a clear oil (10.5 g), identified as linalyl piperonyl sulfide:* nmr δ 6.7 (m, 3), ABC pattern 5.86 (A), 5.08 (B), 4.95 (C) ($J_{AB} = 11$, $J_{AC} = 17$, $J_{BC} = 1.5$ Hz), 5.81 (s, 2), 5.1 (m, 1), 3.47 (s, 2), 2.0 (m, 2), 1.67 (s, 3), 1.59 (s, 3), 1.6 (m, 2), and 1.31 (s, 3).

The Grignard reagent for generating benzyne was made from magnesium (0.6 g, 25 mg-atoms) and 2-bromofluorobenzene (4.0 g, 23 mmol) in dry THF (50 ml). When the Grignard began forming, linalyl piperonyl sulfide was added (6.1 g, 20 mmol) in THF (25 ml). The solution was stirred under nitrogen and heated under reflux for 3 hr before cooling and adding saturated ammonium chloride (65 ml). The layers were separated and the aqueous layer was extracted with ether (75 ml). The combined organic extracts were dried over MgSO$_4$, and the solvent was removed under vacuum to leave a yellow oil. Chromatography over silica gel in hexane–benzene gave a clear oil (5.5 g), identified as 2,6-dimethyl-9-(3,4-methylenedioxyphenyl)-9-phenylthio-2,6-nonadiene: nmr δ 7.2 (m, 5), 6.7 (m, 3), 5.77 (s, 2), 5.1 (m, 2), 4.08 (t, $J = 7$ Hz, 1), 2.57 (t, $J = 7$ Hz, 2), 1.9 (m, 4), and 1.5 (m, 9).

2,6-Dimethyl-9-(3,4-methylenedioxyphenyl)-9-phenylthio-2,6-nonadiene (1 g) was stirred at room temperature for 30 min with W-2 Raney nickel[13] (5 ml settled) in ethanol (60 ml). The nickel was removed by filtration and the ethanol was removed under vacuum. The product was dissolved in ether (60 ml) and washed with water before drying over MgSO$_4$. Evaporation of ether and chromatography over silica gel in hexane–benzene gave a clear oil (0.7 g), identified as 2,6-dimethyl-9-(3,4-methylenedioxyphenyl)-2,6-nonadiene.* Glpc shows that the configuration at the central double bond is 70–75% trans and 25–30% cis. This sample is identical with that formed by another method[10] except for the cis:trans ratio: nmr δ 6.66 (s, 3), 5.86 (s, 2), 5.2 (m, 2), 2.4 (m, 4), 2.0 (m, 4), and 1.6 (d, 9).

Registry No.—**1a**, 39707-18-1; **1c**, 39707-19-2; **1d**, 39707-20-5; **1e**, 5513-30-4; **1f**, 39707-22-7; **1g**, 39707-23-8; **1h**, 39707-24-9; **1i**, 39707-25-0; *cis*-**1j**, 39707-26-1; *trans*-**1j**, 39707-27-2; **1k**, 39707-28-3; **2a**, 39707-29-4; *cis*-**2b**, 39707-30-7; *trans*-**2b**, 39707-31-8; **2c**, 39707-32-9; **2d**, 39707-33-0; **2e**, 18283-54-0; *cis*-**2f**, 39707-35-2; *trans*-**2f**, 39707-36-3; *cis*-**2g**, 39707-37-4; *trans*-**2g**, 39707-38-5; *cis*-**2h**, 39707-39-6; *trans*-**2h**, 39707-40-9; **2i**, 39707-41-0; **2j**, 39707-42-1; **2k**, 39707-43-2; **2l**, 39707-44-3; **2m**, 39707-45-4; **2n**, 39707-46-5; **5**, 39707-47-6; α-vinylbenzyl mercaptan, 39707-48-7; linalyl piperonyl sulfide, 39707-49-8; 2,6-dimethyl-9-(3,4-methylenedioxyphenyl)-9-phenylthio-2,6-nonadiene, 39707-50-1; *cis*-2, 6-dimethyl-9-(3,4-methylenedioxyphenyl)-2,6-nonadiene, 39707-51-2; *trans*-2,6-dimethyl-9-(3,4-methylenedioxyphenyl)-2,6-nonadiene, 39707-52-3; piperonyl chloride, 20850-43-5; 2-bromofluorobenzene, 1072-85-1.

Acknowledgment.—We wish to thank Mr. P. L. Unger and associates for spectral measurements and Mr. G. M. Maciak and associates for elemental analyses.

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Studies on the Pinacol Rearrangement

BRADFORD P. MUNDY* AND RODNEY D. OTZENBERGER

Department of Chemistry, Montana State University, Bozeman, Montana 59715

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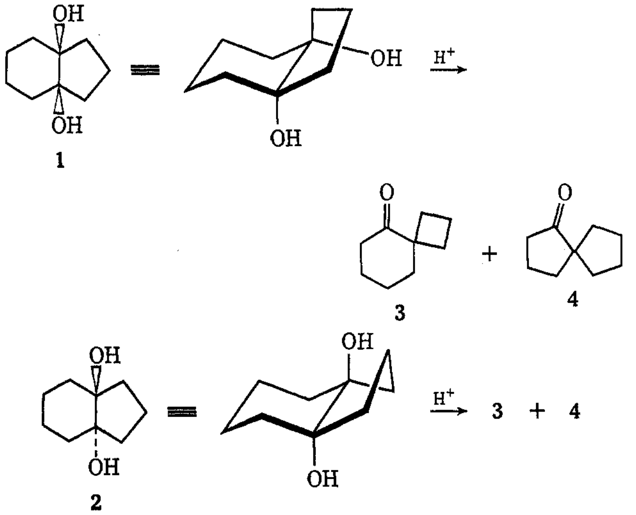
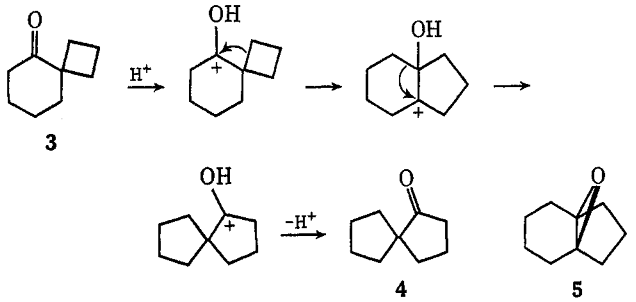
One of the interesting questions regarding the pinacol rearrangement is that concerned with stereochemical requirements. Curtin has demonstrated stereospecificity in semipinacolonic deaminations;[1] however, there exists a paucity of work regarding steric control for the pinacol rearrangement of glycols.[2]

The problem of stereochemistry can be best analyzed with conformationally homogeneous molecules. The *cis*- and *trans*-hydrindan system appeared suitable as a model system in view of the report by Fort that a carbonium ion generated at the ring fusion, under solvolytic conditions, maintained stereochemical integrity.[3]

We were prompted to examine the *cis*- and *trans*-8,9-dihydroxytetrahydroindan in the anticipation that a concerted pinacol rearrangement might be reflected in different product ratios for the two isomers. The glycols **1** and **2** have been previously prepared,[4] as have the spiranones **3**[5] and **4**.[6]



Treatment of either **1** or **2** with concentrated sulfuric acid at 0° for 10 min resulted in *complete* conversion to **4**. The epoxide **5**[3] could not be identified as a reaction product; and a sample, when subjected to the reaction conditions, was shown to undergo rapid rearrangement to **4**. In testing whether **3** was stable to the reaction conditions, it was observed that **3** → **4**.



At this point the results can be rationalized by (a) glycol interconversion,[7] (b) unfavorable energetics for the formation of **3**, or (c) product instability.[8]

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[1] D. Y. Curtin and M. C. Crew, *J. Amer. Chem. Soc.*, **77**, 354 (1955).

[2] B. P. Mundy and R. D. Otzenberger, *J. Chem. Educ.*, **48**, 431 (1971).

[3] R. C. Fort, Jr., R. E. Hornish, and G. A. Liang, *J. Amer. Chem. Soc.*, **92**, 7558 (1970).

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[5] S. J. Etheredge, *J. Org. Chem.*, **31**, 1990 (1966).

[6] H. Christol, M. Mousseron, and M. F. Plenat, *Bull. Soc. Chim. Fr.*, **4**, 543 (1959).

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Unfortunately, these problems will always plague stereochemical studies of the pinacol rearrangement.

Experimental Section

The compounds discussed in this paper, **1–5**, have been reported elsewhere: **1** and **2**,[4] **3**,[5] **4**,[6] **5**.[3] Comparison of physical constants with those reported as well as the agreement of infrared and nmr spectra with the assigned structures confirmed the identity of the products.

General Procedure for Pinacol Rearrangement.—The glycol (0.1 g) was stirred with 5 ml of concentrated sulfuric acid. After 10 min the reaction mixture was poured into ice and water. The resulting aqueous solution was immediately extracted with methylene chloride, and the extracts were washed with 10% bicarbonate solution. The crude product was analyzed by analytical glc (6 ft × 6 mm glass column, packed with 16% hyprose SP 80 on 60–68 mesh Chromosorb W).

The spiranone **3** and the epoxide **5** were subjected to the same reaction conditions and work-up.

Registry No.—**1**, 39837-98-4; **2**, 39837-53-1; **4**, 14727-58-3.

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The Structures of Some of the Minor Alkaloids of *Cephalotaxus Fortunei*

William W. Paudler* and Jerry McKay

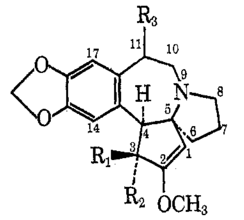
Department of Chemistry, Ohio University, Athens, Ohio 45701

Received January 26, 1973

Some time ago[1] we reported on the isolation and partial structure elucidation of the major alkaloid of *Cephalotaxus fortunei* and *C. drupacea*, and named it cephalotaxine. Since this publication, the complete structure of cephalotaxine (**1**), as its methiodide, has been determined by X-ray crystallography,[2] and the alkaloid has been synthesized.[3,4]

Powell and coworkers[5] have also isolated, along with cephalotaxine, an ester of cephalotaxine, named harringtonine, which has shown significant inhibitory activity against experimental lymphoid leukemia systems L1210 and P388. Two minor alkaloids containing an oxygen function at R_3 in structure **1** have also been described.[5a]

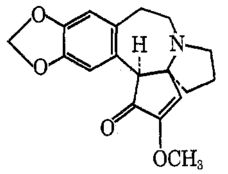
We now wish to report on the isolation and structure determination of some of the minor alkaloids of *Cephalotaxus fortunei.*



1, $R_1 = OH; R_2 = H; R_3 = H$
4, $R_1 = H; R_2 = OH; R_3 = H$

These minor alkaloids were obtained pure by careful column chromatography of the crude alkaloid mixture on neutral grade III alumina.

Alkaloid B.—This alkaloid was obtained in 1.08% yield of the crude alkaloid mixture. Its formula, as established by its mass spectrometric molecular weight and elemental analyses, is $C_{18}H_{19}NO_4$. Thus, it differs from cephalotaxine by having two fewer hydrogens. The infrared spectrum of this alkaloid, which is devoid of the hydroxyl absorption (3500 cm^{-1}) present in cephalotaxine, shows the presence of a carbonyl group (1720 cm^{-1}). Furthermore, the absorption due to the olefinic function in cephalotaxine (1665 cm^{-1}) is shifted to 1625 cm^{-1}. This bathochromic shift of the olefin absorption, in conjunction with the other observations (see Table I), suggests that alkaloid B is cephalotaxinone (**2**). It has now been shown that this alkaloid is also found in *C. harringtonia.*[5d] Furthermore, (±)-cephalotaxinone has recently been prepared as a key intermediate in the synthesis of racemic cephalotaxine,[3,4] and we have prepared it by Oppenauer oxidation of cephalotaxine (see Experimental Section).



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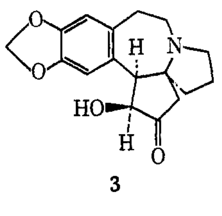
Alkaloid C.—This minor alkaloid constitutes 5.4% of the crude alkaloidal mixture and is identical in every respect (infrared, ultraviolet, proton magnetic resonance spectrum, as well as by a mixture melting point determination) with an authentic sample of acetylcephalotaxine.[1] This alkaloid has also been isolated from *C. wilsoniana.*[1d]

Alkaloid D.—This compound is identical in every respect with demethylcephalotaxine (**3**), the product obtained by mild acid hydrolysis of cephalotaxine.[1]

Since cephalotaxine is stable to the conditions of isolation (as shown by subjecting it to the isolation procedure and recovering it without any loss), this alkaloid cannot be an artifact of isolation but is indeed present in the plant.



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