Tetrahedron Letters No. 38, pp 3575 - 3578. 0040-4039/78/0915-3575$02.00/0

REACTIONS OF ACTIVE METHYLENE AND CARBONYL COMPOUNDS WITH MYRCENE CATALYSED BY PALLADIUM AND NICKEL COMPLEXES

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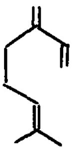
The reactions of 1,3-butadiene with alcohols,[1] amines,[2] carboxylic acids[2,3] and active methylene and methyne[4] compounds have been shown to be catalytic in the presence of palladium(0) complexes. More recently, myrcene has been reported to react with acetic acid[5,6] and alcohols[6,7] catalysed by palladium[5,7] and rhodium[6] complexes. In this laboratory, reactions between 1,3-dienes and active methylene compounds[8,9] with a variety of transition metal complexes have been carried out and we now report the palladium(0) complex catalysed alkylation of diethyl malonate, ethyl acetoacetate and acetylacetone with myrcene. Nickel complex catalysed reactions of myrcene with diethyl malonate, acetaldehyde and acetone have also been studied.

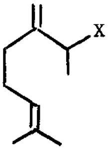
Myrcene (1) (4.2 ml, 25 mmol), diethyl malonate (4.0 ml, 25 mmol), palladium chloride (100 mg, 0.56 mmol), bis(diphenylphosphino)ethane (230 mg, 0.57 mmol) and sodium phenoxide (650 mg, 5.6 mmol) in ethanol (5 ml) were heated at 100°C in a sealed tube for 18 h. A 73% conversion of diethyl malonate to (2a) (30%), (3a) (52%) and (4a) (18%) was obtained. Reaction with ethyl acetoacetate under similar conditions gave higher selectivity to predominantly two products and a conversion of 57% to (2b) (5%), (3b) (50%) and (4b) (45%). In the reaction with acetylacetone a 40% conversion to a 5:3 mixture of ketones and diketones was obtained. The latter consisted of (2c) (6%), (3c) (42%), and (4c) (52%) while the former contained (5) (6) and (7) in the ratio 1:53:46. In all cases the amount of myrcene dimers formed was low, although with other organophosphorus ligands myrcene dimers formed up to 45% of the product mixture. Compounds (3a, b and c) were obtained as a mixture of *cis* and *trans* isomers, but separation was not attempted.

A trend is apparent, both in reactivity and product distribution, over the active methylene reagents employed. Whilst reactivity decreases from diethyl malonate to acetylacetone, the formation of the geranyl adduct (4) increases, so that for acetylacetone it forms 52% of the adduct mixture. Differences in selectivity of reactions of active methylene compounds and π-allyl palladium complexes derived from olefins has previously been noted.[10]

Variation of the organophosphorus ligand used in the reaction has a marked effect on the



(1)



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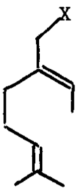
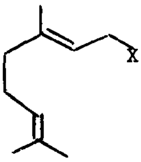


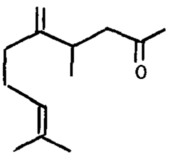
cis and *trans*

(3)



(4)

(a) X = $CH(CO_2Et)_2$ (b) X = $CH(COCH_3)CO_2Et$ (c) X = $CH(COCH_3)_2$



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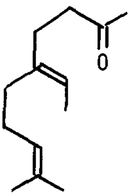
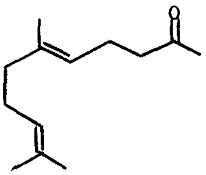


cis and *trans*

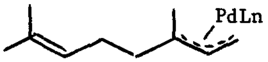
(6)



(7)

anti *syn*

(8)



(9)

extent of alkylation and the product distribution. For example, using $(nBu)_3P$ in a 4:1 ratio with $PdCl_2$, an increased selectivity to formation of (2a) (37%), (3a) (56%) and (4a) (7%) can be obtained in a 77% conversion from reaction of diethyl malonate and myrcene. Under the same conditions, a 51% reaction of myrcene and acetylacetone was obtained, of which 90% of the product was a 1:1 mixture of the ketones (6) and (7), the remainder being diketone. Formation of the monoketones must arise as a result of a reverse Claisen reaction, which appears to be particularly favourable in the presence of tributylphosphine.

In general, the use of other organophosphorus ligands decreases the catalytic activity. A reduced conversion of diethyl malonate was observed with triphenylphosphine and with a range of phosphites. Similarly, ethyl acetoacetate was less reactive in the presence of triphenylphosphine Acetylacetone and myrcene, however, gave a 53% conversion to a 1:1 mixture of ketones [(5) (2%) (6) (70%) and (7) (28%)] and diketones [(2c) (39%), (3c) (33%) and (4c) (28%)] in the presence of triphenylphosphine. The use of this phosphine therefore results in an increased amount of (2) in the product mixture and this was also found in reaction of diethyl malonate and myrcene, where a 52% conversion to (2a) (46%), (3a) (44%) and (4a) (10%) was obtained.

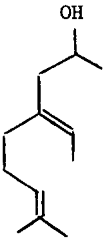
The reactions are considered to involve the π-allyl intermediates (8) and (9). The kinetic and thermodynamic stability of these intermediates and the reactivity of the active methylene compound used determines the product mixture. Previous studies suggest that whilst *syn*-(8) is the thermodynamically more stable complex, formation of *anti*-(8) is kinetically preferred.[11]

Reactions of myrcene and diethyl malonate catalysed by nickel complexes were also examined. In presence of nickel bromide (1 mmol), phenyldiisopropoxyphosphine (3.4 mmol) and sodium phenoxide (4 mmol) in dimethylformamide (5 ml), reaction of diethyl malonate (25 mmol) gave a 65% conversion in 70 h at 100° to a 1:1 mixture of (2a) and (3a). Although in lower yield, complete selectivity to the formation of (2a) was found when a nickel complex catalyst was formed in a different manner. A catalyst solution was prepared at -30° from nickel chloride (3.3 mmol), triphenylphosphine (6.8 mmol) and sodium borohydride (13 mmol) in ethanol (20 ml) in presence of myrcene (6 mmol). Addition of further myrcene (19 mmol) and diethyl malonate (25 mmol) and stirring at room temperature for 24 h gave a 27% conversion to (2a). Thus, under these conditions, reaction takes place through a π-allylnickel complex analogous to (8).

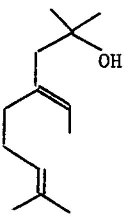
A single product (10) (25% yield) was also obtained from reaction of acetaldehyde (15 mmol) with myrcene (15 mmol) in presence of bis(cyclooctadiene)nickel (15 mmol) and triphenylphosphine (3 mmol) in ethanol at 100° for 18 h. Under similar conditions, reaction of myrcene with acetone gave a 25% conversion to a 4:1 mixture of (11) and (12). This latter product is analogous to the diol formed by the bis(cyclooctadiene)nickel catalysed reaction of butadiene and acetaldehyde.[12]

Further reactions have been carried out on the adducts formed with myrcene to demonstrate the value of these metal complex catalysed reactions. *trans*-Pseudoionone has been formed from (7), and geranyl acetone is also a useful precursor for a number of terpenes such as chromenes,[13] dihydroionones[14] and citronellyl acetone.[15]

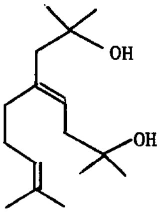
We thank S.R.C. and Burts & Harvey Ltd. for a C.A.S.E. Studentship (RJP).



(10)



(11)



(12)

Products were obtained by distillation and final purification, in some cases, was achieved by preparative g.l.c. All spectroscopic and other analytical results are consistent with the suggested structures.

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(Received in UK 10 July 1978; accepted for publication 20 July 1978)