Table I. Benzyl Radical Coupling Products from Irradiation of Ring-Substituted AH_3 and AF_3 with 0.5 M *p*-Cymene in Benzene[a]

ketone	substituent	log k[b]	% P-P	% P-T	% T-T	P/T
AH_3	*p*-CH_3		*c*	0.38	0.62	0.30
AH_3	none	5.3[d]	0.09	0.37	0.54	0.38
AH_3	*m*-F		*c*	0.47	0.53	0.44
AH_3	*m*-CF_3		*c*	0.51	0.49	0.53
AF_3	*p*-OCH_3	4.7	0.31	0.45	0.24	1.2
AF_3	*p*-CH_3	6.0	0.40	0.45	0.15	1.8
AF_3	*m*-CH_3	6.4	*c*	0.81	0.19	2.1
AF_3	none	7.0	0.62	0.31	0.07	3.5
AF_3	*m*-CF_3	9.0	0.70	0.30	*c*	4.7

[a] 0.05 M ketone, irradiated at 313 nm, room temperature. [b] Bimolecular rate constant for quenching by toluene in acetonitrile, ref 5. [c] Not measurable. [d] Giering, L.; Berger, M.; Steel, C. *J. Am. Chem. Soc.* 1974, *96*, 953.

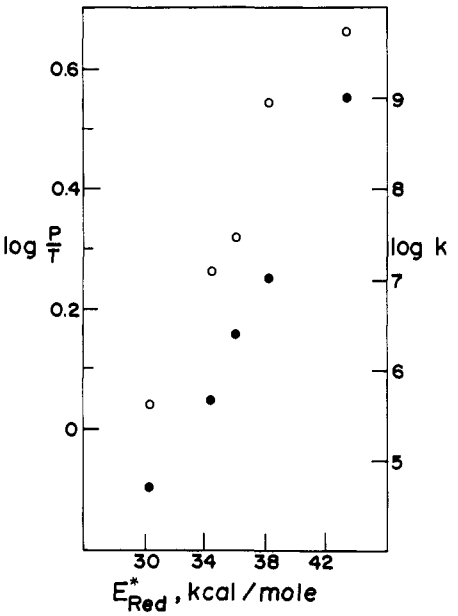

Figure 1. Correlation of rate constants and product ratios with excited ketone reduction potential for ring-substituted α-trifluoroacetophenones: (○) log (P/T) from *p*-cymene; (●) log k for quenching by toluene.

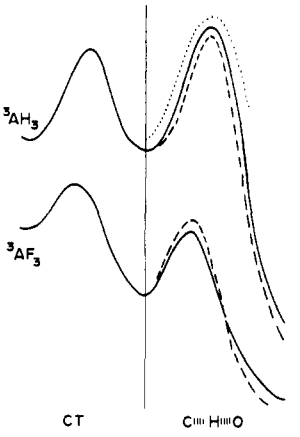

Figure 2. Partial potential-energy diagrams for triplet-state hydrogen abstraction by AH_3 (top) and AF_3 (bottom) from cymene. Reaction coordinate on left corresponds to CT complexation, that on right to H transfer from benzylic C to carbonyl O: (—) primary H; (- - -) tertiary H; (···) direct H abstraction by uncomplexed ketone triplet.

With AF_3, there is so much CT stabilization of the exciplex that proton transfer is no longer rate determining. Figure 2 compares the two situations.

We suspect that the low maximum quantum yields observed in ketone–toluene photoreductions reflect considerable exciplex decay[11] and are currently studying ketyl–benzyl radical–radical reactions to isolate chemical decay processes in photoreduction.[12]

(11) The opposite conclusion has just been reached for ketone–amine photoreductions: Inbar, S.; Linschitz, H.; Cohen, S. G. *J. Am. Chem. Soc.* **1980**, *102*, 1419.

(12) Generous continuing NSF support (Grant No. CHE79-10831) is acknowledged.

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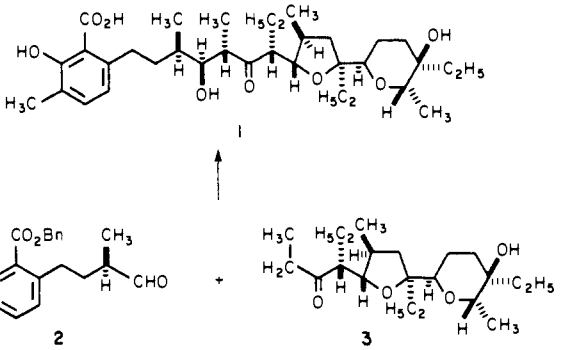
A Chiral Synthesis of the Left-Side Aldehyde for Lasalocid A Synthesis[1]

Sir:

In a recent report[2] from these laboratories, a total synthesis of the ionophore antibiotic lasalocid A (X537A) (**1**) was described. As in the first reported[3] synthesis, this approach is based on the



aldol condensation between the aldehyde fragment **2** and the ketone polyether **3**. At the time, only the ketone polyether **3** had been prepared in optically pure form, and while a new and efficient synthesis of the aldehyde **2** had been developed, only racemic material was available. The total synthesis, then, relied on the previously reported synthesis[3] of the chiral aldehyde **2** and the demonstration[3] that the aldol condensation successfully generated lasalocid A. The present report describes a chiral synthesis of the aldehyde **2** and demonstrates that the previously reported[3] optical rotation of this material from synthetic and natural sources is incorrect.

A common intermediate in the two synthetic schemes is the bromopentene **10**. Previously,[3] the racemic acid **8** was resolved and subsequently transformed into the bromide **10**, $[\alpha]^{22}_D$ −4.77° (*c* 3.02, CH_3OH). In the present work, *both* enantiomers **9** and **10** of this bromopentene were prepared *independently* from *enantiomerically pure*, naturally occurring (−)-citronellene (**4**), $[\alpha]^{25}_D$ −5.63° (*c* 2.14, $HCCl_3$) (Scheme I).

The bromide **9**,[4] $[\alpha]^{25}_D$ +32.7° (*c* 2.74, CH_3OH), ultimately related to the unnatural enantiomer of the aldehyde **2**, was derived from (−)-citronellene by conversion of the vinyl terminus to the acetate **6** and then degradation of the propylidene side chain through the acid **5** to the vinyl group. The resulting olefinic alcohol was converted to the bromide **9** by displacement of the derived mesylate.

(1) Support for this work from grants (HL-21367) from the National Heart and Lung Institute of the U.S. Public Health Service and the Hoffmann-La Roche Foundation is gratefully acknowledged.

(2) Ireland, R. E.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1980**, *102*, 1155–1157.

(3) Nakata, T.; Schmid, G.; Vranesic, B.; Okigawa, M.; Smith-Palmer, T.; Kishi, Y. *J. Am. Chem. Soc.* **1978**, *100*, 2933–2935.

(4) An alternate synthesis of enantiomer **9** from D-ribonic acid γ-lactone confirmed the stereochemical assignments when the *same* rotation for bromide **9** was observed: Fitzsimmons, B., unpublished experiments.

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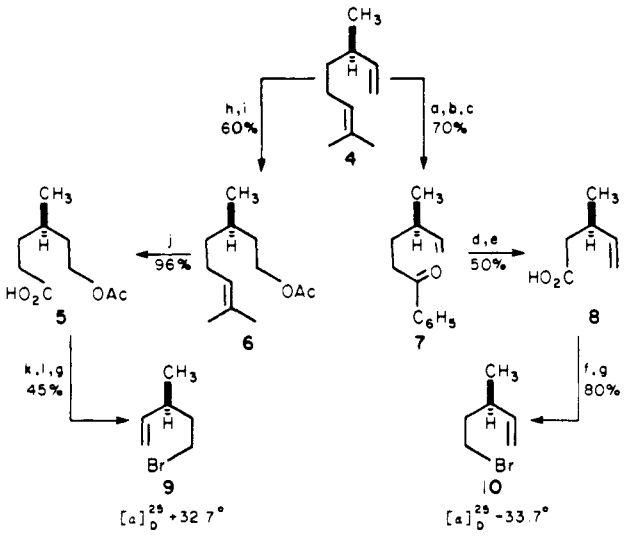
Scheme I. Chiral Synthesis of the Bromopentenes 9 and 10[a]



[a] (a) MCPBA, CH_2Cl_2; (b) H_5IO_6, Et_2O; C_6H_5MgBr, Et_2O; (c) PCC, CH_2Cl_2; (d) $HCO_2C_2H_5$, $NaOCH_3$; (e) $NaIO_4$, aqueous CH_3OH; (f) $LiAlH_4$, Et_2O; (g) $MgCl_2$, Et_3N, CH_2Cl_2; LiBr, acetone; (h) 9-BBN, THF, H_2O_2, OH^-; (i) AcCl, Et_3N; (j) O_2, 8 N H_2CrO_4; (k) $Pb(OAc)_4$, $Cr(OAc)_2$, C_6H_6-pyr; (l) $NaOCH_3$, CH_3OH.

The desired enantiomer **10** of this bromopentene, $[\alpha]^{25}_D$ −33.7° (*c* 2.75, CH_3OH),[5] was obtained from the same (−)-citronellene by a reverse strategy from that used above. Selective oxidative cleavage of the trisubstituted double bond and then phenyl Grignard addition to the resulting aldehyde provided an alcohol which was oxidized to the ketone **7**. Formylation and then oxidative cleavage of ketone **7** produced the desired enantiomer of the acid **8** which was converted into the bromide **10** by the previously described procedure.

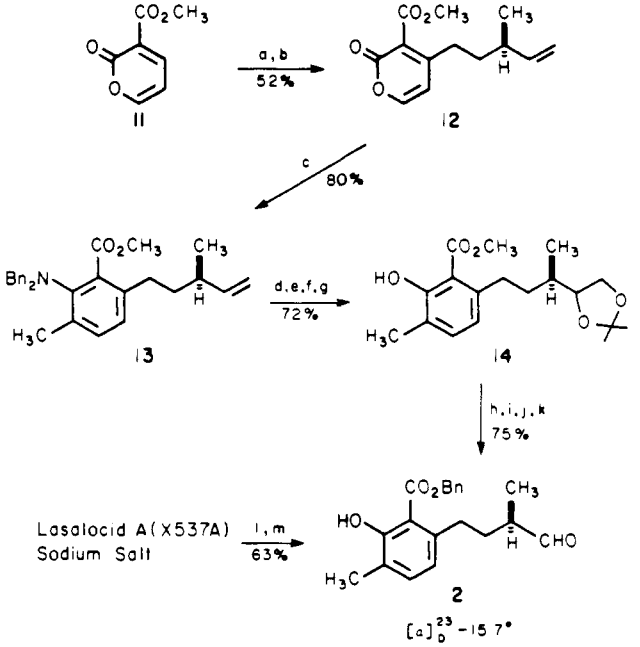
The strategy chosen for the synthesis of the aldehyde **2** entailed the synthetic construction of the aromatic ring rather than substitution of a preformed aromatic system. The reported[6] synthesis of aromatic compounds by the Diels–Alder condensation between ynamines and α-pyrones appeared particularly attractive. The first objective was therefore a synthesis of the α-pyrone **12** (Scheme II).

Initial planning called for the 1,4-conjugate addition of an alkyl residue to the readily available carbomethoxy-α-pyrone **11**. Although organocuprates failed to add to the α-pyrone **11**, Grignard reagents were found to be highly effective. Thus, addition of the Grignard reagent derived from the bromide **10** to the α-pyrone **11** and subsequent dehydrogenation of the adduct produced the desired α-pyrone **12**.

The Diels–Alder reaction between the α-pyrone **12** and *N*,*N*-dibenzyl-1-aminopropyne proved to be much more facile than that reported[6] for similar reactions and regiospecifically gave the aniline derivative **13** in high yield.

With the carbon skeleton thus established, further cosmetic work to manipulate the functionality, oxidation state, and blocking groups led through the phenolic ester **14** to the chiral aldehyde **2**, $[\alpha]^{23}_D$ −15.7° (*c* 0.73, $HCCl_3$). A sample of the aldehyde **2**, $[\alpha]^{23}_D$ −15.4° (*c* 1.00, $HCCl_3$), was also prepared from naturally occurring lasalocid A sodium salt[7] by benzylation and then pyrolysis. The identity of the natural and synthetic samples was established not only by comparison of their optical rotations but also by complete coincidence of their proton magnetic resonance and infrared spectra and their mobility on thin-layer chromatography. The previously reported optical rotation of aldehyde **2**, $[\alpha]^{22}_D$ −0.92° (*c* 0.65, $HCCl_3$),[8] must therefore be in error, and a reinvestigation of the isomeric outcome of the aldol condensation with the optically pure aldehyde **2** under the previously reported[3] conditions as well as recently developed[9] variations is in progress.

Scheme II. Construction of the Chiral Aldehyde 2[a]



[a] (a) $BrMgCH_2CH_2CH(CH_3)CH{=}CH_2$ from 8R, THF; (b) MnO_2, CH_2Cl_2; (c) $Br_2NC{\equiv}CCH_3$, C_6H_6; (d) OsO_4, NHO, aqueous acetone; (e) H_2, Pd/C, C_2H_5OH; (f) *i*-AmONO, HBF_4, C_2H_5OH; H_2O, Δ; (g) $CH_3C(OCH_3)_2CH_3$, H^+, acetone; (h) KH, $CH_3OCH_2OCH_2$-Cl; (i) *n*-C_3H_7SLi, HMPA, BnBr; (j) H_3O^+; (k) $NaIO_4$, aqueous CH_3OH; (l) BnBr, dioxane; (m) 230 °C (0.01 mmHg).

(5) The discrepancy between these values for the optical rotations of the bromopentenes **9** and **10** and those reported by Kishi and co-workers[3] can probably be ascribed to incomplete resolution of the racemic acid **8**. An initially developed synthesis of racemic acid **8** by essentially the same route reported by Kishi and co-workers[3] was discarded when it was determined by proton magnetic resonance spectral experiments with chiral shift reagents [16 mol % tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III)] that classical resolution of the acid **8** by recrystallization of the *l*-(−)-α-methylbenzylammonium and other salts was ineffective, even after numerous recrystallizations. Similar NMR shift reagent experiments with the optically active acid **8** derived from (−)-citronellene established the optical purity of this sample in comparison with the spectra from the racemic material above.

(6) Bryson, T. A.; Donelson, D. M. *J. Org. Chem.* **1977**, *42*, 2930–2931.

(7) The authors are grateful to Drs. W. Leimgruber and J. W. Westley of Hoffmann-La Roche Co., Inc. for their generous contributions of supplies of lasalocid A and supportive encouragement.

(8) The generation of optically impure aldehyde **2** in the previous work[3] by synthesis can be explained as a result of the incomplete resolution of the acid **8**. In private communication, Professor Kishi indicated that the aldehyde **2**, prepared by benzylation of the silver salt of lasalocid A and then pyrolysis, melted at 29–30 °C and showed specific rotations of +17.66° (MeOH) and −11.43° ($HCCl_3$). The latter value was observed to change slowly to the stable −0.92° ($HCCl_3$) value reported[3] for synthetic and naturally derived aldehyde **2**. We have also observed the high positive specific rotation (+12.5°) of the aldehyde **2** in methanol. This may be due to diastereoisomeric hemiacetal formation. We cannot confirm, however, either the low, sharp melting point or the time-dependent change of the specific rotation when chloroform is the solvent. In our hands, the aldehyde **2** appears to be an amorphous solid which after "crystallization" from hexane melts over the range 54–58 °C with perceptible softening at 40 °C. Some samples crystallized from pentane melted from 40 to 48 °C, even though the spectral data (IR, NMR, TLC, $[\alpha]_D$) of both materials were identical. In any case, chloroform solutions of samples of the aldehyde **2** of varying optical purity from −11° to −16° were optically stable over long periods of time (>24 h) with or without added ethanol. The aldehyde **2** appears to be sensitive to prolonged contact with silica gel on chromatography, and unless handled with dispatch, material of lower specific rotation and storage stability is obtained.

(9) Van Horn, D. E.; Masamune, S. *Tetrahedron Lett.* **1979**, 2229–2232. Kleschick, W. A.; Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 247–248. Evans, D. A.; Vogel, E.; Nelson, J. V. *Ibid.* **1979**, *101*, 6120–6123.

(10) Postdoctoral Fellow of the National Cancer Institute, USPHS, 1978–1979.

(11) NRD (Canada) Postdoctoral Fellow, 1978–1979; NSERC (Canada)–NATO Postdoctoral Fellow, 1979–1980.

(12) Fonds National Suisse de la Recherche Scientifique Postdoctoral Fellow, 1979–1980.

(13) NSERC (Canada) Predoctoral Studentship, 1979–1982.

Supplementary Material Available: Infrared and proton magnetic resonance spectra, optical rotations, physical constants, thin-layer chromatographic mobility, and elemental combustion analyses of compounds **2**, **4**–**14**, and isolated intermediates (6 pages). Ordering information is given on any current masthead page.

(14) Upjohn Predoctoral Research Fellow, 1979–1980.

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First Successful ENDOR Studies of Organic Radical Ions in Liquid Crystals

Sir:

The use of liquid crystalline solvents in ENDOR investigations of organic free radicals has proved to give valuable information about anisotropic hyperfine contributions and quadrupole splittings.[1-4] It has to be pointed out, however, that these studies have been restricted to neutral radicals, owing to the low solubility of ionic species in these nonpolar solvents. Until now very few papers exist that deal only with ESR of radical ions in liquid crystals.[5-10] In the present communication, we report on the generation and ENDOR investigation of semiquinone and semidione type radical anions in nematic and smectic phases. To the best of our knowledge, these are the first successful ENDOR experiments on ionic organic radicals in liquid crystals.

The solubility problem might be overcome by using ionophores such as crown ethers to solubilize ions by complexing the alkali counterion[10,11] or by using lipophilic quaternary ammonium counterions, e.g., in the electrolytic generation of radicals in the presence of relatively large amounts of supporting electrolyte.[6] We could achieve a similar effect by using a quaternary ammonium base in the chemical generation of radical anions. The formation of tight ion pairs might severely affect the results.[10,12] With consideration of that possibility, the use of smectic A phases appeared to be especially advantageous as compared to nematic phases, since both the anisotropic and the isotropic hyperfine interactions are accessible under the same experimental conditions.[13]

The samples were prepared in "nematic phase IV licristal" (nematic phase 289–349 K), in 4-cyano-4′-pentylbiphenyl (5CB, nematic phase 295–308 K), or in 4-cyano-4′-octylbiphenyl (8CB, smectic A phase 294–307 K, nematic phase 307–314 K) as follows: A mixture of anthraquinone and benzoin in the liquid crystal was treated with benzyltrimethylammonium hydroxide or with potassium ethoxide in the presence of dibenzo-18-crown-6 to give anthrasemiquinone radical anion (**1**). Benzil semidione radical anion (**2**) and the respective perdeuterated compound (**3**) were obtained similarly from benzil and benzoin or benzil-d_{10} and benzoin-d_{12}. ESR and ENDOR spectra were recorded on a Bruker ER 220D ESR spectrometer equipped with a Bruker ENDOR cavity (ER 200 ENB) and home-built NMR facilities described elsewhere.[14]

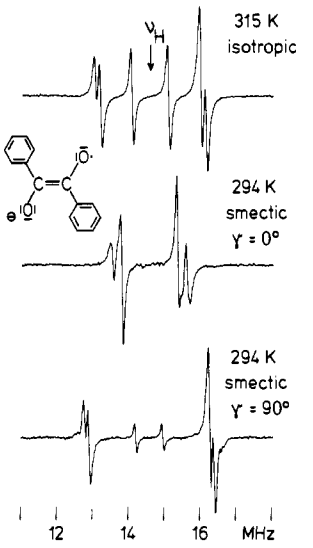

Figure 1. ENDOR spectra of **2** in 8CB, see text.

Table I. Isotropic Proton Hyperfine Coupling Constants and Shifts of 1 (MHz)

	phase IV[a]			8CB[b]		
position	a_{iso} 354 K	Δa 341 K	Δa 294 K	a_{iso} 315 K	a_{iso} 294 K	Δa 294 K
2,3,6,7	−2.74	+0.48	+0.99	−2.73	−2.73	+0.78
1,4,5,8	−0.91	+0.55	+0.74	−0.89	−0.93	+0.97

[a] Counterion K^+/dibenzo-18-crown-6. [b] Counterion benzyltrimethylammonium.

Table II. Isotropic Proton Hyperfine Coupling Constants and Shifts of 2 (MHz)

	5CB			8CB[b]		
position	a_{iso}[a] 315 K	Δa[a] 294 K	Δa[b] 294 K	a_{iso} 315 K	a_{iso} 294 K	Δa 294 K
p	−3.10	+0.77	+0.65	−3.10	−3.13	+1.09
o	−2.82	+0.85	+0.74	−2.82	−2.83	+1.21
m	+1.02	+0.46	+0.41	+1.03	+1.02	+0.60

[a] Counterion K^+/dibenzo-18-crown-6. [b] Counterion benzyltrimethylammonium.

Figure 1 shows the ENDOR spectra of **2** taken in 8CB in the isotropic phase (top) and in the smectic phase at two different angles between the director and the magnetic field.[13] The isotropic hyperfine coupling constants and the shifts are collected in Tables I and II. Our experimental results demonstrate that ENDOR of radical anions can be performed in liquid crystals, that a good signal-to-noise ratio can be achieved, and that the anisotropic hyperfine shifts can accurately be determined from the ENDOR spectra whereas the ESR spectra are poorly resolved. It should be pointed out that the coupling constant shifts are quite large, indicating a high degree of ordering. Actually, the shifts obtained for **1** (Table I) are about five times as large as those reported previously.[7]

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