Avermectin Aglycons[1]

Helmut Mrozik,* Philip Eskola, Byron H. Arison, George Albers-Schönberg, and Michael H. Fisher

Merck Sharp & Dohme Research Laboratories, Rahway, New Jersey 07065

Received June 23, 1981

Reaction of avermectin A_{2a} and B_{2a} (1 and 2) with MeOH containing 1% concentrated H_2SO_4 gave the aglycons 4 and 5; alcoholysis of 1 and 2 in 2-propanol containing 1% concentrated H_2SO_4 gave the monosaccharides 6 and 11. Acid-catalyzed methanolysis of 3, however, gave a mixture of three compounds identified as the aglycon 8 and the two epimeric 22,23-dihydro-23-methoxyaglycons 9 and 10 by addition of MeOH to the 22,23 double bond of 3. The structures were determined by ^1H and ^{13}C NMR and mass spectra. Hydrolysis of 3 in aqueous tetrahydrofuran containing 10% concentrated H_2SO_4 gave a mixture of monosaccharide 7 and aglycon 8, from which pure 7 and 8 were isolated by silica gel column chromatography.

The avermectins are a group of fermentation products[2] with potent anthelmintic[3] and insecticidal[4] activities. Their structure was recently described[5] as 16-membered lactones containing an α-L-oleandrosyl-α-L-oleandrosyl disaccharide attached to the lactone ring through the allylic C_{13}-hydroxy group. Structurally closely related macrolides lacking the C_{13}-hydroxy group and its disaccharide substituent are represented by the milbemycins,[6] a group of microbial metabolites with potent insecticidal activities. We were interested in the preparation of the aglycons of the avermectins A_{2a}, B_{2a}, and B_{1a} (1–3, Chart I), the major products of the fermentation, in order to assess their biological activities and to utilize them as intermediates in the synthesis of 13-deoxyavermectin aglycons[7] for comparison to the milbemycins.

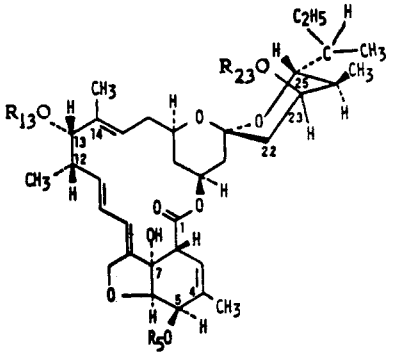
Methanolysis with sulfuric acid catalysis as described for oleandomycin[8] readily cleaved the acid-labile 2-deoxy sugar glycosides and gave in good yield the aglycons 4 and 5 of the avermectins A_{2a} and B_{2a} (1, 2).[5] Any rearrangements occurring under these reaction conditions can be ruled out on the basis of the close relationship of the 300-MHz proton NMR spectra for starting materials and products.[9] In addition, the ^{13}C NMR spectra for 4 and 5 and an X-ray structure determination for 5,[5] confirm the structural assignments. Aromatization[10] of the potentially labile methoxy cyclohexenol or the cyclohexenediol part structure comprising carbons 2–7 of 1 and 2, respectively, was not observed under these reaction conditions. In contrast, application of the acid-catalyzed methanolysis to avermectin B_{1a} (3), which contains a 22,23 double bond, did not yield pure aglycon 8. The reaction proceeded to a large extent with addition of methanol to this double bond and gave a mixture of aglycons. Substitution of 2-propanol for methanol as a bulkier reagent for the alcoholysis resulted in a selective cleavage of only the oleandrosyl–oleandrose bond and furnished the monosaccharide 6 in good yield. Apparently the glycosidic bond to the lactone ring is subject to steric hindrance so that it does not react under the conditions of the oleandrosyl-oleandrose bond cleavage. Aqueous acidic hydrolysis conditions also proceeded very slowly, and comparable acid concentrations without the assistance of methanol as nucleophile gave mainly monosaccharides. It was necessary to use 10% H_2SO_4 in 50% aqueous tetrahydrofuran to obtain a 1:1 mixture of avermectin B_{1a} monosaccharide 7 and the aglycon 8. Addition of water to the double bond was not observed under those conditions.[11]

We then investigated further the acid-catalyzed addition of methanol to the 22,23 double bond, which is part of a latent α,β-unsaturated ketone with the carbonyl protected in the form of a bicyclic spiro ketal. The thin-layer chromatogram of the reaction mixture obtained by methanolysis of avermectin B_{1a} (3) with 5% of *p*-toluenesulfonic acid monohydrate as an acid catalyst barely suggested the presence of two compounds. The reverse-phase HPLC system used to separate the eight naturally occurring avermectins[12] likewise showed only one peak. Analysis of the 300-MHz ^1H NMR spectrum of the reaction products, however, strongly suggested a mixture of three components. The characteristic signal for the vinylic C_{23} H as a doublet of doublets at δ 5.58 (J = 10, 2 Hz) had reduced intensity but showed the presence of some avermectin B_{1a} aglycon (8), and two singlets for two methoxy groups at δ 3.33 and 3.36 suggested two isomeric methoxy derivatives. The mass spectra were in agreement with these assignments. Chromatography of the reaction product on a Corasil A HPLC column[13] with methylene chloride–ethyl acetate as the solvent resolved it into three components. These could be isolated in pure form by high-performance liquid chromatography on a preparative column of Porasil A[13] or Partisil 10.[14] The fastest moving compound was identified as the aglycon 8 by direct comparison with an authentic sample. The mass spectra of the two slower moving compounds are virtually identical and confirm a 1:1 addition of methanol to avermectin B_{1a} aglycon (8). Their ^1H NMR spectra show clearly the absence of the C_{22}

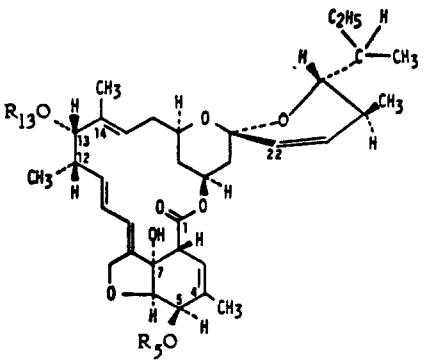
(1) Presented in part at the 178th National Meeting of the American Chemical Society, Washington, DC, Sept 1979; Abstract No. ORGN 259.
(2) Burg, R. W.; Miller, B. M.; Baker, E. E.; Birnbaum, J.; Currie, S. A.; Hartman, R.; Kong, Y. L.; Monaghan, R. L.; Olson, G.; Putter, I.; Tunac, J. B.; Wallick, H.; Stapley, E. O.; Oiwa, R.; Omura, S. *Antimicrob. Agents Chemother.* **1979**, *15*, 361.
(3) Egerton, J. R.; Ostlind, D. A.; Blair, L. S.; Eary, C. H.; Suhayda, D.; Cifelli, S.; Riek, R. F.; Campbell, W. C. *Antimicrob. Agents Chemother.* **1979**, *15*, 372.
(4) Ostlind, D. A.; Cifelli, S.; Lang, R. *Vet. Rec.* **1979**, *105*, 168.
(5) Albers-Schönberg, G.; Arison, B. H.; Chabala, J. C.; Douglas, A. W.; Eskola, P.; Fisher, M. H.; Lusi, A.; Mrozik, H.; Smith, J. L.; Tolman, R. L. *J. Am. Chem. Soc.* **1981**, *103*, 4216. Springer, J. P.; Arison, B. H.; Hirshfield, J. H.; Hoogsteen, K. *Ibid.* **1981**, 103, 4221.
(6) Takiguchi, Y.; Mishima, H.; Okuda, M.; Terao, M.; Aoki, A.; Fukuda, R. *J. Antibiot.* **1980**, *23*, 1120.
(7) Chabala, J. C.; Eskola, P.; Fisher, M. H.; Mrozik, H.; paper in preparation. See also: U. S. Patent 4 171 314.
(8) Hochstein, F. A.; Els, H.; Celmer, W. D.; Shapiro, B. L.; Woodward, R. B. *J. Am. Chem. Soc.* **1960**, *82*, 3225.
(9) See the Experimental Section.
(10) Tolan, J. W.; Eskola, P.; Fink, D. W.; Mrozik, H.; Zimmerman, L. A. *J. Chromatogr.* **1980**, *190*, 367.
(11) Mass spectral evidence was obtained for the addition of HCl and C_4H_9SH to the double bond after treatment of 3 with HCl–dioxane or C_4H_9SH-H_2SO_4–dioxane.
(12) Miller, T. W.; Chaiet, L.; Cole, D. J.; Cole, L. J.; Flor, J. E.; Goegelman, R. T.; Gullo, V. P.; Joshua, H.; Kempf, A. J.; Krellwitz, W. R.; Monaghan, R. L.; Ormond, R. E.; Wilson, K. E.; Albers-Schönberg, G.; Putter, I. *Antimicrob. Agents Chemother.* **1979**, *15*, 368.
(13) Waters Associates, Inc.
(14) Whatman Inc.

0022-3263/82/1947-0489$01.25/0

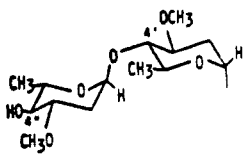
Chart I



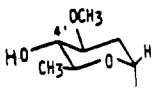
	R_5	R_{13}	R_{23}
1	CH_3	A	H
2	H	A	H
4	CH_3	H	H
5	H	H	H
6	CH_3	B	H
9	H	H	CH_3
11	H	B	H



	R_5	R_{13}
3	H	A
7	H	B
8	H	H



A



B

Table I. NMR Decoupling Experiments[a]

C_{22} H_{ax}	C_{22} H_{eq}	C_{23} H	C_{25} H
	23-*O*-Methylavermectin B_{2a} Aglycon (9)[b]		
1.48 (dd, 14.5, 3.5)	2.20 (dd, 14.5, 3.5)	3.43 (q, 3.5)	3.81 (dd, 10.5, 1.5)
irradiated proton	2.20 (br d, 4)	3.43 (br t, 3.5)	
1.48 (br d, 4)	irradiated proton	3.42 (br t, 3.5)	
1.48 (d, 15)	2.18 (d, 15)	irradiated proton)	
	23-*epi*-*O*-Methylavermectin B_{2a} Aglycon (10)[c]		
1.27 (dd, 13, 10)	2.20 (dd, 13, 5)	3.24 (dt, 10, 10, 5)	3.25 (br d, 10)
irradiated proton	2.20 (br d, 5)	multiplet simplified	
1.28 (br d, 10)	irradiated proton	3.26 (t, 10)	
1.28 (br d, 13)	2.20 (d, 13)	irradiated proton	

[a] The values given are δ values followed by assignments and coupling constants (in hertz) given in parentheses. [b] In CD_3COCD_3. [c] In $CDCl_3$.

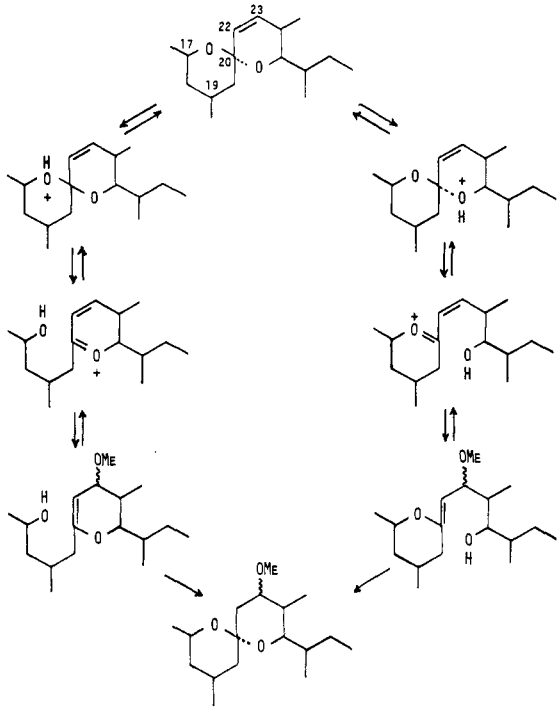
double bond and the presence of one methoxy group. They are essentially superimposable with the exception of the signals assigned to C_{22} H_{axial}, C_{22} $H_{equatorial}$, C_{23} H, and C_{25} H (Table I). This makes any structural rearrangments unlikely and suggests the two epimeric 23-*O*-methylavermectin B_{2a} aglycon structures for products **9** and **10**. The C_{23} H in **9** was assigned to the isolated quartet at δ 3.43 with a coupling constant of 3.5 Hz (CD_3COCD_3 solution), and this assignment was confirmed by irradiation of the adjacent axial and equatorial C_{22} protons. The small coupling constant does not allow for a coupling of an axial C_{23} proton with the adjacent axial C_{22} and C_{24} protons, therefore the C_{23} H must be equatorial, and the C_{23}-methoxy group in **9** has the same axial configuration as the C_{23}-hydroxy group in the aglycon **5** of the natural substance **2**. Consequently, **10** is assigned the structure with an equatorial C_{23} OMe, which is confirmed again by consideration of its ^{1}H NMR spectrum. Although here C_{23} H occurs partially overlapping with C_2 H and C_{25} H (δ 3.24, 3.29, and 3.25, respectively, $CDCl_3$ solution, Table I), irradiations of C_{22} H_{ax} and C_{22} H_{eq} allow the assignment of a triplet of doublets with shift of δ 3.24 and coupling constants of 10, 10, and 5 Hz for a diaxial coupling with C_{22} H_{ax} and C_{24} H_{ax} and axial–equatorial coupling with C_{22} H_{eq} respectively.

Additional evidence for the absence of any rearrangement and the addition of MeOH to the C_{22} double bond with the methoxy group located at the two epimeric C_{23} positions in **9** and **10** is provided by the ^{13}C NMR spectra (Table II). Comparisons with the C_{23}-hydroxy analogue **5** are most revealing. In the axial methoxy compound **9** only carbons 21–23 have changed by more than 1 ppm, and C_{23} was shifted downfield by 7.9 ppm as expected for a change from hydroxy to methoxy. A similar shift of 9 ppm

Table II. ^{13}C NMR Data (δ)

	4	5	9	10
C_{20}	40.9	40.9	41.9 t	41.5
C_{21}	99.6	99.6	98.0 s	99.1
C_{22}	40.9	41.1	36.9	40.5
C_{23}	70.0	70.1	78.0 d	79.1
C_{24}	35.7	35.6	35.7	38.5
C_{24a}	13.8	13.8	13.3	12.6
C_{25}	71.3	71.4	71.7 d	75.9
C_{26}	35.2	35.2	35.8	35.4

Scheme I



is also shown for C_{23} of **10**, where carbons 24, 24a, and 25 are the only additional ones shifted by more than 1 ppm. The 23-methoxy carbons are represented by a new peak at 56.8 ppm.

Under the reaction conditions of alcoholic or aqueous strong acids,[15] the dioxaspirane is partially protonated and exists in an equilibrium with presumably two allyl cations or β,γ-unsaturated oxonium ions resulting from ring opening (see Scheme I). Thermodynamically controlled ring closure gives back the dioxaspirane of natural configuration. Similar stereospecific cyclizations to single dioxaspiranes have been reported recently for synthetic keto diols.[16] We believe that conjugate addition of methanol to the β,γ-unsaturated oxonium ion best explains the facile regiospecific reaction of the double bond at the 23-position of **3**. The resulting enol ether will then readily cyclize to the more stable dioxaspirane of natural configuration. Apparently addition of methanol is not stereospecific, leading to the two epimeric 23-methoxy aglycons **9** and **10**.

Experimental Section

The natural products **1–3** used as starting materials contained up to 8% of the 27-demethyl analogues (the "b" series),[5] which could not readily be removed by chromatography and thus were carried through the reaction sequences. The new derivatives as well as starting materials **1** and **2** were amorphous lyophilates or foams and were therefore vigorously purified by preparative layer chromatography (PLC on silica gel GF, Uniplates, Analtech, 20 × 20 cm) of 0.25–2.0-mm thickness. Their purities were further demonstrated by analytical TLC on silica gel plates (Uniplate, Analtech, 25 × 100 mm) with hexane–EtOAc, CH_2Cl_2–EtOAc, toluene–2-propanol, $CHCl_3$–THF, CH_2Cl_2–THF-EtOH, or CH_2Cl_2–MeOH as an eluting solvent. The spots were observed in UV light and visualized by a ceric sulfate spray. The progress of all reactions was similarly followed by TLC. High-performance column chromatography (Waters Corasil A column[13] with CH_2Cl_2–EtOAc solvent mixtures or Waters C_{18} μ-Bondapak reverse-phase columns[13] with 75–98% aqueous MeOH as solvent) was carried out on certain selected compounds. Silica gel 60 (E. Merck, particle size 0.063–0.200 mm) was used for short-column chromatography.[17] The usual workup means two to three extractions with the solvent specified, washing the extract with water, drying with $MgSO_4$, and concentration to a solid residue in vacuo and under high vacuum. Microanalyses were performed by the staff of Merck Sharp & Dohme Research Laboratories under the direction of Mr. J. Gilbert. The analytical samples, containing in certain instances up to 8% of the homologous "b" compounds, were dried 16 h under high vacuum at 40 °C. This did not remove water completely, as is apparent from the NMR spectra, and the majority of the analyses are only within 0.4% of the calculated values when corrected for a water content of 0.5–1 mol. The structures therefore were further confirmed by high-resolution mass spectra of a prominent peak (aglycon or aglycon – H_2O) recorded on a Varian MAT 731 spectrometer. All compounds were characterized by 300-MHz proton NMR spectra on a Varian SC300 in deuteriochloroform solution with tetramethylsilane as an internal standard, by mass spectra on an LKB Model 9000, and by UV spectra on a Cary 15 instrument. ^{13}C NMR spectra were recorded on a Varian SC-300 or XL-100 instrument in $CDCl_3$ solution with Me_4Si as an internal reference.

Avermectin B_{2a} Aglycon (5). Avermectin B_{2a} (**2**; 2.0 g, 2.25 mmol) was added to a solution of 1% H_2SO_4 in MeOH (0.4 mL of H_2SO_4, 39.6 mL of MeOH) and stirred at 18 °C under N_2 for 16 h. Then $CHCl_3$ (300 mL) was added, and the solution was transferred into a separatory funnel, washed with aqueous $NaHCO_3$ solution and water, dried, and concentrated in vacuo to 2.4 g of a mixture containing mainly **5** and methyl oleandroside. MeOH (5 mL) was added to this residue, which slowly crystallized. The mother liquor was decanted, and the residue was washed with a little cold MeOH to give 1.0 g of a sticky crystalline solid, still containing some methyl oleandroside. The mother liquors gave after concentration an additional 140 mg of crystals. The crystalline residues were recrystallized from MeOH to give **5**: 770 mg (57%); mp 175–180/205–206 °C; $[\alpha]_D$ +96.4° (*c* 0.365, acetone); NMR and mass spectral data (supplementary material); UV (MeOH) 245 nm (ϵ 26 000). Anal. Calcd for $C_{34}H_{50}O_9$: C, 67.75; H, 8.36. Found: C, 67.42; H, 8.51.

Avermectin A_{2a} Monosaccharide (6). Avermectin A_{2a} (**1**; 500 mg, 0.66 mmol) was added to a solution of 0.1 mL of H_2SO_4 in 9.9 mL of 2-propanol and kept at 18 °C for 16 h. Then 125 mL of $CHCl_3$ was added, and the solution was washed with aqueous saturated $NaHCO_3$–solution and water, dried, and concentrated in vacuo to 650 mg of yellow foam. This was further purified by PLC (C_6H_6–EtOAc, 2:1; two successive elutions) to give 367 mg (87%) of **6** as white amorphous foam: NMR and mass spectral data (supplementary material); high-resolution mass spectrum calcd for $C_{35}H_{50}O_8$ *m/e* 598.3502 (M – 162, aglycon – H_2O), found 598.3503.

Avermectin B_{2a} Monosaccharide (11). Avermectin B_{2a} (**2**; 500 mg, 0.56 mmol) was added to a solution of 1% of *p*-toluenesulfonic acid monohydrate in MeOH (600 mg, 2.6 mmol, of *p*-TsOH·H_2O and 60 mL of MeOH) and the mixture stirred at 18 °C for 2.5 h. Neutralization with dilute aqueous $NaHCO_3$ and the usual workup with ether gave 430 mg of white foam. Preparative TLC (2.0-mm SiO_2 layers; CH_2Cl_2–THF–EtOH, 90:9.7:0.3) gave **11**: 342 mg (81%); amorphous foam; $[\alpha]_D$ +27° (*c* 0.545, acetone); UV (MeOH) 244 nm (ϵ 30 070); NMR and mass spectral data (supplementary material); high-resolution mass

(15) No reaction occurs in the presence of weak acids like AcOH.
(16) Evans, D. A.; Sacks, C. E.; Whitney, R. A.; Mandel, N. G. *Tetrahedron Lett.* **1978**, 727. Cresp, T. M.; Probert, C. L.; Sondheimer, F. *Tetrahedron Lett.* **1978**, 3955.
(17) Hunt, B. J.; Rigby, W. *Chem. Ind. (London)* **1962**, 1868.

spectrum calculated for $C_{34}H_{48}O_8$ m/e 584.3346 (M - 162, aglycon - H_2O) found 584.3339.

Avermectin B_{1a} Aglycon (8) and Monosaccharide (7). A mixture of 46.2 mL of H_2O, 46.2 mL of concentrated H_2SO_4, and 170 mL of THF was added over 30 min to a solution of **3** (22.2 g, 0.025 mol) in 200 mL of THF stirred in an ice bath. After the addition was completed, the reaction mixture was left at 18 °C for 24 h under a nitrogen atmosphere. Analysis by TLC and HPLC showed after 2 h about 60% of **3** and 40% of **7** and after 16 h about 60% of **7** and 40% of **8**. It also showed that the product mixture was essentially unchanged after 22 h. The dark brown reaction mixture was cooled in an ice bath followed by addition of 300 mL of ice–water. The usual workup with CH_2Cl_2 (4 × 200 mL) and washing with aqueous $NaHCO_3$ and water gave, after drying and concentration in vacuo, 17.7 g of dark brown foam. This was dissolved in 15 mL of EtOAc, filtered through silica gel (50 g) using 500 mL of EtOAc, and concentrated to give 17.2 g of light foam. Further purification was achieved on a Waters Prep LC/System 500 on two Prep PAK-500/silica cartridges (CH_2Cl_2–EtOAc, 7:3; total volume 8 L), giving 7.5 g (50%) of **8** as pale yellow foam. A 100-mg sample of this was purified for analysis by PLC (CH_2Cl_2–THF–EtOH, 89.7:10:0.3) and gave **8** as a white glass (quantitative recovery): $[\alpha]_D$ +65.5° (c 0.595, $CHCl_3$); NMR and mass spectral data (supplementary material); high-resolution mass spectrum calcd m/e 584.3346, found 584.3281; UV (MeOH) 245 nm (ϵ 28 200).

The second reaction product **7** was obtained pure as 4.67 g (25%) white foam; NMR and MS (supplementary material); UV (MeOH) 245 nm (ϵ 27 200); high resolution mass spectrum calculated for $C_{34}H_{46}O_7$ (M-162:aglycon-H_2O) 566.3240. Found: 566.3249.

23-*O*-Methylavermectin B_{2a} Aglycon (9) and 23-*epi*-*O*-Methylavermectin B_{2a} Aglycon (10). A solution of 1.26 g (1.45 mmol) of **3** and 10 g (53 mmol) of *p*-toluenesulfonic acid monohydrate in 200 mL of MeOH was kept at 18 °C for 22 h. Then it was poured into 1000 mL of ether, washed twice with ice-cold aqueous $NaHCO_3$ and water, dried, and concentrated in vacuo to 1.1 g of light foam. The crude product (1.0 g) was subjected to a preliminary purification by column chromatography (30 g of silica gel; CH_2Cl_2–EtOAc, 7:3) to give 700 mg of crude aglycon mixture as white foam, which shows one spot on TLC (CH_2Cl_2–THF–EtOH, 90:9.5:0.5). Analysis by HPLC (Corasil, 37–50 μm; column i.d. 0.2 cm, length 61 cm; CH_2Cl_2–EtOAc, 9:1) shows three components at retention times of 4.0 (**8**), 7.0 (**9**), and 9.5 (**10**) min. A 200-mg aliquot of this mixture was separated by preparative HPLC (Whatman Partisil M9, 10/50 column; CH_2Cl_2–EtOAc, 9:1) to give 15 mg of **8**, 80 mg of **9**, and 63 mg of **10** as crystalline residues.

8: mp 144–155 °C dec; HPLC (Corasil A, CH_2Cl_2–EtOAc) single peak, retention time 4.0 min; UV (MeOH) 243 nm (ϵ 26 400); H NMR and mass spectra were identical with those of authentic **8**.

9: mp 140–144 °C dec; HPLC, single peak, retention time 7.0 min; UV (MeOH) 245 nm (ϵ 29 100); ^1H and ^{13}C NMR, and mass spectral data (supplementary material); high-resolution mass spectrum calcd m/e 616.3610, found 616.3603.

10: mp 153–156 °C dec; HPLC single peak, retention time 9.5 min; UV (MeOH) 243 nm (ϵ 28 950); ^1H and ^{13}C-NMR and mass spectral data (supplementary material) high-resolution mass spectrum calcd m/e 616.3607, found 616.3661.

Acknowledgment. We are grateful to Drs. B. M. Trost and A. W. Douglas for stimulating discussions. We thank H. Flynn and J. L. Smith for obtaining spectral data. The generous supply of the avermectins by I. Putter and his staff is appreciated.

Registry No. **1**, 65195-53-1; **2**, 65195-57-5; **3**, 65195-55-3; **4**, 71828-13-2; **5**, 71828-15-4; **6**, 71837-28-0; **7**, 71831-09-9; **8**, 71828-14-3; **9**, 80010-05-5; **10**, 80041-02-7; **11**, 71861-20-6.

Supplementary Material Available: Tables of ^1H NMR (compounds **4–11**), ^{13}C NMR (compounds **4**, **5**, **8–10**), and mass spectral (compounds **1–11**) and analytical (compounds **5–11**) data (8 pages). Ordering information is given on any current masthead page.

Pyridinium Ylides Derived from Pyryliums and Amines and a Novel Rearrangement of 1-Vinyl-1,2-dihydropyridines

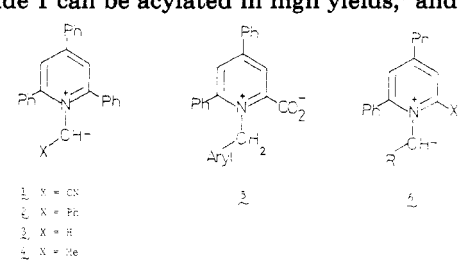
Alan R. Katritzky,* Amornsri Chermprapai, Ranjan C. Patel, and Alberto Tarraga-Tomas

School of Chemical Sciences, University of East Anglia, Norwich, NR4 7TJ, England, and the Department of Chemistry, University of Florida, Gainesville, Florida 32611

Received June 30, 1981

1-Benzyl-2,4-diphenylpyridiniums with benzaldehydes give oxazolopyridines which are dehydrated to 1-styryl derivatives. On pyrolysis the 1-styryl-1,2-dihydropyridine **21a** gave 2,4,6-triphenylpyridine and *m*-chlorostyrene by a ring-enlargement–ring-contraction mechanism: this is a general reaction of 1-vinyl-1,2-dihydropyridines.

Nitrogen ylides are well-known:[1] pyridinium ylides have been considerably utilized in synthesis by Kroehnke[2] and others.[3] The present paper records work which is part of our attempt to utilize synthetically pyridinium ylides derived from amines and pyrylium salts. We have found that ylide **1** can be acylated in high yields,[4] and that betaines of type **5** undergo Kroehnke reaction with *p*-nitroso *N*,*N*-dimethylaniline to afford benzaldehyde nitrones.[5] However, attempts to utilize the ylides derived from 1-benzyl-, 1-methyl-, and 1-ethyl-2,4,6-triphenylpyridinium salts (**2–4**) failed: although the corresponding pyridinium tetrafluoroborates and more soluble trifluoromethane sulfonates on treatment with lithium diisopropylamide in THF at −80 °C gave deep colors, only starting materials were obtained after the addition of various electrophiles.[6]



* To whom correspondence should be addressed at the University of Florida.

(1) Johnson, A. W. "Ylid Chemistry"; Academic Press: New York, 1966.
(2) Kroehnke, F. *Ber. Dtsch. Chem. Ges.* **1935**, *68*, 1177 (and many subsequent papers). Cf.: *Angew, Chem., Int. Ed. Engl.* **1963**, *2*, 225.
(3) Ratts, K. W.; Howe, R. K.; Phillips, W. G. *J. Am. Chem. Soc.* **1969**, *91*, 6115.
(4) Katritzky, A. R.; Burgess, K.; Yeung, W. K.; Patel, R. C., unpublished work.
(5) Katritzky, A. R.; Dabbas, N.; Patel, R. C., unpublished work.

0022-3263/82/1947-0492$01.25/0