Pergamon

Tetrahedron Letters 40 (1999) 1153–1156

TETRAHEDRON
LETTERS

Novel Mercuric Triflate-Catalyzed Condensation of Ketones and Homoallyl Alcohols†

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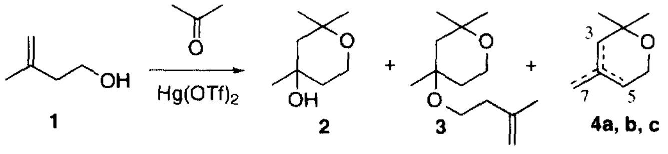
Received 20 October 1998; revised 20 November 1998; accepted 27 November 1998

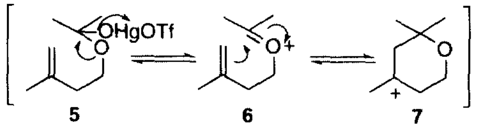
Abstract

Novel condensation of ketones with homoallyl alcohols catalyzed by $Hg(OTf)_2$ has been developed, generating a 6-membered ring ether alcohol, bisether, and olefins. The reaction is initiated by hemiacetal formation, and cyclization of the resulting oxonium cation provides the 6-membered ring carbocation as a common intermediate. Thus, it is a catalytic Prins-type condensation of non-activated homoallyl alcohols and ordinary ketones.

Keywords: Mercury and compounds; Carbonium ions; Condensations; Cyclization.

Mercuric triflate has been developed in this laboratory[1,2] as an efficient olefin cyclization agent and is applied to the synthesis of a variety of polycyclic terpenoids.[3-5] When we examined an intramolecular oxymercuration of olefinic alcohols with $Hg(OTf)_2$, 5-, 6-, and 7-membered ring ethers were formed in high yield; however, the 4-membered ring ether was not obtained.[6] Thus, we investigated the reaction of homoallyl alcohols under various conditions, and a six-membered ring ether alcohol **2** was detected by the reaction of 3-methyl-3-butenol (**1**) with $Hg(OTf)_2$ in acetone via novel hydroxyl migration. Furthermore, we found that a catalytic amount (0.1 equiv.) of $Hg(OTf)_2$ induces a cleaner reaction to give **2** along with a bisether **3** and olefinic products **4a-c**. The reaction should involve a carbonium ion **7** as the common intermediate. Therefore, we would like to describe herein the development of a novel Prins-type condensation of ordinary ketones and non-activated homoallyl alcohols catalyzed by our original mercuric triflate.





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† Dedicated to Professor Ryoji Noyori of Nagoya University on the occasion of his 60th birthday.

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PII: S0040-4039(98)02551-9

Reaction of **1** and Hg(OTf)$_2$ (1.2 equiv.) in acetone at –20 °C afforded ether alcohol **2** (17% yield) along with bisether **3** (7% yield) and a mixture **4a-c** (71% yield) (entry 1). Since regeneration of Hg(OTf)$_2$ was suggested by consideration of the mechanisms, next we examined a catalytic reaction using 0.1 equiv. of Hg(OTf)$_2$ at –20 °C for 2 h (entry 2). The ether alcohol **2** was obtained in 77% yield along with 5% of **3** and 10% of **4a-c**. Upon addition of water (0.5 equiv.), however, the reaction became slower and 13% of the starting material remained even after 48 h and **2** was obtained in 60% yield (entry 3). Then, we investigated the solvent effect using DMF, acetonitrile, dichloromethane, THF, and toluene. Although DMF did not induce any reaction (entry 4), the other solvents gave condensation products slowly and some starting materials remained even after 17 h (entries 5-8). When nitromethane was employed as the solvent, reaction was completed within 2 h affording alcohol **2** in 67% yield (entry 9). Addition of water (0.5 equiv.) to the nitromethane solution also retarded the reaction to give **2** in 52% yield along with 18% of the starting material even after 17 h (entry 10). Using 0.01 equiv. of Hg(OTf)$_2$ (entry 11), slow but clean reaction took place and **2** was obtained in 70% yield along with **3** (12%) and **4** (8%) after 48 h reaction. Limiting the amount of acetone caused an increase in the formation of **3** and the recovery of the starting material (entries 12 and 13). The reaction temperature of -20 °C seems reasonable through comparing entries 9, 14, and 15. When the reaction was carried out in the presence of tetramethylurea (0.1 equiv.), similar reaction took place slowly to give **2**, **3**, and **4a-c** along with 16% of **1** even after 48 h (entry 16).

Table 1

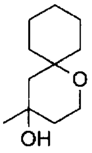
Hg(OTf)$_2$-catalyzed condensation of acetone and 3-methyl-3-butenol (**1**).

Entry	Acetone (equiv.)	Hg(OTf)$_2$ (equiv.)	Solvent	Water (equiv.)	Temp. (°C)	Time (h)	Product (% Yield)[a]			
							2	**3**	**4a-c**	**1**
1	20	1.2	acetone	-	-20	2	17	7	72	0
2	20	0.1	acetone	-	-20	2	77	5	10	0
3	20	0.1	acetone	0.5	-20	48	60	6	7	13
4	10	0.1	DMF	-	-20	17	0	0	0	100
5	10	0.1	acetonitrile	-	-20	17	18	34	5	42
6	10	0.1	dichloromethane	-	-20	17	54	10	17	5
7	10	0.1	THF	-	-20	17	27	12	22	21
8	10	0.1	toluene	-	-20	17	43	22	15	13
9	10	0.1	nitromethane	-	-20	2	67	8	19	0
10	10	0.1	nitromethane	0.5	-20	17	52	7	11	18
11	10	0.01	nitromethane	-	-20	48	70	12	8	4
12	5	0.1	nitromethane	-	-20	17	43	27	16	4
13	1.5	0.1	nitromethane	-	-20	17	17	37	13	27
14	10	0.1	nitromethane	-	0	2	52	13	21	0
15	10	0.1	nitroethane	-	-50	17	31	12	6	21
16	10	0.1[b]	nitromethane	-	-20	48	41	17	10	16

[a] GLC yield using naphthalene as an internal standard. [b] Tetramethylurea (0.1 equiv.) was added.

Since separation of the olefinic products **4a-c** was troublesome due to their volatility, next we examined the Hg(OTf)$_2$ (0.1 equiv.)-catalyzed condensation of **1** with cyclohexanone (5 equiv.) in nitromethane at -20 °C for 1 h, and isolated an ether alcohol **8** in 57% yield along with 3% of **9** and 18% of **10a-c** (7:8:1) after silica gel column chromatography. The olefinic mixture **10a-c** was subjected to HPLC (hexane-ethyl acetate 100:1 using YMC R-Sil-5 column) to give **10a**, and a mixture of **10b** and **10c**. Although the separation of **10b** and **10c** was very difficult, both ^{13}C (150 MHz) and ^{1}H NMR (600 MHz) showed paired signals due to the major **10b** and minor **10c** in 8:1 ratio. Furthermore, GC-MS analysis elucidated that both constituents have nearly identical *m/z*, 166.1369 and 166.1363, respectively, (calcd. for $C_{11}H_{18}O$ 166.1358). Thus, the production of olefinic byproducts was confirmed. Reaction of 3-nonyl-3-butenol (**11**)[7] and acetone (10 equiv.) catalyzed by $Hg(OTf)_2$ (0.1 equiv.) in nitromethane also afforded alcohol **12** (54% yield), bisether **13** (1% yield) and a mixture of olefins **14a-c** (23% yield). Thus, this condensation reaction is shown to be general for ketones and homoallyl alcohols. Since the acetate **15** did not react with acetone under the standard conditions, the reaction should be initiated by a nucleophilic attack of the hydroxyl moiety of **1** to the carbonyl group activated by the chelation with $Hg(OTf)_2$ leading to **5**. The major alcoholic product should be formed via novel migration of the hydroxyl group. Reaction of benzaldehyde with **1** under the standard conditions was not as clean as that of ketone, and alcohol **16** and bisether **17** were isolated in 31% and 8% yield, respectively, along with a complex mixture of less polar products.

Although the $Hg(OTf)_2$-catalyzed condensation of ketones and homoallyl alcohols herein described affords a mixture, the reaction takes place *via* single carbocation and is very simple. When 2-arylethanol **18** was subjected to the reaction with acetone (10 equiv) under the standard conditions, highly selective reaction took place to give **19** in 80% yield along with recovered starting material (15%). The catalyst is not limited to $Hg(OTf)_2$, and similar condensation took place by using triflic acid or BF_3.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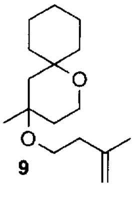
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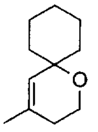
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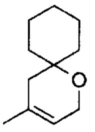
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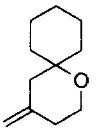
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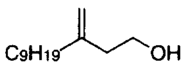
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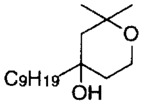
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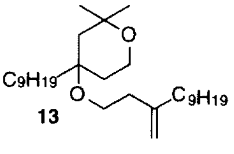
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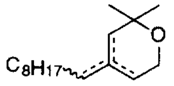
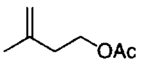

14a, b, c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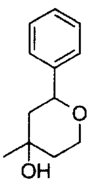
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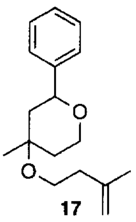
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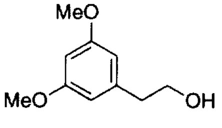
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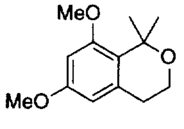
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Lewis acid-promoted condensation of homoallyl alcohols and aldehydes is known as Taddei-Ricci condensation using a stoichiometric amount of Lewis acid that acts as the nucleophile.[8-12] Related allylsilane-iminium salt condensation was reported by Grieco.[13-15] Overman's ring-enlarging tetrahydrofuran annulation,[16] Nokami's allylation of aldehyde with

2-methyl-4-pentene-2-ol catalyzed by $Sn(OTf)_2$ under concomitant loss of the acetone moiety,[17] and Ito's chirality transferred allylsilane cyclization are also C-C bond formations via oxonium cations.[18]

Acknowledgment. This study was financially supported by Japan Private School Promotion Foundation and by the Grant-in-Aid for Scientific Research on Priority Area No. 08245103 from the Ministry of Education, Science, Sports and Culture, of the Japanese Government.

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