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# HIGHLY STEREOSELECTIVE SYNTHESIS OF THE INSECT SEX PHEROMONE OF PHTHORIMAEA OPERCULELLA AND OF PROPYLURE

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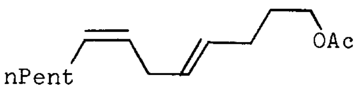
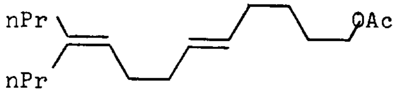
Dienic systems are widely encountered in insect sex pheromones (1). We have recently reported two methods for the obtention of 1-3 dienes namely the synthesis of Bombykol (2) and Pear Ester (3).

We describe herein an extension of our work to 1-4 and 1-5 dienes with the synthesis of the sex pheromone of Phtorimaea Operculella 1 and Propylure, a compound isolated from Pectinophora Gosypiella (1) 2.



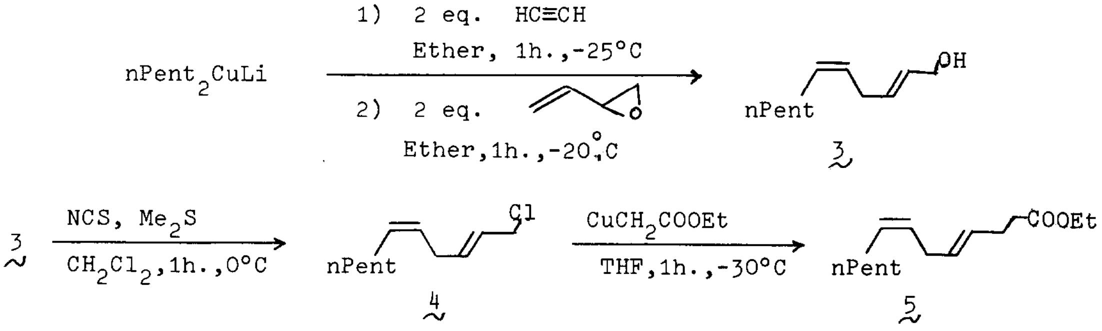
1

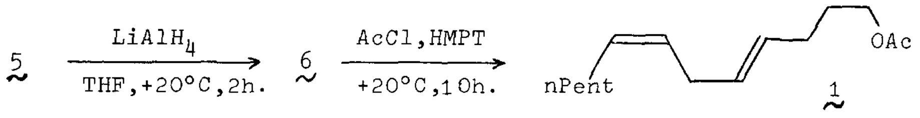


2

The key step of these syntheses is the conjugate opening of acyclic allylic epoxides by vinylic and allylic organocopper reagents (4).

This new reaction appears to be a general and stereospecific method for the obtention of 2-5 and 2-6 dienols (such as 4 and 8 ) which allows a carbon chain extension as depicted below :

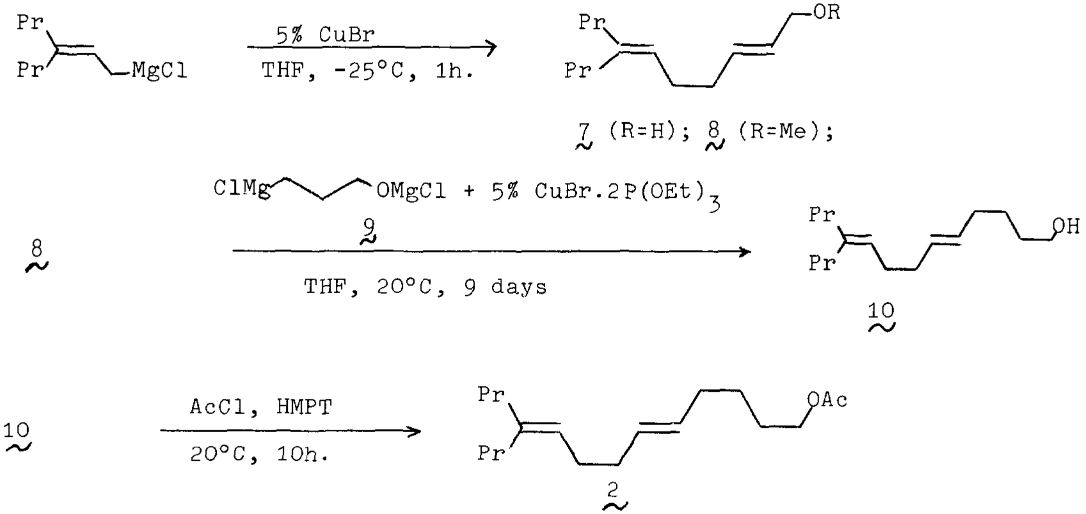




Global yield:60%

Introduction of 740ml. of acetylene ( 33 mmol.) into an ether solution of $nPent_2CuLi$ ( 30mmol. in 150ml solvent) in 10 min. at -45°C (then 1h.at -25°C) gives the Z-heptenyl cuprate (3) to which 2.1g.(30 mmol.) (5) of butadiene oxide are added ( 1h.,-25°C). After $NH_4Cl/HCl$ 1N solution hydrolysis and standard work-up, the crude alcohol 3 (5.08g.) is directly transformed into the chloride 4 by the NCS, $Me_2S$ complex (6). The crude chloride is alkylated with $Cu-CH_2COOEt$ (7), then reduced to the alcohol 6 and acetylated (8). Distillation through a 15cm Vigreux column affords (4E,7Z)-4,7-Tridecadien-1-yl acetate 1 (4.27g) in 60% global yield from the epoxide. Eb:93°/0.005.
IR (neat): 3010, 1740, 1655, 1240, 965, 730$cm^{-1}$; $^1H$ NMR ($CDCl_3$/TMS)
$\delta$ ppm:5.20-5.60ppm (m,4H); 4.04ppm (t,2H); $^{13}C$ NMR ($CDCl_3$/TMS)
$\delta$ ppm:170.4 (C=O), 130.9-130.0-129.6-127.9 (C=C), 63.9 ($CH_2$-O-),31.8 (=CH-$\underline{CH_2}$ -CH = ) with a ratio E-Z/Z-Z=96/4 (9). The high stereoselectivity of this synthesis is determined by the key step which affords 3 with the same steric purity as 1.

For compound 2, the key step was slightly modified by the use of a catalytic amount of Cu(I) salt (4):



Global Yield: 69%

Thus, slow addition of $Pr_2C=CH-CH_2MgCl$ (16 mmol.) (0.85N THF sol.) to a stirred mixture of 1.05g (15 mmol.) butadiene oxide and 100mg CuBr

(0.75 mmol.) in 50ml THF at -25°C, gave after standard work-up and distillation ( Eb:110°/0.1) 2.62g of **7** ( 92% yield based on the epoxide) ( E/Z:94/6) **7** is transformed into its methyl ether **8** (10) ( 90% isolated yield after distillation) which is then hydroxypropylated with the yet unknown Grignard reagent **9** (11) in the presence of catalytic amount of Cu(I) salt (12,13). The crude alcohol **10** is acetylated (8) and affords 2.9g of 10-Propyl-5 (E), 9 Tridecadien-1-yl acetate **2** after distillation through a 15cm Vigreux column Eb:112°/0.001; I.R.(neat):3010, 1740, 1660, 1235,1040,965cm$^{-1}$; $^{1}$H NMR ( $CDCl_3$/TMS: $\delta$ ppm): 5.40ppm (m,2H), 5.12 (t,1H), 4.05 (t,2H); $^{13}$C NMR ( $CDCl_3$/TMS: $\delta$ ppm): 170.6 (C=O), 139.6-131.1-130.2-125.0 ( C=C , C=C), 64.4 ($CH_2$-O).

The global yield is 69% based on epoxide and the purity of **2** is the same as for **7** ( E/Z= 94/6 ).

These syntheses illustrate a concomittent use of three methods ( preparation of dienols (4b), substitution of allylic ethers (12), use of " non protected" hydroxy Grignards ) which represent a general access to ω-functionnalized 1-4 or 1-5 dienes.

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## References and Notes

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4. (a) Only $Me_2CuLi$ and $Ph_2CuLi$ have been already studied:
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   (b) For vinylic and allylic organometallics, see G.Cahiez, A.Alexakis, J.F.Normant: submitted for publication to Synthesis
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9. The purity of 3 and 1 is determined by capillary G.C; (SE 30; 50m) and $^{13}$C NMR.

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11. The use of the Grignard reagent 9 and higher homologs has been developed in this laboratory and will be described in a separate note. Its use is much more practical, efficient and economical than the hydroxy-protected lithium or magnesium derivatives.

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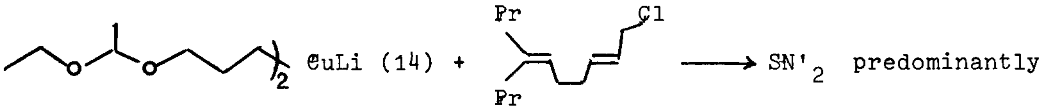
This reaction is performed by mixing of 8 and 9 in the presence of Cu(I) catalyst and stirring the mixture at room temperature until the disappearanceof 8 is complete ( by G.C.). Use of the acetate unstead of the methyl ether gave only carbonyl attack.

13. The reaction of 8 with 9 affords regio and stereo specifically 10 whereas



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