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The fragmentation of *exo*-5-norbornenyl-2-oxychlorocarbene: stereochemistry and mechanism

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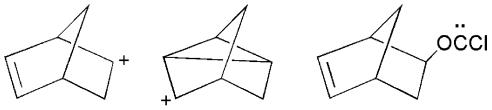
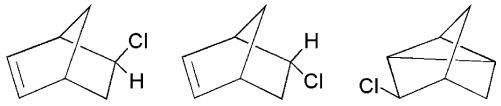
Abstract—The fragmentation of (*S*)-*exo*-5-norbornenyl-2-oxychlorocarbene (**3**) affords (*S*)-*exo*-5-norbornenyl-2-chloride (**4**), (*R*)-*endo*-5-norbornenyl-2-chloride (**5**), and (*S*)-3-nortricyclyl chloride (**6**) with varying degrees of enantiomeric excess. A weighted blend of S_Ni fragmentation and escape to norbornenyl/nortricyclyl ion pairs rationalizes the stereochemical results.

Reactions that formally pass through either the 5-norbornen-2-yl cation (**1**) or the nortricyclyl cation (**2**) usually afford product mixtures that are rich in nortricyclyl derivatives.[1–3] Indeed, cations **1** and **2** are better considered canonical forms of a resonance hybrid whose structure is closer to **2**.[4–7]



1 **2** (*S*)-**3**

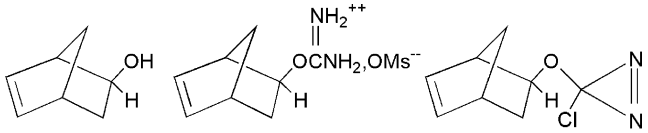
Olah and Liang recognized that ion pairing can affect the norbornenyl/nortricyclyl product distribution from **1/2**,[6] and we recently observed that fragmentation of *exo*-5-norbornenyl-2-oxychlorocarbene (**3**) yielded mixtures dominated by norbornenyl products.[8] For example, fragmentations of **3** in cyclohexane-d_{12} gave 53% of *exo*-5-norbornen-2-yl chloride (**4**), 31% of the isomeric endo chloride (**5**), and 16% of nortricyclyl chloride (**6**); whereas, in the more polar solvent CD_3CN, only chlorides **4** and **6** were obtained (in a 57:43 distribution).[8] Computational studies suggested that S_Ni fragmentations of **3** were largely responsible for the formation of chlorides **4** and **5** in C_6D_{12}, while escape to an ion pair allowed the formation of some **6**. In the more polar solvent, ion pair formation was enhanced, and **4** and **6** formed from $(\mathbf{1/2})^+Cl^-$ in nearly comparable quantities.[8]



4 **5** **6**

Carbene **3** and products **4**–**6** are chiral. Consequently, determining the stereochemical course of the reaction sequence should provide a more nuanced mechanistic scenario. Here we present the first stereochemical investigation of these reactions.

Norbornadiene was hydroborated with dicaranylborane (derived from (+)-3-carene and borane-methyl sulfide) to give (+)-*exo*-norborn-5-en-2-ol (**7**),[9] $[\alpha]_D^{25}$ +4.78 (*c* 8.51, $CHCl_3$). The dextrorotatory alcohol was identical (^1H and ^{13}C NMR) to literature descriptions,[10] and was of (*S*) configuration at C2,[9] with 49% ee.[11] Conversion of the alcohol to isouronium salt **8** (cyanamide, CH_3SO_3H),[12] and thence to diazirine **9** (NaOCl),[13] proceeded as previously described.[8] The diazirine was purified by column chromatography and characterized



(*S*)-(+)-**7** (*S*)-**8** (*S*)-**9**

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by IR, UV, ^{1}H, and ^{13}C NMR spectroscopy; details for racemic **9** appear in Ref. 8.

Photolysis (350 nm) or thermolysis (25 °C) of diazirine (*S*)-**9** in C_6D_{12}, $CDCl_3$ or CD_3CN afforded carbene (*S*)-**3**, and thence fragmentation products **4**–**6**. The (^{1}H NMR) product distributions are recorded in Table 1. Photolysis or thermolysis of **9** led to generally comparable product distributions. As noted previously,[8] the formation of *endo*-norbornenyl chloride **5** was important only in the hydrocarbon solvent; in $CDCl_3$ or CD_3CN, **5** was suppressed in favor of nortricyclyl chloride **6**.

In order to define the stereochemical courses of the (*S*)-**3** to **4**–**6** conversions we required the absolute configurations and associated rotatory properties of these chlorides. This information was unknown, and so we computed it.[14] The structures of **4**–**6** were minimized at the DFT-RB3LYP level with a 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.[15] The computed linkage of absolute configuration and calculated specific rotation for each product chloride is illustrated below, where the computed $[\alpha]_D$ value pertains to solvents like CH_2Cl_2 or $CHCl_3$.

Samples of (*R*)-(−)-**4**, (*S*)-(−)-5, and (*S*)-(−)-**6**) were obtained by chromatographic separations of the product mixtures from fragmentation reactions of (*S*)-nortricyclyloxychlorocarbene[16] and (*S*)-*endo*-5-norbornenyl-2-oxychlorocarbene.[17] These chloride samples helped us to assign peak identities on GC separations of the products from the fragmentations of carbene (*S*)-**3**. Product mixtures were analyzed on a 30 m × 0.25 mm Chiraldex GTA column at 50 °C, which permitted the separation of each enantiomer of **4**–**6**. An example of the GC separation, with peak assignments, appears in Figure 1 for the products from the fragmentation of (*S*)-**3** in C_6D_{12}; peak areas are electronically integrated. The GC results establish that fragmentation of (*S*)-**3** leads predominantly to chlorides (*S*)-**4**, (*R*)-**5**, and (*S*)-**6** (see above for structures and configurations). The product ee's and the % ee's of the conversions are collected in Table 2, corrected for the 49% ee of carbene (*S*)-**3**.

Next, we consider the stereochemistry of formation of each product in turn, starting with *exo*-5-chloro-2-norbornene, **4**, the major fragmentation product of carbene **3**. In C_6D_{12}, carbene (*S*)-**3** gives **4** with 90–100% net retention; there is ~10% racemization when the carbene is photochemically generated, but complete retention

Table 1. Product distributions from the fragmentation of carbene **3**

Solvent	Method[a]	%**4**	%**5**	%**6**
C_6D_{12}	*hv*	54	29	17
C_6D_{12}	Δ	53	31	16
$CDCl_3$	*hv*	61	5	34
$CDCl_3$	Δ	60	4	36
CD_3CN	*hv*	59	5	36
CD_3CN	Δ	63	tr	37

[a] Photolysis or thermolysis of diazirine (*S*)-**9**, both at 25 °C.

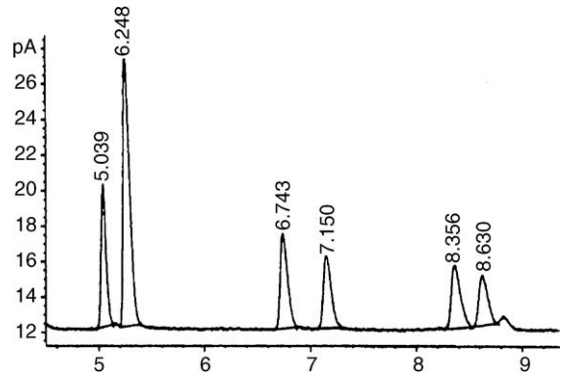


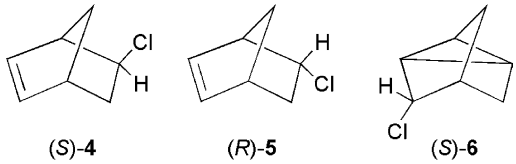
Figure 1. Separation of chloride products from the fragmentation of carbene (*S*)-**3** on a Chiraldex GTA column at 50 °C. The numbers are retention times in minutes. From left to right, the peak assignments are (*R*)-**4**, (*S*)-**4**, (*R*)-**5**, (*S*)-**5**, (*S*)-**6**, and (*R*)-**6**. The final, small peak is an unknown.

Table 2. Stereochemistry of formation of product chlorides[a,b]

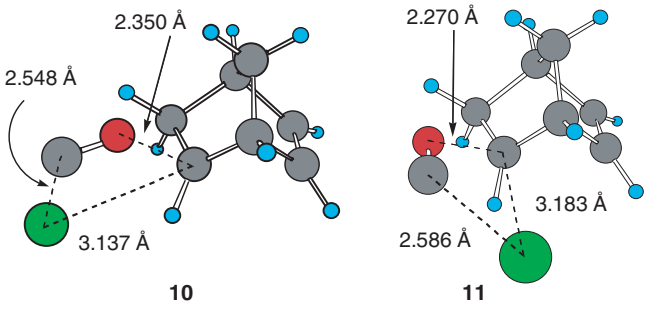
Solvent	Method[c]	(*S*)-**4**		(*R*)-**5**		(*S*)-**6**	
		Ee	% Ee[d]	Ee	% Ee[d]	Ee	% Ee[d]
C_6D_{12}	*hv*	44.3	90.4	8.87	18.1	12.1	24.7
C_6D_{12}	Δ	50.0	100	8.55	17.4	8.68	17.7
$CDCl_3$	*hv*	31.8	64.9	11.3	23.1	7.57	15.4
$CDCl_3$	Δ	33.7	68.8	10.1	20.6	7.81	15.9
CD_3CN	*hv*	29.4	60.0	[e]	[e]	6.56	13.4
CD_3CN	Δ	34.9	71.2	[e]	[e]	12.0	24.5

[a] From (*S*)-**9** via carbene (*S*)-**3**, assuming 49% ee, as in alcohol (*S*)-**7**.
[b] Product ee analysis by GC on a Chiraldex GTA column; see text.
[c] Photolysis or thermolysis of diazirine **9** at 25 °C.
[d] Corrected for 49% ee of carbene (*S*)-**3**.
[e] Inadequate sample size.

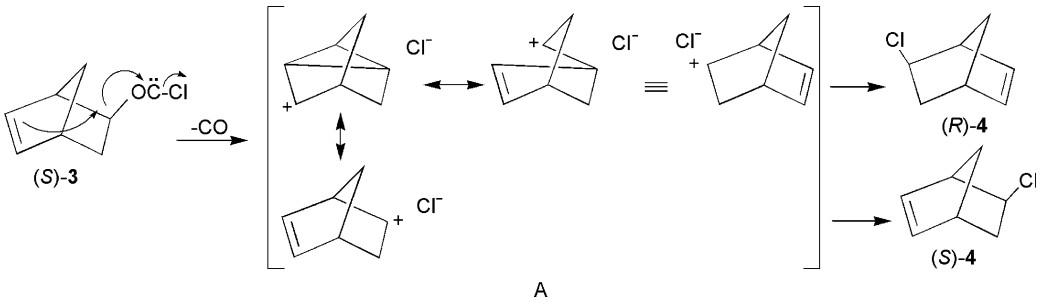
from thermolysis of diazirine (*S*)-**9** (Table 2). This result is in agreement with the S_Ni-like process computed for the **3** → **4** conversion ($\Delta G^{\ddagger}$ = 12.1 kcal/mol in vacuum);[8] cf., transition state (TS) **10**.[18]



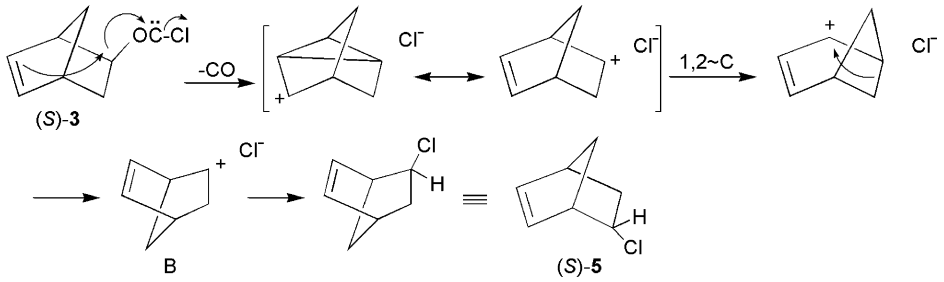
(*S*)-**4** $[\alpha]_D$+28.6 (*R*)-**5** $[\alpha]_D$+124.0 (*S*)-**6** $[\alpha]_D$-113.8



10 **11**



Scheme 1.



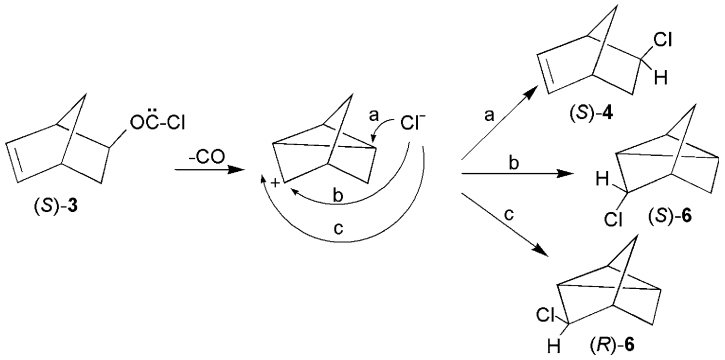
Scheme 2.

In C_6D_{12}, S_Ni formation of **4** with retention dominates, but as the solvent becomes more polar ($CDCl_3$ or CD_3CN), retention in the **3** → **4** conversion decreases to 60–70%. The enhanced racemization can be explained by competitive fragmentation to an ion pair which can give either (*S*)-**4** or (*R*)-**4** upon reopening; cf., ion pair **A** in Scheme 1.[19]

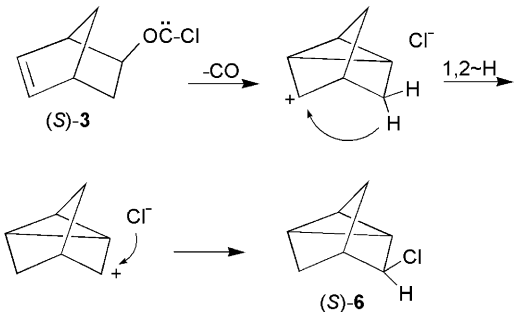
In C_6D_{12}, fragmentation of (*S*)-**3** also produces ~30% of *endo*-5-chloro-2-norbornene (**5**), but with only ~18% net retention. Computational studies predict direct S_Ni formation of (*R*)-**5** from carbene (*S*)-**3** via TS **11**.[8,18] However, the extensive racemization (82%) implies that fragmentation to an ion pair successfully competes with the S_Ni process.[19,20] The dominant enantiomer (*R*)-**5** can be obtained from ion pair **A** of Scheme 1 by migration of Cl^- from the exo to endo face of the norbornenyl cation prior to recombination. Alternatively, a reversible nortricyclyl-bicyclo[3.1.1]heptenyl 1,2-carbon shift[4] can afford chloride (*S*)-**5** from carbene (*S*)-**3**; cf., Scheme 2. In SO_2ClF, the experimental E_a for the 1,2-C shift is ~17 kcal/mol.[4] Collapse of ion pair **B** (Scheme 2) leads to (*S*)-**5**.

As solvent polarity increases from C_6D_{12} to $CDCl_3$ and CD_3CN, the importance of TS **11** declines; only 4–5% of *endo*-chloride **5** (again with ~20% ee) forms upon fragmentation of carbene **3** (Table 1). Most of the product in the polar solvents consists of *exo*-chloride **4** and 3-nortricyclyl chloride **6**,[8] presumably derived from the fragmentation of carbene **3** via TS **10** (for **4**), and the nortricyclyl chloride ion pair derived therefrom (for **6**).

The third product from carbene **3** is 3-nortricyclyl chloride **6**, which forms in ~17% yield in C_6D_{12}, increasing to ~36% in the more polar $CDCl_3$ or CD_3CN (Table 1). It arises mainly as (*S*)-**6**, with ee ~13–25% over the solvent range of Table 2. As we have suggested, even



Scheme 3.



Scheme 4.

in C_6D_{12} there must be some 'leakage' of carbene **3** to a tight norbornenyl/nortricyclyl chloride ion pair; cf., Scheme 3.

Here, return of chloride via path (a) generates product (*S*)-**4**, while chloride migration to the underside of the cation via path (b) generates (*S*)-**6**, the predominant enantiomer of product **6**. This is the 'least motion' pathway to **6**; further motion to the exo face of the cation by path (c) affords (*R*)-**6**, the minor enantiomer.

One could also obtain (*S*)-**6** by a 3,5-hydride shift within the initially formed nortricyclyl chloride ion pair, followed by recombination (Scheme 4), but this process would require an activation energy significantly greater than 18.4 kcal/mol.[4]

In summary, the fragmentation of carbene (*S*)-**3** affords chlorides (*S*)-**4**, (*R*)-**5**, and (*S*)-**6** with varying degrees of enantiomeric excess which depend, in part, on solvent polarity. The stereochemical courses of the transformations can be understood as weighted blends of S_Ni fragmentations, coupled with escape to norbornenyl/nortricyclyl ion pairs in which stereochemical integrity is compromised. Note that the fragmentation of (*S*)-3-nortricyclyloxychlorocarbene via competing S_Ni transition states leads to (*S*)-**6** and (*R*)-**6**, resulting in extensive racemization of the 3-nortricyclyl chloride product.[16] In contrast, fragmentation of (*S*)-**3** proceeds via analogous S_Ni transition states **10** and **11**, which lead to different products, (*S*)-**4** and (*R*)-**5**, with the former produced with essentially complete retention. Clearly, our ability to follow the stereochemistry of product formation from the fragmentation of **3** enables us to refine the available mechanistic possibilities.

Acknowledgements

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