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LETTERS

Rearrangements of cyclopropylmethylchlorocarbene and dicyclopropylmethylchlorocarbene

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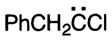
Abstract—Cyclopropylmethylchlorocarbene (**3**) and dicyclopropylmethylchlorocarbene (**4**) give only 1,2-H shift products with $k_H = 2.0 \times 10^7$ and 1.3×10^7 s^{-1}, respectively, at 25°C. © 2001 Elsevier Science Ltd. All rights reserved.

The kinetics and energetics of the 1,2-rearrangements of alkyl- and alkylchlorocarbenes have been much studied, both experimentally and computationally.[1] Benzylchlorocarbene (**1**), in particular, attracted great attention due to the possible occurrence of quantum mechanical tunneling (QMT) coincident with its 1,2-H shift to β-chlorostyrene.[2] However, the most recent experiments do not provide support for QMT in this reaction at ambient or near-ambient temperatures.[1d,3]


$PhCH_2\ddot{C}Cl$

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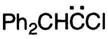
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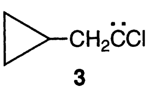

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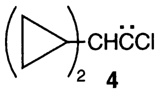

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Benzylchlorocarbene was also a testing ground for the electronic effects of the phenyl 'bystander' substituent on the kinetics of the carbene's 1,2-H shift. The matter has been extensively explored,[1a,d,2–5] with extension to the properties of diphenylmethylchlorocarbene, **2**.[4,6,7] For both carbenes **1** and **2**, 1,2-H migration exceeded 1,2-Ph migration: with **1**, the 1,2-H/1,2-Ph product shift ratio was 13.8 (*hν*, isooctane, 25°C),[3] whereas it was 14.2 (*hν*, 22°C) or 13.7 (Δ, 78°C) for carbene **2** in pentane.[6]

Computationally, it was shown that the preference for 1,2-H shift is mainly due to the greater ability of the bystander Ph substituent to accelerate a 1,2-H shift than that of a bystander H to foster a 1,2-Ph shift.[4,7] The bystander effect dominates an intrinsic Ph>H migratory aptitude for 1,2-carbenic rearrangements, and arises from the superior propensity of the phenyl substituent to stabilize the partial positive charge that develops at C2 during the hydride-like migration of H from C2 to C1.[1,4,8] The bystander effect of Ph is geometry dependent: the Ph group must assume a conformation appropriate for (resonance) electronic interaction with the developing *p* orbital at C2; steric inhibition of the rotational freedom (and hence of resonance) reduces the potency of phenyl as a bystander.

The cyclopropyl (Cy) substituent effectively stabilizes adjacent carbocation centers;[9] indeed "cyclopropylmethyl cations are even more stable than the benzyl type."[10] Cy also strongly interacts with the vacant *p* orbital of an adjacent carbenic center, conferring unusual properties on CyCCl.[11] Indeed, 'resonance' electron donation from the *p*-rich σ bonds of Cy to an adjacent vacant *p* orbital is stronger than the analogous π electron donation from Ph.[12]

Accordingly, we have now examined the products, kinetics, and (computed) transition states of the 1,2-rearrangements of cyclopropylmethylchlorocarbene (**3**) and dicyclopropylmethylchlorocarbene (**4**), the cyclopropyl analogues of carbenes **1** and **2**. Our findings define the comparative rearrangement proclivities and bystander effects of Cy and Ph substituents in 1,2-carbenic rearrangements.

Carbenes **3** and **4** were generated from diazirines **5** and **6**, which required the prior preparation of amidinium salts **7** and **8**. Cyclopropylacetamidinium chloride (**7**) was obtained in 60% yield from α-cyclopropylacetonitrile by sequential treatment with HCl/EtOH and NH_3/EtOH.[13] Dicyclopropylacetamidinium chloride (**8**) was obtained in 60% yield from α,α-dicyclopropylacetonitrile by reaction with methylchloroaluminum amide

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Keywords: carbenes; diazirines; kinetics.

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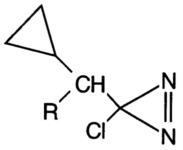
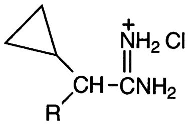
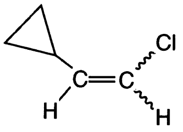
(90°C, 35 h, 2 equiv. of $MeAl(Cl)NH_2$).[14] The nitrile was itself obtained in 40% yield from dicyclopropylketone by reaction with *p*-toluenesulfonylmethyl isocyanide.[15]


5, R=H
6, R=Cy


7, R=H
8, R=Cy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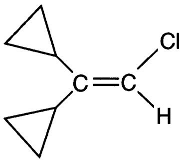
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Amidinium salts **7** and **8** were converted to diazirines **5** and **6** in ~40% yields by Graham oxidation with 12% HOCl.[16] The diazirines were purified by chromatography on silica gel (1:2 CH_2Cl_2/pentane), and exhibited UV maxima in pentane at 342, 358 nm (**5**) and 344, 356 nm (**6**).

Photolysis of diazirine **5** in pentane ($A_{max} = 0.5$, Rayonet reactor, 350 nm, 30 min, 25°C) afforded only *E*,*Z*-1-chloro-2-cyclopropylethene (**9**) via 1,2-H shift of carbene **3**.[17] Capillary GC and GC–MS analysis gave no evidence for the formation of the 1,2-Cy migration product of **3**; i.e. 1-chloro-1-cyclopropylethene. Thermolysis of diazirine **5** in pentane (100°C, 24 h, sealed tube) also afforded only H-shift products **9**.[17] The identity of *E*,*Z*-**9** was established by GC–MS and GC-spiking experiments with the authentic alkenes, obtained in 65% yield from the reaction of cyclopropanecarboxyaldehyde with triphenylphosphonium chloromethylide,[18] purified by preparative GC on SF-96, and characterized by NMR and HRMS.

Photolysis or thermolysis (as above) of diazirine **6** afforded only the 1,2-H shift product of carbene **4**, 1-chloro-2,2-dicyclopropylethene, **10**. Again, capillary GC and GC–MS gave no evidence for the 1,2-Cy migration product. Alkene **10** was identified by GC–MS and GC-spiking experiments with an authentic sample obtained in 45% yield by reaction of dicyclopropylketone with triphenylphosphonium chloromethylide.[18] It was characterized by NMR and GC–MS.

Absolute rate constants (reproducibility ±10%) for the 1,2-H shifts of carbenes **3** and **4** were determined at 25°C in pentane by laser flash photolysis (LFP)[19] at 351 nm of diazirines **5** and **6**. Data were obtained with the pyridine ylide method,[20] monitoring the growth of the **3**/pyridine or **4**/pyridine ylides at 390 nm as [pyr] was varied from 1.2–7.4 mM (**3**) or 6–80 mM (**4**). Details of this methodology, as applied to carbenic rearrangements, have been described.[20,21] In the present instance, excellent linearities ($r > 0.99$) were obtained for correlations of k_{obs} for the formation of the carbene–pyridine ylides and [pyr]. From intercepts of these correlations at [pyr] = 0, we obtained $k_H = 2.0 \times 10^7\ s^{-1}$ for **3** and $k_H = 1.3 \times 10^7\ s^{-1}$ for **4**.[22] These rate constants together with the corresponding data for MeCCl,[23] **1** and **2** are collected in Table 1. Errors in the rate constants are estimated at 10%, so that the small difference between the k_H values of **3** and **4** is probably significant, whereas the k_H values of **2** and **3** are identical within experimental error.

We attempted to determine the activation energy for the 1,2-H shift of **3** by measuring k_H at eight temperatures between −29 and 41°C. However, scatter in the correlation of $\ln k_H$ versus $1/T$ was much too large to permit the extraction of E_a; a value computed at the B3LYP/6-31G* level is included in Table 1, and discussed below.

Table 1 indicates that Cy is slightly inferior to Ph in its bystander effect on k_H: the 1,2-H shift is 2.7 times faster for carbene **1** than its Cy analogue **3**, whereas the kinetic disparity between the 1,2-H shifts of the disubstituted Ph_2 and Cy_2 carbenes, **2** and **4**, is 1.6. Thus, the anticipated superior ability of Cy over Ph in stabilizing an adjacent positive *p* orbital[12] is not fully expressed in these carbenic rearrangements. Moreover, *no* 1,2-Cy shifts are observed with either **3** or **4**, although minor contributions (6–7%) of 1,2-Ph migrations are observed in the rearrangements of **1** and **2**.[3,6] The π mediated 1,2-shift of Ph is clearly more facile than the parallel migration of Cy. This difference is computationally quantified below.

Note that a second Cy substituent (**4**) leads to a lower k_H than a single Cy substituent (**3**), in concord with the behavior of their Ph analogues, **2** and **1**. Just as the second Ph substituent of **2** may prevent either Ph from assuming an appropriate rotational conformation for optimal electronic stabilization of the developing *p* orbital at C2 during the 1,2-H shift,[4,6] the second Cy substituent of **4** similarly interferes, relative to the mono-Cy carbene **3**.

Of course, both α-Ph and α-Cy substitution accelerates the 1,2-H shift: k_H (**1**) is 19 times greater than k_H (MeCCl), and k_H (**3**) is 6.7 times greater. However, an

Table 1. Kinetic data for 1,2-H rearrangements[a]

Carbene	k_H (s^{-1})	E_a (kcal/mol)	Log A (s^{-1})	Refs.
MeCCl	3×10^6	4.9	9.7	23
$PhCH_2CCl$ (**1**)	5.4×10^7	4.5–4.8	11.1–11.3	5
Ph_2CHCCl (**2**)	2.1×10^{7}[b]	[c]	[c]	6
$CyCH_2CCl$ (**3**)	2.0×10^7	6.0–7.1[d]		[e]
Cy_2CHCCl (**4**)	1.3×10^7	5.9[d]		[e]

[a] In hydrocarbon solvents at 25°C.

[b] $k = 1.5 \times 10^6\ s^{-1}$ for 1,2-Ph migration.

[c] In tetrachloroethane, $E_a = 1.65$ kcal/mol and log $A = 8.6\ s^{-1}$.

[d] Computed values; see below.

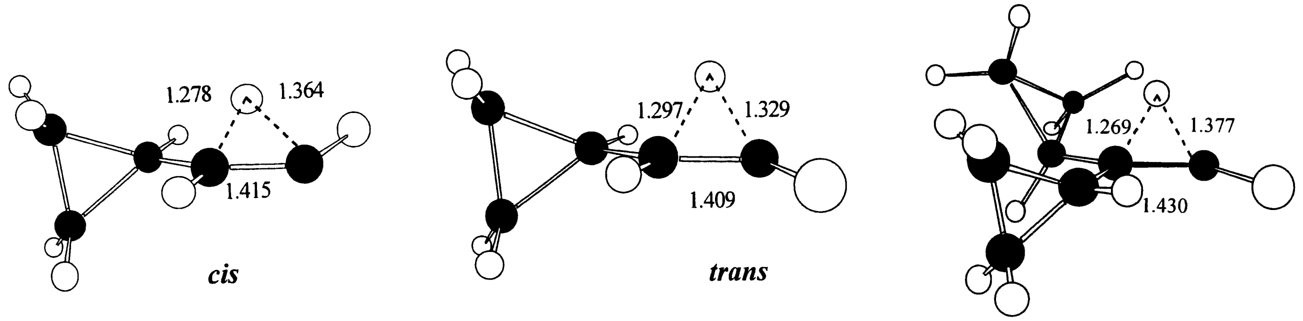
[e] This work.

α-Me substituent is a more effective bystander than either α-Ph or α-Cy; both $MeCH_2CCl$ and Me_2CHCCl exhibit $k_H > 10^8$ s^{-1}.[23] The advantage of Me over Ph or Cy must stem from the former's lack of a stringent conformational requirement in order to exert its bystander electronic effect.

Computational studies at the B3LYP/6-31G* level[24] support the foregoing analysis. Optimized transition states for the 1,2-H migrations of '*cis*' and '*trans*' **3**, and also carbene **4**, appear in Fig. 1.[25] The computed E_a's (0 K, with zero point energy correction) are 6.0, 7.1, and 5.9 kcal/mol, respectively, and the associated $\Delta S^{\neq}$ values (298 K) are −2.5, −2.9, and −1.1 e.u. Fig. 2 depicts optimized transition states for the 1,2-Cy shifts of carbenes **3** ($E_a = 16.3$ kcal/mol) and **4** ($E_a = 10.8$ kcal/mol).

The computed barrier for the 1,2-H migration of **1** (5.5 kcal/mol)[4] is slightly lower than that of **3** (6.0 kcal/mol), consistent with **1**s experimental kinetic advantage of 2.7 (Table 1).[26,27] The computed E_a values for the 1,2-Cy shifts of *cis*-**3** (16.3 kcal/mol) and **4** (10.8 kcal/mol) are considerably higher than the E_a's for the alternative 1,2-H shifts (6.0 and 5.9 kcal/mol, respectively), so that the absence of observable 1,2-Cy shift products from carbenes **3** and **4** is understandable. The operation of bystander effects[1d,4,7] on the 1,2-H shifts can also be discerned in the computed activation barriers (kcal/mol): MeCCl (11.5),[4] $CyCH_2CCl$ (6.0), and $PhCH_2CCl$ (5.5).[4,28]

Finally, given the interest in possible QMT attending the 1,2-H shift of **1**,[2,3] we determined LFP values of k_H and k_D for carbenes **3** and α,α-**3**-d_2 at various temperatures between 5 and 60°C in isooctane. Values of the kinetic isotope effect, k_H/k_D, were 1.09 (60°C), 1.53 (50°C), 1.57 (40°C), 1.73 (30°C), 2.79 (20°C), 4.11 (15°C), and 4.77 (5°C). The last two values are not very reliable because the pyridine ylide signals from which k_{abs} was derived were quite small. However, neither the magnitude nor the trend of these isotope effects provides compelling evidence for QMT in the 1,2-H shift of carbene **3** in the ambient temperature regime.



cis *trans*

Figure 1. Computed 1,2-H transition states for (left to right) carbenes *cis*-**3**, *trans*-**3**, and **4**. The numbers are bond distances in Å.

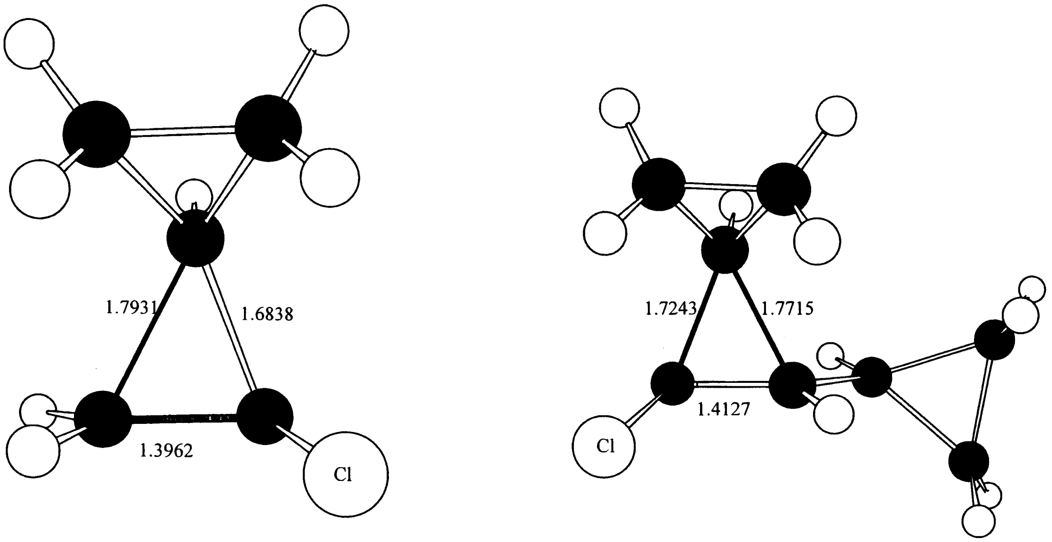


Figure 2. Computed 1,2-Cy transitions states for carbenes **3** (left) and **4**.

Acknowledgements

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22. The slopes of the correlations represent the bimolecular rate constants for the formation of the carbene–pyridine ylide: $k_2 = 8.7\times10^8\ M^{-1}\ s^{-1}$ (**3**), and $k_2 = 3.2\times10^8\ M^{-1}\ s^{-1}$ (**4**).
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25. We compute E_a for the conversion of *cis*-**3** to *trans*-**3** as 1.8 kcal/mol, with an energy difference of only 0.3 kcal/mol favoring *trans*-**3**.
26. For carbene **1**, E_a (1,2-H) is computed at 5.5 kcal/mol and E_a (1,2-Ph) at 9.5 kcal/mol.[4] The 6.5% of 1,2-Ph migration observed for photochemically generated **1**[3] may reflect rearrangement occurring in the excited diazirine precursor of the carbene.[6]
27. A B3LYP/6-31G* calculation carried out for Ph_2CHCCl (**2**) using Gaussian 98.A7 gave $E_a = 7.40$ kcal/mol (with zero point energy correction) for the 1,2-H shift. This value is higher than E_a (**1**), calculated[4] at 5.5 kcal/mol, consistent with the suggestion[4] that the second phenyl group of **2** leads to steric interactions between the *gem*-C_2 phenyl groups, preventing increased stabilization of the 1,2-H shift transition state. The experimental rate constants (Table 1) are in a sequence consistent with these computed E_a's.
28. An additional Cy bystander effect is apparent in the 5.5 kcal/mol computed reduction in E_a for 1,2-Cy migration of carbene **4**, relative to carbene **3**. The second Cy substituent of **4** significantly stabilizes the transition state for migration of the other Cy group.