^{1}H NMR (500 MHz, CD_2Cl_2) δ 4.48 (H6, dd, $J_{6,4}$ = 0.64 Hz, $J_{6,5}$ = 11.76 Hz), 4.10 (H5, dd, $J_{5,4}$ = 6.00 Hz, $J_{5,6}$ = 11.76 Hz), 2.65 (H7, d, $J_{7,8}$ = 6.86 Hz), 2.58 (H2, dd, $J_{2,1}$ = 14.24 Hz, $J_{2,3}$ = 17.25 Hz), 2.33 (H4, d, $J_{4,5}$ = 6.00 Hz), 2.30 (H3, dd, $J_{3,1}$ = 7.60 Hz, $J_{3,2}$ = 17.25 Hz), 2.21 (H9, dd, $J_{9,11}$ = 6.31 Hz, $J_{9,8}$ = 14.73 Hz), 1.98 (H13, d, $J_{13,14}$ = 14.38 Hz), 1.90 (H12, dd, $J_{12,10}$ = $J_{12,11}$ = 3.20 Hz), 1.83 (H8, dddd, $J_{8,7}$ = 6.86 Hz, $J_{8,10}$ = 7.25 Hz, $J_{8,11}$ = 13.22 Hz, $J_{8,9}$ = 14.73 Hz), 1.82 (H14, d, $J_{14,13}$ = 14.38 Hz), 1.72 (H1, dd, $J_{1,2}$ = 14.24 Hz, $J_{1,3}$ = 7.60 Hz), 1.70 (H10, ddd, $J_{10,12}$ = 3.20 Hz, $J_{10,8}$ = 7.25 Hz, $J_{10,11}$ = 13.22 Hz), 1.53 (H11, dddd, $J_{11,12}$ = 3.20 Hz, $J_{11,9}$ = 6.31 Hz, $J_{11,8}$ = $J_{11,10}$ = 13.22 Hz), 1.18 (H18-20, s), 1.12 (H15-17, s).

Circular Dichroism Spectrum of Natural (-)-Quadrone. A 1.00 mM solution was prepared by dissolving 1.326 mg of natural (-)-quadrone in 5.338 mL of methanol (Aldrich Chemical Co.; spectroscopic grade, used as received). The ambient-temperature (25 °C) CD spectrum was recorded on a Jasco J41 spectrometer, together with a blank spectrum of the solvent. The quadrone spectrum was corrected by subtraction of the solvent spectrum. The cuvette path length was 0.1 cm. The instrument was calibrated by using a 2.583 mM standard aqueous solution of camphorsulfonic acid. The latter solution furnished molar ellipticities (θ) of 7670 and -15 100 deg·cm^2/dmol at wavelengths of 291 and 192 nm, respectively, slightly lower than literature[50] values of 7800 and -15 600. Accordingly, the molar ellipticities measured for quadrone were further corrected by dividing by 0.9756. Dichroic absorption ($\Delta\epsilon$) values were calculated by using the relation $\theta = 3300\Delta\epsilon$.

Acknowledgment. We are pleased to acknowledge the support of the National Institutes of Health (National Cancer Institute) through Grant CA-19033. We thank Professor Andrew S. Kende (University of Rochester) and Dr. Matthew Suffness (National Cancer Institute) for samples of enone acid (±)-3 and natural (-)-quadrone, respectively. Professor W. Clark Still (Columbia University) graciously provided the program MACROMODEL, version 2.5. In addition, we thank Drs. W. C. Randall and G. Sanyal of Merck Sharp and Dohme Research Laboratories (West Point, PA) for measuring CD spectra. We also thank Dr. G. Furst and Mr. John L. Wood, Dr. J. Dykins, and Dr. P. Carroll for assistance in obtaining and interpreting NMR spectra, high-resolution mass spectra, and X-ray crystallographic data, respectively. Dr. Christopher S. Shiner provided helpful suggestions and critical comments.

Registry No. (+)-**1**, 87480-01-1; (-)-**1**, 66550-08-1; (±)-**1**, 74807-65-1; (-)-**2**, 93219-11-5; **3** (natural isomer), 117557-24-1; **3** (unnatural isomer), 132831-32-4; (±)-**3**, 78739-64-7; (±)-**6**, 92216-07-4; (+)-**11**, 132831-34-6; (-)-**11**, 132831-33-5; (±)-**11**, 92096-28-1; (+)-**12**, 92216-09-6; (-)-**12**, 132831-35-7; (±)-**12**, 92096-26-9; (+)-**13**, 132831-37-9; (-)-**13**, 132831-36-8; (±)-**13**, 92096-23-6; (+)-**14**, 132831-38-0; (-)-**14**, 132831-39-1; (±)-**14**, 92096-24-7; (+)-**15**, 132751-50-9; (-)-**15**, 132831-40-4; (±)-**15**, 132831-41-5; **16** (natural isomer), 132831-42-6; **16** (unnatural isomer), 132751-51-0; (±)-**16**, 132831-43-7; (+)-**17**, 132831-44-8; (-)-**17**, 132831-45-9; (±)-**17**, 92096-25-8; (+)-**18**, 132831-46-0; (-)-**18**, 132831-47-1; (±)-**18**, 84057-44-3; **19**, 132751-52-1; **20**, 132831-48-2; **21**, 92096-27-0; **22**, 92216-08-5; (+)-**23**, 132831-49-3; (-)-**23**, 132831-50-6; (*S*)-PhCH(OMe)CO_2H, 26164-26-1; (*S*)-PhCH(OAc)CO_2H, 7322-88-5.

Supplementary Material Available: X-ray data for **1** and **21**, Chem3D coordinates for **D**, **E**, and **H-K**, and detailed $\Delta\epsilon$ calculations for **D** and **E** (26 pages). Ordering information is given on any current masthead page.

Biosynthesis of L-671,329, an Echinocandin-Type Antibiotic Produced by *Zalerion arboricola*: Origins of Some of the Unusual Amino Acids and the Dimethylmyristic Acid Side Chain

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Abstract: The biosynthesis of L-671,329, an antibiotic of the echinocandin class, was studied in *Zalerion arboricola* by stable isotope tracer techniques and high-field NMR spectroscopy. The organism incorporates DL-[2-^{13}C]tyrosine into the antibiotic with the label appearing as C-3 of the homotyrosine residue; the C-2 position of this residue can be labeled by [2-^{13}C]acetate. Thus, homotyrosine arises from tyrosine by a chain elongation mechanism involving condensation with acetate. [2-^{13}C]Acetate also labels all the even-numbered carbon atoms (C-2–C-14) of the myristic acid side chain. L-[$^{13}CH_3$]Methionine does not donate its methyl group to 3-hydroxy-4-methylproline but is the origin of both methyl moieties of the 10,12-dimethylmyristoyl side chain. L-[1-^{13}C]Proline is incorporated into only one of the two substituted proline residues, viz, 4-hydroxyproline. Label from L-[2-^{13}C]leucine enriches the 3-hydroxy-4-methylproline residue, suggesting that this proline moiety is formed by cyclization of leucine.

L-671,329 is an acylated cyclic hexapeptide antibiotic (**1**; Figure 1) produced by the fungus *Zalerion arboricola*.[1,2] It is a member of the echinocandin group of antifungal antibiotics, which also includes aculeacin and mulundocandin.[3] The peptide portions of these natural products contain threonine together with residues of the following unusual or nonprotein amino acids: 3,4-dihydroxyhomotyrosine, *trans*-4-hydroxyproline, 2,3-*trans*-3,4-*cis*-3-hydroxy-4-methylproline, and 4,5-dihydroxyornithine. The presence of 3-hydroxyglutamine and a 10,12-dimethylmyristoyl side chain distinguishes L-671,329 from other compounds in this class. Interest in L-671,329 recently intensified with the report

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0002-7863/91/1513-3542$02.50/0

Table I. Incorporation of ^{13}C-Labeled Precursors into L-671,329

precursor fed	possible positions labeled		δ (ppm)[a]	fold ^{13}C enrichement obsd
DL-[2-^{13}C]tyrosine	C-3[b]	3,4-dihydroxyhomotyrosine	76.86	26–28
	C-odd	10,12-dimethylmyristate	various[c]	2.5–3.5
sodium [2-^{13}C]acetate	C-2	3,4-dihydroxyhomotyrosine	56.31	2.4
	C-even	10,12-dimethylmyristate	various[d]	1.5–2.7
L-[$^{13}CH_3$]methionine	C-6	3-hydroxy-4-methylproline	11.20	none
	C-15	10,12-dimethylmyristate	20.78	48
	C-16	10,12-dimethylmyristate	20.25	43
L-[1-^{13}C]proline	C-1	4-hydroxyproline	173.12	22
	C-1	3-hydroxy-4-methylproline	172.40	none
L-[2-^{13}C]leucine	C-2	3-hydroxy-4-methylproline	70.08	16

[a] Previously published values,[2] but three pairs of closely spaced methylene resonances needed to be interchanged (C-3 with C-8; C-4 with C-5; C-6 with C-7). [b] Because of the high incorporation at C-3, ^{13}C–^{13}C satellites at C-2 (δ 56.31, J_{cc} = 41 Hz) and C-4 (δ 75.72, J_{cc} = 46 Hz) were clearly visible. [c] In ascending order for C-1 to C-13:175.47, 27.00, 30.61, 31.19, 38.10, 45.93, 30.37. [d] In ascending order from C-2 to C-14: 36.69, 30.33, 30.76, 28.07, 31.19, 32.94, 11.64.

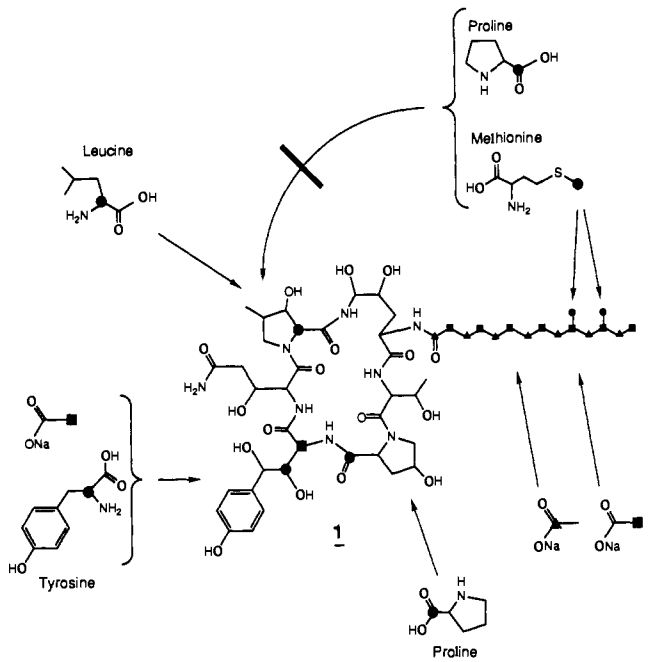

Figure 1. Biosynthetic origins of components of L-671,329 (**1**). Tyrosine and acetate are condensed to form homotyrosine. The backbone of the dimethylmyristoyl side chain is produced from acetate units, and the methyl groups derive from methionine. Only one of the two proline residues in the antibiotic is made from proline; the other arises by the cyclization of leucine.

of an animal study showing that this compound and another inhibitor of β-(1,3)-glucan synthesis are effective in the treatment of *Pneumocystis carinii* infections.[4]

Little is known regarding the biosynthesis of any member in the echinocandin group, but the occurrence of the echinocandins as a series of compounds wherein the ornithine and homotyrosine residues are progressively more hydroxylated[5] suggests that biosynthesis may proceed through a cyclopeptide precursor in which these two amino acids are not hydroxylated. The study reported here was undertaken to explore the biosynthetic origins of the homotyrosine and the two proline residues in L-671,329. Feeding experiments involving ^{13}C-enriched amino acids or acetate were performed, and the data obtained also provided information on the synthesis of the branched fatty acid constituent.

Results

An initial survey of ^{14}C-labeled compounds to determine which could be utilized by *Z. arboricola* in the formation of L-671,329 was done to guide the choice of precursors in experiments with stable isotopes (data not presented). Enrichments obtained by feeding ^{13}C-labeled precursors are summarized in Table I.

DL-[2-^{13}C]Tyrosine was incorporated into the antibiotic with a 26–28-fold enrichment at C-3 of dihydroxyhomotyrosine. The C-2 position of this residue was labeled with [2-^{13}C]acetate, although to a much lesser extent (2.4-fold), showing that elongation of tyrosine to homotyrosine involves condensation with acetate. The process must also include the decarboxylation of tyrosine, for L-671,329 could be radiolabeled with L-[U-^{14}C]tyrosine but not with L-[1-^{14}C]tyrosine (data not shown). As anticipated, label from [2-^{13}C]acetate also appeared in the even-numbered carbons (C-2–C-14) of the 10,12-dimethylmyristoyl side chain; the enrichments were of approximately the same magnitude seen at the C-2 of homotyrosine and ranged from 1.5- to 2.7-fold. Unexpectedly, the odd-numbered carbons (C-1–C-13) in the fatty acid were enriched (2.5-3.5-fold) when DL-[2-^{13}C]tyrosine was the precursor. This may have come about by the metabolism of the labeled tyrosine to the α-ketoacid and the subsequent decarboxylation and oxidation/decarboxylation to generate [1-^{13}C]-malonate/acetate.

The methyl group of L-[$^{13}CH_3$]methionine did not enrich the 3-hydroxy-4-methylproline of L-671,329, but labeling occurred in both the 10-methyl (C-15) and the 12-methyl (C-16) of 10,12-dimethylmyristate (48- and 43-fold enrichment, respectively). Collectively, the acetate and methionine data suggest that the straight-chain myristic acid arises by the condensation of seven molecules of acetate, presumably in the usual fatty acid synthase catalyzed reaction, and that the methylations at C-10 and C-12 occur as *S*-adenosylmethionine-mediated modifications during or after fatty acid assembly.

Since there was no labeling at C-6 of 3-hydroxy-4-methylproline associated with the feeding of L-[$^{13}CH_3$]methionine, it seemed likely that the 3-hydroxy-4-methylproline residue of L-671,329 is not derived from proline. To confirm this hypothesis, labeling from L-[1-^{13}C]proline was examined. Only the C-1 of 4-hydroxyproline was enriched (22-fold) by L-[1-^{13}C]proline; no labeling of the 3-hydroxy-4-methylproline residue was observed.

In our preliminary experiments with radiolabeled precursors, incorporation of L-[U-^{14}C]leucine into L-671,329 was found (data not presented). Although metabolic transformations of leucine can provide a precursor for branched-chain fatty acids,[6] leucine is a progenitor of iso fatty acids[7] and is an unlikely precursor of the branched myristic acid of L-671,329. Furthermore, the data obtained with [2-^{13}C]acetate and L-[$^{13}CH_3$]methionine are inconsistent with the involvement of leucine in 10,12-dimethylmyristic acid synthesis. The possibility remained that leucine was a precursor for 3-hydroxy-4-methylproline. This was verified by a feeding experiment with L-[2-^{13}C]leucine; a 16-fold enrichment was obtained at C-2 of 3-hydroxy-4-methylproline. The results with L-[1-^{13}C]proline and L-[2-^{13}C]leucine demonstrated that the

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(7) A fatty acid with a methyl at the penultimate or ω-1 position.

two substituted proline residues in L-671,329 have different biosynthetic origins and suggested that the producing organism possesses the enzymatic capability to cyclize leucine.

Discussion

The findings of this study are summarized in Figure 1. Several of the amino acids that compose antibiotics of the echinocandin group either are unique to these natural products or are encountered only rarely in fungi.

Homotyrosine is in the former category. During L-671,329 biosynthesis, it is produced by a condensation of tyrosine and acetate and a removal of what was originally the carboxyl function of tyrosine. The mechanism for the synthesis of homophenylalanine in the watercress plant (*Nasturtium officinale*) has similar features.[8,9] Experiments with L-[1-^{14}C]phenylalanine, DL-[2-^{14}C]phenylalanine, [1-^{14}C]acetate, [2-^{14}C]acetate, 2-[2-^{14}C]-benzylmalic acid, and 3-[1,2-^{14}C]benzylmalic acid established that homophenylalanine is produced from phenylalanine by deamination to the ketoacid, condensation with acetate, loss of a one-carbon unit presumably in the form of carbon dioxide and reamination. The *p*-nitro derivative of homophenylalanine is a component of the β-lactone antibiotic obafluorin, which is made by *Pseudomonas fluorescens*. Work on the biosynthesis of this antibiotic suggested that the *p*-nitrohomophenylalanine residue arises from *p*-aminophenylalanine through the addition of a two-carbon unit.[10] None of the enzyme systems involved in the elongation of these aromatic amino acids has been characterized, but by analogy with the well-known metabolic pathway converting valine to leucine each should include an aminotransferase (E. C. 2.6.1.00) and an oxoacid lyase (E. C. 4.1.3.00). Our data are consistent with a view of the hydroxylations of homotyrosine at C-3 and C-4 as late-stage events in the biosynthesis of L-671,329.

Fungi apparently lack hydroxyproline-rich cell surface components[11] corresponding to the matrix collagens in animals[12] or the hydroxyproline-rich glycoproteins typical of plant cell walls,[13] and 4-hydroxyproline is only rarely found in fungal products. It is present as the cis isomer in the cyclopeptide amatoxins and phallotoxins of mushrooms.[14] Our study shows that the *trans*-4-hydroxyproline in L-671,329 is formed from proline. Direct conversion of proline to 4-hydroxyproline has previously been demonstrated for the streptomycete antibiotic actinomycin I, but it is not clear whether hydroxylation precedes incorporation of proline into the peptide.[15,16] However, free *trans*-4-hydroxy-L-proline occurs in seeds of the legume *Afzelia bella*[17] and as an intermediate in the synthesis of the streptomycete antibiotic etamycin (viridogrisein).[18] In the latter case, hydroxylation of free proline has been demonstrated in a cell-free extract of the producing organism,[19] and a mutant defective in the process has been isolated.[20] *cis*-4-Hydroxyproline is found as the free amino acid in sandal wood (*Santalum album L.*) where it is apparently synthesized from proline.[21,22]

To date, 3-hydroxy-4-methylproline has been found only as a component of echinocandin-type antibiotics.[23,24] Our data for L-671,329 indicate that the carbon skeleton of this amino acid is formed by the cyclization of leucine. A related proline derivative (*trans*-4-methylproline) is present in two streptomycete antibiotics, griselimycin,[25] and monamycin,[26] and it has been reported that the monamycin-producing organism *Streptomyces jamaicensis* incorporates radioactivity from L-[U-^{14}C]leucine into the methylproline residue of the antibiotic.[27] Nothing is known about the enzyme system responsible for this conversion. Certain plants produce 4-methylglutamic acid, which may be considered a relative of 4-methylproline since glutamic acid and proline have a precursor/product relationship in primary metabolism. It is interesting in the present context that an investigation of 4-methylglutamic acid formation in the honeylocust *Gleditsia triacanthos* has shown that it derives from leucine.[28]

Branched-chain fatty acids are uncommon in fungi[29] but not in other eukaryotes. In bacteria and other organisms, a branch is introduced during the fatty acid synthase reaction by the utilization of a branched primer unit (e.g., isovaleryl-CoA, isobutyryl-CoA, or 2-methylbutyryl-CoA, which derive from leucine, valine, and isoleucine, respectively) or by the use of methylmalonyl-CoA, which arises from propionyl-CoA.[6] In mycobacteria, methyl groups from *S*-adenosylmethionine can be introduced into preformed glycerol-bound fatty acids,[30] and our data for *Z. arboricola* suggest that the introduction of the methyl moieties to form 10,12-dimethylmyristate similarly involves methionine. Fatty acid alkylation in mycobacteria occurs at a point of unsaturation; the nature of the methyl acceptor in the L-671,329-producing fungus is not presently known. The utilization of methionine in the formation of methyl branch points in polyketide products has been well-documented for fungi.

Experimental Section

Materials. Stable isotopes were of 99% ^{13}C atom purity and were purchased from two sources: DL-[2-^{13}C]tyrosine, sodium [2-^{13}C]acetate, L-[2-^{13}C]leucine from MSD Isotopes; L-[1-^{13}C]proline and L-[^{13}CH$_3$]-methionine from Cambridge Isotopes.

Microbiological Procedures. *Z. arboricola* ATCC 20868 was grown in the seed medium previously described[1] or in a production medium consisting of D-mannitol, 4% (w/v); NZ Amine type E, 3.3% (Sheffield Products); yeast extract, 1% (Fidco); KH_2PO_4, 0.9%; and $(NH_4)_2SO_4$, 0.5%. A standardized inoculum was prepared by mixing a culture grown in seed medium with an equal volume of 20% glycerol and freezing portions of the mixtures at −70 °C. Transfers were made by 25-fold dilution with fresh medium when the culture was passed from this source into seed medium and then from seed medium to production medium. Cultures were incubated for 3 days at 25 °C with shaking at 220 rpm.

Feeding Experiments. In production medium, the synthesis of L-671,329 commences on day 3. At this point, the mycelia were harvested aseptically by low-speed centrifugation at room temperature and transferred to sterile 100 mM potassium phosphate buffer (pH 5.5) containing 0.5% D-mannitol. The transfer included washing the cells with buffered mannitol by two cycles of suspension and centrifugation before the final suspension was made, and in each step the volume of buffered mannitol was equal to that of the original culture. The addition of a ^{13}C-enriched precursor was made in four equal doses at 6–8-h intervals (cumulatively 100 mg/L) during incubation of the cell suspension at 25 °C with shaking at 220 rpm. The total incubation time was 48 h. To obtain the labeled product, the cells were collected by centrifugation and extracted with a volume of methanol equivalent to 40% of that of the cell suspension.[31]

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Isolation of L-671,239. Cell extracts were diluted with water to lower the methanol concentration to 50%, and the labeled product was adsorbed onto a column of SP-207 resin (Mitsubishi) previously equilibrated with 50% methanol. The resin was washed with 3 bed volumes of 65% methanol before the L-671,329 was eluted with 100% methanol. The resulting material was adsorbed to a column of HP-20 resin (Mitsubishi) and eluted in a similar fashion. As a final purification step, preparative-scale HPLC was performed with a Dupont Zorbax C18 column (21.2 mm × 25 cm) eluted isocratically at 37 °C with acetonitrile/water (48:52) at a flow rate of 15 mL/min. Under these conditions, the retention time of L-671,329 was approximately 12 min. Analytical HPLC on a Beckman Ultrasphere C18 column (4.6 mm × 25 cm) was used to monitor the purification. The column was operated isocratically at 37 °C with acetonitrile/water (50:50) at a flow rate of 0.75 mL/min. The column effluent was monitored at 210 nm, and L-671,329 had a retention of 11.2 min. Fractions with >98% purity (by peak integration) were combined, and yields from feeding experiments performed on a 1-L scale ranged from 10 to 20 mg.

Spectroscopy. ^{13}C NMR spectra were acquired in CD_3OD at 100 MHz with use of Waltz 16-proton decoupling on a Varian XL-400 instrument at ambient temperature. Chemical shifts are given in parts per million referenced to CD_3OD at 49.0 ppm as internal standard. Spectra of labeled and natural abundance L-671,329 were recorded with identical operating parameters. Conclusions regarding positions enriched with ^{13}C were based upon the assignments published previously,[2] although some of the myristate methylene carbons needed to be reassigned (see Table I).

(31) The experiments with ^{14}C precursors were performed in the same way except that the radionuclides were added as a single dose to a final concentration of 0.5 μCi/10 mL, and the incubations were allowed to proceed for only 6 h, which was sufficient time for the uptake of >90% of the precursor by the cells. The presence of radiolabeled L-671,329 in methanol extracts was demonstrated by TLC on silica gel 60 F (Merck) with a mobile phase of 1-butanol/acetic acid/5% ammonium hydroxide (12:3:1.5 by volume) followed by radioautography with X-Omat AR film (Kodak).

Acknowledgment. We thank our colleagues R. Schwartz and D. Sesin for useful suggestions regarding purification procedures and C. Caldwell, P. Durette, M. Hammond, and E. Inamine for stimulating discussions regarding this research.

Registry No. L-671,329, 120692-19-5; L-Tyr, 60-18-4; L-Pro, 147-85-3; L-Leu, 61-90-5.

Metal Ion Catalysis in Nucleophilic Displacement Reactions at Carbon, Phosphorus, and Sulfur Centers.[1] 4. Mechanism of the Reaction of Aryl Benzenesulfonates with Alkali-Metal Ethoxides: Catalysis and Inhibition by Alkali-Metal Ions

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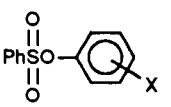
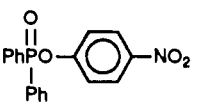
Abstract: The rates of the nucleophilic displacement reactions of aryl benzenesulfonates (**1a–f**) with alkali-metal ethoxides (LiOEt, KOEt, and KOEt in the presence of complexing agents) in anhydrous ethanol at 25 °C have been studied by spectrophotometric techniques. For all esters studied, the order of reactivity is LiOEt < EtO^- < KOEt. Metal ion catalysis (K^+) and inhibition (Li^+) are proposed to occur via reactive alkali-metal ethoxide ion pairs. Second-order rate constants for free ethoxide and metal–ethoxide ion pairs are calculated. Hammett treatment of leaving-group effects results in correlation of rate data with σ^0 substituent constants and large ρ values of 3.0 (KOEt), 3.1 (LiOEt), and 3.4 (EtO^-). A rate-determining transition state having well-advanced EtO–S bond formation but little S–OAr bond breakage is proposed. The similarity of the ρ values for KOEt, LiOEt, and EtO^- implies that alkali-metal ions do not significantly alter the extent of S–OAr bond breakage in the transition state. However, metal ions do stabilize the transition state to differing degrees. Equilibrium constants for association of K^+ and Li^+ with the transition state are calculated, and it is concluded from the relative magnitudes of these values ($Li^+ < K^+$) that solvated metal ions interact with the transition state, rather than bare metal ions. Hammett plots of the free energy of association of metal ions with the transition state indicate that leaving-group substituent effects on metal ion binding in the transition state are small (ρ = –0.39 (K^+) and –0.23 (Li^+)) and lead to the conclusion that more electron-rich transition states bind metal ions more strongly.

Introduction

We have undertaken systematic studies of the mechanism of the nucleophilic substitution reactions of carbon-, phosphorus-, and sulfur-based esters, including the effects of alkali-metal ions on these reactions. Previous reports have outlined the observation of alkali metal ion catalysis in the reactions of alkali-metal ethoxides and phenoxides with *p*-nitrophenyl diphenylphosphinate (**2**),[1c,d,f] as well as alkali metal ion catalysis and inhibition in the



1a: X = *p*-NO_2
b: X = *m*-NO_2
c: X = *p*-CF_3
d: X = *m*-Br
e: X = *p*-Cl
f: X = H



2

reactions of alkali-metal ethoxides with *p*-nitrophenyl benzenesulfonate (**1a**).[1e-g] The present study deals with the mechanism of the nucleophilic displacement reactions of alkali-metal ethoxides (KOEt, LiOEt, and EtO^-) with aryl benzenesulfonates (**1a–1f**)

(1) This paper is an extension of our series on Bond Scission in Sulfur Compounds. Previous papers in this series are the following: (a) Buncel, E.; Wilson, H.; Chuaqui, C. *J. Am. Chem. Soc.* **1982**, *104*, 4896. (b) Buncel, E.; Chuaqui, C.; Wilson, H. *J. Org. Chem.* **1980**, *45*, 2825. (c) Buncel, E.; Dunn, E. J.; Bannard, R. A. B.; Purdon, J. G. *J. Chem. Soc., Chem. Commun.* **1984**, 162. (d) Dunn, E. J.; Buncel, E. *Can. J. Chem.* **1989**, *67*, 1440. (e) Buncel, E.; Pregel, M. J. *J. Chem. Soc., Chem. Commun.* **1989**, 1566. (f) Dunn, E. J.; Molr, R. Y.; Buncel, E.; Purdon, J. G.; Bannard, R. A. B. *Can. J. Chem.* **1990**, *68*, 1837. (g) Pregel, M. J.; Dunn, E. J.; Buncel, E. *Can. J. Chem.* **1990**, *68*, 1846.

0002-7863/91/1513-3545$02.50/0