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STEREOSELECTIVE SYNTHESES OF SUBSTITUTED METHYL (Z,E,E)-DECA-2,7,9-TRIENOATES AND SUBSTITUTED METHYL (Z,E,E)-UNDECA-2,8,10-TRIENOATES

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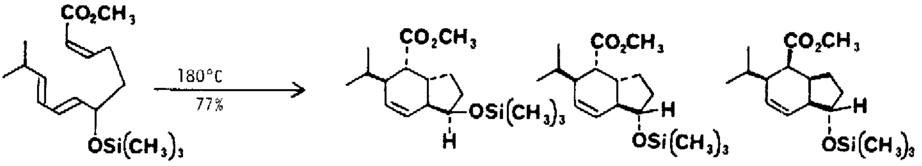
Summary: Lindlar hydrogenation of substituted methyl (E,E)-deca-7,9-dien-2-ynoates and substituted methyl (E,E)-undeca-8,10-dien-2-ynoates affords selectively the corresponding (Z,E,E)-trienes.

We have recently reported that triene 1 undergoes an intramolecular Diels-Alder reaction to afford a mixture of cycloadducts in which trans-fused 2a and 2b, products of exo Diels-Alder reactions, predominate.[1] We have initiated studies to determine the factors responsible for the failure of the endo-rule to apply to this reaction. The low availability of (Z,E,E)-trienes such as 1 by our original method[1,2] prompted us to develop a new route to these systems. Herein we report that Lindlar hydrogenation[3] of the corresponding diene acetylenes constitutes an efficient and, in most cases, highly selective route to the desired (Z,E,E)-trienes (Table I). In future publications we describe the Diels-Alder reactions of these compounds.



1 2a (49%) 2b (28%) 3 (23%)

Syntheses of the substrates for the Lindlar hydrogenation are outlined in Scheme I. Each route involves the addition of an appropriate Grignard reagent, either that prepared from chloride 4[4] or bromide 5,[5] to a diene aldehyde (either 6,[6] 13,[7] or 16). In all cases, the

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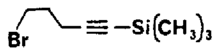

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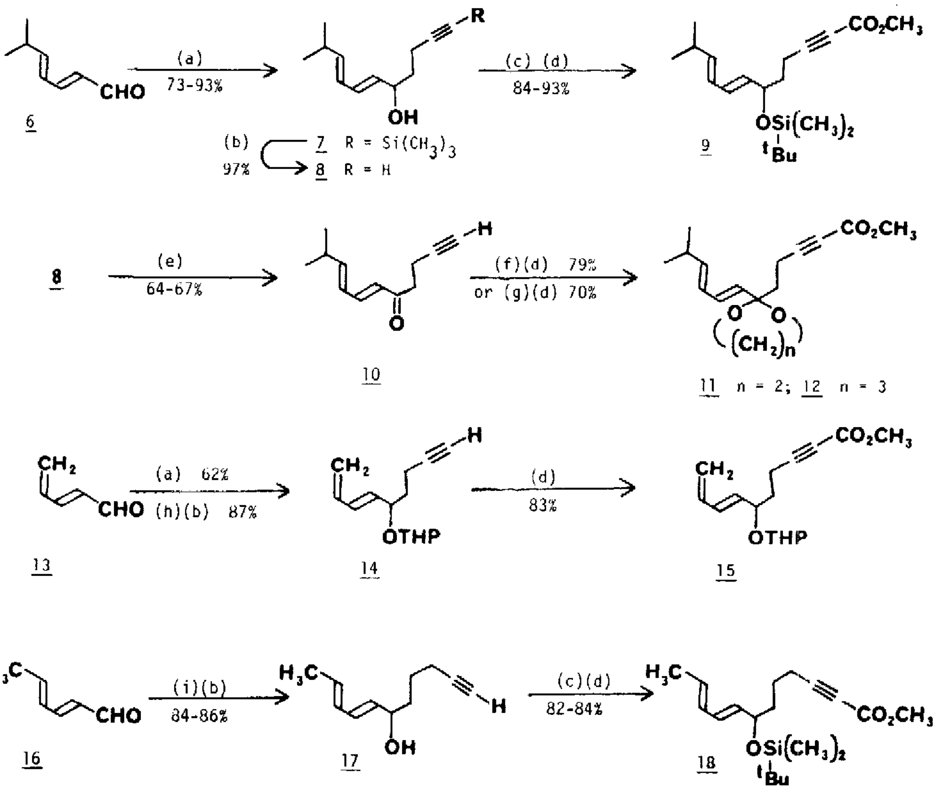
products of the Grignard reactions (e.g., 7[8a,b]) were desilylated by the action of KF in an aqueous DMF mixture (91-97% yields).[4] The routes to 9,[8a,b] 15,[8a,b] and 18[8a,b] were completed by hydroxyl protection as indicated in the appropriate equations (89-95% yield) followed by acetylene carbomethoxylation. This step was performed by treating the terminal acetylenes with a slight excess of n-butyllithium in THF at -78°C followed by excess methyl chloroformate (-78°C → 25°C; 83-94% yield).

Scheme I

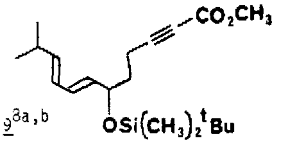
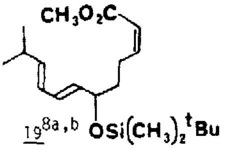
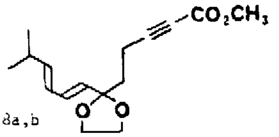
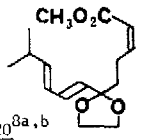
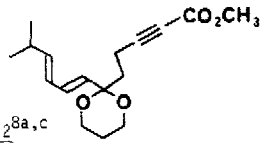
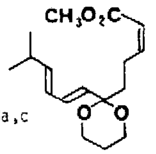
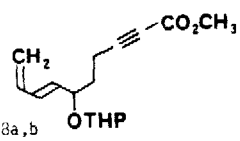
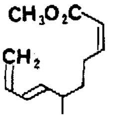
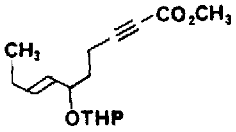
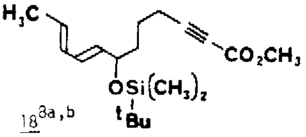
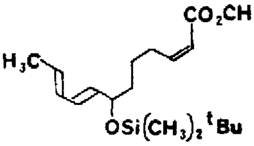


Key: (a) $ClMgCH_2CH_2C{\equiv}C\text{-}Si(CH_3)_3$,$Et_2O$, 0°C; (b) KF, H_2O, DMF; (c) $(CH_3)_2{}^tBuSiCl$, DMF, imidazole; (d) (i) n-BuLi, THF, -78°C; (ii) $ClCO_2CH_3$, THF, -78°C → 25°C; (e) DMSO, $(COCl)_2$, CH_2Cl_2, -78°C, then Et_3N; (f) 2-methoxy-1,3-dioxolane, $HOCH_2CH_2OH$, pTsOH; (g) 2-methoxy-1,3-dioxane, $HOCH_2CH_2CH_2OH$, pTsOH; (h) dihydropyran, CH_2Cl_2, pTsOH; (i) $BrMgCH_2CH_2CH_2C{\equiv}C\text{-}Si(CH_3)_3$, THF, 0°C.

Ketals 11[8a,b] and 12[8a,c] were prepared starting from 8.[8a,c] Thus, oxidation of 8 with the reagent prepared from DMSO and oxalyl chloride[9] afforded 10[8a,c] in 64-67% yield. Treatment of 10 with ethylene glycol, catalytic p-toluenesulfonic acid, and 2-methoxy-1,3-dioxolane[10] (84% yield of ethylene ketal) or with 2-methoxy-1,3-dioxane,[11] propylene glycol, and p-TsOH (77% of propylene ketal) followed by acetylene carbomethoxylation afforded ketals 11[8a,b] and 12,[8a,c] respectively, in 79% and 70% overall yields from 10.

The Lindlar hydrogenations of 9, 11, 12, 15, and 18 were performed in toluene using 10% (w/w) of Lindlar catalyst (5% $Pd/CaCO_2$, lead poisoned). The progress of these reactions was

Table I - Lindlar Hydrogenation of Acetylenic Dienes

Substrate	Product(s)	Isolated Yield
 9[8a,b]	 19[8a,b]	82%[a]
 11[8a,b]	 20[8a,b]	87%
 12[8a,c]	 21[8a,c]	88%
 15[8a,b]	 22  23	74% (~3:1)[b,c]
 18[8a,b]	 24[8a,b]	83%[d]

(a) Compound 9 was recovered (9%).
(b) Compounds 22 and 23 were inseparable by tlc; compound 15 was recovered (13%).
(c) Quinoline (1% w/w) added. In the absence of quinoline, this reaction was much less selective.
(d) Compound 18 was recovered (7%), and an overreduction product of unassigned structure was also obtained (5%).

monitored by tlc and by H_2 uptake, and the reactions were stopped when starting material could no longer be detected by tlc, or when the theoretical amount of H_2 had been absorbed. Under these carefully monitored conditions, the site selectivity was excellent for all substrates except 15 (Table I); evidently, the steric bulk of the isopropyl or methyl substituents of 9, 11, 12, and 18 supresses the rate of butadiene reduction in these systems. Moreover, these reductions are highly stereoselective. High field (250 or 270 MHz) ^1H NMR spectroscopy clearly indicated that the dienophilic double bonds of all reduction products are cis (19,[8a,b] $J_{2,3}$ = 11.3 Hz; 20,[8a,b] $J_{2,3}$ = 11.4 HZ; 21,[8a,c] $J_{2,3}$ = 11.5 Hz; 24,[8a,b] $J_{2,3}$ = 11.2 Hz). In no cases were trans-unsaturated esters observed. Compound 19 prepared in this manner was identical in all respects

(NMR, IR, tlc, mass spectrum) with an authentic sample prepared by t-butyldimethylsilylation[12] (t-butyldimethylsilyl chloride, imidazole, DMF, 43%) of the corresponding alcohol.[1,6]

The interesting Diels-Alder chemistry of the compounds described herein will be the subject of future publications from this laboratory.

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11. 2-Methoxy-1,3-dioxane was prepared by the general method described in reference 10a and was used without purification.
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