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PROPARGYLIC CARBONATES AS AN a^1, a^2 SYNTHON IN ANNULATION REACTIONS. A CONVENIENT SYNTHESIS OF 3-METHYLENE DIHYDROPYRAN DERIVATIVES

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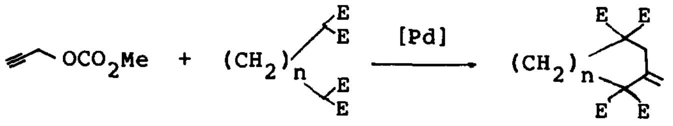
Abstract: Propargylic carbonates react with 2,3-diacylsuccinates in the presence of Pd(0) and phosphine ligands to give 3-methylene dihydropyran derivatives in moderate to good yields.

The use of propargylic derivatives as starting materials in organic synthesis is of current interest. Propargylic halides, propargylic alcohols and their derivatives are known to react with organocopper reagents to give substituted allenes.[1] Organomagnesium or zinc reagents react with propargylic compounds in the presence of palladium,[2] copper,[3] or nickel[4] catalyst to form carbon-carbon bonds. Tsuji reported the reaction of propargylic carbonates with carbon nucleophiles and a novel synthesis of exo-methylene furan derivatives was developed.[5] In Tsuji's reaction, propargylic carbonates could be regarded as an a^1, a^2 synthon which was attacked first by the carbon nucleophile and then by the oxygen nucleophile. It occurs to us that propargylic carbonates are possible to react with a dicarbanion to form the annulated products as shown in the following equation:



1a **2** **3**

Based on this idea, diethyl 2,3-diacetylsuccinate (**4a**) was used as the nucleophile to react with **1a** in the presence of $Pd_2(dba)_3 \cdot CHCl_3$-dppe, besides the expected methylene cyclobutane derivative **5a**, the six-membered 3-methylene dihydropyran derivative **6a**, which may result from the first attack by the carbon nucleophile and then by the oxygen nucleophile, was obtained. The reaction condition is crucial. The ratio of **5a** and **6a** was influenced by both the solvents and the ligands used as shown in Table 1.

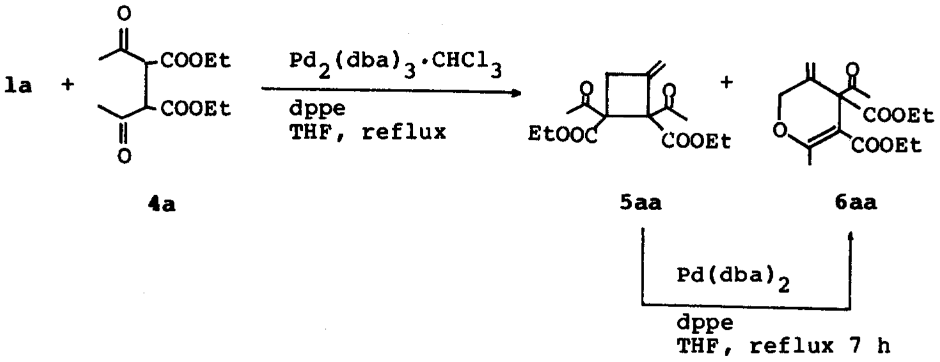


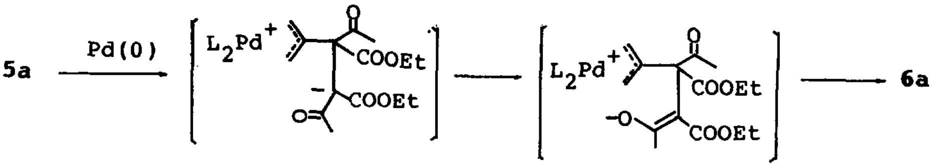
Table 1. Reaction of Propargyl carbonate (**1a**) with diethyl 2,3-diacetyl succinate (**4a**)[a]

Entry	Solvent	Catalyst[b]	Ligand[c]	Temp.	Time (h)	Yield[d] (%)	
						5a	**6a**
1	THF	A	dppe	r.t.	14	No reaction	
2	THF	A	dppe	reflux	7	45	52
3	THF	A	Ph_3P	reflux	10	27	68
4	THF/CH_3CN(1/1)	B	-	r.t.	10	60	-
5	CH_3CN	A	dppe	reflux	5	-	52

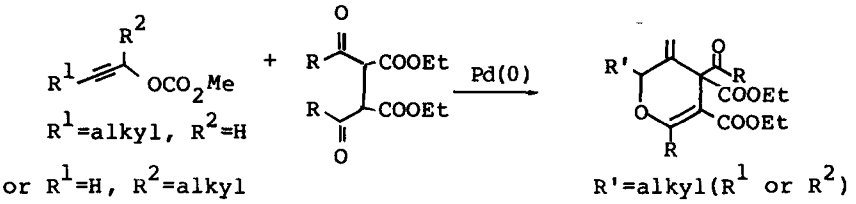
a: **1a** (1.3 mmol) and **4a** (1 mmol) were used.
b: Catalyst: 0.05 mmol; A: $Pd_2(dba)_3 \cdot CHCl_3$, B: $Pd(Ph_3P)_4$.
c: Dppe (0.1 mmol) or Ph_3P (0.2 mmol) was added.
d: The products were isolated by preparative TLC (petroleum ether/ethyl acetate=1/10) and characterized by ^{1}H NMR, ^{13}C NMR, IR, MS and elementary analysis[6].

From Table 1, it is shown that acetonitrile as the solvent and $Pd_2(dba)_3 \cdot CHCl_3$ as the catalyst favor the formation of **6a**, while the reaction is preferable to form **5a** in THF/CH_3CN(1/1) under the catalysis of $Pd(Ph_3P)_4$.

It was also found that the yield of **6a** increased with the increase of the reaction time implying that **5a** may be the intermediate of this reaction. Indeed, **6a** was isolated in 33% yield when pure **5a** was refluxed for 7 h in THF under the catalysis of $Pd(dba)_2$ and dppe, but **6a** could not be converted to **5a** under the same reaction condition, showing that **6a** is more stable than **5a**. The mechanism is suggested as follows:



Although transition metal complexes could react with cyclobutane derivatives[7] with special structure in stoichiometric amount to give metallacycles, it is worth noting that the transition metal complexes catalyzed carbon-carbon bond cleavage of four membered rings is scarcely reported in literature.



1 **4** **6**

Table 2. Reaction of Propargylic Carbonates (**1**) and 2,3-Diacylsuccinates (**4**)[a]

Entry	Propargylic carbonates(**1**) R^1	R^2	2,3-Diacyl-succinates(**4**) R	Time (h)	Product **6** R'	R	Yield[b] (%)
1	n-C_3H_7	H (**1b**)	CH_3 (**4a**)	48	n-C_3H_7	CH_3	65
2	H	n-C_3H_7 (**1c**)	**4a**	42	n-C_3H_7	CH_3	62
3	H	n-C_7H_{15}(**1d**)	**4a**	72	n-C_7H_{15}	CH_3	51
4	H	Ph (**1e**)	**4a**	9	Ph	CH_3	81
5	H	H (**1a**)	Ph (**4b**)	47	H	Ph	76[c]

a: **4** (1 mmol) and **1** (1.3 mmol) in THF (5 ml) in the presence of $Pd(dba)_2$ (0.05 mmol) and dppe (0.1 mmol) were heated at reflux.

b: All structures of products were determined by ^1H NMR, IR , MS and elementary analysis.

c: **4b** (1 mmol) and **1a** (1.3 mmol) in dioxane (2 ml) and CH_3CN (2 ml) in the presence of $Pd(dba)_2$ (0.05 mmol) and Ph_3P (0.2 mmol) were heated at 80°C.

When substituted propargylic carbonates were used in this reaction, only 3-methylene dihydropyran derivatives **6** could be isolated. No cyclobutane derivative was detected. The results are shown in Table 2. The reaction mechanism may be similar to Tsuji's mechanism of the formation of exo-methylene furan derivatives.[5] The fact that reaction of isomeric carbonates **1b** or **1c** with **4a** gives tha same product (entries 1 and 2) supports this mechanism.

The presence of a six membered oxygen heterocycle ring in a range of naturally occurring compounds stimulated the development of synthetic routes to these compounds.[8] Our results provide a convenient and simple synthetic method for these compounds from the easily accessible propargylic carbonates. Especially, this reaction can simultaneously introduce the exocyclic methylene group as a useful functionality for further structural elaboration.

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6. **5a**: IR(neat, cm^{-1}): 3005, 2990, 1740, 1720, 1620, 1460, 1240, 1100, 930; ^{1}H NMR(, CCl$_4$, 60 MHz): 1.22(t, 6H), 2.30(s, 6H), 3.90-4.20(m, 4H), 4.30(s, 2H), 5.23(s, 1H), 5.32(s, 1H); MS(m/e): 298(M^{+}+1), 252, 224, 209, 179; calculated for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80; found: C, 60.97; H, 6.37.
   6a: IR(neat, cm^{-1}): 3005, 2990, 1705, 1650, 1450, 1390, 1120, 850; ^{1}H NMR(, CCl$_4$, 60 MHz): 1.25(t, 6H), 1.43(s, 3H), 2.23(s, 3H), 3.85-4.28(m, 4H), 4.38(m, 2H), 5.08(m, 1H), 5.30(m, 1H); MS(m/e): 297 (M^{+}), 251, 223, 208; calculated for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80; found: C, 60.70; H, 6.86.
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