Tetrahedron Letters No. 16, pp 1385 - 1388, 1973. Pergamon Press. Printed in Great Britain.

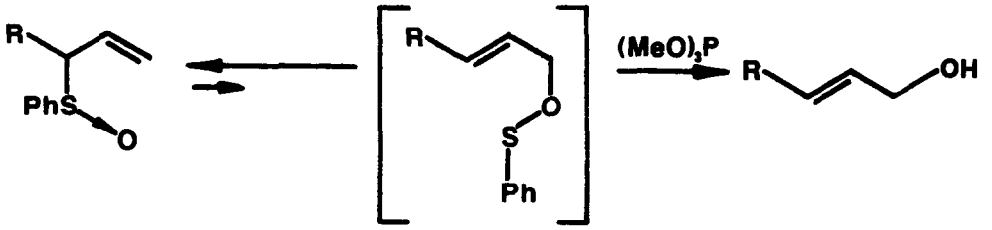
THE APPLICATION OF ALLYLIC SULFOXIDE ANIONS AS VINYL ANION EQUIVALENTS. A GENERAL SYNTHESIS OF ALLYLIC ALCOHOLS.

D. A. Evans,[1] G. C. Andrews, T. T. Fujimoto, D. Wells

Contribution No. 3113 from the Department of Chemistry,
University of California, Los Angeles, California 90024

(Received in USA 26 January 1973; received in UK for publication 12 March 1973)

Recently we reported a general procedure for the reversible interconversion of allylic sulfoxides and alcohols with allylic rearrangement (e.g. 1⇄3) and alluded to the possible applications of this transformation to a new synthesis of allylic alcohols.[2,3] The purpose of this communication is to define the utility of sulfoxide stabilized anions such as 4 as a synthon for the vinyl anion 5 in a new approach to the synthesis of allylic alcohols.



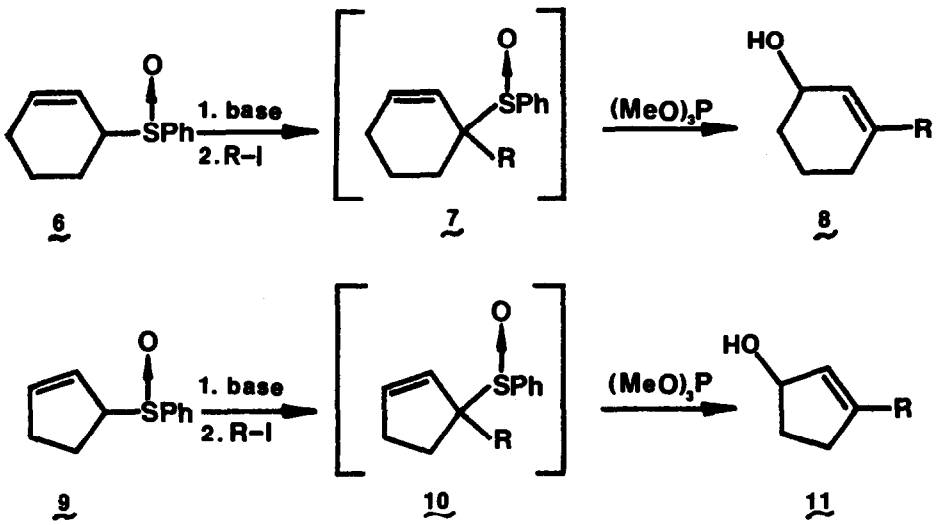
1 2 3

4 5

The general conditions for the alkylation of allylic sulfoxides and for subsequent transformation into the rearranged allylic alcohols are described below.

Alkylation: To a cooled (-60°) solution of lithium diisopropylamide[4] (11.0 mmol) in 30 ml of

dry THF under a nitrogen atmosphere was added 10 mmol of the allylic sulphoxide *via* syringe. The resulting yellow anion[5] was allowed to stir for 15 min and the alkyl halide (1-2 equiv) was then added in one portion. The temperature was raised to between -50° and -30° until the color of the anion was dissipated (see Table for specific conditions). The reaction was quenched with saturated NH_4Cl solution and extracted with methylene chloride. Removal of the solvent afforded the crude α-and γ-alkylated sulfoxides. Cleavage: The crude sulfoxide (10 mmol) was dissolved in 10 ml of methanol and 20 mmol of freshly purified trimethyl phosphite[6] at room temperature. The rate of cleavage depends upon the degree of α-substitution (α-disubstituted sulfoxides require ≈ 1 hr, monosubstituted sulfoxides require ≈ 12 hr). A saturated aqueous solution of $NaHCO_3$ was added to the reaction, and the desired allylic alcohol was isolated by chromatography (Florisil). The methanol-phosphite solution may also be added directly to the alkylation mixture after quenching the allylic anion with alkylating agent.

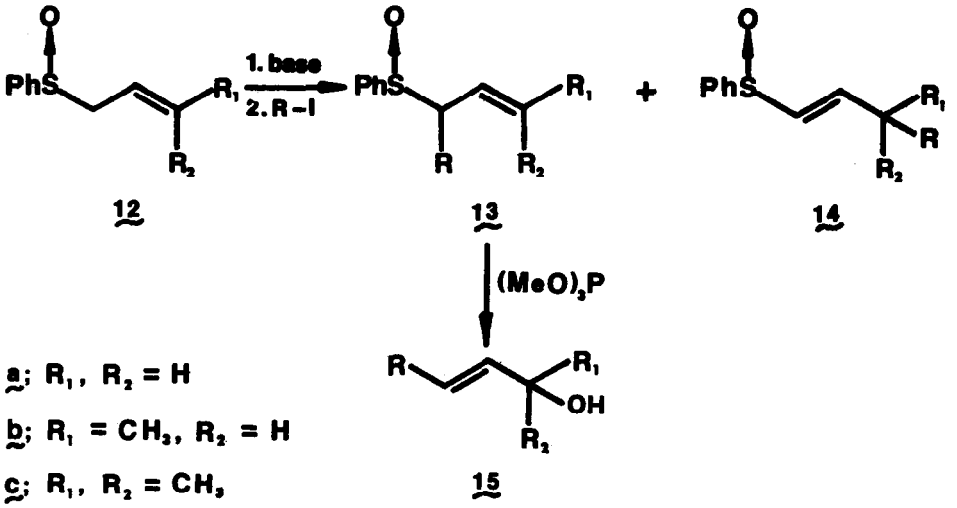


6 7 8

9 10 11

As illustrated above, the anion derived from cyclohexenylphenyl sulfoxide 6[2] may be readily alkylated with methyl iodide and the resulting alkylated derivative 7 transformed *in situ* (MeOH, $(MeO)_3P$, 1 hr) to 8 (R = CH_3) in nearly quantitative yield. In a similar fashion cyclopentenylphenyl sulfoxide 9 afforded the 3-substituted cyclopentenols 11 (R = CH_3, C_2H_5, C_3H_5) in good yields.[9] The isolated yields of these alcohols (Table) reflect the difficulties encountered in purification due to dehydration. In the alkylation of the anions derived from both 6 and 9 only α-alkylation was observed. As little as 2-3% of the γ-alkylation product could have been detected by nmr analysis.

Alkylation of the acyclic allylic sulfoxides 12a-c with a variety of alkyl iodides afforded both the α- and γ-alkylated adducts 13a-c and 14a-c respectively,[9] the product ratio being dependent upon the structure of both the alkyl halide and the sulfoxide (see Table). *In situ* cleavage of the crude alkylation mixtures with methanol-trimethyl phosphite afforded the trans-



disubstituted allylic alcohols 15a-c and the corresponding γ-alkylated sulfoxides 14a-c which were readily isolated by chromatography (Florisil).

As summarized in the Table, the yields of allylic alcohols depend upon the extent of γ-alkylation. Attempts to alter the proportion of 13 and 14 by changing solvent or introducing metal ion complexing agents (TMEDA) were unsuccessful. In contrast to the high regioselectivity toward α-protonation[10] and to a lesser extent toward α-alkylation, we have observed that the conjugate bases of both 9 and 12a exhibit little site selectivity in addition reactions to both aldehydes and ketones even at temperatures as low as -100°.

Table. Alkylation-Rearrangement of Allylic Sulfoxides

Sulfoxide	R-X	Alkylation Conditions	α:γ Ratio[a]	ROH[9]	Yield,%[b]
6[2]	CH_3I	-50°, 1hr	>>10	8	(99)
9[7,8]	CH_3I	-40°, 1hr	>>10	11	(100)
	C_2H_5I	-40°, 3/4hr	>>10		45 (75)
	CH_2=$CHCH_2Br$	-50°, 1/2hr	>>10		32 (73)
12a[7]	CH_3I	-35°, 1/2hr	5.6	15a	74
	C_2H_5I	-50°, 5hr	2.9		60
	CH_2=$CHCH_2Br$	-30°, 1hr	1.3		49
12b[7]	CH_3I	-50°, 1hr	>>10	15b	85
	C_2H_5I	-30°, 4hr	6.7		50 (56)
12c[7]	n-$C_6H_{13}I$	-40°, 2hr	>>10	15c	70 (80)

a The γ-alkylation products were isolated and characterized.[9] The α:γ ratios were determined by nmr. b Figures in parenthesis refer to glc or nmr yields relative to an internal standard; other figures refer to isolated yields based on starting sulphoxide.

There are several significant features in this approach to the synthesis of allylic alcohols. It offers a new method of establishing carbon-carbon bonds applicable to a wide variety of structurally dissimilar systems. In addition, the concerted nature of the sulfoxide rearrangement results in the stereoselective formation of specific olefin geometries. The application of this approach to the synthesis of trisubstituted olefins is discussed in the accompanying communication.[11]

Acknowledgement. We wish to thank the U. S. Public Health Service, the National Science Foundation and the Petroleum Research Fund administered by the American Chemical Society for their support of this research.

References

1. Camille and Henry Dreyfus Teacher-Scholar recipient, 1971-1976, A. P. Sloan Fellow, 1972-1974.
2. D. A. Evans, G. C. Andrews, C. L. Sims, J. Amer. Chem. Soc., 93, 4956 (1971).
3. D. A. Evans, G. C. Andrews, ibid., 94, 3672 (1972).
4. Prepared by the addition of n-butyllithium in hexane to a cooled ($t \leq 0°$) solution of amine in THF.
5. The anions may also be formed by direct treatment with n-butyllithium, however, byproducts (5-10%) result using this procedure, cf. K. K. Anderson, S. A. Yeager, J. Org. Chem., 28, 865 (1963).
6. Freshly distilled from sodium metal. This purification step appears to be important.
7. Prepared from the corresponding sulfide which was oxidized according to the procedure of N. J. Leonard and C. R. Johnson, J. Org. Chem., 27, 282 (1962).
8. Sulfoxide 9 is unstable toward molecular distillation and was used without purification.
9. Satisfactory spectra and elemental analyses have been obtained.
10. C. D. Broaddus, Accounts Chem. Res., 1,231 (1968), and references cited therein.
11. D. A. Evans, G. C. Andrews, T. T. Fujimoto, D. Wells, Tetrahedron Lett., 0000 (1972).