Cyclopropanes *via* Nucleophilic Attack at the Central Carbon of (π-Allyl)palladium Complexes

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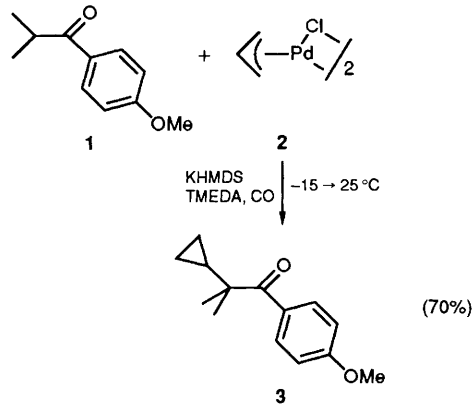
A variety of carbanions (pK_a of protonated carbanion ≥ 20) combine with (π-allyl)palladium complexes in the presence of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) *via* a new reaction mode, giving functionalized cyclopropanes.

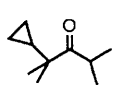
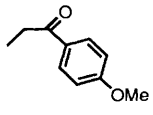
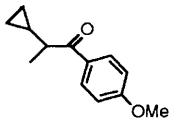
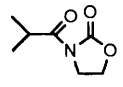
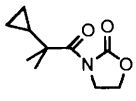
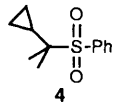
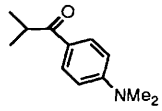
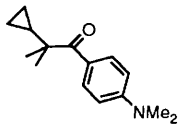
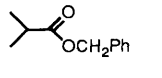
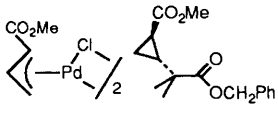
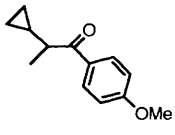
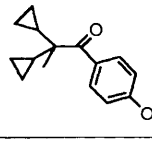
Generally, (π-allyl)palladium complexes react with a variety of nucleophiles to afford the products of allylic alkylation. The reaction is of wide ranging synthetic utility for the formation of carbon–carbon bonds.[1] As yet, nucleophilic attack at the central carbon of the allyl ligand with formation of cyclopropanes has only rarely been observed.[2–4] However, we have found recently that (π-allyl)palladium complexes react with a variety of ester enolates to give α-cyclopropyl esters in good and reproducible yields, provided the ligand sphere of palladium is altered by adding TMEDA as a donor ligand.[5]

We now show that the type of nucleophile for the energetically uphill cyclopropanation is not limited to ester enolates. We have successfully employed a variety of deprotonated ketones as well as deprotonated *N*-isobutyryloxazolidinone and isopropyl phenyl sulfone (Scheme 1, Table 1).†‡ In most of these reactions the amount of conventional allylic alkylation product is very low. Ion pairing and the nature of the counterion of the nucleophile play an important role since the yield of cyclopropanes increases when the enolate becomes more ionic (Table 1, entries 5–7). Therefore, TMEDA exerts a double function, *i.e.* not only complexing palladium (increasing the electron density at palladium), but also activating the nucleophile. As yet, cyclopropanation of acceptor-substituted (π-allyl)palladium complexes results in only very low yields (entry 8). Entry 9 shows that a second cyclopropanation is feasible although it does not occur *in situ*, *i.e.* as a consecutive reaction under the experimental conditions chosen in entry 2.



Scheme 1

Table 1 Cyclopropanes from (π-allyl)palladium complexes[a]

Entry	Protonated nucleophile	Base	π-Allyl palladium complex	Product	Yield (%)[b]
1		LDA–TMEDA[c]	2		65
2		KHMDS[c]	2		63
3		KHMDS–TMEDA	2		74
4		LDA–TMEDA	2	 4	63[d]
5		LDA–TMEDA	2		22
6		KHMDS	2		34
7		KHMDS–TMEDA	2		54
8		LDA–TMEDA	2		13
9		KHMDS–TMEDA	2		25[e]

[a] All products were fully characterized by spectroscopic methods (IR, ^{1}H and ^{13}C NMR, and mass spectra). [b] Isolated yields. [c] LDA = lithium diisopropylamide; KHMDS = potassium bis(trimethylsilyl)-amide. [d] Separation of **4** and the allylic alkylation product by column chromatography proved difficult. However, pure cyclopropane derivatives were obtained after treatment with OsO_4–H_2O_2 and chromatographic separation of the resulting diol. [e] Nucleophile and palladium complex have been employed in equimolar amounts.

To summarize, the scope of the unusual cyclopropane formation from (π-allyl)palladium complexes has been broadened. This transformation has been induced with a variety of nucleophiles ($pK_a \geq 20$) in the presence of TMEDA as ligand. Furthermore, the applicability of allylic alkylation (pK_a of protonated nucleophile usually < 20)[1] is also defined more clearly.

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† *Preparation of enolates*: Potassium bis(trimethylsilyl)amide (KHMDS) (1.66 ml, 1.1 mmol, 15% in toluene) in dry tetrahydrofuran (THF) (5 ml) was placed in an oven-dried flask under N_2. After cooling the mixture to −78 °C the protonated nucleophile (1.1 mmol) was added. The solution was then stirred at 0 °C for 5 min, after which it was cooled to −78 °C and TMEDA (0.17 ml, 1.1 mmol) was added. The solution was stirred at −78 °C until required (*ca.* 20 min).

Cyclopropanation reaction: A dimeric (π-allyl)palladium chloride complex (0.275 mmol) in dry THF (5 ml) was placed in an oven-dried flask under N_2. The solution was cooled to −78 °C and TMEDA (0.17 ml, 1.1 mmol) was added. After warming the mixture to −15 °C, the carbanion solution (see above) was added dropwise through a double-tipped needle. Attachment of a CO balloon caused the reaction mixture to turn black and palladium to precipitate. After stirring for 30 min, the solvent was removed by evaporation *in vacuo* and diethyl ether (50 ml) was added. The mixture was filtered and the filtrate washed with water. The aqueous layer was back extracted with diethyl ether and the combined organic layers were washed with brine (10 ml), dried ($MgSO_4$) and concentrated. The resulting oil was purified by flash column chromatography (silica gel, cyclohexane–diethyl ether, 3 : 1) to give the product as a colourless oil.

‡ In the absence of CO, the yields of cyclopropane derivatives are lower.