

THE STEREOCHEMICAL COURSE OF FRAGMENTATION OF BENZYLOXYCHLOROCARBENE

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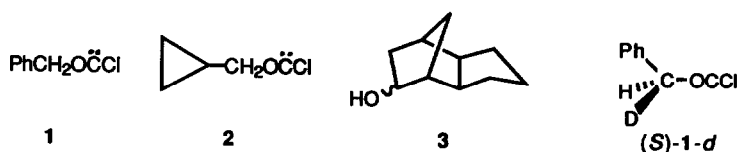
Summary. The fragmentation of α -deuteriobenzyloxychlorocarbene to α -deuteriobenzyl chloride in acetonitrile occurs with at least 60% net retention of stereochemistry.

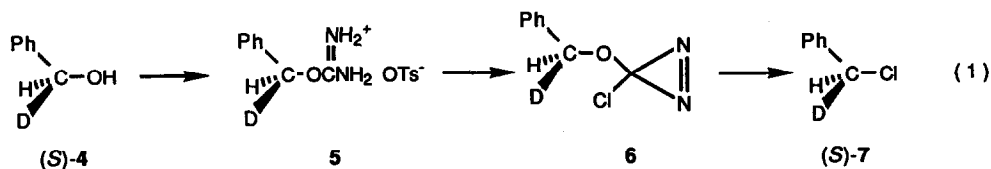
Benzyloxychlorocarbene (1) or cyclopropylmethoxychlorocarbene (2), generated by room temperature thermolyses of the appropriate diazirines in MeCN, undergo fragmentation to (CO and) R^+Cl^- ion pairs that collapse to alkyl chlorides in high yield.^{1,2} Related carbene fragmentations were earlier encountered by Hine^{3a} and Skell^{3b} in reactions of haloforms (i.e., dihalocarbenes) with alkoxides, and by Stevens in thermolyses of methoxy- and isobutoxychlorodiazirines.⁴ More recently, Jones *et al.* examined the reactions of phase-transfer-generated CCl_2 with the epimeric alcohols 3, where the derived alkoxychlorocarbenes are putative intermediates.⁵

In the fragmentation of 2, the intermediacy of tight cyclopropylmethyl cation-chloride ion pairs was signalled by the variety and distribution of the isomeric C_4 -chloride products.² The intervention of ion pairs in the benzyloxychlorocarbene fragmentation, however, was inferred from the absence of radical products, and the outcome of competitive intermolecular trapping with methanol.¹ In contrast, the absence of H- or C-shifted, rearranged chloride products from the reactions of 3 with CCl_2 was attributed to competitive S_N1 decomposition and halide displacement on alkoxychlorocarbenes derived from 3 or their (ylide) precursors.⁵

Now we describe the fragmentation of (*S*)- α -deuteriobenzyloxychlorocarbene [(*S*)-1-d]. Monitoring the stereochemical fate of the benzylic center of 1-d as it fragments to α -deuteriobenzyl chloride allows a closer examination of mechanism in this reaction. This appears to be the first report concerning chirality in a carbene fragmentation reaction.

Benzaldehyde-*formyl*-d, prepared by the reaction of benzil with KCN in D_2O /dioxane,⁶ was stereoselectively reduced to (*S*)-(+)- α -deuteriobenzyl alcohol (4) with the chiral organoborane derived from (+)- α -pinene and 9-BBN.⁷ The alcohol was purified by distillation, followed by chromatography (silica gel, 1:1 CH_2Cl_2 /hexane), and obtained in 50% yield with >98.5% purity by gc. Over 8 separate preparations, $[\alpha]_D^{25}$ of 4 (in MeOH) ranged from +1.25° to +1.61° ($\pm 0.04^\circ$), or 78-100% of optical purity.⁸ (*S*)-(+)-4 was





converted to the α -deuteriobenzylisourea tosylate, 5, by stirring with cyanamide and anhydrous *p*-toluenesulfonic acid in dry CHCl_3 (25°C, 2 days), followed by precipitation with ether and recrystallization from 2-butanone.¹ Importantly, although 5 is optically active (e.g., $[\alpha]_D^{25} +1.17^\circ$ (MeOH) from 4 with $[\alpha]_D^{25} +1.25^\circ$), there is evidence for some acid catalyzed racemization of 4 concurrent with its conversion to 5. Over 4 experiments, recovered and repurified 4 retained only ~80% of its initial optical purity. Thus 5 may be as much as 20% racemized, relative to its precursor alcohol.

Hypochlorite oxidation⁹ of (S)-(+)-5 in a 2-phase aqueous DMSO/pentane system at $\leq 15^\circ\text{C}$ afforded a pentane solution of diazirine 6.¹ This solution was dried over CaCl_2 , stripped of pentane at 0°C, and the resulting diazirine was redissolved in dry MeCN. The MeCN solution was stirred at 25°C for 24 h, whereupon diazirine 6 underwent quantitative fragmentation¹ to benzyl chloride- α -d, 7, which was isolated by gc (SE-30, 70°C), and repurified ($\geq 99\%$, gc) by chromatography over silica gel (hexane). A summary of the stereochemical results for several (S)-4 to (S)-7 conversions appears in Table I;¹⁰ the chemical transformations are outlined in eq.(1).

Due to the low intrinsic optical activity of 7,⁸ and the difficulty of obtaining highly purified 7 in quantity, the observed rotations recorded in the table are low. Nevertheless, four repetitions of the 4 \rightarrow 7 conversion are in reasonable agreement, and indicate that the overall process proceeds with ~60-80% net retention. Indeed, noting the potential for up to 20% racemization in the conversion of 4 to 5 (see above), we conclude that the conversion of diazirine (S)-6 to chloride (S)-7, via the fragmentation of carbene (S)-1-d in MeCN, occurs with very substantial, but probably incomplete, stereochemical retention.¹¹⁻¹³

Retention of this magnitude is consistent with the intervention of tight ion pair 8 in the fragmentation of 1-d to 7. The process seems analogous to the formation of alkyl chlorides by the thermolytic extrusion of SO_2 from alkyl chlorosulfites. Initially designated " $\text{S}_{\text{N}}1$ ", the mechanism of the latter reaction is now considered to involve an ion pair:¹⁴ "although the $\text{S}_{\text{N}}1$ mechanism at one time was postulated to involve front-side displacement involving a four-center transition state, no such process has been

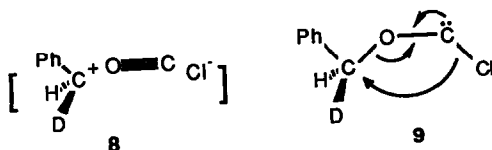


Table I. Stereochemical Course of Conversion of 4 to 7^a

Expt	Opt. purity		[7] ^c	Opt. purity		Net retn, % ^e
	of 4, %	α_D^{25} of 7, deg ^b		$[\alpha]_D^{25}$ of 7, deg	of 7, % ^d	
1	90	0.016 ^f	0.016	1.0	65	72
2	90	0.012 ^f	0.011	1.1	72	80
3	97	0.023 ^g	0.251	0.92	60	62
4	97	0.023 ^g	0.270	0.85	56	58

^aPolarimetric readings were determined with a Perkin-Elmer model 141 polarimeter, accurate to $\pm 0.002^\circ$ for microcells. ^bObserved rotations of 7, reproducibility $\pm 0.002^\circ$. ^cConcentration of 7 expressed in g/cc in CHCl_3 . ^dBased upon $[\alpha]_D^{25} = 1.53^\circ$ for optically pure 7.¹⁰ ^eAll samples of 7 were dextrorotatory when obtained from dextrorotatory 4 via eq.(1). This corresponds to stereochemical retention.¹⁰ The values are minima because of possible racemization during the preparation of 5; see text. ^fPathlength = 1 dm. ^gPathlength = 0.1 dm.

demonstrated in nucleophilic substitution at carbon.^{14b} Indeed, it is probably inappropriate to describe the fragmentation of alkoxychlorocarbenes as S_N1 (in the sense of 9), and unnecessary to use this mechanistic descriptor to emphasize the absence of free carbocationic intermediates in these reactions. Thus, textbooks that were contemporary with Hine's study^{3a} had already incorporated the ion pair formulation of " S_N1 " reactions.¹⁵

With regard to the specific case of primary alkyl moieties, we note that the decomposition of purified 1-butyl-1-d chlorosulfite in a carbocation supportive solvent (e.g., dioxane) proceeded with 34% inversion and 66% racemization, rationalized as S_N2 chloride attack on the chlorosulfite (inversion) in competition with front-side chloride return in an ion pair (retention).¹⁶ We suggest that the fragmentation of benzyloxychlorocarbene in acetonitrile is also best regarded as occurring with the intermediacy of an ion pair (8). In this case, the extremely rapid fragmentation of the carbene,¹ coupled with the absence of external nucleophiles, ensures the return of chloride anion to the benzyl cation with high stereochemical retention.¹⁷

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References and Notes

- (1) R.A. Moss, B.K. Wilk, and L.M. Hadel, Tetrahedron Lett., 28, 1969 (1987).
- (2) R.A. Moss, G-J. Ho, and B.K. Wilk, Tetrahedron Lett., 30, 2473 (1989).
- (3) (a) J. Hine, E.L. Pollitzer, and H. Wagner, J. Am. Chem. Soc., 75, 5607 (1953); (b) P.S. Skell and I. Starer, Ibid., 81, 4117 (1959).
- (4) N.P. Smith and I.D.R. Stevens, J. Chem. Soc. Perkin Trans. II, 1298 (1979).
- (5) I.R. Likhovorik, M. Jones, Jr., A.G. Yurchenko, and P.A. Krasutsky, Tetrahedron Lett., 30, 5089 (1989).

- (6) A.W. Burgstahler, D.E. Walker, Jr., J.P. Kuebrich, and R.L. Showen, J. Org. Chem., **37**, 1272 (1972).
- (7) M.M. Midland, A. Tramontano, and S.A. Zderic, J. Am. Chem. Soc., **99**, 5211 (1977).
- (8) Based upon $[\alpha]_D^{25} +1.58^\circ$ for optically pure 4: K.S.Y. Lan, P.K. Wong, and J.K. Stille, J. Am. Chem. Soc., **98**, 5832 (1976). Note that gc indicated that α -pinene was absent in our optically active 4.
- (9) W.H. Graham, J. Am. Chem. Soc., **87**, 4396 (1965).
- (10) Absolute configurations and maximum rotations are summarized in ref. 8.
- (11) Optically active 7 underwent minimal (<7%) racemization when stirred in MeCN for 1 day at room temperature.
- (12) An attempt to study the stereochemical course of the reaction in MeOH/MeCN was inconclusive because of the extremely low intrinsic optical activity of product chiral PhCHDOME,¹³ and the very low (<0.01°) observed rotations of product 7.
- (13) The corresponding ethyl ether has $[\alpha]_D 0.098^\circ$: A. Streitwieser, Jr., and J.R. Wolfe, Jr., J. Am. Chem. Soc., **81**, 4912 (1959). In our hands, (S)-PhCHDOME [from (S)-4, NaH, and MeI in THF] had $[\alpha]_{365} +0.31^\circ$.
- (14) (a) J. March, "Advanced Organic Chemistry," 3rd Ed., Wiley, New York, 1985, pp. 286-7. (b) F.A. Carey and R.J. Sundberg, "Advanced Organic Chemistry, 2nd Ed., Plenum, New York, 1984, pp. 286-7.
- (15) J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, 1956, pp. 114ff. E.S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rhinehart, and Winston, New York, 1959, pp. 294-5.
- (16) A. Streitwieser, Jr., and W.D. Schaeffer, J. Am. Chem. Soc., **79**, 379 (1957).
- (17) One might suggest that the acetonitrile solvent, in which 8 collapses to (S)-7, could function in a manner analogous to dioxane in the decomposition of butyl chlorosulfite; i.e., holding the benzylic configuration by rear side N: participation while Cl⁻ returns from the front side with retention. We view this as unlikely, however, because a sufficiently strong MeCN-benzylic cation interaction should divert the cation to MeCCl=NCHDPh, as in a Ritter reaction. No such product is observed, and the yield of benzyl chloride is quantitative.¹

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