Bioscience, Biotechnology, and Biochemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/tbbb20

Enantioselective Synthesis of Ancepsenolide and its Analogs

Katsuki TAKAI[a] & Ryozo IRIYE[a]
[a] Department of Bioscience and Biotechnology, Faculty of Agriculture, Shinshu University (United Graduate School of Gifu University)
Published online: 22 May 2014.

To cite this article: Katsuki TAKAI & Ryozo IRIYE (2001) Enantioselective Synthesis of Ancepsenolide and its Analogs, Bioscience, Biotechnology, and Biochemistry, 65:8, 1903-1906, DOI: 10.1271/bbb.65.1903

To link to this article: http://dx.doi.org/10.1271/bbb.65.1903

Biosci. Biotechnol. Biochem., **65** (8), 1903–1906, 2001

Note

Enantioselective Synthesis of Ancepsenolide and its Analogs

Katsuki TAKAI and Ryozo IRIYE†

Department of Bioscience and Biotechnology, Faculty of Agriculture, Shinshu University (United Graduate School of Gifu University), 8304 Minamiminowa, Kamiina, Nagano 399-4598, Japan

Received February 2, 2001; Accepted March 12, 2001

Ancepsenolide (1a-s) and the enantiomer (1a-r) were respectively synthesized from (*S*)- and (*R*)-2-[(*R*)-*O*-MEM-mandeloyloxy]propanal (3a-s and 3a-r) and diisopropyl hexadecanedioate (5). The analogs (1b, 2a and 2b) were synthesized by a similar method.

Key words: ancepsenolide; aldol reaction; optical resolution; butenolide

Novel lipids with one or two butenolide moieties have been isolated from gorgonians.[1-6] Although they are considered to be defense substances of these organisms,[1,6,7] their activity is not clear. Ancepsenolide (**1a-s**) is one component and has been isolated from *Pterogorgia anceps*,[1-3] *P. citrina*[5] and *P. guadalupensis*.[6] Ancepsenolide (**1a-r**) has two (*S*)-4-methyl-2-buten-4-olide moieties at both terminal positions of dodecane (see the Scheme). The presence of a butenolide moiety with (*S*)-configuration relates it to Annonaceous acetogenins[7-10] in structural classification. Many acetogenins are known for their potent biological activities as cytotoxic, antitumorial, antimalarial, microbicidal, immunosuppressive, antifeeding and pesticidal substances, and their (*S*)-4-methyl-2-buten-4-olide group has been reported to be important for these activities.[7-11] Although many papers on the synthesis of ancepsenolide (**1a-s**) have been published,[12,13] a simple synthesis was investigated in order to elucidate the biological activity of ancepsenolide (**1a-s**) and related compounds. We have already reported that the γ-acyloxy-β-hydroxy carbonyl moiety obtained by aldol reaction could be transformed into a γ-hydroxy-α,β-unsaturated carbonyl moiety by treating with AcONa.[14-16] A modification of this method was used to synthesize the (*R*,*R*)- and (*S*,*S*)-forms of ancepsenolide (**1a**) and its derivatives (**1b**, **2a** and **2b**).

The starting compound, (*S*)-(−)-2-[(*R*)-*O*-MEM-mandeloyloxy]propanal (**3a-s**), was prepared with sodium (*R*)-*O*-MEM-mandelate by the methods described previously.[15,16] Aldehyde **3a-s** was treated with the dienolate of diisopropyl hexadecanedioate (**5**) to form the hydroxyester (**7a-s**). Hydroxyester **7a-s** was transformed into **8a-s** by treating with AcONa (44% yield), since **7a-s** was unstable. **8a-s** was transformed into (*S*,*S*)-ancepsenolide (**1a-s**) by treating with NaH,[17] and then by successive purification by TLC and recrystallization (24% yield). Similarly, the (*R*,*R*)-form compound (**1a-r**) was synthesized from **3a-r** and **5** in a 13% yield.

(*R*,*R*)- and (*S*,*S*)-bis-4-pentyl-2-buten-4-olide derivatives with a dodecamethylene (**1b-r** and **1b-s**) were respectively prepared from the aldehydes (**3b-r** and **3b-s**) and **5** *via* **7b-r** and **7b-s**, and respectively transformed to **8b-r** and **8b-s** in 36.9% and 49.7% yields.

(*R*,*R*)- and (*S*,*S*)-bis-4-methyl-2-buten-4-olide derivatives with an octamethylene (**2a-r** and **2a-s**) were similarly synthesized from the respective aldehydes (**3a-r** and **3a-s**) and diisopropyl dodecanedioate (**6**) *via* **9a-r** and **9a-s** and then transformed into **10a-r** and **10a-s**.

(*R*,*R*)- and (*S*,*S*)-4-pentyl-2-buten-4-olide derivatives with an octamethylene (**2b-r** and **2b-s**) were also respectively synthesized from **3b-r** and **3b-s**, and **6** in a similar manner described above (see the Scheme).

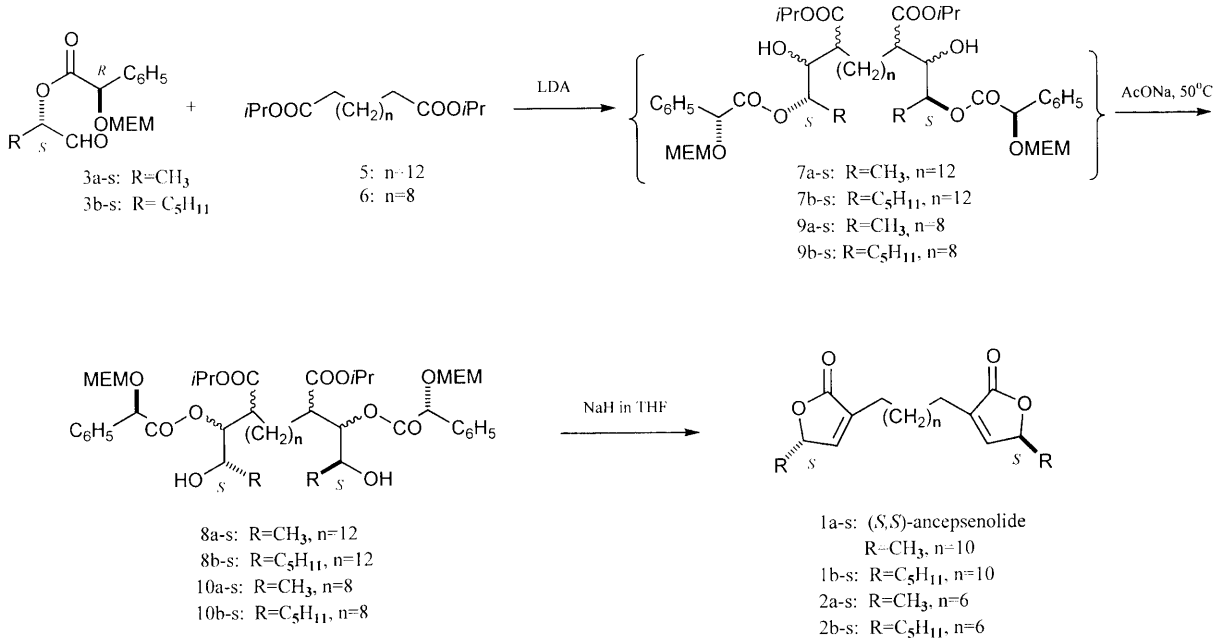
Experimental

NMR spectra were measured with a Bruker DRX-500 spectrometer (^{1}H at 500.13 MHz, ^{13}C at 125.77 MHz) with the Bruker pulse program and TMS as an internal standard. Mass spectra were taken with a JEOL JMS-700 spectrometer using the JEOL data processing system, and optical rotation was measured with a JASCO DIP-1000 polarimeter. NMR spectral data resulting from similar structures and protective groups are not repeatedly described.

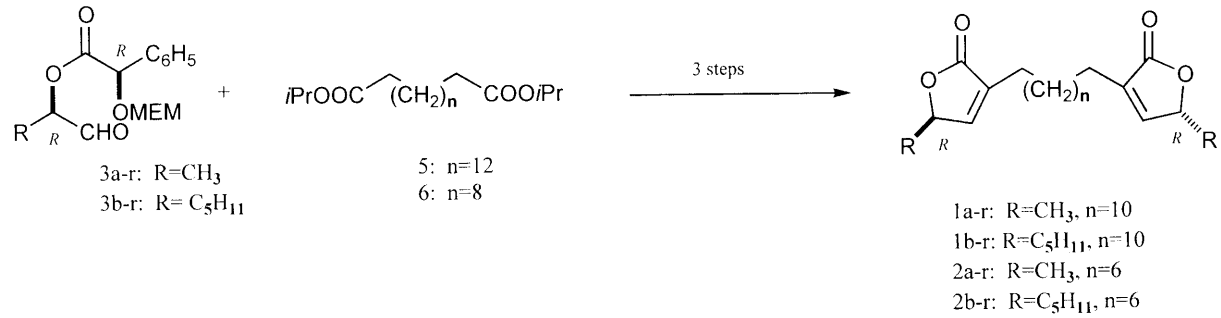
(R)-(−)- and (S)-(−)-2-[(R)-O-MEM-mandeloyloxy]alkanal (3a-r and 3a-s, and 3b-r and 3b-s). (*R*)-(−)- and (*S*)-(−)-2-[(*R*)-*O*-MEM-mandeloylox-

† To whom correspondence should be addressed. Tel: +81-265-77-1604; Fax: +81-265-77-1629; E-mail: kn53278@gipmc.shinshu-u.ac.jp

Abbreviations: MEM, 2-methoxyethoxymethyl; AcONa, sodium acetate; DMF, *N*,*N*-dimethylformamide; HMPA, hexamethylphosphoric triamide



Scheme a



Scheme b

y]alkanal (**3a-r** and **3a-s**, and **3b-r** and **3b-s**) were prepared by the method described previously.[15,16] The mixture of **3a-r** and **3a-s** was prepared by adding an ether solution of an excess amount of 2-bromopropanal to a suspension of sodium (*R*)-*O*-MEM-mandelate in DMF and HMPA.

(*R*)-(−)-2-[(*R*)-*O*-MEM-mandeloyloxy]propanal (**3a-r**): 10.3% yield, $[\alpha]_D = -52.5°$, *c* 0.10 (EtOH). **3a-s**: 9.1% yield, $[\alpha]_D = -72.8°$, *c* 0.10 (EtOH). **3a-r** was separated with a flash column (silica gel, hexane:EtOAc = 4:1), and **3a-s**, by preparative TLC (hexane:EtOAc = 5:3, 5 developments) from the residual mixture. **3a-r**: NMR δ_H ($CDCl_3$): 1.39 (3H, d, J = 7.2 Hz, CH_3), 3.37 (3H, s, MEM), 3.45–3.57 (2H, m, MEM), 3.69 (1H, ddd, J = 3.7, 5.5, 11.2 Hz, MEM), 3.81 (1H, ddd, J = 3.7, 5.5, 11.0 Hz, MEM), 4.81 (1H, d, J = 7.1 Hz, MEM), 4.90 (1H, d, J = 7.1 Hz, MEM), 5.09 (1H, q, J = 7.1 Hz, CH), 5.32 (1H, s, CH), 7.28–7.43 (3H, m, Ph), 7.49 (2H, d, J = 7.2 Hz, Ph), 9.33 (1H, s, CHO). NMR δ_C: 14.20, 58.98, 67.63, 71.64, 75.21, 94.23, 127.49, 128.77, 128.99, 135.80, 170.39, 197.94. HR-MS *m/z*: calcd. for $C_{15}H_{20}O_6$ (M^+), 296.1260; found, 296.1243. **3a-s**: NMR δ_H ($CDCl_3$): 1.31 (3H, d, J = 7.1 Hz, CH_3), 3.37 (3H, s, MEM), 3.45–3.58 (2H, m, MEM), 3.67 (1H, ddd, J = 0.5, 5.6, 11.0 Hz, MEM), 3.80 (1H, ddd, J = 3.8, 5.3, 11.3 Hz, MEM), 4.82 (1H, d, J = 7.0 Hz, MEM), 4.89 (1H, d, J = 7.0 Hz, MEM), 5.09 (1H, q, J = 6.9 Hz, CH), 5.34 (1H, s, CH), 7.29–7.42 (3H, m, Ph), 7.48 (2H, d, J = 6.0 Hz, Ph), 9.54 (1H, s, CHO). NMR δ_C: 14.00, 58.98, 67.67, 71.62, 75.29, 94.32, 127.43, 128.74, 128.94, 135.72, 170.39, 197.99. HR-MS *m/z*: calcd. for $C_{15}H_{20}O_6$ (M^+), 296.1260; found, 296.1260.

(*R*)-(−)- and (*S*)-(−)-2-[(*R*)-*O*-MEM-mandeloyloxy]heptanal (**3b-r** and **3b-s**) were identified with (*R*)-(+)- and (*S*)-(+)-2-[(*S*)-*O*-MEM-mandeloyloxy]heptanal[16] on the NMR spectra. (*R*)-(−)-2-[(*R*)-*O*-MEM-mandeloyloxy]heptanal (**3b-r**): $[\alpha]_D = -26.7°$, *c* 0.25 (EtOH); and the (*S*)-(−)-form (**3b-s**):

$[\alpha]_D = -53.0°$, *c* 0.17 (EtOH).

Diisopropyl 2,15-bis{(2S)-2-hydroxy-1-[(R)-O-MEM-mandeloyloxy]propy}hexadecanedioate(8a-s). **3a-s** (183.9 mg, 0.62 mM) was added to a THF solution of the dienolate of diisopropyl hexadecanedioate [which had been prepared from diisopropyl hexadecanedioate (**5**), 100.0 mg, 0.27 mM and LDA (0.62 mM) at −78°C for 1.5 hr in dry THF] at −78° C, and the mixture was stirred for 40 min at −78°C to give **7a-s** (139.1 mg, quantitative yield). NMR δ_H ($CDCl_3$): 3.6–3.8 (CH-OH), 4.7–4.9 (CH-Omandeloyl). NMR δ_C: 67.05, 70.00, 70.28, 71.05 (C-OH), 73.18, 74.40, 75.68 (CH-Omandeloyl). HR-MS *m/z*: calcd. for $C_{52}H_{74}O_{14}$ ($M^+-2H_2O-2H_2$), 922.5079; found, 922.5058. Since **7a-s** was unstable, it was transformed to **8a-s**. **7a-s** (139.1 mg, 0.14 mM) was treated with an excess amount of AcONa (1.0 g) in a mixed solvent of DMF:HMPA = 3:1 at 50°C for 5 hr, and the crude products (100.2 mg) were separated by preparative TLC (hexane:EtOAc = 1:2) to give **8a-s** (61.6 mg, 44.4% yield). NMR δ_H ($CDCl_3$): 1.09–1.36 (20H, m, CH_2), 1.25 (12H, d, J = 7.1 Hz, $-CH_3$), 1.43 (6H, d, J = 6.6 Hz, CH_3), 1.49–1.70 (8H, m, HO-C-CH_2&OCO-C-CH_2), 2.35–2.50 (2H, m, CO-CH_2), 3.36 (3H, s, MEM), 3.43–3.54 (4H, m, MEM), 3.54–3.70 (2H, m, MEM), 3.70–3.83 (2H, m, MEM), 3.7–4.0 (2H, m, CH-OH), 4.72–4.82 (2H, m, J = 7.1 Hz, CH-Omandeloyl), 4.78 (2H, d, J = 6.7 Hz, MEM), 4.87 (2H, d, J = 6.6 Hz, MEM), 4.91–5.10 (4H, m, CH of isopropyl), 5.21 (2H, d, J = 7.1 Hz, CO-CH(OMEM)Ph), 7.30–7.43 (6H, m, Ph), 7.43–7.49 (4H, m, Ph). NMR δ_C: 69.27, 69.53 (CH-OH), 77.17 (CH-Omandeloyl). HR-MS *m/z*: calcd. for $C_{52}H_{74}O_{14}$ ($M^+-2H_2O-2H_2$), 922.5079; found, 922.5079.

(S,S)-(+)-Ancepsenolide (1a-s). **8a-s** (61.6 mg, 0.064 mM) in dry THF (2 ml) was added to a stirred suspension of NaH (a 60% dispersion in mineral oil, 11.5 mg (0.19 mM)) in THF (1 ml) at 0°C, and the mixture stirred for 1 hr at room temperature.[17] The reaction mixture was poured into an aqueous NH_4Cl solution (2 ml) and ether (10 ml). The organic materials were extracted with ether and EtOAc, and successively washed with 2 N HCl, sat. $NaHCO_3$ and sat. NaCl. After drying over $MgSO_4$, the solvents were evaporated to give crude products (38.1 mg) which were purified with silica gel TLC (benzene) and successive crystallization (hexane) to give optically active (*S,S*)-(+)-ancepsenolide (**1a-s**, 5.5 mg, 23.8% yield, $[\alpha]_D = +\mathbf{20.0}°$, *c* 0.133 ($CHCl_3$)). The NMR spectra of **1a-s** agreed with those of ancepsenolide. **1a-s**. NMR δ_H ($CDCl_3$): 1.07–1.38 (16H, m, CH_2), 1.43 (6H, d, J = 6.8 Hz, CH_3), 1.49–1.69 (4H, m, =C-CH_2-CH_2), 2.26 (4H, t, J = 7.7 Hz, =C-CH_2), 4.99 (2H, dq, J = 1.6 Hz, COOCH), 6.98 (2H, d, J = 1.3 Hz, =CH). NMR δ_C: 19.24, 25.20, 27.43, 29.19, 29.30, 29.50, 29.57, 77.27, 134.37, 148.85, 173.89. HR-MS *m/z*: calcd. for $C_{22}H_{34}O_4$ (M^+), 362.2457; found, 362.2454.

The (*R,R*)-(−)-isomer (**1a-r**) was also synthesized from the aldehyde (**3a-r**) and **5** in a 14% yield by a procedure similar to that just described. The structure was identified with that of **1a-s** by their ^1H- and ^{13}C-NMR spectra. $[\alpha]_D = -\mathbf{21.7}°$, *c* 0.273 ($CHCl_3$).

(R,R)- and (S,S)-2,2'-dodecamethylene-bis(2-nonen-4-olide) (1b-r and 1b-s). **3b-r** (173 mg, 0.50 mM) was stirred with the lithium enolate of diisopropyl hexadecanedioate [which had been prepared from **5** (80 mg, 0.022 mM) and LDA at −78°C for 1.5 hr in dry THF] at −78°C for 40 min in dry THF to give **7b-r** (237.5 mg, 0.22 mM, quantitative yield). **7b-r** (237.5 mg, 0.22 mM) was transformed into diisopropyl 2,15-bis{(2*R*)-2-hydroxy-1-[(*R*)-*O*-MEM-mandeloyloxy]heptyl}hexadecanedioate (**8b-r**, 85.9 mg, 0.08 mM, 36.1% yield. HR-MS *m/z*: calcd. for $C_{57}H_{90}O_{13}$ ($M^+-CH_3OCH_2CH_2O-H_2O$), 982.6381; found, 982.6390) by a method similar to that just described. **8b-r** (85.9 mg, 0.08mM) was transformed into bis-butenolide (**1b-r**, 4.7 mg, 0.01 mM, 12.4% yield). **1b-r**: $[\alpha]_D = -\mathbf{19.1}°$, *c* 0.27 ($CHCl_3$). NMR δ_H ($CDCl_3$): 0.89 (6H, t, J = 6.6 Hz, CH_3), 1.18–1.38 (24H, m, CH_2), 1.38–1.50 (4H, m, CH_2), 1.50–1.59 (4H, m, CH_2), 1.59–1.67 (2H, m, C_5-H&C_{24}-H), 1.67–1.78 (2H, m, C_5-H&C_{24}-H), 2.27 (4H, t, J = 7.5 Hz, C_9&C_{20}), 4.88 (2H, t, J = 5.6 Hz, COOCH), 6.98 (2H, s, =CH). NMR δ_C: 13.94, 22.46, 24.69, 25.27, 27.48, 29.20, 29.32, 29.52, 29.58, 31.54, 33.57, 81.24, 134.57, 147.81, 174.00. HR-MS *m/z*: calcd. for $C_{30}H_{48}O_4$ (M^+-H_2), 472.3553; found, 472.3569.

1b-s was also synthesized from **3b-s** (220.0 mg, 0.062 mM) and lithium enolate of diisopropyl hexadecanedioate (**5**) [which had been prepared from **5** (100.0 mg, 0.027 mM) and LDA at −78°C for 1.5 hr in dry THF] at −78°C for 40 min in dry THF to give **7b-s** (300.8 mg, 0.028 mM, quantitative yield). **7b-s** (300.8 mg, 0.028 mM) was transformed into diisopropyl 2,15-bis{(2*S*)-2-hydroxy-1-[(*R*)-*O*-MEM-mandeloyloxy]heptyl}hexadecanedioate (**8b-s**, 122.8 mg, 0.11 mM) by a method similar to that just described (40.3% yield), and **8b-s** (122.8 mg, 0.11 mM) was then transformed into (*S,S*)-bis-4-pentyl-2-butenolide (**1b-s**, 16.3 mg, 0.034 mM, 30.1% yield). **1b-s**: $[\alpha]_D = +21.3°$, *c* 1.08 ($CHCl_3$). The ^1H- and ^{13}C-NMR spectra of **1b-s** agreed with those of **1b-r**.

(R,R)- and (S,S)-2,2'-octamethylene-bis(2-penten-4-olide) (2a-s and 2a-r). **3a-s** (103.7 mg, 0.35 mM) and the lithium enolate of isopropyl dodecanedioate (**6**, 50.0 mg, 0.16 mM) were reacted to give **9a-s** (149.7 mg, 0.35 mM, quantitative yield. HR-MS *m/z*: calcd. for $C_{48}H_{69}O_{14}$ (M^+-2H_2O+H),

869.4687; found, 869.4648) which was transformed into **10a-s** (34.6 mg, 23.1% rough yield. HR-MS *m/z*: calcd. for $C_{45}H_{65}O_{13}$ (M^+-$CH_3OCH_2CH_2O$-H_2O), 813.4425; found, 813.4457). **10a-s** (34.6 mg, 3.8×10^{-2} mM) similarly yielded optically active **2a-s** (5.0 mg, 42.8% yield, $[\alpha]_D=+$**26.4°**, *c* 0.33 ($CHCl_3$)). **2a-s**: NMR δ_H ($CDCl_3$): 1.20–1.37 (8H, m, $-CH_2$), 1.41 (6H, d, *J*=6.8 Hz, CH_3), 1.48–1.62 (4H, m, $=C-CH_2-CH_2$), 2.26 (4H, dt, *J*=7.7, 1.5 Hz, $=C-CH_2$), 5.00 (2H, qq, *J*=6.8, 1.6 Hz, CO-O-CH), 6.99 (2H, d, *J*=1.5 Hz, C=CH). NMR δ_C: 19.23, 25.17, 27.39, 29.10, 29.12, 77.42, 134.29, 148.93, 173.88. HR-MS *m/z*: calcd. for $C_{18}H_{26}O_4$ (M^+), 306.1831; found, 306.1862.

Bis-(4*R*)-4-methyl-2-butenolide (**2a-r**) was similarly synthesized from **3a-r** and **6** in a 5.5% yield. $[\alpha]_D=-$**22.9°**, *c* 0.14 ($CHCl_3$). **2a-r** was identified with **2a-s** by their NMR spectra.

(R,R)- and (S,S)-octamethylene-bis(2-nonen-4-olide) (2b-s and 2b-r). **2b-s** was similarly prepared by the reaction of **3b-s** and **6** *via* **9b-s** in a 17.4% yield. $[\alpha]_D=+$**10.4°**, *c* 0.40 ($CHCl_3$). NMR δ_H ($CDCl_3$): 0.89 (6H, t, *J*=6.8 Hz, CH_3), 1.23–1.37 (16H, m, CH_2), 1.37–1.49 (4H, m, O-CH-CH_2-CH_2), 1.54 (4H, t, $=C-CH_2-CH_2$), 1.58–1.67 (2H, m, O-CH-CH-H), 1.67–1.77 (2H, m, O-CH-CH-H), 2.26 (4H, t, *J*=7.6 Hz, $=C-CH_2$), 4.89 (2H, t, *J*=5.7 Hz, CO-O-CH), 6.99 (2H, d, *J*=1.4 Hz, C=CH). NMR δ_C: 13.94, 22.46, 24.70, 25.24, 27.45, 29.13, 29.15, 31.54, 33.57, 81.26, 134.49, 147.89, 173.98. HR-MS *m/z*: calcd. for $C_{26}H_{42}O_4$ (M^+), 418.3083; found, 418.3056. The (4*R*)-isomer (**2b-r**) was similarly prepared (6.5% yield). $[\alpha]_D=-$**9.5°**, *c* 0.40 ($CHCl_3$). **2b-r** was identified with the authentic sample of **2b-s** by their NMR spectra.

References

1) Ciereszko, L. S., Sifford, D. H., and Weinheimer, A. J., Chemistry of coelenterates I. Occurrence of terpenoid compounds in gorgonians. *Ann. N.Y. Acad. Sci.*, **90**, 917–919 (1960).
2) Schmitz, F. J., Kraus, K. W., Ciereszko, L. S., Sifford, D. H., and Weinheimer, A. J., Ancepsenolide: A novel bisbutenolide of marine origin. Chemistry of coelenterates V. *Tetrahedron Letters*, **1**, 97–104 (1966).
3) Schmitz, F. J., Lorance, E. D., and Ciereszko, L. S., Chemistry of Coelenterates XII. *J. Org. Chem.*, **34**, 1989–1990 (1969).
4) Guo, Y., Gavagunin, M., Mollo, E., Trivellone, E., and Cimino, G., Three new butenolide lipids from the Caribbean gorgonian Pterogorgia anceps. *J. Nat. Prod.*, **62**, 1194–1196 (1999).
5) Rodríguez, A. D. and Ramírez, C., Further butenolides from the Caribbean octocoral, *Pterogorgia citrina*. *J. Nat. Prod.*, **57**, 339–347 (1994).
6) Schmitz, F. J. and Lorance, E. D., Chemistry of coelenterates XXI. Lactones from the gorgonian *Pterogorgia guadalupensis*. *J. Org. Chem.*, **36**, 719–721 (1971).
7) Rupprecht, J. K., Hui, Y., and McLaughlin, J. L., Annonaceous acetogenins: a review. *J. Nat. Prod.*, **53**, 237–278 (1990).
8) Fang, X., Rieser, M. J., Gu, Z., Zhao, G., and McLaughlin, J. L., Annaceous acetogenins: An update review. *Phytochem. Anal.*, **4**, 27–48 (1993).
9) Cavé, A., Figadère, B., Laurens, A., and Cortes, D., Acetogenins from *Annonaceae*. In "*Progress in the Chemistry of Natural Products*," eds. Herz, W., Kirby, G. W., Moore, R. E., Steglich, W., and Tamm, Ch., Springer, Wien, **70**, pp. 81–288 (1997).
10) Alali, F. Q., Liu, X., and McLaughlin, J. L., Annoceous acetogenins: Recent progress. *J. Nat. Prod.*, **62**, 504–540 (1999).
11) Hoppen, S., Emide, U., Friedrich, T., Grubert, L., and Koert, U., Natural-product hybrids: Design, synthesis, and biological evaluation of quinone-annonaceous acetogenins. *Angew. Chem. Int. Ed.*, **39**, 2099–2102 (2000).
12) Podraza, K. F. and Sneden, A. T., A short synthesis of ancepsenolide. *J. Nat. Prod.*, **48**, 792–795 (1985).
13) Trost, B. M., Müller, T. J. J., and Martinez, J., Ruthenium catalyzed synthesis of butenolides and pentenolide *via* contra-electronic α-alkylation of hydroxyalkynoates. *J. Am. Chem. Soc.*, **117**, 1888–1899 (1995).
14) Iriye, R., Nakamura, A., and Takeshita, M., Synthesis of 2-(2-hydroxyalkylidene)cyclopentanones and their bio-antimutagenic activity. *Biosci. Biotechnol. Biochem.*, **59**, 401–407 (1995).
15) Iriye, R., Takai, K., and Noguchi, M., The synthesis of (*R*)-1-(2-oxocyclopentyliden)-2-alkanols and the (*S*)-forms, and their bio-antimutagenic activity against UV-induced *Escherichia coli* WP2 B/r *Trp*$^-$. *Bioorg. Med. Chem. Lett.*, **7**, 199–202 (1997).
16) Noguchi, M., Takai, K., Takei, Y., and Iriye, R., Synthesis of (*R*)- and (*S*)-13-hydroxy-10-oxo-*trans*-11-octadecenoic acid and their antimutagenic activity. *Biocontrol Sci.*, **5**, 91–95 (2000).
17) van Delft, F. L., Timmers, C. M., van der Marel, G. A., and van Boom, J. H., Preparation of 2-oxazolidinones by intramolecular nucleophilic substitution. *Synthesis*, 450–454 (1997).