Tetrahedron Letters,Vol.27,No.28,pp 3255-3256,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

Total Synthesis of (±)-Baiyunol

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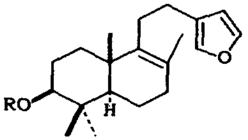
Abstract: On the basis of highly efficient cationic cyclization of 13-oxo-ambliofuran with mercury(II) triflate/N,N-dimethylaniline complex, the first total synthesis of (±)-baiyunol, an aglycon of a sweet substance, is accomplished in a short-step sequence.

Recently we have reported that the cyclizations of ambliofuran (**3a**) and its sulfonyl analog **3b** induced by mercury(II) triflate/N,N-dimethylaniline complex (**2**) show a unique cyclization mode affording a variety of products.[1] Thus, the cyclization of acyclic furano terpenoids must be controlled not only the initiation point but also the termination mode in order to promote the efficient synthesis of (±)-baiyunol (**1a**).[2] The ketone analog **3c** is the best substrate and gives the desired bicyclic ketone **4** in 64% yield. A transformation of the ketone **4** into **1a** is realized via short steps.



1a R = H
1b R = β-glc-^{2}-β-xyl

$Hg(OSO_2CF_3)_2 \cdot C_6H_5N(CH_3)_2$

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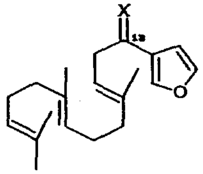
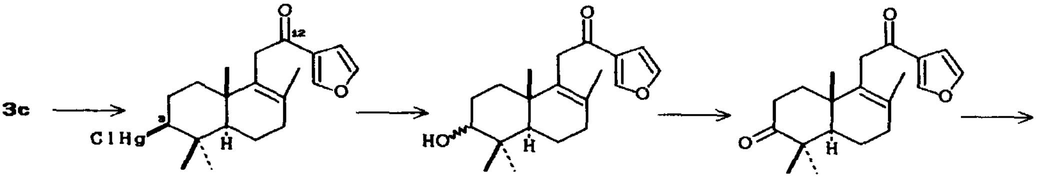
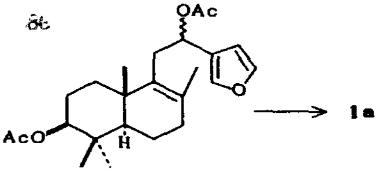


3a X = H_2
3b X = H, $SO_2C_7H_7$
3c X = O
3d X = $S_2C_3H_6$



4 **7** **8**



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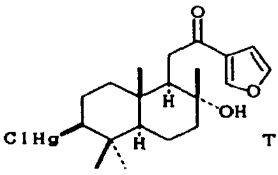

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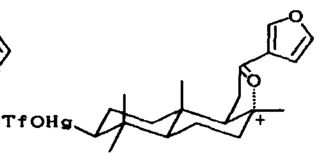

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1,3-Dithiane derivative of 3-furancarboxaldehyde was metalated with lithium diisopropyl amide[3] and treated with (E,E)-farnesyl bromide (-78 ℃, 1.5 h) to give **3d** in 93% yield. Thallium trinitrate-induced hydrolysis of **3d** in methanol and tetrahydrofuran (room temperature for 5 min) afforded 13-oxoambliofuran (**3c**) in 84% yield.[4] On the cyclization of **3c** with **2**, we have observed that quenching conditions of the reaction is very important to control the reaction course. For example, the addition of brine after the reaction period of 1.5 h at -20 ℃ gave the desired ketone **4** in 31% yield along with a hydroxylated product **5** (33%), while the quenching after warming up to 0 ℃ afforded **4** as a major product in 64% yield.[5] These results suggested the intervention of a stable cationic intermediate **6** under the reaction conditions.[6] However, it is still difficult to explain why the proton elimination occurred predominantly at C-9 in **6**. The ketone **4** was subjected to Whitesides' hydroxylation ($NaBH_4/O_2/DMF$)[7] to give a mixture of 3α- and 3β-hydroxylated ketones **7** in 81% yield. The carbonyl moiety at C-12 was entirely inert under the conditions. The mixture **7** was oxidized with Jones reagent to a single diketone **8** (86% yield). Lithium aluminum hydride reduction of **8**, followed by the acetylation, afforded a diastereomeric mixture of diacetates **9** in 93% yield. Upon lithium/ammonia reduction of the mixture **9**, an alcohol **1a** was obtained in 58% yield (conversion yield 100%) via simultaneous cleavage of the acetoxyl moiety at C-12 and the acetyl group at C-3. The spectral properties of **1a** were indistinguishable from those of the authentic (+)-baiyunol derived from baiyunoside (**1b**).

Acknowledgment: We thank Professor O. Tanaka of Hiroshima University for the identification of baiyunol, Professor Y. Tsuda of Kanazawa University for helpful discussion, and Dr. Y. Fujita of Kuraray Co. Ltd. for the kind gift of (E,E)-farnesol.

References and Note

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5. $\Delta^{7,8}$ Isomer was also produced in ca 10% and was removed by recrystallization at the stage of diketone **8**. The stereochemistry of 5 was established by ^{13}C NMR chemical shift analogy with our previous results (ref 1).
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(Received in Japan 1 May 1986)