Tetrahedron Letters,Vol.25,No.29,pp 3055-3058,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

A STEREOSPECIFIC SYNTHESIS OF CHIRAL 1,3-DISUBSTITUTED BROMOALLENES

E. J. Corey and Neil W. Boaz
Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138

Summary: Optically active 1,3-disubstituted propargyl alcohols undergo S_Ni' rearrangements with thionyl bromide in the presence of propylene oxide to yield bromoallenes without loss of optical purity.

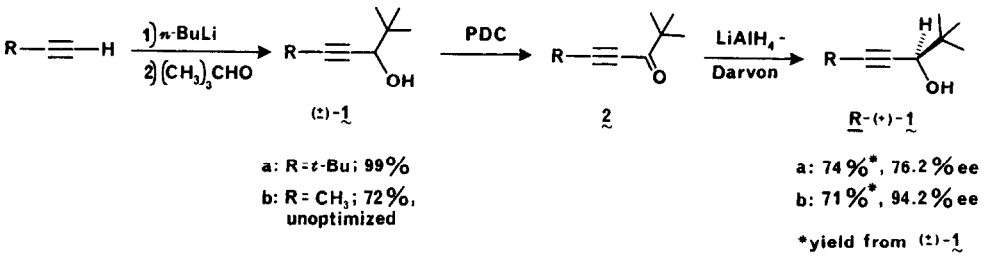
Haloallenes are versatile synthetic intermediates in organic chemistry. For example, they have been used to prepare leukotrienes,[1] allenic hydrocarbons,[2] and naturally occurring allenediynes.[3] We were interested in synthesizing optically active haloallenes of known optical purity in order to study the stereochemistry of S_N2' displacements thereof.[4]

Bromoallenes were the most desirable substrates because of their relatively good stability and reactivity. Unfortunately, few methods for preparing optically active haloallenes are known,[5,6] and the optical purity of the haloallenes has never been precisely determined. The most promising process was the reported synthesis of optically active chloroallenes (optical purity unknown) from optically active propargyl alcohols using thionyl chloride via S_Ni' rearrangement of an initially formed chlorosulfinate.[5] We sought to extend this method to the formation of optically active bromoallenes with a minimum of racemization.

The preparation of the optically active propargyl alcohol starting materials is shown in Scheme I. The lithium anion of the desired terminal acetylene (n-butyllithium, tetrahydrofuran) was condensed with trimethylacetaldehyde at 0° to give the racemic alcohol (±)- 1. This was oxidized to the corresponding ketone (pyridinium dichromate, 3Å molecular sieves, CH_2Cl_2), and the crude 2 was then asymmetrically reduced with the lithium aluminum hydride-Darvon alcohol complex (ether, -78°).[7,8] This reagent has been shown to reduce α,β-acetylenic ketones consistently from the si face to produce the corresponding R-alcohols,[8] with this configuration proven for (+)- 1a.[9] The optical purity of each alcohol was determined by 270 MHz ^{1}H nmr analysis of the corresponding d-10-camphorsulfonate ester (d-10-camphorsulfonyl chloride, triethylamine, benzene).

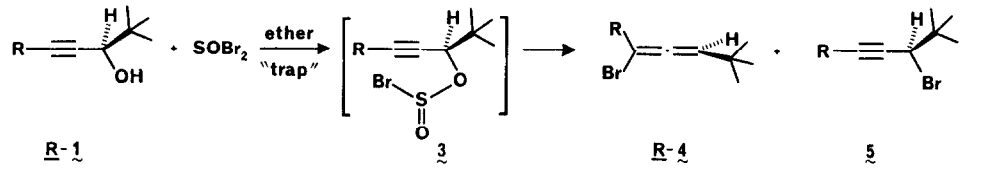
Thionyl bromide converted R-1 to bromoallene (-)- 4 along with smaller amounts of propargyl bromide 5. To minimize racemization, reaction conditions which encouraged the S_Ni' rearrangement to the exclusion of other pathways were sought. Since the most probable competing reactions involved bromide ion, removal of the HBr generated in the formation of bromosulfinate intermediate 3 was desirable. The use of an amine as an acid scavenger has been shown to result in racemization for an

analogous chloroallene case, presumably due to competing S_N2' reactions by chloride ion,[5a] so other HBr acceptors were investigated. The results of experiments on the thionyl bromide rearrangement of R-1 are presented in Table 1.



SCHEME I

TABLE I



R	Optical Purity of 1	Temp.	"Trap"	4 : 5[a]	Yield of 4[b]	$[\alpha]_D$ of 4[c]
^{t}Bu	76.2%	RT	None	65 : 35	35.8%	-100.9°
^{t}Bu	76.2%	RT	Propylene oxide	74 : 26	60.1%	-111.1°
^{t}Bu	76.2%	RT	4 Å Molecular Sieves	74 : 26	39.8%	-114.0°
^{t}Bu	76.2%	RT	Dihydropyran	74 : 26	11.5%	-116°[d]
CH_3	94.2%	RT	Propylene oxide	85 : 15	56.4%	-187.3°
CH_3	94.2%	O°C	Propylene oxide	90 : 10	51.8%	-203.2°

a) By ^{1}H nmr integration. b) Yield of purified, isolated 4. c) c ~ 1.25, chloroform. d) ± 5°.

The solvent used for this investigation was diethyl ether because it was found to produce the highest ratios of allene 4 to acetylene 5. For R-1a and R-1b, the best results in terms of operational ease and stereospecificity were obtained with propylene oxide as scavenger.

That the configuration of (-)-4 was R as expected for the S_Ni' mechanism was confirmed by application of Lowe's extension of Brewster's rules,[10] which predicts a negative rotation for the R configuration of 4 using a polarizability order of Br > CH_3 > tert-butyl > H.[10,11] Further, the chemical transformations delineated in the accompanying paper have shown that the stereospecificity of the R-1 ⟶ R-4 conversion under optimal conditions is > 99%.[4a]

Typical Procedure for the Preparation of R-4a.

To a dry flask equipped with a magnetic stir bar under a nitrogen atmosphere was added R-1a (1.25g; 7.43 mmol; 76.2% ee) in 75 ml of ether. Propylene oxide (1.30 ml; 18.6 mmol) was added, followed by dropwise addition of distilled thionyl bromide (1.44 ml; 18.6 mmol) to the stirred reaction mixture. The light yellow solution was stirred at room temperature under a nitrogen atmosphere for 30 h, at which time tlc analysis showed complete consumption of 1a. The reaction was quenched by addition of 1 : 1 (v:v) brine: pH 7 phosphate buffer, and the mixture of R-4a and 5a along with trapping products was isolated by extraction with ether. Chromatography on silica gel with hexane as eluant gave 1.03 g (60%) of R-4a (R_f 0.54), $[\alpha]_D^{18}$ -111.1° (c 1.27, chloroform), as a clear, colorless liquid, ^{1}H nmr ($CDCl_3$) (δ): 5.22 (s, 1H); 1.17 (s, 9H); 1.07 (s, 9H). ^{13}C nmr ($CDCl_3$) (δ): 195.07; 109.48; 106.92; 36.92; 32.70; 29.68; 29.22. IR (neat film): 1960 $cm.^{-1}$ Further elution yielded 0.25 g (15%) of 5a (R_f 0.44).

Typical Procedure for the Preparation of R-4b.

A solution of R-1b (1.04g; 8.23 mmol; 94.2% ee) in 85 ml of ether was added to a dry flask containing a magnetic stir bar. After cooling this solution to 0°, propylene oxide (1.45 ml; 20.7 mmol; 2.5 equiv) and distilled thionyl bromide (1.60 ml; 20.7 mmol; 2.5 equiv) were added sequentially. The reaction mixture was stirred at 0° under nitrogen for 20 hr, at which time no 1b was visible by tlc. The reaction was quenched and the crude product was isolated as above. Chromatography on silica gel utilizing 20-40 petroleum ether for elution gave 0.81 g (52%) of R-4b (R_f 0.51) as a clear liquid, $[\alpha]_D^{22}$ -203.2° (c 1.29, chloroform). ^{1}H nmr ($CDCl_3$) (δ): 5.193 (q, J=2.97 Hz, 1H); 2.263 (d, J=2.97 Hz, 3H); 1.066 (s, 9H). ^{13}C nmr ($CDCl_3$) (δ): 197.01; 109.21; 88.74; 32.84; 29.63; 25.52. IR (neat film): 1960 $cm.^{-1}$ [12]

References and Notes

1. (a) E. J. Corey and J. Kang, J. Am. Chem. Soc., 103, 4618 (1981); (b) E. J. Corey and J. Kang, Tetrahedron Letters, 23, 1651 (1982); (c) E. J. Corey and S. G. Pyne, Tetrahedron Letters, 24, 3291 (1983).
2. M. Kalli, P. D. Landor, and S. R. Landor, J. Chem. Soc. Perkin I, 1347 (1973).
3. P. D. Landor, S. R. Landor, and P. Leighton, J. Chem. Soc. Perkin I, 1628 (1975).
4. (a) E. J. Corey and N. W. Boaz, Tetrahedron Letters, following paper; (b) see also E. J. Corey and W. T. Borden, Tetrahedron Letters, 313 (1969).
5. (a) R. J. D. Evans, S. R. Landor, R. Taylor-Smith, J. Chem. Soc., 1506 (1963); (b) R. J. D. Evans and S. R. Landor, J. Chem. Soc., 2553 (1965).
6. (a) O. J. Muscio, Jr., Y. M. Juva, and J. B. Philip, Jr., Tetrahedron Letters, 2379 (1978); C. J. Elsevier, J. Meijer, G. Tadema, P. M. Stehouwer, H. J. T. Bos, and P. Vermeer, J. Org. Chem., 47, 2194 (1982); (b) S. R. Landor, B. Demetriou, R. J. Evans, R. Grzeskowiak, and P. Pavey, J. Chem. Soc. Perkin II, 1995 (1972).
7. S. Yamaguchi and H. S. Mosher, J. Org. Chem., 38, 1870 (1973).
8. R. S. Brinkmeyer and V. M. Kapoor, J. Am. Chem. Soc., 99, 8339 (1977); N. Cohen, R.J. Lopresti, C. Neukom, and G. Saucy, J. Org. Chem., 45, 582 (1980).
9. W. M. Butler, Y. Tanaka, and M. Koreeda, J. Org. Chem., 46, 4620 (1981).
10. G. Lowe, Chem. Comm., 411 (1965).
11. J. H. Brewster, J. Am. Chem. Soc., 81, 5475 (1959).

12. This research was assisted in part by a grant from the National Science Foundation.

(Received in USA 13 April 1984)