

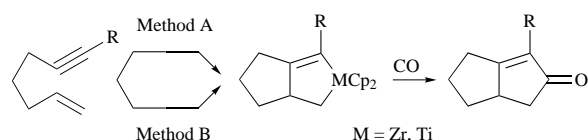
Trapping bicyclic titanacyclopentenones with bis(trichloromethyl) carbonate (BTC): a new method to bicyclic cyclopentenones

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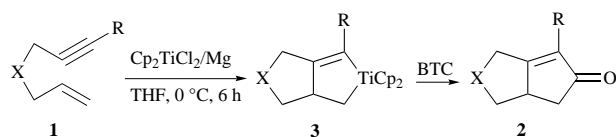
Bis(trichloromethyl) carbonate is found to trap bicyclic titanacyclopentenones providing a new method for bicyclization of enynes into bicyclic cyclopentenones.

The intramolecular Pauson–Khand cyclization of enynes, mediated by $\text{Co}_2(\text{CO})_8$, is one of the most versatile synthetic routes to bicyclic cyclopentenones.¹ In recent years, several modifications, including the dry-state adsorption techniques² and the introduction of additives,³ have been reported. Owing to the importance of this transformation in the synthesis of natural products,⁴ other metal complexes⁵ have also been introduced into this reaction with various results. However, most of those cases need a high pressure of CO atmosphere, elevated temperature, long reaction time and expensive metal complexes. More recently, Negishi,⁶ Buchwald⁷ and their co-workers have reported alternatives using Group IV metallacycles to fulfil this conversion (Scheme 1).



Scheme 1 Method A, Cp_2TiCl_2 , 2 equiv. Bu^nLi , -78°C . Method B, $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$ or Cp_2TiCl_2 , 2 equiv. EtMgCl

In the course of our research on reactions promoted by bis(cyclopentadienyl)titanium dichloride (Cp_2TiCl_2),⁸ we found that bis(trichloromethyl) carbonate (BTC), a stable white crystal which has been recently devoted to introducing a carbonyl group in organic synthesis,^{9,10} was able to trap titanacycles resulting in bicyclic cyclopentenones in lieu of carbon monoxide (Scheme 2). It should be pointed out that **3** can also be



Scheme 2

trapped with isocyanides or trialkylsilyl cyanide, two kinds of CO equivalents, and then hydrolyzed to furnish bicyclic cyclopentenones.¹¹

In an initial attempt, a mixture of 3-phenylprop-2-ynyl allyl ether (**1a**), 1.1 equiv. of Cp_2TiCl_2 and excess amount of activated Mg turnings in dry THF was stirred at 0°C for 6 h to afford the titanacycle.¹² After being treated with 1.5 equiv. of BTC, the desired product was isolated in a yield of 57.5%. However, isolated yields were increased to 75.0% (Table 1, Entry 1) when the reaction was conducted in the presence of 2 equiv. of $\text{P}(\text{OEt})_3$, probably because it can stabilize the key

intermediate **3** generated from Cp_2TiCl_2 and Mg.¹³ Owing to the finding that Mg turnings can slowly react with BTC in THF solution at room temperature, a little excess of BTC is required in our procedure.

The results (see Table 1) demonstrate the generality of this methodology for bicyclization of enynes to the corresponding cyclopentenones (**2a–f**),[‡] although the procedure does not afford good isolated yields in many cases. Substrate **1c**, which contains a 1,2-disubstituted olefin, was also found to afford the corresponding bicyclic product (Entry 3). This result, in a sense, represented another merit of our system, since this kind of enyne did not cyclize using trialkylsilyl cyanide or CO as trapping reagent even in the presence of stoichiometric $\text{Cp}_2\text{Ti}(\text{PMe}_3)_2$.^{11b} An attempt to convert an enyne containing a terminal alkyne, namely **1g**, was proven to be unsuccessful (Entry 7), this outcome was, in principle, consistent with what has been published elsewhere.¹⁴

The present reaction is also interesting from a mechanistic point of view. We found that bubbling phosgene gas for 5 min, instead of adding BTC, to the titanacycles resulting from **1a** affords the desired product in a yield of 56.7%. Thus, it seems that BTC acts as a COCl_2 equivalent. In this way there seems to be similarity in some aspects with the known procedure of the production of heterocycles containing main-group elements from zirconacycles.¹⁵ It should be noted that Cp_2TiCl_2 can be recovered in a yield of about 40% when the reaction mixture was filtered through a short silica gel plug followed by concentration and recrystallization from chloroform. This observation suggested that the titanacycle **3** might abstract two chlorine atoms from BTC, or phosgene generated *in situ*.

In conclusion, we have found a new method to prepare bicyclic cyclopentenones from enynes through the trapping of titanacycles with BTC. Our procedure features a short reaction time, mild reaction conditions and relatively stable starting materials, although BTC is toxic and the yields are moderate in most cases. Now we are continuing to investigate the scope of this kind of reaction and are also interested in the mechanism of the reaction.

[‡] The data for **2a** and **2b** are identical with those presented in the literature. Selected spectroscopic data for **2c**: δ_{H} (300 MHz, CDCl_3) 7.14–7.34 (m, 5H), 4.62 (d, J 15.6, 1H), 4.52 (d, J 15.6, 1H), 4.35 (m, 1H), 3.27–3.38 (m, 3H), 1.82 (s, 3H); MS (EI) 214 (M^+ , 52.8%) (HRMS: calc. for $\text{C}_{14}\text{H}_{14}\text{O}_2$, 214.0993. Found, 214.0990). **2d**: δ_{H} (300 MHz, CDCl_3) 7.20–7.41 (m, 5H), 4.80 (d, J 13.7, 1H), 4.25 (d, J 13.7, 1H), 4.06 (m, 1H), 3.64 (dt, J 1.8 and 12, 1H), 2.93 (m, 1H), 2.75 (dd, J 6.6 and 18.8, 1H), 2.08–2.23 (m, 2H), 1.64 (dq, J 4.4 and 12.2, 1H); MS (EI) 214 (M^+ , 70%) (HRMS: calc. for $\text{C}_{14}\text{H}_{14}\text{O}_2$, 214.0993. Found, 214.1012). **2e**: δ_{H} (300 MHz, CDCl_3) 4.61 (d, J 15.5, 1H), 4.51 (d, J 15.6, 1H), 4.31 (m, 1H), 3.18 (m, 2H), 2.66 (dd, J 5.6 and 17.6, 1H), 2.07–2.30 (m, 3H), 1.21–1.49 (m, 6H), 0.88 (t, J 7, 3H); MS (EI) 195 ($\text{M}^+ + 1$, 100%) (HRMS: calc. for $\text{C}_{12}\text{H}_{18}\text{O}_2$, 194.1306. Found, 194.1291). **2f**: δ_{H} (300 MHz) 7.24–7.58 (m, 5H), 4.14–4.32 (m, 4H), 3.64 (d, J 19.2, 1H), 3.30 (d, J 17.9, 1H), 2.72–2.96 (m, 2H), 2.38–2.62 (m, 1H), 2.30 (dd, J 3.3 and 17.9, 1H), 1.76 (t, J 12.6, 1H), 1.20–1.34 (m, 6H); MS (EI) 343 ($\text{M} + 1$, 100%), 342 (M^+ , 38%) (HRMS: calc. for $\text{C}_{20}\text{H}_{22}\text{O}_5$, 342.1467. Found, 342.1467).

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Table 1 Conversion of Enynes to Bicyclic Cyclopentenones

Entry	Substrate	Product	Isolated yield (%)
1		1a	2a 75.0
2		1b	2b 42.0
3		1c	2c 32.7 ^a
4		1d	2d 30.3
5		1e	2e 37.5
6 ^b		1f	2f 46.7
7		1g	2g 0 ^c

^a Only one diastereoisomer was isolated. ^b E = CO₂Et. ^c The isolated product was cinnamyl alcohol.

Experimental

Typical procedure

Under an argon atmosphere, to a solution of 1,2-dibromoethane (50 µl) in dry THF (0.8 ml) was added well-pestled Mg turnings (5 mmol). After being stirred for 15 min, the solvent was removed at reduced pressure and dry THF (20 ml), Cp₂TiCl₂ (2.2 mmol), the enyne (2 mmol) and P(OEt)₃ (4 mmol) were added. A solution of BTC (2.5 mmol) in dry THF (5 ml) was added dropwise to the mixture after being stirred at 0 °C for 6 h. The mixture was allowed to reach room temperature, stirred for additional 1–3 h and then diluted with diethyl ether (50 ml), washed with water, dried over MgSO₄, concentrated *in vacuo* and chromatographed on silica gel to afford the product.

Acknowledgement

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References

- For reviews, see: (a) N. E. Schore, *Org. React.*, 1991, **40**, 1; (b) N. E. Schore, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, vol. 5, p. 1037. For recent examples of this reaction, see: (c) M. Ahmar, C. Locatelli, D. Colombier and B. Cazes, *Tetrahedron Lett.*, 1997, **38**, 5281; (d) L. Jordi, S. Ricart, J. M. Vinas and J. M. Moretó, *Organometallics*, 1997, **16**, 2808.
- W. A. Smit, S. L. Kireev, O. M. Nefedov and V. A. Tarasov, *Tetrahedron Lett.*, 1989, **30**, 4021.
- (a) Y. K. Chung, B. Y. Lee, N. Jeong, M. Hudecek and P. L. Pauson, *Organometallics*, 1993, **12**, 220; (b) S. Shambayati, W. E. Crowe and S. L. Schreiber, *Tetrahedron Lett.*, 1990, **31**, 5289.
- There are many natural products that have been synthesized using this protocol. For examples, see: (a) T. F. Jamison, S. Shambayati, W. E. Crowe and S. L. Schreiber, *J. Am. Chem. Soc.*, 1994, **116**, 5505; (b) J. Tormo, A. Moyamo, M. A. Pericàs and A. Rieca, *J. Org. Chem.*, 1997, **62**, 4851; (c) E. G. Rowley and N. E. Schore, *J. Org. Chem.*, 1992, **57**, 6853; (d) A. L. Veretenov, D. O. Koltun, W. A. Smit and Y. A. Strelenko, *Tetrahedron Lett.*, 1995, **36**, 4651.
- For Fe, see: (a) B. E. Eaton and B. Rollman, *J. Am. Chem. Soc.*, 1992, **114**, 6245; (b) A. J. Pearson and R. A. Dubbert, *Organometallics*, 1994, **13**, 1656. For Mo and W, see: (c) T. R. Hoye and J. A. Suriano, *J. Am. Chem. Soc.*, 1993, **115**, 1154; (d) T. R. Hoye and J. A. Suriano, *Organometallics*, 1992, **11**, 2044. For Ru, see: (e) T. Kondo, N. Suzuki, T. Okada and T. Mitsudo, *J. Am. Chem. Soc.*, 1997, **119**, 6187. For Ni, see: (f) K. Tamao, K. Kobayashi and Y. Ito, *J. Am. Chem. Soc.*, 1988, **110**, 1286. For Pd, see: (g) N. C. Ihle and C. H. Heathcock, *J. Org. Chem.*, 1993, **58**, 560; (h) W. Oppolzer, *Pure Appl. Chem.*, 1990, **62**, 1941 and references cited therein.
- (a) E. Negishi, S. J. Holmes, J. M. Tour and J. A. Miller, *J. Am. Chem. Soc.*, 1985, **107**, 2568; (b) E. Negishi, S. J. Holmes, J. M. Tour, J. A. Miller, F. E. Cedarbaum, D. R. Swanson and T. Takahashi, *J. Am. Chem. Soc.*, 1989, **111**, 3336.
- (a) F. A. Hicks and S. L. Buchwald, *J. Am. Chem. Soc.*, 1996, **118**, 11 688; (b) N. M. Kablaoui, F. A. Hicks and S. L. Buchwald, *J. Am. Chem. Soc.*, 1997, **119**, 4424.
- (a) Y. Ding, Z. Zhao and C. Zhou, *Tetrahedron*, 1997, **53**, 2899; (b) Y. Ding and G. Zhao, *J. Chem. Soc., Chem. Commun.*, 1992, 941.
- For an extensive review, see: L. Cotarca, P. Delogu, A. Nardelli and V. Sunjić, *Synthesis*, 1996, 553.
- In our initial results, we found one case involving the trapping of diselenotitanacycle with BTC. See: R. Kato, H. Kobayashi and A. Kobayashi, *Synth. Met.*, 1991, **41–43**, 2093.
- (a) R. B. Grossman and S. L. Buchwald, *J. Org. Chem.*, 1992, **57**, 5803; (b) S. C. Beck, R. B. Grossman and S. L. Buchwald, *J. Am. Chem. Soc.*, 1994, **116**, 8593.
- K. Miura, M. Funatsu, H. Saito and A. Hosomi, *Tetrahedron Lett.*, 1996, **37**, 9059.
- Y. Horikawa, M. Watanabe, T. Fujiwara and T. Takeda, *J. Am. Chem. Soc.*, 1997, **119**, 1127.
- (a) T. V. Rajanbabu, W. A. Nugent, D. F. Taber and P. J. Fagan, *J. Am. Chem. Soc.*, 1988, **110**, 7128; (b) 11b.
- (a) P. J. Fagan and W. A. Nugent, *J. Am. Chem. Soc.*, 1988, **110**, 2310; (b) 14a.

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