

Conjugate Addition of the Anion Derived from 3-(Phenylsulfinyl)prop-1-ene to Cyclopent-2-en-1-one

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Abstract

The title anion in tetrahydrofuran containing one equivalent of hexamethylphosphoric triamide at -78° undergoes a rapid conjugate addition reaction with cyclopent-2-en-1-one. The sole product obtained, in 73% yield, is (*E*)-3-[3-(phenylsulfinyl)prop-2-enyl]cyclopentan-1-one.

Introduction

The anion (1) derived from allyl phenyl sulfide undergoes a rapid conjugate addition reaction with cyclopentenone in the presence of one equivalent of hexamethylphosphoric triamide to yield the α -addition product (2) and a small amount of the γ -addition product (3).^{1,2} Reactions of the corresponding anions of allylic sulfoxides, such as that, (4), derived from allyl phenyl sulfoxide, with conjugated enones have not been recorded. If (4) were to react with cyclopentenone in the same way as (1), the reaction would be of some importance from a synthetic standpoint, as the product (5) is structurally similar to intermediates of several highly stereospecific syntheses of prostaglandins.³ However, we find that the reactivity of (4) towards cyclopentenone is markedly different from that of (1), and herewith report our results.

Results and Discussion

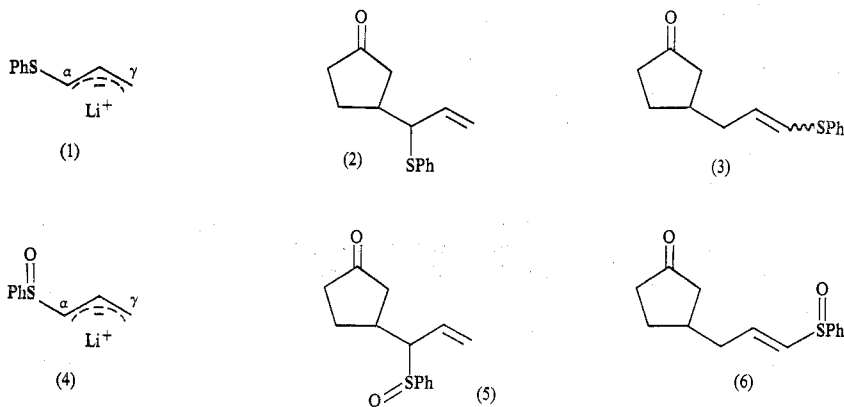
Treatment of allyl phenyl sulfoxide with lithium diisopropylamide in tetrahydrofuran containing 1 equiv. of hexamethylphosphoric triamide at -78° produced the yellow anion (4), which reacted rapidly with cyclopentenone at the same temperature. The only product, which was obtained in 73% yield, was the vinylic sulfoxide (6), arising from reaction through the γ -position of (4). None of the isomeric, allylic sulfoxide (5), prepared from the sulfide (2) and *m*-chloroperbenzoic acid, could be detected in the reaction mixture. In addition, (6) was obtained as a single geometric

¹ Binns, M. R., Haynes, R. K., Houston, T. L., and Jackson, W. R., *Tetrahedron Lett.*, 1980, 573.

² Binns, M. R., and Haynes, R. K., *J. Org. Chem.*, 1981, 45, in press.

³ Miller, J. G., Kurz, W., Untch, K. G., and Stork, G., *J. Am. Chem. Soc.*, 1974, 96, 6774; Grieco, P. A., Yokoyama, Y., Nicolau, K. C., Barnette, W. E., Smith, J. B., Ogletree, M., and Lefer, D. M., *Chem. Lett.*, 1978, 1001; Kondo, K., Unemoto, T., Yako, K., and Tunemoto, D., *Tetrahedron Lett.*, 1978, 3937; Luthy, C., Konstantin, P., and Untch, K. G., *J. Am. Chem. Soc.*, 1978, 100, 6211; Davis, R., and Untch, K. G., *J. Org. Chem.*, 1979, 44, 3755.

isomer possessing the (*E*) configuration. This contrasts with the analogous reaction of the anion (1), in which case the small amount of reaction which does proceed through the γ -position produces the vinylic sulfide (3) as a mixture of (*E*) and (*Z*) isomers.^{1,2} Treatment of the allylic sulfoxide (5) with an equivalent amount of lithium diisopropylamide in tetrahydrofuran in the presence of hexamethylphosphoric triamide at -78° did not induce any detectable conversion into (6). It thus appears that the γ -mode of conjugate addition is a kinetic process.



The remarkable difference in the regiochemistries displayed by the anions (1) and (4) in their reaction with cyclopentenone is not apparent in reactions with other electrophiles.^{4,5} Both the sulfenyl and sulfinyl substituents are donors according to the terminology of Gompper and Wagner,⁴ and thus a current theory on the reactivity of ambient nucleophiles breaks down in the present case. Solvation of the lithium cation by the hexamethylphosphoric triamide will enhance repulsive interactions between the occupied orbitals of the allylic anions (1) and (4) and cyclopentenone. This may be one factor which leads to conjugate (as opposed to a 1,2) addition to cyclopentenone, as has been discussed elsewhere.⁶ The repulsive interaction will be more pronounced at the α -carbon atom of (4) than at the corresponding atom of (1). Whether this stereoelectronic effect is sufficient to account entirely for the differences in regiochemistries of (1) and (4) in their conjugate addition reactions cannot be assessed. Finally it should be noted that the anion derived from allyl phenyl sulfone reacts in conjugate fashion with cyclohex-2-en-1-one through the γ -position.⁷

Experimental

General experimental conditions have been given elsewhere.²

Preparation of (*E*)-3-[3'-(Phenylsulfinyl)prop-2'-enyl]cyclopentan-1-one (6)

Butyllithium (1.4 M in hexane, 12.6 ml, 0.018 mol) was added to a stirred solution of hexamethylphosphoric triamide (2.7 ml, 0.015 mol) and diisopropylamine (2.5 ml, 0.018 mol) in tetrahydrofuran (40 ml) at -70° under nitrogen. Freshly distilled allyl phenyl sulfoxide (2.5 g,

⁴ Gompper, R., and Wagner, H.-U., *Angew. Chem., Int. Ed. Engl.*, 1976, **15**, 321.

⁵ Evans, D. A., and Andrews, G. C., *Acc. Chem. Res.*, 1974, **7**, 147.

⁶ Loupy, A., Lefour, J. M., Deschamps, B., and Seyden-Penne, J., *Nouv. J. Chim.*, 1980, **4**, 121.

⁷ Kraus, G. A., and Frazier, K., *Synth. Commun.*, 1978, **8**, 483.

0.015 mol) was then added dropwise to the solution, which acquired a yellow colour as formation of the anion (4) took place. After 15 min, the solution was treated carefully with neat cyclopentenone (1.23 g, 0.015 mol). The reaction is exothermic, and addition of the cyclopentenone was maintained at such a rate as to keep the solution temperature below -65° . After addition of the cyclopentenone, the reaction mixture was stirred for 5 min and then quenched with aqueous ammonium chloride (7 g in water, 30 ml) at -70° . The mixture was treated with water (30 ml) and extracted with ether (3×50 ml). The ether extracts were washed successively with dilute sulfuric acid (1 M, 20 ml), water (20 ml), saturated aqueous sodium bicarbonate (20 ml), brine (20 ml) and then dried (Na_2SO_4). Removal of ether under reduced pressure left a pale yellow oil (3.1 g), a ^1H n.m.r. and t.l.c. examination of which indicated that it consisted entirely of the one product. Purification by preparative t.l.c. over silica gel with dichloromethane as eluent afforded (E)-3-[3'-(phenylsulfinyl)prop-2'-enyl]-cyclopentan-1-one (6) (2.72 g, 73%) as an unstable, light yellow oil (Found: C, 67.8; H, 6.6. $\text{C}_{14}\text{H}_{16}\text{O}_2\text{S}$ requires C, 67.8; H, 6.5%). ν_{max} (thin film) 3065w, 2975m, 2942m, 2905m, 1736s (C=O), 1478w, 1445m, 1401m, 1246w, 1164m, 1084m, 1044s (S=O), 998, 968m, 748m, 688, cm^{-1} . ^1H n.m.r. spectrum: δ 1.42–2.58, 9H, m, $\text{H}1'$, H2, H3, H4, H5; 6.31, 1H, dt, $J_{3',2'}$ 15.2, $J_{3',1'}$ c. 0.6 Hz, H3'; 6.64, 1H, dt, $J_{2',3'}$ 15.0, $J_{2',1'}$ 6.2 Hz, H2; 7.3–7.8, 5H, m, C_6H_5 . Irradiation at δ 2.3 caused collapse of the signals at 6.31 and 6.64 to an AB quartet with J c. 15 Hz. ^{13}C n.m.r. δ 29.1, C4; 36.1, C5; 37.5, C3; 38.1, C2; 44.5, C1'; 124.5, Cpara, C_6H_5 ; 129.5, Cmeta, C_6H_5 ; 131.1 Cortho, C_6H_5 ; 136.7, C2'; 137.4, C3'; 144.0, Cipso, C_6H_5 ; 218.2, C1. Absorptions due to diastereotopic protons or carbon atoms were absent in the foregoing spectra, recorded from CDCl_3 solutions. Mass spectrum: m/e 248 (M, 17%), 200 (85), 150 (20), 126 (66), 123 (97), 112 (100), 109 (71), 95 (43).

Preparation of 3-[1'-(Phenylsulfinyl)prop-2'-enyl]cyclopentan-1-one (5)

m-Chloroperbenzoic acid (1.63 g, 9 mmol) in dichloromethane (20 ml) was added slowly dropwise to a stirred solution of 3-[1'-(phenylthio)prop-2'-enyl]cyclopentan-1-one (1) (2.0 g, 8.6 mmol) (prepared as a 7 : 6 mixture of diastereomers as described elsewhere²) in dichloromethane (30 ml) under dry nitrogen at -78° . After 30 min, the mixture was quenched with aqueous sodium hydrogen carbonate (4 g in water, 30 ml) and the organic phase was separated, washed with water, dried (Na_2SO_4) and evaporated to give a pale yellow oil (2.0 g). This was purified by preparative layer t.l.c. on silica gel with light petroleum/ethyl acetate (7 : 3) to yield 3-[1'-(phenylsulfinyl)prop-2'-enyl]-cyclopentan-1-one (5) (1.73 g, 81%) as an inseparable mixture of diastereomers (Found: C, 67.7; H, 6.4. $\text{C}_{14}\text{H}_{16}\text{O}_2\text{S}$ requires C, 67.75; H, 6.5%). ν_{max} (thin film) 3060w, 2978m, 1741s (C=O), 1630w, 1582w, 1476m, 1441s, 1399m, 1161m, 1039s (S=O), 935m, 745s, 688s. ^1H n.m.r. spectrum δ 1.73–2.58, 7H, m, H2, H3, H4, H5; 3.47, 1H, m, $\text{H}1'$; 4.71, 1H, dt, $J_{3'(E),2'}$ 17.0, $J_{3'(E),3'(Z)}$ 1.5, $J_{3'(E),1'}$ 1.5 Hz, H3'(E); 5.17 and 5.19, 1H, dd(?), $J_{3'(Z),2'}$ 10.0, $J_{3'(Z),3'(E)}$ c. 1.5 Hz, H3'(Z); c. 5.2–5.9, 1H, m, H2'; 7.3–7.74, 5H, m, C_6H_5 . ^{13}C n.m.r. δ 28.0, C4; 36.7, C5; 38.2 and 43.1, C3; 53.6, C2; 73.6 and 73.9, C1'; 122.2 and 122.4, Cmeta, C_6H_5 ; 124.4, Cpara, C_6H_5 ; 127.4 and 127.6, C3'; 128.8 and 129.2, Cortho, C_6H_5 ; 130.8 and 131.5, Cipso, C_6H_5 ; 136.4, C2'; 216.5, C1. Mass spectrum: m/e 248 (M, 33%), 126 (93), 123 (100), 109 (36), 95 (70), 81 (53), 79 (46), 77 (43), 69 (83), 67 (77).

Acknowledgment

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