Tetrahedron Letters,Vol.24,No.25,pp 2581-2584,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

A NEW OLEFIN CYCLIZATION AGENT, MERCURY(II) TRIFLUOROMETHANESULFONATE—AMINE COMPLEX[1]

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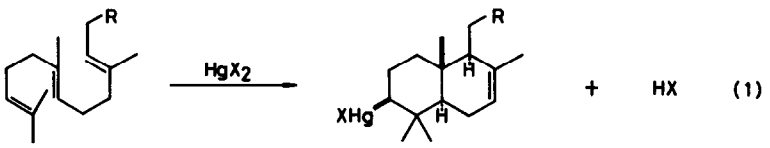
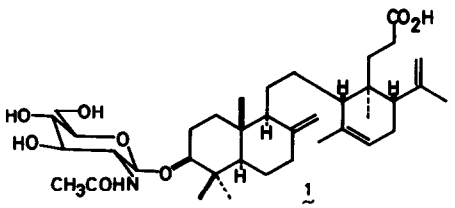
Summary: A new reagent, mercury(II) trifluoromethanesulfonate—amine complex, has been developed for effective cyclization of various farnesol derivatives in good yield and high selectivity.

Olefin cyclization reactions, affording carbocycles, have been intensively studied[2], since it was first reported as a chemical mimic of terpenoid biosynthesis. Of many synthetic applications of this methodology[3], a process initiated by a mercury reagent occupies a particularly important situation because it allows to give functionalized carbocycles (eq 1). However, there has not been recorded any efficient mercury reagent which generally provides cyclized products in high yield and high selectivity[4]. Described herein is the development of a new olefin cyclization agent and its application to the synthesis of (±)-drimenol (22) and (±)-driman-8,11-diol (23).



During the course of our investigation in the total synthesis of lansioside A (1)[5], we have attempted to develop an efficient procedure of this cyclization. After several fruitless efforts[6], we have found a complex 2, mercury(II) trifluoromethanesulfonate—amine[7], shows a remarkable innovation in yield and selectivity for the cyclization of various farnesol derivatives.



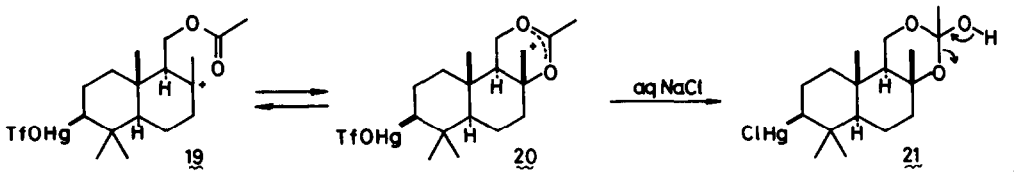
$(CF_3SO_3)_2Hg \cdot amine$

2

When trifluoromethanesulfonic anhydride (188 mg, 0.67 mmol) was added to a suspension of dried yellow mercuric oxide (144 mg, 0.67 mmol) in nitromethane

(10 mL), the yellow color slowly turned to milky white. After 18 h stirring at room temperature, N,N-dimethylaniline (86 mg, 0.71 mmol) was added. The suspension immediately turned to a clear pale yellow solution. The mixture was cooled to -20 °C, and a solution of E,E-farnesyl sulfone 3 (200 mg, 0.56 mmol) in nitromethane (2 mL) was added slowly. After stirring for 2 h at this temperature, an excess of sodium chloride solution was added, and the resulting heterogeneous solution was stirred for an additional 20 h at room temperature. The mixture was acidified with 1N HCl, and extractive workup, followed by silica gel column chromatography, afforded a bicyclic product 4 (249 mg, 74% yield): mp 231-232.5 °C; IR ($CHCl_3$) 3060, 1595, 1310, 1300 cm^{-1}; ^1H NMR (δ, $CDCl_3$) 0.71, 1.04, 1.07 (each 3H, s), 1.68 (3H, br s), 2.24 (3H, s), 2.84 (1H, dd, J = 11, 5 Hz), 3.05 (2H, m), 5.44 (1H, br), 7.30 (2H, d, J = 8 Hz), 7.76 (2H, d, J = 8 Hz), and the exo-isomer 5 (17 mg, 5% yield). The former was the desired intermediate for lansioside synthesis.

As shown in Table I, a variety of farnesol derivatives were converted to cyclization products 9, 11, 16, and 18 in high selectivity under the same conditions. The keto ester 6 afforded only O-cyclization product 7 with the endocyclic double bond[4e]. E,E-Farnesyl acetate (12) behaves in a different manner. A tert-alcohol 13 was produced together with an expected endo-olefin product 14[8]. The generation of 13 is recognized by considering the participation of the neighboring acetyl group, which stabilizes the intermediary tert-cation as shown by 19 and 20[9]. Hydrolysis on the workup stage gave the less crowded primary acetate 13 exclusively via 21. As expected from electronic reason, trichloroacetate 15 did not give such type of a carbinol product.

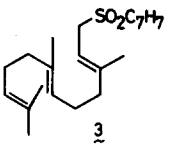
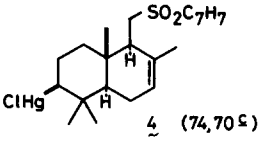
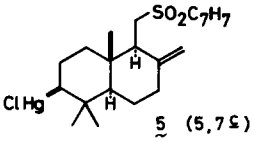
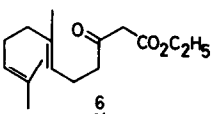
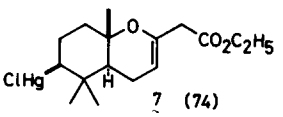
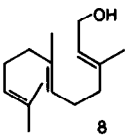
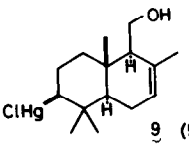
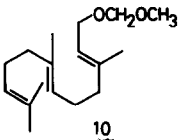
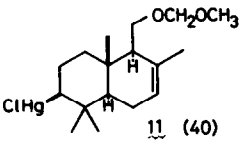
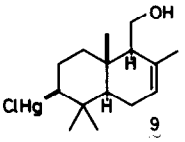
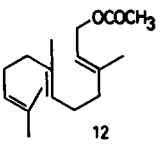
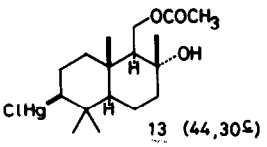
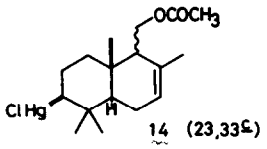
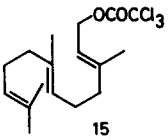
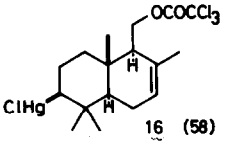
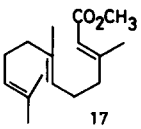
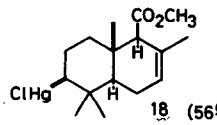


The structures of alcohol 9, methoxymethyl ether 11, trichloroacetate 16, and ester 18 were established by the correlation with known (±)-drimenol (22) via reductive demercuration[4e]. The tert-alcohol 13 was converted to a demercuration product 23, which was identified with (±)-driman-8,11-diol, a sesquiterpene isolated from Greek Nicotiana tabacum[10]. Most of the cyclization products obtained in this study would be very useful intermediates for the synthesis of many natural products. Thus, the mercury moiety of these compounds could be

replaced easily by hydrogen[4e], hydroxyl[11], or bromine[4d] by the reported procedure.

Although the isolation of complex 2 has never been successful, some efforts to the characterization of its structure and the application to other useful olefinic substrates are in progress.

Table I. Cyclization of Farnesol Derivatives with 2[a].

entry	substrate	product (% yield)[b]	
1	 3	 4 (74,70%)	 5 (5,7%)
2	 6	 7 (74)	
3	 8	 9 (51)	
4	 10	 11 (40)	 9 (10)
5	 12	 13 (44,30%)	 14 (23,33%)
6	 15	 16 (58)	
7	 17	 18 (56[d])	

[a] Reactions were conducted at -20 °C for 2 h by using 1.2 equiv of 2 with N,N-dimethylaniline in nitromethane. [b] Isolation yield after column chromatography. [c] Result obtained by using 2 with 2,6-di-tert-butylpyridine. [d] Ca 10% of monocyclic product was included.

Acknowledgment: We are indebted to Professor T. Kato of Tohoku University for the gift of drimenol, Professor C. R. Enzell of Swedish Tabacco Co. for sending the spectral data of driman-8,11-diol, and Dr. Y. Fujita of Kuraray Co. for the gift of pure E,E-farnesol. We also thank, for the financial aids, The Naito Foundation (1981), The Toyota Foundation (1981), and the Grant-in-Aid for Special Project Research of the Ministry of Education, Japanese Government.

REFERENCES AND NOTES

(1) Dedicated to Emeritus Professor Takeo Sakan on the 70th anniversary of birth.

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(4) Mercury(II) trifluoroacetate is recorded to give cyclization products in the following cases. See (a) M. Kurbanov, A. V. Semonovsky, W. A. Smit, L. V. Shmelev, and V. F. Kucherov, Tetrahedron Lett., 2175 (1972). (b) E. J. Corey, M. A. Tius, and J. Das, J. Am. Chem. Soc., 102, 1742, 7612 (1980). (c) C. Sato, S. Ikeda, H. Shirahama, and T. Matsumoto, Tetrahedron Lett., 23, 2099 (1982). (d) T. R. Hoye and M. J. Kurth, J. Org. Chem., 44, 3461 (1979). (e) T. R. Hoye, A. J. Caruso, and M. J. Kurth, ibid., 46, 3550 (1981).

(5) M. Nishizawa, H. Nishide, Y. Hayashi, and S. Kosela, Tetrahedron Lett., 23, 1349 (1982).

(6) Without using the amine, a complicated mixture of products was obtained.

(7) Among the variety of amines examined, N,N-dimethylaniline or 2,6-di-tert-butylpyridine gave much satisfactory result.

(8) Surprisingly, the endo-olefin product 14 was not a single compound. Spectral examinations showed this product to be a stereoisomeric mixture at C-9 (ca 1:1), and the polar isomer was determined to be C-9β product by the correlation with (±)-drimenol. The reason of the generation of the C-9α epimer only in this case is still not obvious.

(9) This type of participation is recognized in the glycosidation reaction of 2-acetoxy sugar derivatives. See H. Tsutsumi and Y. Ishido, J. Syn. Org. Chem. Japan, 38, 473 (1980).

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(Received in Japan 3 March 1983)