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Endo Entry to the Nortricyclyl−Norbornenyl Cation System: Stereochemistry in the Fragmentation of *endo*-5-Norbornenyl-2-oxychlorocarbene

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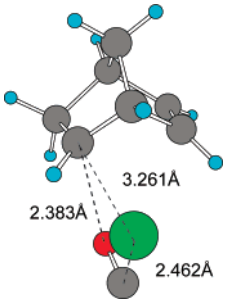
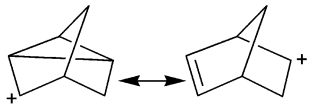


Fragmentation of (*S*)-*endo*-5-norbornenyl-2-oxychlorocarbene [(*S*)-**8**] in cyclohexane-d_{12} gives ∼20% (*S*)-*endo*-2-chloro-5-norbornene [(*S*)-**7**] with ∼50% ee, 65−70% (*R*)-*exo*-2-chloro-5-norbornene [(*R*)-**4**] with >95% ee, and ∼12% (*R*)-3-nortricyclyl chloride [(*R*)-**5**] with ∼22% ee. (Analogous stereochemical results were also obtained starting with the enantiomeric carbene (*R*)-**8**.) The (*S*)-**8** to (*S*)-**7** and (*S*)-**8** to (*R*)-**4** conversions are ascribed mainly to retention and inversion S_Ni transition states, respectively. These have been located by computational methods and are nearly isoenergetic. In more polar solvents ($CDCl_3$ and CD_3CN), the fragmentation of (*S*)-**8** increasingly occurs via competitive ion pair pathways in which steroselectivity is diminished, and escape to the norbornenyl−nortricyclyl cation directs the products away from *endo*-2-chloro-5-norbornene toward *exo*-chloride **4** and nortricyclyl chloride **5**.

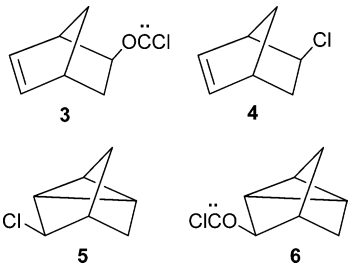
Introduction

The 3-nortricyclyl (**1**) and 5-norbornen-2-yl (**2**) cations can be considered canonical forms of a resonance hybrid,



1 **2**

with a structure which is closer to **1**.[1−4] Not surprisingly, therefore, reactions which should transit either **1** or **2** generally yield mixtures of nortricyclyl and norbornenyl products that are weighted toward the former.[5−7] Ion pairing, however, can bias the product distribution from **1** ↔ **2**;[3] for example, fragmentation of *exo*-5-norbornenyl-2-oxychlorocarbene (**3**) in MeCN affords 57% *exo*-2-chloro-5-norbornene (**4**) and 43% 3-nortricyclyl chloride (**5**), whereas the fragmentation of 3-nortricyclyloxychlorocarbene (**6**) in CD_3CN produces chlorides **4** and **5** in a 10:90 distribution.[8]



3 **4** **5** **6**

† Rutgers, the State University of New Jersey.
‡ University of Pittsburgh.

(1) Jarret, R. M.; Veniero, J. C.; Byrne, T. P.; Saunders, M.; Laidig, K. E. *J. Am. Chem. Soc.* **1998**, *110*, 8287.
(2) Olah, G. A.; Liang, G. *J. Am. Chem. Soc.* **1973**, *95*, 3792.
(3) Olah, G. A.; Liang, G. *J. Am. Chem. Soc.* **1975**, *97*, 1920.
(4) Saunders, M.; Jarret, R. M.; Pramanik, P. *J. Am. Chem. Soc.* **1987**, *109*, 3735.

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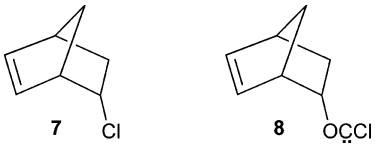
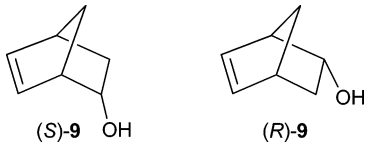
Remarkably, fragmentations of carbenes **3** and **6** also occur readily in nonpolar solvents such as pentane and cyclohexane. Under these conditions, **3** uniquely gives 28−31% *endo*-2-chloro-5-norbornene (**7**), in addition to 53−56% **4** and 16% **5**. As the solvent is made more polar, however, product **7** disappears in favor of chlorides **4** and **5**.[8] Computational studies implicate S_Ni mechanisms in these ROCCl fragmentations, particularly in nonpolar solvents, whereas a blend of S_Ni and ion pair mechanisms can rationalize the changes in product distributions that accompany increasing solvent polarity.



Noting that carbenes **3** and **6** as well as products **4**, **5**, and **7** are chiral, we suggested[8] that a stereochemical study of these transformations would permit a more precise mechanistic analysis. To that end, we examined the fragmentations of carbenes (*S*)-**3**[9] and (*S*)-**6**[10] in several solvents and determined the stereochemical courses of formation of their chloride products. Here, we complete our stereochemical survey, focusing on the fragmentation of (*S*)-*endo*-5-norbornenyl-2-oxychlorocarbene [(*S*)-**8**], as well as its (*R*)-enantiomer, to chlorides **4**, **5**, and **7**. The new results are considered in the context of our previous studies,[8−10] and provide detailed mechanistic scenarios.

Results

Chiral Precursors and Products. *endo*-5-Norbornen-2-ol (**9**) was prepared by the $NaBH_4$ reduction of 5-norbornen-2-one.[11,12] The alcohol was resolved into its enantiomers (*R*)-**9** and (*S*)-**9** by kinetic resolution with the



lipase from *Candida cylindracea*[13,14] (purchased from a commercial supplier). Thus, racemic **9** was acetylated (Ac_2O, pyridine),[13] and the racemic acetate was catalytically hydrolyzed with the lipase in aqueous phosphate buffer at pH 7.5.[13] After GC monitoring indicated 40% conversion, the hydrolysis was stopped and a simple ethereal extraction, followed by chromatography over silica gel, gave (*R*)-(+)-**9**.[13] Our sample was obtained in 34% chemical yield and had $[\alpha]_D^{25}$ 121 (*c* 6.32, $CHCl_3$), corresponding to 73.3% ee.[15,16]

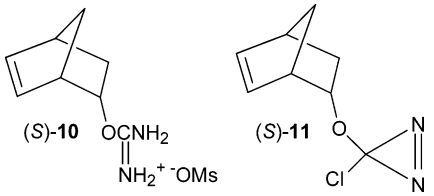
TABLE 1. Product Distributions from the Fragmentation of Carbene 8[a]

solvent	method[b]	% **4**	% **5**	% **7**
C_6D_{12}[c]	*hν*	64−65	13−14	21−22
C_6D_{12}	Δ	71−72	9−12	16−19
$CDCl_3$	*hν*	56−60	34−39	5−6
$CDCl_3$	Δ	57−58	39−40	2−4
CD_3CN	*hν*	61−63	33−35	4−5
CD_3CN	Δ	62−66	30−31	3−7

[a] Data are ranges of percent distributions from (*S*)-**8** and (*R*)-**8**. [b] Photolysis or thermolysis of diazirine (*S*)-**11** or (*R*)-**11**, both at 25 °C. [c] Perdeuteriocyclohexane.

The *endo*-norbornenyl acetate recovered from the lipase-catalyzed hydrolysis was resubmitted to the hydrolytic conditions until an additional 20% hydrolysis had occurred.[13] Workup then gave (*S*)-(−)-*endo*-5-norbornenyl-2-acetate, $[\alpha]_D^{25}$ −84.7 (*c* 12.5, $CHCl_3$). This was saponified (NaOH, MeOH) to (*S*)-(−)-**9**[13] in 34% chemical yield with $[\alpha]_D^{25}$ −113 (*c* 4.42, $CHCl_3$), corresponding to 68.5% ee.[15,16] Further characterization of (*R*)-**9** and (*S*)-**9** appears in the Experimental Section.

Racemic and optically active samples of **9** were converted to isouronium salts **10** (here depicted as (*S*)-**10**) by reaction with cyanamide and methanesulfonic acid.[17] The isouronium salts were significantly contaminated with urea. Without purification, they were oxidized to diazirines **11** with aqueous NaOCl.[18] The diazirines could be purified by chromatography over silica gel (eluted with pentane), and were characterized by UV and ^1H and ^{13}C NMR spectroscopy.



Photolysis (350 nm) or thermolysis (25 °C) of diazirine (*S*)-**11** or (*R*)-**11** in several solvents afforded norbornenyl and nortricyclyl chlorides **4**, **5**, and **7**,[19] as well as small quantities (<4%) of the elimination product norbornadiene. The relative distributions of the chlorides were determined by ^1H NMR integration of the product mixtures and are recorded in Table 1, where they are expressed as ranges that incorporate results from both

(5) Cristol, S. J.; Seifert, W. K.; Johnson, D. W.; Jurale, B. J. *J. Am. Chem. Soc.* **1962**, *84*, 3918.
(6) Roberts, J. D.; Lee, C. C.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1955**, *77*, 3034.
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(10) Moss, R. A.; Fu, X.; Tian, J.; Sauers, R.; Wipf, P. *Org. Lett.* **2005**, *7*, 1371.
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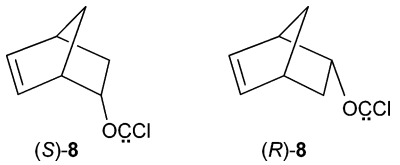
(14) Oberhauser, Th.; Bodenteich, M.; Faber, K.; Penn, G.; Griengl, H. *Tetrahedron* **1987**, *43*, 3931.
(15) Based upon $[\alpha]_D^{25}$ 165 for optically pure material, extrapolated from $[\alpha]_D^{25}$ 160 (*c* 0.5, $CHCl_3$) for material determined to have an ee of 97%: Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P.; Rosini, G. *Tetrahedron: Asymmetry* **1994**, *5*, 1635.
(16) See ref 14 for correlations of optical rotation and absolute configuration.
(17) Moss, R. A.; Kaczmarczyk, G.; Johnson, L. A. *Synth. Commun.* **2000**, *30*, 3233.
(18) Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.
(19) For details of product identification, independent preparations, and NMR spectra of chlorides **4** and **5**, see ref 8. The ^1H NMR spectrum of *endo*-chloride **7** is described by R. V. Moen and H. S. Makowski (*Anal. Chem.* **1967**, *39*, 1860) and P. Laszlo and P. v. R. Schleyer (*J. Am. Chem. Soc.* **1963**, *85*, 2709; **1964**, *86*, 1171).

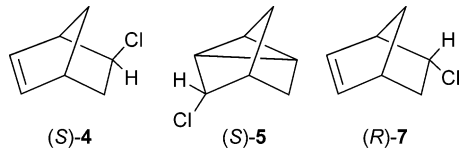
(*R*)- and (*S*)-diazirine precursors. We attribute the products to fragmentations of carbenes (*S*)-**8** and (*R*)-**8**, which are generated by the photolysis or thermolysis of diazirines (*S*)-**11** and (*R*)-**11**, respectively.



(*S*)-**8** (*R*)-**8**

To define the stereochemistry of the (*S*)-**8** or (*R*)-**8** conversions to chlorides **4**, **5**, and **7**, we need the absolute configurations and associated rotational properties of the products. This information was unknown when we began our studies, so we computed it.[9,20] The structures of **4**, **5**, and **7** were minimized at the DFT-RB3LYP level with the 6-31G(d) basis set, and the optical rotations at the sodium D line were calculated with RB3LYP/6-311++G-(2d,p) from the Gaussian 03 suite.[21]The computed connection between absolute configuration and calculated specific rotation for each of the product chlorides is shown below, where the computed $[\alpha]_D$ value pertains to solvents such as CH_2Cl_2 or $CHCl_3$.[9]

Samples of (*S*)-(+)-**4**, (*S*)-(−)-**5**, and (*R*)-(+)-**7** were obtained by chromatographic separations of the product mixtures from the fragmentations of (*S*)-*exo*-5-norbor-



(*S*)-**4** (*S*)-**5** (*R*)-**7**

$[\alpha]_D$+28.6 $[\alpha]_D$-113.8 $[\alpha]_D$+124.0

nenyl-2-oxychlorocarbene [(*S*)-**3**],[9] (*S*)-nortricyclyloxychlorocarbene [(*S*)-**6**],[10] and (*R*)-*endo*-5-norbornenyl-2-oxychlorocarbene [(*R*)-**8**] (this work). For example, (*R*)-*endo*-5-norbornen-2-ol,[13,14] via the derived isouronium salt (*R*)-**10** and diazirine (*R*)-**11**, ultimately afforded carbene (*R*)-**8**, which gave *endo*-2-chloro-5-norbornene. The purified 4.8 mg sample had α_D^{25} 0.034 ± 0.002, as read in a 1 cm cell (*c* 0.0048, $CDCl_3$).[22] The dextrorotatory character of this material establishes it as the (*R*)-enantiomer (see above). In parallel fashion, we obtained samples of (S)-(−)-**5** with α_D^{25} −0.117 (*c* 0.0167, $CDCl_3$) and (*S*)-(+)-**4** with α_D^{25} 0.008 (*l* = 0.1 dm, *c* = 0.002, $CDCl_3$).[23]

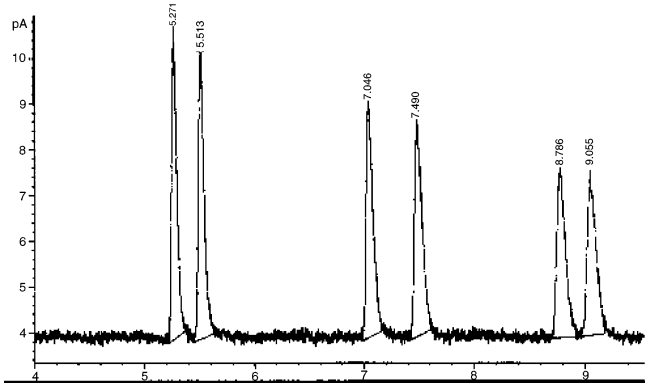


FIGURE 1. Separation of a mixture of racemic chlorides **4**, **5**, and **7** on a Chiraldex GTA column at 50 °C. The numbers are retention times in minutes. From left to right the peak assignments are (*R*)-**4**, (*S*)-**4**, (*R*)-**5**, (*S*)-**5**, (*S*)-**7**, and (*R*)-**7**.

With chloride samples of known absolute configuration thus in hand, we could assign peak identities in GC separations of the enantiomeric chloride products from fragmentations of carbenes **3**, **6**, and **8**. Product mixtures were analyzed on a 30 m × 0.25 mm Chiraldex GTA column at 50 °C, where both enantiomers of each of the chlorides **4**, **5**, and **7** could be separated. Figure 1 illustrates the separation of a mixture of the three racemic chlorides. For separations of product mixtures from the fragmentations of the enantiomerically enriched carbenes, product GC peak areas were electronically integrated.

Stereochemical Results. (*S*)-(−)-5-Norbornen-2-ol, (*S*)-(−)-**9** with $[\alpha]_D^{25}$ −113, 68.5% ee,[15,16] was converted to isouronium salt (*S*)-**10** and then to diazirine (*S*)-**11** as described above. Photolysis or thermolysis of (*S*)-**11** in cyclohexane-d_{12}, $CDCl_3$, or CD_3CN afforded chloride mixtures via carbene (*S*)-**8** which were analyzed on the Chiraldex capillary GC column. The product ee's and the % ee's of the conversions are collected in Table 2, corrected for the 68.5% ee assumed for carbene (*S*)-**8**.

Given that enantiomeric carbene (*R*)-**8** was available from an analogous sequence beginning with alcohol (*R*)-**9**, we could obtain an independent check on the stereochemistry of product formation. The product ee's and % ee's of a parallel series of conversions via fragmentations of (*R*)-**8** are collected in Table 3, corrected for the 73.3% ee assumed for carbene (*R*)-**8** derived from (*R*)-**9** with $[\alpha]_D^{25}$ 121, 73.3% ee.[15,16]

Examination of the sterochemical results in Tables 2 and 3 reveals a reasonable consistency: there are only small differences between the ee's of products formed by photochemical or thermal decompositions of diazirine (*S*)-**11** or (*R*)-**11** (i.e., carbene (*S*)-**8** or (*R*)-**8**), and the product

(20) For examples of the assignment of absolute configuration by ab initio theory and the calculation of $[\alpha]_D$, see: (a) Kondru, R. K.; Wipf, P.; Beratan, D. N. *J. Am. Chem. Soc.* **1998**, *120*, 2204. (b) Kondru, R. K.; Wipf, P.; Beratan, D. N. *Science* **1998**, *282*, 2247. (c) Ribe, S.; Kondru, R. K.; Beratan, D. N.; Wipf, P. *J. Am. Chem. Soc.* **2000**, *122*, 4608. (d) Specht, K. M.; Nam, J.; Ho, D. M.; Berova, N.; Kondru, R. K.; Beratan, D. N.; Wipf, P.; Pascal, R. A.; Kahne, D. *J. Am. Chem. Soc.* **2001**, *123*, 8961. Review: (e) Polavarapu, P. L. *Chirality* **2002**, *14*, 768.

(21) Gaussian 03, Revision B.03: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A.; Jr,; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M..C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; and Pople, J. A., Gaussian, Inc., Pittsburgh, PA, 2003.

(22) Optical rotations were obtained on an automated polarimeter; readings were reproducible to ±0.002°.

(23) The observed rotation of (*S*)-(+)-**4** is admittedly small, but the consequent dextrorotatory assignment to the (*S*)-enantiomer verifies that the fragmentation of carbene (*S*)-**3** to chloride **4** (now assigned as (*S*)-**4**) occurs with 90−100% *retention* in cyclohexane, in keeping with the computed S_Ni mechanism.[9]

TABLE 2. Stereochemistry of Product Chlorides from Carbene (*S*)-8[a,b]

		(*S*)-**7**		(*R*)-**4**		(*R*)-**5**	
solvent	method[c]	ee (%)	% ee[d]	ee (%)	% ee[d]	ee (%)	% ee[d]
C_6D_{12}	*hν*	35.4	51.7	66.9	97.7	16.8	24.5
C_6D_{12}	Δ	32.0	46.7	65.4	95.5	14.1	20.6
$CDCl_3$	*hν*	49.5[e]	72.3	37.1	54.2	10.3	15.0
$CDCl_3$	Δ	e		33.9	49.5	14.4	21.0
CD_3CN	*hν*	e		30.4	44.4	13.8	20.1
CD_3CN	Δ	e		31.2	45.5	13.4	19.4

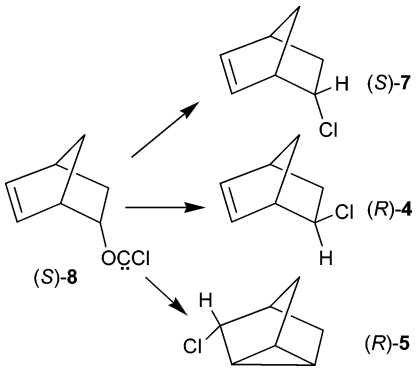
[a] From diazirine (*S*)-**11** via carbene (*S*)-**8**, assuming 65.8% ee, as in alcohol (*S*)-**9**. [b] Product ee analysis by GC on a Chiraldex GTA column; see the text. [c] Photolysis or thermolysis of diazirine (*S*)-**11** at 25 °C. [d] Corrected for the 68.5% ee of carbene (*S*)-**8**. [e] Inaccurate or unavailable due to inadequate product yield and GC peak size.

TABLE 3. Stereochemistry of Product Chlorides from Carbene (*R*)-8[a,b]

		(*R*)-**7**		(*S*)-**4**		(*S*)-**5**	
solvent	method[c]	ee (%)	% ee[d]	ee (%)	% ee[d]	ee (%)	% ee[d]
C_6D_{12}	*hν*	44.7	61.0	76.3	100	10.2[e]	13.9
C_6D_{12}	Δ	32.4	44.2	76.8	100	16.5	22.5
$CDCl_3$	*hν*	37.4[e]	51.0	44.4	60.6	14.1	19.2
$CDCl_3$	Δ	e		45.6	62.2	11.6	15.8
CD_3CN	*hν*	e		38.5	52.5	15.7	21.4
CD_3CN	Δ	e		42.0	57.3	16.0	21.8

[a] From diazirine (*R*)-**11** via carbene (*R*)-**8**, assuming 73.3% ee, as in alcohol (*R*)-**9**. [b] Product ee analysis by GC on a Chiraldex GTA column; see the text. [c] Photolysis or thermolysis of diazirine (*R*)-**11** at 25 °C. [d] Corrected for the 73.3% ee of carbene (*R*)-**8**. [e] Inaccurate or unavailable due to inadequate product yield and GC peak size.

SCHEME 1

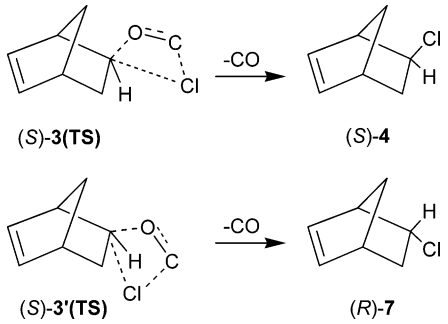


chirality reverses, as required, when the diazirine's chirality is reversed. (A reviewer suggested that the intervention of excited diazirines masquerading as carbenes could be responsible for the very minor differences between the stereochemical results noted in Tables 2 and 3.) Qualitatively, we can represent the stereochemical sense of the carbene to chloride transformations as shown in Scheme 1, using carbene (*S*)-**8** for illustrative purposes.

Discussion

Reactions that generate the nortricyclyl (**1**) or norbornenyl (**2**) cation usually lead to product mixtures that contain 3-nortricyclyl and *exo*-5-norbornen-2-yl products.[5−7] *endo*-5-Norbornen-2-yl products normally do not form,

SCHEME 2



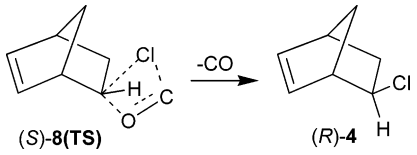
even from an *endo*-5-norbornen-2-yl precursor. Thus, the nitrous acid deamination of *endo*-2-amino-5-norbornene gives mainly 3-nortricyclanol,[24] accompanied by minor amounts of *exo*-5-norbornen-2-ol and 3-norpinen-2-ol.[25] Similarly, buffered acetolysis of *endo*,*endo*-5-norbornen-2,3-ditosylate, as well as its *endo*,*exo*-isomer, yields mainly nortricyclyl diacetates; derivatives of *endo*-norbornenyl acetate do not form.[26]

In contrast, oxychlorocarbene fragmentations do lead to *endo*-2-chloro-5-norbornene (**7**), particularly in hydrocarbon solvents. Thus, fragmentation of *exo*-carbene **3** in pentane gives 28% **7**, as well as 56% *exo*-chloride **4** and 16% nortricyclyl chloride **5**.[8] And, in the present study, *endo*-carbene **8** affords up to 22% **7** in C_6D_{12}, accompanied by ∼70% **4** and minor quantities of **5** (Table 1). We attribute the formation of *endo*-norbornenyl chloride **7** from carbenes **3** and **8** to S_Ni fragmentation mechanisms, which are particularly important in hydrocarbon solvents.

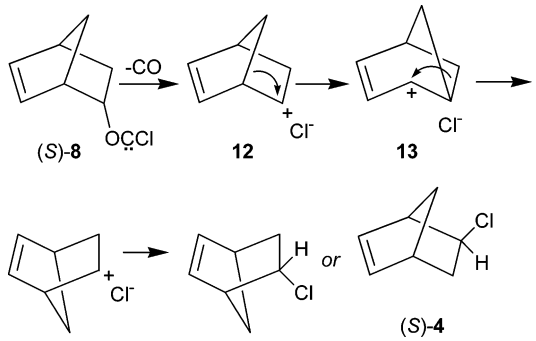
Both theory and experiment show that S_Ni mechanisms can give products with either retention or (surprisingly) inversion.[8,27] For example, transition states of nearly equal computed energy lead from *exo*-carbene **3** to either *exo*-chloride **4** or *endo*-chloride **7**; cf. Scheme 2.[8,9] (See Figure 2, below, for alternative depictions of these transition states.) Thermolysis of (*S*)-**3** in C_6D_{12} gives 53% (*S*)-**4** with complete retention (100% ee), and 31% "inverted" **7** with an 18% excess of the (*R*)-enantiomer.[9] The former result is in accord with the computed S_Ni transition state, whereas the extensive racemization observed in the formation of **7** implies that fragmentation to an ion pair effectively competes with the computed S_Ni process.[28] The dominant (*R*)-**7** enantiomer arises either by the S_Ni process depicted in Scheme 2 or by formation of an ion pair from carbene (*S*)-**3** followed by loss of CO and migration of Cl^- from the exo to the endo face of the norbornenyl cation followed by anion−cation recombination.[9] Formation of minor enantiomer (*S*)-**7** can occur via a more complicated intra ion pair process.[9]

(24) Parham, W. E.; Hunter, W. T.; Hanson, R. *J. Am. Chem. Soc.* **1951**, *73*, 5068.
(25) Kirmse, W. Knöpfel, N.; Loosen, K.; Siegfried, R.; Wroblowsky, H.-J. *Chem. Ber.* **1981**, *114*, 1187.
(26) (a) Lambert, J. B.; Mark, H. W. *J. Am. Chem. Soc.* **1978**, *100*, 2501. (b) Lambert, J. B.; Halcomb, A. G. *J. Am. Chem. Soc.* **1971**, *93*, 2994.
(27) (a) Schreiner, P. R.; Schleyer, P.v. R.; Hill, R. K. *J. Org. Chem.* **1993**, *58*, 2822. (b) Schreiner, P. R.; Schleyer, P.v. R.; Hill, R. K. *J. Org. Chem.* **1994**, *59*, 1849.
(28) Fragmentation of ROCCl to short-lived ion pairs occurs in hydrocarbon solvents when R = (e.g) cyclopropylmethyl: Moss, R. A.; Sauers, R. R.; Zheng, F.; Fu, X.; Bally, T.; Maltsev, A. *J. Am. Chem. Soc.* **2004**, *126*, 8466.

SCHEME 3



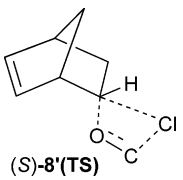
SCHEME 4



Retention and inversion S_Ni mechanisms analogous to those in Scheme 2 also dominate the fragmentation of nortricyclyloxychlorocarbene (**6**) in hydrocarbon solvents. Here, retention and inversion mechanisms do not lead to structural isomers (as in Scheme 2), but to opposite enantiomers of 3-nortricyclyl chloride (**5**), resulting in an essentially racemic chloride product.[10]

In the present instance, a combination of S_Ni and ion pair mechanisms can rationalize the experimental findings. Thus, in C_6D_{12}, *endo*-carbene (*S*)-**8** affords ~20% *endo*-chloride (*S*)-**7** with ~50% ee, ~65−70% *exo*-chloride (*R*)-**4** with >95% ee, and ~12% nortricyclyl chloride (*R*)-**5** with ~22% ee (see Tables 1 and 2).[29] The conversion of (*S*)-**8** to (*R*)-*exo*-2-chloro-5-norbornene [(*R*)-**4**] with >95% ee in C_6D_{12} is completely consistent with the operation of an inverting S_Ni reaction via transition state **8(TS)** (see Scheme 3), and is also supported by our computational studies (see below). As the solvent is made more polar, the ee of product (*R*)-**4** decreases to ~52% (in $CDCl_3$) and ~45% (in CD_3CN), reflecting the incursion of ion pair processes. For example, fragmentation of (*S*)-**8** to ion pair **12**, followed by a (reversible) 1,2-carbon shift to the bicyclo[3.1.1]heptenyl cation **13**,[1] can give *exo*-chloride (*S*)-**4** and thus contribute to a loss of stereospecificity in the (*S*)-**8** to (*R*)-**4** transformation (see Scheme 4). In SO_2ClF, the activation energy for the **12** → **13** 1,2-C shift is ~17 kcal/mol.[1]

Also consistent with a (retention) S_Ni mechanism is the fragmentation of (*S*)-**8** to *endo*-chloride (*S*)-**7**, which occurs with ~52% ee in C_6D_{12}. Here S_Ni TS **8′(TS)** leads



directly from (*S*)-**8** to (*S*)-**7** (cf. Scheme 1). Computational studies below provide support for this pathway. Even in C_6D_{12}, however, (*S*)-**7** forms with only ~50% ee. We can account for the racemization by the incursion of competitive ion pair processes which lead to both (*R*)-**7** and (*S*)-**7**; cf. Scheme 5. Leakage to tight norbornenyl−nortricyclyl ion pairs can be expected even in hydrocarbon solvents.[28]

As the solvent becomes more polar, *endo*-chloride **7** becomes a very minor component of the product mixture from carbene (*S*)-**8** while nortricyclyl chloride (*R*)-**5** increases in importance; in $CDCl_3$ or CD_3CN, the yield of **7** decreases to 2−7% while (*R*)-**5** forms from **8** in 30−40% yield with ~20% ee (Tables 1 and 2). The (*S*)-**8** to (*R*)-**5** conversion can be understood in terms of Scheme 6, where ion pair **12** gives the major enantiomer of nortricyclyl chloride (*R*)-**5**, by recombination on the underside of the nortricyclyl cation (path a), which is a "least motion" pathway for the chloride anion. A slightly longer relocation via path b brings the chloride to the exo face of the cation, leading, after recombination, to minor enantiomer (*S*)-**5**.

Direct recombination of **12** at C-2 leads, of course, to (*S*)-**7**, but we suggest that this product is formed mainly by the S_Ni process via **8′(TS)** (see above). In polar solvents, however, **8′(TS)** is disfavored relative to fragmentation to **12**, which features a delocalized positive charge, and favors collapse to either enantiomer of nortricyclyl chloride (Scheme 6) or to *exo*-2-chloro-5-norbornene by migration of Cl^- to the exo face of the cation at C-2 or by the rearrangement shown in Scheme 4.

Computational studies support the importance of S_Ni mechanisms for the fragmentation of *endo*-carbene **8** in a vacuum (and presumably in hydrocarbon solvents). Thus, B3LYP/6-31G(d) calculations[21,30,31] located two transition states for the fragmentation of carbene **8** to the norbornenyl chlorides; cf. Figure 2. The lower energy *inversion* TS ($\Delta H^{\ddagger} = 17.1$ kcal/mol) converts *endo*-carbene **8** to *exo*-chloride **4**. The *retention* TS, which is slightly higher in activation enthalpy ($\Delta H^{\ddagger} = 17.6$ kcal/mol), converts **8** to *endo*-chloride **7**. The computed inversion TS of Figure 2 is equivalent to the schematic inversion TS **8(TS)** in Scheme 3, whereas the computed retention TS of Figure 2 matches the schematic **8′(TS)**.[32] IRC calculations reveal no ion pair minima between these transition states and their products; both fragmentations are direct S_Ni processes. Mulliken charge distributions for ground-state carbene **8** and for the inversion and retention transition states of Figure 2 appear in the Supporting Information. There it can be seen that the positive charge developed on C-2(H) of the carbene is small in both transition states (0.04−0.05) while the negative charge developed on Cl is larger (0.40−0.44). We estimate that the charge character of these transition

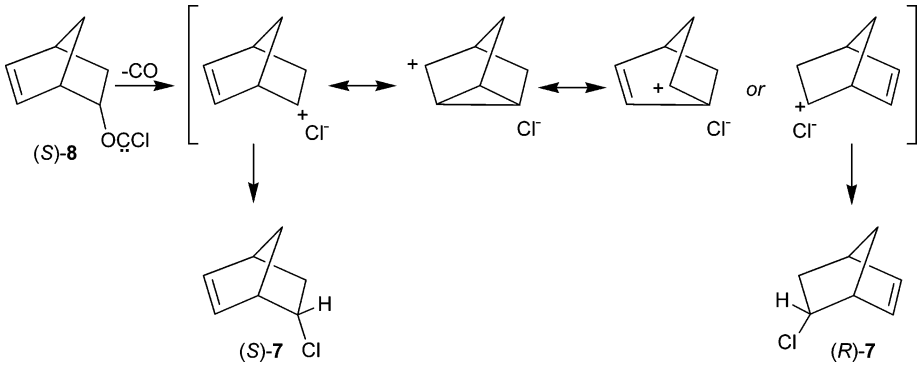
(29) The data quoted here are "averages" from photochemical and thermal generations of the carbene. The stereochemical data obtained from the enantiomeric carbene (*R*)-**8** are comparable (Table 3).

(30) All structures were fully optimized by analytical gradient methods using the Gaussian 03 Suite[21] and DFT calculations at the 6-31G(d) level, the exchange potentials of Becke,[31a] and the correlation functional of Lee, Yang, and Paar.[31b] Activation energies were corrected for zero-point energy differences (ZPVE, unscaled) and thermal effects at 298.150 K. Vibrational analyses established the nature of all stationary points as either energy minima (no imaginary frequencies) or first-order saddle points (one imaginary frequency).

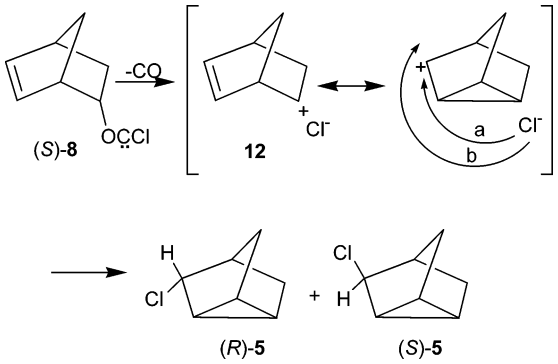
(31) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Lee, C.; Yang, W.; Paar, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(32) Note, however, that the computed transition states pertain to (*R*)-**8** whereas the schematic transition states are drawn for (*S*)-**8**.

SCHEME 5



SCHEME 6



states is midway between that of a covalent structure and an ion pair.

We also find a transition state (not shown) for elimination of HCl from carbene **8** leading to norbornadiene. At $\Delta H^{\ddagger} = 16.5$ kcal/mol, the elimination TS is computed to be 0.5−1.0 kcal/mol more favorable than either **8(TS)** or **8′(TS)**. However, as indicated above, experiment shows norbornadiene to be a very minor product (<4%) from carbene **8**, even in hydrocarbon solvent. On the other hand, the yield of inversion chloride **4** does exceed that of retention chloride **7** in C_6D_{12} (Table 1), in accord with the 0.5 kcal/mol lower computed $\Delta H^{\ddagger}$ for the inversion S_Ni TS. For details of the computations, see the Supporting Information.

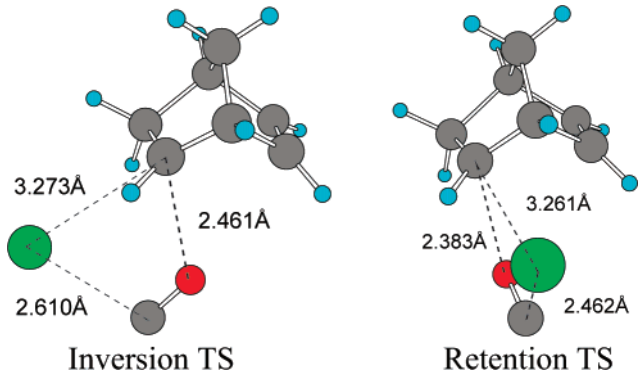


FIGURE 2. B3LYP/6-31G(d) transition states for the fragmentations of *endo*-carbene **8** to *exo*-chloride **4** (inversion TS) or to *endo*-chloride **7** (retention TS).

Conclusions

S_Ni fragmentation of ROCCl to RCl seems to be a common pathway in nonpolar solvents for *exo*-5-norbornenyl-2-oxychlorocarbene (**3**),[8,9] 3-nortricyclyloxychlorocarbene (**6**),[8,10] and *endo*-5-norbornenyl-2-oxychlorocarbene (**8**) (this work). In the latter case, fragmentation of (*S*)-**8** in cyclohexane-d_{12} gives ∼20% *endo*-chloride (*S*)-**7** with ∼50% ee, 65−70% *exo*-chloride (*R*)-**4** with >95% ee, and ∼12% 3-nortricyclyl chloride (*R*)-**5** with ∼22% ee. The (*S*)-**8** to (*S*)-**7** and (*S*)-**8** to (*R*)-**4** conversions are mediated by retention and inversion S_Ni transition states, respectively. These transition states are locatable by computational methods and are nearly isoenergetic. In more polar solvents, the fragmentations also transit competitive ion pair pathways so that stereoselectivity is increasingly lost, and escape to the norbornenyl−nortricyclyl cation system directs the products away from *endo*-2-chloro-5-norbornene (**7**), and toward *exo*-chloride **4** and nortricyclyl chloride **5**.

Experimental Section

***O*-(*endo*-5-Norbornen-2-oxy)isouronium Methansulfonate (10).** This material was prepared from *endo*-5-norbornen-2-ol (**9**),[11,12] mp 107−108 °C (lit.[33] mp 109.4−110.8 °C). The NMR spectra of (*S*)-**9**, (*R*)-**9**, and (*S*,*R*)-**9** were identical. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 0.76 (m, 1H), 1.29 (m, 1H), 1.47 (m, 1H), 2.01 (m, 1H), 2.81 ("s", 1H), 2.99 ("s", 1H), 4.47 (m, 1H), 6.06 and 6.44 (dd each, $J = 4.0$, 7.2 Hz, 1H each). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 37.8, 42.9, 48.1, 48.3, 72.4, 130.7, 140.2.

Following our standard procedure,[8,17] *endo*-5-norbornen-2-ol (6.0 g, 55.5 mmol), cyanamide (2.33 g, 55.5 mmol), and methansulfonic acid (5.33 g, 55.5 mmol) were stirred magnetically for 24 h in a 250 mL round-bottom flask protected with a $CaCl_2$ drying tube. The reaction mixture was diluted with 150 mL of ether and stored in the refrigerator. After several days, the product remained as an oily phase. It was washed with a large amount of ether, separated, and dried under vacuum for 8 h. We obtained 7.26 g (26%) of crude **10**. This material contained 56% urea by ^{1}H NMR. ^{1}H NMR (400 MHz, DMSO-d_6, δ): 8.46 (br s, 4H) 8.00 (br s, urea), 6.40 (m, 1H), 6.00 (m, 1H), 5.28 (m, 1H), 3.18 (m, 1H), 3.14 (m, 1H), 2.48 (s, 3H), 0.90−2.34 (m, 4H). ^{13}C NMR (75 MHz, DMSO-d_6, δ): 161.2, 139.3, 130.8, 80.9, 47.3, 45.6, 41.9, 39.7, 34.0.

3-(*endo*-5-Norbornen-2-oxy)-3-chlorodiazirine (11). A Graham oxidation[18] was used to convert isouronium salt **10** into the diazirine. To a mixture of ∼5 g of LiCl in 100 mL of DMSO were added 1.5 g of crude isouronium salt **10** and 100 mL of pentane. The mixture was kept below 20 °C while 150 mL of commercial 12% aqueous NaOCl ("pool chlorine") was added dropwise, with stirring, over 30 min. The mixture was then transferred to a separatory funnel, and the aqueous layer

(33) Roberts, J. D.; Trumbull, E. R., Jr.; Bennett, W.; Armstrong, R. *J. Am. Chem. Soc.* **1950**, *72*, 3116.

was drained. The pentane layer was washed twice with ice−water. The diazirine−pentane solution was dried over $CaCl_2$ at 0 °C for 2 h and then chromatographed over silica gel with pentane elution. Diazirine **11** was concentrated by rotary evaporation. Diazirine **11** had λ_{max} 351 nm (pentane). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 6.27 (dd, J = 4.0, 7.6 Hz, 1H), 5.80 (dd, J = 4.0, 7.6 Hz, 1H), 4.89 (m, 1H), 3.29 (m, 1H), 2.83 (m, 1H), 2.10 (m, 1H), 1.52 (m, 1H), 1.32 (m, 1H), 0.92 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 138.4, 131.1, 79.5, 70.8, 47.5, 46.2, 41.9, 37.7.

(*S*)-(−)-*endo*-5-Norbornen-2-ol [(*S*)-(−)-9]. This material was prepared in 34% yield as described by Griengl et al.[13,14] The waxy solid had mp 108−109 °C (lit.[34] mp 105−111 °C) and $[\alpha]_D^{25}$ 112.7 (*c*, 4.42, $CHCl_3$), corresponding to 68.5% ee.[15,16]

(*R*)-(+)-*endo*-5-Norbornen-2-ol [(*R*)-(+)-9]. This material was prepared in 34% yield as described by Griengl et al.[13,14] The waxy solid had mp 102−103 °C. A similar "low" melting point has been reported for the (−)-enantiomer, mp 103−107 °C.[35] We determined $[\alpha]_D^{25}$ 121 (*c* 6.32, $CHCl_3$), corresponding to 73.3% ee.[15,16]

Chloride Products. *exo*-2-Chloro-5-norbornene (**4**) and 3-nortricyclyl chloride (**5**) are fully described in ref 8.[19] Literature references to the ^{1}H NMR spectrum of *endo*-2-chloro-5-norbornene (**7**)[19] are available but old. We redetermined the NMR spectrum. Chloride **7** was isolated by silica gel chromatography (pentane) from the photolysis of diazirine **11** in pentane. GC−MS: *m/e* 128, 130 (M^+). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 6.34 (dd, J = 4.0, 7.2 Hz, 1H), 6.09 (dd, J = 4.0, 7.2, Hz, 1H), 4.40 (m, 1H), 3.13 (m, 1H), 2.89 (m, 1H), 2.28 (m, 1H), 1.54 (m, 1H), 1.28 (m, 1H), 1.15 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 137.8, 132.2, 58.0, 49.0, 48.2, 42.7, 37.4.

GC Separations. Product mixtures were analyzed on a 30 m × 0.25 mm Chiraldex GTA column. Operating conditions included a column temperature of 50 °C, with He carrier gas at 29 psig; cf. Figure 1.

Acknowledgment. We are grateful to the National Science Foundation for financial support and to the National Center for Computer Applications for an allocation of time on the IBM P Series 690 (to R.R.S.).

Supporting Information Available: Computational details for the fragmentation of carbene **8**. This information is available free of charge via the Internet at http://pubs.acs.org.

JO051222O

(34) Sandman, D. J.; Mislow, K. *J. Org. Chem.* **1968**, *33*, 2924.
(35) Lightner, D. A.; Beavers, W. A. J. *Am. Chem. Soc.* **1971**, *93*, 2677.