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DIALKYLATION AND METHOXYALKYLATION OF BUTADIENE WITH DIETHYL MALONATE ANIONS

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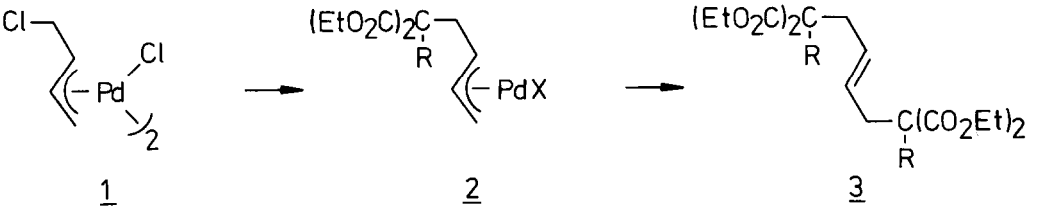
Summary: Butadiene has been transformed into diethyl 2,7-diethoxycarbonyl-4-octenedioates and ethyl 2-ethoxycarbonyl-6-methoxy-4-hexenoates by reacting π-4-chloro- and 4-methoxybutenylpalladium complexes, respectively, with malonate anions.

The industrial production of adiponitrile *via* metal catalyzed 1,4-addition to butadiene[2] and the preparation of 1,4-diacetoxybutene from butadiene and acetate[3] demonstrate the synthetic usefulness of 1,4-addition to 1,3-dienes. As recently shown by diamination of 1,3-cyclohexadiene, this type of addition may be stereospecific.[4]

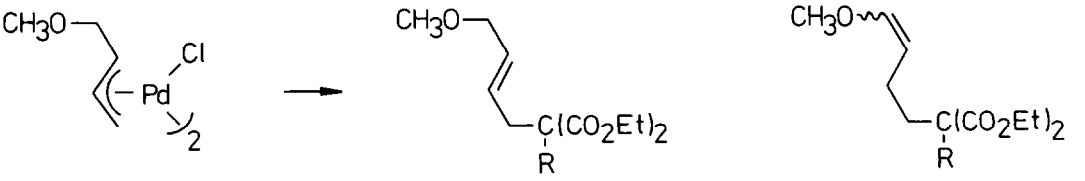
In order to study the scope of 1,4-addition reactions we have investigated the 1,4-dialkylation and 1,4-methoxyalkylation of butadiene, in THF-solution, using malonates as alkylating agents. The exploratory experiments have utilized the π-allylcomplexes 1[5] and 4[6] which were reacted with sodium diethyl malonates (Table 1).[7,8]

The success of both dialkylation and methoxyalkylation is highly dependent on the reaction conditions. In the dialkylation reaction a primary reason is the lability of the chlorobutenyl complex 1, which readily reverts to free butadiene and palladium dichloride complexes. A ligand like diphos is particularly effective in promoting this type of reaction, probably due to the insolubility of diphospalladium chloride. This type of ligand must therefore be added after reacting the complex 1 with malonate to yield 2. This reaction probably generally proceeds *via* nucleophilic displacement of the chloride but could perhaps also take place *via* attack of malonate on complexed butadiene.

Steric effects are clearly important in both dialkylation and methoxyalkylation. This is shown by the fact that diethyl methylmalonate gave high yields of the desired products 3 and 5. As the substituent R became more bulky, the yields decreased (Table 1). With the parent diethyl malonate the yields were unexpectedly low, in the methoxyalkylation reaction due to the formation of diethyl bis(methoxybutenyl)malonate (7). As in the classical alkylation reaction,[9] the selectivity may be improved by the use of phase transfer conditions under which 5a may be obtained as the exclusive product[10] (Table 1).

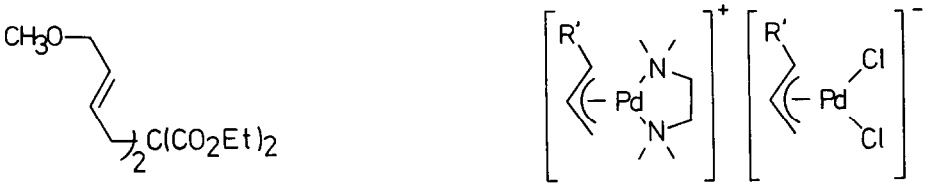


1 2 3



4 5 6

a R=H; b R=CH_3; c R=Ph; d R=$PhCH_2$; e R=HCONH



7 8

When the methoxyalkylation reaction was run under an atmosphere of nitrogen the primary products 5 were partly or completely isomerized to the vinyl ethers 6. This isomerization was inhibited by the presence of oxygen. It was also observed, that the palladium(0) which is formed in the last step (4 → 5) precipitates when nitrogen atmosphere is used but remains in solution when oxygen is present. The presence of oxygen also leads to an increase in the yields. A tentative explanation for these observations is that in the absence of oxygen small amounts of palladium hydrides or very active palladium(0) species are formed, which catalyze both isomerization of the products 5 and the precipitation of palladium metal.

TABLE 1

Reaction of anions of diethylmalonates with the π-butenylcomplexs 1 and 4.

Starting complex	Malonate	Auxiliary ligand	Product (yield %)
1	$CH_2(CO_2Et)_2$	TMEDA[a]	3a (40)
1	$CH_3CH(CO_2Et)_2$	DIPHOS[b]	3b (40)
1	$CH_3CH(CO_2Et)_2$	TMEDA	3b (80)
1	$PhCH(CO_2Et)_2$	TMEDA	3c (30)
1	$PhCH_2CH(CO_2Et)_2$	TMEDA	3d (35)
1	$CHONHCH(CO_2Et)_2$	TMEDA	3e (30)
2	$CH_2(CO_2Et)_2$	TMEDA[c]	5a (15), 7 (60)
2	$CH_2(CO_2Et)_2$	Ph_3P[e]	5a (90)
2	$CH_3CH(CO_2Et)_2$	TMEDA[c]	5b (90)
2	$CH_3CH(CO_2Et)_2$	TMEDA[d]	6b[d] (80)
2	$PhCH(CO_2Et)_2$	TMEDA[c]	5c (85)
2	$PhCH(CO_2Et)_2$	TMEDA[d]	5c (35), 6c (35)
2	$PhCH_2CH(CO_2Et)_2$	TMEDA[c]	5d (70)
2	$PhCH_2CH(CO_2Et)_2$	TMEDA[d]	5d (30), 6d (30)
2	$CHONHCH(CO_2Et)_2$	TMEDA[c]	5e (50)
2	$CHONHCH(CO_2Et)_2$	TMEDA[d]	5e (35)

a) N-tetramethyldiaminoethane b) di-1,2-diphenylphosphinoethane c) under air
d) under nitrogen e) phase transfer conditions, ref. 10

In order to ensure a reasonable yield in the final alkylation step (2 → 3 or 4 → 5) it was necessary to add an auxiliary ligand presumably to stabilize the leaving group (Pd(0)) and to induce the formation of cationic intermediates.[11] Phosphines were believed to be efficient in both these aspects and were therefore used in the early experiments. However, recent studies in this laboratory have shown that in THF, no cationic intermediates are formed on addition of phosphines to π-allyl systems.[12] We therefore switched to TMEDA which induces the formation of an ion pair of the type 8, which does have a cationic part.[12] In accordance it was found that the use of TMEDA as ligand led to a considerable improvement of the yields in the malonate reactions (Table 1).

Although the synthetic applications of the reported reactions have not been explored, it appears that the final products 3 and 5 should be capable of undergoing a number of interesting transformations. This is particularly true for the compounds 5 which are readily isomerized to the protected aldehydes 6.

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6. The literature procedures, Ref. 5 and J.M. Rowe and D.H. White, *J. Chem. Soc. A*, 1967, 1451, where modified in that bisbenzonitrilepalladiumchloride was used in the place of sodium tetrachloropalladite.
7. The following conditions were used in the dialkylation reaction of butadiene with malonates: butadiene (2 mmol) was added at -30°C to the complex 1, (0.231 g, 0.5 mmol) in THF (tetrahydrofuran) (30 ml). After 5 min, the malonate anion (1.2 mmol) was added, followed after 5 min by the ligand (TMEDA or diphos, 1.1 mmol), causing the formation of a precipitate. After another 2 min, more anion (2 mmol) was added, the cooling bath was removed and stirring continued for 18 h. Isolation by extraction gave the dialkylation products 3, contaminated with the ligand and small amounts of the starting material. The pure compounds were obtained by column chromatography.
8. The following conditions were used for the methoxyalkylation of butadiene: TMEDA (165 µl, 1.1 mmol) was added to a THF solution (10 ml) of the π-allyl complex 4 (0.226 g, 0.5 mmol) at 0°C. After 2 min the appropriate malonate anion (2 mmol) was added. The reaction mixture was then left for 5 min at 0°C and then for 2 h at 20°C under an atmosphere of either nitrogen or air. Work up and removal of TMEDA by extraction gave the essentially pure product 5 which could be obtained completely pure by column chromatography.
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10. A solution of sodium hydroxide (0.10 g, 2.2 mmol) and tetrabutylammonium hydrogen sulphate (0.205 g, 0.6 mmol) in water (5 ml) was mixed with a solution of diethyl malonate (0.08 g, 0.55 mmol) and triphenyl phosphine (0.262 g, 1 mmol) in dichloromethane (5 ml). The mixture was vigorously stirred and cooled to 0°C, and the complex 4 (0.06 g, 0.5 mmol), in dichloromethane (1 ml) was added dropwise over a period of 5 min. After 4 h the product was isolated by extraction. Essentially pure 5a was obtained, contaminated only by small amounts of triphenylphosphine.
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