A New Synthesis of Substituted Dienes and its Application to an Alkylated Taxane Model System

Roger V. Bonnert and Paul R. Jenkins*

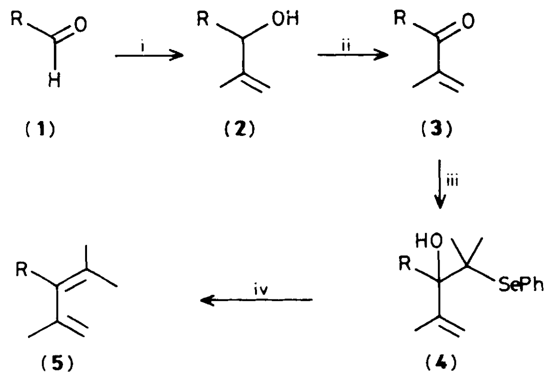
Department of Chemistry, Leicester University, Leicester LE1 7RH, UK

A new synthesis of highly substituted dienes using $LiCMe_2SePh$ is reported, along with its application to the synthesis of the taxane model compound 8,12,15,15-tetramethyltricyclo[9.3.1.$0^{3,8}$]pentadecane.

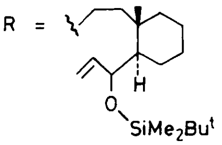
Our synthetic programme on the taxane natural products has resulted in a successful stereocontrolled synthesis of the ring system containing three chiral centres in the required orientation.[1] In order to extend this work we required a reliable synthesis of alkyl-substituted butadienes, and we have produced an answer to this problem based on silicon chemistry.[2] The reagent used in this work is $LiCMe_2SiMe_3$, and while it works well with simple aldehydes, attempts to apply it to our taxane model were unsuccessful. It appeared that the reagent was acting as a base instead of a nucleophile on the aldehyde used. We now report an alternative synthesis of substituted dienes using the selenium reagent $LiCMe_2SePh$,[3] which has enabled us to synthesise an alkylated taxane ring system. Scheme 1† summarises the method of diene synthesis. Addition of the propenyl Grignard reagent to the aldehydes (**1a**—**d**) gave the allylic alcohols (**2a**—**d**) which on Collins oxidation afforded the enones (**3a**—**d**). The reagent $LiCMe_2SePh$, prepared from $Me_2C(SePh)_2$ and BuLi according to a literature procedure[3] added readily to the series of

---

† All new compounds gave satisfactory spectroscopic data; correct microanalytical data were obtained for crystalline derivatives of (**5a**—**c**) along with high resolution mass spectral data for (**3d**), (**5d**), and (**7**).



a; R = Ph
b; R = CH_2CH_2Ph
c; R = $[CH_2]_5CH_3$
d; R =



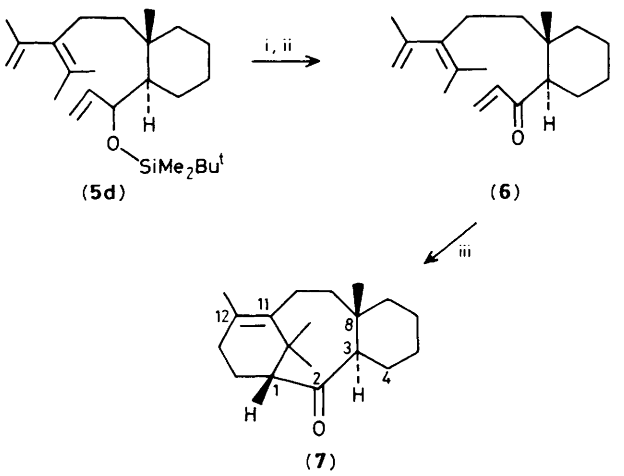
% Yields

	a	b	c	d
(3)	70	60	72	51
(4)	29§	73	86	85
(5)	66	62	65	54

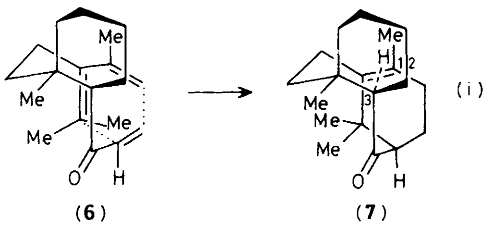
Scheme 1. *Reagents:* i, $CH_2{=}CMeMgBr$ (1.1 equiv.), THF, 0 °C; ii, CrO_3 (6 equiv.), pyridine (12 equiv.), CH_2Cl_2, room temp.; iii, $Me_2C(SePh)_2$, BuLi, THF, −78 °C; iv, $SOCl_2$ (2 equiv.), Et_3N (7 equiv.), CH_2Cl_2, room temp.

enones (**3a**—**d**) to produce the hydroxy selenides (**4a**—**d**). Although the conversion of a 2-methylselenobut-3-enol unit into a diene has been mentioned as unpublished results by Krief,[4] full details and specific applications to highly substituted dienes have not been reported. We now report that the hydroxy selenides (**4a**—**d**) readily undergo elimination with thionyl chloride to give the dienes (**5a**—**d**) in good yield.

The diene (**5d**) produced was subjected to deprotection and oxidation to give the enone (**6**). Treatment of (**6**) with $BF_3{\cdot}OEt_2$ at −40 °C caused an intramolecular Diels-Alder reaction and the alkylated taxane model system (**7**) was isolated as an oil‡ [55% from (**5d**)] (Scheme 2).



Scheme 2. *Reagents:* i, HF, H_2O, MeCN, room temp., 6 h; ii, CrO_3 (6 equiv.), pyridine (12 equiv.), CH_2Cl_2, room temp., iii, $BF_3{\cdot}OEt_2$ (1 equiv.), toluene, −40 °C, 24 h.



The stereochemistry of the Diels-Alder reaction (**6**)→(**7**) is consistent with that found in our previous unalkylated model[1] and may be summarised by the representation (i), where cyclisation occurs to give the chair-boat conformation for the eight-membered ring in the product (**7**). The importance of the nuclear Overhauser effect between the proton at C-3 and the methyl group at C-12 (see footnote ‡) can be clearly seen in (i); this is the clearest evidence for the stereochemical assignment of (**7**).

We thank Dr. O. W. Howarth and Dr. A. Harrison of the University of Warwick for extensive n.m.r studies on the taxane model (**7**). We also thank the S.E.R.C. for financial support.

Received, 21st May 1987; Com. 695

References

1 P. A. Brown and P. R. Jenkins, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1303.
2 P. A. Brown, R. V. Bonnert, P. R. Jenkins, and M. R. Selim, *Tetrahedron Lett.*, 1987, **28**, 693.
3 D. Van Ende, W. Dumont, and A. Krief, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 700; A. Krief, *Tetrahedron*, 1980, **36**, 2632.
4 J. Rémion and A. Krief, *Tetrahedron Lett.*, 1976, 3743.

---

‡ *Spectroscopic data* for (**7**): $\nu_{max.}$ 1678 cm^{-1}; ^{1}H n.m.r. (400 MH) δ 0.94 (3H,s), 0.98—1.21 (4H,m), 1.08 (3H,s), 1.24 (3H,s), 1.47—1.74 (6H,m), 1.82 (1H, ddd, *J* 15.5, 12.68, and 5.51 Hz, 9β-H) overlapping 1.83 (3H), 1.97 (1H, dddd, *J* 15.37, 11.25, 8.69, and 2.64 Hz, 14β-H), overlapping 2.02 (1H, ddd, *J* 18.29, 10.05, and 2.3 Hz, 13α-H), 2.09—2.17 (1H,m,10β-H), 2.40 (1H, d, *J* 8.63 Hz, 1-H), 2.44—2.59 (1H, m, 13β-H), 2.81 (1H, ddd, *J* 14.19, 12.65, and 5.60 Hz, 10α-H), and 2.96 (1H, dd, *J* 12.22 and 2.96 Hz, 3-H); 3% nuclear Overhauser enhancement between δ 1.83 and 2.96 and 1% in the reverse direction. Extensive n.O.e. and COSY experiments were carried out to assist in assigning the proton spectrum.

§ In the case of (**3a** → **4a**) a product resulting from Michael addition of $LiCMe_2SePh$ to the enones was also isolated in 38% yield.