

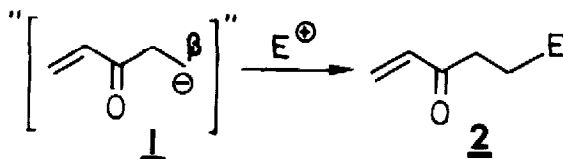
ELECTROPHILIC SUBSTITUTIONS OF 3-TRIETHYLSILYLOXPENTADIENYL LITHIUM

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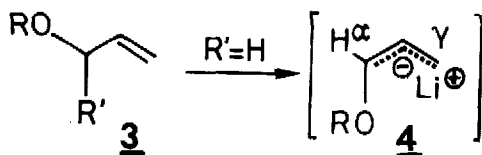
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The preparation of fused carbocyclic systems by the intramolecular Diels-Alder reaction is restricted by the accessibility of suitably functionalised dienes and dienophiles as well as by the CC-bond formation which couples the reactive units.^[2]



Thus, in connection with one of our synthetic projects an equivalent for the (hypothetical) homoenolate ion of ethylvinyl ketone (1) was required.



Whereas it is known that metallated allylic ethers, 4 ($R'=H$), react with electrophiles in the γ -position (and also in the α -position), thereby representing a formal synthon of the *n*-propanal-homoenolate ion^[3-5], a corresponding metallation of the ethers 3 ($R'=alkyl$) proved to be extremely slow^[4].

In contrast, we now wish to report the efficient deprotonation of 3-triethylsilyloxy-1,4-pentadiene (6)^[6,7] to form the symmetrical anion 7 which is quenched with a range of alkyl and carbonyl electrophiles.

Treatment of the silylether 6, readily prepared from the carbinol 5^[8], with *sec.* butyllithium in THF at -78° ^[9], followed by addition of methyl iodide furnished, regio- and stereo-selectively, the γ -substituted silyloxydiene 8b^[10]. The (*Z*)-configuration of 8b (and therefore the depicted *W*-configuration of 7) follows from its smooth bimolecular cycloaddition (proceeding between 25 and 80°) to *N*-phenylmaleimide to give the adduct 9^[6] in 91% yield.

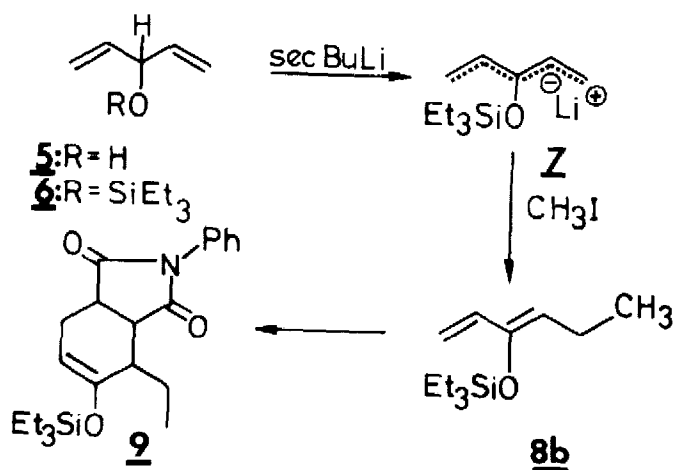
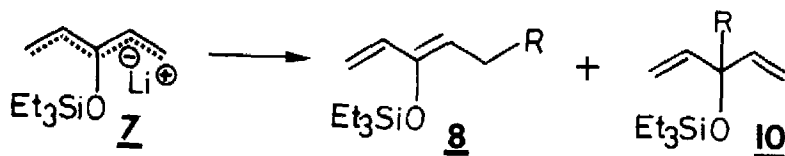
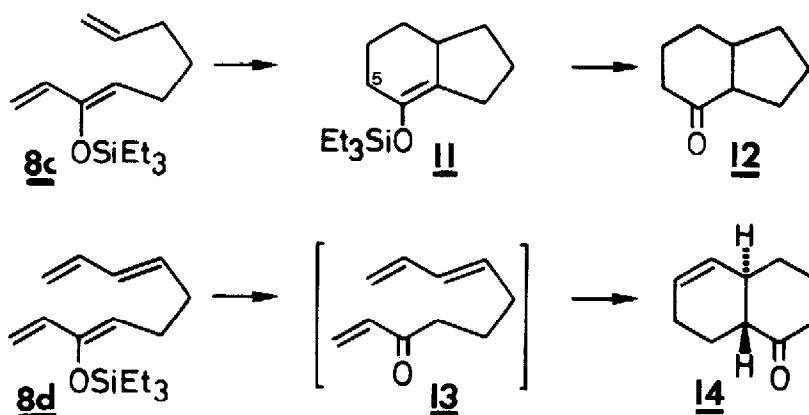


Table 1 - Reactions of the Anion 7 with Electrophiles



Electrophile	PRODUCTS [6]			
	R	Total Yield (8+10)	Rel. % 8(γ-)	Rel. % 10(α-)
H ₂ O	a: H-	87	100	-
CH ₃ I	b: CH ₃ -	86	100	-
CH ₂ =CH-(CH ₂) ₂ -I	c: CH ₂ =CH(CH ₂) ₂ -	77	67	33
CH ₂ =CH-(CH ₂) ₂ -Br	c: "	77	65	35
CH ₂ =CH-(CH ₂) ₂ -OTs	c: "	68	10	90
CH ₂ =CH-(CH ₂) ₂ -OSO ₂ CF ₃	c: "	71	2	98
CH ₂ =CH-CH=CH-CH ₂ Br	d: CH ₂ =CH-CH=CH-CH ₂ -	79	75	25
CH ₂ =CH-CH ₂ Br	e: CH ₂ =CH-CH ₂ -	77	60	40
C ₆ H ₅ CH ₂ Br	f: C ₆ H ₅ CH ₂	84	80	20
C ₆ H ₅ CH ₂ Cl	f: "	82	80	20
oxirane	g: HO-CH ₂ -CH ₂ -	87	40	60
CH ₃ CHO	h: CH ₃ CH(OH)-	92	100	-
C ₆ H ₅ CHO	i: C ₆ H ₅ CH(OH)-	87	100	-
(CH ₃) ₂ CO	j: (CH ₃) ₂ CH(OH)-	93	100	-
cyclohexanone	k: 1-cyclohexanol-	73	100	-
(C ₆ H ₅) ₂ CO	l: (C ₆ H ₅) ₂ C(OH)-	86	100	-
CH ₃ COCl	m: CH ₃ C(O)-	75	100	-

Moreover, the anion 7 reacts with a range of other electrophiles, as shown in Table 1; it appears that, on alkylation, γ -rather than α -attack is preferred when the alkylating agent is a halide^[11] whereas with oxirane, 1-butenyl p-toluenesulphonate or trifluoromesylate α -substitution becomes increasingly important: in the last case the α -product 10c being formed almost exclusively. In contrast, carbonyl electrophiles such as aldehydes, ketones, and acetyl chloride consistently reacted with 100% selectivity at the γ -position.



The preferred formation of γ -substituted products 8 in good overall yields made it possible to exploit the anion 7 as a five-carbon synthon for the preparation of both functionalised diene and dienophile units. Accordingly, intramolecular cycloaddition of the crude triene 8c occurred at 160° in toluene to afford the enol ether 11^[5,7] (the double bond having shifted into the more stable position^[12]). Subsequent cleavage with KF in methanol at 0° gave the cis-fused indanone 12^[5,13] in 55% overall yield. Alternatively, treatment of the unpurified tetraene 8d with KF in methanol at 0° for 16h gave directly the trans-octalone 14^[5,14,15] as the sole adduct in 62% yield. Evidently the initially formed vinyl ketone 13 undergoes an exceedingly smooth and stereoselective intramolecular cycloaddition to the diene unit. The mild conditions, coupled with the observation that no deuterium was found in 14 after similar reaction of 8f with KF in CD₃OD are in accord with a kinetically controlled Diels-Alder process favouring an exo-orientation of the carbonyl group in the transition state.^[2] Other possibilities provided by this approach to vinyl ketones may include their intramolecular photo- or conjugate additions. Further work to exploit this concept in the synthesis of natural products is being actively pursued.

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References and Notes

1. Presented (W.O) at the CNRS Gif-sur-Yvette, June 1976.
2. For reviews on intramolecular [4+2]-additions see: R.G. Carlson, Ann.Rep. Med.Chem., 9, 270 (1974); W. Oppolzer, Angew.Chem., in preparation.
3. D.A. Evans, G.C. Andrews and B. Buckwalter, J.Amer.Chem.Soc., 96, 5560 (1974).
4. W.C. Stills and T.L. Macdonald, J.Amer.Chem.Soc., 96, 5561 (1974).
5. J. Hartmann, M. Stähle and M. Schlosser, Synthesis, 888 (1974).
6. Mobile oil: the ir-, ¹H-nmr- and mass spectra are in agreement with the assigned structure. The isomer ratios 8/10 were determined by g.l.c.
7. Purified by distillation: b.p. 100-120^o (bath)/0.03mm.
8. E.J. Corey and A. Venkateswarlu, J.Amer.Chem.Soc., 94, 6190 (1972).
9. It appears that the presence of hexamethylphosphoramide (HMPA), not required here, is essential for the metallation 3→4.
10. Similarly the less stable trimethylsilylether corresponding to 6, prepared from the carbinol 5 with trimethylsilylacetamide, on subsequent treatment with *sec.* BuLi and MeI afforded the trimethylsilyl analogue of 8b in 85% yield.
11. It is worth noting that neither introduction of HMPA or TMEDA nor exchange of the counterion by Z⁺⁺ or by K⁺ significantly alters the γ/α ratio.
12. The 4,5-unsaturated isomer of 11 rearranges to 11 at 160^o.
13. The *cis* stereochemistry was proved by an independent synthesis of the ketone 12 using classical methods (9 steps from cyclopentanone, <10% overall yield).
14. Purified by chromatography on silica gel.
15. The *trans* stereochemistry of 14 was confirmed by hydrogenation to *trans*-1-decalone and comparison with an authentic sample independently synthesised.