Tetrahedron Letters, Vol.32, No.44, pp 6449-6452, 1991
Printed in Great Britain

0040-4039/91 $3.00 + .00
Pergamon Press plc

# A New Pathway to Alkynyl Ketones via Palladium-Catalyzed Carbonylative Coupling of Vinyl Triflates with 1-Alkynes

**Pier Giuseppe Ciattini, Enrico Morera, and Giorgio Ortar***

Dipartimento di Studi Farmaceutici e Centro di Studio per la Chimica del Farmaco del C.N.R.,
Università 'La Sapienza', 00185 Roma, Italy

*Key words: organopalladium; carbonylative coupling; vinyl triflates; 1-alkynes; 1-alken-4-yn-3-ones.*

***Abstract:*** *The palladium-catalyzed coupling reaction of vinyl triflates with 1-alkynes in the presence of carbon monoxide takes place under mild conditions to produce 1-alken-4-yn-3-ones in moderate to good yields.*

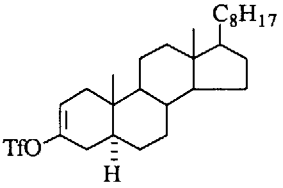
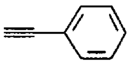
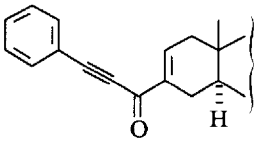
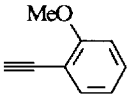
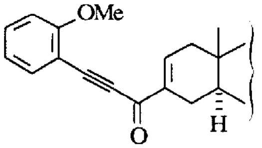
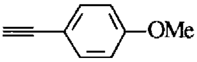
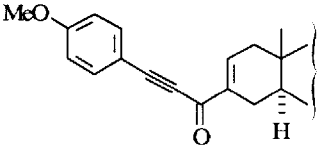
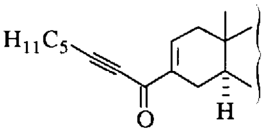
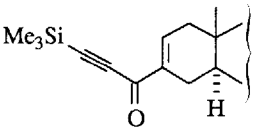
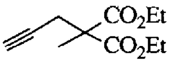
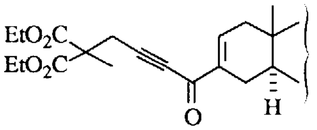
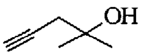
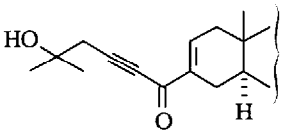
α,β-Acetylenic ketones are not only useful synthetic intermediates, particularly for further elaboration to heterocyclic systems,[1] but also exhibit interesting biological properties.[2] Of the various methods that have been developed for their preparation,[3] the acylation of terminal acetylenes or of metal acetylides has been by far the most common. As concerns in particular procedures involving acylpalladium(II) species as acylating agents, the conversions of aryl and vinyl halides[4] and of acyl chlorides[1c] into 2-alkyn-1-ones by palladium-catalyzed reactions with 1-alkynes and carbon monoxide and with alkynylstannanes, respectively, have been described. Isolated examples of carbonylative couplings of vinyl halides[5a] and triflates[5b] and of aryl halides[5c] and triflates[5d] with alkynylstannanes have been also reported.

We have now found that vinyl triflates react under mild conditions with carbon monoxide and 1-alkynes in the presence of a palladium catalyst to afford 1-alken-4-yn-3-ones in synthetically useful yields.

The results obtained are summarized in the Table. In a typical procedure (entry 1), a mixture of cholest-2-en-3-yl triflate (518 mg, 1 mmol), phenylacetylene (0.132 mL, 1.2 mmol), triethylamine (0.28 mL, 2 mmol), palladium acetate (7 mg, 0.03 mmol), and 1,3-bis(diphenylphosphino)propane (dppp) (14 mg, 0.034 mmol) in DMF (3 mL) was purged with carbon monoxide for 5 min and stirred under a CO balloon at 60°C for 2.5 h. The reaction mixture was then diluted with brine, extracted with ether, washed twice with brine, dried ($Na_2SO_4$), and evaporated. Chromatography of the residue (554 mg) on silica gel (17 g) using hexane/$CH_2Cl_2$ = 6/4 as eluent gave 412 mg (83%) of 1-(cholest-2-en-3-yl)-3-phenylpropyn-1-one: mp 132-134°C (acetone); IR ($CHCl_3$) 2200 (C≡C), 1619 (C=O) $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) δ 0.67 (3H, s, 13-Me), 0.74 (3H, s, 10-Me), 7.36-7.60 (6H, m, C-2 H and aromatics).

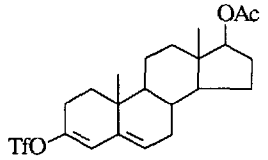
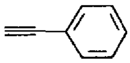
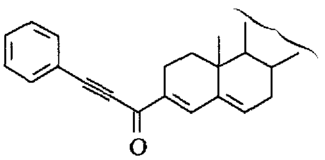
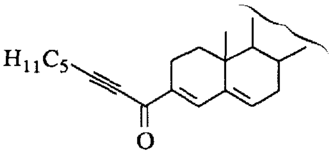
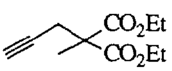
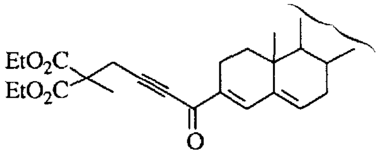
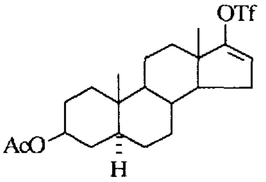
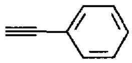
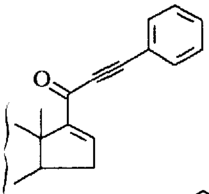
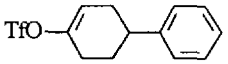
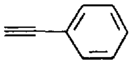
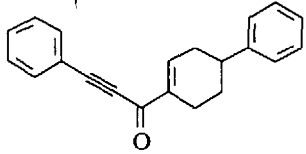
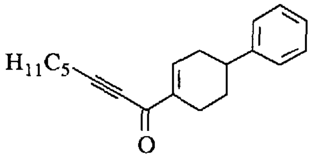
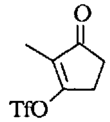
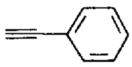
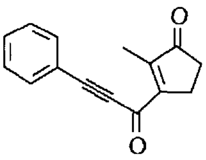
For most vinyl triflates, satisfactory results were obtained by using $Pd(OAc)_2$ (dppp) as the catalytic system. Dppp was found to be a slightly better ligand than 1,1'-bis(diphenylphosphino)ferrocene (dppf) regarding the yield of the alkynyl ketone (compare entries 1 and 2). In any case, the presence of bidentate phos-

Table. Palladium-Catalyzed Carbonylative Coupling of Vinyl Triflates with 1-Alkynes[a]

| Entry | Enol Triflate[b] | 1-Alkyne | Product[c] | Yield[d] (%) |
|---|---|---|---|---|
| 1 |  |  |  | 83 |
| 2 | " | " | " | 73[e] |
| 3 | " |  |  | 80 |
| 4 | " |  |  | 75 |
| 5 | " | ≡—$C_5H_{11}$ |  | 77 |
| 6 | " | ≡—$SiMe_3$ |  | 53[f] |
| 7 | " |  |  | 77 |
| 8 | " |  |  | 75 |

(continued)

Table. (continued)

| Entry | Enol Triflate[b] | 1-Alkyne | Product[c] | Yield[d] (%) |
|---|---|---|---|---|
| 9 |  |  |  | 80 |
| 10 | " | ≡—$C_5H_{11}$ |  | 82 |
| 11 | " |  |  | 74 |
| 12 |  |  |  | 60[g] |
| 13 |  |  |  | 75 |
| 14 | " | ≡—$C_5H_{11}$ |  | 70 |
| 15 |  |  |  | 72 |

---

[a] All reactions were carried out for 2-3 h in the same manner as described in the text, unless otherwise noted. Disappearance of starting material was monitored by TLC. [b] Enol triflates were prepared according to ref. 6. [c] All the products were adequately characterized spectroscopically. [d] Yields of isolated products. [e] Dppf (3.3 mol%) was used as the ligand. [f] Reaction performed at 50°C. [g] Reaction carried out at room temperature in the presence of CuI (1 mol%) as the cocatalyst.

phine ligands was required for achieving a good selectivity for carbonyl-containing products formation. Thus, for istance, the use of $Pd(OAc)_2(PPh_3)_2$ in the carbonylation of cholest-2-en-3-yl triflate with phenylacetylene resulted in extensive formation of the noncarbonylated coupled product (63%) while only a 29% of the desired alkynyl ketone was obtained. Similar observations in regard with the use of the bidentate ligand dppf in the carbonylation of organic halides in the presence of terminal acetylenes have been reported by Tanaka.[4]

The reaction of 3β-acetoxy-5α-androst-16-en-17-yl triflate with phenylacetylene required somewhat different conditions (entry 12). In fact, under standard conditions, the triflate was completely consumed but only a 16% of the expected alkynyl ketone was produced. However, upon addition of 1% mol of CuI and carrying out the reaction at room temperature in order to minimize direct coupling, the alkynyl ketone could be obtained in synthetically useful yield.

The major drawback which we were not able to overcome was the failure to obtain satisfactory results with electron-poor acetylenes such as ethyl propynoate[7] and 3,3-diethoxy-1-propyne.

Attempts to extend our procedure to aryl triflates met with substantial failure as well. Thus, although 2-naphtyl triflate reacted with phenylacetylene under standard conditions to give the carbonylative coupling product in acceptable yield (59%), 4-carbomethoxyphenyl triflate, 4-methoxyphenyl triflate, and 3-triflyloxyestra-1,3,5(10)-trien-17-one were all recovered practically unchanged when reacted as above. Higher reaction temperature and/or the use of CuI as cocatalyst did not lead to substantial improvements.

In conclusion, we have developed an efficient method for the transformation of ketones, via their enol triflates, into 1-alken-4-yn-3-ones. The method merits attention, despite its limitations, due to the use of readily available starting materials and the simplicity and mildness of the experimental procedure.

The reaction pathway is clearly related to that of the carbonylative coupling between organic halides and terminal acetylenes, for which a nucleophilic attack of an acetylide anion on an acylpalladium halide has been proposed by different authors.[8] The mechanistic details of this attack, e.g. Pd attack *vs* CO attack, remain however obscure.

## REFERENCES AND NOTES

1. (a) Sheng, H.; Lin, S.; Huang, Y.Z. *Tetrahedron Lett.* **1986**, *27*, 4893-4894. (b) Cupps, T.L.; Boutin, R.H.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 3972-3979 and references therein. (c) Logue, M.W.; Teng, K. *J. Org. Chem.* **1982**, *47*, 2549-2553 and references therein.
2. Nicolaou, K.C.; Skokotas, G.; Furuya, S.; Suemune, H.; Nicolaou, D.C. *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1064-1067. Jones, E.R.H.; Thaller, V. *The Chemistry of the Carbon-Carbon Triple Bond*; Patai, S. Ed.; Wiley: New York, 1978; Vol. 2, p 631. Metcalf, B.W.; Wright, C.L.; Burkhart, J.P.; Johnston, J.O. *J. Am. Chem. Soc.* **1981**, *103*, 3221-3222.
3. Larock, R.C. *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*; VCH Publisher: New York, 1989; pp 1060-1061.
4. Kobayashi, T.; Tanaka, M. *J. Chem. Soc., Chem. Commun.*, **1981**, 333-334.
5. (a) Goure, W.F.; Wright, M.E.; Davis, P.D.; Labadie, S.S.; Stille, J.K. *J. Am. Chem. Soc.* **1984**, *106*, 6417-6422. (b) Crisp, G.T.; Scott, W.J.; Stille, J.K. *J. Am. Chem. Soc.* **1984**, *106*, 7500-7506. (c) Bumagin, N.A.; Bumagina, I.G.; Kashin, A.N.; Beletskaya, I.P. *Dokl. Akad. Nauk SSSR* **1981**, *261*, 1141-1144. (d) Echavarren, A.M.; Stille, J.K. *J. Am. Chem. Soc.* **1988**, *110*, 1557-1565.
6. Cacchi, S.; Morera, E.; Ortar, G. *Synthesis* **1986**, 320-322.
7. When ethyl propynoate was tried as the alkyne, sodium acetate replaced $Et_3N$ as the base; see ref. 6.
8. Heck, R.F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985; p 359. Hegedus, L.S. *The Chemistry of the Metal-Carbon Bond*; Hartley, F.R.; Patai, S. Eds.; Wiley: New York, 1985; Vol 2, p 431.

(Received in UK 18 July 1991)