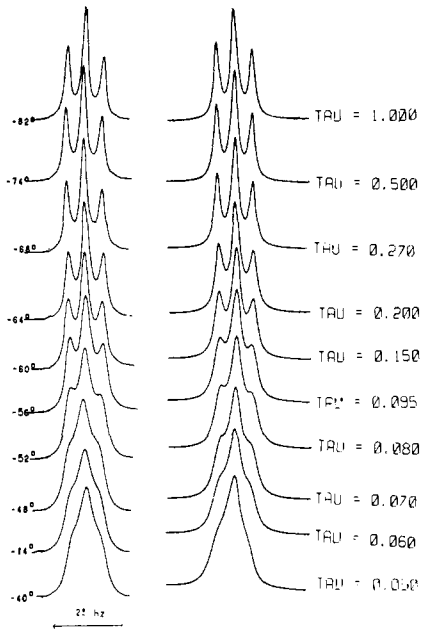


Figure 1. Temperature-dependent pmr spectra of exchanging complex, $(CH_3)_2SiF_2 \rightarrow SbF_5$, in SO_2ClF (left) and calculated spectra (right).

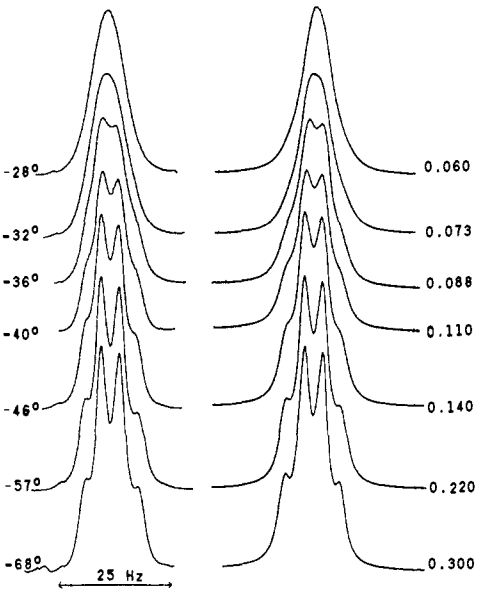
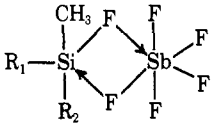


Figure 2. Temperature-dependent pmr spectra of exchanging complex, $CH_3SiF_3 \rightarrow SbF_5$, in SO_2ClF (left) and calculated spectra (right).

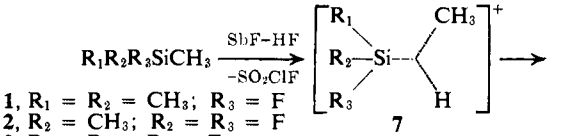
the analogous carbenium ion, $CH_3{}^+CF_2$, has been recently directly observed.[12] Again, the formation of a donor–acceptor complex, $CH_3SiF_3 \rightarrow SbF_5$, is indicated by the above observations. Temperature-dependent ^1H and ^{19}F nmr spectra were obtained when equal molar amounts of **3** and SbF_5 were mixed in SO_2ClF (Figure 2). Theoretical spectra were calculated to fit the experimental proton spectra. The energy of activation, E_a, of this exchange process was estimated to be 4.3 ± 0.9 kcal/mol.

The direct observation of a silicenium ion was not achieved even in the low nucleophilicity SbF_5–SO_2ClF media used in this study. In comparison to the chemistry of carbocations, the available empty 3d orbitals of the silicon atom seem to be responsible for the failure to directly observe silicenium ions. This is because the empty 3d orbital of silicon is capable of changing the tetrahedral sp^3 hybridization to the trigonal pyramidal sp^3d hybridization. Consequently, we conclude that the rapidly exchanging complexes of **1–3** with SbF_5 could have structures **4–6** as shown (or containing dimeric antimony pentafluoride, *i.e.*, $R_1R_2CH_3SiF$, Sb_2F_{10}).



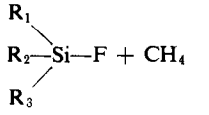
4, $R_1 = R_2 = CH_3$
5, $R_1 = CH_3$; $R_2 = F$
6, $R_1 = R_2 = F$

We have also studied the behavior of the methylfluorosilanes (**1–3**) in SbF_5–HF–SO_2ClF solution. Silicocations were not observed. Instead, protolytic cleavage of Si–C single bonds (assumed through a three-center bound[13] transition state **7**, a pentacoordinated siliconium ion) took place to give methane and the higher homologous methylfluorosilanes. Similar types of Si–C single bond cleavage reactions in strong acid have been observed by O'Brien.[14]



1, $R_1 = R_2 = CH_3$; $R_3 = F$
2, $R_2 = CH_3$; $R_2 = R_3 = F$
3, $R_1 = R_2 = R_3 = F$

7



Acknowledgment. Support of our work by the National Science Foundation and the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

(12) G. A. Olah and Y. K. Mo, *J. Org. Chem.*, in press.
(13) (a) G. A. Olah, Y. Halpern, J. Shen, and Y. K. Mo, *J. Amer. Chem. Soc.*, **93**, 1251 (1971); (b) G. A. Olah and J. A. Olah, *ibid.*, **93**, 1256 (1971); (c) G. A. Olah and H. C. Lin, *ibid.*, **93**, 1259 (1971).
(14) D. H. O'Brien and C. M. Harbordt, *J. Organometal. Chem.*, **21**, 321 (1970); **24**, 327 (1971).

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Tirandamycin. I. Structure Assignment

Sir:

Tirandamycin, a new antibacterial agent isolated from the culture broth of *Streptomyces tirandis* sp. n.,[1] has been the subject of two recent reports describing its mode of action.[2,3] The compound shows potent inhibition of RNA polymerase in bacterial cell-free systems[2] and interferes with oxidative phosphorylation

(1) C. E. Meyer, *J. Antibiot.*, **24**, 558 (1971).
(2) F. Reusser, *Infec. Immun.*, **2**, 77 (1970).
(3) F. Reusser, *ibid.*, **2**, 82 (1970).

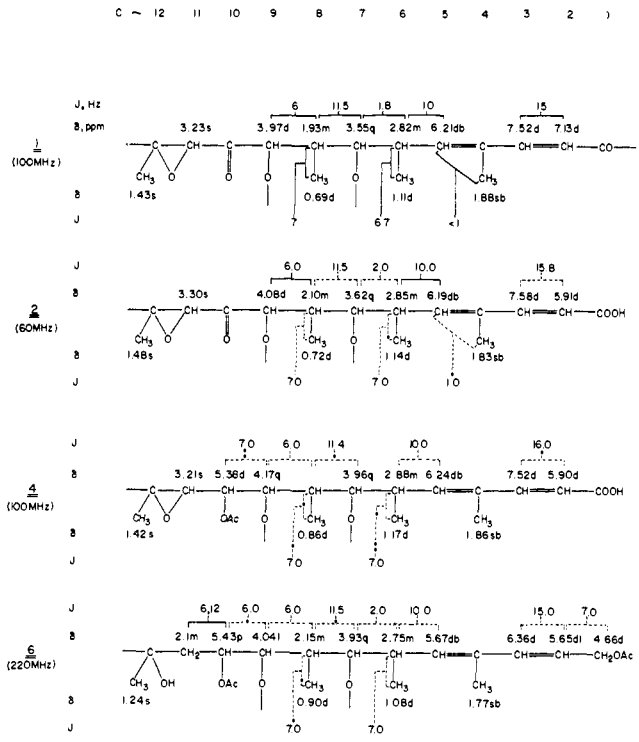
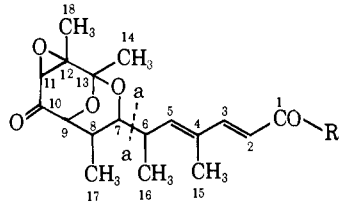
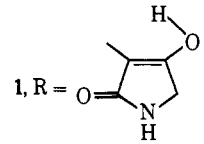


Figure 1. Nmr ($CDCl_3$ solutions) for compounds described in the text. Abbreviations of multiplicities are: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, b = broad. Solid lines join those absorptions for which decoupling was carried out. Funds contributing to the purchase of the HR-220 nmr spectrometer were provided by the National Science Foundation.

in rat liver mitochondria.[3] In the present report we assign structure **1** to tirandamycin.





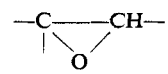
1, R =

2, R = OH

Tirandamycin has been assigned the empirical formula $C_{22}H_{27}NO_7$ on the basis of high-resolution mass spectral measurements (calcd, 417.1786; found, 417.1792) and microanalyses of a bromobenzene adduct.[1] The chemical nature of the antibiotic is adumbrated by the close similarity of its peculiar ultraviolet spectral properties [$\lambda\lambda_{max}$ 287,331 nm ($\epsilon\epsilon_{max}$ 16,200, 16,700, respectively) in 0.01 *N* potassium hydroxide in 95% ethanol; λ_{max} 353 (ϵ_{max} 32,700), shoulder 366 nm (ϵ 30,000) in 0.01 *N* sulfuric acid in 95% ethanol] to those of the dienoyltetramic acid antibiotic streptolydigin,[4] and by the similarity of the nmr spectra (Figure 1) of tirandamycin and streptolic acid,[5] a periodate degradation product of sodium streptolydigin, in the olefinic region. The modes of antibacterial action of streptolydigin[6] are also the same as those of tirandamycin. Accordingly, periodate oxidation of sodium tirandamycin was carried out, affording tirandamycic acid (**2**; $C_{18}H_{24}O_6$;[7,8] mp 70–74°) in 58% yield. As expected, the ultraviolet spectrum of **2** (λ_{max} 260 nm (ϵ_{max} 27,400)) and its nmr spectrum (Figure 1) show it to be a dienoic acid, whose chromophoric region is nearly identical with that of streptolic acid (λ_{max} 261 nm (ϵ_{max} 28,200)).[5] Two sharp doublets ($J_{2,3}$ = 15.8 Hz) at δ 5.91 (H-2) and 7.58 (H-3, at characteristically low field),[9] indicate trans substitution[9] of the α,β double bond and no proton in the γ position. The γ-methyl peak is identified at δ 1.83, coupled ($J_{5,15}$ = 1.0 Hz) with the δ proton at 6.19, which appears as a doublet ($J_{5,6}$ = 10.0 Hz) broadened by coupling with the γ-methyl protons. Other aspects of the substitution pattern of C-1 through C-9 were established by spin decoupling, as indicated in Figure 1. In addition, the nmr spectrum ($CDCl_3$) of tirandamycic acid contains CH_3CO singlets at δ 1.48 and 1.58 and a CH–O singlet at 3.30.

The nature of the functional groups beyond C-9 and their juxtaposition to the C(1)–C(9) unit were established by hydride reductions. Sodium borohydride reduction of **2** in 50% aqueous ethanol gave a secondary alcohol, **3** ($C_{18}H_{26}O_6$;[7,8] mp 199–201°) in 89% yield. The nmr spectra of **3** (CD_3COCD_3) and its acetate (Figure 1), **4** ($C_{20}H_{28}O_7$;[7,8] mp 67–72°; prepared in 90% yield by acetylation of **3** with acetic anhydride–pyridine), show the H-10 proton near δ 4.1 (**3**) and at 5.38 (**4**) (doublet, $J_{9,10}$ = 7.0 Hz) and the H-9 proton as a multiplet ($J_{8,9}$ = 6.0 Hz) at 3.8 (**3**) and 4.17 (**4**). In both compounds' spectra the epoxide proton at H-11 (δ 3.10 in **3**) remains effectively a singlet. A model shows the dihedral angle between H-10 and H-11 to be *ca.* 90°, in accord with a coupling constant near zero.

Lithium aluminum hydride reduction of **2** in ether gave the triol **5** ($C_{18}H_{30}O_5$;[8,10] oil) in 38% yield, while similar reduction of **3** in tetrahydrofuran afforded **5** in 56% yield. The nmr spectrum ($CDCl_3$) of **5** shows loss of the epoxide proton and change of the adjacent H-10 proton's absorption to a multiplet at δ 4.47 ($J_{9,10}$ = ~6 Hz). Acetylation of **5** in acetic anhydride–pyridine produced the diacetate **6** ($C_{22}H_{34}O_7$;[8,10] oil) in 80% yield. In the nmr spectrum (Figure 1) of **6** the H-10 proton appears as a pentet at δ 5.43 ($J_{9,10}$ = 6.0 Hz; $J_{10,11}$ = 12, 6 Hz) and the H-11 methylene protons as a multiplet near δ 2.14, thereby establishing C-10 as being linked to the CH–O unit (C-11) noted above. The chemical shift of H-11 in the spectra of **1**–**4** (δ 3.1–3.3) is in agreement with its formulation as part of an epoxide



as indicated by the lithium aluminum hydride reduction of **2** and **3**, thus giving the unit

(4) K. L. Rinehart, Jr., J. R. Beck, D. B. Borders, T. H. Kinstle, and D. Krauss, *J. Amer. Chem. Soc.*, **85**, 4038 (1963).

(5) K. L. Rinehart, Jr., J. R. Beck, W. W. Epstein, and L. D. Spicer, *ibid.*, **85**, 4035 (1963).

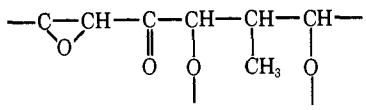
(6) F. Reusser, *J. Bacteriol.*, **100**, 1335 (1969).

(7) Elemental analyses agree with the formula given.

(8) Low-resolution mass spectra, obtained on a Varian MAT CH5 mass spectrometer by the direct inlet technique, were in agreement with the formula cited.

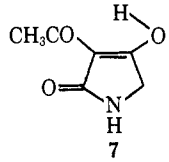
(9) L. M. Jackman and R. H. Wiley, *J. Chem. Soc.*, 2886 (1960).

(10) High-resolution mass spectral data, obtained on a Varian MAT SM-1B mass spectrometer, were in agreement with the formula cited.



for C(7)–C(12). If the oxygen at C-7 or that at C-9 were attached to C-12, a hemiketal would be generated in the reduction of **2** and **3** and that would have been further reduced rather than giving **5**. Thus, the extra CH_3C unit must be attached to both O-7 and O-9, and at C-12 as well, along with the remaining methyl group. The structure of tirandamycic acid is then **2**. It is of interest that the carbon skeletons of **2** and streptolic acid[5] are identical, the two acids differing only in functional groups on the tetrahydropyran ring. As expected,[11] **2** and all its degradation products, as well as **1**, show facile mass spectral fragmentations along line a···a to give intense peaks (at *m/e* 197 for **1** and **2**, at *m/e* 199 for **3**, at *m/e* 241 for **4**, at *m/e* 201 for **5**, and at *m/e* 243 for **6**).

Subtraction of the acyl group ($C_{18}H_{23}O_5$) from the molecular formula of tirandamycin ($C_{22}H_{27}NO_7$) leaves $C_4H_4NO_2$ for the tetramic acid portion of the molecule, *i.e.*, the tetramic acid must be unsubstituted except for the 3-acyl group. In agreement with this assignment is a mass spectral peak due to cleavage between C-1 and C-2 of the acyl group (calcd for $C_5H_4NO_3$, 126.0191; found, 126.0193). Moreover, the nmr spectrum ($CDCl_3$) of **1** contains an amide NH at δ 6.95 and an isolated methylene group at 3.76, as well as an enolic OH at 13.16; synthetic 3-acetyltetramic acid, **7**, exhibits nmr absorptions[12] for the amide NH at δ 6.82 and the isolated methylene at 3.72 (as well as the enolic OH at 11.8, reflecting the difference in the functions of **1** and **7** α to the enolic carbon).



7

Acknowledgment. This work was supported in part by Public Health Service Grants AI 01278 and AI 04769 from the National Institute of Allergy and Infectious Diseases and CA 11388 from the National Cancer Institute.

(11) K. L. Rinehart, Jr., *Carygraph*, 3 (2), 1 (1964).
(12) A. Aebi, H. U. Daeniker, and J. Druey, *Pharm. Acta Helv.*, 38 (1963).

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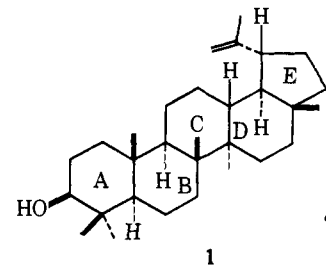
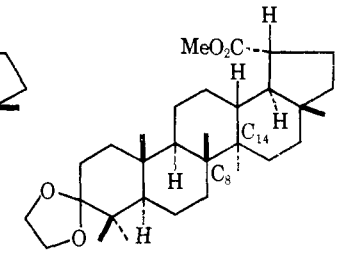
The Total Synthesis of Lupeol

Sir:

Lupeol (**1**), said to be the most abundant of the pentacyclic triterpenes,[1] became of interest to us, not only because of the stereochemical challenge of its ten asymmetric centers, but also because this rather complex structural problem presented us with the opportunity of using and extending the enolate trapping method.[2]

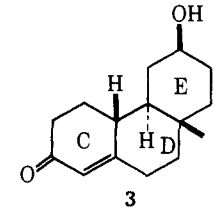


1



2

The goal of the synthesis was the pentacyclic ketal ester **2** which embodies essentially all the asymmetry of lupeol into which it presumably should be easily convertible. The correctness of this assumption was checked by demonstrating that **2**, mp 204–206°, made from natural lupeol,[3] could, indeed, be reconverted to lupeol by (a) treatment with excess lithium methyl in refluxing dioxan, followed by phosphorus oxychloride–pyridine dehydration, to establish the isopropenyl group and (b) deketalization and sodium borohydride reduction. The identity of the lupeol thus formed was established by comparison of its benzoate, mp 250–252°, with that of an authentic sample (mixture melting point, tlc, ir, and nmr spectra).



3

We now report the synthesis of **2** from the previously described[4] tricyclic enone **3**. The first major problem in the elaboration of **3** toward **2** involves the critical introduction of the two vicinal *trans*-methyl groups at C_8 and C_{14}, together with a substituent at C_8 to serve as a precursor of ring B. The goal at this stage thus became **9**, the construction of which, starting with the benzoate, mp 143–144°, of **3**,[5] was initiated by thermal rearrangement (refluxing pyridine, 20 hr) of its allyl enol ether (allyl orthoformate–allyl alcohol in tetrahydrofuran–*p*-toluenesulfonic acid, room temperature 1 hr) to **4**, mp 134–135° (70% from **3**). Addition of diethylaluminum cyanide[6] to the enone **4** (4:1 benzene–toluene, 0°, followed by 1 hr at 45°) gave the cyano

(1) J. Simonsen and W. C. J. Ross, "The Terpenes," Vol. IV, Cambridge University Press, Cambridge, 1957, p 329. In all structural formulas heavy and dotted lines stand for methyl groups unless otherwise labeled.
(2) G. Stork, P. Rosen, N. Goldman, R. V. Coombs, and J. Tsuji, *J. Amer. Chem. Soc.*, 87, 275 (1965). For a different approach to pentacyclic triterpene synthesis, *cf.* the total synthesis of germanicol: R. E. Ireland, *et al.*, *ibid.*, 92, 5743 (1970).
(3) Starting from the known 3β-hydroxy ester corresponding to **2** (L. Ruzicka and G. Rosenkranz, *Helv. Chim. Acta*, 23, 1311 (1940); E. R. H. Jones and R. J. Meakins, *J. Chem. Soc.*, 1335 (1940)) by Jones' oxidation and ketalization. We thank Professors K. Nakanishi and R. Stevens for samples of natural lupeol.
(4) G. Stork, H. J. E. Loewenthal, and P. C. Mukharji, *J. Amer. Chem. Soc.*, 78, 501 (1956).
(5) All intermediates had mass nmr and ir spectra in accord with their expected structures. Some were further characterized by carbon and hydrogen analyses or (as indicated in the text) by exact masses.
(6) *Cf.* W. Nagata, *Nippon Kagaku Zasshi*, 90, 837 (1969).