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$Hg(OTf)_2$-Catalyzed cyclization of alkynyl *tert*-butylcarbonate leading to cyclic enol carbonate

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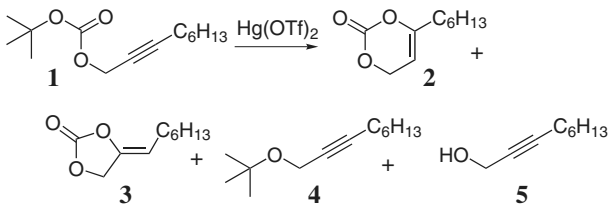
Abstract—Mercuric triflate was shown to be a powerful catalyst for the cyclization of alkynyl *tert*-butylcarbonates giving rise to cyclic enol carbonates under mild conditions. Internal alkynyl carbonate affords *endo* cyclization product selectively, while terminal alkynyl carbonate provides only *exo* cyclization product.

Mercuric triflate was developed in 1983 as an olefin cyclization agent,[1] and its catalytic activities have been recently demonstrated for the hydration of terminal alkynes leading to methyl ketones,[2] the hydroxylative 1,6-enyne cyclization to give exomethylene five-membered ring products,[3] cyclization of 1-alkyn-5-ones leading to 2-methylfurans,[4] arylalkyne cyclization leading to dihydronaphthalene derivatives,[5] biomimetic tandem cyclization of an alkynyl alkenyl aryl derivative to give polycarbocycles,[6] and the reaction of propargyl acetate with water affording vinyl ketones.[7] These reactions likely involve a protodemercuration step of the vinylmercury intermediate, which is induced by in situ-generated TfOH.

We envisioned that $Hg(OTf)_2$-catalyzed cyclizations of alkynyl *tert*-butylcarbonates might provide an attractive and efficient synthesis of cyclic enol carbonates. Although cyclic enol carbonates can serve as useful building blocks, the classical preparation of cyclic enol carbonates by the fixation of CO_2 with propargylic alcohols requires the presence of catalyst under high temperature or high CO_2 pressure.[8] Recently, Buzas and Gagosz demonstrated Au(I)-catalyzed *exo* cyclizations of propargylic *tert*-butyl carbonates to give five-membered ring 4-alkylidene-1,3-dioxolan-2-ones even from an internal alkyne after cationic rearrangement.[9] Therefore, most of the known preparations of cyclic alkylidene carbonates are limited to the formation of five-membered ring compounds. The sole example of a six-membered ring *endo* type enol carbonate was prepared by a multi-step synthetic sequence[10] (Scheme 1).

We have discovered that $Hg(OTf)_2$ induces *endo* cyclization selectively with internal alkynyl carbonates, and only *exo* cyclization with terminal alkynes. We first examined the reaction of an internal alkynyl carbonate, *tert*-butyl-2-nonynyl carbonate (**1**)[11] with 5 mol % of $Hg(OTf)_2$ in acetonitrile at room temperature. An *endo* cyclization product **2** was obtained in 35% yield along with *exo* cyclization product **3** in 3% yield and fragmentation products **4** and **5** in 29% and 14% yields, respectively (Table 1, entry 1). The *Z*-configuration of **3** was confirmed by the NOE experiment. The reaction in toluene, however, afforded **2** in 83% yield along with 5% of **3** (entry 2). Although ether and nitromethane gave lower yields (entries 3 and 4), dichloromethane was found to be the solvent of choice affording **2** in 93% yield after 5 min reaction. *exo* Cyclization product **3** was the only by-product in 4% yield (entry 5).[12] Yields were neither significantly increased nor decreased with varying catalyst loadings (entries 6 and 7). However, 1 mol %



Scheme 1.

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Table 1. $Hg(OTf)_2$-Catalyzed cyclization of **1**

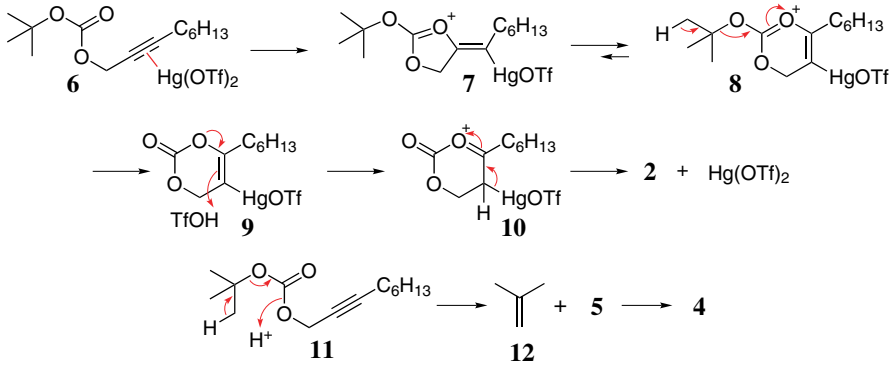
Entry	Solvent	$Hg(OTf)_2$ (mol %)	Time (min)	Yield[a] (%)				
				2	**3**	**4**	**5**	**1**
1	CH_3CN	5	60	35	3	29	14	17
2	$C_6H_5CH_3$	5	5	83	5	—	—	—
3	$(C_2H_5)_2O$	5	15	72	5	—	—	—
4	CH_3NO_2	5	60	58	2	6	2	—
5	CH_2Cl_2	5	5	93	4	—	—	—
6	CH_2Cl_2	10	5	89	4	—	—	—
7	CH_2Cl_2	3	60	77	4	—	—	—
8	CH_2Cl_2	1	60	76	4	11	—	—
9	CH_2Cl_2	1[b]	120	57	3	8	7	15
10	CH_2Cl_2	1[c]	1440	17	1	—	—	69
11	CH_2Cl_2	0.5	60	46	2	11	8	21
12	CH_2Cl_2	5[d]	60	—	—	21	34	43

[a] NMR yield using naphthalene as the internal standard.
[b] Reaction with $Hg(OTf)_2$·TMU.
[c] Reaction with $Hg(OTf)_2$·3TMU.
[d] Reaction with TfOH.

of catalyst was sufficient to consume starting material **1** to give **2** in 76% yield along with significant quantity of fragmentation product **4** (11%) (entry 8). The cyclization catalyzed by $Hg(OTf)_2$·tetramethylurea (hereafter TMU) also afforded larger amounts of fragmentation products **4** and **5** (8% and 7%, respectively), however, $Hg(OTf)_2$·3TMU formed neither **4** nor **5**, and gave rise to **2** in only 17% yield after 24 h with a larger amounts of starting material (entries 9 and 10). The catalyst at 0.5 mol % also produced **4** and **5**, indicating that the fragmentation reaction to give **4** as well as **5** occurred by the contaminated acidic moiety such as TfOH. Probably the reaction using 5 mol % catalyst completes the cyclization before fragmentation. Of course TfOH did not show any catalytic activity for the cyclization but provided fragmentation products **4** and **5** in 21% and 34% yields, respectively, along with 43% of starting material by the reaction in CH_2Cl_2 for 1 h (entry 12).

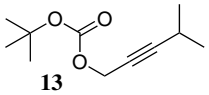
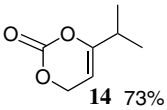
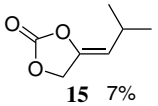
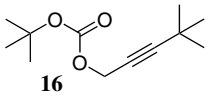
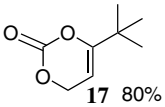
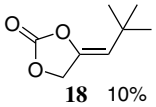
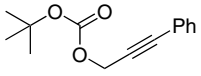
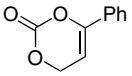
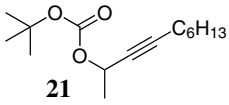
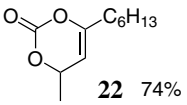
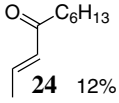
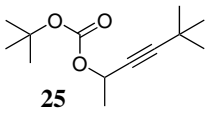
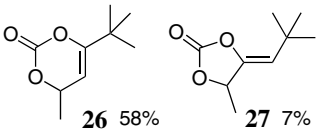
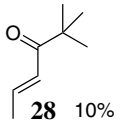
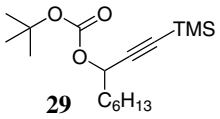
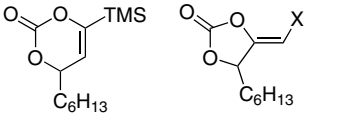
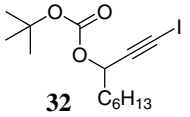
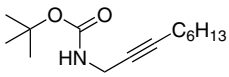
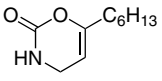
The cyclization of **1** is thought to proceed as shown in Scheme 2. The reaction is initiated by π-complexation of an alkynyl group with $Hg(OTf)_2$ as seen in **6**, followed by the nucleophilic participation of the carbonyl group leading to an equilibrium of *exo* cyclic oxonium cation **7** and *endo* cyclic oxonium cation **8**. Deprotonative fragmentation from the thermodynamically more stable **8** will be the major path and producing vinylmercuric intermediate **9**. The protonation of **9** by in situ-generated TfOH forms the alternative oxonium cation **10** and yields product **2** as well as regenerated catalyst $Hg(OTf)_2$. Fragmentation as seen in **11** results in the formation of 2-nonynol (**5**) along with 2-methylpropene (**12**) and CO_2, and acid mediated coupling of **12** and **5** provides *tert*-butyl ether **4**.

When the standard procedure (5 mol % $Hg(OTf)_2$, CH_2Cl_2) was applied to the reaction of the *tert*-butylcarbonate derivative of 4-methyl-2-pentyn-1-ol (**13**), *endo* cyclization product **14** was obtained in 73% yield along with *exo* cyclization product **15** in 7% yield (Table 2). The 4,4-dimethyl-2-pentyn-1-ol derivative **16** also afforded *endo* cyclization product **17** in 80% yield along with *exo* cyclization product **18** in 10% yield. Phenyl substituted **19** afforded *endo* cyclization product **20** in 72% yield along with a significant quantity of less polar complex mixture, however, occurrence of the corresponding *exo* cyclization product was not detected. Internal alkynyl secondary alcohol derivatives **21** was again converted into *endo* mode cyclization products **22** in 74% yield along with *exo* cyclization product **23** (5%) and the third product **24** in 12% yields. Compound **22** was unstable and decomposed through acidic hydrolysis to



Scheme 2.

Table 2. $Hg(OTf)_2$-Catalyzed cyclization of alkynyl carbonates[a]

Substrate	Time	Product[b]
 **13**	10 min	 **14** 73%  **15** 7%
 **16**	60 min	 **17** 80%  **18** 10%
 **19**	30 min	 **20** 72%
 **21**	10 min	 **22** 74% **23** 5%  **24** 12%
 **25**	30 min	 **26** 58% **27** 7%  **28** 10%
 **29**	15 min	 **30** 20% **31a**: X = TMS **31b**: X = H 64%
 **32**	24 h	No reaction
 **33**	30 min	 **34** 84%

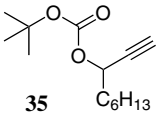
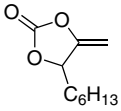
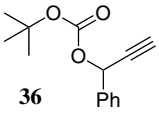
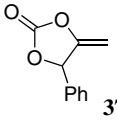
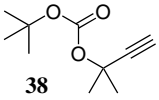
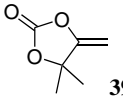
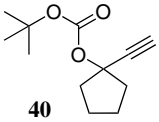
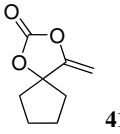
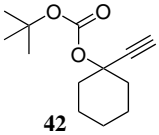
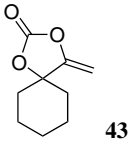
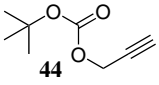
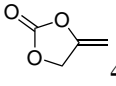
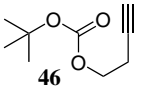
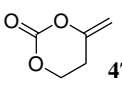
[a] Reaction was carried out using 5 mol % of $Hg(OTf)_2$ in CH_2Cl_2 at room temperature.
[b] NMR yield using naphthalene as the internal standard.

form **24** during column chromatography. *tert*-Butyl substituted alkyne **25** also produced three products **26**–**28** in 58%, 7%, and 10% yield, respectively. The reaction of TMS substituted alkyne **29** afforded a mixture of *endo* cyclization product **30** and *exo* cyclization product **31a**. Since the separation of **30** and **31a** was very difficult and *exo* product **31a** was shown to be unstable against acid, we treated the mixture with 0.8 equiv of TfOH in CH_2Cl_2 at room temperature for 5 min. The TMS group of the *exo* cyclization product **31a** was selectively cleaved to give **31b**, and the separation of **30** and **31b** was easily achieved by a column chromatography on silica gel to give pure **30** and **31b** in 20% and 64% yield, respectively. Iodine substituted alkyne **32** was entirely inert under these condition and starting material was recovered after 24 h. The reaction of nitrogen analog **33** with 5 mol % of $Hg(OTf)_2$ afforded *endo* cyclization product **34** selectively in 84% yield.

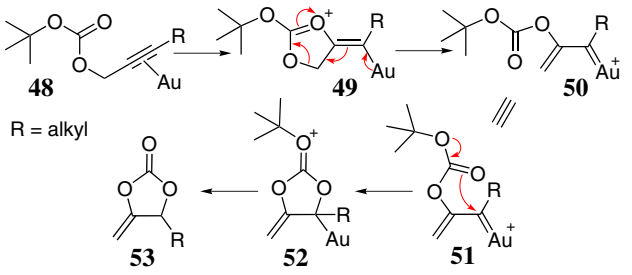
In contrast terminal alkynyl substrates uniformly underwent *exo* cyclizations. For instance, substrate **35** afforded *exo* cyclization product **31b** in a quantitative yield after only after 10 min reaction. The yield was also observably diminished for the corresponding cyclization of 1-phenyl analogue **36** affording **37** in 62% yield with the formation of a complex mixture of less polar products. *tert*-Alcohol derivatives **38**, **40**, and **42** afforded **39** (72% yield), **41** (73% yield), and **43** (94% yield), respectively. The treatment of **44** with 5 mol % of $Hg(OTf)_2$ afforded complex mixtures, however, the reaction with $Hg(OTf)_2{\cdot}3TMU$ with **44** effectively took place in $CDCl_3$ at room temperature.[13] All starting material was consumed after 5 h and the yield of **45** was determined to be 80% by direct NMR experiment. The reaction of 3-butynol derivative **46** with $Hg(OTf)_2{\cdot}3TMU$ in $CDCl_3$ also afforded six-membered ring *exo* cyclization product **47** in 70% yield (Table 3).

Therefore, we have developed $Hg(OTf)_2$- and $Hg(OTf)_2{\cdot}3TMU$-catalyzed cyclization of alkynyl *tert*-butylcarbonate to give *endo* cyclized enol carbonates from internal alkynes and *exo* cyclized products from terminal alkynes in good to excellent yields under mild conditions. The thermodynamic stability of oxonium cation **8** over **7**, which induces *endo* selective cyclization, may be the result of stereoelectronic effects. However, *exo* selective cyclization occurs with terminal alkynes following the Markovnikov rule to lead nucleophilic addition at the more substituted carbon. The Au(I)-catalyzed cyclization of internal alkyne **48** reported by Buzas and Gagosz takes place via *exo* cyclization generating **49**, which rearranges into cationic carbene **50**. A second cyclization from **51** to **52** furnishes *exo* olefin **53** after demetalation. The Au(I)-catalyzed reaction should be directed by carbenoid formation to **50**, whereas the $Hg(OTf)_2$-catalyzed reaction should be controlled by the intensive cationic character of **8** (Scheme 3).

Table 3. $Hg(OTf)_2$-Catalyzed cyclization of alkynyl carbonates[a]

Substrate	Time	Product[b]
 **35**	10 min	 **31b** 99%
 **36**	30 min	 **37** 62%
 **38**	30 min	 **39** 72%
 **40**	5 min	 **41** 73%
 **42**	5 min	 **43** 94%
 **44**	5 h[c]	 **45** 80%
 **46**	2 h[c]	 **47** 70%

[a] Reaction was carried out using 5 mol % of $Hg(OTf)_2$ in CH_2Cl_2 at room temperature.
[b] NMR yield using naphthalene as the internal standard.
[c] Reaction using $Hg(OTf)_2{\cdot}3TMU$ in $CDCl_3$.



Scheme 3.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.09.067.

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11. *tert*-Butyl-2-nonynyl carbonate (**1**) was prepared from 2-nonyny-1-ol by the reaction with NaH and followed by the addition of di-*tert*-butyl dicarbonate in THF at room temperature.
12. Typical experimental procedure is as follows. A stock solution of $Hg(OTf)_2$ in CH_3CN (0.05 M solution, 0.41 mL, 0.02 mmol) was transferred to a two-necked flask under argon atmosphere, and the solvent was replaced with CH_2Cl_2 (1 mL) after the removal of CH_3CN under reduced pressure. To this was added a solution of *tert*-butyl-2-nonynyl carbonate (**1**) (100 mg, 0.41 mmol) in CH_2Cl_2 (0.4 mL) at 0 °C. The solution was stirred for 5 min at room temperature, and the reaction was quenched by the addition of aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2 and dried with magnesium sulfate. The NMR yield of **2** (93%) and **3** (4%) were determined by using naphthalene as the internal standard. Purification of products was achieved by a column chromatography on silica gel (hexane/ethyl acetate 10:1) to give **2** (70 mg, 93%) and **3** (3 mg, 4%).
13. The reactions of **44** (and also **46**) with both $Hg(OTf)_2$·TMU and $Hg(OTf)_2$·2TMU also gave complex mixtures.