dimethyl sulfide in ether at −25 °C for 20 min) to enone **12** produces a solution of **5b**. Addition of (phenylseleno)acetaldehyde (**6**; 1.5 equiv) to this enolate (at −78 °C) affords crude alcohol **7b** upon workup. Treatment of **7b** with mesyl chloride and triethylamine in methylene chloride[6] generates trans-ketone **8b** in 65% yield after chromatography. In contrast with the nine-step literature route,[1] this two-step synthesis of ketone **8b** from cyclohexenone dramatically illustrates the utility of our new vinylation procedure.

For less hindered ketones, e.g., **13** and **17**, method A fails; deprotonation α to the carbonyl leads both to conjugation of the initially formed olefin products (producing **15** and **19**) and to mesylate elimination without selenium loss (affording **16**). Such problems are avoided in method B by diisobutylaluminum hydride reduction (4 equiv at −78 °C in methylene chloride) of the aldol product to a diol (e.g., **7b** → **9b**) *prior* to olefin formation. The diol (e.g., **9b**) is treated with 4 equiv of trifluoroacetic anhydride and 6 equiv of triethylamine (in CH_3CN at ~15 °C) to form the bis(trifluoroacetate); then trimethyl phosphite (3 equiv) is added and the solution refluxed (11 h) to unmask the olefin via this modified procedure of Krief.[7] Finally the reaction mixture is quenched with aqueous sodium hydroxide solution (excess, 2 h at room temperature) to hydrolyze the remaining trifluoroacetyl group. The 59% overall yield of alcohols **2b** obtained via this three-step procedure compares well with the 60% yield from method A.

The results shown in Table I[8-14] illustrate the generality of method B, which effects conversion of ketones **13**, **17**, **20**, and **22** into vinyl alcohols in overall yields of 65–78%. It should be noted that, while vinyl ketones are not intermediates in this procedure (as they are in method A), simple Jones oxidation of the homoallylic alcohols affords the nonconjugated enones in nearly quantitative yield for those cases examined (**2a,b**, **23**). Thus both methods A and B, while intended to effect reductive vinylation to the homoallylic alcohols, can be used to obtain the vinylated ketones as well. Use of these procedures should provide ready access to a variety of substituted Cope–Claisen precursors, and natural products, not easily synthesized by other means; such applications are currently under way.

Acknowledgment. Support of this investigation was provided by the Science and Education Administration of the U.S. Department of Agriculture under Grant No. 7800894, by the National Institutes of Health under Biomedical Sciences Support Grant No. RR07033-13, and by the National Cancer Institute, DHEW, under Grant No. 27157-01.

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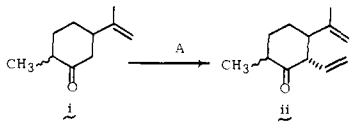
Received August 18, 1980

(5) Seebach, D.; Newmann, H. *Chem. Ber.* **1974**, *107*, 847.
(6) See Table I, note *e*.
(7) Addition of trimethyl phosphite is essential to effect olefin formation on these bis(trifluoroacetates); this extra reagent was not employed in the mono(trifluoroacetate) systems investigated by: Rémion, J.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1976**, 1385.
(8) Ketone **1** was obtained from *l*-carvone in 75% yields by conventional reductive methylation in ammonia; a related preparation was recently reported by: Mueller, R. H.; Gillick, J. G. *J. Org. Chem.* **1978**, *43*, 4647.
(9) Obtained for these new compounds were IR and NMR spectral data consistent with the assigned structures, as well as satisfactory combustion or exact mass spectral analyses.
(10) Edwards, H. N.; Wycpoleki, A. F.; Corbin, N. C.; McChesney, J. D. *Synth. Commun.* **1978**, 563.
(11) Crandall, J. K.; Arrington, J. P.; Hen, J. *J. Am. Chem. Soc.* **1967**, *89*, 6208.
(12) Akenhaim, D.; Henry-Basch, E.; Freon, P. *Bull. Soc. Chim. Fr.* **1969**, 4038.
(13) Chau, T. M.; Beaute, C.; Thoai, N.; Niemann, J. *Bull. Soc. Chim. Fr.* **1971**, 4138.
(14) Katzenellenbogen, J. A.; Lenox, R. S. *J. Org. Chem.* **1973**, *38*, 326.
(15) Reich, H. J; Reich, I. L.; Renga, J. M. *J. Am. Chem. Soc.* **1973**, *95*, 5813.
(16) After submission of the manuscript, an alternative vinylation procedure appeared in the literature: Chang, T. C. T.; Rosenblum, M.; Samuels, S. B. *J. Am. Chem. Soc.* **1980**, *102*, 5930.
(17) At the suggestion of one referee, *l*-dihydrocarvone, i, was submitted to our vinylation procedure; ketone ii was obtained in 65% yield after purification, using method A without the lithium aluminum hydride reduction step.



i ii

Alkylaluminum Chloride Induced Cyclization of Unsaturated Carbonyl Compounds

Sir:

We have recently reported that alkylaluminum chlorides are useful catalysts for ene and Diels–Alder reactions[1] and cation–olefin cyclizations,[2] since they are proton scavengers as well as Lewis acids. We report here studies of the alkylaluminum chloride induced cyclization of unsaturated aldehydes and ketones which indicate the advantages of these reagents in Lewis acid initiated reactions. Proton-catalyzed reactions do not occur, the alkyl group can enter into the reaction in a synthetically useful manner, and the type of reaction can often be controlled by variation of the temperature and the strength and amount of Lewis acid. These reactions should be of considerable value in synthesis, as illustrated by the synthesis of the CD ring system of androstanone.

The reactions of 2,6-dimethyl-5-heptenal (**1**) (in the text **1–9** refer to the alcohol or carbonyl compounds obtained after workup from the structures shown in Scheme I), which are shown in Table I, indicate that either concerted or stepwise reactions can be made to occur selectively. With 1 equiv of Me_2AlCl at −80 °C, a concerted Lewis acid catalyzed ene reaction, which gives **2a** and **2b** in a 3:1 ratio, is the predominant process.[3,6] The ene adduct·Me_2AlCl complex loses CH_4 to give the aluminum alkoxide, thereby preventing reversal of the ene reaction and decomposition of **2**.[1] We believe that **2** is formed by a concerted process since ene reactions of 1,6-dienes have been shown to give mainly cis-substituted cyclopentanes[4,6] and **3** has the wrong stereochemistry to give **2**.

With 2 equiv of Me_2AlCl a more electrophilic aldehyde·$(Me_2AlCl)_2$ complex is formed, so that formation of **3** by a more rapid reaction becomes the major process. At −80 °C, a high yield of chloro alcohol **4** is isolated. At 0 °C, formation of **4** is reversible, so that products obtained from **3** by three competing irreversible reactions are obtained. A 1,5-methyl shift gives **6**,[7] a reversible 1,5-proton shift gives **5**, which irreversibly loses CH_4,[1] and two 1,2-hydride shifts give **8**.[8,9]

Treatment of **1** with 2 equiv of $MeAlCl_2$ at −80 °C gives mainly **8**. This is due to the greater acidity of $MeAlCl_2$, which makes

(1) Snider, B. B. *Acc. Chem. Res.*, in press. Snider, B. B.; Rodini, D. J. *Tetrahedron Lett.* **1980**, *21*, 1815. Snider, B. B.; Rodini, D. J.; Conn, R. S. E.; Sealfon, S. *J. Am. Chem. Soc.* **1979**, *101*, 5283.
(2) Snider, B. B.; Rodini, D. J.; Van Straten, J. W. *J. Am. Chem. Soc.* **1980**, *102*, 5872.
(3) The stereochemical assignments of **2** and **5** are based on the NMR signals for the olefin hydrogens which absorb as one singlet for **5** and two singlets separated by 0.14 ppm for **2**.[4] The C*H*OH absorbs at the following δ: **2a**, 3.74 (br d, J = 4.6 Hz); **2b**, 3.93 (dd, J = 2.9, 3.1 Hz); **5a**, 3.42 (dd, J = 8.8, 8.1 Hz); **5b**, 3.93 (dd, 1, J = 6.3, 6.3 Hz); **4a**, 3.60 (dd, J = 7.3, 7.3 Hz); **6a**, 3.42 (br, $W_{1/2}$ = 15 Hz); **7a**, 3.44 (dd, J = 6.7, 6.7 Hz); **9a**, 3.28 (dd, 1, J = 7, 7 Hz).[5]
(4) McQuillin, F. J.; Parker, D. G. *J. Chem. Soc., Perkin Trans. 1* **1974**, 809.
(5) Rei, M.-H. *J. Org. Chem.* **1978**, *43*, 2173.
(6) For a review of intramolecular ene reactions of aldehydes, see ref 15 and: Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476.
(7) Varech, D.; Jacques, J. *Bull. Soc. Chim. Fr.* **1969**, 3505.
(8) Similar reactions have been reported with other unsaturated aldehydes[9] and we have found that 2 equiv of $RAlCl_2$ will induce the conjugate addition of alkenes to enones to give zwitterions which undergo similar hydride shifts.[2]
(9) (a) Kulkarni, B. S.; Rao, A. S. *Org. Prep. Proced. Int.* **1978**, *10*, 73. (b) Sakai, K.; Ide, J.; Oda, O.; Nakamura, N. *Tetrahedron Lett.* **1972**, 1287. (c) Baldwin, J. E.; Lusch, M. J. *J. Org. Chem.* **1979**, *44*, 1923. (d) Cookson, R. C.; Smith, S. A. *J. Chem. Soc., Chem. Commun.* **1979**, 145.

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Scheme I

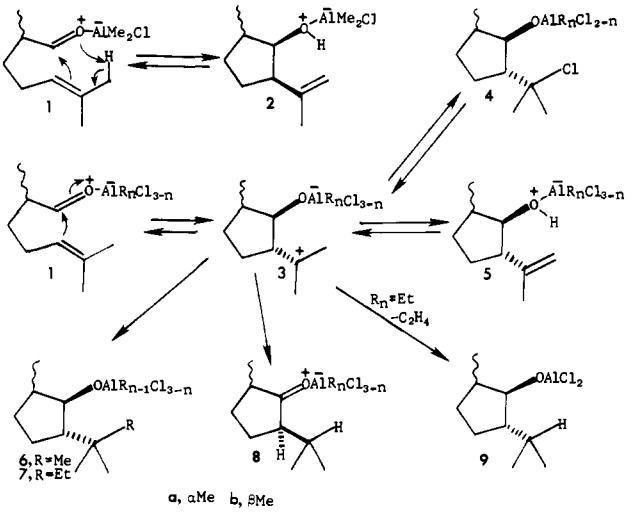


Table I. Cyclization of 2,6-Dimethyl-5-heptenal (1)[a]

Lewis acid (equiv)	temp, °C (time, h)	% yield[b] 2a (2b)	4a	5a (5b)	6a/7a	8a (8b)	9a
Me_2AlCl (1)[c]	−80 (0.2)	30 (11)	5	2			
Me_2AlCl (2)	−80 (0.2)	1	75[d]				
Me_2AlCl (2)	0 (4.0)	7 (2)		34 (1)	30	22 (2)	
$MeAlCl_2$ (2)	−80 (0.2)	4 (1)		9 (1)	4	72 (6)	
$EtAlCl_2$ (2)	−80 (0.2)				14	8 (3)	73[e]
$EtAlCl_2$ (2)	0 (1.0)				7	43 (4)	41

[a] Reactions were conducted by adding a 15–25% solution of the Lewis acid in heptane to a 0.3 M solution of 1 in anhydrous CH_2Cl_2 under nitrogen. The reactions were quenched by addition to 10% NaOH solution. The product was isolated by extraction into pentane, which was dried and evaporated at reduced pressure. [b] Determined by GC analysis. All compounds were isolated by preparative GC or column chromatography on silica gel and fully characterized. [c] 20% unreacted 1 was recovered. [d] 54% isolated yield. [e] 51% isolated yield.

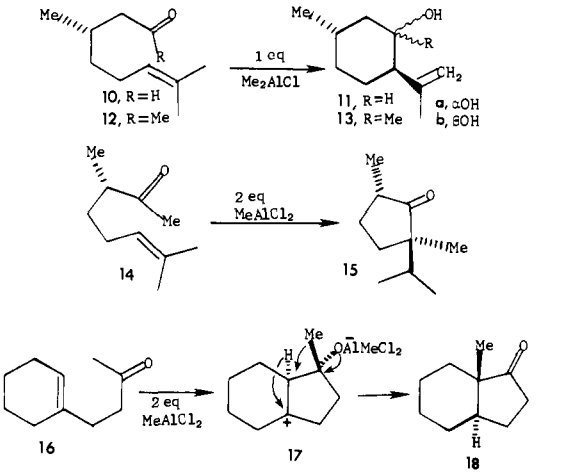
4 unstable, even at −80 °C.[10a] Since the methyl group of $MeAlCl_2$ is less basic and nucleophilic than that of Me_2AlCl, 5 reverts to 3 faster than it loses CH_4 and formation of 6 is less facile. Formation of 8 has been previously observed by treatment of 1 with BF_3·Et_2O.[9a]

With 2 equiv of $EtAlCl_2$ at −80 °C, a reductive cyclization to give 9 is the major process.[10] Apparently the zwitterion 3 reacts via hydride delivery from the β-hydrogen of the ethyl group to give 9 and C_2H_4, possibly through an eight-membered ring transition state. At 0 °C, 8 and 9 are formed in a 1:1 ratio. The proposed mechanism for the formation of 9 would have a large negative $\Delta S^{\ddagger}$, which is consistent with the selective formation of 9 at lower temperature.

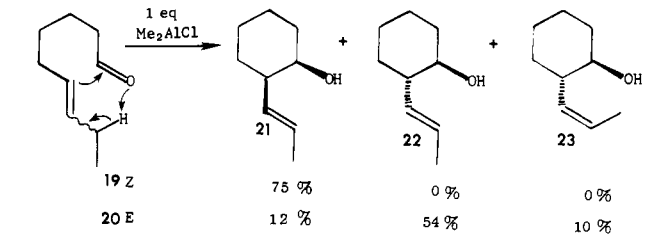
In all cases, stepwise reaction appears to occur exclusively or predominantly through the trans,trans-zwitterion **3a**. No **4b**, **6b**, **7b**, or **9b** is detected and only small amounts of **5b** and **8b** are formed. This selectivity may be due to kinetic or thermodynamic control, since formation of 3 from 1 is probably reversible. Ketone 8 is ≈95% **8a** which is consistent with reaction proceeding through **3a** and indicates that equilibration does not occur since a 70:30 mixture of **8a** and **8b** is present at equilibrium.[11]

Citronellal (**10**) does not show a similar variation in reactivity, giving, under all of the above conditions, mixtures of isopulegol

Scheme II



Scheme III



(**11a**) and neoisopulegol (**11b**) with traces of the other isomers, similar to those obtained with other Lewis acids.[12] The difference in reactivity between 1 and **10** is due, at least in part, to the equilibrium constant of the ene reaction. Using Benson's group additivity rules[13] we calculate $\Delta H = -3.3$ kcal/mol and $\Delta S = -22.7$ eu for the ene reaction of 1 and $\Delta H = -9.6$ kcal/mol and $\Delta S = -31$ eu for the ene reaction of **10**. The difference in ΔH is due to the cyclopentane ring strain of 6.3 kcal/mol. This estimate suggests that the aldehyde 1 should exist in equilibrium with ene adducts 2 and 5.[14] The facile formation of 8 from 1 and the lack of formation of menthone from **10** may also be due to the thermodynamics of the first 1,2-hydride shift. A 1,2-hydride shift in the α,α-dimethylcyclopentylmethyl cation to give the 1-isopropylcyclopentyl cation is exothermic while the corresponding 1,2-hydride shift in the α,α-dimethylcyclohexylmethyl cation is endothermic.[16]

The corresponding ketones **12** and **14** react similarly to **10** and 1. Treatment of **14** with 2 equiv of $MeAlCl_2$ at 0 °C for 4 h gives a 60% yield of **15**.[17] The ketone **12** gives a 58% yield of a 4.5:1 mixture of **13a** and **13b**[18] on treatment with 1 equiv of Me_2AlCl at 25 °C for 24 h. The isolation of a tertiary alcohol in the presence of a Lewis acid is remarkable and is presumably due to the rapid loss of CH_4 from the alcohol·Me_2AlCl complex to give the aluminum alkoxide, which is stable. Me_2AlCl should be especially useful for intramolcular ene reactions of ketones since the adducts are often not stable at the temperatures required for uncatalyzed reactions. For instance, Conia has reported that

(10) (a) Treatment of chloro alcohol **4a** with 1 equiv of Et_2AlCl and 1 equiv of $EtAlCl_2$ at −78 °C gives the chloro alkoxide which would be obtained from 1 ·$(EtAlCl_2)_2$. This species is unstable giving 1, **7a**, 8, and **9a**. (b) The ethyl group is more nucleophilic than the methyl group and β-hydride delivery is a kinetically facile process. See: Ashby, E. C.; Noding, S. A. *J. Org. Chem.* **1979**, *44*, 4792.

(11) Sisido, K.; Kurozumi, S.; Utimoto, K.; Isida, T. *J. Org. Chem.* **1966**, *31*, 2795.

(12) Nakatani, Y.; Kawashima, K. *Synthesis* **1978**, 147 and references cited therein.

(13) Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley: New York, 1976.

(14) We have observed partial reversion of 2, but not 5, to 1 during GC at 125 °C and **2a** is rapidly converted to 8, presumably via 1, on treatment with BF_3·Et_2O at 0 °C. Andersen has reported that similar ene adducts undergo facile reversion to aldehydes.[15]

(15) Andersen, N. H.; Ladner, D. W. *Synth. Commun.* **1978**, *8*, 449 and references cited therein.

(16) Saunders, M., Yale University, personal communication, 1980.

(17) Doering, W. von E.; Willcott, M. R., III; Jones, M. Jr., *J. Am. Chem. Soc.* **1962**, *84*, 1224. Several minor products were also formed. Reaction of **14** with 1 equiv of Me_2AlCl gave only the aldol dimer.

(18) Watanabe, S. *J. Sci. Hiroshima Univ., Ser. A.* **1973**, *37*, 91. The aldol dimer was formed in 20% yield.

pyrolysis of **12** for 46 h at 350 °C gives a 50% yield of 2,4-dimethylisopropylbenzene, which most likely arises via dehydration and dehydrogenation of the ene adduct **13**.[19]

The cyclization of **16** was investigated as a model study for the synthesis of steroids by annealation of the D ring. Treatment of **16** with 2 equiv of $MeAlCl_2$ for 24 h at 0 °C gives a 50% yield of *trans*-hydrindanone **18**[20] via the intermediate **17**. Baldwin and Lusch have reported the cyclization of ketones, but only at 100–140 °C in the presence of $AlCl_3$.[9c]

The reactions of **19** and **20** were explored to determine the effect of double-bond stereochemistry on the stereochemistry of the ene adduct, and if the less nucleophilic 1,2-disubstituted double bond could be used as the ene. The *Z* isomer **19**[21] gives exclusively the cis-substituted adduct **21** with 1 equiv of Me_2AlCl for 2 h at 0 °C, while the *E* isomer gives mainly the trans-substituted isomers **22** and **23** (see Scheme III). Due to the less nucleophilic double bond of **19** and **20**, reaction is much slower than with **10** and methyl addition to the aldehyde competes, giving 15–20% of 7-decen-2-ol. The exclusive formation of **21** from **19** is due to geometrical constraints on the transition state.[6] The ene reaction thus offers a promising route to 2-alkenylcyclohexanols with control of stereochemistry.

The above examples indicate that alkylaluminum halides are Lewis acids with many unique properties which make them attractive reagents for organic synthesis.

Acknowledgment. We thank the Research Corp., the National Institutes of Health, and the Mobil Foundation for financial support. The synthesis of **18** was carried out by Ketih McDaniel.

Supplementary Material Available: Physical data for all products (4 pages). Ordering information is given on any current masthead.

(19) Rouessac, F.; Le Perchec, P.; Conia, J.-M. *Bull. Soc. Chim. Fr.* **1967**, 818.

(20) Johnson, W. S. *J. Am. Chem. Soc.* **1944**, *66*, 215. Lansbury, P. T.; Briggs, P. C.; Demmin, T. R.; Du Bois, G. E. *Ibid.* **1971**, *93*, 1311. Zeeh, B.; Jones, G.; Djerassi, C. *Chem. Ber.* **1967**, *100*, 3204. Three minor products in a total of 25% yield are also formed in the cyclization of **16**.

(21) We thank Bedoukian Research Inc. for a generous gift of **19**.

(22) Fellow of the Alfred P. Sloan Foundation, 1979–1981.

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Received August 18, 1980

Myricoside, an African Armyworm Antifeedant: Separation by Droplet Countercurrent Chromatography

Sir:

Our continuing search for insect antifeedant compounds from natural sources[1] has led us to examine the active constituents from the roots of *Clerodendrum myricoides* (Verbenaceae). This shrub was collected in East Africa, mainly on the basis of information provided by "Bwana Mganga", the local medicine man.[2] Extracts from the roots revealed potent insect antifeedant activity when tested against the African armyworm *Spodoptera exempta*, using the leaf disk bioassay with *Zea* mays.[3] Separation of the active material was monitored by this antifeedant bioassay,[1a,c] using a combination of polyamide chromatography and droplet countercurrent chromatography (DCCC).[4] This latter technique proved to be extremely efficient for the separation of the desired bioactive compound; all other semipreparative-scale methods failed or led to decomposition of material. We now report the structure of the active component, myricoside, as 3,4-dihydroxy-β-phenethyl-*O*-β-D-apiofuranosyl-(1→3)-α-L-rhamnopyranosyl-(1→3)-4-*O*-caffeoyl-β-D-glucopyranoside (**1**) (Figure 1). It is a potent antifeedant against *S. exempta*, the 10-ppm activity level being comparable to that of ajugarin.[5,6]

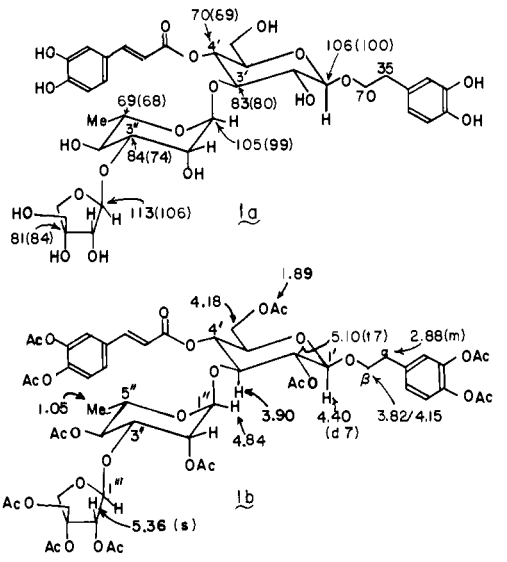

Figure 1. (a) Myricoside. Pertinent ^{13}C NMR peaks are shown; values in parentheses are chemical shifts in the peracetate. (b) Myricoside peracetate. Pertinent ^1H NMR peaks are shown.

Addition of ether to the aqueous methanolic extract of the roots (500 g) gave a precipitate (1 g) which was eluted from polyamide (Woelm) with H_2O. Further fractionation was carried out by DCCC. The active fraction (125 mg) was partitioned between a $CHCl_3$–MeOH–H_2O (7:13:8) equilibrated solvent mixture, with passage of the upper aqueous phase as mobile ascending droplets (flow rate 5 mL/h) through the stationary organic phase.[4c] Base-line separation into four fractions (I–IV) was achieved after 12 h, using a total of only 60 mL of solvent (collected in 1-mL aliquots, 254-nm detection). The bioactive fraction II was finally passed through polyamide (H_2O) to yield 10 mg of myricoside (**1**): mp 165–167 °C (aqueous MeOH); IR (Nujol) 3400 (br, OH), 1705 (conjugated ester), 1600 cm^{-1} (aromatic); UV (MeOH) 216 (ε 19 900), 246 sh (ε 11 000), 288 (ε 13 700), 300 (ε 14 400), 330 nm (ε 20 600; shifts to 375 nm (ε 21 200) on addition of base). These data suggested that **1** contained caffeate and catechol moieties as chromophores in a 1:1 ratio; this was corroborated by actual simulation experiments with a 1:1 mixture of methyl caffeate and catechol carried out in the pH range 2–9.

^1H and ^{13}C NMR showed **1** to have aromatic and sugar moieties. Acid hydrolysis of myricoside (1 mg) in refluxing aqueous 2 N HCl/MeOH (1:1) yielded D-apiose, L-rhamnose, and D-glucose[7] as well as caffeic acid. Mild hydrolysis of **1** in refluxing aqueous 0.1 N HCl for 20 min gave apiose as the only detectable sugar, suggesting this sugar to be the terminal unit. The following

(1) (a) Nakanishi, K. *Pontif. Acad. Sci. Scr. Varia* **1977**, *No. 41*, 185. (b) Kubo, I.; Nakanishi, K. *ACS Symp. Ser.* **1977**, *No. 62*, 165. (c) In "Advances in Pesticide Science, Part 2"; Geissbühler, H., Ed.; Pergamon: Oxford and New York, 1977; p 284.

(2) Taniguchi, M.; Chapya, A.; Kubo, I.; Nakanishi, K. *Chem. Pharm. Bull.* **1978**, *26*, 2910.

(3) The *S. exempta* bioassays were carried out at the International Centre of Insect Physiology and Ecology (ICIPE), Nairobi, Kenya.

(4) (a) Tanimura, T.; Pisano, J. J.; Ito, Y.; Bowman, R. L. *Science* **1971**, *169*, 54. (b) Hostettmann, K.; Hostettmann-Kaldas, M.; Nakanishi, K. *Helv. Chim. Acta* **1978**, *61*, 1990. (c) Hostettmann, K.; Hostettmann, M.; Nakanishi, K. *J. Chromatogr.* **1979**, *170*, 355. (d) The apparatus is handled by Tokyo Rikakikai Co. Ltd., Nishikawa Bldg., Toyama-cho, Kanda, Tokyo.

(5) Kubo, I.; Lee, W.-W.; Balogh-Nair, V.; Nakanishi, K.; Chapya, A. *J. Chem. Soc., Chem. Commun.* **1976**, 949.

(6) In tests carried out at Columbia University, myricoside is not active against the Southern armyworm *S. eridania* or the Mexican bean beetle *Epilachna varivestis*.

(7) The sugars were detected in the free form by TLC (silica gel, 4:1:5 *n*-BuOH-AcOH-H_2O), and as their dansylhydrazone derivatives: Avigad, G. *J. Chromatogr.* **1977**, *139*, 343.

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