

HEXACHLOROACETONE/TRIPHENYLPHOSPHINE: A REAGENT FOR THE REGIO- AND STEREOSELECTIVE CONVERSION OF ALLYLIC ALCOHOLS INTO CHLORIDES

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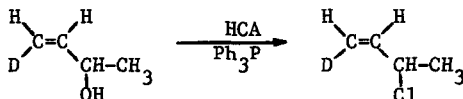
The preparation of an allylic halide from the alcohol in a regio- and stereospecifically predictable fashion has been of concern to synthetic and mechanistic organic chemists. Numerous methods (of varying generality) have been developed, among which are the following: (a) reaction with conventional halide-producing reagents like SOCl_2 ¹ or PX_3 ²; (b) formation of a sulfonate ester^{3,4} or other reactive group⁵ followed by displacement with halide ion in an aprotic solvent; (c) reaction with dimethyl sulfide and an *N*-halosuccinimide.^{6,2b,4c}

The reagent system triphenylphosphine/carbon tetrachloride and its several variants⁷ have proved very versatile for the conversion of alcohols and carboxylic acids into halides,⁸ the dehydration of amides and oximes to nitriles,⁹ the dihalomethylenation of carbonyl groups,¹⁰ and condensations leading to esters, amides, and peptides.¹¹ Application of this method to the production of allylic halides seemed most promising in light of the report by Snyder¹² that $\text{Ph}_3\text{P}/\text{CCl}_4$ transforms 2-buten-1-ol exclusively into unrearranged chloride, and that only 11% of rearranged material is formed from 1-buten-3-ol. Similarly high regioselectivity has been reported for other allylic alcohols in their reactions with $\text{Ph}_3\text{P}/\text{CX}_4$.¹³ Nevertheless, one's enthusiasm is tempered by the fact that low-boiling allylic chlorides such as 1-chloro-2-butene (bp 85° (E), bp 84° (Z)) and 3-chloro-1-butene (bp 65°) are only with difficulty separable from reagent CCl_4 (bp 77°) and product CHCl_3 (bp 62°); similar isolation troubles have been noted by others.^{2g,3c,14}

We felt that one could circumvent this problem and, at the same time, facilitate the reaction by letting Ph_3P attack a higher-boiling halogen compound which also possesses a better leaving group than CCl_3 .¹⁵ Such reasoning led us naturally to an investigation of hexachloroacetone (HCA) as a substitute for CCl_4 . We have, in fact, found that $\text{Ph}_3\text{P}/\text{HCA}$ is a very useful system for the production of allylic chlorides under very mild conditions, resulting in excellent yields, high regio- and stereoselectivity, and great ease of product purification. The recent report¹⁶ on the use of HCA as a source of positive halogen prompts us now to communicate our preliminary observations on the reactions of the α - and γ -methylallyl alcohols.

Reaction of an allylic alcohol in HCA with a slight excess of Ph_3P is rapid (<20 min at 10-15°) and exothermic. Flash distillation at ambient temperature produces allylic chlorides as the only volatile products (accompanied by small amounts of CCl_4 in some cases). Significantly, the high boiling reagent HCA (bp 202°) and product pentachloroacetone (bp 192°) are

left behind. As indicated in the Table, not only are the yields and regioselectivity very high, but also the geometrical integrity of the double bond is quantitatively preserved in the reactions of (*E*)- and (*Z*)-2-buten-1-ol. Similarly, (*Z*)-1-buten-3-ol-1-d¹⁷ is cleanly transformed into chloride having unchanged stereochemistry. High stereoselectivity at the saturated



carbon is demonstrated by the conversion of (*R*)-(-)-1-buten-3-ol,^{17a,18} $[\alpha]_D^{25} -9.2^\circ$ (neat), 27.7% optically pure,¹⁹ into (*S*)-(+)-3-chloro-1-butene, $\alpha_D^{25} +15.1^\circ$ (neat, $l = 1$), 24.8% optically pure,¹⁹ with 90% inversion and only 10% racemization (as is typical of $\text{Ph}_3\text{P}/\text{CCl}_4$ reactions²⁰). We are currently extending our studies to the behavior of more highly substituted allylic systems, and will report these results in a full paper.

TABLE Reaction of Allylic Alcohols with Triphenylphosphine/Hexachloroacetone			
Alcohol	Allylic Chloride, % Yield ^a		
	$\begin{array}{c} \text{H}_3\text{C} \quad \text{H} \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{H} \quad \text{CH}_2\text{Cl} \end{array}$	$\begin{array}{c} \text{H}_3\text{C} \quad \text{CH}_2\text{Cl} \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{H} \quad \text{H} \end{array}$	$\begin{array}{c} \text{H}_3\text{C}-\text{CH}-\text{CH}=\text{CH}_2 \\ \\ \text{Cl} \end{array}$
$\begin{array}{c} \text{H}_3\text{C} \quad \text{H} \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{H} \quad \text{CH}_2\text{OH} \end{array}$ ^b	99.3%	---	0.7%
$\begin{array}{c} \text{H}_3\text{C} \quad \text{CH}_2\text{OH} \\ \diagdown \quad / \\ \text{C}=\text{C} \\ / \quad \diagdown \\ \text{H} \quad \text{H} \end{array}$ ^c	--- ^d	98.0% ^d	0.5%
$\begin{array}{c} \text{H}_3\text{C}-\text{CH}-\text{CH}=\text{CH}_2 \\ \\ \text{OH} \end{array}$ ^e	6.0%	---	94%

^aAbsolute yields, as determined by quantitative glpc analysis of the flash-distilled mixture. ^bCommercial sample (Chemical Samples Co.) >99% pure. ^cA 94/6 mixture (glpc), respectively, of (*Z*)- and (*E*)-2-buten-1-ol, prepared by Zn/Cu²¹ reduction in ethanol^{22,3d} of 2-butyne-1-ol. ^dA 94/6 mixture (glpc), respectively, of (*Z*)- and (*E*)-1-chloro-2-butene. ^eCommercial sample (Aldrich Chemical Co.), >99% pure.

Experimental Procedure: Into a 100-ml, round-bottomed flask equipped with magnetic stirrer were placed 17 ml (30 g, 0.11 mole) of HCA and 4.25 ml (3.58 g, 0.0496 mole) of (*E*)-2-buten-1-ol. The clear solution was cooled to 0° and 13.5 g (0.0515 mole) of Ph_3P was added in small portions over 20 min; an ice bath maintained the reaction mixture at 10°. The clear solution was allowed to warm to room temperature over 10 min during which time a thick slurry formed. Flash distillation (3 torr, 30 min, ambient temperature) into a Dry Ice-cooled receiver gave 4.8 g of volatile material. Quantitative glpc analysis (SE-30 on Chromosorb W) revealed the presence of

4.46 g (0.0493 mole, 99.3% yield) of (E)-1-chloro-2-butene, 0.03 g (0.0003 mole, 0.7% yield) of 3-chloro-1-butene, and 0.3 g of CCl₄.

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REFERENCES AND NOTES

- (a) W. G. Young, F. F. Caserio, Jr., and D. D. Brandon, Jr., *J. Am. Chem. Soc.*, **82**, 6163 (1960); (b) W. S. Johnson, T. Li, C. A. Harbert, W. R. Bartlett, T. R. Herrin, B. Staskun, and D. H. Rich, *ibid.*, **92**, 4461 (1970); (c) E. Meléndez and M. Pardo, *Bull. Soc. Chim. Fr.*, 632 (1974).
- (a) E. J. Corey, D. E. Cane, and L. Libit, *J. Am. Chem. Soc.*, **93**, 7016 (1971); (b) B. M. Trost, D. F. Taber, and J. B. Alper, *Tetrahedron Lett.*, 3857 (1976); (c) D. F. Taber, *J. Am. Chem. Soc.*, **99**, 3513 (1977); (d) P. A. Grieco and Y. Masaki, *J. Org. Chem.*, **39**, 2135 (1974); (e) J. H. Babler, *ibid.*, **41**, 1262 (1976); (f) A. G. Anderson, Jr., N. E. T. Owen, F. J. Freenor, and D. Erickson, *Synthesis*, 398 (1976); (g) J. A. Katzenellenbogen and A. L. Crumrine, *J. Am. Chem. Soc.*, **98**, 4925 (1976).
- (a) E. W. Collington and A. I. Meyers, *J. Org. Chem.*, **36**, 3044 (1971); (b) A. I. Meyers and E. W. Collington, *Tetrahedron*, **27**, 5979 (1971); (c) C. Georgoulis and G. Ville, *Bull. Soc. Chim. Fr.*, 607 (1975); (d) S. J. Cristol and C. S. Ilenda, *Tetrahedron Lett.*, 3681 (1976).
- (a) G. Stork, P. A. Grieco, and M. Gregson, *ibid.*, 1393 (1969); (b) Y. Bensimon and E. Ucciani, *C. R. Acad. Sci., Paris, Ser. C*, **276**, 683 (1973); (c) C. Chuit, G. Cahiez, J. Normant, and J. Villieras, *Tetrahedron*, **32**, 1675 (1976); (d) R. F. Borch, A. J. Evans, and J. J. Wade, *J. Am. Chem. Soc.*, **99**, 1612 (1977).
- S. Czernecki and C. Georgoulis, *Bull. Soc. Chim. Fr.*, 405 (1975).
- E. J. Corey, C. U. Kim, and M. Takeda, *Tetrahedron Lett.*, 4339 (1972).
- Reviews: (a) R. Appel, *Angew. Chem., Int. Ed. Engl.*, **14**, 801 (1975); (b) J. I. G. Cadogan and R. K. Mackie, *Chem. Soc. Rev.*, **2**, 87 (1974).
- (a) I. M. Downie, J. B. Lee, and M. F. S. Matough, *J. Chem. Soc., Chem. Commun.*, 1350 (1968); (b) J. B. Lee, *J. Am. Chem. Soc.*, **88**, 3440 (1966); (c) S. L. Regen and D. P. Lee, *J. Org. Chem.*, **40**, 1669 (1975); (d) P. Hodge and G. Richardson, *J. Chem. Soc., Chem. Commun.*, 622 (1975); (e) P. J. Kocienski, G. Cernigliaro, and G. Feldstein, *J. Org. Chem.*, **42**, 353 (1977); (f) J. D. Morrison, J. E. Tomaszewski, H. S. Mosher, J. Dale, D. Miller, and R. L. Eisenbaumer, *J. Am. Chem. Soc.*, **99**, 3167 (1977).
- (a) E. Yamato and S. Sugawara, *Tetrahedron Lett.*, 4283 (1970); (b) C. R. Harrison, P. Hodge, and W. J. Rogers, *Synthesis*, 41 (1977).
- (a) N. S. Isaacs and D. Kirkpatrick, *J. Chem. Soc., Chem. Commun.*, 443 (1972); (b) E. J. Corey and P. L. Fuchs, *Tetrahedron Lett.*, 3769 (1972); (c) G. H. Posner, G. L. Loomis, and H. Sawaya, *ibid.*, 1373 (1975); (d) W. G. Salmond, *ibid.*, 1239 (1977); (e) C. Gadreau and A. Foucaud, *Bull. Soc. Chim. Fr.*, 2068 (1976).
- (a) L. E. Barstow and V. J. Hruby, *J. Org. Chem.*, **36**, 1305 (1971); (b) R. Appel and L. Willms, *J. Chem. Research (S)*, 84 (1977).
- E. I. Snyder, *J. Org. Chem.*, **37**, 1466 (1972).
- (a) E. H. Axelrod, G. M. Milne, and E. E. van Tamelen, *J. Am. Chem. Soc.*, **92**, 2139 (1970); (b) G. Stork, M. E. Jung, E. Colvin, and Y. Noel, *ibid.*, **96**, 3684 (1974); (c) H. L. Goering and S. L. Trenbeath, *ibid.*, **98**, 5016 (1976).
- (a) B. Stephenson, G. Solladié, and H. S. Mosher, *ibid.*, **94**, 4184 (1972); (b) H. S. Mosher, *Tetrahedron*, **30**, 1733 (1974).

15. (a) R. Appel, F. Knoll, W. Michel, W. Morbach, H-D. Wihler, and H. Veltmann, Chem. Ber., 109, 58 (1976); (b) R. Appel and H-D. Wihler, ibid., 109, 3446 (1976); (c) R. Appel and H. Veltmann, Tetrahedron Lett., 399 (1977); (d) L. A. Jones, C. E. Sumner, Jr., B. Franzus, T. T-S. Huang, and E. I. Snyder, Abstracts, 173rd National Meeting of the American Chemical Society, New Orleans, LA, March 1977, ORGN 192; we thank Professor Franzus for making his results available to us before publication; (e) I. Tömösközi, L. Gruber, and L. Radics, Tetrahedron Lett., 2473 (1975); (f) B. Castro, Y. Chapleur, and B. Gross, ibid., 2313 (1974).
16. F. M. Laskovics and L. M. Schulman, ibid., 759 (1977).
17. (a) R. M. Magid and E. C. Nieh, J. Org. Chem., 36, 2105 (1971); (b) Prepared from 1-butyn-3-ol by reduction with LiAlH_4 followed by D_2O : B. Grant and C. Djerassi, ibid., 39, 968 (1974).
18. Resolved via the brucine salt of the phthalate half-ester.^{17a}
19. (a) W. G. Young and F. F. Caserio, J. Org. Chem., 26, 245 (1961); (b) K. G. Oliver and W. G. Young, J. Am. Chem. Soc., 81, 5811 (1959).
20. (a) R. G. Weiss and E. I. Snyder, J. Chem. Soc., Chem. Commun., 1358 (1968); (b) R. G. Weiss and E. I. Snyder, J. Org. Chem., 35, 1627 (1970); (c) R. G. Weiss and E. I. Snyder, ibid., 36, 403 (1971); (d) I. M. Downie, H. Heaney, and G. Kemp, Angew. Chem., Int. Ed. Engl., 14, 370 (1975); (e) R. Aneja, A. P. Davies, and J. A. Knaggs, Tetrahedron Lett., 67^a (1974).
21. R. T. Rawson and I. T. Harrison, J. Org. Chem., 35, 2057 (1970).
22. R. G. Bergman, J. Am. Chem. Soc., 91, 7405 (1969).