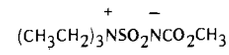
Ring Contraction of Oleandrose on the Macrolide Antibiotic Oleandomycin with [(Methoxycarbonyl)sulfamoyl]triethylammonium Hydroxide Inner Salt

Arthur A. Nagel,* Joseph DiBrino, Lawrence A. Vincent, and James A. Retsema

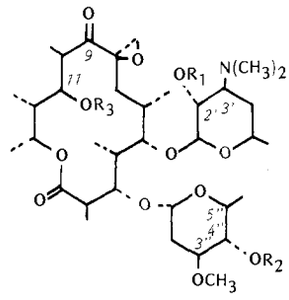
Pfizer Central Research, Groton, Connecticut 06340. *Received December 11, 1981*

Ring contraction of the neutral oleandrose sugar in the 14-membered-ring macrolide antibiotic oleandomycin (**2**) has been accomplished using [(methoxycarbonyl)sulfamoyl]triethylammonium hydroxide inner salt (**1**). The product of this interesting rearrangement, after methanolic hydrolysis of the 2′-acetate, is the 11-acetyl-3-*O*-(3″-methoxy-4″-vinylfuranosyl)oleandomycin (**12**). The in vitro activity of furanoside **12** is only moderately less than that of 11-acetyloleandomycin (**13**).

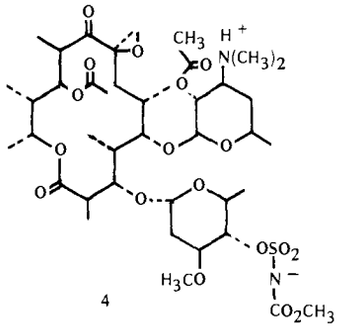
The neutral sugar of 14-membered-ring macrolides has been shown to be an important functionality necessary for achievement of maximum antibacterial activity.[1,2] The 14-membered-ring macrolide antibiotic oleandomycin (**2**)



1



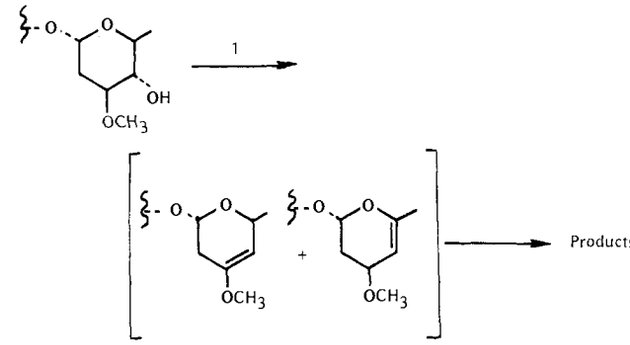
	R_1	R_2	R_3
2	H	H	H
3	$COCH_3$	H	$COCH_3$
5	$COCH_3$	SO_2NH_2	$COCH_3$
8	$COCH_3$	$SO_2C_6H_5$-CH_3 (p)	$COCH_3$
9	$COCH_3$	SO_2CH_3	$COCH_3$
13	H	H	$COCH_3$



4

has the neutral sugar oleandrose attached to the 3-position of the aglycon. It was of interest to determine whether the spectrum and/or potency of oleandomycin could be affected by neutral sugar modification. Since glycosidation of the 3-hydroxyl group on 14-membered-ring macrolides has met with limited success,[3,4] chemical modification was carried out on the intact macrolide. Herein is reported one aspect of this work which describes the conversion of oleandrose in oleandomycin to a vinyl furanoside via an interesting glycoside ring contraction.

Chemistry. [(Methoxycarbonyl)sulfamoyl]triethylammonium hydroxide inner salt (**1**), first described by Burgess and co-workers,[5] has been shown to be an effective dehydrating reagent for secondary and tertiary alcohols.[6] If inner salt **1** were to react with the 4″-alcohol on the oleandrose sugar of oleandomycin (**2**), dehydration would require the elimination of either the 3″ or 5″ axial hydrogens, both of which are adjacent to an oxygen functionality. This resulting transformation would lead to the formation of either (or both) of two enol ethers or their expected hydrolysis products.



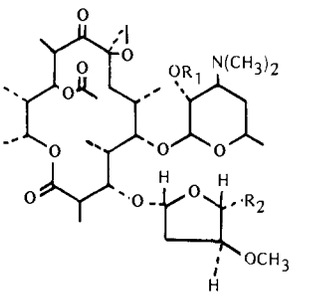
While the formation of enol ethers by this method was not realized, the reaction of **1** with the 4″-alcohol of oleandomycin led to an interesting oleandomycin derivative.

Stirring a mixture of 2′,11-diacetyloleandomycin (**3**)[7] [mp 162 °C; R_f 0.55 (acetone/ethyl acetate, 3:1)] and inner salt **1** in anhydrous benzene under a nitrogen atmosphere (room temperature, 20 h) affords, after standard workup,

(1) J. M. Wilhelm, N. L. Oleinick, and J. W. Corcoran, *Antimicrob. Agents Chemother.*, 236 (1967).
(2) R. A. LeMahieu, M. Carson, R. W. Kierstead, L. M. Fern, and E. Grunberg, *J. Med. Chem.*, 17, 953 (1974).
(3) (a) R. A. LeMahieu, M. Carson, R. W. Kierstead, and S. Pestka, *J. Med. Chem.*, 18, 849 (1975). (b) W. D. Celmer, U.S. Patent 3144466 (1964); *Chem. Abstr.*, 61, 10664*h* (1964).
(4) The ease of glycosidation of the 3-hydroxyl group in erythromycin is apparently effected by the oxidation state of Cg. See R. B. Woodward, B.-W. Au-Yeung, P. Balaram, L. J. Browne, P. J. Card, C. H. Chen, R. B. Chênevert, A. Fliri, K. Frobel, H.-J. Gais, D. G. Garratt, K. Hayakawa, W. Heggie, D. P. Hesson, D. W. H. Hoppe, I. Hoppe, J. A. Hyatt, D. Ikeda, P. A. Jacobi, K. S. Kim, Y. Kobuke, K. Kojima, K. Krowicki, V. J. Lee, T. Teutert, E. Logusch, S. Malchenko, J. Martens, R. S. Matthews, K. P. Nambiar, B. S. Ong, J. B. Press, T. V. Rajan Babu, G. Rousseau, K. Sakan, H. M. Sauter, M. Suzuki, K. Tatsuta, L. M. Tolbert, E. A. Truesdale, I. Uchida, Y. Ueda, T. Uyehara, A. T. Vasella, W. C. Vladuchick, P. A. Wade, D. E. Ward, R. M. Williams, and H. N.-C. Wong, *J. Am. Chem. Soc.*, 103, 3215 (1981).
(5) G. M. Atkins, Jr., and E. M. Burgess, *J. Am. Chem. Soc.*, 90, 4744 (1968).
(6) E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Am. Chem. Soc.*, 92, 5224 (1970). E. M. Burgess, H. R. Penton, Jr., and E. A. Taylor, *J. Org. Chem.*, 38, 26 (1973).
(7) W. D. Celmer, *Antibiot. Annu.*, 277 (1958).

0022-2623/82/1825-0881$01.25/0

a polar [R_f 0.05 (acetone/ethyl acetate, 3:1)], crystalline (mp 214–215 °C) compound whose spectral and analytical properties are consistent with the 4″-sulfamoyl-*N*-carbomethoxy ester **4**. Refluxing intermediate **4** in dry xylene produces, as the only xylene-soluble macrolide product, the interesting oleandomycin furanoside **6** in 15–20% yield.



	R_1	R_2
6	$COCH_3$	$CH=CH_2$
7	$COCH_3$	CH_2-CH_3
12	H	$CH=CH_2$

Spectral evidence (^{13}C and ^1H NMR) clearly indicates the presence of a vinyl group, and the mass spectrum indicates a *m/e* of 127.0763 ($C_7H_{11}O_2$) for the neutral sugar fragment. Hydrogenation of **6** occurs smoothly to yield the 4″-ethylfuranosyl macrolide derivative **7**. Stirring vinyl pyranoside **6** in methanol at room temperature for 48 h removes the 2′-acetyl group to produce the 2′-hydroxy vinyl pyranoside **12**.

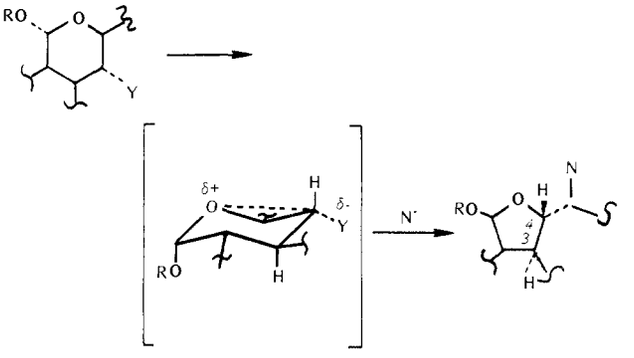
If water is present in the reaction mixture, **4** undergoes a slow conversion to the N-decarbomethoxylated derivative **5**. In fact, a 70% isolated yield of the crystalline (mp 192–194 °C) macrolide **5** could be realized by refluxing **4** (4 h) in xylene, in the presence of water. Mechanistically, it is interesting that attempted ring contraction of the 4″-sulfamate **5**, tosylate **8**, and mesylate **9** in the presence or absence of bases and in a variety of solvents fails to yield the expected furanoside derivative. In most cases, only the initial starting material is recovered; if vigorous reaction conditions are used, aglycon degradation products are produced. Addition of external nucleophiles (N_3^- or acetate) rapidly lead to aglycon degradation (epoxide opening and/or elimination of the 11-acetate to form an α,β-unsaturated ketone).

Ring contractions of pyranosides to furanosides, using a variety of experimental conditions *in the presence of external nucleophiles*, are well documented in the literature.[8-13] The conditions favorable to ring contraction appear to be that the glycoside must exist in a chair conformation in which the ring oxygen is oriented trans-antiparallel to the developing carbonium ion so that 1,3-oxonium ion participation can take place.[8] In such cases the ring contraction results in a trans relationship between the 3 and 4 substituents on the newly created five-membered ring. Previous conformational studies of oleandomycin[14] indicate that the oleandrose sugar exists in a chair form in which the ring oxygen exists in a trans-antiparallel relationship with the 4″-alcohol functionality.

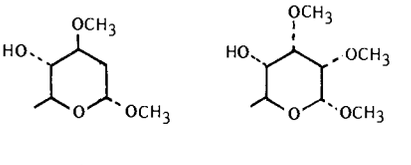
Table I. In Vitro Activity of 11-Acetyl-3-(3″-methoxy-4″-vinylfuranosyl)oleandomycin (12) as Compared to 11-Acetyloleandomycin (13)[a]

organism[b]	12	13
St.a. 01A005	3.12	0.39
01A052	6.25	0.39
01A111	0.78	0.78
01A400	25	1.56
S.f. 02A006	12.5	1.56
S.p. 02C203	0.39	0.10
S.pn. 02J012	≤0.01	≤0.01
B.s. 06A001	1.56	0.78
E.c. 51A470	50	6.25
51A125	>800	400
P.m. 59A001	50	6.25
N.s. 66C000	6.25	1.56

[a] Reported as the minimum inhibitory concentration. Broth dilution minimal inhibitory concentrations were determined as described previously.[19] Average of two determinations. [b] *St.a.* = *Staphylococcus aureus*; *S.f.* = *Streptococcus facecalis*; *S.p.* = *Streptococcus pyogenes*; *S.pn.* = *Streptococcus pneumoniae*; *B.s.* = *Bacillis subtilis*; *E.c.* = *Escherichia coli*; *P.m.* = *Pasteurella multocida*; *N.s.* = *Neisseria sicca*.



The stereochemistry of the vinyl furanoside **6** is assigned based primarily on the mechanism of the ring contraction. While assignment of stereochemistry of five-membered ring substituents based on NMR coupling constants is not straightforward, a 270-MHz NMR spectrum of **6** reveals a coupling constant between the resulting 3″ and 4″ hydrogens of 3.6 Hz (see Experimental Section). This is in good agreement with published coupling constants for similar 2-deoxyfuranosides.[15] Several attempts were made to effect the ring contraction of α-methyloleandrose (**10**)[16]



10 **11**

or α-methylmycinose (**11**)[17] with inner salt **1**. While TLC indicates that the starting pyranosides are rapidly consumed, the reaction yields a variety of products, none of which possess a vinyl moiety. Apparently, the oleando-

(8) S. Hanessian, *Chem. Commun.*, 796 (1966).
(9) K. Kefurt, J. Jary, and Z. Samek, *Chem. Commun.*, 213 (1969).
(10) C. L. Stevens, R. P. Glinoki, G. E. Gutowski, and J. P. Dickerson, *Tetrahedron Lett.*, 649 (1967).
(11) C. L. Stevens, R. P. Glinoki, K. G. Taylor, P. Blumbergo, and F. Sirokman, *J. Am. Chem. Soc.*, **88**, 2073 (1966).
(12) G. Fronza, C. Fuganti, and P. Grasselli, *Tetrahedron Lett.*, 2999 (1980).
(13) Amino sugars have been ring contracted via diazotization; for example, see C. Erbing, B. Lindberg, S. Svensson, *Acta. Chem. Scand.*, **27**, 3699 (1973).
(14) W. D. Celmer, *Pure Appl. Chem.*, **28**, 413 (1971).
(15) J. A. Gerlt and A. V. Youngblood, *J. Am. Chem. Soc.*, **102**, 7433 (1980).
(16) W. D. Celmer and D. C. Hobbs, *Carbohydr. Res.*, 1, 137 (1965).
(17) H. W. Dion, P. W. K. Woo, and Q. R. Bartz, *J. Am. Chem. Soc.*, **84**, 880 (1962).

mycin aglycon and/or basic desosamine sugar must exert some stabilizing influence on the above reaction which permits the isolation of vinyl furanoside **6**.

Biology. Table I summarizes the in vitro biological activity of 11-acetyl-3-*O*-(3″-methoxy-4″-vinylfuranosyl)-oleandomycin (**12**) as compared with that of 11-acetyl-oleandomycin (**13**).[7] As can be seen, the rearrangement of oleandrose to the vinyl pyranoside results in a rather modest decrease of in vitro potency against Gram-positive and Gram-negative organisms. This is in spite of the fact that (1) the spatial orientation of the 3″-methoxy group has been shifted[18] and (2) the initial 4″-hydroxy group in oleandrose has been completely eliminated. Whether this potency decrease is the result of reduced penetration of the bacterial cell wall and/or loss of intrinsic antibacterial activity (i.e., inhibition of bacterial protein synthesis) is under study.

Experimental Section

General Methods. Melting points (uncorrected) were determined with a Thomas-Hoover capillary apparatus. ^{1}H NMR spectra were recorded with a Varian T-60, Varian XL-100-15, or Varian 270 MHz spectrometer using tetramethylsilane as an internal standard. ^{13}C NMR spectra were obtained in the FFT mode on a Varian XL-100-15 (25 MHz) spectrometer equipped with a Nicolet Technology 1080 data system. Chemical shifts are reported in parts per million relative to tetramethylsilane as an internal standard. Mass spectra were recorded with an AEI MS-30 spectrometer equipped with a D5-50 data system. TLC was performed using precoated 0.25-mm thick silica gel 60 plates (Merck) and column chromatography with silica gel (Merck) 70–230 mesh.

2′,11-Diacetyl-4″-*O*-[(methoxycarbonyl)sulfamoyl]-oleandomycin (4). A solution of 10.0 g (0.013 mol) of 2′,11-diacetyloleandomycin (**3**) and 9.0 g (0.039 mol) of [(methoxycarbonyl)sulfamoyl]triethylammonium hydroxide inner salt (**1**) was stirred in 75 mL of anhydrous benzene under a nitrogen atmosphere for 20 h at room temperature. TLC (acetone/$CHCl_3$, 3:1) indicated that all of the macrolide **3** had been consumed. To the solution was added 300 mL of anhydrous ether, which caused precipitation of a white solid. The solid was collected by filtration and redissolved in $CHCl_3$. The $CHCl_3$ solution was washed with saturated $NaHCO_3$ and H_2O, dried with Na_2SO_4, and evaporated to afford 11.0 g of a white amorphous solid. Crystallization of 1.0 g of the amorphous solid from ethyl acetate gave 0.4 g of **4**: mp 214–215 °C; TLC (acetone/$CHCl_3$, 3:1) R_f 0.30; NMR ($CDCl_3$) δ 3.73 (s, 3 H), 3.46 (s, 3 H), 2.70 (s, 6 H), 2.20 (s, 3 H), 2.10 (s, 3 H). Anal. Calcd for $C_{41}H_{68}O_{18}N_2S\cdot H_2O$: C, 53.12; H, 7.61; N, 3.02; S, 3.46. Found: C, 53.21; H, 7.26; N, 2.97; S, 3.60.

2′,11-Diacetyl-4″-*O*-sulfamoyloleandomycin (5). The crystalline 4″-*N*-carbomethoxy ester **4** (3.3 g, 0.0036 mol) was suspended in a biphasic system consisting of 400 mL of xylene and 20 mL of water and heated to reflux for 4 h. Upon refluxing, the suspension gradually dissolved to give a colorless solution. TLC indicated that the reaction was complete, and the solution was cooled to room temperature. The solution was added to 200 mL of water, and the pH was adjusted to 2.0 with 1 N HCl. The water layer was separated from the organic layer and added to 300 mL of ethyl acetate, and the pH was adjusted to 9.5 with 1 N NaOH. The ethyl acetate layer was separated from the water layer, dried (Na_2SO_4), and evaporated to yield 2.15 g (70%) of crystalline sulfamoyloleandomycin **5**: mp 192–194 °C; TLC (acetone/ethyl (3:1) acetate, R_f 0.70; NMR ($CDCl_3$) δ 3.4 (s, 3 H), 2.26 (s, 3 H), 2.08 (s, 3 H), 2.06 (s, 3 H). Anal. Calcd for $C_{39}H_{64}O_{15}N_2S$: C, 55.06; H, 7.76; N, 3.29; S, 3.76. Found: C, 54.90; H, 7.83; N, 3.14; S, 3.49.

2′,11-Diacetyl-4″-*O*-(toluenesulfonyl)oleandomycin (8). A mixture of 1.0 g (0.0012 mol) of diacetyloleandomycin **3** and 2.46 g (0.0129 mol) of *p*-toluenesulfonyl chloride was stirred in 10 mL of distilled pyridine at room temperature for 15 h. TLC indicated the reaction was complete, and the pyridine was evaporated under reduced pressure. The residue was dissolved in a mixture of 50 mL of ethyl acetate and 50 mL of water. The pH was adjusted to 9.5 with aqueous K_2CO_3. The ethyl acetate layer was separated from the aqueous layer, dried, and evaporated to yield 1.5 g of a brown amorphous solid. The solid was chromatographed on 70 g of silica gel using 2:1 ethyl acetate/acetone as an eluant. Appropriate fractions were combined and evaporated to yield 825 mg (69%) of tosylate **8** as a white amorphous foam: TLC ($CHCl_3$/acetone, 3:1) R_f 0.40; NMR ($CDCl_3$) δ 7.77, 7.29 (AB q, J = 8 Hz, 4 H), 2.91 (s, 3 H), 2.41 (s, 3 H), 2.25 (s, 6 H), 2.03 (s, 3 H), 1.96 (s, 3 H). Anal. Calcd for $C_{46}H_{71}O_{16}NS$: C, 59.66; H, 7.73; N, 1.51. Found: C, 59, 96; H, 7.70; N, 1.43.

2′,11-Diacetyl-4″-*O*-(methanesulfonyl)oleandomycin (9). A mixture of 1.0 g (0.0013 mol) of diacetyloleandomycin **3** and 1.0 mL (0.0129 mol) of methanesulfonyl chloride was stirred in 10 mL of dry pyridine for 2 h at 0 °C. Workup of the reaction was essentially the same as that described for oleandomycin tosylate **8**. Chromatography afforded 300 mg (28%) of crystalline mesylate **9**: mp 183–185 °C; TLC (ethyl acetate/acetone, 2:1) R_f 0.60; NMR ($CDCl_3$) δ 3.36 (s, 3 H), 3.10 (s, 3 H), 2.31 (s, 6 H), 2.08 (s, 3 H), 1.98 (s, 3 H). Anal. Calcd for $C_{40}H_{67}O_{16}NS$: C, 56.52; H, 7.94; N, 1.65. Found: C, 56.39; H, 7.89; N, 1.61.

2′,11-Diacetyl-3-*O*-(3″-methoxy-4″-vinylfuranosyl)-oleandomycin (6). A suspension of the crystalline 4″-*N*-carbomethoxy ester **4** (2.5 g, 0.0027 mol) was refluxed in 100 mL of dry xylene under a nitrogen atmosphere in the presence of a Dean–Stark apparatus for 1.5 h. During the reflux, ester **4** gradually went into solution, and a dark oily xylene-insoluble substance collected on the sides of the reaction flask. TLC indicated that starting material was absent in the reaction, and the mixture was cooled to room temperature. The xylene solution was decanted from the oily residue and mixed with 100 mL of water.[20] The pH of the biphasic mixture was adjusted to 2.0, and the aqueous layer was separated from the organic layer. The pH of the aqueous layer was adjusted to 9.5, and the aqueous layer was extracted with ethyl acetate. The ethyl acetate extracts were combined, dried (Na_2SO_4), and evaporated. The residue was chromatographed on 50 g of silica gel using 1:1 chloroform/ethyl acetate as the eluant. Appropriate fractions were combined and evaporated to yield 0.300 g (15%) of the furanosyloleandomycin **6** as a white amorphous foam: TLC ($CHCl_3$/acetone 1:1) R_f 0.71; NMR ($CDCl_3$) δ 5.96 (ddd, J = 17.3, 10.2, and 7.3 Hz, 1 H, $C_{5''}$ H), 5.36 (d, J = 17.1 Hz, 1 H, $C_{6''}$ H), 5.29 (t, J = 4.5 Hz, 1 H, $C_{1''}$ H), 5.17 (d, J = 10.5 Hz, 1 H, $C_{6''}$ H), 4.33 (dd, J = 7.3 and 3.7 Hz, 1 H, $C_{4''}$ H), 3.76 (t, d, J = 5.2 and 3.7 Hz, 1 H, $C_{3''}$ H), 3.36 (s, 3 H, $C_{4''}$ OCH_3), 2.25 [s, 6 H, $C_{3''}$ $N(CH_3)_2$], 2.16 (t, J = 5 Hz, 2 H, $C_{2''}$); mass spectrum, m/e 754 (P − H), 627 (P − 127), 411 (P − 342), 351.2191 ($C_{21}H_{31}O_5$ ± 1.9 ppm), 200.1284 ($C_{10}H_{18}NO_3$ ± 0.2 ppm, base peak), 127.0763 ($C_7H_{11}O_2$ ± 0.4 ppm), 95.0493 (C_6H_7O ± 0.3 ppm); ^{13}C NMR ($CDCl_3$) 138.3, 116.6 ppm (vinyl carbons).

2′,11-Diacetyl-3-*O*-(3″-methoxy-4″-ethylfuranosyl)-oleandomycin (7). To a solution of 150 mg (0.19 mmol) of vinyl furanoside **6** in 20 mL of ethyl acetate was added 150 mg of 10% palladium on carbon. The suspension was hydrogenated at room temperature for 18 h at 50 psi. The suspension was filtered, and the ethyl acetate was evaporated. The residue (140 mg) was chromatographed on 6 g of silica gel using 2:1 $CHCl_3$/acetone as an eluant. The appropriate fractions were combined and evaporated to yield 0.102 g (67%) of ethyl furanoside **7** as a white amorphous foam: TLC ($CHCl_3$/acetone, 2:1) R_f 0.42; NMR ($CDCl_3$) δ 3.40 (s, 3 H, 3″-OCH_3), 2.21 [s, 6 H, 3′-$N(CH_3)_2$], 2.11

(18) The spatial orientation of the 3″-methoxy group in oleandomycin is important for antibacterial potency. See R. A. LeMahieu, H. A. Ax, J. F. Blount, M. Carson, C. W. Despreaux, D. L. Pruess, J. P. Scannell, F. Weiss, and R. W. Kinstead, *J. Antibiot.*, **29**, 728 (1976).

(19) J. A. Retsema, A. R. English, and A. E. Girard, *Antimicrob. Agents Chemother.*, **17**, 615 (1980).

(20) Characterization of the insoluble oily residue indicated that it was a complex mixture of products, some of which contained macrolide residues. Since no single macrolide-containing product was dominant in the mixture, attempted purification of various derivatives was not pursued.

(s, 6 H, $COCH_3$); ^{13}C NMR ($CDCl_3$) 22.7, 9.5 (5″; 6″ ethyl group); mass spectrum, *m/e* 756 (P + H), 627 (P − 129), 411 (P − 344), 351.2155 ($C_{20}H_{31}O_5$ ± 1.6 ppm), 200.1283 ($C_{10}H_{18}NO_3$ ± 0.3 ppm, base peak), 129.0908 ($C_7H_{13}O_2$ ± 0.7 ppm).

11-Acetyl-3-*O*-(3″-methoxy-4″-vinylfuranosyl)-oleandomycin (12). A solution of 0.4 g (0.00053 M) of the 2′,11-diacetyl vinyl furanoside derivative **6** was dissolved in 100 mL of methanol and stirred at room temperature for 48 h. The solvent was evaporated under reduced pressure to yield 0.35 g of **12** as a white amorphous solid: TLC ($CHCl_3$/acetone, 1:1) R_f 0.12; NMR ($CDCl_3$) δ 5.96, 5.36, 5.17 (m, 3 H, vinyl protons), 3.36 (s, 3 H, OCH_3), 2.31 [s, 6 H, $N(CH_3)_2$], 2.02 (s, 3 H, $COCH_3$); mass spectrum, *m/e* 351.2187 ($C_{21}H_{31}O_5$ ± 3.1 ppm), 158.1181 ($C_8H_{16}NO_2$ ± 0.0 ppm, base peak), 127.0758 ($C_7H_{11}O_2$ ± 0.5 ppm). Anal. Calcd for $C_{37}H_{61}O_{12}N$: C, 62.43; H, 8.64; N, 1.97. Found: C, 62.28; H, 8.71, N, 2.12.

Book Reviews

Kirk-Othmer Encyclopedia of Chemical Technology. Third Edition. Volume 16. Edited by Martin Grayson and David Eckroth. Wiley, New York. 1981. xxvi + 971 pp. 18.5 × 26 cm. ISBN 0-471-02069-9. $145.00.

Volume 16 of this third edition includes articles from noise pollution to perfumes. Articles of particular interest to medicinal chemists include a brief discussion on nomenclature. While not the last word on naming organic compounds, this article does identify appropriate sources for further information, and as a last resort one can always write to Kurt Loening at Chemical Abstracts Service (the author) for further help. A thorough (93 pp) article on patents includes discussions on practice and management and patent literature detailing the various primary and secondary sources of information. Industrial chemists would be well advised to review this article, and those academic chemists who may also find it necessary to file patent applications in the U.S. or overseas would benefit too.

The articles on Perfumes and Essential Oils will be a useful source of information for those who find it necessary to be updated in this field.

Staff

Receptors and Recognition, Series B. Volume 9. Neurotransmitter Receptors. Part 1. Amino Acids, Peptides, and Benzodiazepines. Edited by S. J. Enna and H. I. Yamamura. Chapman & Hall, London. 1980. xi + 212 pp. 16.5 × 24 cm. $37.50 (with Part 2, $70.00).

Receptors and Recognition, Series B. Volume 10. Neurotransmitter Receptors. Part 2. Biogenic Amines. Edited by H. I. Yamamura and S. J. Enna. Chapman & Hall, London. 1981. xi + 273 pp. 16.5 × 24 cm. $37.50 (with Part 1, $70.00).

These two volumes are the most recent additions to the *Receptors and Recognition* series. Together, they present a series of reviews on neurotransmitter receptors by recognized authorities. Part 1 contains reviews on receptors for excitatory amino acids (Coyle), glycine, GABA and benzodiazepines (Enna and Defrance), substance P (Hanley and Iversen), enkephalins and endorphins (Childrens), and other peptides, including angiotensin, bombesin, VIP, etc. (Burt). Part 2 reviews biogenic amine receptors, including serotonergic receptors (Haigler), histamine receptors (Taylor and Richelson), acetylcholine receptors (Wastek and Yamamura), dopamine receptors (Creese), and adrenergic receptors (Minneman). Each chapter presents evidence on the chemical, physiological, and pharmacological criteria for the classification and subclassification of receptors and, where appropriate, discusses the mechanisms of signal transduction, receptor regulation. It is particularly interesting to note how major the contributions of ligand–receptor binding studies have been to our understanding of receptors and yet, in the absence of appropriate pharmacological and biochemical measurements, how sterile such studies can be.

Each chapter thus serves as a useful and usually quite comprehensive analysis of a particular receptor system within limits set by necessary publication time and the very rapid developments taking place. This discrete character of each chapter is both the strength and the weakness of the two volumes. The volumes probably will be of use to workers, both junior and senior, wishing to explore a particular receptor field. However, nowhere in either volume will they find the necessary general discussions of the principles of recognition, of mechanisms of receptor transduction, receptor regulation, etc. This is a great pity, since much that is useful could have been surveyed in this fashion. The Editors have missed a valuable opportunity.

However, the books are of considerable value to workers in the receptor field. The prices of these volumes are quite reasonable and, to a large extent, they fulfill the editors purpose of presenting expert, separate reviews on a number of neurotransmitter receptors. These volumes should certainly be in every health sciences library, and many individuals, including myself, will be glad that we own these and previous volumes in the series.

Department of Biochemical Pharmacology
School of Pharmacy
State University of New York at Buffalo
Buffalo, New York 14260

David J. Triggle