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α:γ RATIOS IN PHENYLTHIOMETHYLATION OF SILYL DIENOL ETHERS[1]

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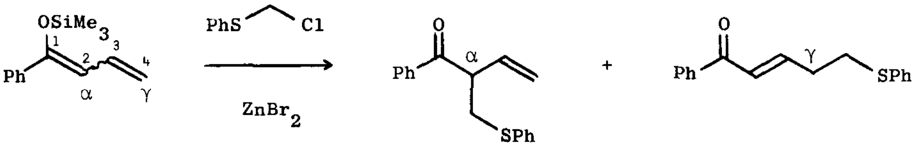
Summary: We report α:γ ratios for the electrophilic attack of phenylthiomethyl chloride on all the possible 2- and 4-methylated 1-phenyl-1-trimethylsilyloxybutadienes **(7a-7e)**; the methyl groups appear to reduce the proportion of attack taking place at the carbon atom carrying the methyl groups.

We reported earlier[2] that silyl dienol ethers show a promising degree of d^4 reactivity; that is they react with electrophiles at the γ-position, in contrast to the corresponding lithium enolates, which react almost always at the α-position. We also reported[3] that phenylthiomethylation is the reaction giving the lowest degree of γ-attack: thus the silyl dienol ether **(1)** and phenylthiomethyl chloride give the α- and γ-products **(2** and **3)** in a ratio of 55:45,

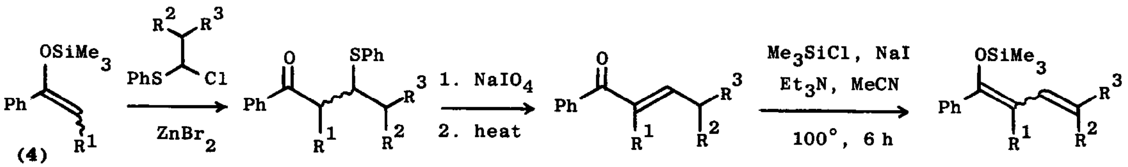


(1) **(2)** **(3)**

and this ratio is higher than that for any other electrophile we have tried. The proportion of γ-attack was substantially raised (α:γ = 10:90) when the triphenylsilyl ether was used in place of the trimethylsilyl ether,[3] even with this, the least γ-selective electrophile. So far, we have examined the silyl dienol ether **(1)**, and its analogues in which the phenyl group is replaced by alkoxy,[2] or hydrogen,[2,4] but we have barely touched upon the problem of more highly substituted silyl dienol ethers, other than to find that a 3-methyl group understandably increases the proportion of γ-attack.[2,5] We now report the effect on the α:γ ratio of having methyl groups in the 2- and 4-positions. It was not obvious whether the presence of an alkyl group would raise or lower the proportion of attack on the atom to which it was attached, so we studied systematically all possible combinations of the 2- and 4-substituted silyl dienol ethers **(7a-7e)**.

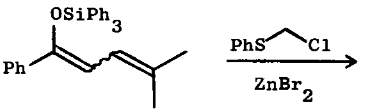
We prepared each of the unsaturated ketones **(6a-6e)** using the appropriate phenylthioalkylation reaction[6] followed by oxidation and elimination (Scheme 1), and we prepared the silyl enol ethers **(4)** and the silyl dienol ethers **(7a-e)** using the very effective and easy method[7] based on the generation, *in situ*, of trimethylsilyl iodide.[8] We recommend this method when there are no problems of regiochemistry (as here) or where thermodynamic silyl enol ethers are wanted. The results of phenylthiomethylation are shown in Scheme 2,[9] where the α:γ ratios are calculated from the yields of separated and isolated products. These ratios were supported by the ^{1}H-NMR spectrum of the crude reaction mixture, indicating that no gross errors had been introduced during the separation.

Scheme 1 Synthesis of the Silyl Dienol Ethers



a	R^1 = Me R^2 = R^3 = H	**(5a)** 79%	**(6a)** 93%	**(7a)** 81%
b	R^1 = R^2 = Me R^3 = H	**(5b)** 73%	**(6b)** 73%	**(7b)** 59%
c	R^1 = R^2 = R^3 = Me	**(5c)** 62%	**(6c)** 61%	**(7c)** 51%
d	R^1 = R^2 = H R^3 = Me	**(5d)** 76%	**(6d)** 69%	**(7d)** 63%
e	R^1 = H R^2 = R^3 = Me	**(5e)** 69%	**(6e)** 77%	**(7e)** 54%

There is a fairly consistent pattern to these results. An α-methyl group lowers the proportion of attack at the α-position (compare **7a** with **1**, or **7b** with **7d**, or **7c** with **7e**), and a γ-methyl group lowers the proportion of attack at the γ-position (compare **7d** and **7e** with **1**, or **7c** with **7b**, or **7b** with **7a**). However, all the effects are small, and the errors probably at least as large as some of the changes in the ratios. The triphenylsilyl enol ether **(10)** is again more γ-selective than its trimethylsilyl analogue **(7e)**. The conclusion is that alkyl groups on the diene portion of the silyl dienol ether have a small effect on the α:γ ratio, and usually lower the proportion of attack on the atom to which they are attached. It is not of course possible from these results to say whether the effect is caused by a reduction in the rate of attack at the position to which the methyl group is attached or by an increase in the rate of attack at the other position. It must be remembered that the electrophile used in

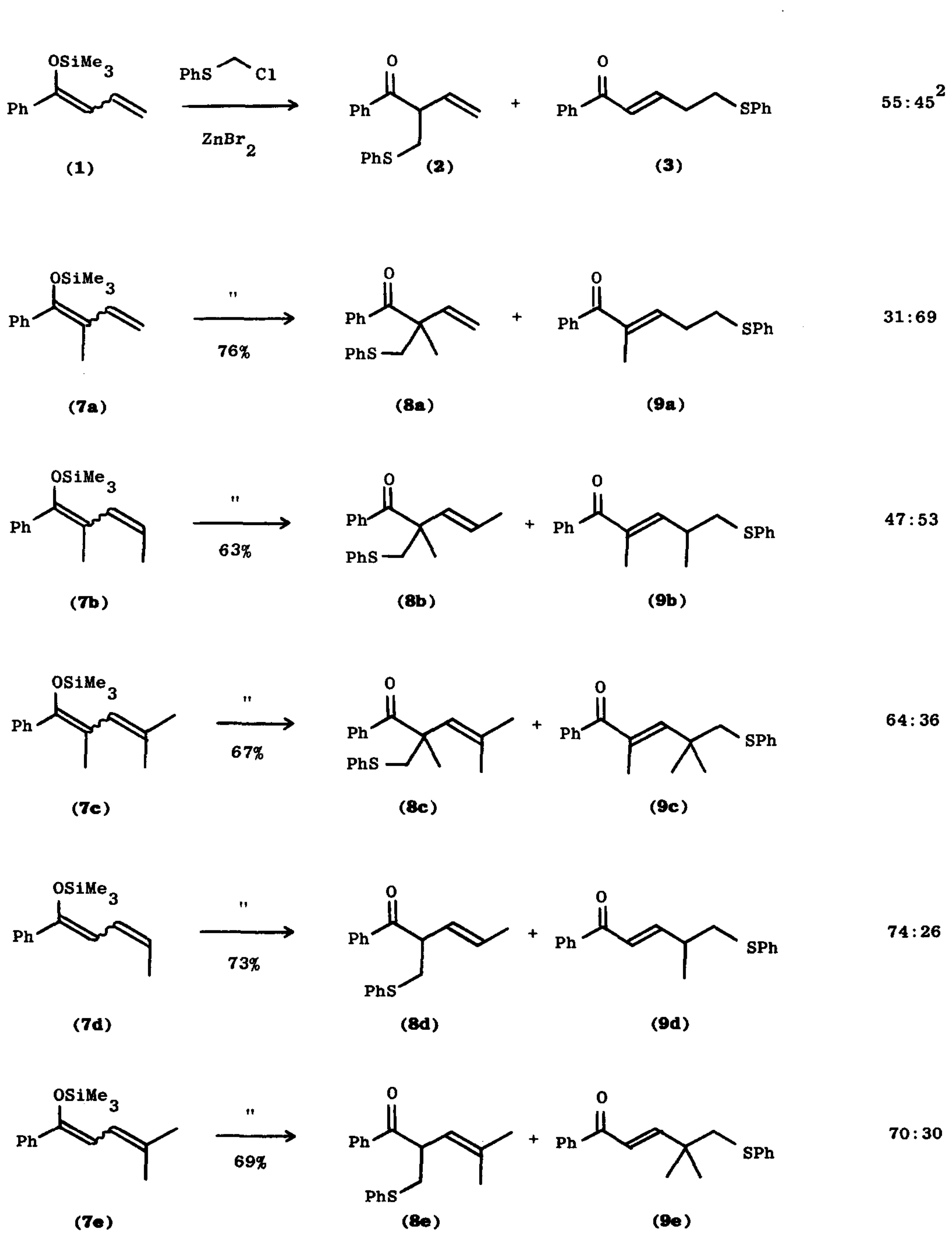


(10) 43% 59%

(8e) + **(9e)**

α:γ
51:49

Scheme 2 Phenylthiomethylation of Silyl Dienol Ethers



this work is the one giving inherently the lowest degree of selectivity for the γ-position, and that other electrophiles can be expected to be more γ-selective. However, it is possible that larger electrophiles may meet resistance to attack at heavily substituted γ-positions. We have not yet investigated this point. Silyl dienol ethers remain an attractive solution to the problem of getting d^4 reactivity from enones, and it is now easier to predict when preparatively useful levels of γ-attack can be expected.

NOTES and REFERENCES:

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5. A silyloxy substituent on the 3-position also encourages γ-attack: T. H. Chan and P. Brownbridge, *J. Chem. Soc.*, *Chem. Commun.*, 578 (1979) and 20 (1981), *J. Am. Chem. Soc.*, **102**, 3534 (1980), and *Tetrahedron* **37**, Supplement 1, 387 (1981); P. Brownbridge and T. H. Chan, *Tetrahedron Lett.*, 4437 (1979) and **21**, 3427 and 3431 (1980).
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9. The experimental conditions are the same as those used earlier.[2] Typically, the silyl dienol ether (7 mmol), phenylthiomethyl chloride (7.5 mmol) and anhydrous zinc bromide (*ca.* 20 mg) were stirred in dichloromethane (20 ml) at room temperature for 3 h under nitrogen. The mixture was then poured into water (50 ml) and the aqueous layer extracted with dichloromethane (2 × 20 ml). The combined organic layer was dried ($MgSO_4$) and the solvent removed by evaporation *in vacuo*. The residue was chromatographed on silica gel eluting with ether-light petroleum (b.p. 40-60 °C) 1:1.5 to give successively the α- and the γ-alkylated products (**8** and **9**). New compounds had the following spectroscopic data. (**6b**) 7.92-7.08 (5H, m), 6.12 (1H, t, *J* 7Hz), 2.18 (2H, quintet, *J* 7Hz), 1.91 (3H, s), 1.02 (3H, t, *J* 7Hz), *M*, 174.2435; (**6c**) 7.95-7.04 (5H, m), 6.14 (1H, d, *J* 7Hz), 2.69-2.15 (1H, m), 1.93 (3H, s), 1.05 (6H, d, *J* 7Hz), *M*, 188.2706; (**6d**) 7.98-7.12 (5H, m), 6.90-6.55 (2H, m), 2.16 (2H, m), 0.96 (3H, t, *J* 7Hz), *M*, 160.2153; (**6e**) 8.0-7.06 (5H, m), 6.97-6.6 (2H, m), 2.45 (2H, m), 0.96 (6H, d, *J* 7Hz), *M*, 174.2451; (**7a**) 7.91-7.13 (5H, m), 6.12 (1H, dd, *J* 12 and 7Hz), 5.29 (1H, d, *J* 10Hz), 5.29 (1H, d, *J* 17Hz), 1.96 (3H, s), 0.45 (9H, s), *M*, 232.3930; (**7b**) 7.57-7.1 (5H, m), 6.15 (1H, d, *J* 16Hz), 5.5 (1H, m), 1.98 (3H, s), 1.65 (3H, d, *J* 6Hz), 0.49 (9H, s), *M*, 246.4266; (**7c**) 7.52-7.06 (5H, m), 5.55 (1H, br s), 1.87 (3H, s), 1.79 and 1.70 (3H each, s), 0.39 (9H, s), *M*, 260.4533; (**7d**) 7.67-7.12 (5H, m), 6.07 (1H, d, *J* 18Hz), 5.8-5.2 (2H, m), 1.8 (3H, d, *J* 7Hz), 0.33 (9H, s), *M*, 232.3941; (**7e**) 7.7-7.17 (5H, m), 6.21 (2H, m), 1.91 (6H, 2 br s), 0.3 (9H, s), *M*, 246.4269; (**8a**) 7.97-7.13 (10H, m), 6.22 (1H, dd, *J* 17 and 10Hz), 5.27 (1H, d, *J* 17Hz), 5.27 (1H, d, *J* 10Hz), 3.43 (2H, s), 1.52 (3H, s), *M*, 282.4057; (**9a**) 7.98-7.08 (10H, m), 6.28 (1H, m), 2.92 (2H, t, *J* 7Hz), 2.59 (2H, m), 1.88 (3H, s), *M*, 282.4061; (**8b**) 7.96-7.13 (10H, m), 5.73 (2H, m), 3.37 (2H, s), 1.67 (3H, d, *J* 6Hz), 1.49 (3H, s), *M*, 296.4329; (**9b**) 8.17-7.15 (10H, m), 6.2 (1H, m), 2.98 (2H, d, *J* 7 Hz), 2.26 (1H, m), 1.88 (3H, s), 1.05 (3H, d, *J* 7Hz), *M*, 296.4333; (**8c**) 8.1-7.1 (10H, m) 5.54 (1H, br s), 3.42 (2H, s), 1.57 (3H, s), 1.55 (3H, s), 1.33 (3H, s), *M*, 310.4584; (**9c**) 7.63-6.88 (10H, m), 6.06 (1H, br s), 2.87 (2H, s), 1.88 (3H, s), 1.09 (6H, s), *M*, 310.4592; (**8d**) 8.05-6.89 (10H, m), 5.56 (2H, m), 4.2 (1H, m), 3.3 (2H, m), 1.62 (3H, d, *J* 6Hz), *M*, 282.4062; (**9d**) 8.05-6.89 (10H, m), 5.56 (2H, m), 3.15 (2H, m), 2.45 (1H, m), 0.97 (3H, d, *J* 7Hz), *M*, 282.4062; (**8e**) 7.98-7.2 (10H, m), 5.56 (1H, br d), 4.45 (1H, m), 3.53 (1H, dd, *J* 9 and 7.5Hz), 3.06 (1H, dd, *J* 9 and 6Hz), 1.66 (6H, s), *M*, 296.4331; (**9e**) 8.17-7.21 (10H, m), 6.96 (2H, AB system, *J* 15Hz), 3.12 (2H, s), 1.29 (6H, s), *M*, 296.4330; (**10**) 8.1-7.17 (20H, m), 3.65 (2H, m), 1.7 and 1.62 (3H each, 2 × br s), *M*, 432.6388.

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