Pergamon

Tetrahedron: Asymmetry Vol. 6, No. 2, pp. 375-376, 1995
Elsevier Science Ltd
Printed in Great Britain
0957-4166/95 $9.50+0.00

0957-4166(95)00017-8

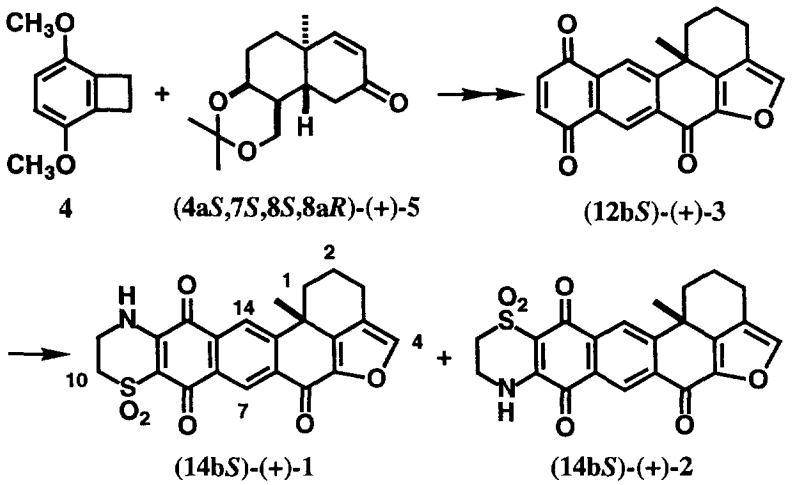
Synthesis and Absolute Stereochemistry of (+)-Adociaquinones A and B

Nobuyuki Harada,*[a] Tatsuo Sugioka,[a,b] Tomomi Soutome,[b] Norie Hiyoshi,[a] Hisashi Uda,[a] and Takeo Kuriki[b]

[a] Institute for Chemical Reaction Science, Tohoku University, 2-1-1 Katahira, Aoba, Sendai 980-77, Japan
[b] Pharma Research Laboratory, Hoechst Japan Ltd., 1-3-2 Minamidai, Kawagoe, Saitama 350, Japan

Abstract: Adiciaquinones A (+)-**1** and B (+)-**2** were synthesized and their absolute configurations were determined to be (14b*S*).

A series of quinone and hydroquinone compounds of the halenaquinol family have been isolated from tropical marine sponges as biologically active natural products: antibiotics, cardiotonic and cytotoxic constituents, etc. Schmitz and his co-worker isolated adociaquinones A (+)-(**1**) and B (+)-(**2**) from a sponge *Adocia sp.* collected in Truk Lagoon, together with halenaquinone and xestoquinone **3**.[1] Compounds **1** and **2** are unique in their 1,4-thioaza heterocyclic structures. However, the absolute configurations of these heterocyclic compounds have remained undetermined. The absolute stereochemistry of halenaquinone and xestoquinone compounds had already been determined by us by the theoretical calculation of the CD spectra.[2] We had also proven that the absolute configurations theoretically determined were correct by achieving the first total synthesis of (+)-halenaquinone, (+)-halenaquinol,[3] xestoquinol, (+)-xestoquinone **3**,[4] and (-)-prehalenaquinone[5] in natural enantiomeric forms (Scheme 1). As an extension of our synthetic project, we report here the synthesis and absolute stereochemistry of adociaquinones A (+)-**1** and B (+)-**2**.



4 **(4a*S*,7*S*,8*S*,8a*R*)-(+)-5** **(12b*S*)-(+)-3**

(14b*S*)-(+)-1 **(14b*S*)-(+)-2**

Scheme 1. Synthetic Route of Adociaquinones A (+)-**1** and B (+)-**2**.

According to the procedure reported by Schmitz,[1] the synthetic sample[4,5] of xestoquinone (12b*S*)-(+)-**3** was converted to adociaquinones A and B. To a solution of **3** in ethanol/acetonitrile/water was added hypo-

taurine (1.5 eq), and the reaction mixture was stirred at 40 °C for 1.5 h, during which time fine yellow crystals appeared and additional hypotaurine (1.5 eq) was added at every 30 min. The crude product obtained was separated by preparative HPLC on silica gel ($CHCl_3$/MeOH 9:1) yielding adociaquinone A (+)-**1** (17%) as yellow crystals:[6] $[\alpha]_D^{20}$ +70 (*c* 0.107, $CHCl_3$/MeOH 2:1); ref[1,8] $[\alpha]_D$ +25 (*c* 0.075, DMSO). From more polar fractions, adociaquinone B (+)-**2** (59%) was obtained as yellow crystals:[7] $[\alpha]_D^{20}$ +74 (*c* 0.0668, $CHCl_3$/MeOH 2:1), ref[1,8] $[\alpha]_D$ +22 (*c* 0.085, DMSO). Since the CD spectral data of the synthetic and natural samples agreed with each other, the absolute configurations of adociaquinones A (+)-**1** and B (+)-**2** were determined to be (14b*S*).[6,7,9]

Acknowledgment. This work was supported in part by grants from the Ministry of Education, Science, and Culture, Japan (General (B) No. 01470026, Priority Areas Nos. 02250103, 03236101, 04220101, and 06240204, and International Joint Research No. 02044014 to N.H.).

References and Notes

1. Schmitz, F. J.; Bloor, S. J. *J. Org. Chem.* **1988**, *53*, 3922.
2. Kobayashi, M.; Shimizu, N.; Kitagawa, I.; Kyogoku, Y.; Harada, N.; Uda, H. *Tetrahedron Lett.* **1985**, *26*, 3833. Harada, N.; Uda, H.; Kobayashi, M.; Shimizu, N.; Kitagawa, I. *J. Am. Chem. Soc.* **1989**, *111*, 5668.
3. Harada, N.; Sugioka, T.; Ando, Y.; Uda, H.; Kuriki, T. *J. Am. Chem. Soc.* **1988**, *110*, 8483.
4. Harada, N.; Sugioka, T.; Uda, H.; Kuriki, T. *J. Org. Chem.* **1990**, *55*, 3158.
5. Harada, N.; Sugioka, T.; Uda, H.; Kuriki, T.; Kobayashi, M.; Kitagawa, I. *J. Org. Chem.* **1994**, *59*, 6606.
6. (+)-**1**: mp > 300 °C (decomposed); TLC (silica gel, $CHCl_3$/MeOH 9:1) R_f = 0.53; IR (KBr) ν_{max} 3269, 2942, 1674, 1639, 1591, 1552, 1446, 1327, 1213, 1147, 1124, 1045, 748, 441 cm^{-1}; ^1H NMR (500.0 MHz, DMSO-d_6) δ 1.499 (3 H, s, 14b-CH_3), 1.658 (1 H, ddd, J = 12.9, 12.9, 4.2 Hz, 1ax-H), 2.080 (1 H, m, 2-H), 2.230 (1 H, m, 2-H), 2.559-2.630 (2 H, m, 1eq- and 3ax-H), 2.843 (1 H, dd, J = 17.4, 8.2 Hz, 3eq-H), 3.403 (2 H, t, J = 6.0 Hz, 10-H), 3.887 (2 H, br s, 11-H), 8.002 (1 H, s, 4-H), 8.266 (1 H, s, 14-H), 8.691 (1 H, s, 7-H), 9.340 (1 H, br s, 12-H); UV (MeOH) λ_{max} 416.6 nm (ε 2,500), 302.0 (23,000), 243.4 (18,500); CD (MeOH) λ_{ext} 401.0 nm (Δε +1.9), 339.0 (–4.4), 302.8 (+4.5), 277.5 (–1.1), 242.5 (–8.3); MS (FD) *m/z* 423 (parent, relative intensity 100%), 446 ($(M+Na)^+$, 82).
7. (+)-**2**: mp > 300 °C (decomposed); TLC (silica gel, $CHCl_3$/MeOH 9:1) R_f = 0.47; IR (KBr) ν_{max} 3273, 2950, 1673, 1587, 1551, 1446, 1332, 1307, 1288, 1209, 1157, 1030, 1028, 750 cm^{-1}; ^1H NMR (500.0 MHz, DMSO-d_6) δ 1.500 (3 H, s, 14b-CH_3), 1.631 (1 H, ddd, J = 12.8, 12.8, 4.2 Hz, 1ax-H), 2.067 (1 H, m, 2-H), 2.210 (1 H, m, 2-H), 2.587 (1 H, dd, J = 16.9, 9.0 Hz, 3ax-H), 2.648 (1 H, ddd, J = 12.8, 3.0, 3.0 Hz, 1eq-H), 2.842 (1 H, dd, J = 16.9, 7.7 Hz, 3eq-H), 3.883 (2 H, t, J = 5.9 Hz, 10-H), 7.997 (1 H, s, 4-H), 8.278 (1 H, s, 14-H), 8.719 (1 H, s, 7-H), 8.90 (1 H, br s, 9-H). The signal of 11-H around δ 3.40 ppm was buried in the peak of water contained in the solvent; ^{13}C NMR (125.7 MHz, DMSO-d_6) δ 16.19, 17.76, 30.35, 31.61, 36.83, 48.29, 111.42, 121.62, 123.39, 124.77, 130.91, 131.77, 137.95, 143.08, 146.14, 147.09, 147.88, 154.60, 169.36, 173.69, 178.34. The one carbon signal around δ 40 ppm was buried in the peak of the solvent; UV (MeOH) λ_{max} 417.0 nm (ε 2,100), 347.6 (10,400), 292.2 (28,700), 278.0 (26,600), 222.4 (18,600); CD (MeOH) λ_{ext} 413.0 nm (Δε +2.3), 345.0 (–4.3), 301.0 (+2.9), 281.5 (+6.9), 261.0 (–4.6), 245.0 (–7.3); MS (FD) *m/z* 423 (parent, relative intensity 100%), 446 ($(M+Na)^+$, 21).
8. Prof. F. J. Schmitz, Oklahoma University, kindly informed us of the solvent and concentration used.
9. The natural sample of (+)-**1**, CD (MeOH) λ_{ext} 398.7 nm (Δε +1.8), 337.3 (–3.5), 303.6 (+4.0), 277.2 (–1.2), 243.2 (–6.6); the natural sample of (+)-**2**, CD (MeOH) λ_{ext} 414.2 nm (Δε +2.0), 345.6 (–4.0), 303.2 (+2.8), 282.2 (+6.3), 258.3 (–4.0), 239.0 (–6.7). The authors thank Prof. F. J. Schmitz, Oklahoma University, for a generous gift of the natural samples of (+)-**1** and (+)-**2**.

(*Received in Japan* 7 *December* 1994)