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Comparative stereochemistry of the fragmentations of oxychlorocarbenes, chlorocarbonates, and chlorosulfites in the 3-nortricyclyl/5-norbornen-2-yl system

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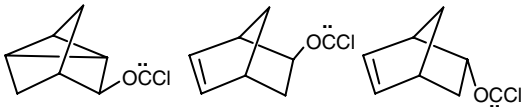
Abstract—Fragmentations of the title precursors in polar solvents proceed via similar ion pairs to mixtures of *exo*-2-chloro-5-norbornene and 3-nortricyclyl chloride. The stereochemical course of the conversions is mainly determined by least motion chloride return in ion pair intermediates.

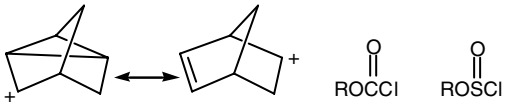
1. Introduction

We recently completed a stereochemical study of the fragmentations of 3-nortricyclyloxychlorocarbene (**1**),[1] *exo*-5-norbornenyl-2-oxychlorocarbene (**2**),[2] and *endo*-5-norbornenyl-2-oxychlorocarbene (**3**).[3] The products



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

were mixtures of the corresponding chlorides whose formation was attributed to competing retention and inversion S_Ni mechanisms in hydrocarbon solvents, and competitive ion pair pathways in more polar solvents.[1–3] In the latter cases, the nortricyclyl–norbornenyl cation[4] was centrally involved.[5] Cation **4**, shown here as a resonance hybrid, has a structure that more closely resembles the nortricyclyl canonical form,[6] but ion pairing can affect the nortricyclyl/norbornenyl product distribution.[5,6c]



4 **5** **6**

The fragmentation of ROCCl to RCl is mechanistically related to the decompositions of alkyl chlorocarbonates (**5**)[7] and alkyl chlorosulfites (**6**),[8] which can also be formulated as S_Ni or ion pair processes leading to RCl. The differences between the three reactions involve the identity of the molecule extruded during fragmentation: CO from the carbenes, CO_2 from the chlorocarbonates, or SO_2 from the chlorosulfites.

Having in hand the optically active alcohol precursors to carbenes **1**–**3**,[1–3] we decided to generate the analogous chlorocarbonates and chlorosulfites in order to carry out a thorough stereochemical comparison of the three types of reaction with each of the three isomeric nortricyclyl/norbornenyl precurors. The results, described here, confirm that the fragmentations of these secondary alkyl oxychlorocarbenes, chlorocarbonates, and chlorosulfites do indeed pass through closely related ion pairs in polar solvents.[9]

2. 3-Nortricyclyl precursors

(*S*)-(−)-3-Nortricyclanol with $[\alpha]_D^{25}$ −19.0 (*c* 5.0, $CHCl_3$), corresponding to 46.5% ee,[10] was prepared from *exo*-norbornene oxide as previously described.[1,11] The optically active alcohol was then converted in 66% yield to oily (*S*)-3-nortricyclyl chlorocarbonate (**7a**) with triphosgene in toluene.[7b] The chlorocarbonate was characterized by IR, GC–MS, and ^1H and ^{13}C NMR spectroscopy. Thermal decomposition of (*S*)-**7a** in

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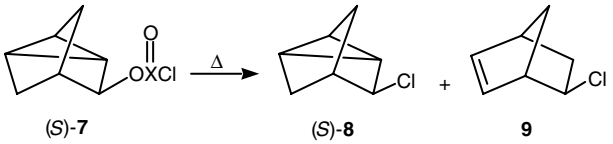
Table 1. Stereochemistry of formation of 3-nortricyclyl chloride[a]

Precursor	Solvent	Temperature (°C)	Yield (%)	(*S*)-**8**	
				ee	ee[b] (%)
(*S*)-**1**[c]	$CDCl_3$	25	93	6.0	13
(*S*)-**1**[c]	CD_3CN	25	86	10.5	23
(*S*)-**7a**	$CDCl_3$	70[d]	98	10.2	22
(*S*)-**7a**	CD_3CN	70[e]	90	13.0	28
(*S*)-**7b**	THF[f]	Refl.	70[g]	12.9	28
(*S*)-**7b**	THF, Py[f]	Refl.	58[g]	7.2	16

[a] From precursors (*S*)-**1**, (*S*)-**7a**, or (*S*)-**7b**, assuming 46.5% ee, as in (*S*)-3-nortricyclanol.
[b] Product analysis by GC on a Chiraldex GTA Column, corrected for 46.5% ee of precursor.
[c] From Ref. 1.
[d] 48 h at 70 °C.
[e] 2 h at 70 °C.
[f] $SOCl_2$ and pyridine (Py) were in 5- and 10-fold excess, respectively. Solutions were refluxed for 12 h.
[g] Isolated yield.

$CDCl_3$ or CD_3CN afforded (*S*)-3-nortricyclyl chloride (**8**) in $\geqslant$90% yield; see Eq. 1 and Table 1.[9,12] Additionally, 2-10% of *exo*-2-chloro-5-norbornene was formed, but not in sufficient quantity to accurately determine its stereochemistry. The stereoselectivity of the (*S*)-**7a** to (*S*)-**8** conversion is shown in Table 1, where it is compared to that of the (*S*)-**1** to (*S*)-**8** reaction.[1] Control experiments demonstrated the configurational stability of chloride (*S*)-**8** under all the reaction conditions of Table 1.



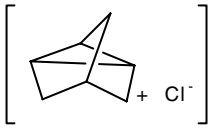
(*S*)-**7** (*S*)-**8** **9**

a, X=C; **b**, X=S

(1)

Next, we generated chlorosulfite (*S*)-**7b** by reacting (*S*)-3-nortricyclanol (46.5% ee) with excess $SOCl_2$ in THF. The unstable chlorosulfite was not isolated, but formed and decomposed in situ.[5,13] The stereochemical results of the thionyl chloride reactions, with or without added pyridine, also appear in Table 1.

The fragmentations of carbene (*S*)-**1**, chlorocarbonate (*S*)-**7a**, and chlorosulfite (*S*)-**7b** afford (*S*)-3-nortricyclyl chloride with similar and modest net retention in $CDCl_3$ or CD_3CN. In particular, the similar stereochemical results in $CDCl_3$ and CD_3CN suggest that specific involvement of the CD_3CN solvent is *not* important. The outcome is consistent with a combination of inversion and retention S_Ni transition states,[1] and with the intermediacy of ion pair **10**,[5] from which chloride return with net retention would be expected. It is reasonable to conclude that similar ion pairs are formed from each precursor. From a synthetic standpoint, the chlorocarbonate reaction is the cleanest and simplest procedure; the thionyl chloride reaction gives a number of (unidentified) side products, while the carbene fragmentation requires prior synthesis of an unstable diazirine.



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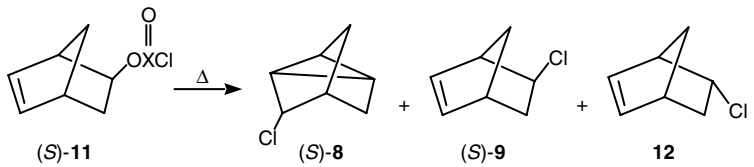
3. *exo*-5-Norbornen-2-yl precursors

(*S*)-(+)-*exo*-5-Norbornen-2-ol was obtained by the asymmetric hydroboration of norbornadiene,[14] and had $[\alpha]_D^{25}$ 5.37 (*c* 6.2, $CHCl_3$), corresponding to 55.1% ee.[15] The alcohol was converted to the oily (*S*)-*exo*-5-norbornen-2-chlorocarbonate (**11a**) in 66% yield by reaction with triphosgene in toluene.[7b] The chlorocarbonate was characterized by IR, GC–MS, and ^1H and ^{13}C NMR spectroscopy.

Thermal decomposition of (*S*)-**11a** in $CDCl_3$ or CD_3CN gave (*S*)-*exo*-2-chloro-5-norbornene (**9**), (*S*)-3-nortricyclyl chloride (**8**), and (traces of) *endo*-2-chloro-5-norbornene (**12**); see Eq. 2 and Table 2. Stereoselectivities of the (*S*)-**11a** to (*S*)-**8** and (*S*)-**9** conversions were determined by GC[12] and are recorded in Table 2, where they are compared to those of the (*S*)-**2** fragmentations.[2] Products **8** and **9** were shown to be configurationally stable under all the conditions in Table 2, but insufficient *endo*-chloride **12** was obtained for accurate stereochemical analysis.



(*S*)-**11** (*S*)-**8** (*S*)-**9** **12**

a, X=C; **b**, X=S

(2)

Table 2. Stereochemistry of products from *exo*-5-norbornen-2-yl precursors[a]

Precursor	Solvent	Temperature (°C)	Yield (%)	(*S*)-**8**		Yield (%)	(*S*)-**9**	
				ee	ee[b] (%)		ee	ee[b] (%)
(*S*)-**2**[c]	$CDCl_3$	25	36	7.81	15.9	60	33.7	68.8
(*S*)-**2**[c]	CD_3CN	25	37	12.0	24.5	63	34.9	71.2
(*S*)-**11a**	$CDCl_3$	90[d]	39	10.9	19.8	60	38.5	89.9
(*S*)-**11a**	CD_3CN	90[d]	27	15.7	28.5	68	22.9	41.6
(*S*)-**11b**	THF[e]	Refl.	21[f]	22.3	40.5	40[f]	20.6	37.4
(*S*)-**11b**	THF, Py[e]	Refl.	19[f]	14.1	25.6	35[f]	12.1	22.0

[a] From precursors (*S*)-**2**, (*S*)-**11a**, or (*S*)-**11b**. Ee is 49% for (*S*)-**1** and 55.1% for (*S*)-**11a** and (*S*)-**11b**, based on the ee of the initial (*S*)-(+)-*exo*-5-norbornen-2-ol.
[b] Product analysis by GC on a Chiraldex GTA column, corrected for the ee of the precursor.
[c] From Ref. 2.
[d] 48 h in $CDCl_3$; 2 h in CD_3CN.
[e] $SOCl_2$ and pyridine (Py) were in 5- and 10-fold excess, respectively. Solutions were refluxed overnight.
[f] Isolated yield.

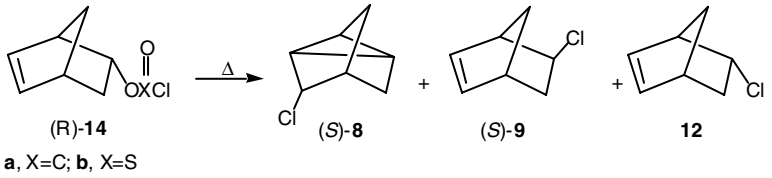
Chlorosulfite **11b** was generated and decomposed in situ by reaction of (*S*)-(+)-*exo*-5-norbornen-2-ol (55.1% ee) with excess $SOCl_2$ in refluxing THF.[5,13] The stereoselectivity of product formation from this reaction, in the presence or absence of pyridine, also appears in Table 2.

Allowing for differences in reaction temperature and solvent, the data of Table 2 again point to similar mechanisms for the fragmentations of the *exo*-5-norbornen-2-yl precursors: oxychlorocarbene **2**, chlorocarbonate **11a**, and chlorosulfite **11b**. Ion pairs are the most reasonable intermediates[2] and can readily account for the observed moderate stereoselectivity. After the loss of CO, CO_2, or SO_2, each (*S*) precursor can afford ion pair **13**, from which either (*S*)-**9** or (*R*)-**9** can arise; cf. Scheme 1. Return of Cl^- at C-2 (**13A**), the least motion option, exceeds Cl^- return at C-1 (**13C**), accounting for the observed excess of (*S*)-**9** over (*R*)-**9** (i.e., net retention). Similarly, a least motion return of Cl^- at C-5 (**13B**) affords (*S*)-**8** in excess over (*R*)-**8**, as is observed (Table 2).

4. *endo*-5-Norbornen-2-yl precursors

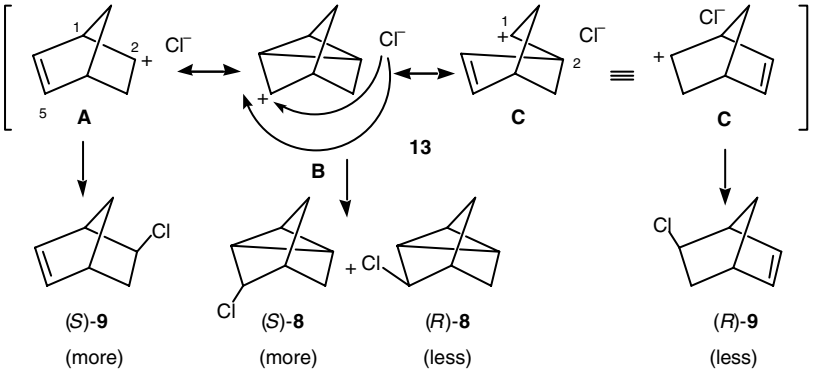
(*R*)-(+)-*endo*-5-Norbornen-2-ol was obtained from its racemic acetate ester by kinetic resolution with the lipase from *Candida cylindracea*.[3,16,17] The alcohol had $[\alpha]_D^{25}$ 121 (*c* 6.32, $CHCl_3$), corresponding to 73.3% ee.[18] As above, the alcohol was converted to the oily (*R*)-*endo*-5-norbornen-2-yl chlorocarbonate (**14a**) in 61% yield by reaction with triphosgene in toluene.[7b] The chlorocarbonate was characterized by IR, GC–MS, and ^1H and ^{13}C NMR spectroscopy.

Thermal decomposition of (*R*)-**14a** in $CDCl_3$ or CD_3CN at 95 °C gave mainly (*S*)-**8** and (*S*)-**9**; only trace quantities (⩽5%) of *endo*-chloride **12** were formed; cf. Eq. 3 and Table 3. The stereoselectivities of the (*R*)-**14a** to (*S*)-**8** and (*S*)-**9** conversions appear in Table 3, where they are compared to the fragmentations of carbene (*R*)-**3**.



(3)

Chlorosulfite **14b** was generated and decomposed in situ by reaction of (*R*)-(+)-*endo*-5-norbornen-2-ol with



Scheme 1.

Table 3. Stereochemistry of products from *endo*-5-norbornen-2-yl precursors[a]

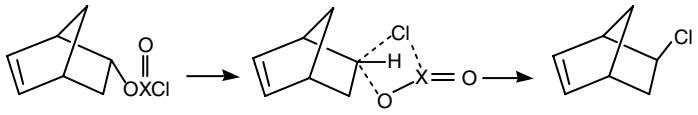
Precursor	Solvent	Temperature (°C)	Yield (%)	(*S*)-**8**		Yield (%)	(*S*)-**9**	
				ee	ee[b] (%)		ee	ee[b] (%)
(*R*)-**3**[c]	$CDCl_3$	25	40	11.6	16	58	45.6	62
(*R*)-**3**[c]	CD_3CN	25	31	16.0	22	66	42.0	57
(*R*)-**14a**	$CDCl_3$	95[d]	39	16.3	22	57	39.7	54
(*R*)-**14a**	CD_3CN	95[e]	37	15.6	21	63	34.3	47
(*R*)-**14b**	—[f]	—[f]	7[g]	47.8	65	35[g]	30.8	42
(*S*)-**14b**[h]	Py[f]	—[f]	7[g]	24.5[h]	36[h]	38[g]	21.4[h]	31[h]

[a] From precursors (*R*)-**3**, (*R*)-**14a**, or (*R*)-**14b**. Ee is 73.3% for each precursor, based on the ee of the initial (*R*)-(+)-*endo*-5-norbornen-2-ol.
[b] Product analysis by GC on a Chiraldex GTA column, corrected for the ee of the precursor.
[c] From Ref. 3.
[d] 5 days.
[e] 3 days.
[f] 50% Ethylene glycol dimethyl ether and 50% THF; reflux 48 h. $SOCl_2$ and Py were in 5- and 10-fold excess, respectively.
[g] Isolated yield.
[h] Note the use of (*S*)-**14b**; the products are (*R*)-**8** and (*R*)-**9**.

excess $SOCl_2$ in refluxing 1:1 ethylene glycol dimethyl ether and THF. The stereoselectivity of product formation, in the presence or absence of pyridine, appears in Table 3.

Except for the formation of (S)-**8** in 65% ee from chlorosulfite (*R*)-**14b** in the absence of pyridine, the stereochemical consequences of the fragmentations of the *endo*-norbornenyl oxychlorocarbene, chlorocarbonate, and chlorosulfite are rather similar. Note again the minimal differences in stereochemical outcomes in $CDCl_3$ and CD_3CN, suggesting that CD_3CN is not specifically involved in the reactions. The major product is *exo*-2-chloro-5-norbornene (*S*)-**9**, formed from the endo precursor with net inversion, whereas the minor product is (*S*)-**3**-nortricyclyl chloride, (*S*)-**8**.

The substantial inversion seen in the formation of (*S*)-**9** from all 3 *endo* precursors suggests the persistence in polar solvents of inverting S_Ni processes similar to that first identified in the conversion of *endo* carbene (*R*)-**3** to chloride (*S*)-**9** in hydrocarbon solvents.[3] We illustrate this process here for the fragmentation of the *endo* precursors (*R*)-**14a** or (*R*)-**14b**, via transition state **15**, to *exo*-chloride (*S*)-**9**; cf. Eq. 4.



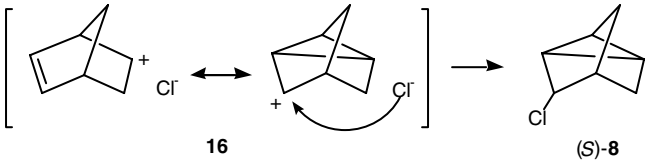
(R)-**14**
a, X=C; **b**, X=S

15
(X = C or S)

(*S*)-**9**

(4)

The conversion of the (*R*) *endo* precursors to minor product **8**, mainly with (*S*) configuration, can be rationalized by a least motion collapse of ion pair **16** predominantly on its *endo* face; cf. Eq. 5.



16

(*S*)-**8**

(5)

Further motion of the chloride to the *exo* face would lead to (minor) enantiomer (*R*)-**8**. Note that little (⩽5%) *endo*-2-chloro-5-norbornene forms from endo precursors **3**, **14a**, or **14b** in polar solvents, in contrast with ~20% of the *endo*-chloride that forms from *endo*-carbene **3** in hydrocarbon solvents.[3] This points to a reduced role for S_Ni fragmentation with retention on the *endo* face of the precursors in polar solvents, where ion pair processes dominate.

5. Conclusion

The fragmentations of 3-nortricyclyl, *exo*-5-norbornen-2-yl, and *endo*-5-norbornen-2-yl oxychlorocarbenes, chlorocarbonates, and chlorosulfites *in polar solvents* proceed via similar ion pairs to mixtures of *exo*-2-chloro-5-norbornene and 3-nortricyclyl chloride (with small quantities of *endo*-2-chloro-5-norbornene). The stereochemical course of the conversions is mainly determined by least motion chloride return in ion pair intermediates.

Acknowledgements

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