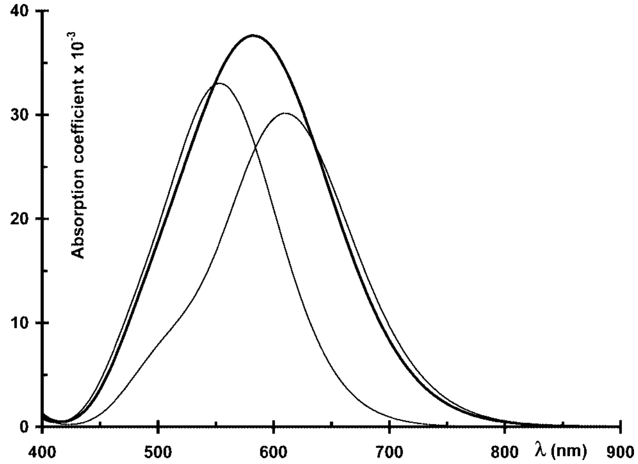


Figure 15. Absorption spectra for ylides **Y1** and **Y2** calculated by ZINDO after optimization of the geometries by MOPAC with PM3 parameters. The bold curve represents the absorption spectrum of a mixture of **Y1** and **Y2** in 2:3 proportions.

c) In a polar solvent, **TS1** and **TS2** are close in energy (125.7 and 124.1 kcal mol^{-1}, respectively), so the cyclization should give a mixture of **P1** and **P2** with the latter as major component, again in agreement with our interpretation of the experimental results obtained in CH_2Cl_2.

These calculations support the idea that the use of a polar solvent opens the way to cyclization to **P2** by stabilizing **TS2** more efficiently than **TS1**, as we expected intuitively, because interactions between the free N lone pair and a polar solvent are sterically easier for the *anti* species than for the *syn* one in which the free N atom is shielded by the carbene moiety.

When we started this study, we expected **P1** to be a stable product and we hoped that it could be photodissociated into **PCC** and **bipy**. This would provide a convenient source of **PCC** by excitation in the 400–500 nm wavelength range,[19] more easily accessible than the 250–300 nm region in which Jones'[20,21] and Johnson's[22] non-nitrogenous precursors of carbenes must be photolyzed. According to our calculations this is energetically possible, but **P1** has too short a lifetime to be of practical interest as a potential source of **PCC**. The elimination of Cl$^-$ is driven by a strong energetic factor, **P1** being a polyene, whereas **C1** is an stable aromatic system, unaffected by boiling aqueous NaOH solutions or by sodium methoxide.[3] The cation **C2**, being polyenic, is probably less stable. This may be the reason why we were unable to isolate it.

The phenyl substituent contributes to the stabilization of **C1**.[23] It seems impossible to eliminate it to produce the "Arduengo-type carbene" such as has been obtained by deprotonation of the dipyridoimidazolium salt in a case in which the phenyl is exchanged for an H atom.[24]

Conclusions

This work demonstrates that the synthesis of indolizines by cyclization of the 2-vinylpyridinium ylides of singlet aryl chlorocarbenes may be extended to systems in which the vinyl double bond is exchanged for an aromatic group such as a pyridyl or a phenyl. This study also reveals some limitations. The formation of the intermediate ylide requires good availability of the N lone pair of the pyridine moiety, indicated by a pK_a larger than 4. For instance, no ylide would be expected to be formed with 4-phenylpyrimidine because of the low pK_a value of the pyrimidine. Additionally, the flexibility of the arylpyridine system must be sufficient to allow first the formation of the ylide, and then its cyclization. The reaction should not occur with compounds such as 5*H*-indeno[1,2]pyridine or benzo[*h*]quinoline.

Finally, we wish to emphasize two points concerning rotamerism: *i)* the nature of the product(s) is not determined by the relative energies (and thus the populations) of the two ylide rotamers but by the relative energies of the transition states leading to the products of cyclization, and *ii)* the polarity of the solvent affects these energies and therefore the nature of the products.

Experimental Section

We prepared phenylchlorodiazirine (**PCD**) from benzamidine hydrochloride (Aldrich) by Graham's procedure.[25] Aldrich products **bipy** (99+%), ***o*-phen** (99+%), and **ph-py** (98%) were used as received. Isooctane and dichloromethane solvents (SDS or Aldrich) were "UV spectroscopy" or "HPLC" grades. We kept isooctane over molecular sieves in order to minimize its water content. We performed continuous irradiations with a medium-pressure mercury lamp (Philips HPK 125) with a set of filters to isolate the 366 nm line. We used a diode-array spectrophotometer (HP, 8452A) to record the evolution of the UV/Vis spectrum of the solutions after continuous irradiations. This spectrophotometer also enables us to record a series of spectra at regular time interval, down to 0.5 s for a 200 nm range. This proved to be useful for following the evolution of the spectrum over several seconds or minutes after excitation of the sample, inside the spectrophotometer, by a millisecond flash of light provided by a photographic flash.

For flash-photolysis measurements in the 10 ns–1 ms range, the set-up (kinetics type, right angle arrangement) used a frequency tripled mode-locked Nd-YAG laser (Quantel), providing 200-ps single pulses with 30 mJ energy at 355 nm as excitation and a pulsed 75-W Xe-arc as the source for the analytical light beam. The detection system had a 3-ns response time. We collected the data on a digital oscilloscope (Tektronix TDS 620B), operated in oversampling mode to improve the signal/noise ratio. For measurements in the 10 ms–10 s range, the excitation was given by the millisecond light pulse of a photographic flash and we obtained an extremely stable analytical light beam from a 12 V/50 W quartz tungsten halogen lamp powered by a car battery. In addition, to avoid the effect of macroscopic diffusion from highly excited fractions of the sample to less excited ones, we used a small cell (10 mm analytical path × 3 mm excitation path × 4 mm high) to ensure a homogeneous excitation of the entire volume.

We used a package of molecular mechanics and semiempirical methods, CAChe 3.2 for Windows, to calculate the geometries, the enthalpies of formation (MOPAC with PM3 parameters), and the UV/Vis absorption spectra (ZINDO) of various species involved in this study.

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[6] 4 mL portions, added at 1 hour intervals so that the diazirine concentration never exceeds 7 mM in order to minimize the formation of azine.

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[17] The frequency factor for the cyclization of the **ph-py** ylide is even lower, $A \approx 10^7\ \text{s}^{-1}$.

[18] CAChe 3.2, Oxford Molecular Ltd., includes a COSMO module.

[19] Calculated ΔH_f = 155 kcal mol^{-1} for **PCC + bipy** and 102 kcal mol^{-1} for **P1**; from the onset of the calculated and experimental UV spectra of **P1**, around 540 nm, **P1*** should be 53 kcal mol^{-1} above the ground state so that ΔH for the reaction **P1*** → **PCC + bipy** would be close to zero. The ΔG value would be negative because the entropy factor favors the dissociation.

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