Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2011, **21**, 140–141
Mendeleev Communications

Triethylsilyl triflate-promoted skeletal rearrangement of bottrospicatols

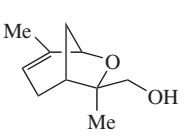
Seda A. Torosyan, Fanuza A. Gimalova, Ruslan F. Valeev and Mansur S. Miftakhov*

Institute of Organic Chemistry, Ufa Scientific Centre of the Russian Academy of Sciences, 450054 Ufa, Russian Federation. Fax: +7 347 235 6066; e-mail: bioreg@anrb.ru

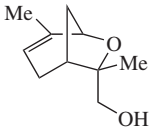
DOI: 10.1016/j.mencom.2011.04.008

Treatment of diastereomeric (1*R*,5*R*,6*R*)- and (1*R*,5*R*,6*S*)-6-hydroxymethyl-2,6-dimethyl-7-oxabicyclo[3.2.1]oct-2-enes with Et_3SiOTf leads to scalemic (1*R*,5*R*,6*R*)- and (1*R*,5*R*,6*S*)-6-hydroxy-2,6-dimethyl-8-oxabicyclo[3.3.1]non-2-enes.

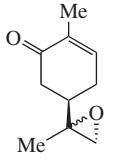
Previously, bottrospicatol **1** and isobottrospicatol **2** were obtained by fermenting of (–)-*cis*-carveol with *Streptomyces* microorganisms.[1–3] Bottrospicatol **1** revealed a strong inhibiting effect on the growth of lettuce and other plant seeds.



1



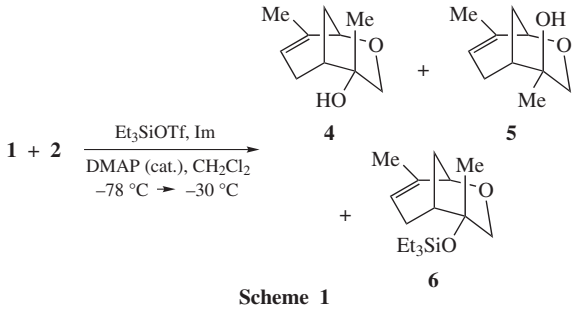
2



3

diastereomeric ratio of ~3:2

We prepared an isomeric mixture of compounds **1** and **2**[4] from (*R*)-(–)-carvone 7,8-epoxide **3**[5] and subjected them to silylation by treatment with the Et_3SiOTf – imidazole (Im)–DMAP (cat.) system.[6] Once the starting compounds **1**+**2** were consumed (TLC), the reaction was stopped and three new products, namely alcohols **4**, **5** and silyl ether **6**, were isolated in an overall yield of 80% (Scheme 1).† The latter compound is obviously formed from alcohol **4**. Upon prolonged storage of the reaction mixture, alcohol **5** is fully converted into its triethylsilyl ether isomeric to ether **6**. Of diastereomeric pairs **4** and **5**, only the all-*R* isomer **4** isolated from *Haplopappus multifolius* essential oil is known.[7] The same compound is also formed in a low yield in zeolite-catalysed reactions of *R*-(+)-citrene diepoxide.[8] The motive force of the entire rearrangement results from lowering of steric and other strains in the reactions **1**+**2** → **4**+**5**.



4 **5** **6**

Scheme 1

A plausible mechanism of conversion of compounds **1** and **2** to compound **5** is outlined in Scheme 2. First, Et_3SiOTf silylates the hydroxy groups of compounds **1** and **2** with evolution of TfOH. This is followed by protonation and opening in the furan

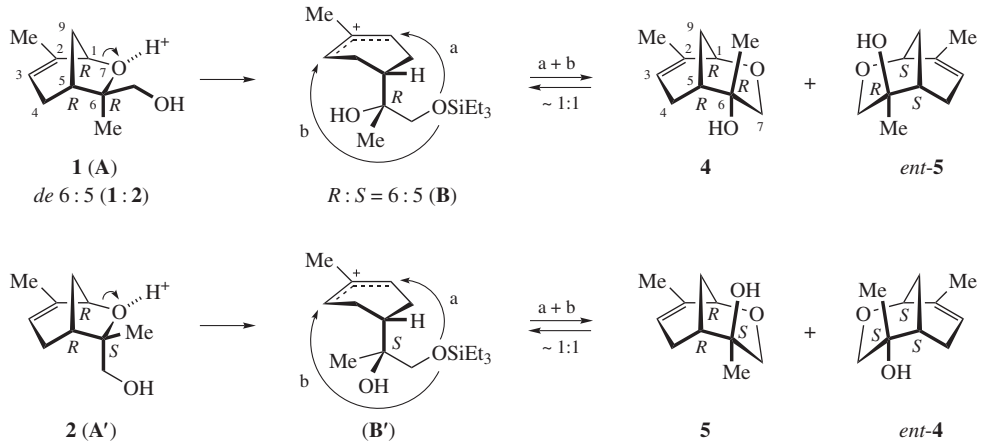
† NMR spectra were recorded on a Bruker AM-300 spectrometer at 300 (^{1}H) and 75.47 MHz (^{13}C), using TMS as the internal standard. IR spectra were recorded on an IR Prestige-21 Fourier Transform Shimadzu spectrophotometer using samples prepared as thin films or dispersed in Nujol. Mass spectra were recorded on a Thermo Finnigan MAT 95XP spectrometer. Optical rotations were measured at 25 °C on a Perkin–Elmer-341 polarimeter. Elementary analyses of the compounds obtained match the calculated values.

Reaction of bicycles **1** *and* **2** *with triethylsilyl triflate*. Triethylsilyl triflate (0.31 g, 1.20 mmol), imidazole (0.10 g, 1.20 mmol) and 4-dimethylaminopyridine (0.01 g) were added to a solution of a mixture of compounds **1**, **2** (~6:5, ^{1}H NMR) (0.1 g, 0.59 mmol) in 10 ml of anhydrous CH_2Cl_2 at –78 °C. The reaction mixture was warmed to –30 °C and stirred at this temperature until the starting compounds were consumed (3 h, TLC monitoring), and quenched by adding several drops of Et_3N. Then the mixture was washed with a saturated NaCl solution; the aqueous layer was extracted with $CHCl_3$, the combined organic layers were dried with $MgSO_4$ and concentrated. The residue was chromatographed in a column [SiO_2, EtOAc–light petroleum (10:3)] to give 0.04 g (24%) of silyl ether **6** and 0.02 g (20%) and 0.03 g (30%) of compounds **4** and **5**, respectively.

*(1*R*,5*R*,6*R*)-2,6-Dimethyl-8-oxabicyclo[3.3.1]non-2-en-6-ol* **4**. Oily compound, $[\alpha]_D^{20}$ +3.5 (*c* 0.33, $CHCl_3$), *ee* 7% {lit.,[8] $[\alpha]_{580}^{20}$ +50 (*c* 0.2, $CHCl_3$)}. IR (ν/cm^{-1}): 3418, 2963, 2928, 2874, 1448, 1435, 1375, 1300, 1263, 1136, 1093, 1072, 1051, 1036, 999, 905, 831. ^{1}H NMR ($CDCl_3$) δ: 1.44 (s, 3H, Me), 1.70 (s, 3H, Me), 1.63 (d, 1H, 9-CH, *J* 12.6 Hz), 1.85 (br.s, 1H) and 2.07–2.15 (m, 2H, CH, CH_2), 2.44 (m, 1H, 4-CH, *J* 19.0 Hz), 3.26 (d, 1H, *J* 10.7 Hz) and 3.43 (d, 1H, OCH_2, *J* 10.5 Hz), 3.95 (br. s, 1H, 1-CH), 5.74 (br. s, 1H, 3-CH). ^{13}C NMR, δ: 21.31 (Me), 27.36 (Me), 26.09 (4-C), 29.52 (9-C), 36.26 (5-C), 67.45 (OCH_2), 69.64 (1-C), 69.69 (6-C), 126.61 (3-C), 129.94 (2-C).

*(1*R*,5*R*,6*S*)-2,6-Dimethyl-8-oxabicyclo[3.3.1]non-2-en-6-ol* **5**. Oily compound, $[\alpha]_D^{20}$ –4.6 (*c* 1.55, $CHCl_3$), *ee* 9.2%. IR (ν/cm^{-1}): 3412, 2960, 2927, 2875, 1446, 1375, 1336, 1259, 1236, 1159, 1126, 1099, 1070, 1049, 1033, 991, 943, 929, 829. ^{1}H NMR ($CDCl_3$) δ: 1.06 (s, 3H, Me), 1.69 (s, 3H, Me), 1.42 (m, 1H, 9-CH), 1.83 (m, 1H), 1.98–2.06 (m, 1H) and 2.22–2.36 (m, 2H, CH, 9-CH, CH_2), 2.77 (s, 1H, OH), 3.32 (d, 1H, *J* 12.1 Hz) and 3.50 (d, 1H, OCH_2, *J* 12.1 Hz), 3.98 (br. s, 1H, 1-CH), 5.67 (br. s, 1H, 3-CH). ^{13}C NMR, δ: 21.43 (Me), 23.32 (Me), 27.62 (4-C), 28.53 (9-C), 35.99 (5-C), 68.20 (OCH_2), 69.85 (1-C), 70.47 (6-C), 125.80 (3-C), 129.78 (2-C). MS, *m*/*z* (%): 168 $[M]^+$ (0.5), 150 $[M-H_2O]^+$ (1), 139 $[M-CHO]^+$ (12), 123 (18), 94 (100), 93 (36), 79 (35), 43 $[MeCO]^+$ (53). Found (%): C, 71.88; H, 9.80. Calc. for $C_{10}H_{16}O_2$ (%): C, 71.39; H, 9.59.

*(1*R*,5*R*,6*R*)-6-(Triethylsilyloxy)-2,6-dimethyl-8-oxabicyclo[3.3.1]non-2-ene* **6**. Oily compound, $[\alpha]_D^{20}$ +12.6 (*c* 4.43, MeOH). ^{1}H NMR ($CDCl_3$) δ: 0.58 (q, 6H, $SiCH_2$, *J* 8.0 Hz), 0.94 (t, 9H, $SiCH_2Me$, *J* 8.0 Hz), 1.44 (s, 3H, Me), 1.70 (s, 3H, Me), 1.60 (m, 1H), 1.80 (m, 1H) and 1.95–2.10 (m, 2H, CH, CH_2), 2.50 (d, 1H, 9-CH, *J* 19.0 Hz), 3.20 (d, 1H, *J* 11.0 Hz) and 3.40 (d, 1H, OCH_2, *J* 11.0 Hz), 3.90 (br. s, 1H, 1-CH), 5.57 (br. s, 1H, 3-CH). ^{13}C NMR, δ: 6.88 ($SiCH_2$), 7.06 ($SiCH_2Me$), 21.41 (Me), 26.76 (Me), 26.38 (4-C), 29.43 (9-C), 37.04 (5-C), 68.10 (OCH_2), 69.74 (1-C), 72.39 (6-C), 127.11 (3-C), 129.59 (2-C). Found (%): C, 68.68; H, 10.59; Si, 10.31. Calc. for $C_{16}H_{30}O_2Si$ (%): C, 68.03; H, 10.70; Si, 9.94.



Scheme 2

part of bicycles **A** and **A′** promoted by the acidic agents (TfOH, $[Im–SiEt_3(H)]^+TfO^-$, *etc.*) to give delocalised carbocations **B** and **B′**, which are stabilised by cyclisations involving the electron-donating O atoms of the siloxy moieties (see pathways a and b), these epimeric cations **B** and **B′** producing diastereomeric alcohols **5** + *ent*-**6** and **6** + *ent*-**5**, respectively. The resulting alcohols **5** and **6** are the mixtures of enantiomers the ratios of which approximately matches those in the starting mixture of diastereomeric alcohols being **1** : **2** = 6 : 5.

In conclusion, the ring expansion of natural monoterpenoids **1** and **2** can find synthetic application, while rearrangement products **4** and **5** may be of interest for biological studies.

We are grateful to Professor K. K. Pivnitsky (N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Moscow) for his valuable comments on the mechanistic concept of the rearrangements in question.

References

1 Y. Noma and H. Nishimura, *Agric. Biol. Chem.*, 1987, **51**, 1845.
2 H. Nishimura and Y. Noma, in *Biotechnology for Improved Food and Flavors*, ACS, Washington, DC, 1996, vol. 637, ch. 16, pp. 173–187.
3 H. Nishimura, Sh. Hiramoto, J. Mizutani, Y. Noma, A. Furusaki and T. Matsumoto, *Agric. Biol. Chem.*, 1983, **47**, 2697.
4 J. E. Baldwin and B. M. Broline, *J. Am. Chem. Soc.*, 1982, **104**, 2857.
5 (*a*) S. A. Torosyan, F. A. Gimalova, R. F. Valeev and M. S. Miftakhov, *Zh. Org. Khim.*, 2011 (in press); (*b*) O. Smitt and H.-E. Högberg, *Tetrahedron*, 2002, **58**, 7691.
6 C. H. Heatcock, S. D. Vong, J. P. Hagen, R. Pilli and U. Badertcher, *J. Org. Chem.*, 1985, **50**, 2095.
7 G. T. Maatooq, A. A. Gohar and J. J. Hoffmann, *Pharmazie*, 2002, **57**, 282.
8 O. V. Salomatina, O. I. Yarovaya, D. V. Korchagina, M. P. Polovinka and V. A. Barkhash, *Mendeleev Commun.*, 2005, 59.

Received: 30th December 2010; Com. 10/3653