dated in the cavity. The environments of the O(2′) and the O(3′) atoms are substantially different upon the complex formation, resulting in the selective cleavage of the P–O(3′) bonds. The regioselective catalysis is applicable to the cleavage of ribonucleotide dimers.

The regioselectivity of β- and γ-CyD is opposite to the selectivity (the P–O(2′) cleavage) of ribonuclease, whereas the specificity of α-CyD is parallel to that of the enzyme. The remarkable dependence of the regioselectivity on the kind of CyD originates from the difference of the structure of the CyD–substrate complex (the inclusion type for β- and γ-CyDs and the hydrogen-bonding type for α-CyD).

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Ferroelectric Liquid Crystals. 6. Synthesis of Nonracemic Aryl Cyanohydrin Ethers

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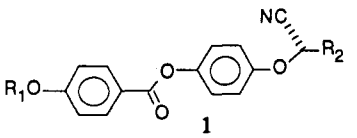
In connection with our project directed toward the design and synthesis of high-performance ferroelectric liquid crystals, we have developed a generally applicable synthetic route to chiral nonracemic aryl cyanohydrin ethers. The synthesis is illustrated herein by preparation of the arylbenzoate **1** (R_1 = *n*-decyl, R_2 = *n*-pentyl), which results in a straightforward manner from benzoylation of the key phenol intermediate **7**. Phenol **7** derives from Mitsunobu coupling of *p*-(benzyloxy)phenol (**3**) with nonracemic *N*-(α-hydroxyacyl)oxazolidone **2** prepared by the method of Evans. It is shown that this coupling proceeds predominantly with inversion of configuration. Conversion of the resulting *N*-(α-(aryloxy)acyl)oxazolidone **4** to amide **5** by treatment with dimethylaluminum amide, dehydration to nitrile **6** by the action of trimethylsilyl polyphosphoric acid, and then debenzylation promoted by trimethylsilyl iodide gives **7** in 51% overall yield from **2**.

Introduction

In connection with a project directed toward the design and synthesis of high-performance ferroelectric liquid crystals (FLCs),[1] we required an efficient route to nonracemic aryl cyanohydrin ethers of type **1**, where R_1 and R_2 are branched or straight-chain alkyl groups. Access to both enantiomers of the target materials in high enantiomeric purity was required, and a high degree of structural flexibility in the alkyl grouping R_2 was considered desirable.



1

We report herein a simple solution to this problem[2] based upon chiral oxazolidone chemistry recently reported by Evans,[3] as illustrated in Scheme I for R_1 = *n*-decyl and R_2 = *n*-pentyl. The route involves Mitsunobu coupling of a phenol with nonracemic α-hydroxy-*N*-acyloxazolidones such as **2**. Aminolysis of the *N*-acyloxazolidone, followed by dehydration of the resulting amide, leads to the key aryl cyanohydrin ethers of type **7**. Details of the illustrative synthesis of compound **1** (R_1 = *n*-decyl, R_2 = *n*-pentyl) follow.

Mitsunobu Coupling of *p*-(Benzyloxy)phenol (3) with Alcohol 2. The starting material, nonracemic α-hydroxyoxazolidone **2**, is easily prepared using the Evans protocol.[3] Coupling of alcohol **2** with *p*-(benzyloxy)phenol (**3**) under standard Mitsunobu conditions[4] (diethyl azodicarboxylate (DEAD)/triphenylphosphine, THF, room temperature) is extremely slow, presumably due to the hindered nature of the secondary alcohol substrate. While benzene has been shown to be an excellent solvent for the inversion of hindered hydroxyl groups in steroids using the Mitsunobu procedure,[5] phenol **3** is only slightly soluble in benzene, and coupling in this solvent is very sluggish. Efficient coupling could be achieved, however, using dichloromethane as solvent, affording the target aryl ether **4** in 73% yield, along with a minor amount (3–5%) of diastereomeric product.[6] The major product was purified by chromatography.

† University of Colorado Department of Chemistry X-ray lab.

(1) (a) Walba, D. M.; Slater, S. C.; Thurmes, W. N.; Clark, N. A.; Handschy, M. A.; Supon, F. *J. Am. Chem. Soc.* **1986**, *108*, 5210–5221. (b) Walba, D. M.; Vohra, R. T.; Clark, N. A.; Handschy, M. A.; Xue, J.; Parmar, D. S.; Lagerwall, S. T.; Skarp, K. *J. Am. Chem. Soc.* **1986**, *108*, 7424–7425. (c) Walba, D. M.; Clark, N. A. Model for the Molecular Origins of the Polarization in Ferroelectric Liquid Crystals, *Spatial Light Modulators and Applications II*; Efron, U., Ed.; Proc. SPIE 825, 81–87, 1988. (d) Walba, D. M.; Clark, N. A. *Ferroelectrics* **1988**, *84*, 65–72. (e) Walba, D. M.; Razavi, H. A.; Clark, N. A.; Parmar, D. S. *J. Am. Chem. Soc.* **1988**, *110*, 8686–8691.

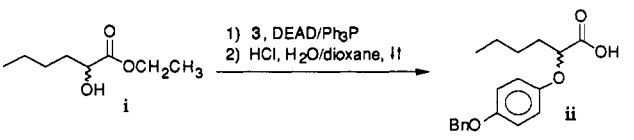
(2) This work was first presented at the 11th International Liquid Crystal Conference, Poster Θ-040-FE, June 30–July 4, 1986.

(3) Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346.

(4) Mitsunobu, O. *Synthesis* **1981**, 1.

(5) Loibner, H.; Zbiral, E. *Helv. Chim. Acta* **1977**, *60*, 417.

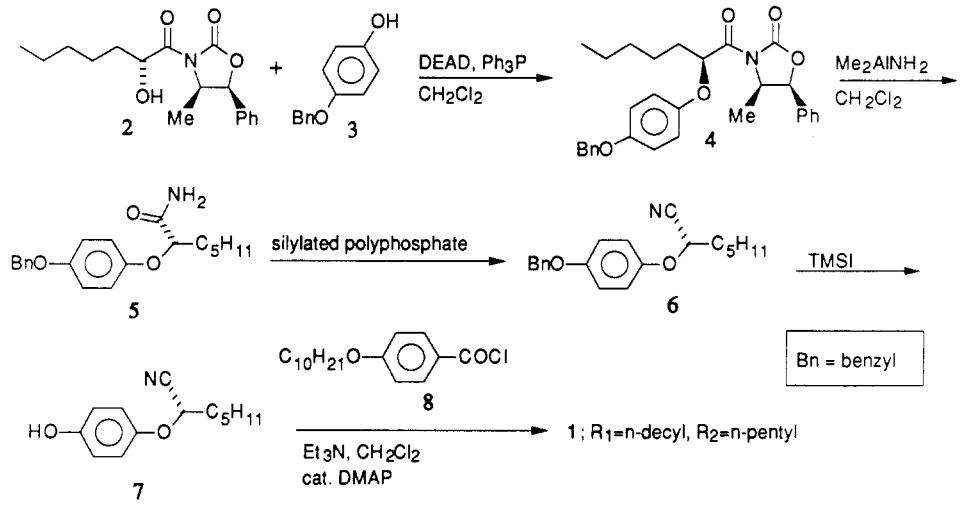
(6) In the case of the Mitsunobu coupling of alcohol **2** with phenol **3**, the minor diastereomer was tentatively identified as a component of the crude reaction mixture by ^{1}H NMR. This assignment is quite firm, however, since in the homologous series leading to compounds **1**, R_2 = *n*-butyl, the minor diastereomer was isolated from a coupling reaction and was shown to be identical by ^{1}H NMR with one of the diastereomers produced by coupling of the racemic acid **ii** (prepared from ethyl α-hydroxypentanoate (**i**) as shown) with the norephedrine-derived oxazolidone. The other diastereomer deriving from the latter process was, of course, identical with the major product of the Mitsunobu coupling.



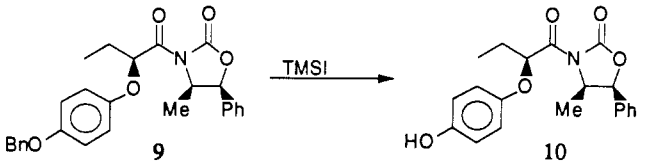
i **ii**

0022-3263/89/1954-4939$01.50/0

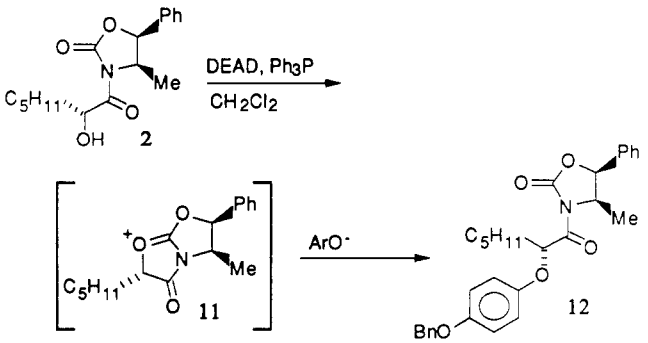
Scheme I. Synthesis of Compound 1, R_1 = *n*-Decyl, R_2 = *n*-Pentyl



A priori, there is no way of assigning the relative configuration of the major product of this coupling reaction. While no crystalline derivative of compound **4** was obtained, treatment of benzyl ether **9** (prepared as for compound **4**) with trimethylsilyl iodide in dichloromethane[7] gave the nicely crystalline phenol **10**. The stereochemistry of this material was established unequivocally by X-ray crystallography, showing that the coupling proceeds predominantly with inversion.



Thus, the minor diastereomer formed in the coupling is produced with overall retention of configuration. While it is possible that epimerization is responsible for formation of the minor diastereomer, an attractive alternative mechanism for formation of the product with retention is given below. Reaction of alcohol **2** with DEAD/Ph_3P gives an intermediate alkoxyphosphonium salt, which normally reacts in an intermolecular fashion with phenoxide to give the major product. An apparently disfavored intramolecular attack by the oxazolidone carbonyl can, however, given cation **11**. Subsequent reaction with phenoxide would then produce the minor product (benzyl ether **12**) with overall retention of configuration.



Conversion of the *N*-Acyloxazolidone Function to a Nitrile. To accomplish the required transformation to nitrile **6**, we thought it would be interesting to attempt displacement of the chiral auxilliary from ether **4** with bis(trimethylsilyl) amide. If successful, we felt that dehydration of the resulting bissilyl amide would be readily accomplished with trimethylsilyl triflate. Unfortunately, treatment of compounds of type **4** with sodium bis(trimethylsilyl) amide gave only epimerization, leading to isolation of a mixture of diastereomeric benzyl ethers, presumably due to enolization. This result was somewhat surprising, since enolization of α,α-disubstituted oxazolidones of type **4** gives an enolate ion with considerable A-strain.[8] Clearly, however, the hindered nature of the silyl amide base causes enolization to compete effectively with addition to the relatively hindered exocyclic carbonyl grouping.

With the failure of the bis(trimethylsilyl) amide approach, a more standard sequence to the nitrile via dehydration of an intermediate amide (**5**) was explored.[9] Thus, treatment of *N*-acyloxazolidones **4** with Weinreb's reagent (dimethylaluminum amide)[10] in dichloromethane at room temperature gave the desired amide **5** reproducebly in high yield, and the oxazolidone chiral auxiliary could be recovered in high yield after workup. Dehydration of amide **5** to give the desired cyanohydrin ether **6** was readily accomplished by treatment of the amide with (trimethylsilyl)polyphosphate in refluxing benzene or toluene.[11]

The enantiomeric purity of the product cyanohydrin ethers was established in order to rule out the possibility of racemization. Thus, analysis of racemic cyanoether **6** by ^1H NMR using the Pirkle chiral solvating agent (+)-2,2,2-trifluoro-1-(9-anthryl)ethanol[12] allowed "resolution"of the enantiomers. Similar analysis of **6** prepared as indi-

(7) Jung, M. E.; Lyster, M. A. *J. Org. Chem.* **1977**, *42*, 3761.

(8) (a) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127. (b) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.

(9) The use of lithium amide for accomplishing the required transformation of oxazolidone **4** to amide **5** proved unsatisfactory. Thus, when **4** was treated with 1 equiv of $LiNH_2$ in THF, deprotonation of initially formed amide **5** at nitrogen gave an aza enolate which reacted rapidly with starting material affording a symmetrical urea. Dimerization could be avoided by the use of 2 equiv of $LiNH_2$ in THF. Small quantities of excess ammonia, however, led to varying amounts of undesired carbamate byproduct resulting from attack on the ring carbonyl of **4** rather than the exocyclic carbonyl. The carbamate was the exclusive product in liquid ammonia solvent.

(10) (a) Basha, A.; Lipton, M.; Wienreb, S. M. *Tetrahedron. Lett.* **1977**, 4171. (b) Lipton, M.; Basha, A.; Wienreb, S. M. *Org. Synth.* **1979**, *159*, 49.

(11) Yokoyama, M.; Yoshida, T.; Tsuneo, I. *Synthesis* **1982**, 591.

(12) (a) Pirkle, W. H.; Hoekstra, M. S. *J. Am. Chem. Soc.* **1976**, *98*, 1832. (b) Pirkle, W. H.; Rinadli, P. L. *J. Org. Chem.* **1977**, *42*, 3217.

cated in Scheme I showed no detectable amount of the minor enantiomer, indicating an enantiomeric purity of >95%.

Completion of the Synthesis of Compound 1 (R_1 = *n*-Decyl, R_2 = *n*-Pentyl). Preparation of the target liquid crystal compound 1 now simply required debenzylation of cyanohydrin ether 6 to give the key phenol 7, followed by benzoylation. Hydrogenolysis of compounds of type 6 with palladium hydroxide on carbon in ethanol led to reduction of the nitrile group at a rate comparable to the debenzylation of the benzyl ether. The required deprotection was cleanly achieved, however, utilizing trimethylsilyl iodide in dichloromethane, giving phenol 7 in excellent yield. Benzoylation of this phenol with *p*-(decyloxy)benzoyl chloride (8) under standard conditions (CH_2Cl_2, 2 equiv of Et_3N, catalytic DMAP) produced the final target phenylbenzoate 1 (R_1 = *n*-decyl, R_2 = *n*-pentyl) in a straightforward manner.

Liquid Crystal Properties of Phenylbenzoates of Type 1. Using this route, nine compounds of type 1 were prepared and characterized, including materials with R_2 = ethyl, *n*-propyl, *n*-butyl, and *n*-pentyl. Several of the new compounds possessed monotropic chiral nematic and/or smectic A phases. For example, crystalline 1 (R_1 = *n*-decyl, R_2 = *n*-pentyl) melts directly into the isotropic liquid at 42 °C and shows the phase sequence [I–41.3° → N*–39° → A–24° → X] upon cooling from the isotropic liquid (temperatures in degrees celsius I = isotropic liquid, A = smectic A, N* = chiral nematic, X = crystalline solid). In addition, this material exhibited a large extrapolated ferroelectric polarization of +100 nC/cm^2 when evaluated as guest with standard FLC hosts.[13]

To our knowledge, compounds 1 were the first liquid crystals possessing a cyano grouping at a stereocenter. Since our initial disclosure,[2] several similar FLC components have been reported, including the cyanohydrin esters of Gray et al.,[14] the novel 2-methyl-2-cyanoalkanoic acid esters of the E. Merck group,[15] and some 2-((cyanoalkyl)phenyl)benzoates from our own laboratories.[16] While it is clear the chiral nitriles represent a useful class of FLCs, in our estimation the level of understanding of the orientation of cyano groups in ferroelectric liquid crystal phases is poor. Experiments aimed at improving this situation are under way and will be reported in due course.

Conclusion

A general route from *N*-(α-hydroxyacyl)oxazolidones of type 2 to cyanohydrin ether phenylbenzoates of type 1 is illustrated with a synthesis of compound 1 (R_1 = *n*-decyl, R_2 = *n*-pentyl). The key step in the synthesis is Mitsunobu coupling of compound 2 with *p*-(benzyloxy)phenol (3) to give (aryloxy)oxazolidone 4. The route is quite efficient, affording the target in 46% overall yield from compound 2.

Experimental Section

All glassware was dried at 120 °C overnight. All reactions were performed under a positive pressure of argon using standard manifold techniques unless otherwise stated. All reagent solutions were transferred using glass syringes or stainless steel cannulas with an argon overpressure. The syringes and cannulas were dried overnight at 120 °C oven before use. Melting points are uncorrected.

Analytical thin-layer chromatography was performed on glass silica gel plates (0.25 mm thick E. Merck silica gel 60-F254), using the solvent mixtures indicated. Preparative chromatographic purifications were performed by employing flash chromatography on E. Merck 40–63 μm normal-phase silica gel. All solvent mixtures were prepared by combining the indicated relative volumes of solvent.

Dry solvents were prepared using standard techniques. Tetrahydrofuran (THF) was distilled from a purple solution of sodium benzophenone ketyl just prior to use. Dichloromethane was prepared by continuous distillation from calcium hydride. Toluene and benzene were dried by distillation from calcium hydride and were stored under argon.

Sodium bis(trimethylsilyl)amide, as a 1.0 M solution in THF, was used as received from Aldrich Chemical Co., as were diethyl azodicarboxylate (DEAD) and triphenylphosphine. 4-(Benzyloxy)phenol (3) was purchased from Eastman Kodak and purified by repeated recrystallization from ethanol or benzene. Trimethylaluminum was purchased from Aldrich Chemical Co. as a 2.0 M solution in hexanes or toluene and was converted to a standard 1.0 M solution of dimethylaluminum amide by literature methods.[10] (*S*)-(+)-2,2,2-Trifluoro-(9-anthryl)ethanol was used as received from Aldrich Chemical Co. Poly(trimethylsilyl)-phosphate was prepared as a standard 1.14 M solution in toluene or benzene from hexamethyldisiloxane and phosphorus pentoxide as reported.[11] Trimethylsilyl iodide was used as received from Aldrich Chemical Co.

4-(Decyloxy)benzoic acid was purchased from Frinton Laboratories and was purified by recrystallization from ethanol. 4-(Decyloxy)benzoyl chloride was obtained through chlorination of the acid with oxalyl chloride in refluxing toluene and was purified before further use by high-vacuum distillation.

[3(2*R*),4*R*,5*S*]-3-(2-Hydroxy-1-oxoheptyl)-4-methyl-5-phenyl-2-oxazolidinone (2) was prepared by the method of Evans,[3] and was obtained in 66% yield: crystalline solid recrystallized from hexanes as plates, mp 59.5–60.5 °C; R_f 0.26 (CH_2Cl_2); IR ($CHCl_3$, cm^{-1}) 3550 (broad), 3020, 3005, 2960, 2930, 2860, 1785 (s), 1695 (s), 1455, 1365, 1345, 1305, 1195, 1145, 1120, 1090, 1060, 1030, 990, 960; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.93 (t, *J* = 6.7 Hz, 3 H), 0.955 (d, *J* = 6.7 Hz, 3 H), 1.20–1.45 (m, 5 H), 1.45–1.75 (m, 3 H), 1.82 (m, 1 H), 3.41 (d, *J* = 8.1 Hz, 1 H, OH), 4.75 (quin, *J* = 6.7 Hz, 7.0 Hz, 1 H), 5.05 (m, 1 H), 5.74 (d, *J* = 7.2 Hz, 1 H), 7.15–7.50 (m, 5 H, arom); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ 13.78, 14.02, 22.30, 24.78, 31.20, 34.32, 55.12, 70.67, 79.54, 125.37, 128.52, 128.67, 132.61, 152.47, 174.94; mass spectrum (70 eV, *m/z*) 305 (P^+), 235, 234, 205, 177, 118, 109, 91.

Anal. Calcd for $C_{17}H_{23}O_4N$: C, 66.86; H, 7.59. Found: C, 66.93; H, 7.50.

[3(2*S*),4*R*,5*S*]-3-(2-((4-(Benzyloxy)phenyl)oxy)-1-oxoheptyl)-4-methyl-5-phenyl-2-oxazolidinone (4). To 1.701 g (5.57 mmol) of alcohol 2, 1.33 g (6.69 mmol, 1.2 equiv) of *p*-(benzyloxy)phenol (3), and 1.75 g (6.69 mmol, 1.2 equiv) of triphenylphosphine was added 30 mL of dry dichloromethane. To an additional 5 mL of dry dichloromethane was added 1.05 mL of diethyl azodicarboxylate (DEAD, 6.69 mmol, 1.2 equiv). This solution was added to the reaction flask dropwise over 4 h at 25 °C.

The resulting light yellow reaction mixture was allowed to stir for 12 h. To isolate the product, approximately 50% of the reaction solvent was removed by rotary evaporation, and the resulting slurry was poured into 150 mL of hexanes. The organic layer was washed with three 50-mL portions of water and 50 mL of brine and dried over anhydrous Na_2SO_4. The majority of the

(13) An illustration of the host–guest approach for evaluation of FLC properties can be found in ref 1e and in: Walba, D. M.; Clark, N. A.; Razavi, H. A.; Parmar, D. S. A Novel Application of the Host-Guest Paradigm: Design of Organic Optoelectronic Materials, In *Proceedings of the 5th International Symposium on Inclusion Phenomena and Molecular Recognition*; Atwood, J. L., Ed.; Plenum Publishing Corp, in press. Details of the evaluation of the cyanohydrin ethers as FLC components will be published separately.

(14) Sage, I.; Jenner, J.; Chambers, M.; Bradshaw, M. J.; Brimmell, V.; Constant, J.; Hughes, J. R.; Raynes, E. P.; Samra, A. K.; Gray, G. W.; Lacey, D.; Toyne, K.; Chan, L.; Shenouda, I.; Jackson, A. *Ferroelectrics* **1988**, *85*, 351–359.

(15) Geelhaar, T.; Krause, J.; Reiffenrath, V.; Wächtler, A. Technical digest of the 1988 Optical Society of America Annual Meeting in Santa Clara, California, October 30–November 4, 1988, abstract no. TUAA1.

(16) Walba, D. M.; Clark, N. A.; Razavi, H. A.; Eidman, K. F.; Haltiwanger, R. C.; Parmar, D. S. A Novel Application of the Molecular Recognition Paradigm: Design of Ferroelectric Liquid Crystals, *Liquid Crystal Chemistry, Physics, and Applications*; Doane, J. W., Yaniv, Z., Eds.; Proc. SPIE 1080, in press.

triphenylphosphine oxide byproduct was removed with the drying agent by filtration. Solvent evaporation gave 5.18 g of a moist solid. This was subjected to flash chromatography on 300 g of silica gel with 8:2 hexanes/ethyl acetate as eluting solvent to give 1.99 g (73%) of pure ether **4** as a white solid. Recrystallization from methanol gave white needles: mp 74 °C; R_f 0.47 (4:1 hexanes/ethyl acetate); IR ($CHCl_3$, cm^{-1}) 3005, 2920, 2860, 1778, 1715, 1505, 1458, 1365, 1345, 1200, 1165, 1125; ^1H NMR (200 MHz, $CDCl_3$) δ 0.85 (d, 3 H, $NCHCH_3$), 0.90 (t, J = 5.4 Hz, 3 H, CH_2CH_3), 1.34 (m, 4 H, $CH_2(CH_2)_2CH_3$), 1.62 (m, 2 H, $CHCH_2CH_2CH_2$), 1.92 (m, 2 H, $CHCH_2CH_2$), 4.85 (quin, 1 H, $NCHCH_3$), 5.01 (s, 2 H, $PhCH_2O$), 5.75 (d, 2 H, $NCH(CH_3)CHPh$), 5.75 (d of d, 1 H, $PhOCH(C_5H_{11})CO$), 6.88 (s, 4 H, O*Ph*O), 7.25–7.44 (m, 10 H, arom); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ 13.95, 14.32, 22.40, 25.10, 31.27, 32.69, 54.27, 70.34, 76.63, 79.38, 115.75, 116.63, 125.56, 127.38, 127.75, 128.42, 128.58, 128.69, 133.21, 137.16, 152.09, 152.62, 153.66, 171.58; mass spectrum (70 eV, m/z) 487 (P^+), 288, 149, 91.

Anal. Calcd for $C_{30}H_{33}O_5N$: C, 73.90; H, 6.82. Found: C, 73.59; H, 6.75.

[3(2*S*),4*R*,5*S*]-3-(2-((4-(Benzyloxy)phenyl)oxy)-1-oxobutyl)-4-methyl-5-phenyl-2-oxazolidinone (9). A procedure similar to that described above for the synthesis of ether **4** was utilized to convert the known [3(2*R*),4*R*,5*S*]-3-(2-hydroxy-1-oxobutyl)-4-methyl-5-phenyloxazolidinone[3] to ether **9**: The product was purified by flash chromatography to afford an 80% yield of product pure by TLC. Recrystallization from hexanes or 2-propanol produced white plates: mp 76–78 °C; R_f 0.31 (4:1 hexanes/ethyl acetate); $[\alpha]^{25}_D$ = 50.5° (c = 0.0789, CH_2Cl_2); IR (CCl_4, cm^{-1}) 3000–2850, 1780, 1715, 1505 (s), 1450, 1383, 1363, 1340, 1228, 1198, 1150, 1110; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (d, 3 H, $NCH(CH_3)$), 1.11 (t, 3 H, CH_2CH_3), 1.99 (m, 2 H, $CHCH_2CH_3$), 4.81 (quin, 1 H, $NCH(CH_3)$), 5.01 (s, 2 H, $PhCH_2O$), 5.71 (d, 1 H, $NCH(CH_3)CH(Ph)O$), 6.88 (s, 4 H, O*Ph*O), 7.27–7.40 (broad m, 10 H, arom); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ 9.73, 14.33, 26.07, 54.31, 70.36, 77.63, 79.40, 115.67, 116.69, 125.47, 127.31, 127.70, 128.36, 128.59, 128.72, 133.00, 137.04, 151.97, 152.59, 153.58, 171.34; mass spectrum (70 eV, m/z), 445 (P^+), 246, 160, 117, 91, 69, 28.

Anal. Calcd for $C_{27}H_{27}O_5N$: C, 72.81; H, 6.06; N, 3.15. Found: C, 72.60; H, 5.89; N, 3.29.

[3(2*S*),4*R*,5*S*]-3-(2-((4-Hydroxyphenyl)oxy)-1-oxobutyl)-4-methyl-5-phenyloxazolidinone (10). To 339 mg (1.00 mmol) of ether **9** was added dichloromethane (2.0 mL), followed by 210 mg (0.14 mL, 1.05 mmol, 1.05 equiv) of neat trimethylsilyl iodide. The dark red solution which resulted was stirred for 45 min until the starting material was consumed (TLC, 4:1 hexanes/ethyl acetate). When the reaction was judged complete, methanol was added to destroy the remaining TMSI, and the volatile byproducts were removed under vacuum. The crude product was taken up in ether, washed with 1.0 M HCl, 1.0 M $Na_2S_2O_3$, and brine, and dried (Na_2SO_4). Solvent removal gave 338 mg of crude phenol **10**. Chromatography on silica gel eluting with 3:1 hexanes/ethyl acetate produced 230 mg (68.0%) of pure phenol **10**. Recrystallization from hexanes/ethyl acetate gave fine plates with the following physical properties: mp 116–117.5 °C; R_f 0.37 (3:1 hexanes/ethyl acetate); IR ($CHCl_3$, cm^{-1}) 3590 (sharp), 3310 (broad), 2980, 2950, 1780 (s), 1715 (s), 1515 (s), 1460, 1390, 1375, 1350, 1220, 1165, 1125, 1070, 1038, 995, 962; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (d, J = 6.0 Hz, 3 H, $NCHCH_3$), 1.14 (t, J = 8.0 Hz, 3 H, $CHCH_2CH_3$), 1.88–2.05 (m, 2 H, $CHCH_2CH_3$), 4.81 (quin, 1 H, $NCH(CH_3)$, 5.70 (d of d, 1 H, $CHCH_2CH_3$), 5.70 (d, 1 H, $NCHCH_3$), 5.75 (broad s, 1 H, OH), 6.69–6.82 (AA'XX', 4 H, HO*Ph*O), 7.26–7.43 (m, 5 H, arom); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ 14.44, 26.14, 54.53, 77.76, 79.68, 116.12, 116.99, 125.56, 128.72, 128.88, 132.91, 150.62, 151.60, 152.84, 171.95; mass spectrum (70 eV, m/z) 355 (P^+), 246, 160, 117, 91, 69.

Anal. Calcd for $C_{20}H_{21}O_5N$: C, 67.60; H, 5.92; O, 22.53; N, 3.94. Found: C, 67.36; H, 5.63.

Slow crystal growth from hexanes/ethyl acetate gave thick plates of sufficient quality to allow a single-crystal X-ray analysis.

(*S*)-2-((4-(Benzyloxy)phenyl)oxy)heptanecarboxamide (5). To 721 mg (1.48 mmol) of oxazolidinone **4** was added 3.70 mL (3.70 mmol, 2.5 equiv) of 1.0 M dimethylaluminum amide in 1:1 hexanes/dichloromethane. The resulting homogeneous solution was stirred for 7 h at 25 °C until the reaction was judged complete by TLC (4:1 hexanes/ethyl acetate).

The reaction mixture was poured into a separatory funnel containing 20 mL of ice, 20 mL 1.0 M HCl, and 20 mL of ether. When methane production ceased the layers were separated, and the aqueous layer was extracted with two additional 20-mL portions of ether. The combined organic layers were washed with brine and dried ($MgSO_4$). Filtration and solvent removal yielded 707 mg of a white solid. TLC analysis showed that only the chiral auxiliary and product were present (19:1 dichloromethane/acetone). Both products were isolated by flash chromatography on 50 g of silica gel, eluting with 19:1 dichloromethane/acetone to yield 227 mg of recovered chiral auxiliary (87%) and 431 mg of amide **5** (89%) as a solid: mp 136–142 °C; R_f 0.37 (19:1 dichloromethane/acetone); $[\alpha]^{25}_D$ 16.07° (c = 0.0862, $CHCl_3$); IR ($CHCl_3$ cm^{-1}) 3510, 3400, 3050, 2960, 2940, 2875, 1695, 1578, 1515, 1210; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, J = 6.4 Hz, 3 H, CH_2CH_3), 1.33 (m, 4 H, $CH_2(CH_2)_2CH_3$), 1.49 (m, 2 H, $CH_2CH_2(CH_2)_2CH_3$), 1.92 (m, 2 H, $CH_2CH_2(CH_2)_2CH_3$), 4.43 (t, 1 H, $OPhOCH(C_5H_{11})CO$), 5.01 (s, 2 H, $PhCH_2OPh$), 5.81 (broad s, 1 H, CO_2NH_2), 6.37 (broad s, 1 H, CO_2NH_2), 6.81–6.93 (AA'XX', 4 H, O*Ph*O), 7.31–7.44 (m, 5 H, $PhCH_2O$); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ 13.89, 22.34, 24.59, 31.36, 32.83, 70.45, 79.65, 115.85, 116.36, 127.32, 127.83, 128.45, 136.92, 151.71, 153.72, 175.24; mass spectrum (70 eV, m/z) 327 (P^+), 128, 91 (100).

Anal. Calcd for $C_{20}H_{25}O_3N$: C, 73.37; H, 7.70. Found: C, 73.28; H, 7.57.

(*S*)-2-((4-(Benzyloxy)phenyl)oxy)heptanenitrile (6). To 244 mg (0.747 mmol) of amide **5** was added 5 mL of dry benzene and 1.46 mL of 1.14 M polyphosphoric trimethylsilyl ester (PPSE)[11] in benzene. The resulting solution was heated to reflux for 8 h until the reaction was judged complete by TLC (R_f of product = 0.37, 19:1 dichloromethane/acetone).

The cooled reaction mixture was diluted with 50 mL of ether, washed twice with 20 mL of water and 20 mL of brine, and dried ($MgSO_4$). Filtration and solvent removal gave 217 mg (94%) of the nitrile **6** showing only trace impurities by TLC. Chromatography over a short column of silica gel with 85:15 hexanes/ethyl acetate gave 207 mg of pure **6** (90%). An analytical sample was recrystallized from hexanes as fine needles: mp 48.5 °C; R_f 0.40 (85:15 hexanes/ethyl acetate); $[\alpha]^{25}_D$ = −136° (c = 0.0170, CH_2Cl_2); IR ($CHCl_3$, cm^{-1}) 3300, 2960, 2950, 2865, 1505 (s), 1465, 1380, 1225, 1205, 1015; ^1H NMR (200 MHz, $CDCl_3$) δ 0.93 (t, J = 6.9 Hz, 3 H, $(CH_2)_2CH_3$), 1.38 (m, 4 H, $CH_2(CH_2)_2CH_3$), 1.55 (m, 2 H, $CH_2CH_2(CH_2)_2CH_3$), 2.01 (m, 2 H, $OCH(CN)CH_2CH_2$), 4.65 (t, 1 H, $PhOCH(C_5H_{11})CN$), 5.03 (s, 2 H, $PhCH_2O$), 6.95 (s, 4 H, O*Ph*O), 7.25–7.41 (m, 5 H, $PhCH_2O$); ^{13}C NMR (50.1 MHz, $CDCl_3$) δ 13.84, 22.32, 24.32, 31.01, 33.49, 68.31, 70.45, 115.88, 117.64, 117.97, 127.38, 127.91, 128.50, 136.87, 150.78, 154.78; mass spectrum (70 eV, m/z) 309 (P^+), 91.

Anal. Calcd for $C_{20}H_{23}O_2N$: C, 77.64; H, 7.49. Found: C, 77.56; H, 7.41.

(*S*)-2-((4-Hydroxyphenyl)oxy)heptanenitrile (7). To 198 mg (0.641 mmol) of benzyl ether **6** was added 1 mL of dry dichloromethane and 0.10 mL (141 mg, 0.70 mmol) of neat trimethylsilyl iodide (TMSI). The reaction mixture turned deep red and was allowed to stand at room temperature. After 1 h ethanol was added to destroy any remaining TMSI. Volatile materials were removed under vacuum, and TLC analysis showed only the presence of phenol product and one high R_f compound (probably benzyl iodide). These were separated on 5 g of silica gel using 25% ethyl acetate/hexanes as eluting solvent to provide 122 mg of pure phenol **7** as a clear, colorless oil (83% yield): R_f 0.23 (3:1 hexanes/ethylacetate); ^1H NMR (200 MHz, $CDCl_3$) δ 0.90 (t, J = 6.3 Hz, 3 H, CH_2CH_3), 1.34 (broad s, 6 H, $(CH_2)_3CH_3$), 1.60 (broad m, 2 H, $OCH(CN)CH_2CH_2$), 2.06 (broad m, 2 H, $OCH(CN)CH_2CH_2$), 4.65 (t, J = 6.4, 6.8 Hz, 1 H, $OCH(C_6H_5)CN$), 5.25 (broad s, 1 H, OH), 6.90 (AA'XX', 4 H, HO*Ph*O); ^{13}C NMR (50.2 MHz, $CDCl_3$) δ 13.97, 22.41, 24.60, 28.53, 31.42, 33.46, 68.64, 116.28, 117.96, 128.54, 150.39, 151.78.

4'-[[(*S*)-1-Cyanoheptyl]oxy]phenyl 4-(*n*-Decyloxy)benzoate (1; R_1 = *n*-Decyl, R_2 = *n*-Pentyl). To 66.4 mg (0.224 mmol) of (decyloxy)benzoyl chloride (**8**) and 52.6 mg (0.240 mmol) of phenol **7** was added 2 mL of dry dichloromethane, 33 mg of triethylamine (0.336 mmol, 0.047 mL, 1.5 equiv), and a few small crystals of 4-(dimethylamino)pyridine (DAMP). The condensation was complete in 5 min at 25 °C as indicated by TLC (3:1 hexanes/ethyl acetate). After 10 min, the reaction mixture was

transferred into a 60-mL separatory funnel with ether, and the ethereal solution was washed with 20 mL of 1.0 M HCl followed by 20 mL of 1.0 M sodium hydroxide. Drying with brine and $MgSO_4$, followed by solvent removal, gave a thick oil. The crude product (nearly pure by TLC) was purified by flash chromatography on silica gel (1:9 hexanes/ethyl acetate) to yield 103 mg (96% yield) of pure product. This material was further purified by recrystallization from spectral grade methanol, to give the target compound 1; R_1 = *n*-decyl, R_2 = *n*-pentyl, of sufficient purity for liquid crystal studies: mp 42 °C; IR ($CHCl_3$, cm^{-1}) 3060, 2960, 2930, 2760, 1730, 1605, 1510, 1500, 1260, 1225, 1210, 1195, 1175, 1075; ^1H NMR (500 MHz, $CDCl_3$) δ 0.885 (t, J = 7.5 Hz, 3 H), 0.929 (t, J = 9.5 Hz, 3 H), 1.25–1.40 (large m, alkyl region), 1.47 (m, CH_2), 1.62 (m, CH_2), 1.83 (m, CH_2), 2.09 (m, $OCH(CN)CH_2$), 4.04 (t, J = 6.5 Hz, 2 H, CH_2O), 4.739 (t, $OCH(CN)CH_2$, J = 6.7 Hz, 1 H), 6.96 (d, J = 8.5 Hz, 2 H), 7.055 (d, J = 8.5 Hz, 2 H), 7.179 (d, J = 9.0 Hz, 2 H), 8.127 (d, J = 9.0 Hz, 2 H); mass spectrum (CI^+, methane, m/z) 480 ($(M + 1)^+$), 261.

Anal. Calcd for $C_{30}H_{41}O_4N$: C, 75.12; H, 8.62. Found: C, 74.65; H, 8.59.

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Supplementary Material Available: Details of the crystal structure determination of compound **10**, including tables of atomic coordinates, bond lengths and angles, anisotropic displacement parameters, H-atom coordinates and isotropic displacement parameters, and an ORTEP drawing of the structure showing the numbering scheme used in the tables (9 pages). Ordering information is given on any current masthead page.

Reaction Pathways of 3-(3′-Methylenecyclobutyl)propyl and 2-(3′-Methylenecyclobutyl)ethyl Radicals

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Molecular mechanics (MM2) calculations were used to predict the efficacy and regiochemical outcome of radical cyclizations involving the title radicals and others with further substitution at C_1 on the ring. The MM2 results were generally ratified by experiment and showed the preference for exo closure to give the bicyclo[3.1.1]-heptylmethyl and bicyclo[2.1.1]hexylmethyl radicals, respectively. However, due to subsequent radical rearrangements and, in the case of the former, internal H transfer, these cyclizations are not synthetically viable.

Introduction

Currently there is a great deal of interest in free-radical cyclizations from their extensive use as kinetic and mechanistic probes[1] and successful application in synthesis.[2] Similarly, small-ring bicyclic alkanes have also commanded considerable attention due to the intriguing chemistry attributed to them over recent years. Most of the interest has arisen through NMR[3] and photoelectron spectra,[4] gas-phase ion studies,[5] and solvolytic chemistry[6] in which transannular bridgehead–bridgehead interactions have been implicated, with substantial theoretical support,[7] to explain observations. It seemed appropriate to investigate the possibility of ring-forming reactions of the type

Scheme I

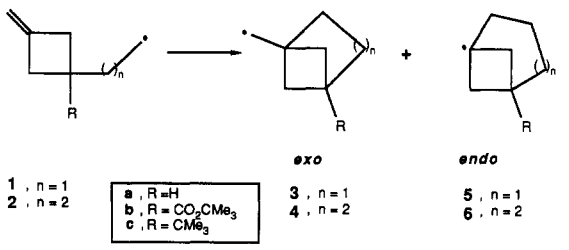

Table I. Transition Structure MM2 Strain Energies for the Ring Closure of 1 and 2

radical	ΔE_s^a (radical) exo	endo
1a	11.1 (3a)	27.4 (5a)
1b	9.5 (3b)	26.3 (5b)
1c	6.4 (3c)	24.2 (5c)
2a	13.1 (4a)	16.9 (6a)
2b	10.8 (4b)	14.5 (6b)
2c	9.6 (4c)	12.9 (6c)

[a] Kilocalories/mole.

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