July, 1985] © *1985 The Chemical Society of Japan* NOTES *Bull. Chem. Soc. Jpn., 58, 2137—2138 (1985)* 2137

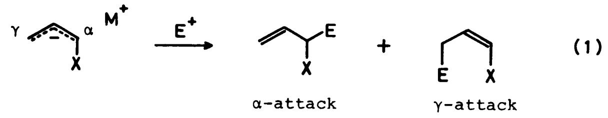
Regioselectivity of the Coupling of Phenoxyallyllithium with Allylic Electrophiles

Yasuo Butsugan,* Tomokazu Goto, and Shuki Araki
Department of Synthetic Chemistry, Nagoya Institute of Technology, Gokiso-cho, Showa-ku, Nagoya 466

(Received January 14, 1985)

Synopsis. The regioselectivity of the coupling of phenoxyallyllithium with allylic electrophiles was investigated. The allylation pattern corresponded with the hardness of the leaving group and the highest α-selectivity was observed in the reaction with allylic phosphate.

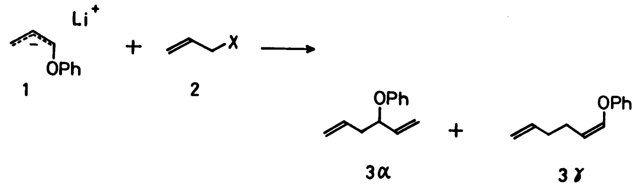
The reaction of heteroatom-substituted allylic anion with electrophiles can lead to two regioisomers, α-attack and γ-attack products (Eq. 1). The regioselectivity (α/γ ratio) is a function of a number of factors including the nature of X, and the nature of other substutuents, electrophiles, solvents, and additives.[1] For example, alkyloxyallyl carbanion (X=OR) is reported to yield predominantly γ-attack product by the reaction with alkyl halides, whereas with carbonyl electrophiles α-attack product is formed selectively.[2] In order to define the effect of the leaving group of electrophiles on the α/γ ratio, we examined the reaction of phenoxyallyllithium (**1**) with a series of allylic electrophiles and it was found that the proportion of the α-product increased with increasing hardness of the electrophiles.



(1)

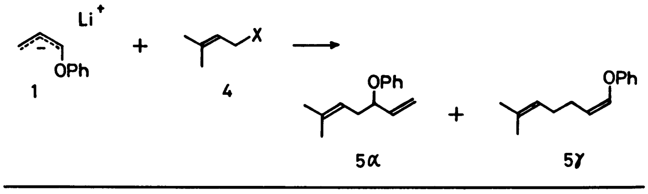
To a solution of phenoxyallyllithium (**1**), generated from allyl phenyl ether and butyllithium in tetrahydrofuran-*N*,*N*,*N′*,*N′*-tetramethylethylenediamine, was added allyl halides (**2a**—**c**), tosylate (**2d**), or phosphate (**2e**) at −78 °C, and the reaction mixture was gradually warmed to room temperature. After stirred for 1 h, the reaction was quenched and the products were extracted with ether. The separation of the α- and γ-products (**3α** and **3γ**) was easily performed by column chromatography on silica gel and the structures were deduced by their elemental and spectral data. It should be noted that the stereochemistry of **3γ** was confirmed to be *Z* by the ^{1}H NMR analysis. The yields of **3α** and **3γ** and the α/γ ratios are summarized in Table 1. The reaction of **1** with allyl iodide predominantly gave the γ-attack product (**3α**/**3γ**=28/72). The proportion of **3α** increased as the hardness of the electrophiles increased, and with allyl diphenyl phosphate the α/γ ratio was reversed (**3α**/**3γ**=53/47). These facts can be reasonably explained by the terms of HSAB principle,[3] that is, the softer halides preferentially attack the softer γ-terminus, while the harder tosylate and the phosphate attack the harder α-position. Similar tendency was also observed in the reactions with prenyl and geranyl compounds (Tables 2 and 3). By the reaction of allylic phosphates (**4c**—**e** and **6c**—**e**), the lesser amount of enol ethers (**5γ** and **7γ**) was formed compared with the reaction of the softer halides (**4a**—**b** and **6a**—**b**). Of the three allylic phosphates (diethyl, diisopropyl, and diphenyl phosphates) which were examined, diphenyl phosphates (**4e** and **6e**) gave the largest α/γ ratio. It is worthwhile to note that all the reactions of **1** with allylic electrophiles (**4** and **6**) gave the products coupled at the α-position of the allylic system, no trace of the products coupled at the γ-position being found. Although the yields of the coupling products (**3**, **5**, and **7**) are not high, considerable amounts (30—50%) of starting electrophiles were recovered in many cases. Furthermore, the coupling products are stable enough under the reaction and separation condi-

Table 1. Reaction of **1** with allyl halides tosylate, and phosphate



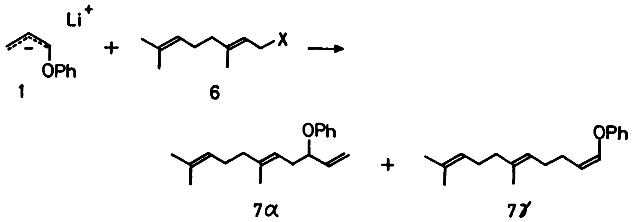
Run	X	Yield/%		**3α**/**3γ**
		3α	**3γ**	
a	I	10	25	28/72
b	Br	21	35	38/62
c	Cl	23	23	50/50
d	OTs	24	25	49/51
e	$OP(O)(OPh)_2$	19	16	53/47

Table 2. Reaction of **1** with prenyl halides and phosphates



Run	X	Yield/%		**5α**/**5γ**
		5α	**5γ**	
a	Br	17	39	30/70
b	Cl	24	32	42/58
c	$OP(O)(OEt)_2$	36	28	56/44
d	$OP(O)(OPr^i)_2$	26	16	63/37
e	$OP(O)(OPh)_2$	29	10	74/26

TABLE 3. REACTION OF **1** WITH GERANYL HALIDES AND PHOSPHATES



Run	X	Yield/%		**7α**/**7γ**
		7α	**7γ**	
a	Br	13	24	35/65
b	Cl	29	19	61/39
c	$OP(O)(OEt)_2$	26	18	60/40
d	$OP(O)(OPr^i)_2$	20	9	69/31
e	$OP(O)(OPh)_2$	29	12	70/30

tions. Therefore, the isolated yields of the α- and γ-products are considered to reflect the regioselectivity (α/γ ratio).

In summary, it is found that the regioselectivity of the coupling of **1** with allylic electrophiles largely depends on the nature of the leaving group of the electrophile and the highest α-selectivity could be attained by the use of allylic phosphate.

Experimental

General. Infrared spectra were recorded on a JASCO IRA-1 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-24A spectrometer (60 MHz) in CCl_4. Chemical shifts (δ) are recorded in ppm downfield from Me_4Si. Mass spectra were determined using a Hitachi M-52 mass spectrometer at 20 eV. Elemental analyses were performed at the Elemental Analysis Center of Kyoto University.

Reaction of Phenoxyallyllithium (1) with Allylic Electrophiles (2, 4, and 6). The following reaction of **1** and allyl diphenyl phosphate (**2e**)[4] is a representative. To a solution of allyl phenyl ether (419 mg, 3.12 mmol) in THF (12 cm^3) was added a solution of *n*-BuLi in hexane [1.64 M(1 M=1 mol dm^{-3}), 1.85 cm^3, 3 mmol] and then *N,N,N′,N′*-tetramethylethylenediamine (0.75 cm^3) at −78 °C. The mixture was stirred at −30—−40 °C for 1.5 h. The solution of **1** thus prepared was cooled again to −78 °C and a solution of **2e** (946 mg, 3.26 mmol) in THF (6 cm^3) was added dropwise. The reaction mixture was gradually warmed to room temperature and further stirred for 1 h. After the addition of saturated aqueous ammonium chloride, the products were extracted with ether, washed with brine, and dried (Na_2SO_4). The solvent was evaporated and the residue was chromatographed on silica gel (light petroleum–benzene 10:1) to give 3-phenoxy-1,5-hexadiene (**3α**) (95 mg, 19%) and 1-phenoxy-1,5-hexadiene (**3γ**) (86 mg, 16%). The reactions with prenyl (**4**) and geranyl compounds (**6**) were similarly carried out. Results are summarized in Tables 1 to 3.

3-Phenoxy-1,5-hexadiene (3α): IR (neat), 3060, 2900, 1640, 1590, 1580, 1490, 1235, 1165, 980, 915, 745, and 685 cm^{-1}; ^{1}H NMR 7.38—6.64 (m, 5H, Ph), 6.39—5.51 (m, 2H, olefin), 5.41—4.82 (m, 4H, olefin), 4.82—4.36 (m, 1H, CH), 2.66—2.27 (m, 2H, CH_2); MS *m/z* (rel. intensity) 174 (M$^+$, 7.8) and 80 (100); Found: C, 82.61; H, 8.16. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10%.

(Z)-1-Phenoxy-1,5-hexadiene (3γ): IR (neat) 3030, 2910, 1665, 1640, 1595, 1490, 1385, 1255, 1220, 1165, 910, 750, and 685 cm^{-1}; ^{1}H NMR 7.44—6.72 (m, 5H, Ph), 6.28 (d, 1H, *J*=6 Hz, C<u>H</u>(OPh)), 6.09—5.46 (m, 1H, olefin), 5.26—4.53 (m, 3H, olefin), 2.41—2.03 (m, 4H, CH_2); MS *m/z* (rel. intensity) 174 (M$^+$, 4.7) and 133 (100); Found: C, 83.19; H, 8.19. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10%.

6-Methyl-3-phenoxy-1,5-heptadiene (5α): IR (neat) 2930, 1650, 1602, 1590, 1499 1242, 1175, 1035, 992, 930, 755, and 695 cm^{-1}; ^{1}H NMR 7.33—6.56 (m, 5H, Ph), 6.24—5.54 (m, 1H, olefin), 5.54—4.95 (m, 3H, olefin), 4.70—4.30 (m, 1H, CH), 2.58—2.18 (m, 2H, CH_2), 1.69 (s, 3H, CH_3), 1.61 (s, 3H, CH_3); MS *m/z* (rel. intensity) 202 (M$^+$, 8.0) and 109 (100); Found: C, 83.71, H, 9.12. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97%.

(Z)-6-Methyl-1-phenoxy-1,5-heptadiene (5γ): IR (neat) 2940, 1670, 1600, 1499, 1394, 1260, 1230, 1170, 1090, 1035, 758, and 695 cm^{-1}; ^{1}H NMR 7.44—6.72 (m, 5H, Ph), 6.26 (d, 1H, *J*=6 Hz, C<u>H</u>(OPh)), 5.37—4.95 (m, 1H, olefin), 4.95—4.45 (m, 1H, olefin), 2.54—1.85 (m, 4H, CH_2), 1.64 (s, 3H, CH_3), 1.58 (s, 3H, CH_3); MS *m/z* (rel. intensity) 202 (M$^+$, 7.9) and 133 (100); Found: C, 83.33; H, 9.11. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.97%.

(E)-6,10-Dimethyl-3-phenoxy-1,5,9-undecatriene (7α): IR (neat) 2940, 1648, 1600, 1590, 1499, 1242, 1175, 1032, 992, 928, 755, and 695 cm^{-1}; ^{1}H NMR 7.48—6.60 (m, 5H, Ph), 6.16—5.56 (m, 1H, olefin), 5.39—4.97 (m, 4H, olefin), 4.56 (m, 1H, CH), 2.62—2.21 (m, 2H, CH_2), 2.21—1.92 (m, 4H, CH_2), 1.82—1.50 (m, 9H, CH_3); MS *m/z* (rel. intensity) 270 (M$^+$, 0.8) and 133 (100); Found: C, 84.13; H, 9.82. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69%.

(1Z,5E)-6,10-Dimethyl-1-phenoxy-1,5,9-undecatriene (7γ): IR (neat) 2925, 1665, 1595, 1493, 1448, 1386, 1255, 1235, 1225, 1165, 1070, 1025, 750, and 690 cm^{-1}; ^{1}H NMR 7.42—6.71 (m, 5H, Ph), 6.27 (d, 1H, *J*=6 Hz, C<u>H</u>(OPh)), 5.35—4.55 (m, 3H, olefin), 2.51—1.87 (m, 8H, CH_2), 1.87—1.48 (m, 9H, CH_3); MS *m/z* (rel. intensity) 270 (M$^+$, 3.1) and 133 (100); Found: C, 84.35; H, 9.91. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69%.

References

1) E. Negishi, "Organometallics in Organic Synthesis," John Wiley and Sons, Inc., 1980, New York, Vol. 1, pp 163—166.

2) D. A. Evans, G. C. Andrews, and B. Buckwalter, *J. Am. Chem. Soc.*, **96**, 5560 (1974); W. C. Still and T. L. Macdonald, *ibid.*, **96**, 5561 (1974); *Idem, J. Org. Chem.*, **41**, 3620 (1976).

3) T-L. Ho, "Hard and Soft Acids and Bases Principle in Organic Chemistry," Academic Press, 1977, New York.

4) J. A. Miller and H. C. S. Wood, *J. Chem. Soc., C*, **1968**, 1837.