Lifetime Determinations. The three-phase test modified by using the "Poliphasic Dynamic Reactor" (PDR)[9] has been applied to determine the lifetime of 1 and 2. In PDR, resins are separated to a constant distance and a variable flow of the liquid phase is introduced. The intermediate is generated from a polymeric precursor in a vessel of PDR and trapped in another vessel. The reagent solution flows inside the PDR from precursor to trap through a conduit of known volume and outside the PDR from trap to precursor through an adjustable peristaltic pump. We found, in the same experimental conditions, the value of 2.0 ± 0.5 s for 2-aza-2,4-cyclopentadienone and 63.5 ± 0.5 s for 2,3-diaza-2,4-cyclopentadienone.

Conclusions

2,3-Diaza-2,4-cyclopentadienone, 2, is able to act as an azadienophile, but seems not be able to act as an azadiene. Thus, its reactivity differs from that of 2-aza-2,4-cyclopentadienone, 1, which behaves as a diene or as a dienophile in Diels–Alder reactions.

Lifetime values show that 1 is a very unstable intermediate compared to homocyclic 2,4-cyclopentadienone (lifetime 13.0 s).[9] This fact seems likely to depend on the high reactivity of the C=N bond. 2,3-Diaza-2,4-cyclopentadienone, 2, has also a very reactive bond (N=N); still, it is more stable than homocyclic annulenone. Probably, 2 does not dimerize, since its behavior as a diene has never been detected. Thus, the disappearance of this intermediate might follow a different pathway, and this fact could explain its larger lifetime.

Further theoretical and experimental studies on these and related azaannulenones will show us the relationship between number and positions of ring nitrogens and reactivity of these species. Such studies are under way.

Experimental Section

Preparation of the Polymeric Sulfonate of 3-Pyrazolin-5-one (3). Polymeric tosyl chloride[5] (2.0 g), 3-pyrazolin-5-one (5.1 g, 0.061 mol), and pyridine (24 mL) were stirred in 200 mL of ethanol for 3 days at room temperature. After the reaction, the resin was filtered and washed with aqueous 10% HCl, dioxane, acetone, and ether to obtain 3: IR (KBr) 3010, 2910, 1617, 1478, 1440, 1151, 1017 cm^{-1}. Analysis indicated 1.70 mequiv/g (1.95% N).

Preparation of the Bromo Compound 6. A mixture of 2,3-dimethyl-1,3-butadiene (3.86 g), NBS (4.88 g), and benzoyl chloride (0.12 g) in 34 mL of CCl_4 was heated in a steam bath for 1 h, and then the solution was chilled and filtered. The organic phase was washed with saturated sodium thiosulfate solution/iced water (1:1), dried, and evaporated to give 6: IR 2910, 1690, 1600, 1450, 1225, 1180, 1030, 1000, 705 cm^{-1}; ^1H NMR (CCl_4) δ 5.00 (m, 4 H), 4.90 (s, 2 H), 1.90 (s, 3 H); MS 162, 160, 135, 133, 97, 95, 81, 79, 67, 53, 41; bp 50 °C/30 Torr. Anal. Calcd: C, 44.72; H, 5.59. Found: C, 44.70; H, 5.60.

Preparation of Trapping Polymer 5. The polymeric acid (2 g) was added to a solution of 0.36 g of KOH in 40 mL of water. After 10 min, $AgNO_3$ (1.12 g) was added and the solution stirred at room temperature for 30 min. The silver salt of polymeric acid was separated by filtration and washed with ether: IR (KBr) 3015, 2910, 1580–1560, 1450, 1380 cm^{-1}; 2.04 mequiv/g (21.99% Ag).

Compound 6 (0.37 g) and 1.0 g of the so obtained polymer in 20 mL of dioxane were heated in a steam bath for 24 h. After filtration, the solid AgBr was removed with a solution of KCN and the resin 5 washed with dioxane, acetone, and ether: IR (KBr) 3010, 2917, 1600–1560, 1450, 1390–1370, 1020 cm^{-1}. Titration indicated 2.15 mequiv of ester/g.

Reaction of 2 as a Dienophile. Compound 3 (1.0 g) and 1.02 g of 5 were suspended in 7 mL of HMPT. Lithium amide (0.6 g in 10 mL of HMPT) was added dropwise at 30 °C, and then the mixture was stirred for an additional 24 h at room temperature. Washing and separation of the resin gave 8 (2.00 mequiv/g): IR (KBr) 3015, 2905, 1703, 1490, 1445, 1020 cm^{-1}. Compound 8 (0.83 g) was stirred in 200 mL of acetonitrile with 0.51 g of NaI, then 0.27 g of trimethylsilyl chloride was added slowly, and the reaction mixture was kept for 3 h in a steam bath. The polymer was separated by filtration, and the solution was diluted in 100 mL of HMPT and treated with $NaBH_4$, 64.4 mg, in a steam bath for 1 h. Then 200 mL of water was added and the solution extracted with CH_2Cl_2. From the evaporated mixture, 7 could be separated by TLC (silica gel as stationary phase and benzene/ethanol, 1:1, as eluent): IR (KBr) 2915, 2850, 1615, 1450, 1370 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.35 (d, 1 H), 5.55 (d, 1 H), 4.15 (s, 2 H), 4.00 (s, 2 H), 1.80 (ds, 6 H); mp 115–117 °C. It was identical with an authentic sample.[4]

Behavior of 2 as a Diene. As an example, 0.1 g of 3 and 0.43 g of polymeric monoester of acetylenedicarboxylic acid were suspended in 7 mL of HMPT, and then 0.6 g of lithium amide in 10 mL of HMPT was added dropwise. The solution was allowed to stand at 40 °C for 24 h. Unchanged polymeric trapping agent was then isolated.

Lifetime Determinations. Lifetime determinations were made as described.[9] In a series of experiments, a suspension of 6.5 mequiv of polymeric precursor (3 or 5-polymeric sulfonate of the 3-pyrrolin-2-one[1]) with 1.5 g of lithium amide in HMPT was heated and stirred at 30 °C in a vessel of PDR. Trapping agent 5 (4.5 mequiv) was stirred in the other vessel. Reagent solution flowed from precursor to trapping agent through a conduit of known volume. The run time through this conduit was adjusted by the peristaltic pump. After each experiment, the polymeric trapping agent was tested for the presence of the azaannulenone moiety. This presence showed the transfer of azaannulenone and a lifetime for the intermediate higher than the run time. The lifetime values so obtained were 2.0 ± 0.5 s for 1 and 63.5 ± 0.5 s for 2.

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Registry No. 1, 54036-77-0; 2, 56240-95-0; 4, 137-45-1; 6, 74793-41-2; 7, 73977-45-4; 2,3-dimethyl-1,3-butadiene, 513-81-5.

Determination of a New Tetracyclic Diterpene Skeleton through Selective INEPT Spectroscopy

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Salvia prionitis Hance (Labiateae) is native to the Southern Provinces of the People's Republic of China and is used as an antibacterial, antitubercular and antiphlogistic drug in traditional Chinese medicine. Previous phytochemical studies on this plant have described the isolation of several abietane and 4,5-seco-5,10-*friedo*-abietane diterpenoids.[3,4]

We report here on the isolation and structure elucidation of a new type of tetracyclic diterpene, prionitin (1), obtained by chromatographic separation of the chloroform-soluble part of the crude ethanolic extract of the roots of

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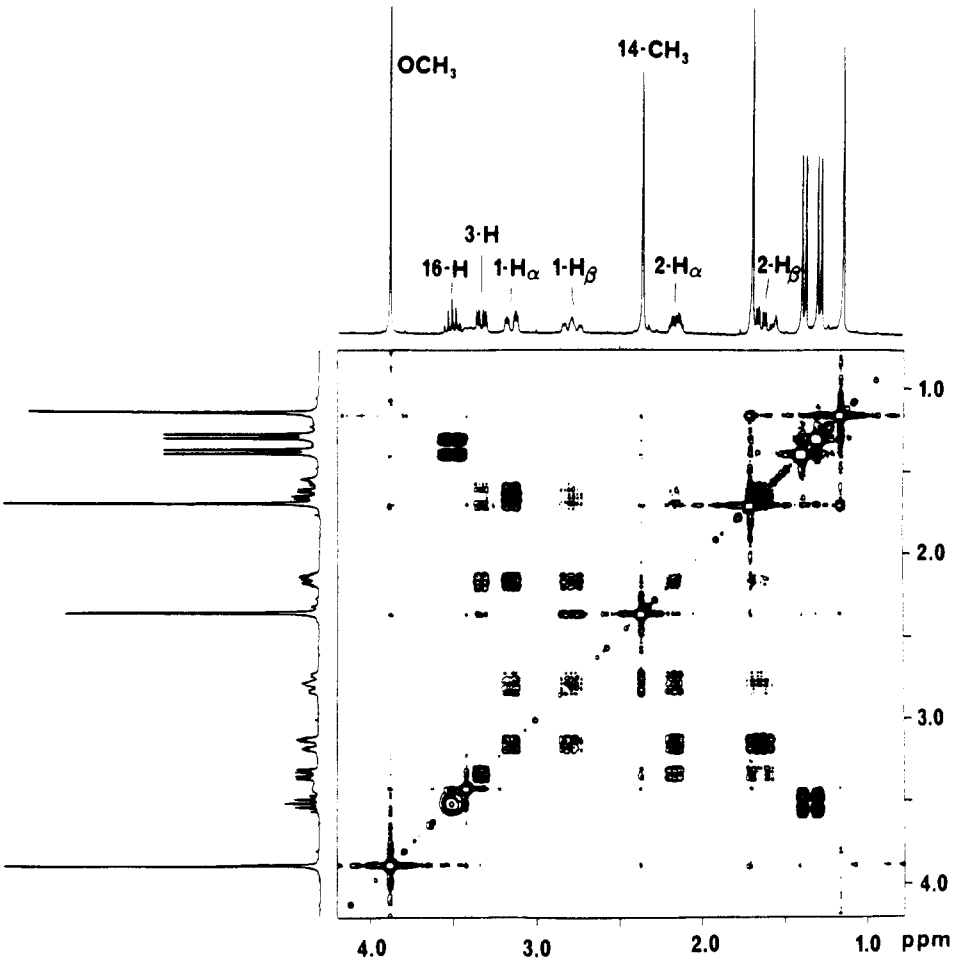
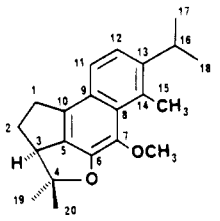


Figure 1. Homonuclear COSY spectrum of prionitin (1).

S. prionitis Hance. High-resolution mass spectrometric analysis of prionitin (1), mp 98–100 °C, $[\alpha]_D$ −11.9° (0.042,



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MeOH) indicated a molecular ion at m/z 310.1922 corresponding to $C_{21}H_{26}O_2$ (calcd 310.1952). Intense absorptions in the UV spectrum (MeOH), λ_{max} (log ϵ) 254 (4.41), 296 (3.56) nm, and the IR spectrum (KBr), ν_{max} 2975, 2955, 1645, 1575, 1470, 1370, 1300, and 1100 cm^{-1}, suggested the presence of a naphthalene chromophore. The ^1H NMR spectrum (see Table I) indicated the presence of an isopropyl group (δ 1.31 d, J = 6.7 Hz; δ 1.38 d, J = 6.7 Hz; δ 3.52 sept, J = 6.7 Hz), an aromatic methyl (δ 2.37 s), an aromatic methoxyl (δ 3.88 s), and two nonequivalent aliphatic methyl groups (δ 1.17 s and 1.71 s), and these data suggested the presence of an abietane type diterpene skeleton. However, the degree of unsaturation indicated that the molecule possessed four condensed rings instead of the usual three. The homonuclear COSY spectrum of prionitin (1) (see Figure 1) displayed an unusual coupling pattern for the 1-H_2, 2-H_2, and 3-H protons, suggesting that ring A of 1 was five membered instead of the normal six-membered ring A of the abietane diterpenes.[5,6] The nonequivalent methylene protons appeared as geminally coupled pairs of signals at 3.16 and 2.80 as well as at δ 2.16 and 1.66. The latter two signals are showing further coupling with the dd of 3-H at δ 3.34, thereby permitting their assignment as 2-H_2 absorptions. The multiplet (dddd) at δ 2.16 exerted two small couplings (4.4 Hz and 2.5 Hz) toward 3-H (δ 3.34) and one of the 1-H_2 signals, which appears at δ 3.16, indicating the peudoequatorial (α) orientation of both hydrogens. The ^{13}C NMR and APT spectra of prionitin (1) exhibited six methyl carbons (δ 18.89, 21.33, 21.53, 21.95, 28.07, and 47.74), two methylene carbons (δ 23.71 and 26.64), and two aliphatic (δ 25.68 and 62.87) and two aromatic methine carbons (δ 119.98 and 126.07). One aliphatic quaternary carbon appeared in the APT spectrum at δ 93.58 together with eight quaternary aromatic carbons (δ 118.07, 120.81, 123.47, 127.33, 129.46, 152.12, and 153.22) of which the latter two could be assigned as oxygen-bearing. The unusual downfield chemical shift of the aliphatic quaternary carbon (δ 93.58) could only be explained by the presence of a highly substituted oxygen-bearing carbon.

Determination of the carbon framework and substitution pattern of prionitin was made by series of selective INEPT,[7] CSCM 1D,[8] and NOE experiments, which also permitted the unambiguous assignment of the ^{13}C NMR spectrum. Due to the limited amount of prionitin avail-

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Table I. ^1H and ^{13}C NMR Assignments of Prionitin (1)[a]

carbon	^1H	^{13}C
1-Hα	3.16 (ddd, 16.8, 4.2, 2.6)	26.64
1-Hβ	2.80 (ddd, 17.0, 12.3, 4.4)	
2-Hα	2.16 (dddd, 17.4, 12.1, 4.4, 2.5)	23.71
2-Hβ	1.66 (ddd, 17.4, 12.3, 4.5)	
3	3.34 (dd, 12.2, 4.6)	62.87
4		93.58
5		127.33
6		152.12
7		153.22
8		118.07
9		130.81
10		129.46
11	7.08 (d, 8.8)	126.07
12	7.68 (d, 8.8)	119.98
13		124.87
14		120.81
15	2.37 (s)	28.07
16	3.52 (sept, 6.7)	25.68
17	1.31* (d, 6.7)	21.33†
18	1.38* (d, 6.7)	21.53†
19	1.71 (ns)	21.95
20	1.17 (s)	18.89
OCH_3	3.88 (s)	47.74

[a] Spectra were recorded in $CDCl_3$. Proton chemical shifts are reported as δ values (ppm) from internal TMS at 300 MHz. Carbon chemical shifts are reported as δ values (ppm) at 90.8 MHz. (*,†) Interchangeable.

able, the use of one-bond or long-range HECTOR spectroscopic techniques were precluded. Magnetization transfer via irradiation of 3-H resulted in enhancements of δ 26.64, 129.46, and 152.12, which could be assigned as C-1, C-10, and C-6, respectively. Irradiation of 1-Hα enhanced the aliphatic methine carbon at δ 62.87, which should be C-3, and the aromatic quaternary carbons at δ 127.33 and 130.81. The latter two signals, C-5 and C-9, were distinguished through the irradiation of 2-Hα, which resulted in enhancements at δ 93.58 (C-4), 127.33 (C-5), and 129.46 (C-10). Selective INEPT irradiation of 12-H enhanced the signals at δ 130.81 (C-9) and 120.81, assigned as C-14, indicating that this latter carbon was substituted by the aromatic methyl group. CSCM 1D irradiation of the ^{13}C satellite of 12-H enhanced the signal at δ 119.98, permitting the assignment of C-12, and consequently the other aromatic methine carbon, C-11 (δ 126.07). Finally, selective INEPT irradiation of 11-H confirmed the assignment of C-10 (δ 129.46) and permitted the assignment of C-13 at δ 124.87. The complete assignment of the ^{13}C NMR spectra of prionitin (1) is shown in Table I. The relative location of the isopropyl, methyl, and methoxy groups was firmly established by a NOE experiment. Irradiation of the methyl singlet at δ 2.37 resulted in enhancement of the methoxyl (δ 3.88) and the isopropyl methyl groups (δ 1.31 and 1.38), thereby placing the aromatic methyl group at C-14.

Prionitin (1), which represents a novel diterpenoid skeleton, was evaluated in the P-388 cytotoxicity assay where an ED_{50} value at 9.2 μg/mL was observed. Compounds displaying an ED_{50} 4 μg/mL are regarded as active.[9] Studies of the remaining active compounds present in the plant are in progress.

Experimental Section

Melting point was determined on a Kofler-type hot-stage apparatus and is uncorrected. Optical rotation was measured with a Perkin-Elmer 241 polarimeter. Ultraviolet spectra were recorded with a beckman DU-7 spectrophotometer, and infrared spectra were obtained with a Nicolet MX-1 interferometer. Mass spectrum was determined on a Varian MAT 112S double-focusing mass spectrometer at 80 eV. The ^1H NMR spectra were obtained with a Nicolet NMC 360 instrument operating at 360 MHz. The ^{13}C NMR measurements were performed with a Nicolet NMC 360 instrument operating at 90.8 MHz. Tetramethylsilane (TMS) was used as the internal standard, and chemical shifts are reported as δ values (ppm).

Homonuclear COSY spectra were recorded at 1 K with a Varian XL-300 spectrometer. Standard Varian pulse sequences were used. The one-dimensional heteronuclear ^1H–^{13}C shift correlation (CSCM 1D) and selective INEPT experiments were performed on a Nicolet NMC 360 spectrometer. Data sets of 16K covering a spectral width of 10 000 Hz were acquired. Proton pulse widths were calibrated by using a sample of acetic acid in 10% $C6D_6$ (^1J = 6.7 Hz) in a 5-mm NMR tube. The radio frequency field strength for the soft proton pulse was on the order of 25 Hz in these experiments. For 1-Hα, 2-Hα, and 3-H protons, 4 Hz was used as the ^3J value and 6 Hz was used for the irradiation 11-H and 12-H. Twenty thousand acquisitions were accumulated in each irradiation.

Plant Material. The plant material of *S. prionitis* Hance was collected in the Jiang-Xi Province of China in June 1986 and identified by Dr. X.-L. Huang. A voucher sample is deposited in the herbarium of the Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, People's Republic of China.

Isolation of Prionitin (1). Dried and powdered roots of *S. prionitis* (11 kg) were extracted with EtOH (140 L), and the combined extracts were evaporated in vacuo. The residue was distributed between $CHCl_3$ (10 L) and H_2O (10 L), and the organic layer was washed with H_2O (2 × 2 L), dried, and evaporated to a residue (520 g), which was subjected to column chromatography on Si gel (3 kg), eluting with $CHCl_3$. The fractions were evaporated, examined by TLC, and purified further through preparative TLC to yield prionitin (5 mg, 0.001%) having the following physical and spectroscopic properties: mp 98–100 °C; IR (KBr) ν_{max} 2975, 2955, 1645, 1575, 1470, 1370, 1300, and 1100 cm^{-1}; UV (MeOH) λ_{max} (log ϵ) 254 (4.41) and 296 (3.56) nm; ^1H NMR, see Table I; ^{13}C NMR, see Table I; mass spectrum, m/z (relative intensity) 310 (M^+, 100), 295 (7), 267 (12), 253 (8), 237 (10), 195 (4), 165 (6).

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Synthesis of Acylpyrroles via α-(Dimethylamino)-α-pyrrolylacetonitriles[1]

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Acylpyrroles are intermediates of considerable importance and numerous methods have been devised to provide synthetic access thereto. The 2-acyl compounds are most efficaciously prepared by the direct acylation of α-unsubstituted pyrroles with acid chlorides (in the presence or absence of a Lewis acid catalyst),[3] Vilsmeier–Haack

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