The larger portion was placed in a glass ampule and sealed with a torch. The ampule was then placed in the constant-temperature bath at 91 °C for 2 h, after which it was removed from the bath and cooled by immersing in cold water. The extent of reaction was determined by withdrawing a small aliquot and measuring the optical densities at both 248 and 259 nm. These optical densities were then compared to those for complete reaction. The infinity points were measured independently for known concentrations of methyl benzoate under the experimental conditions of the isotope effect experiments. Approximately the same slit width was used for all experiments, and the extinction coefficient change resulting from hydrolysis was found to be 44.7 M^{-1} cm^{-1} at 259 nm and 221 M^{-1} cm^{-1} at 248 nm. After determination of percent reaction, the reaction solution was neutralized with KOH and extracted twice with 2-g portions of Norit. The Norit was filtered off after each extraction with Whatman No. 42 filter paper.

To the smaller 75-mL portion was added enough freshly prepared KOH to bring the pH around 13. Hydrolysis was allowed to proceed beyond 10 half-lives, after which the solution was neutralized with sulfuric acid, diluted to 250-mL total volume, and extracted with Norit as described above. At this point the large and small portions were treated in an identical manner.

The remaining procedure for concentration, purification, and chemical conversion of the methanol to either carbon monoxide or carbon dioxide is identical with that which we have previously published.[5]

Registry No. Methyl benzoate, 93-58-3.

Rearrangements and Demethylation of 2-*o*-Anisyl-2-*endo*-fenchyl Alcohol

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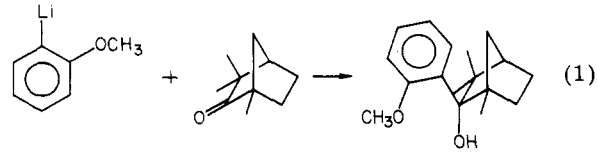
As part of a plan to prepare chiral compounds for studies in asymmetric synthesis, we have attempted the chlorination of the title compound by several methods and have observed some unusual chemical results which we now report.

Addition of (+)-fenchone to *o*-anisyllithium gave alcohol product consisting of a single isomer in 82% isolated yield. On the basis of analogy with the formation of 2-*p*-anisyl-2-*endo*-camphenilol by exo attack of *p*-anisylmagnesium bromide on the structurally similar ketone camphenilone,[1-3] the structure of this alcohol was assigned that of 2-*o*-anisyl-2-*endo*-fenchyl alcohol (1, eq 1). All spectral and analytical data were consistent with that assignment (see Figure 1).



(1)

1

An attempt was made to chlorinate 1 using an adaptation of the method of Brown and Rei.[4] Passage of anhydrous hydrogen chloride gas through a chloroform solution of 1 at 25 °C resulted in the formation of two new products 2 and 3. The reaction was followed by VPC: 2 was formed first and changed into 3 with time under the reaction conditions. The conversion of 2 to 3 was slowed when the reaction was run at 0 or −60 °C, but it was not stopped.

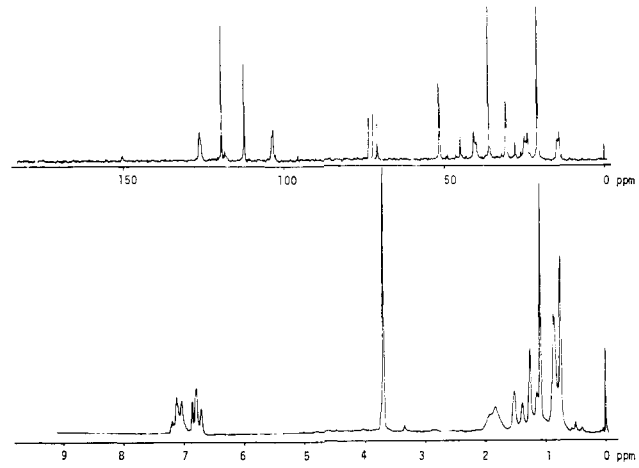
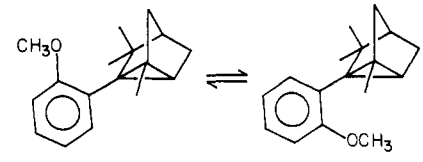


Figure 1. Upper trace: 22.5-MHz ^{13}C NMR spectrum of 2, completely decoupled, 301 K, 5000-Hz sweep width. Lower-trace: 90-MHz ^{1}H NMR spectrum of 2, 301 K, 1000-Hz sweep width.

Phosphorus pentachloride and calcium carbonate, a reagent combination which rapidly leads to chlorination with retention of configuration in many,[5] but not all,[6] tertiary alcohols, gave the same pair of products, 2 and 3, when alcohol 1 was added. The only difference between this reaction system and use of anhydrous hydrogen chloride was that the conversion of 2 to 3 was slow even at room temperature with the $PCl_5/CaCO_3$ combination.

A reaction mixture containing components 2 and 3 was separated by silica gel chromatography. Compound 2 was eluted first with pentane and was then purified into a colorless oil by preparative VPC. Compound 3 was eluted from the column with diethyl ether and, following Kugelrohr distillation, formed snow-white crystals.

Microanalyses of both 2 and 3 showed that both were devoid of chlorine and contained only carbon, hydrogen, and oxygen. Both the proton NMR and the completely decoupled carbon-13 NMR spectra of 2 showed uncharacteristically broad signals (Figure 1). The broadness of the signals suggested the existence of two rotational isomers of 2 which interconvert slowly enough at ambient probe temperature (301 K) for signals of the nuclei of both isomers to be seen. Indeed, at 273 K, every signal in the carbon-13 NMR spectrum of 2 was split into two signals. On the basis of the spectral data, the assignment of the two rotational isomer structures 2 and 2' was made for this compound.



2 2'

The coalescence temperature of the pair of signals in the carbon-13 spectrum of 2 centered at δ 15.3 ($\Delta\nu$ = 19.5 Hz) was found to be 318 K (Figure 2). From this an activation

(1) Bartlett, P. D.; Webster, E. R.; Dills, C. E.; Richey, H. G., Jr. *Justus Liebigs Ann. Chem.* **1959**, *623*, 217.
(2) Brown, H. C.; Takeuchi, K. *J. Am. Chem. Soc.* **1977**, *99*, 2679.
(3) Brown, H. C.; Takeuchi, K.; Ravindranathan, M. *J. Am. Chem. Soc.* **1977**, *99*, 2684.
(4) Brown, H. C.; Rei, M-H *J. Org. Chem.* **1966**, *31*, 1090.
(5) Carman, R. M.; Shaw, I. M. *Aust. J. Chem.* **1976**, *29*, 133.
(6) Hückel, W.; Volkmann, D. *Justus Liebigs Ann. Chem.* **1963**, *664*, 31.

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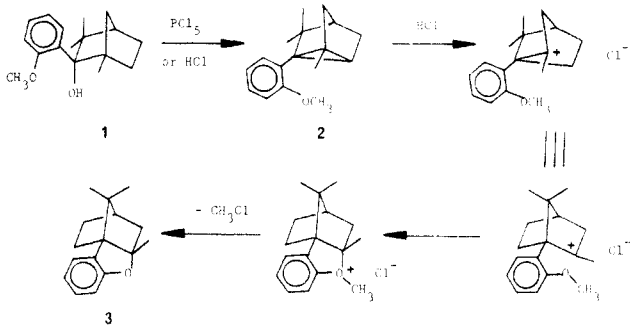
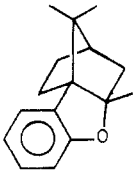
Scheme I



energy ($\Delta G^{\ddagger}$) barrier to rotation for the interconversion of **2** ⇄ **2'** was calculated to be 16.3 kcal.[7] The size of this barrier, when compared with that of sterically less congested phenylcyclopropane (2.0 ± 0.3 kcal/mol[8]), suggests that steric components to the barrier in **2** may be of greater importance than electronic components.

Remarkably, both the proton and the carbon-13 NMR spectra of compound **3** revealed the absence of an *o*-anisyl methoxyl group. Consideration of all the spectral and analytical data led to the assignment of the cyclic ether structure to **3** as shown.[9]

A possible mechanism for understanding the behavior of this system is shown in Scheme I. Although the dehydration in the first step to the tricyclene **2** has a precedent in the behavior of related systems,[1-3] the subsequent formation of the cyclic oxonium ion and demethylation to ether **3** appear to be dependent upon the unique ortho relationship of the ring methoxyl group to the carbenium ion center of this system.



3

Experimental Section

All nuclear magnetic resonance spectra were measured on ca. 10–20% solutions in deuteriochloroform containing tetramethylsilane as an internal standard by using either a Varian Associates Model T-60A spectrometer or a JEOL Model FX-90Q Fourier transform spectrometer. Chemical shifts are reported in parts per million (δ) downfield from Me_4Si.

Optical rotations were determined by using a Rudolph Research Model 26202 automatic digital polarimeter capable of a precision of ±0.003°. Both neat liquids and solutions were analyzed by using 1.6 mm × 1 dm and 3.0 mm × 1 dm polarimeter tubes. All rotations are reported as specific rotations and have been corrected for density and pathlength as necessary.

Infrared absorption spectra were recorded on a Perkin-Elmer 621 or a Pye Unicam SP3-200 spectrophotometer by using neat films, KBr pellets, or CCl_4 solutions. All absorptions are recorded in wavenumbers (cm^{-1}).

Vapor-phase chromatography (VPC) analyses were performed on a Hewlett-Packard Model 5722A gas chromatograph. The following columns were employed: column A (2 m × 6.4 mm), 10% Carbowax 20 M on Anakrome ABS 80/90; column B (2 m × 6.4 mm), 10% Apiezon L on Anakrome ABS 80/90. Preparative gas chromatography was performed on a Hewlett-Packard Model 776 gas chromatograph equipped with a (2 m × 19 mm) column packed with 20% diisodecyl phthalate on Chromasorb P (column C).

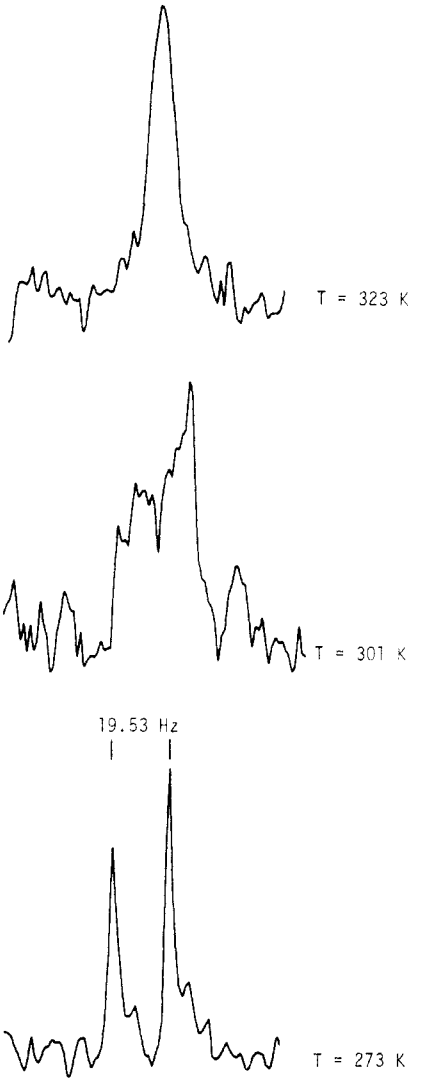


Figure 2. Temperature dependence of signals centered at δ 15.3 in proton-decoupled 22.5-MHz ^{13}C NMR spectrum of **2**.

Melting points were determined in open capillary tubes by using a Thomas-Hoover melting point apparatus. Melting points and boiling points are uncorrected.

Elemental analyses were performed by Spang Microanalytical Laboratory.

All glassware was oven dried and assembled while still hot.

2-*o*-Anisyl-2-*endo*-fenchyl Alcohol (1). To a solution of 25 g (0.134 mol) of *o*-bromoanisole (Aldrich) in 60 mL of diethyl ether contained in a three-necked, 300-mL, round-bottomed flask fitted with a reflux condenser, rubber septum, and gas inlet was added 100 mL (0.16 mol, Aldrich 1.6 M in hexane) of *n*-butyllithium via syringe. The reaction was stirred magnetically under an atmosphere of argon for 12 h, and then a solution of 20.7 g (0.136 mol) of fenchone (Fluka, $[\alpha]^{20}_{546}$ +75°) in 50 mL of diethyl ether was added dropwise over a period of 30 min. This solution was stirred for an additional 12 h, quenched with 80 mL of saturated aqueous ammonium chloride, and stirred until the ether layer became clear. The ether layer was removed and washed three times with water. The combined aqueous portion was extracted with two 10-mL portions of pentane. The combined organic extract was dried (Na_2SO_4), concentrated to a thick yellow liquid, and then dissolved in 50 mL of boiling 95% ethanol. Ice-water (150 mL) was added to induce crystallization. Subsequent vacuum filtration afforded 37.4 g of light yellow crystals. Vacuum sublimation of these yielded 27.1 g (82%) of snow-white crystals: mp 65–66 °C; $[\alpha]^{28}_{589}$

(7) Lambert, J. B.; Shurvell, H. F.; Verbit, L.; Cooks, R. G.; Stout, G. H. "Organic Structural Analysis", Macmillan, New York, 1977, pp 116–117.

(8) Parr, W. J. E.; Schaefer, T. *J. Am. Chem. Soc.* **1977**, *99*, 1033.

(9) The structure of **3** was previously shown incorrectly: Fry, J. L.; West, J. W. "Abstracts of Papers", 2nd Chemical Congress of the North American Continent, Las Vegas, NV, Aug 25–29, 1980; ORGN 129.

+118.46° (c 10, absolute EtOH).

The proton NMR spectrum ($CDCl_3$) showed resonances at δ 0.43 (3 H, s), 1.12 (3 H, s), 1.32 (3 H, s), 1.3–2.6 (7 H, overlapping m), 3.77 (3 H, s), 5.09 (1 H, br s), and 6.9–7.7 (4 H, overlapping m). Addition of D_2O to the sample resulted in the collapse of the broad singlet at δ 5.09. The C^{13}, completely decoupled NMR spectrum ($CDCl_3$) showed signals at δ 18.3 (q), 22.4 (q), 24.7 (t), 29.4 (q), 33.4 (t), 40.7 (t), 44.7 (s), 50.1 (d), 52.5 (s), 55.1 (q), 85.2 (s), 111.1 (d), 119.7 (d), 126.8 (d), 128.7 (d), 132.7 (s), 157.8 (s). The IR spectrum (CCl_4) had absorptions at 3545, 3070, 2970, 2935, 2880, 2840, 1460, 1435, 1380, 1360, 1305, 1290, 1225, 1180, 1130, 1110, 1070, 1050, 1030, and 922 cm^{-1}.

Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.46; H, 9.23. Found: C, 78.23; H, 9.23.

Attempted Chlorination of 1 with Anhydrous Hydrogen Chloride. Anhydrous hydrogen chloride was passed through a solution of 0.024 g (0.125 mmol) of **1** in $CDCl_3$ contained in a glass NMR tube at 25 °C for 0.5 h. Analysis of the reaction solution by VPC (column A, 170 °C, 40-mL/min flow rate) showed two major products and no starting material. The first product (**2**) had a retention time of 1.8 min (5%) and the second (**3**) one of 2.7 min (90%). The remaining 5% of the solution was comprised of three unknown components. The reaction mixture was then subjected to an additional hour of hydrogen chloride treatment. Analysis of this reaction mixture by VPC, under the same conditions, showed only one major product comprising 95% of the mixture and having a retention time of 2.7 min.

The reaction was rerun in chloroform at 0 °C. After 2 h, only **2** and **3** were present in a 2:1 ratio. After an additional 7 h reaction time, the product distribution had shifted to 45% **2** and 55% **3**. The experiment was performed again at ca. −60 °C. After 9 h, VPC analysis showed the presence of unreacted starting material and **2** and **3** in a 2:1 ratio.

Attempted Chlorination of 1 with Phosphorus Pentachloride. To a solution of 4.00 g (15.4 mmol) of **1** and 2.15 g (21.5 mmol) of calcium carbonate in 70 mL of chloroform at 9 °C contained in a dry, 250-mL round-bottomed flask fitted with a magnetic stirrer, reflux condenser, and gas inlet was added with stirring 4.17 g (20 mmol) of phosphorus pentachloride. The reaction was stirred under a nitrogen atmosphere for 1.5 h, at which time an excess of potassium carbonate was added, and the reaction mixture was then filtered. The filter cake was rinsed with chloroform, and the volatile solvents were removed by rotary evaporation. VPC analysis of the resulting yellow liquid (column A, 190 °C, 40-mL/min flow rate) showed two major components making up 95% of the mixture in a distribution of 52% and 48%. Coinjection of this mixture with the mixture resulting from HCl treatment of **1** indicated the two major components in each reaction to be the same (**2** and **3**).

The yellow liquid was introduced onto a silica gel (35–70 mesh) chromatography column (16.5 cm × 5 cm), and elution was followed by VPC analysis (column A, 190 °C, 40-mL/min flow rate). After component **2** was completely eluted from the column with pentane, the solvent was changed to diethyl ether and **3** was washed from the column. Removal of volatile solvents by rotary evaporation resulted in the formation of thick yellow liquids for both **2** and **3**.

Kugelrohr distillation [60 °C (0.1 torr)] of **2** left it unchanged both in appearance and in its measured proton NMR spectrum. Purification of **2** by VPC (column B, 250 °C, 40 mL/min flow rate) resulted in the formation of a colorless liquid. The proton NMR spectrum ($CDCl_3$, 28 °C) remained identical with the non-VPC-purified **2** and showed resonances at δ 0.66–1.00 (6 H, br s), 1.1 (3 H, s), 1.11–2.22 (6 H, overlapping m), 3.64 (3 H, s), and 6.67–7.33 (4 H, overlapping m). The fully decoupled carbon-13 NMR spectrum showed at least six signals which were very broad (see Figure 1). The carbon-13 NMR spectrum at 0 °C showed that each of the signals was split into two signals, indicating the existence of a rotational barrier in the molecule. The coalescence temperature representing the activation energy for the rotational barrier was investigated by variable-temperature carbon-13 NMR and was found to be 45 °C. The proton NMR spectrum of **2** at 0 °C showed the signals corresponding to the three methyl groups [δ 0.66–1.00 (br s) and 1.1 (s)] to each be split into two signals. At 60 °C, the carbon-13 spectrum ($CDCl_3$) of **2** consisted of sharp signals at δ 15.3 (q), 22.1 (2 superimposed q), 26.3 (d), 29.8 (s), 32.9 (t), 38.6 (t), 43.4 (d), 48.4 (s), 55.1 (q), 84.9 (s), 111.0 (d), 120.5 (d), 126.6 (s), 128.1 (d), 135.1 (d), and 161.2 (s). The IR spectrum (between NaCl plates) showed major absorptions at 3100, 2900–3000, 1800–1950, 1500, 1460, 1360, 1380, 1000–1020 cm^{-1}.

Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.25; H, 9.40.

Compound **3** was subjected to Kugelrohr distillation [60 °C (0.1 torr)] to afford 0.57 g of white crystals. The proton NMR spectrum ($CDCl_3$) for **3** showed resonances at δ 1.16 (3 H, s), 1.21 (3 H, s), 1.33 (3 H, s), 0.75–2.1 (7 H, overlapping m), and 6.63–6.2 (4 H, overlapping m). The carbon-13, completely decoupled spectrum ($CDCl_3$) showed signals at δ 17.8 (q), 19.6 (q), 22.0 (q), 22.9 (t), 33.8 (t), 42.2 (t), 49.3 (d), 50.7 (s), 56.0 (s), 97.8 (s), 109.3 (d), 120.0 (d), 124.0 (d), 128.4 (d), 134.2 (s), 159.1 (s). The IR spectrum showed major absorptions at 3100, 2950, 1600, 1380, 1390, 1240, 1090, and 755 cm^{-1}. The mass spectrum showed peaks at m/e 228 (M^+) and 213 (base peak, $M^+ - 15$).

Anal. Calcd for $C_{16}H_{20}O$: C, 84.21; H, 8.77; O, 7.02. Found: C, 84.19; H, 8.86; O, 6.94.

Acknowledgment. We thank Drs. J. E. Gano and D. A. Horne for their help in obtaining and interpreting a number of NMR spectra and The University of Toledo Faculty Research Awards and Fellowships Program for support.

Registry No. **1**, 76833-22-2; **2**, 76847-44-4; **3**, 76833-23-3; *o*-bromoanisole, 578-57-4; (+)-fenchone, 7787-20-4.

Diels–Alder Reaction of Heterocyclic Azadienes. 1. Thermal Cycloaddition of 1,2,4-Triazine with Enamines: Simple Preparation of Substituted Pyridines

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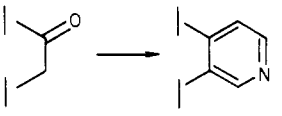
Department of Medicinal Chemistry, The University of Kansas, Lawrence, Kansas, 66045

Received November 24, 1980

During the course of synthetic studies designed for the preparation of substituted pyridine derivatives[1] we have had the occasion to investigate methods for the construction or annelation of a pyridine ring onto a saturated precursor. Most useful for our purposes would be a direct and simple process for the annelation of a pyridine ring onto a preexisting ketone as illustrated in eq 1.[2] Though



(1)

multistep procedures are available for carrying out this transformation, the overall yields and effort involved discourage their general utility.[2]

In the search for a more direct and convenient method, we were intrigued by the possible use of 1,2,4-triazine (**2**) as a dependable, azadiene component in a Diels–Alder route to substituted pyridines.[3,4] Previous studies have

(1) Typified by sesbanine, a cytotoxic constituent of *Sesbania drummondii*; see: Powell, R. G.; Smith, C. R., Jr.; Weisleder, D.; Muthard, D. A.; Clardy, J. *J. Am. Chem. Soc.* **1979**, *101*, 2784.

(2) Weissberger, A.; Taylor, E. C. Eds. *Chem. Heterocycl. Comp.* **1974**, *14*, *Suppl., Part 2*; **1975**, *14*, *Suppl., Part 4*; **1960–1964**, *14*, *Parts 1–4*.

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