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FACILE SYNTHESIS OF VINYLIC CYCLOPROPANES CARBOXYLATES WITH BIS [ETHYLENE BIS(DIPHENYLPHOSPHINE)] PALLADIUM (0) AS CATALYST

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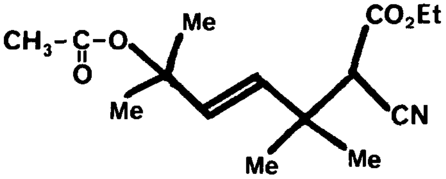
Abstract. *SN_i' cyclisation of 6-acetoxy 4-heptenoate promoted by Bis [ethylene bis(diphenylphosphine)] palladium (0) as catalyst gave cyclopropanes carboxylates with unsaturated side chain in high stereoselectivity*

Functionalized vinyl cyclopropanes are widely distributed in nature and possess interesting physiological properties , they exhibit antibiotic (1) and insecticidal (2) activities They also have a high potential in organic synthesis (3) Previously, we have shown (4) that allylic acetate 1 by SN_1' cyclisation was useful precursor in the preparation of substituted cyclopropanes related to chrysanthemic acid It was of interest to investigate the cyclisation of unsymmetrical derivatives such as 2 potentially valuable for the synthesis of natural cyclopropanes (5)



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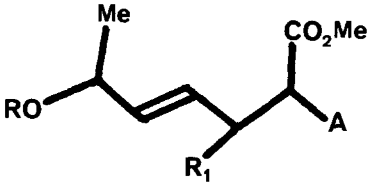


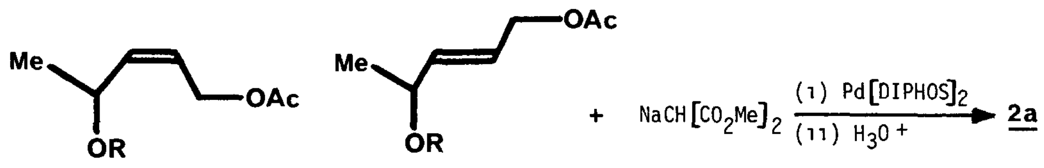
2

a) R = H, R_1 = H, A = CO_2Me ; b) R = H, R_1 = Me, A = CO_2Me
c) R = H, R_1 = Me, A = CN , d) R = $COCH_3$, R_1 = H, A = CO_2Me
e) R = $COCH_3$, R_1 = Me, A = CN , f) R = COϕ, R_1 = Me, A = CN

Now, we wish to report our investigation concerning SN_1' reactions of secondary substrates such as 2 into vinyl cyclopropanes carboxylates

The utility of this vinylic cyclopropane synthesis depends on the availability of the requisite acyclic precursors 1 or 2 We have recently shown (6) that symmetrical secondary allylic alcohols 2b-c are easily prepared by palladium catalyzed allylation (7)

In the same way, the (E)unsymmetrical precursors are readily available from the tetrahydropyranyl acetates 5a, 6a or hydroxy-acetates 5b, 6b (8) Alkylation with sodio malonate gave 2a (9) We obtained a complete regioselectivity for the formation of the C-C bond (10) *in 1,4 position* to the acyloxy or hydroxy groups (11). Subsequent transformation of 2a-c into the corresponding acetates 2d-e or benzoate 2f proceeds in high yields (80-90 %) by treatment with acetic or benzoic anhydride in CH_2Cl_2 with 4-dimethylamino pyridine (DMAP) as catalyst.



5 or **6** **a, R = THP** **b, R = H**

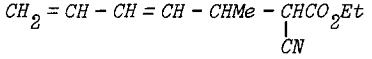
Cyclisation of such substituted substrates 2d-f appears quite difficult (table 1) In contrast with the preceding observation with tertiary derivatives 1, (4) we do not observe cyclisation in the uncatalyzed process with the acetate 2d or with a better leaving group such as the benzoate 2f (run 1,2)

Moreover the catalyzed cyclisation with tetrakis(triphenylphosphine)palladium, $(PPh_3)_4$ Pd, failed at room temperature starting material was recovered (run 3) , at more elevated temperature still with $(PPh_3)_4$ Pd as catalyst, we observed clean elimination with formation of diene (12) (run 4) table 1

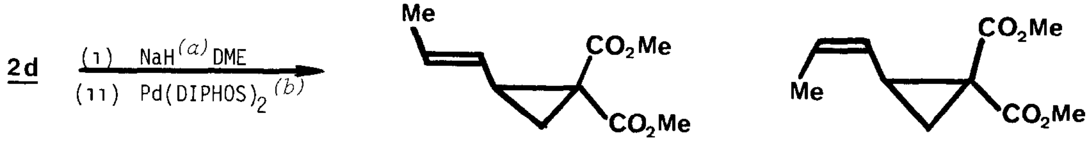
Table 1

run	starting mat	reactions temp (°C)	conditions[(a)] time (hr)	catalyst	results
1	2d	25	80	no	*(b)*
2	2f	65	48	no	*(b)*
3	2d	25	72	$(PPh_3)_4Pd$	*(b)*
4	2d	60	6	$(PPh_3)_4Pd$	elimination *(c)*

(a) Typically 1 mmole of the ester 2 was added to 1,1 eq of NaH in 3ml of THF or DME after complexion of the anion, to the stirred reaction mixture 5-10 % of catalyst was added (run 3,4) - (b) Starting material recovered -

(c) 
$CH_2=CH-CH=CH-CHMe-\underset{CN}{\underset{|}{C}}HCO_2Et$ *(13).*

However Pd(DIPHOS)$_2$ is an efficient catalyst the cyclisation of <u>2d</u> was achieved under very mild conditions 40°C 30 min, into the vinylic cyclopropanes carboxylates <u>7</u> and <u>8</u>, with (E) and (Z) stereochemistry (7 1 ratio) (15) for the propenyl chain



<u>**7**</u> <u>**8**</u>

(a) The neutral catalyzed cyclisation with Pd(DIPHOS)$_2$ undergoes after 4h at 50°C elimination reaction - (b) 10 % of catalyst was used

The utilisation of Pd(DIPHOS)$_2$ appears as an interesting and useful catalyst, for performing cyclopropanation of functionalized allylic acetates <u>1</u> or <u>2</u> in $S_N{}_1'$ fashion (16), with some degree of stereoselectivity (17) Further studies of this $S_N{}_1'$ cyclisation are in progress and synthetic applications for natural product syntheses are under investigation (18)

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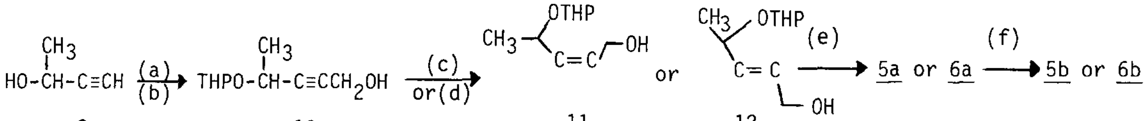
(5) Dictyopterene isolated from <u>Dictyopteris</u> possesses an (E) disubstituted unsaturated side chain , J A Pettus, R E Moore , J Amer Chem Soc <u>93</u> 3087 (1971)

(6) a) J P Genêt, M Balabane, Y Legras , Tetrahedron Lett <u>23</u>, 331 (1982)
b) M Balabane, Thèse 3ème cycle, Université P & M Curie (juin 1982)

(7) Reviews, see B M Trost , Aldrichimica Acta <u>14</u> 43 (1981), and reference (6a) for exhaustive citation therein

(8) Prepared as follows



<u>9</u> <u>10</u> <u>11</u> <u>12</u>

for <u>9</u> → <u>10</u> P D Landlor, S R Landlor, E S Pepper , J Chem Soc 185, (1967)

a) Dihydropyran, PTSA, RT (75 %) , b) EtMgBr, THF then $\mathrm{^{H}_{H}{>}C{=}O}$ (70 %) , c) Pd Lindlar/H_2/ Quinoleine or Na/NH_3 - 33°C (90-100 %) , e) Ac_2O/DMAP NEt_3 in CH_2Cl_2(90 %) , f) HCl 0,1N (70 %)

(9) 2a IR heat 3,400, 1725 cm^{-1} , NMR'H ($CDCl_3$) 1,2 (dJ = 6 Hz, 3 H) , 2,56 (m, 2H) , 3,42 (t J = 7 Hz, 1H) , 3,7 b (s, 6 H) , 4,2 (m, 1 H) 5,46-5,6 (m,2H) irradiation at 2,56 d centered at 5,4 J = 16 Hz, 1 H, irradiation at 4,2 gave d at (5,58 J = 16 H, 1 H), 3(s OH)

(10) For a regioselective 1,4 formation of C-N bond by palladium induced reaction from 1,3 dienes , J E Backvall, R E Nordberg, J E Nystrom , Tetrahedron Lett 23, 1617 (1982)

(11) This interesting regioselectivity was also observed by alkylation of diene monoepoxides a) J Tsuji, H Kataoka, Y Kobayashi , Tetrahedron Lett 22, 2575 (1981) - b) B M Trost, G A Molander , J Amer Chem Soc 103, 5969 (1981)

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(13) IR (neat) 2220, 1730, 1580, 1430 cm^{-1} , 'H RMN $CDCl_3$ 60 MHz 1,35(m, 6H) , 3(m, 1H) , 3,5 (d J = 6 Hz, 1H) , 4,3 (q J = 7 Hz, 2 H) , 4,9 - 6,5 (m, 5H)

(14) Bis [ethylene(bisdiphenylphosphine)] Palladium (0), commercially available from Aldrich

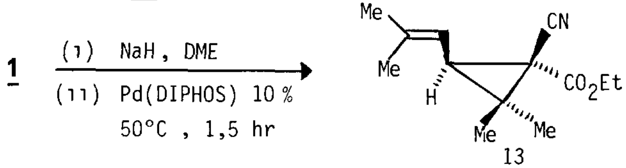
(15) Purification of the reaction mixture flash chromatography on silica (ether/hexane 1 2) gave for 7 and 8

7 IR (neat) 1720, 1620 (w) cm^{-1} , H'RMN ($CDCl_3$) 250 MHz 1,5-1,64 (m, 2H) , 1,66 (d,d J = 7 Hz, 3 H) , 2,54 (q, J = 8 Hz 1 H) 3,76 (s) and 3,77 (s) 6 H , 4,9 - 5,14 (m, 1 H) irradiation at 2,54 gave at 5,1 (d J = 16 Hz 1 H) , 5,62 - 5,84 (m, 1 H) irradiation at 1,6 gave at 5,75 (d J = 16 Hz)

8 IR (neat) 1720, 1620 (w) cm^{-1} , 'H RMN ($CDCl_3$) 250 MHz 1,5 - 1,64 (m, 2 H) , 1,74 (d,d 3 H) , 2,74 (q, J = 8 Hz 1 H) , 3,76 (s) and 3,77 (s) 6 H , 4,9 (t, J = 10 Hz 1 H) 5,6-5,65 (m, 1 H)

(16) Review R Magid , Tetrahedron 36, 1101, (1980) for a mechanistic study in cyclopentane series, G Stork, A R Schoofs , J Amer Chem Soc 101, 5081 (1979)

(17) In the cyclopropanation of 1 Pd(DIPHOS)$_2$ also induces a remarkable stereoselectivity with the exclusive formation of 13 key intermediate for synthesis of cis pyrethroīds



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