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Carbopalladation of β—allenylmalonates : a way to cyclopentenyl or vinylcyclopropyl derivatives.

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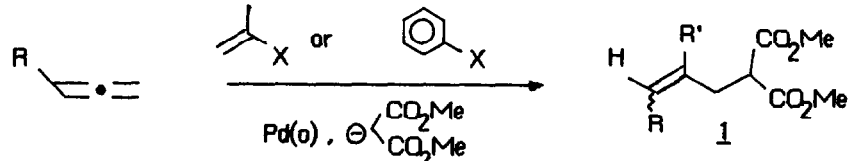
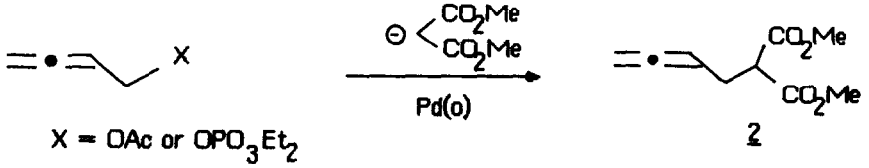
Summary : The palladium—catalyzed addition of a vinyl or aryl halide to the enolate of β—allenyl malonate 2 leads to the formation of either of the two cyclized products 3 and 4 depending mainly on the bulk of the starting unsaturated halide.

We recently described that the carbometallation of allenic hydrocarbons by vinylic or arylic palladium (II) derivatives (resulting from the oxidative addition of the corresponding halides with a palladium (O) complex) certainly produces a π—allyl Palladium species which can be trapped by the enolate of dimethylmalonate leading to diesters 1 ; this regiospecific and highly stereoselective process is catalytic referred to the palladium (O) complex (1).



R' = vinyl or phenyl

The cyclisation of an internal nucleophile with a π—allyl complex being a known process (2) (3), we were interested in studying this reaction in a case where the enolate and the allenic moeity are part of the same molecule. One of the necessary starting materials, namely β—allenic malonate 2 , can be easily obtained with a fairly good yield (∽70%) by the reaction of the enolate of dimethyl malonate with α—allenic acetate or phosphate in the presence of a Palladium (O) complex (4).



X = OAc or OPO_3Et_2 2

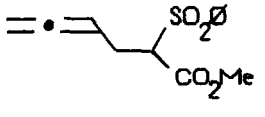
The treatment in THF of the enolate of diester 2 (formed by using sodium hydride) with isopropenyl bromide in the presence of 0,04 molar equivalent of the catalytic system Pd(dba)$_2$–dppe[bis(dibenzylideneacetonato)palladium + 1eq. 1,2–bis(diphenylphosphino)ethane] leads after 16 hours at 40°C to a mixture of 3a (75%) and 4a (25%) corresponding to the attack of the internal enolate on either of the two electrophilic poles of the intermediate π–allyl complex. Both products 3a and 4a are separated by analytical capillary GC or by preparative HPLC and their structures were established mainly by ^{1}H NMR spectroscopy. They are formed by two independant ways since their ratio remains constant during the reaction time as proved by GC analysis every 30 minutes from the begining of the process to the complete disappearance of the starting diester 2. Moreover, they don't interconvert in the reaction conditions since the same ratio is maintained even after heating the reaction mixture 16 hours at 40°C and then 3 hours at 70°C.

The high yield and the regioselectivity of that palladium–catalyzed cyclization was also observed with other unsatured halides but, surprisingly, the site of the attack of the enolate is dramatically dependant of the nature of the entering group as shown by the results of the table : with vinyl bromide, the exclusive formation of the cyclopropyl derivative 4b is observed while with 1–bromocyclohexene and with iodobenzene the only or very preponderant product of the reaction is the cyclopentene 3c and 3d respectively.

At least, the regioselectivity is also influenced by the nature of the solvent since the reaction of isopropenyl bromide in dimethyl sulfoxide at 40°C leads, with a yield of 80%, to an equimolecular mixture of 3a and 4a ; in this last solvent, the reaction is faster than in THF and the starting material is completely consumed in only 4 hours.

It appears from these results that the reaction is highly regioselective in every case with the exception of isopropenyl bromide. This point was resolved by using the sulfone–ester 5 in place of the β–allenyl malonate 2.

No reaction was observed when the enolate of 5 was treated in THF at 40° and during 24 hours with isopropenyl bromide in the presence of 4% of the palladium (0) complex. However, the same reaction and conditions in DMSO lead to the exclusive formation of the cyclopentenyl derivative 6 (yield : 50%). This last result shows that the regioselectivity of this cyclisation is also dependent on the nature of the internal nucleophile.



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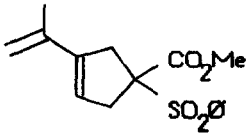

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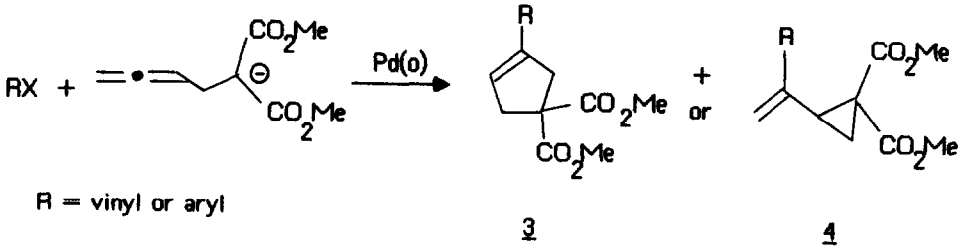
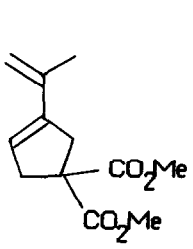
The whole study proves clearly that the formation of the cyclopentenyl derivative is the favored process except in the case of the less substituted vinyl bromide. The reasons for this difference in regioselectivity are currently under investigation ; the most reasonable

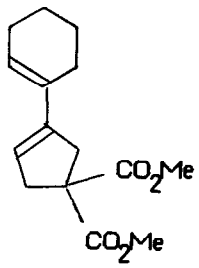


R = vinyl or aryl

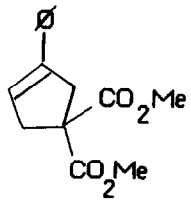
3 4



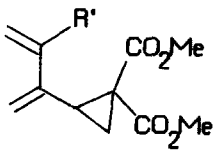
3a



3c



3d



4 a R' = CH_3

b R' = H

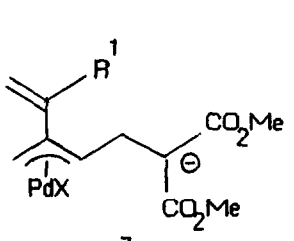
entering halide RX	Conditions *	Yield	% 3	% 4
Isopropenyl bromide	16H–40°	71%	75	25
Vinyl bromide **	15H–65°	80%	–	100
Cyclohexenyl bromide	12H–65°	50%	96	4
Iodo benzene	5H–65°	65%	100	–

Table

* All the reactions were performed in tetrahydrofuran on a 2 mmoles scale. The yields are calculated on quantities of products recovered after column–chromatography.

** The reaction with vinyl bromide was run in a stainless steel bomb and was not followed by GC as in the other cases.

hypothesis is that it comes from a dissimilarity of configuration of the π−allyl intermediate : the syn configuration 7 would be favored when R^1 is an hydrogen and would lead exclusively to the formation of a cyclopropane ring while in other cases the anti configuration 8 would only be present and will cyclize to the primary pole of the allyl moeity (5) giving the cyclopentenyl product.



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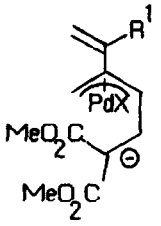

8

Whatever the degree of exactness of this hypothesis would be, it appears that the cyclopentene annelation is interesting from the synthetic point of view since it gives raise to substrate that could subsequently be converted to bicyclic and polycyclic compounds by using the Diels−Alder reaction.

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