Journal of Organometallic Chemistry, 417 (1991) 305–311
Elsevier Sequoia S.A., Lausanne
JOM 21791

The palladium-catalyzed reactions of 2-alkynyl carbonates with terminal acetylenes. A new synthetic method for 1,2-dien-4-ynes *

Tadakatsu Mandai, Hiroshi Murayama, Tatsuya Nakata, Hiromasa Yamaoki, Masakazu Ogawa, Mikio Kawada and Jiro Tsuji *

Department of Applied Chemistry, Okayama University of Science, Ridai-cho, Okayama 700 (Japan)

(Received December 21st, 1990)

Abstract

The reaction of substituted 2-alkynyl carbonates with terminal acetylenes in the presence of palladium-phosphine complex and copper iodide as catalysts proceeds in THF to give 1,2-dien-4-ynes (allenyl acetylenes) in good yields. The reaction proceeds by the formation of allenylpalladium complex as an intermediate.

Introduction

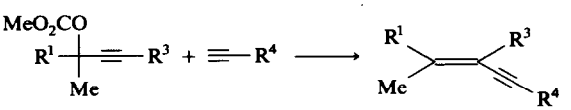
Various allylic compounds, particularly allylic acetates, undergo several palladium-catalyzed transformations via π-allylpalladium complexes, and these reactions are useful in organic synthesis [1]. We found that allylic carbonates have higher reactivity than allylic acetates, and, particularly under mild and neutral conditions, undergo several transformations which are not possible with corresponding acetates [2]. In contrast to the extensive research carried out on the palladium-catalyzed reactions of allylic compounds, few studies have been carried out on such reactions of 2-alkynyl (or propargyl) compounds **1**, which have a triple bond instead of a double bond. The conversion of 2-alkynyl acetate or halides to substituted 1,2-dienes by the reaction of hard carbonucleophiles such as alkyl zinc or magnesium compounds in the presence of palladium catalysts has been reported [3]. In view of the high reactivity of allyl carbonates in the presence of palladium catalyst, we have initiated systematic studies on the palladium-catalyzed transformations of 2-alkynyl carbonates **1**, and have found that the reaction with soft carbonucleophiles such as malonates or β-keto esters proceeds smoothly to give furan derivatives [4]. Also the palladium-catalyzed carbonylation of 2-alkynyl carbonates **1** affords 2,3-alkadienoates in high yields [5]. In addition, 1,2-dienes are obtained by

* This paper is dedicated to the memory of Professor Piero Pino.

0022-328X/91/$03.50

palladium-catalyzed hydrogenolysis with ammonium formate [6]. We have also attempted the palladium-catalyzed reaction of 2-alkynyl carbonates **1** with terminal acetylenes in a search for a new synthetic method for 1,2-dien-4-ynes (or allenyl acetylenes) **3**.

Reasons for our interest are as follows. Allenyl acetylenes **3** are present in compounds produced naturally by some microorganisms [7], and a simple synthetic method is highly desirable. This study is also part of our research on cumulative ene-yne-allene systems which are noteworthy for their DNA cleavage action [8]. The best synthetic method for allenyl acetylenes known so far is the palladium-catalyzed reaction of allenyl bromides with acetylenes or zinc acetylides [3a,9]. But 2-alkynyl carbonates **1** can be prepared more easily than allenyl bromides. As expected, we observed the formation of 1,2-dien-4-ynes **3** according to the following scheme. A preliminary report was published [10] and details of the reaction and improved results are presented in this paper.



(1) (3)

The reaction of alkenyl or aryl halides with terminal acetylenes, catalyzed by palladium complexes and copper iodide to give aryl or alkenyl acetylenes, is well-known [11]. Here, the first step is the oxidative addition of halides. Then transmetallation with copper acetylides, followed by reductive coupling gives the coupled products. The first step in the palladium-catalyzed reaction of 2-alkynyl carbonates **1** mentioned in the above, is the formation of the allenylpalladium alkoxide **2** by the oxidative addition, or S_N2' type displacement of the carbonate group with zero-valent palladium, followed by decarboxylation. In view of the fact that the allenylpalladium complex **2** is formed from 2-alkynyl carbonates **1**, we expected that, similar to alkenyl halides, a reaction with terminal acetylenes should take place to form allenyl acetylenes **3**.

Results and discussion

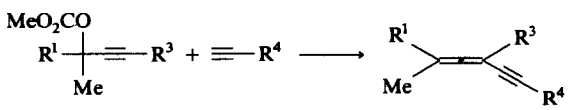
The first attempted reaction of the rather simple 2-alkynyl carbonates **1** in which either R^1 or R^3 is hydrogen, with terminal acetylenes in the presence of catalytic amounts of palladium acetate, triphenylphosphine, copper iodide, and an excess of triethylamine gave a complex mixture of reaction products. There are increasing numbers of reports that some added salts such as alkali halides or tetraalkyl ammonium halides have a remarkable influence on several palladium-catalyzed coupling reactions [12]. In order to study the effect of added salts, we added an excess of lithium chloride to the reaction mixture. Under these conditions the reaction mixture was somewhat cleaner. But we still could not isolate the desired product. We had an impression that the desired reaction took place under these conditions, but the products were reactive and underwent further tranformation. Then we tried the reaction of 2-alkylnyl carbonates which have no hydrogen (R^1, R^2, and R^3 are not hydrogen). The coupling reaction with acetylene took place at room temperature to give the desired allenyl acetylenes **3**, although the yield was low.

In the course of studies on reaction conditions in order to improve the yields of

the reaction, we found that diethylamine was much better than triethylamine. Thus we could isolate the desired allenyl acetylenes **3** in good yields by the reaction of **1** and terminal acetylenes in the presence of excess amounts of diethylamine, and lithium chloride or potassium bromide. Results of the reactions carried out under these conditions have been reported [10]. Then we investigated the reaction conditions more precisely, particularly the effect of the added salts, and finally we confirmed that the reaction of these substituted 2-alkynyl carbonates proceeds smoothly to give the desired allenyl actylenes even in the absence of lithium chloride or potassium bromide. But the reaction is cleaner and gives somewhat improved yields by the addition of the salts as shown in Table 1. The addition of an excess of diethylamine, rather than triethylamine is very important. With the latter, poor results were obtained.

The reaction of several 2-alkynyl carbonates **1** with various terminal acetylenes was carried out under similar reaction conditions. The reaction proceeded smoothly to give the allenyl acetylenes in good yields within 30 min. The representative results obtained in the presence and absence of the salts are shown in Table 1. The limitation of this coupling reaction is the structure of 2-alkynyl carbonates **1**. The coupling products **3** were isolated as stable compounds only when R^1, R^2, and R^3 in the 2-alkynyl carbonates **1** are alkyls. Although the reactants disappeared rapidly within 30 min, no stable coupling product could be isolated when one of the R^1, R^2 and R^3 groups is hydrogen. The product is probably very reactive in the presence of the palladium catalyst. It seems that the products of the reaction that we could isolate are not stable under the reaction conditions. When the reaction was carried out over a longer period of time, the yields tended to decrease probably because of further palladium catalyzed transformations. The reaction proceeded rapidly in less than 30 min with 5 mol% of the palladium catalyst. Also we noticed that the

Table 1



(1) (3)

entry	R^1	R^3	R^4	Additive	Yield [a] (%)	Products
1	C_6H_{13}	CH_2OTHP	CH_2OH	KBr	86 (72.9)	**1**
2			CH_2OTHP	KBr	76 (78.0)	**2**
				LiCl	73	
3			C_4H_9	KBr	85	**3**
4	C_6H_{13}	C_4H_9	CH_2OTHP	LiCl	69 (55.5)	**4**
5			CH_2OH	KBr	85 (65.0)	**5**
6		C_4H_9	CH_2OTHP	LiCl	83 (57.8)	**6**
7			CH_2OH	LiCl	72	**7**
8		CH_2OTHP	CH_2OTHP	KBr	74 (60.1)	**8**

[a] Yields in parentheses were obtained in the absence of the salts.

Table 2

Elemental analyses for compounds **1–8**

Compound	Formula	Analyses (Found (calc.) (%))	
		C	H
1	$C_{19}H_{30}O_3$	74.38 (74.47)	10.10 (9.87)
2	$C_{24}H_{38}O_4$	73.67 (73.81)	9.94 (9.81)
3	$C_{22}H_{36}O_2$	79.42 (79.46)	11.21 (10.91)
4	$C_{22}H_{36}O_2$	79.30 (79.46)	11.82 (10.91)
5	$C_{17}H_{28}O$	82.30 (82.19)	11.63 (11.36)
6	$C_{21}H_{32}O_3$	72.20 (72.38)	9.35 (9.26)
7	$C_{16}H_{24}O_3$	72.62 (72.69)	9.29 (9.15)
8	$C_{23}H_{34}O_6$	67.75 (67.96)	8.51 (8.43)

reaction mixture was cleaner when the reaction was carried out in the dark (by covering the reaction vessel with aluminium foil). The intermediate, or product, seems to be somewhat sensitive to light. The allenyl acetylenes produced by the reaction are not stable even after isolation. The correct elemental analyses shown in Table 2 for all allenyl compounds prepared in this study were obtained when the products were analyzed as soon as they were isolated and purified by column chromatography. But the products can be stored for a longer period of time without change at a low temperature in a refrigerator after the addition of a small amount of triethylamine.

The correct elemental analyses and NMR data clearly support the structure of the products. Thus this reaction offers a good synthetic method for substituted allenyl acetylenes. Also it offers another example that allenyl carbonates are good substrates for palladium-catalyzed reaction.

Experimental

General

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were taken in $CDCl_3$ as a solvent. Chemical shifts are given in δ units relative to tetramethylsilane as an internal standard. The elemental analyses were carried out with a Perkin Elmer 2400 CHN Elemental Analyzer.

Preparation of 2-alkynyl carbonates

All 2-alkynyl alcohols were prepared by the reaction of ketones or aldehydes with magnesium or lithium acetylide. Without isolation, the 2-alkynyl alcohols thus prepared were treated with methyl chloroformate to give the 2-alkynyl carbonates **1**. A typical example of the preparation of **1** is the following. To a THF solution of the

tetrahydropyranyl ether of propargyl alcohol (1.68 g, 12 mmol, 3 ml), ethylmagnesium bromide (THF solution 10.9 ml, 11 mmol) was added and the mixture refluxed for 15 min at room temperature. The mixture was cooled to 0 °C and 2-octanone (1.57 ml, 1.28 g, 10 mmol) was added dropwise and the reaction mixture stirred at room temperature for 30 min. Then methyl chloroformate (0.93 ml, 1.13 g, 12 mmol) was added and the solution was stirred for one hr at room temperature. The reaction was quenched by the addition of aqueous sodium bicarbonate (50 ml) and extracted with ethyl acetate. The ethyl acetate solution was dried over magnesium sulphate and the solvent was evaporated under vacuum to give an oily product, which was purified by column chromatography (silica gel) and pure propargyl carbonate was obtained, 2.27 g (69.8% yield).

1-(2-Tetrahydropyranyloxy)-4-methyl-4-methoxycarbonyloxy-2-decyne. ^{1}H NMR: 0.87 (t, $J = 6.96$ Hz, CH_3); 1.22–1.98 (m, 16H, CH_2); 1.68 (s, 3H, CH_3); 3.48–3.55 (m, 1H, CHO); 3.74 (s, 3H, CH_3); 3.78–3.87 (m, 1H, CHO); 4.30 (s, 2H, CH_2O); 4.82 (t, $J = 3.2$ Hz, 1H, OCHO). ^{13}C NMR: 14.0, 19.0, 22.5, 24.0, 25.4, 26.3, 29.1, 30.2, 31.6, 41.4, 54.0, 54.2, 62.0, 77.5, 81.6, 81.7, 85.5, 96.5, 153.4.

The coupling reaction

A typical example of the coupling reaction is the following (entry 1 in Table 1). A mixture of CuI (9.5 mg, 0.05 mmol), Et_2NH (1.04 ml, 731 mg, 10 mmol), KBr (119 mg, 1 mmol), $Pd(PPh_3)_4$ (28.9 mg, 0.025 mmol) in THF (3 ml) was placed in a reaction flask, and a mixture of the carbonate (163 mg, 0.5 mmol) and propargyl alcohol (28 mg, 0.5 mmol) in THF (2 ml) added. The reaction mixture was stirred at room temperature for 25 min. The disappearance of the carbonate was confirmed by TLC, and the reaction was quenched by the addition of water. The reaction mixture was extracted with ethyl acetate. The organic layer was dried and evaporated under vacuum to give an oily product. Short column chromatography afforded 4-(2-tetrahydropyranyloxy)methyl-6-methyldodeca-4,5-dien-2-yn-1-ol, 132.7 mg, (86.7% yield). The NMR spectra shown below fully support the structure, and indicate that this compound is an inseparable mixture of the diastereomers.

4-(2-Tetrahydropyranyloxy)methyl-6-methyldodeca-4,5-dien-2-yn-1-ol (entry 1). ^{1}H NMR: 0.83 (t, $J = 6.59$ Hz, 3H, CH_3); 1.15–2.00 (m, 16H, CH_2); 1.68, 1.79 (s, 3H, CH_3); 2.88 (bs, 1H, OH); 3.42–3.50 (m, 1H, CHO); 3.79–3.87 (m, 1H, CHO); 3.99 (d, $J = 11.7$ Hz, 1H, CH_2O); 4.02 (d, J = 11.7 Hz, 1H, CH_2O); 4.12 (d, $J = 11.7$ Hz, 1H, CH_2O); 4.31 (s, 2H, CH_2O); 4.66–4.72 (m, 1H, OCHO). ^{13}C NMR: 13.9, 18.4, 18.5, 19.1, 19.2, 22.5, 25.3, 27.0, 27.1, 28.7, 30.2, 30.3, 31.5, 33.7, 33.8, 51.3, 61.9, 62.0, 67.7, 67.8, 80.4, 80.5, 86.1, 86.3, 88.0, 88.1, 96.6, 96.9, 102.8, 102.9, 207.0, 207.2.

The NMR spectra of other allenyl acetylenes are shown below.

1-(2-Tetrahydropyranyloxy)-4-(2-tetrahydropyranyloxy)methyl-6-methyldodeca-4,5-dien-2-yne (entry 2). ^{1}H NMR: 0.85 (t, $J = 7.0$ Hz, 3H, CH_3); 1.18–2.00 (m, 20H, CH_2); 1.68, 1.69 (s, 3H, CH_3); 3.42–3.52 (m, 2H, CH_2O); 3.76–3.90 (m, 2H, CH_2O); 4.00–4.03 (d, $J = 11.7$ Hz, 1H, CH_2O); 4.13–4.14 (d, $J = 11.7$ Hz, 1H, CH_2O); 4.30 (d, $J = 15.8$ Hz, 1H, CH_2O); 4.38 (d, $J = 15.8$ Hz, 1H, CH_2O); 4.67–4.72 (m, 1H, OCHO); 4.78–4.82 (m, 1H, OCHO). ^{13}C NMR: 14.0, 18.5, 18.6, 18.8, 19.0, 19.1, 19.2, 22.5, 25.2, 25.3, 25.4, 27.1, 27.2, 28.7, 30.1, 30.2, 30.3, 30.4, 31.5, 31.6, 33.7, 33.8, 45.9, 54.3, 54.8, 61.8, 61.9, 62.0, 67.6, 67.7, 80.9, 81.0, 85.4, 85.5, 86.4, 86.5, 96.6, 96.7, 96.8, 96.9, 97.0, 102.7, 102.9, 207.0, 207.3.

7-(2-Tetrahydropyranyloxy)methyl-9-methylpentadeca-7,8-dien-5-yne (entry 3). ^{1}H NMR: 0.88 (t, $J = 7.32$ Hz, 3H, CH_3); 0.90 (t, $J = 7.33$ Hz, 3H, CH_3); 1.20–2.04 (m, 20H, CH_2); 1.70, 1.72 (s, 3H, CH_3); 2.30 (t, $J = 6.96$ Hz, 2H, CH_2); 3.45–3.52 (m, 1H, OCHO); 3.85–3.94 (m, 1H, OCHO); 4.00, 4.03 (d, $J = 11.7$ Hz, 1H, CH_2O); 4.14, 4.15 (d, $J = 11.7$ Hz, 1H, CH_2O); 4.71–4.70 (m, 1H, OCHO). ^{13}C NMR: 13.6, 14.1, 18.7, 18.8, 19.2, 19.3, 19.4, 22.0, 22.6, 25.5, 27.2, 27.3, 28.8, 30.5, 30.9, 31.7, 34.0, 61.9, 62.1, 68.2, 68.3, 75.1, 75.2, 87.1, 87.3, 90.9, 91.0, 96.8, 97.1, 102.3, 102.5, 206.3, 206.5.

1-(2-Tetrahydropyranyloxy)-4-butyl-6-methyldodeca-4,5-dien-2-yne (entry 4). ^{1}H NMR: 0.86 (t, $J = 7.0$ Hz, 3H, CH_3); 0.89 (t, $J = 7.0$ Hz, 3H, CH_3); 1.20–1.88 (m, 18H, CH_2); 1.68 (s, 3H, CH_3); 1.90–2.00 (m, 2H, $CH_2C{=}C$); 2.06 (t, $J = 7.3$ Hz, $CH_2C{=}C$); 3.48–3.54 (m, 1H, CHO); 3.81–3.89 (m, 1H, CHO); 4.33 (d, $J = 15.4$ Hz, 1H, CHO); 4.40 (d, $J = 15.4$ Hz, 1H, CHO); 4.82 (t, $J = 3.30$ Hz, 1H, OCHO). ^{13}C NMR: 13.9, 14.1, 18.8, 19.1, 22.0, 22.6, 25.4, 27.3, 28.9, 30.0, 30.3, 31.7, 33.9, 34.0, 55.0, 61.9, 83.1, 84.5, 88.2, 96.7, 101.5, 206.3.

4-Butyl-6-methyldodeca-4,5-dien-2-yn-1-ol (entry 5). ^{1}H NMR: 0.86 (t, $J = 7.0$ Hz, 3H, CH_3); 0.88 (t, $J = 7.3$ Hz, 3H, CH_3); 1.20–1.46 (m, 12H, CH_2); 1.67 (s, 3H, CH_3); 1.90–2.00 (m, 2H, $CH_2C{=}C$); 2.04 (t, $J = 7.33$ Hz, $CH_2C{=}C$); 2.11 (bs, 1H, OH); 4.35 (s, 2H, CH_2O). ^{13}C NMR: 13.8, 14.0, 18.7, 21.9, 22.6, 27.3, 28.9, 30.0, 31.7, 33.8, 34.0, 51.6, 82.8, 86.8, 88.1, 101.6, 206.2.

4-Methyl-6-butyl-9-(2-terahydropyranyloxy)nona-4,5-dien-7-yn-2-one ethylene acetal (entry 6). ^{1}H NMR: 0.87 (t, $J = 6.96$ Hz, CH_3); 1.25–1.85 (m, 10H, CH_2); 1.34 (s, 3H, CH_3); 1.76 (s, 3H, CH_3); 2.05 (t, $J = 7.33$ Hz, 2H, $CH_2C{=}C$); 2.27 (s, 2H, $CH_2C{=}C$); 3.45–3.53 (m, 1H, CHO); 3.78–3.86 (m, 1H, CHO); 3.92 (s, 4H, OCH_2CH_2O); 4.31 (d, $J = 15.8$ Hz, 1H, CHO); 4.37 (d, $J = 15.8$ Hz, 1H, CHO); 4.79 (m, 1H, OCHO). ^{13}C NMR: 13.8, 19.1, 19.7, 21.9, 23.9, 25.3, 29.9, 30.2, 33.6, 43.1, 54.8, 61.9, 64.5, 64.6, 82.4, 85.0, 87.2, 96.5, 96.8, 109.9, 208.94, 208.98.

4-Methyl-6-butylnona-4,5-dien-7-yn-9-ol-2-one ethylene acetal (entry 7). ^{1}H NMR: 0.87 (t, $J = 6.96$ Hz, CH_3); 1.25–1.35 (m, 2H, CH_2); 1.39–1.48 (m, 2H, CH_2); 1.34 (s, 3H, CH_3); 1.75 (s, 3H, CH_3); 2.04 (t, $J = 7.33$ Hz, 2H, $CH_2C{=}C$); 2.27 (s, 2H, $CH_2C{=}C$); 2.35 (bs, 1H, OH); 3.92 (s, 4H, OCH_2CH_2O); 4.33 (s, 2H, CH_2O). ^{13}C NMR: 13.8, 19.7, 21.9, 23.9, 29.8, 33.5, 43.0, 51.4, 64.4, 64.5, 82.0, 87.2, 87.5, 96.8, 109.9, 208.8.

4-Methyl-6-(2-tetrahydropyranyloxy)methyl-9-(2-tetrahydropyranyloxy)nona-4,5-dien-7-yn-2-one ethylene acetal (entry 8). ^{1}H NMR: 1.35, 1.36 (s, 3H, CH_3); 1.45–1.90 (m, 12H, CH_2); 1.79, 1.80 (s, 3H, CH_3); 2.31, 2.32 (s, 2H, CH_2); 3.45–3.54 (m, 2H, CHO); 3.79–3.90 (m, 2H, CHO); 3.93, 3.94 (s, 4H, OCH_2CH_2O); 4.05 (dd, $J = 12.1$, 3.66 Hz, 1H, CHO); 4.17 (d, $J = 11.7$ Hz, 1H, CHO); 4.33 (d, $J = 15.7$ Hz, 1H, CHO); 4.39 (d, $J = 15.7$ Hz, 1H, CHO); 4.69–4.74 (m, 1H, OCHO); 4.81 (t, $J = 3.25$ Hz, 1H, OCHO). ^{13}C NMR: 19.0, 19.2, 19.3, 19.5, 19.6, 23.9, 25.3, 25.4, 30.2, 30.4, 42.9, 43.0, 54.8, 61.9, 62.0, 64.6, 67.5, 80.5, 80.6, 85.4, 85.6, 86.0, 86.1, 96.6, 96.9, 97.2, 98.2, 98.4, 109.7, 109.8, 209.49, 209.52, 209.71.

References

1 (a) J. Tsuji, Organic Synthesis with Palladium Compounds, Springer Verlag, Berlin, 1980. (b) R.F. Heck, Palladium Reagents in Organic Synthesis, Academic Press, New York, 1985.

2 (a) J. Tsuji, I. Minami and I. Shimizu, Tetrahedron Lett., (1983) 24; (b) J. Tsuji, I. Shimizu, I. Minami, Y. Ohashi, T. Sugiura and K. Takahashi, J. Org. Chem., 50 (1985) 1523.

3 (a) T. Jeffery-Luong and G. Linstrumelle, Tetrahedron Lett., 21 (1980) 5019; (b) K. Ruitenberg H. Kleijn, J. Meijer and P. Vermeer, ibid., 22 (1981) 1451; (c) H. Kleijn, J. Meijer, G.C. Overbeek and P. Vermeer, Recl. Trav. Chim. Pays-Bas, 101 (1982) 97; (d) E. Keinan and E. Bosch, J. Org. Chem., 51 (1986) 4006.
4 (a) J. Tsuji, H, Watanabe, I. Minami and I. Shimizu, J. Am. Chem. Soc., 107 (1985) 2196; (b) I. Minami, M. Yuhara, H. Watanabe and J. Tsuji, J. Organomet. Chem., 334 (1987) 225.
5 J. Tsuji, T. Sugiura and I. Minami, Tetrahedron Lett., 27 (1986) 731.
6 J. Tsuji, T. Sugiura, M. Yuhara and I. Minami, Chem. Commun., (1986) 922.
7 (a) D. Celmer and I.A. Solomons, J. Am. Chem. Soc., 75 (1953) 1372; (b) R.E. Bew, J.R. Chapman, E.R.H. Jones, B.E. Lowe and G. Lowe, J. Chem. Soc., (1966) 129 and 135.
8 For example, R. Nagata, H. Yamanaka, E. Murahashi and I. Saito, Tetrahedron Lett., 31 (1990) 2907, and references cited therein.
9 T. Jeffery-Luong and G. Linstrumelle, Synthesis, (1983) 32.
10 T. Mandai, T. Nakata, H. Murayama, H. Yamaoki, M. Ogawa, M. Kawada and J. Tsuji, Tetrahedron Lett., 31 (1990) 7179.
11 K. Sonogashira, Y. Tohda and N. Hagihara, Tetrahedron Lett., (1975) 4467.
12 For example: T. Jeffery, Tetrahedron Lett., 26 (1985) 2667.