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PYRIDINES AS PRECURSORS OF CONJUGATED DIENE PHEROMONES (II) [1] : STEREOSELECTIVE SYNTHESIS OF (7E,9Z)-DODECADIEN-1-YL ACETATE, SEX PHEROMONE OF LOBESIA BOTRANA [2]

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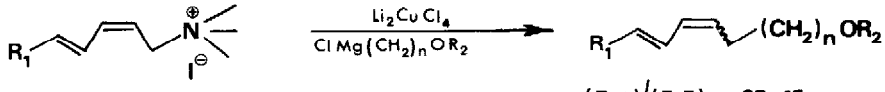
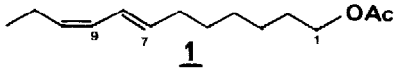
Abstract: 2-Alkyl pyridines are convenient precursors of (E,Z) diene ammonium salts which can be substituted by activated Grignard reagents or a lithium diorgano cuprate reagent. The synthesis of (7E,9Z) dodecadien-1-yl acetate, sex pheromone of Lobesia botrana, is an illustration of this methodology.

Our approach to the synthesis of conjugated dienes allowed us to prepare Z,E diene pheromones using pyridines as starting materials [1]. However, nucleophilic substitution of a (Z,E) diene ammonium salt by an activated Grignard reagent resulted in a partial isomerization of the diemic system (Scheme I).



SCHEME I

In order to extend this method by testing the stereoselectivity of the same reaction on an (E,Z) diene ammonium salt and to compare the reactivity of an activated Grignard reagent versus a lithium diorgano cuprate, we decided to undertake a synthesis of (7E,9Z) dodecadien-1-yl acetate 1 [3] which is the sex pheromone of Lobesia botrana, a major pest of vineyards.

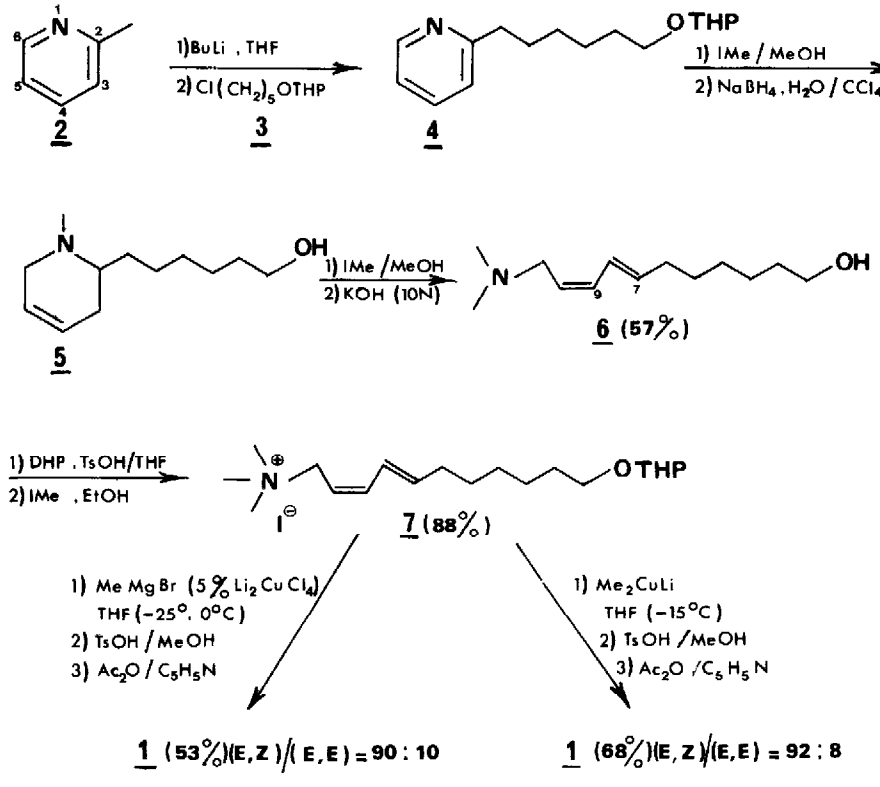


1

Thus, 2-picoline 2 transformed into the corresponding lithio salt [4] was alkylated by 2-(5'-chloropentyloxy) tetrahydropyran 3 [5]. The resulting derivative 4 was transformed into the corresponding N-methyl pyridinium salt [6] and was reduced by sodium borohydride. Quaternization of the 1,2,3,6-tetrahydropyridine 5 [7] followed by an Hofmann elimination reaction afforded the 11-dimethyl-amino (7E,9Z)-undecadien-1-ol 6 [8] as the sole isomer (overall yield from 4 : 57%).

After protection of the alcoholic group, the corresponding ammonium salt 7 was treated either with methyl magnesium chloride in the

presence of lithium tetrachloro cuprate[9] or with lithium dimethyl cuprate to give, after hydrolysis, acetylation and purification by HPLC [10], pure 1 [11] (Scheme II).



SCHEME II

In a typical experiment, a solution of Me_2CuLi in THF (0.2 M ; 10 ml) is added slowly under Argon to a stirred suspension of ammonium salt 7 (2.10^{-3} mole) in THF (15 ml) at - 30°C. Stirring is continued for 4 h at - 15°C. The mixture is then hydrolysed with satured aqueous ammonium chloride and extracted with ether, the organic phases are then washed with satured aqueous sodium chloride dried with sodium sulfate, fitered off and

evaporated in vacuo.

The use of lithium diorgano cuprate in this type of nucleophilic substitution improved both the yield and the stereoselectivity of the reaction. This synthesis constitues a practically stereoselective route which can be used to prepare 1 and other dienic E,Z compounds related to bombykol [2b] on a large scale.

References and Notes

(1) G. Decodts, G. Dressaire and Y. Langlois, Synthesis, 510 (1979).

(2) (a) W.L. Roelofs, J. Kochansky, R. Carde, H. Arn and R. Rauscher, Bull. Soc. Entomol. Suisse, 46, 71 (1973). (b) C.A. Henrick, Tetrahedron, 33, 1845 (1977). (c) R. Rossi, Synthesis, 817 (1977).

(3) For preceding synthesis of 1 see : (a) J.N. Labovitz, C.A. Henrick and V.L. Corbin, Tetrahedron Letters, 4209 (1975). (b) C. Descoins and D. Samain, ibid., 745 (1976). (c) E. Negishi and A. Abramovitch, ibid., 411 (1977). (d) D. Samain, C. Descoins and Y. Langlois, Nouveau Journal de Chimie, 2, 249 (1978). (e) H.J. Bestman, J. Suß and O. Vostrowsky, Tetrahedron Letters, 2467 (1979). (f) For synthesis of related compounds J.F. Normant, A. Commerçon and J. Villieras, Tetrahedron Letters, 1465 (1975).

(4) M. Kaiser and J.D. Petty, Synthesis, 705 (1975).

(5) M.E. Synerholm, J. Amer. Chem. Soc., 69, 2581 (1947).

(6) Unexpectedly, the acetal group was hydrolysed during this reaction.

(7) IR (ν cm^{-1}) (neat) : 3200, 1655, 1455, 1130. MS m/e : 197 ($M^{+\cdot}$), 98, 96, 57. NMR (400 MHz) [12] ($CDCl_3$ TMS, δ = 0 ppm) : 1.33 (m, 8H, C_1,-H_2 to C_4,-H_2), 1.56 (m, 2H, C_5,-H_2), 2.16 (m, 2H, C_3-H_2), 2.31 (s, 3H, N-CH_3), 2.44 (m, 1H, C_2-H), 2.97 and 3.09 (2d, $J_{6a,6b}$ = 20, 2H, C_6-H_2), 3.60 (t, 2H, J = 7, C_6, = H_2), 5.65 (m, 2H, C_4-H and C_5-H).

(8) IR : 3200, 1650, 1460, 990, 955, 730. MS : 212, 211 ($M^{+\cdot}$), 196, 180, 166, 124, 110, 71. NMR (400 MHz) : 1.37 (m, 6H, C_3-H_2, C_4-H_2, C_5-H_2), 1.54 (q, 2H, J = 7, C_2-H_2), 2.10 (q, 2H, J = 7, C_6-H_2), 2.24 (s, 6H, N-$(CH_3)_2$), 3.04 (d, 2H, J = 7, C_1-H_2), 3.61 (t, 2H, J = 7, C_{11}-H_2), 5.33 and 5.35 (2t, 1H, J_{9-10} = 11.6, J_{10-11} = 7, C_{10}-H), 5.68 and 5.70 (2t, 1H, J_{7-8} = 15, J_{6-7} = 7, C_7-H), 6.05 and 6.08 (2d, 1H, J_{9-10} = 11.6, J_{8-9} = 11.6, C_9-H), 6.25 and 6.28 (2d, 1H, J_{7-8} = 15, J_{8-9} = 11.6, C_8-H).

(9) M. Tamura and J. Kochi, Synthesis, 303 (1971).

(10) HPLC : Waters 660. Detector UV 440. Adsorbant : Silica Lichroprop Si 60 + silver nitrate 20%. Eluent : cyclohexane/chloroform = 85:15.

(11) IR : 1740, 1460, 980, 950, 730. MS : 224 ($M^{+\cdot}$), 164, 135, 121. NMR (250 MHz) : 1.00 (t, 3H, J = 7, C_{12}-H_3), 1.34 and 1.62 (2m, 8H, C_2-H_2 to C_5-H_2), 1.90 to 2.2 (m, C_6-H_2 and C_{11}-H_2), 2.04 (s, 3H, CH_3-CO) 4.05 (t, 2H, J = 7, C_1-H_2), 5.23 and 5.27 (2t, J_{9-10} = 11, J_{10-11} = 7, C_{10}-H), 5.55 and 5.63 (2t, J_{7-8} = 15, J_{7-6} = 7, C_7-H), 5.81 and 5.87 (2d, J_{9-10} = 11, J_{9-8} = 11, C_9-H), 6.22 and 6.28 (2d, J_{9-8} = 11, J_{7-8} = 15, C_8-H).

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