CHEMISTRY LETTERS, pp. 455-456, 1978. Published by the Chemical Society of Japan

A SYNTHESIS OF DIASTEREOMERS OF (±)-LABDA-7,14-DIEN-13-OL THROUGH STEREOSPECIFIC CYCLIZATION OF FARNESYL PHENYL SULFONE 1)

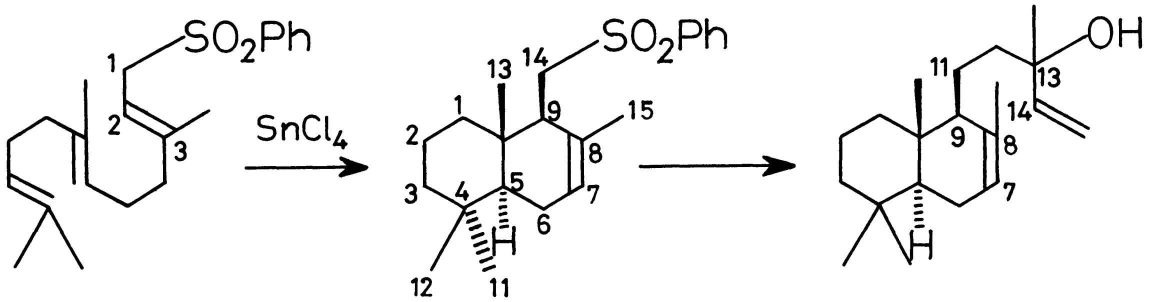
Sigeru TORII,* Kenji UNEYAMA, Ichiro KAWAHARA, and Manabu KUYAMA
Department of Industrial Chemistry, School of Engineering, Okayama University, Okayama 700

The cyclization of farnesyl phenyl sulfone 1 by treatment with $SnCl_4$ in benzene gave a drimane-type compound 2, which was converted to diastereomers of (±)-labda-7,14-dien-13-ol 3.

Transformation of acyclic terpenoids into alicyclic correlates is a current subject for synthetic chemists. The fascinating functional group attached to the terminal of the acyclic isoprenoids should ensure on cyclization in strong acidic media and promise smooth alkylation and versatile functionalization of alicyclic products. Here, we describe a stereospecific cyclization of sulfone 1 into 2 and an efficient conversion of 2a to diastereomers of (±)-labda-7,14-dien-13-ol 3, which has been isolated from *Aster spathulifolius* Maxim. by S. Hayashi. 2), 3)

Thus, the all trans-sulfone 1 was treated with 1 eq. of $SnCl_4$ in dry benzene at room temperature for 32 h affording 2a (77%) after chromatography (SiO_2) as colorless crystals. The isomer 2b on C-9 was not obtained. While, the mixture (2-trans/2-cis = 2.3/1) of 1 provided 2 (80%, 2a/2b = 2.3/1).4) Therefore, the cyclization of 1 was stereospecific.5) Meanwhile, the cyclization seemed to proceed in a stepwise manner *via* the carbonium ion 5 since the monocyclic product 4 was obtained along with 2 when the cyclization was interrupted after 5 h and the conversion of 4 into 2a could be carried out on treatment with $SnCl_4$.

The sulfone 2a was transformed into diastereomers on C-13 of (±)-3. Thus, 2a was treated with BuLi in THF-HMPA (4:1) at -78 °C followed with propylene oxide at 42-45 °C for 8 h providing 6 (90%). Subsequently, the sulfone 6 was reduced with lithium in liquid ammonia affording the alcohol 7 (92%). Oxidation of 7 with pyridinium chlorochromate provided the ketone 8 quantitatively. Finally, the ketone 8 was allowed to react with vinyl magnesium bromide providing

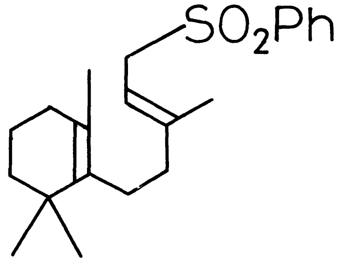


1

2a 9-Hα

2b 9-Hβ

3



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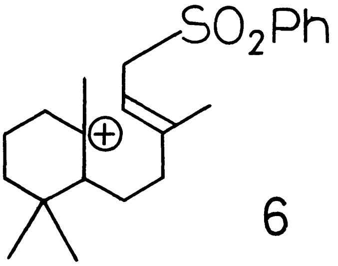

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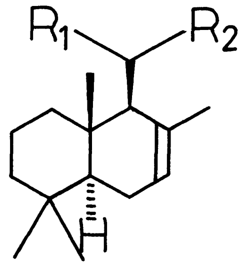

	R_1	R_2
6	$=SO_2Ph$,	$=CH_2CH(OH)CH_3$
7	H	$CH_2CH(OH)CH_3$
8	H	CH_2COCH_3

diastereomers on C-13 of (±)-3 (78%), which was homogeneous in HLC analysis and whose IR and NMR spectra were well consistent with those of the authentic sample.

Acknowledgment The authors are grateful to Professor S. Hayashi and Drs M. Nakayama, A. Matsuo, and Y. Uchio, Department of Chemistry, Hiroshima University for the authentic spectra of 3.

References and Notes

1) Alicyclic Terpenoids from Cyclocitryl Phenyl Sulfides VII. Part VI of the series: S. Torii, K. Uneyama, and M. Kuyama, in contribution.

2) Y. Uchio, A. Matsuo, M. Nakayama, and S. Hayashi, Preprint on the Annual Meeting of the Chemical Society of Japan, Osaka (1977).

3) The compound 3 was also obtained by the base-catalyzed isomerization of manool; R. M. Carman, W. J. Craig, and I. M. Shaw, Aust. J. Chem., 26, 215 (1973).

4) The structures of the compounds 2 were confirmed by PMR, CMR, MS, IR, and elemental analyses along with the conversion of 2a into (±)-3. 2a: mp 111-111.5 °C; IR ($CHCl_3$) 1320, 1151 (SO_2) cm^{-1}; MS m/e 346 (1, M^+), 204 (100, M^+-$PhSO_2H$); PMR ($CDCl_3$) δ 7.98-7.43 (m, 5H, ArH), 5.57-5.40 (m, 1H, CH=), 3.14 (d, 2H, J=4 Hz, CH_2SO_2), 2.73-2.53 (m, 1H, CHC=), 2.1-1.8 (m, 2H, CH_2C=), 1.72 (br s, 3H, Me), 1.6-1.1 (m, 7H, CH_2, CH), 0.85 (s, 6H, Me), 0.68 (s, 3H, Me). 2b: mp 162.5-163 °C; IR ($CHCl_3$) 1316, 1151 (SO_2) cm^{-1}; MS m/e 346 (1, M^+), 204 (100, M^+-$PhSO_2H$); PMR ($CDCl_3$) δ 8.07-7.43 (m, 5H, ArH), 5.38-5.22 (m, 1H, CH=), 3.42 (dd, 1H, J_1=15 Hz, J_2=4 Hz, CH_2SO_2), 2.82 (dd, 1H, J_1=15 Hz, J_2=3 Hz, CH_2SO_2), 2.04 (t, 1H, J=4 Hz, CHC=), 2.0-1.7 (m, 2H, CH_2C=), 1.57 (br s, 3H, Me), 1.6-1.1 (m, 7H, CH_2, CH), 0.96 (s, 3H, Me), 0.88 (s, 3H, Me), 0.82 (s, 3H, Me). The chemical shifts on CMR (PMR) of C-11, C-12, C-13, and C-15 methyls for 2a and 2b which were assigned by selective decoupling method are 32.8 (0.85), 21.6 (0.85), 13.7 (0.68), and 22.0 (1.72) and 32.8 (0.96), 21.7^*(0.88), 21.3^*(0.82), and 22.4 (1.57) ppm from Me_4Si in $CDCl_3$, respectively. The highest field absorption for the protons on C-13 of 2a is due to the shielding effect of phenylsulfonyl group. The β-configuration of phenylsulfonylmethyl group of 2a could be determined by the higher field absorption of C-13 (13.7) and C-14 (54.4) on CMR than those (21.3 and 58.9 for C-13 and C-14, respectively) of 2b.
   * The chemical shifts may be reversed.

5) The farnesic acid was cyclized to bicyclofarnesic acid with formic acid in 10% yield and with BF_3 etherate in 35% yield. A. Caliezi and H. Schinz, Helv. Chim. Acta, 32, 2556 (1949); G. Stork and A. W. Burgstahler, J. Am. Chem. Soc., 77, 5068 (1955); P. A. Stadler, A. Eschenmoser, H. Schinz, and G. Stork, Helv. Chim. Acta, 40, 2191 (1957).

(Received January 23, 1978)