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Effect of Chain Length on Radical to Carbanion Cyclo-Coupling of Bromoaryl Alkyl-Linked Oxazolines: 1,3-Areneotropic Migration of Oxazolines

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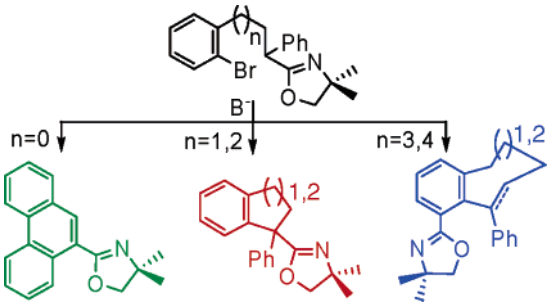

2-Halophenylalkyl-2-oxazolines with alkyl chain spacers of two to six C atoms ($n = 0-4$) were prepared and their $S_{RN}1$-type reactions with several base systems examined. The best conditions to promote cyclo-coupling to the corresponding benzocycloalkane derivatives involved use of LDA in THF. The precursors with 3-C-atom and 4-C-atom spacers gave good yields of 2-(1′-phenylindan-1′-yl)-2-oxazolines and 2-(1-phenyl-1,2,3,4-tetrahydronaphthalen-1-yl)-2-oxazoline, respectively. The major products from the precursor with a 5-C-atom spacer were derivatives of benzocycloheptane in which the oxazoline group had undergone a novel areneotropic migration from the end of the spacer to the benzo ring. The product from reaction of the corresponding 2-C-atom precursor was a 9-oxazolinophenanthrene derivative. EPR spectroscopy showed the intermediates of the LDA-promoted reactions to be radical anions of the product benzocycloalkanes. This supported an $S_{RN}1$-type chain mechanism involving initial production of aryl radicals connected to azaenolate ions via the spacer groups. Intramolecular radical to carbanion coupling then generated ring-closed benzocycloalkane radical anions that transferred an electron to more precursor. Diastereoselective radical to carbanion cyclo-coupling reactions were carried out with 2-bromophenylpropyl precursors containing chiral 2-oxazolines. The diastereoselectivity achievable was modest, but the product diastereoisomeric Indane derivatives were easily separable by chromatography.

Introduction

The quest for alternatives to organotin compounds as mediators of free-radical-based syntheses[1a,b] has not only led to the identification of several new families of reagents[2a−g] but also heightened interest in new ring-closure strategies.[2e,3a−c] Coupling together of a radical with a carbanion during an $S_{RN}1$ process is frequently fast and may even be diffusion controlled.[4a,b] Interest in the intramolecular version of this reaction, i.e., cyclo-coupling, is gathering momentum because of its radical chain character, its potential to routinely produce a range of ring sizes, the possibility of smoothly forming *quaternary* centers, and because the process works for a different range of functionality

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from the classic 5-*exo*-ring closures onto alkene type acceptors. Wolfe and Goehring used this strategy to prepare several types of heterocycles via base-promoted carbanion formation from aromatic amides. For example, indol-2-one derivatives were made from *N*-acyl-*o*-haloanilines,[5] and 2-phenyl-1,3-benzothiazoles were prepared by analogous routes.[6] Six-membered and larger rings have been made in good yields using methodology of this type.[7] Several alkaloids such as eupoulauramine, (±)-tortuosamine[8] and an ergot-type alkaloid[9] have also been synthesized by routes in which radical anion cyclo-couplings were the key steps. Rossi et al. reviewed the limited number of such ring closures in the context of $S_{RN}1$ reactions in general.[10]

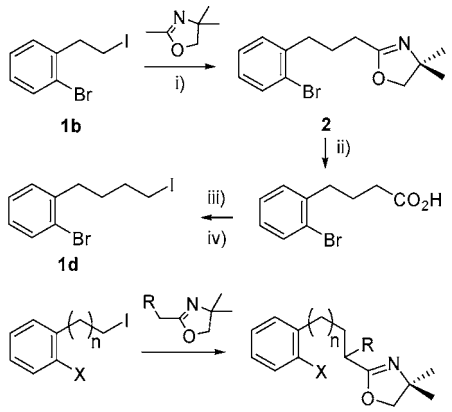
Many bioactive molecules, such as the anticonvulsant benzocaramiphen,[11] contain an Indane, tetralin, or analogous heterocyclic ring, embodying a *quaternary* center. The radical carbanion cyclo-coupling strategy appeared promising as a synthetic approach to such structures. Our primary objectives, therefore, were to test the response of the $S_{RN}1$ ring-closure process to the size of the forming ring and explore ways of controlling stereochemistry during this step.

Wolfe and co-workers showed that carbanions derived from 2-alkyl-2-oxazolines took part in intermolecular $S_{RN}1$ reactions with aromatic and heteroaromatic radicals, giving coupled products in moderate to high yields.[12] Suitably functionalized 2-oxazolines are useful chiral auxiliaries[13] and readily undergo further functional-group manipulations.[14] These factors prompted us to choose haloaromatics, substituted with alkyl spacers of different lengths bearing 2-oxazoline units, as our model precursors. Part of this research was reported in a preliminary communication.[15]

Results and Discussion

Synthesis of Haloaromatics with Oxazolino-alkyl Arms. 2-Halophenylalkyl iodides with a range of chain lengths were required for assembly of our chosen 2-haloaryl-2-oxazoline precursors. 2-Bromophenethyl iodide **1b** was made from commercial 2-bromophenylacetic acid by reduction with $LiAlH_4$ followed by iodination with a mixture of iodine, imidazole, and triphenylphosphine. To avoid debromination during the reduction step, the published procedure[16] was modified to involve only 1 equiv of $LiAlH_4$ at 0 °C for 20 min. Chain elongation was accomplished by a novel sequence that involved coupling **1b** with 2,4,4-trimethyl-2-oxazoline, hydrolysis of the resulting oxazoline **2** to afford the corresponding acid, and reduction of the latter with $LiAlH_4$. The desired 2-bromophenylbutyl iodide **1c** was obtained in 6 steps from 2-bromophenylacetic acid in 41% overall yield (Scheme 1). 2-Bromophenylpropanoic acid was obtained from 2-bromobenzaldehyde and Meldrum's acid.[17] Conversion to the corresponding iodide was achieved by the same reduction/iodination process. Chain elongation followed an oxazoline-mediated sequence similar to that of Scheme 1 and afforded 2-bromophenylpentyl iodide in 45% overall yield in 7 steps.

SCHEME 1. Preparation of 2-Halophenylalkyloxazoline Precursors



1a, n = 0, X=Br
b, n = 1, X=Br
b' n = 1, X=Cl
c, n = 2, X=Br
d, n = 3, X=Br
e, n = 4, X=Br

3, n=0, R=Ph, X=Br, 52 %;
4a, n=1, R=Ph, X=Br, 66 %
4b, n=1, R=Ph, X=Cl, 48 %
4c, n=1, R=H, X=Br, 80 %
4d, n=1, R=H, X=Cl, 54 %
5, n=2, R=Ph, X=Br, 69 %
6, n=3, R=Ph, X=Br, 60 %
7, n=4, R=Ph, X=Br, 61 %

i) *n*-BuLi(1.1 eq.), THF:hexanes (2:1) 80 %.
ii) 5M HCl, reflux 1 h, 92 %. iii) $LiAlH_4$, 20 min, 91 %
iv) I_2, PPh_3, imidazole, 82 %.

The oxazolino precursors **3**−7 were obtained by alkylation of 2,4,4-trimethyl-2-oxazoline or 2-benzyl-4,4-dimethyl-2-oxazoline with the appropriate phenalkyl iodide (or bromide) mediated with *n*-BuLi. During the alkylations control of solvent polarity was found to be crucial. By using a 3:2 mixture of THF:hexane, loss of halogen from the aryl ring was essentially completely suppressed and the (2-haloaryl)alkyl-2-oxazolines **3**−7 were obtained in satisfactory yields (Scheme 1).

Production of Five- and Six-Membered Benzocycloalkanes by Radical to Carbanion Cyclo-Coupling. The projected radical to carbanion cyclo-coupling process is shown in Scheme 2. Treatment of each precursor with base was expected to generate the azaenolate moiety of **8**. Transient intermediate **8** will be generated by electron transfer (ET) to the azaenolate

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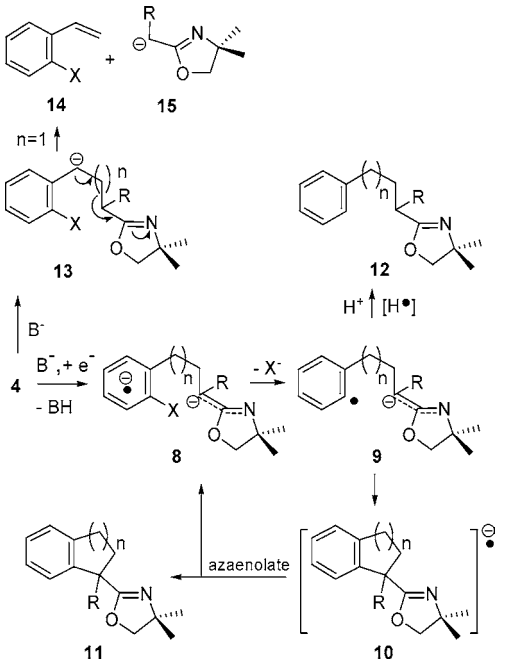
SCHEME 2. $S_{RN}1$ Chain Mechanism for Cyclo-Coupling of Intermediates from (2-Haloaryl)alkyl-2-oxazolines



and should very rapidly eject bromide to produce the distonic radical anion **9**. Rapid cyclo-coupling of the reactive centers in **9** closes the ring and yields benzocycloalkane radical anion **10**. SET from **10** to another precursor azaenolate then yields a functionalized benzocycloalkane **11** while also propagating the chain.

Several sets of conditions for promoting ring closure, embodying different bases and solvents, were examined. One of the traditional conditions for $S_{RN}1$ processes utilizes *t*-BuOK as base in DMSO. However, when **4a** or **4d** was treated with this base, no cyclized product was obtained, even in the presence of added Et_3N as a photoelectron transfer agent (Table 1, entries 1 and 2). Possibly efficient deprotonation of the precursors did not take place. A solution of dimsyl sodium was prepared from sodium hydride and DMSO, and precursor **4a** was added. On photolysis at rt for 4 h mainly the reduced product **12** ($n = 1$, R = Ph) was obtained, but on photolysis at 100 °C a 66% yield of the desired Indane **11** ($n = 1$, R = Ph) was observed (Table 1, entries 3 and 4). Alkali metal amides in liquid ammonia were also tested as bases. The oxazolines in THF were added to the gray suspensions of metal amide in liquid NH_3, and the solutions were irradiated for 1−2 h in quartz apparatus. When bromide **4a** was reacted a poor yield of the Indane (16%) was obtained together with nearly twice as much of the reduced product (entry 5). The reactants were diluted by a factor of 10, but no Indane was observed (entry 6). The chloride **4d** gave only a trace amount of reduced product together with mainly unreacted precursor (entry 7).

LDA in THF has been used as an alternative base/solvent pair for $S_{RN}1$ reactions, and the results we obtained with this combination under various conditions also appear in Table 1. For precursor **4a** the cyclo-coupling proceeded smoothly at room temperature without photostimulation, but 48 h was needed for full consumption of the reactant. This was the cleanest and most efficient reaction and afforded the Indane **11** ($n = 1$, R = Ph) in 75% yield (compare entries 7−9). The reaction was accelerated by use of UV irradiation but was not so clean, giving appreciable reduced product **12** plus minor styrenes **14** (X = Br, H) (entry 11). The advantage of using 3 equiv of LDA was demonstrated by reaction with 1 equiv of LDA, which gave a mixture of products in lower yields (entry 12). This may be because the LDA acts as an electron-transfer reagent as well as a base (see below). The similar yields of **11** ($n = 1$, R = Ph) and **11** ($n = 1$, R = H) under matching conditions in the LDA-promoted reactions (cf. entries 11 and 14) demonstrated that ring closure to give the *quaternary* center took place just as readily as ring closure to give the *tertiary* center. A less polar solvent system consisting of THF/hexane (2:1) was also tried (entry 13). The Indane yield (41% after 3 h) was comparable to that obtained in neat THF (57% after 6 h), so solvent polarity was not crucial. It has been reported that Fe(II) salts significantly enhanced the rates of some $S_{RN}1$ reactions.[18] We found, however, that for 2-oxazoline precursors addition of $FeCl_2$ (0.1−1 equiv) depressed the yield of **11** and made workup more difficult (entries 15 and 16). Stable complexes are known to form between Fe(II) salts and oxazolines,[19] and this may account for the deleterious effect. The cleanest and most efficient conditions, i.e., those of entry 9, were adopted as standard (method A) for most subsequent $S_{RN}1$ processes.

In many of the reactions reduced compound **12** was an important byproduct, particularly when photostimulation was employed. Possibly **12** was formed by hydrogen-atom abstraction by the aryl radical **9** from either solvent or other reactants before cyclo-coupling could take place. Alternatively, LDA might transfer an electron under irradiation to the aryl radical intermediate, giving an anion which is subsequently protonated to **12**. The reaction mixtures were strongly basic, so the final protonation step giving **12** probably occurred during workup. For precursors **4a**−**d** reacting with LDA, 2-bromostyrene and styrene **14** (X = Br, H) were also formed as byproducts (Table 1). The bromostyrene may have originated from deprotonation of the substrate at the benzyl position followed by *β*-elimination of the oxazolinyl moiety **15** (Scheme 2). The 2-bromostyrene can itself undergo electron capture and loss of bromide to afford the 2-vinylphenyl radical, which will rapidly abstract an H atom to give the observed styrene. The fact that styrenes were not observed for precursors with $n \neq 1$ fits this pattern because *β*-elimination of their nonstabilized oxazolinylalkyl moieties would be thermodynamically much less favorable.

The analogous coupling reaction to produce a 6-membered ring was next examined. Treatment of bromophenylbutyl-2-oxazoline **5** with 3 equiv of LDA for 48 h gave a 55% yield of the tetralin derivative **11** ($n = 2$, R = Ph) (Table 1, entry 17), and 50% was obtained with photostimulation in 6 h (entry 18). No reduced product **12** or styrenes were detected. The slightly lower yield of tetralin compared to Indane might possibly be due to a slower rate of six-membered ring closure. In this case crystals of the tetralin **11** ($n = 2$, R = Ph) were obtained and X-ray structure analysis showed a single conformer with the six-membered ring in a half-chair having the oxazoline in the pseudo-equatorial orientation and the phenyl in the pseudo-axial orientation. As expected, the C−C bonds to the quaternary C atom (1.542 Å to benzo, 1.547 Å to ring CH_2, 1.547 Å to Ph, and 1.532 Å to oxazoline) were significantly longer than unstrained C−C bonds.

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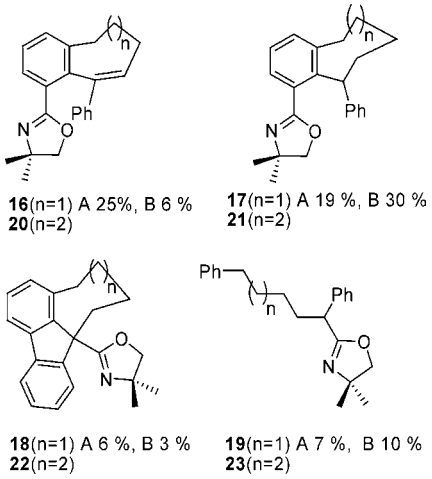
TABLE 1. $S_{RN}1$-Type Reactions of Propyl- (4) and Butyl-2-oxazolines (5) with Various Bases[a]

entry	precursor	conditions	cyclized, **11** ($n = 1$, R = Ph) %	reduced, **12** ($n = 1$, R = Ph) %	styrenes, **14** (X = Br, H) %
1	**4a** (X = Br)	*t*-BuOK, Et_3N, DMSO, UV, rt, 4 h	0	2	0
2	**4d** (X = Cl)	*t*-BuOK, Et_3N, DMSO, UV, rt, 3 h	0	0	0
3	**4a** (X = Br)	NaH, DMSO, UV, rt, 4 h	0	96	0
4	**4a** (X = Br)	NaH, DMSO, UV, 100 °C, 4 h	66	0	0
5	**4a** (X = Br)	KNH_2, liq. NH_3, UV, −33 °C, 1 h	16	31	0
6	**4a** (X = Br)	KNH_2, liq. NH_3, UV, −33 °C, 1 h, 1/10 dil.[c]	0	1	0
7	**4d** (X = Cl)	$LiNH_2$, liq. NH_3, UV, −33 °C, 1 h	0	1	0
8	**4a** (X = Br)	LDA (3 equiv), THF, rt, 20 h	50	0	8
9	**4a** (X = Br)	LDA (3 equiv), THF, rt, 48 h	75[b]	0	2[b]
10	**4a** (X = Br)	LDA (3 equiv), THF, reflux, 3h	45	0	5
11	**4a** (X = Br)	LDA (3 equiv), THF, UV, rt, 6 h	57[b]	15[b]	7[b]
12	**4a** (X = Br)	LDA (1 equiv), THF, rt, 2 h	11	13	2
13	**4a** (X = Br)	LDA(3 equiv), THF/hexane,[d] rt, 3 h	41[b]	12[b]	6[b]
14	**4c** (X = Br, R = H)	LDA (3 equiv), THF, UV, rt, 6 h	58[b] (R = H)	0	0
15	**4a** (X = Br)	LDA (3 equiv), THF, $FeCl_2$ (1 equiv), rt, 1 h	23	16	8
16	**4a** (X = Br)	LDA (3 equiv), THF/hexane,[d] $FeCl_2$ (0.1 equiv)	25	17	8
17	**5**	LDA (3 equiv), THF, rt, 48 h	55[b] ($n = 2$)	0	0
18	**5**	LDA (3 equiv), THF, UV, rt, 6 h	50[b] ($n = 2$)	0	0

[a] Yields (mol %) determined by NMR except as indicated otherwise. In most experiments the shortfall in product mass was shown to be unreacted starting material. [b] Isolated yields. [c] All reactants diluted by 1/10. [d] THF:hexane = 2:1.

SCHEME 3. Products from LDA-Promoted Reactions (methods A and B) of Pentyl 6 and Hexyl 7 Precursors



Rearrangements Accompanying Seven- and Eight-Membered Ring Formation. When bromophenylpentyl-oxazoline **6** was treated with LDA and the solution warmed to room temperature and stirred for 48 h in daylight (method A), the product mixture contained two major and two minor components,[20] none of which was the expected 5-phenyl-5-oxazolinobenzocycloheptene **11** ($n = 3$, R = Ph). The reaction was also carried out over 6 h, in quartz apparatus, with UV irradiation (method B) and yielded the same products, though in different proportions (Scheme 3). The four components were separated by chromatography and characterized by spectroscopic and other means.

The first eluting major component was found to be benzosuberene derivative **16** in which an unprecedented migration of the oxazoline group from the end of the pentyl chain to the aromatic ring had taken place. Crystals of this component were eventually obtained, and X-ray analysis fully confirmed this structure (see Supporting Information). The second major component did not crystallize but was shown by 2D NMR spectroscopy to be the saturated analog **17**. Closure of the seven-membered ring and attachment of the oxazoline group to the aromatic ring were confirmed by COSY $^1H-^1H$ and HMBC $^1H-^{13}C$ correlations (see Supporting Information). One of the minor products was shown to be **19**, derived by reductive dehalogenation. The second minor component crystallized, and it was shown by X-ray diffraction to be the fluorene derivative **18**. It was evident that closure to the seven-membered ring had taken place but that this was followed, in the case of the major products, by migration of the oxazoline group onto the aromatic ring.

The homologous hexyl-precursor **7** was reacted with LDA using the conditions of both methods A and B. In each case a complex mixture of products was obtained that could not be separated by chromatography. Individual fractions from the columns were examined by ^1H NMR spectroscopy and GC-MS. Comparison of the spectroscopic data with that obtained from products **16**−**19** demonstrated that the major products were most probably the eight-membered ring analogs, i.e., benzocyclooctene **20**, benzocyclooctane **21** and the analogous fluorene derivative **22**, accompanied by several minor unidentified byproducts. Thus, a similar areneotropic migration of the oxazoline unit took place, although the process was less efficient.

EPR Spectroscopic Study of the Intermediates. To probe the nature of the intermediates, the reactions of three homologous bromophenylalkyl dimethyl-2-oxazoline precursors **4a**, **5**, and **6**, promoted by LDA in THF solution, were examined by 9 GHz EPR spectroscopy. Solutions (2.5 and 1.5 mM) were prepared with 3 equiv of LDA in the same way as for the preparative work, and 0.02 mL aliquots were transferred to quartz capillary tubes (1 mm i.d.) and hence to the resonant cavity of the EPR spectrometer. When even traces of oxygen were present the spectrum of a nitroxide (aminoxyl) radical ($g = 2.0064$) was obtained in each case. Comparison of the hyperfine splittings (hfs) $a(N) = 14.6$ G and $a(2H) = 4.2$ G at 290 K with the literature[21] showed that this was due to the diisopropyl nitroxide **24**. Minor signals from other nitroxides accompanied this spectrum.

(20) In some experiments a fifth minor component, 2-(1,5-diphenylnonan-5-yl)4,4-dimethyl-2-oxazoline, derived from reaction of an intermediate with excess butyl lithium (or degradation product there from) was also obtained.

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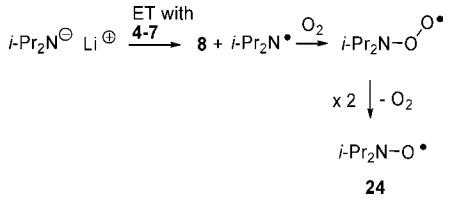
TABLE 2. Comparison of Experimental EPR with DFT Computed EPR Parameters[a]

species/method (basis set)	hydrogen and nitrogen atom hfs/G												
	1	2	3	4	5	6	7	8	9	10	11	12	13
10 ($n = 1$)/exptl. EPR[b]	5.7	1.5	4.2	4.2	1.5		1.5			4.2	1.5		4.2
10 ($n = 1$)/DFT(6-31G(d))	−5.6	1.0	−4.4	−3.8	−1.0	−0.7	1.0	0.1	0.2	−3.6	−1.4	0.1	−4.0
10 ($n = 1$)/DFT(epr-ii)	−4.4	0.5	−2.8	−3.6	−1.0	−0.6	1.4	0.4	−0.6	−3.2	−0.1	−0.7	−3.0
25e /exptl EPR[c]		1.5	3.4	3.4	1.5				1.5	3.4		1.5	3.4
25e /DFT(6-31G(d))	−0.2	−1.4	−6.4	−4.0	3.3	0.5	−0.2	−0.2	−0.5	−3.1	−0.2	−0.5	3.1
25e /DFT(epr-ii)	0.0	−1.0	−5.1	1.7	1.9	0.4	−0.3	0.0	−0.3	−2.7	−0.3	−0.4	−2.7
25a /exptl EPR[c]	1.8			1.8					3.4	1.8	5.1	1.8	3.4
25a /DFT(6-31G(d))	−1.4	−0.3	0.0	−1.2	0.3	0.7	0.0	0.0	−1.4	−0.4	−7.1	0.7	−3.7
25a /DFT(epr-ii)	−1.2	−0.1	−0.1	−1.2	0.3	0.4	0.0	0.0	−1.1	−0.5	−6.4	0.6	−3.2
	N	2	3	4	5	6	7	8	9	10	11	12	13
27/DFT(6-31G(d))	4.9	−3.4	0.3	−8.1	−0.5	−1.6	0.2	−0.2	−0.1	0.1	0.0	0.1	0.0
27/DFT(epr-ii)	3.8	−2.3	−0.4	−7.1	−0.5	−1.5	0.3	−0.2	−0.1	0.1	0.0	0.1	0.1

[a] Numbering shown in structure **26**; DFT computations using UB3LYP with a 6-31G(d) or epr-ii basis set. Tentative assignments of the experimental hfs to individual H atoms are shown. [b] $g = 2.0030$. [c] $g = 2.0028$.

SCHEME 4. Formation of Di-isopropyl Nitroxide



Detection of di-isopropyl nitroxide in the presence of oxygen is evidence in favor of the radical-mediated chain. The nitroxide is probably derived from the di-isopropylaminyl radical generated from LDA (Scheme 4). The *i*-Pr_2N^- anion could transfer an electron to a precursor molecule, thus initiating a new chain and generating the *i*-$Pr_2N^\bullet$ radical together with species **8**.[22] This amounts to an initiation step and would account for the fact that excess LDA was always found to be advantageous. The *i*-$Pr_2N^\bullet$ radical will capture dioxygen to give the corresponding peroxyl radical, and coupling of two peroxyls will produce the observed persistent di-isopropyl nitroxide together with oxygen. Radical **24** is a secondary nitroxide and will decay slowly by disproportionation to the corresponding oxime and nitrone. However, it will also inhibit the $S_{RN}1$ chain, and this is consistent with the observed sensitivity of the reactions to oxygen.

When oxygen was rigorously excluded from the reaction of the propyl precursor **4a**, a longer lived species having $g = 2.0030$ was observed. The isotropic EPR signal was broad at 300 K, and its intensity increased with UV photolysis. On lowering the temperature the intensity increased again, and best resolution was obtained at temperatures of about 205 K. This spectrum was observable for many hours, although its intensity gradually weakened. Broadly similar long-lived EPR spectra, with essentially identical *g* factors, were obtained on treatment of precursors **5** and **6** with LDA in THF and illumination with UV light. A good computer simulation ($R = 0.991$) was obtained for the spectrum from **4a** with the hfs listed in Table 2. The spectrum obtained from precursor **5** was considerably broader than the others with asymmetry caused by the presence of an additional signal originating from the quartz tube; a reliable simulation could not be derived. However, the *g* factor (2.0031), spectral width, and lifetime all suggested the species responsible for this spectrum was analogous to that derived from the other precursors. The spectrum obtained from pentyl precursor **6** was

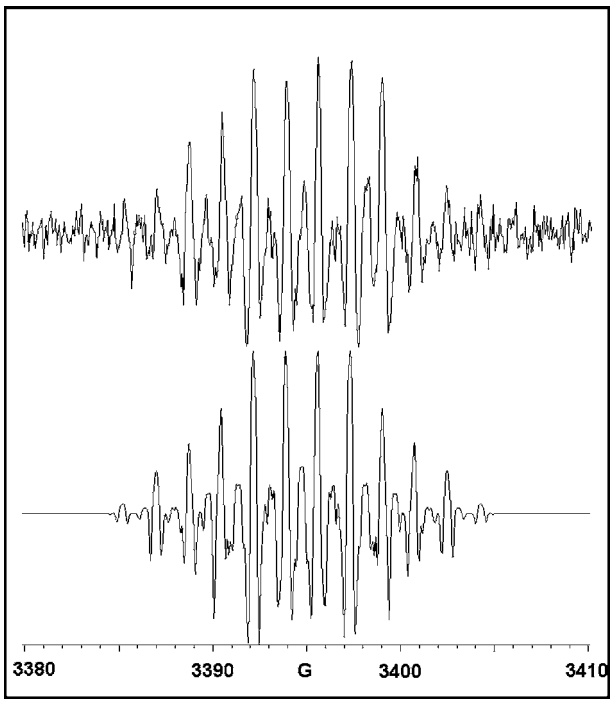


FIGURE 1. EPR spectrum obtained on treatment of **6** with LDA: (top) experimental at 195 K in THF (second derivative); (bottom) computer simulation including both species.

well resolved, and the second-derivative presentation (Figure 1) suggested that two similar paramagnetic species were present. A satisfactory simulation including both species ($R = 0.922$) was obtained, with the parameters shown in Table 2, and this is also displayed in Figure 1.

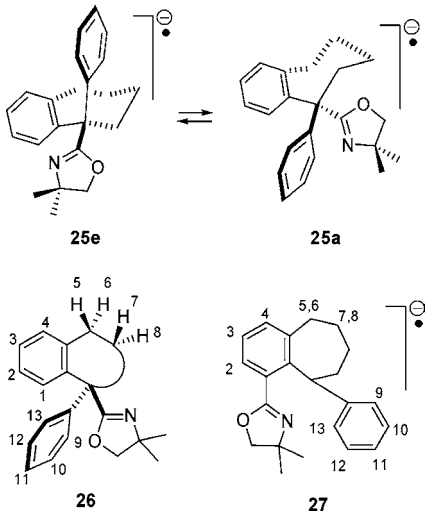
The *g* factors and magnitudes of the hfs of these species suggested they were aromatic radical anions. Cyclo-coupling of the aromatic radical carbanions derived from **4a**, **5**, and **6** will give radical anions that contain a benzocycloalkane unit substituted by phenyl and oxazoline rings, i.e., **10**. EPR data from the literature for the model radical anions of diphenylmethane[23] and Indane[24] (which had been prepared by treatment of the corresponding hydrocarbons with K metal) were similar in terms of *g* factor and hfs magnitudes. The experimental hfs

(22) Alternatively, *i*-$Pr_2N^\bullet$ could be formed by some other radical (or radicals) in the system ($X^\bullet$) abstracting an H atom from adventitious *i*-Pr_2-NH.

(23) Gerson, F.; Martin, W. B., Jr. *J. Am. Chem. Soc.* **1969**, *91*, 1883−1891.

(24) Bauld, N. L.; Farr, F. R. *J. Am. Chem. Soc.* **1974**, *96*, 5633−5634.

SCHEME 5. Radical Anions Derived from Precursor 6



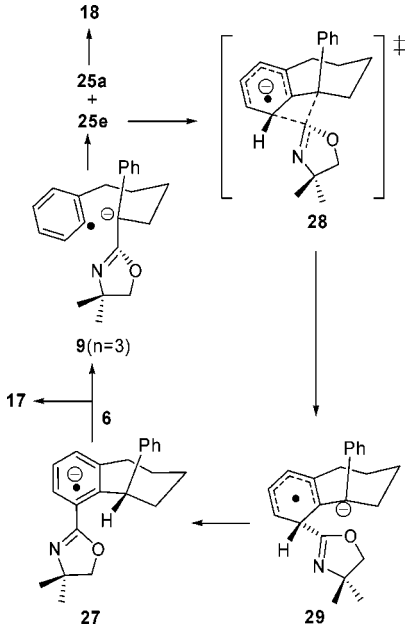
were tentatively assigned to specific H atoms of **10** with the aid of DFT computations (see below) and are compared in Table 2. A noteworthy feature is that the spin density is equally distributed to both phenyl rings in the radical anion of diphenylmethane. In radical anions **10** spin density is also distributed to both rings but the two rings are not equivalent, so the spin is not equally partitioned.

The radical anion concentrations, measured by double integration of the EPR signals at 200 K, ranged from 4×10^{-6} for **10** ($n = 3$) to 3×10^{-4} M for **10** ($n = 1$). The concentrations decreased at higher temperatures, but at 290 K (temperature of the preparative experiments) the ratios of the radical anion to initial precursor were found by extrapolation to be 1.5%, 0.8%, and 0.6% for **10** ($n = 1$)/**4a**, **10** ($n = 2$)/**5**, and **10** ($n = 3$)/**6**, respectively. These values represent a significant proportion of the initial concentration of the precursor molecules, and hence, the EPR spectra are not from minor stray species but important intermediates.

The data are consistent with the $S_{RN}1$ chain process of Scheme 2 (Scheme 6 for **6**) with a modest chain length. The observed increase in radical concentration at lower temperatures is consistent with the expected slower chain propagation at lower temperatures. In particular, Scheme 2 proposes that the radical anions **10** decay by bimolecular electron transfer to more precursor (**4**, **5**, or **6**). This step would slow down as temperature was lowered, and hence, if this is the rate-limiting step, the concentration of the radical anions would be expected to build up, exactly as observed.

The computer fits for the spectra obtained with precursor **6** were "soft" because of the limited S/N but indicated a major species (60%) and a minor species (40%). In this case rapid cyclo-coupling within **9** will give the ring-closed radical anion as a pair of enantiomers, each of which can exist in two conformations, **25e** and **25a**, having the oxazoline group pseudo-equatorial and −axial, respectively (Scheme 5). DFT computations,[25] carried out on **25e** and **25a** at the UB3LYP/epr-ii//UB3LYP/6-31G(d) level of theory,[26] predicted that **25a** was 3.9 kcal/mol lower in energy than **25e**. It may be expected, therefore, that ring inversion will be slow at 195 K, and hence, the two

SCHEME 6. Mechanism for Oxazoline Migration



EPR spectra correspond to the two conformers. The DFT computations showed that the SOMO of **25a** was associated mainly with the two aromatic rings. The SOMO of **25e** was similar but had higher amplitude on the phenyl ring. These properties were reflected in the computed hfs which correlated satisfactorily with the experimental EPR data (Table 2).

The equatorial oxazoline moiety is sited comparatively close to the aromatic ring in conformer **25e** so that 1,3-migration of the oxazoline group toward the "southernmost" C atom (C-1) of the aromatic ring can be envisaged via a four-membered transition state such as **28**. 1,3-Proton transfer in radical anion **29** will yield the rearranged radical anion **27**. DFT computations (UB3LYP/epr-ii//UB3LYP/6-31G(d)) on **27** predicted the overall transformation from **25e** to **27** to be strongly exothermic (by 25 kcal/mol). The computed SOMO for **27** was mainly confined to the aromatic ring and the oxazoline unit with very little amplitude on the Ph ring. Consequently, only four hydrogen hfs >0.1 mT and a comparatively large N-hfs were obtained (Table 2). The predicted EPR spectrum of **27** is, therefore, very different from either of the experimentally observed spectra, in agreement with our assignment of them to **25a** and **25e**. Transfer of an electron from rearranged radical anion **27** to more precursor **6** will yield product **17** and simultaneously propagate the chain (Scheme 6). The most plausible mechanism for formation of the unusual alkene **16** involves lithiation of product **17** at the bisaryl C atom by the excess base followed by loss of LiH. Precedents for this kind of elimination are known,[27] and it is supported by the greater yield of **16** from the longer running experiment (method A) where more **17** would have been available.

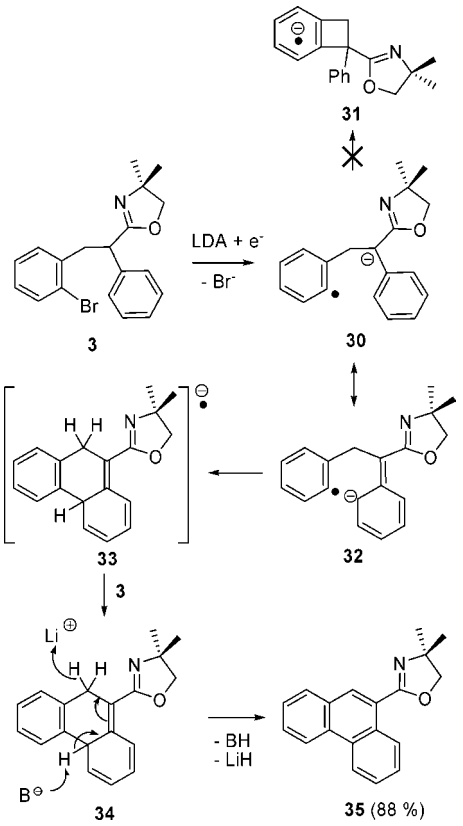
In conformer **25a** it is the equatorial phenyl ring that is comparatively close to the southernmost C-1 of the aromatic ring. It follows that cyclo-coupling from C-1 to an *ortho*-C atom of the phenyl ring would afford a ring-closed radical anion, containing the fluorenyl unit, that could readily be transformed to product **18** by electron transfer and rearomatization by oxidative loss of two H atoms.

(25) Frisch M. J. et al. *Gaussian 03*, Revision A.1; Gaussian Inc.: Pittsburgh, PA, 2003 (see Supporting Information for full citation).

(26) Barone, V. In *Recent Advances in Density Functional Theory*; Chong, D. P., Ed.; World Scientific Publishing Co.: Singapore, 1996.

(27) Withnall, R.; Dunkin, I. R.; Snaith, R. *J. Chem. Soc., Perkin Trans.* **1994**, *2*, 1973−1977 and references cited therein.

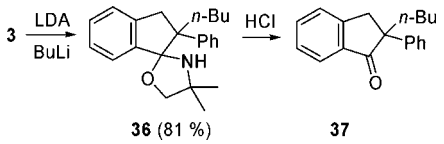
SCHEME 7. Formation of a Phenanthrene Derivative from Ethyl Precursor 3



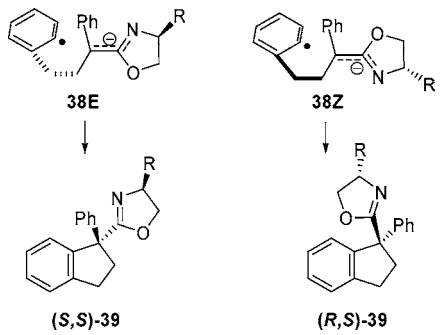
The emerging pattern is that cyclo-coupling of aryl radicals with azaenolate-type carbanions readily takes place for ring sizes from five- to eight-membered. This is in good accord with the known rapidity of intermolecular radical anion coupling.[28] For benzocycloalkane radical anions containing seven- and eight-membered rings, α-substituents take part in subsequent unique rearrangements in which the 1,3-oxazoline group migrates to the benzo moiety. An intriguing question is why the seven- and eight-membered benzocycloalkane radical anions rearrange whereas the five-and six-membered analogs do not. Stereoelectronic factors are likely to be important. In the ring-closed radical anions **10** much of the unpaired electron density resides in the benzo ring. Increasing the adjacent cycloalkane ring size brings the pseudo-equatorial substituent closer to the benzo ring. For example, the DFT-computed, direct, through-space, distances from C(1) of the benzo ring to the C(═N) atom of the oxazoline unit were 3.41, 3.16, 2.79, and 2.91 Å in the equatorial conformers of the five-, six-, seven-, and eight-membered ring anions, respectively. The considerably closer approach for the seven- and eight-membered intermediates would mean less strain in the transition states for migration (**28**), and hence, their energies would be lowered.

Attempted Ring Closure to a Benzocyclobutane Derivative. The precursor **3** with the shorter ethyl-type spacer was also examined to see if radical anion cyclo-coupling could take place to form benzocyclobutene **31** containing a four-membered ring. However, when precursor **3** was treated with LDA (method A) none of **31** was obtained but instead 9-oxazolino-phenanthrene derivative **35** (88%) was isolated. A plausible mechanism to account for this involves initial formation of azaenolate **30** (analogous to **9** proposed for the longer chain precursors). Cyclo-coupling to give the radical anion of **31** appears to be disfavored because of the strain in the four-membered ring. Instead cyclo-coupling with closure to a six-membered ring occurred via the resonance structure **32** affording radical anion **33**. Transfer of an electron from **33** to more **3** will propagate an $S_{RN}1$-type chain and generate dihydrophenanthrene derivative **34**. In view of the strongly basic solution, aromatization to **35** probably occurs as shown in Scheme 7 by deprotonation and loss of lithium hydride. Alternatively, the mechanism might involve oxidative loss of two H atoms, as proposed above for formation of fluorene derivative **18**. A small sample of the reaction mixture was examined by EPR spectroscopy, which showed a strong and long-lived spectrum ($g = 2.003$). The signal was not well enough resolved for definitive analysis, but the observation supports the idea that radical anions were the main intermediates.

SCHEME 8. Preparation of a Dihydroindene-1-one Derivative from Compound 3



SCHEME 9. Stereochemistry of the Cyclo-Coupling Step



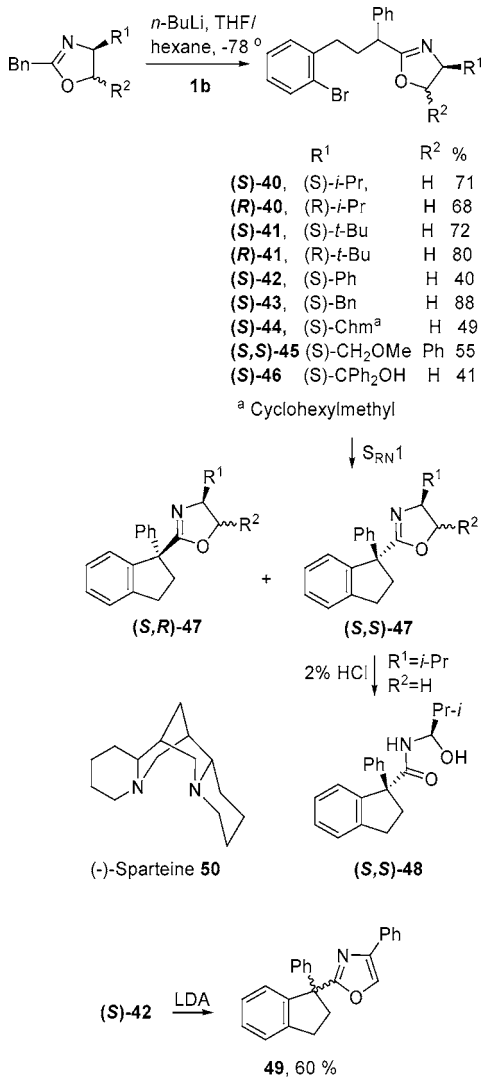
We also carried out an LDA-promoted reaction with compound **3** but with an additional 1 equiv of *n*-BuLi added to the THF solution. Interestingly, the reaction took a completely different course in this case and gave spiro-Indane derivative **36** in good yield. Hydrolysis of the oxazoline moiety in **36** with dilute HCl yielded dihydroindene-1-one derivative **37**, and the latter was fully characterized. A possible mechanism for formation of **36** involves rapid butylation of the azaenolate anion (possibly by attack on BuBr formed from the *n*-BuLi). Subsequent electron transfer and loss of bromide would generate an aryl-type radical that could undergo a normal 5-*exo*-cyclization onto the C═N bond of the oxazoline moiety. Final H-atom abstraction from the THF by the resulting cyclic aminyl radical would then yield **36**.[29]

Diastereoselective Radical Carbanion Cyclo-Coupling Reactions. The stereochemistry of the ring-closure step is an important consideration. It seemed possible that diastereoselectivity could be achieved in our intramolecular $S_{RN}1$ reactions using precursors containing chiral 2-oxazolines. The

(28) Alternative mechanisms involving initial formation of arynes are possible but are less likely because the EPR evidence proves the participation by radical anions because of the sensitivity of the reactions to oxygen and UV radiation and because of literature precedents for analogous S_{RN} 1 processes mediated by LDA (see refs 7, 12, and 15).

(29) Alternatively, after the butylation step, debrominative lithiation of the aryl ring would lead to an aryllithium that could undergo nucleophilic attack at the C═N bond of the oxazoline.

SCHEME 10. Cyclo-Coupling with Chiral Oxazolines



ring-closure step involves coupling of an aryl radical to the azaenolate moiety, and clearly any diastereoselectivity will depend on one of the two possible azaenolate anion conformations **38E** and **38Z** predominating. It was anticipated that approach from *below* azaenolate **38E** (shown) would be sterically favored by bulky oxazoline substituents R and would give the (*S*,*S*)-**39**-diastereomer

However, approach from *above* in azaenolate **38Z** (shown) would be sterically favored by bulky substituents in the oxazoline and would lead to the (*R*,*S*)-**39**-diastereomer. Thus, any stereoselectivity will depend on the relative concentrations of the azaenolates **38E** and **38Z**.

To test this possibility, a set of chiral 3-(2-bromophenyl)-propyl-2-oxazolines **40**−**46** was prepared. Chiral 2-benzyl-2-oxazolines were made by condensing benzyl acetimidate ethyl ester hydrochloride (BnC(OEt)═NH·HCl) with the appropriate chiral 1,2-aminoalcohol.[30] The desired precursors were then obtained in yields ranging from 40% to 88% by *n*-BuLi-promoted alkylation of each oxazoline with 2-bromophenylethyl iodide (**1b**). Each precursor was obtained as a mixture of diastereoisomers (at the 3 position), but this should not affect the outcome of the $S_{RN}1$ cyclo-coupling because the C(3) stereocenter becomes sp^2 on deprotonation. The $S_{RN}1$ reactions of the chiral precursors were then examined using the previously developed methods A and B and Indane product de's were determined using ^{1}H NMR spectroscopy and/or chiral GC-MS (Table 3).

(30) Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297−2360.

TABLE 3. Yields and Diastereoselectivities in Cyclo-Coupling Reactions[a] of Chiral Oxazolines

entry	precursor (R^1)	method/conditions	yield **47**%	de%
1	(*S*)-**40** (*i*-Pr)	A	72	42[b]
2	(*S*)-**40** (*i*-Pr)	A at 0 °C	50	48[c]
3	(*S*)-**40** (*i*-Pr)	B	55	18[b]
4	(*S*)-**44** (Chm)[e]	A	nd[f]	16
5	(*S*)-**44** (Chm)[e]	B	nd[f]	16
6	(*S*)-**41** (*t*-Bu)	B	60	33[c]
7	(*S*)-**41** (*t*-Bu)	A	85	16[d]
8	(*S*)-**41** (0.036M)	A + (−)-**50** (3.5 equiv)	nd	2
9	(*S*)-**41** (0.1 M)	A + (−)-**50** (3.5 equiv)	nd	−4
10	(*S*)-**41** (0.1 M)	A + (−)-**50** (10 equiv)	nd	−14
11	(*R*)-**41** (0.1 M)	A + (−)-**50** (3.5 equiv)	nd	21
12	(*R*)-**41** (0.1 M)	A + (−)-**50** (10 equiv)	nd	14

[a] Method A: LDA (3 equiv), THF, rt, 48 h. Method B: LDA (3 equiv), THF, rt, UV, 6 h. [b] From the ratio of isolated products. [c] Obtained by GC-MS. [d] Obtained from NMR spectra. [e] Chm = cyclohexylmethyl. [f] nd = not determined.

The $S_{RN}1$ reaction of isopropyl precursor (*S*)-**40** without photostimulation (entry 1) gave a 72% yield of the two Indane diastereoisomers, which was comparable to that obtained for the dimethyl analogue under these conditions (Table 1, entry 9). A moderate selectivity (42% de) was obtained, and this increased to 48% (entry 2) when the reaction was carried out at 0 °C. An attempt to carry out the reaction at −33 °C resulted in an intractable mixture in which no product was evident. When the reaction mixture was UV irradiated for 6 h (entry 3) both the yield and selectivity decreased. The two diastereoisomers were easily separable by column chromatography. Neither oxazolino-Indane diastereoisomer crystallized, but mild hydrolysis of the major isomer with dilute HCl gave the *β*-hydroxyamide (*S*,*S*)-**48**. Crystals of this compound were obtained, and an X-ray structure revealed the configuration to be *S*,*S* (see Supporting Information), and thus the absolute configuration of the major oxazolino-Indane was also (*S*,*S*). This suggested that the major conformer of the azaenolate was (*S*,*S*)-**39**. Chiral oxazoline (*S*)-**41** containing the larger *tert*-butyl group was also reacted under similar conditions. The 85% yield obtained in the unstimulated experiment (entry 7) was the highest achieved in our intramolecular $S_{RN}1$ series. However, the de's obtained were actually poorer than those with the isopropyl substituent (presumably the proportion of **38E** was lower in this case).

An attempt was made to carry out the reaction at −33 °C but as before, this resulted in an intractable mixture. The cyclohexylmethyl-substituted oxazoline **(*S*)-44** was also examined, but under both sets of conditions only about one-third of the precursor was consumed and the stereoselectivity was poor (entries 4 and 5). A possible reason might be poor solubility in the reaction medium.

When the phenyl-substituted oxazoline (*S*)-**42** was treated with LDA (method A) the only product (apart from unreacted starting material) was probably oxazole derivative **49** (60%). Formation of **49** may be a consequence of the acidity of the proton at C(4) of the oxazoline ring in (*S*)-**42**. Removal of this proton by the base would give a delocalized anion that could undergo lithiation and subsequent loss of LiH to yield **49**. Alternatively, SET from the anion could give the corresponding benzyl-type radical, which could convert to **49** by oxidative

removal of an H atom. Chiral GC-MS was employed in an attempt to determine any selectivity at the Indane site, but only one peak of the required mass was observed, so the result was inconclusive. Precursor (*S*,*S*)-**45**, derived from the classic Meyers' oxazoline, was reacted with LDA (method A), but only an intractable mixture of products was obtained. The spectra of the mixture indicated many aromatic environments and complete loss of the signals of the oxazoline moiety. This suggested that the 2-oxazoline ring proton(s) had been lost. Similar behavior was observed for the diphenylmethanol derivative (*S*)-**46**. An extra equivalent of LDA was used to ensure deprotonation of the hydroxyl group, but only a complex mixture resulted. The benzyl-substituted oxazoline (*S*)-**43** also gave a multitude of products with either method A or method B. When only 1 equiv of LDA was employed a 2:1 mixture of starting material and the reduced product (analogous to **12**) was obtained. An excess of the weaker base *t*-BuOK in THF gave no reaction at rt for 48 h and gave only reduced product on UV photostimulation for 6 h. The base LiHMDS in THF was also tried with a short irradiation period (1 h) but to no avail, yielding only an intractable mixture. We concluded that oxazolines with substituents that increase the acidity of the ring protons degrade under the $S_{RN}1$ reaction conditions, resulting in a range of products and loss of stereoinduction.

(−)-Spartiene **50** has been used as a bidentate ligand for lithium cations in several stereoselective syntheses with varying success.[31] When a chiral lithium ligating agent is used in conjunction with a chiral auxiliary in the precursor there is the possibility of either enhancement (matched pair) or decrease/reversal in selectivity (mismatched pair). In an attempt to improve the diastereoselectivity in our $S_{RN}1$ ring closures several experiments were carried out using different amounts of **50**. The (*S*)-*tert*-butyl substrate (*S*)-**41** was chosen for study because it delivered the cleanest $S_{RN}1$ ring closure. The reaction was carried out using method A conditions with 3.5 equiv of **50**, but this gave a reduced selectivity (2% de, Table 3, entry 8) compared to the result without spartiene (16%, entry 7). When the substrate concentration was increased (0.1 M) a reversal of selectivity (−4%) was obtained, and on increasing the amount of spartiene to 10 equiv, the reverse selectivity increased to −14% (Table 3, entries 9 and 10). Clearly this data indicated that (*S*)-**41** and (−)-sparteine formed a mismatched pair. The opposite precursor diastereoisomer (*R*)-**41** was prepared from (*R*)-*tert*-leucinol, and the $S_{RN}1$ reactions were carried out with 3.5 and 10 equiv of **50**. A slightly increased selectivity was observed when 3.5 equiv of **50** was employed (21%, entry 11), but a poorer selectivity was obtained in the case of 10 equiv (entry 12). The final experiment had to be carried out on a very small scale due to the expense of the substrate, and serious solvent loss occurred during the reaction; hence, the result may not represent the true selectivity. However, entries 11 and 12 showed that although (*R*)-**41** and **50** formed a matched pair, the enhancement in selectivity was very modest.

Conclusions

2-Halophenylalkyl-2-oxazolines containing propyl and butyl spacers cyclized with reasonable efficiency on treatment with LDA to give Indane and tetralin derivatives, respectively. Ring closure forming a *quaternary* center took place just as readily as ring closure forming a *tertiary* center. The reactions lent themselves to study by EPR spectroscopy, which supported an $S_{RN}1$-type chain mechanism involving a radical to carbanion cyclo-coupling step producing a 1-phenyl-benzocycloalkane radical anion as the main intermediate. Interestingly, although the phenyl and benzo groups in individual radical anions were separated by sp^3-hybridized C atoms, the unpaired electron was distributed to both aromatic rings. For benzocycloalkane radical anions containing seven- and eight-membered rings (pentyl and hexyl spacers), α-oxazoline substituents took part in subsequent unique rearrangements toward the adjacent benzo unit, i.e., 1,3-oxazoline migration (cyclo-coupling for phenyl substituents). This can be attributed to the closer approach of the 2-oxazoline substituent to the benzo ring in the pseudo-equatorial conformers of the seven-membered rings. Overall the alkyl arms served to escort the comparatively remote oxazoline units into the orbit of the arene radical anions. With the bromophenylethyl-oxazoline precursor (ethyl spacer) cyclo-coupling to produce a four-membered ring did not compete. Instead, coupling occurred with the phenyl ring to form the six-membered ring of a phenanthrene derivative. Diastereoselective cyclo-coupling of 2-bromophenyl)propyl precursors containing chiral oxazolines yielded diastereoisomeric Indanes. However, the maximum selectivity achieved with a 4-isopropyl substituent in the oxazoline (48% de) was modest. A redeeming feature was the separability of the two diastereoisomers by conventional chromatography. It was found that substituents that enhanced the acidity of the oxazoline protons were not tolerated.

Experimental Section

General Method for the Preparation of 2-(Arylalkyl)-2-oxazolines. *n*-BuLi (2.5 M) in hexanes (1.05 equiv) was added dropwise to a stirring solution of the 2-oxazoline (1 equiv) in dry THF (0.75 mL/mmol) and dry hexane (0.38 mL/mmol) under nitrogen at −78 °C. After stirring for 5 min *o*-halophenethyl halide (1.05 equiv) in dry THF (0.38 mL/mmol) and dry hexane (0.2 mL/mmol) was added over a 10 min period. The solution was then allowed to warm to room temperature slowly over 3 h; then water (3 × 2 mL/mmol) was added. The aqueous layer was extracted with ether (3 × 3.2 mL/mmol), and the combined organic layers were washed with water (3.2 mL/mmol), dried ($MgSO_4$), and concentrated to give the crude substituted 2-oxazoline. Purification was achieved by column chromatography using SiO_2 or Al_2O_3 and ethyl acetate/hexanes mixtures as eluant.

2-[2-(2-Bromophenyl)-1-phenylethyl]-4,4-dimethyl-2-oxazoline (3). Yellow/orange oil which crystallized as orange crystals (52%), mp 62 °C; R_f (SiO_2, 8:2 hexane:EtOAc) 0.35; IR ν_{max}(film)/cm^{-1} 1664 (C═N); ^{1}H NMR δ 1.20 (3H, s, CH_3), 1.26 (3H, s, CH_3), 3.19 (1H, dd, J = 6.6 and 13.5 Hz, CH_AH$_B$), 3.49 (1H, dd, J = 9.0 and 13.5 Hz, CH), 3.86 (2H, s, CH_2O), 4.06 (1H, dd, J = 6.6 and 9.0 Hz, CH$_A$$H_B$), 7.00−7.14 (3H, m, ArH), 7.21−7.37 (5H, m, ArH), and 7.49−7.55 (1H, m, HCCBr); ^{13}C NMR δ 28.6 (CH_3), 28.8 (CH_3), 41.0 (CH_2), 45.3 (CH), 67.4 ((CH$_3$)$_2$*C*), 79.3 (CH_2O), 125.2 (CBr), 127.3 (CH_{Ar}), 127.6 (CH_{Ar}), 128.1 (CH_{Ar}), 128.5 (CH_{Ar}), 129.0 (CH_{Ar}), 132.2 (CH_{Ar}), 133.2 (CH_{Ar}), 138.8 (C_q), 140.0 (C_q), and 166.1 (C═N); *m*/*z* (CI) 358 [99%, $(MH)^+$)]. Calcd for $C_{19}H_{21}ON^{79}Br$ $(MH)^+$: 358.0807. Found: 358.0812.

2-[3-(2-Chlorophenyl)propyl]-4,4-dimethyl-2-oxazoline (4d). Clear oil (54%); R_f (Al_2O_3, 9:1, hexane:EtAc) 0.3; ν_{max}(film)/cm^{-1} 1648 (C═N); ^{1}H NMR δ 1.27 (6H, s, 2 × CH_3), 1.91−2.01 (2H, m, CH_2(CH$_2$)$_2$), 2.31 (2H, t, J = 7.5 Hz, CH_2), 2.79 (2H, t, J = 7.7 Hz, ArCH_2), 3.91 (2H, s, CH_2O), 7.10−7.24 (3H, m, ArH), and 7.31−7.34 (1H, m, HCCCl); ^{13}C NMR δ 26.1 (CH_2), 27.6 (CH_2), 28.4 (2CH_3), 32.8 (CH_2), 66.9 ((CH$_3$)$_2$*C*H), 78.9 (CH_2O), 126.7 (CH_{Ar}), 127.4 (CH_{Ar}), 129.4 (CH_{Ar}), 130.5 (CH_{Ar}), 133.9 (CCl),

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139.1 (C_q), and 165.6 (C═N); *m*/*z* (CI) 252 [100%, $(MH)^+$]. Calcd for $C_{14}H_{19}ON^{35}Cl$ $(MH)^+$: 252.1155. Found: 252.1147.

2-[3-(2-Bromophenyl)propyl]-4,4-dimethyl-2-oxazoline (4c). Clear oil (80%); R_f (Al_2O_3, 9:1, hexanes:EtAc) 0.25; ν_{max}(film)/cm^{-1} 1668 (C═N); ^1H NMR δ_H 1.27 (6H, s, 2 × CH_3), 1.88−2.00 (2H, m, $CH_2CH_2CH_2$), 2.32 (2H, t, J = 7.7 Hz, CH_2), 2.79 (2H, t, J = 7.8 Hz, $ArCH_2$), 3.91 (2H, s, CH_2O), 7.01−7.07 (1H, m, ArH), 7.21−7.28 (2H, m, ArH), and 7.50−7.53 (1H, m, HCCBr); ^{13}C NMR δ 26.2 (CH_2), 27.6 (CH_2), 28.4 (2 × CH_3), 35.3 (CH_2), 66.9 ($(CH_3)_2CH$), 78.9 (CH_2O), 124.4 (CBr), 127.3 (CH_{Ar}), 127.6 (CH_{Ar}), 130.4 (CH_{Ar}), 132.7 (CH_{Ar}), 140.8 (C_q), and 165.5 (C═N); *m*/*z* (CI) 296 [100%, $(MH)^+$]. Anal. Calcd for $C_{14}H_{18}ONBr$: C, 56.8; H, 6.1; N, 4.7. Found: C, 56.3; H, 6.6; N, 4.7.

2-[3-(2-Chlorophenyl)-1-phenylpropyl]-4,4-dimethyl-2-oxazoline (4b). Clear oil (48%); R_f (Al_2O_3, 19:1, hexane:EtAc) 0.2; ν_{max}(film)/cm^{-1} 1635 (C═N); ^1H NMR δ 1.27 (3H, s, CH_3), 1.28 (3H, s, CH_3), 2.07−2.19 (1H, m, $CHCH_AH_BCH_2$), 2.32−2.44 (1H, m, $CHCH_AH_BCH_2$), 2.63−2.80 (2H, m, $ArCH_2$), 3.60 (1H, t, J = 7.8 Hz, CH), 3.87 (2H, s, CH_2O), 7.07−7.20 (3H, m, ArH), and 7.22−7.37 (6H, m, ArH); ^{13}C NMR δ 28.1 (CH_3), 28.3 (CH_3), 31.4 (CH_2), 33.5 (CH_2), 44.9 (CH), 66.8 ($(CH_3)_2CH$), 78.9 (CH_2O), 126.6 (CH_{Ar}), 127.0 (CH_{Ar}), 127.3 (CH_{Ar}), 127.7 (CH_{Ar}), 128.5 (CH_{Ar}), 129.3 (CH_{Ar}), 130.4 (CH_{Ar}), 133.8 (CCl), 139.0 (C_q), 139.6 (C_q), and 166.5 (C═N); *m*/*z* 328 (CI) [100%, $(MH)^+$]. Calcd for $C_{20}H_{23}ON^{35}Cl$ $(MH)^+$: 328.1468. Found: 328.1478.

2-[3-(2-Bromophenyl)-1-phenylpropyl]-4,4-dimethyl-2-oxazoline (4a). White solid (66%); R_f (SiO_2, 9:1 hexanes:EtOAc) 0.25; mp 69.5−71.5 (EtOAc:hexanes); ν_{max}(nujol)/cm^{-1} 1668 (C═N); ^1H NMR δ 1.28 (3H, s, CH_3), 1.30 (3H, s, CH_3), 2.05−2.19 (1H, m, $CHCH_ACH_BCH_2$), 2.31−2.43 (1H, m, $CHCH_ACH_BCH_2$), 2.60−2.81 (2H, m, $ArCH_2$), 3.61 (1H, t, J = 7.8 Hz, CH), 3.90 (2H, s, CH_2O), 7.00−7.06 (1H, m, ArH), 7.16−7.38 (7H, m, ArH), and 7.48−7.51 (1H, m, HCCBr); ^{13}C NMR δ 28.1 (CH_3), 28.3 (CH_3), 33.6 (CH_2), 34.0 (CH_2), 44.9 (CH), 67.0 ($(CH_3)_2CH$), 79.0 (CH_2O), 124.3 (CBr), 127.1 (CH_{Ar}), 127.3 (CH_{Ar}), 127.6 (CH_{Ar}), 127.8 (CH_{Ar}), 128.5 ($CH_{Ar}H$), 130.4 (CH_{Ar}), 132.7 (CH_{Ar}), 139.7 (C_q), 140.8 (C_q), and 166.6 (C═N); *m*/*z* (CI) 372 [95%, $(MH)^+$]. Calcd for $C_{20}H_{23}ON^{79}Br$ $(MH)^+$: 372.0963. Found: 372.0945. Anal. Calcd for $C_{20}H_{22}ONBr$: C, 64.5; H, 6.0; N, 3.8. Found: C, 64.7; H, 5.75; N, 3.6.

(4*S*)-2-[3-(2-Bromophenyl)propyl]-4-isopropyl-2-oxazoline. Yield (50%); R_f (SiO_2, 4:1 hexanes:EtOAc) 0.25; ν_{max}/cm^{-1} (film) 1670 (C═N); ^1H NMR δ 0.88 (3H, d, J = 6.9, CH_3), 0.96 (3H, d, J = 6.7 Hz, CH_3), 1.74 (1H, dqq, J = 6.9, 6.9 and 6.7, $(CH_3)_2CH$), 1.75 (2H, qu, J = 7.8 Hz, CH_2), 2.35 (2H, t, J = 6.8, CH_2C═N), 2.80 (2H, t, J = 6.8 Hz, $ArCH_2$), 3.84−3.95 (2H, m, CHN and CH_AH_BO), 4.14−4.23 (1H, m, CH_AH_BO), 7.00−7.10 (1H, m, ArH), 7.16−7.30 (2H, m, ArH), and 7.50−7.54 (1H, m, HCCBr); ^{13}C NMR δ 18.1 (CH_3), 18.8 (CH_3), 26.3 (CH_2), 27.6 (CH_2C═N), 32.5 ($(CH_3)_2CH$), 35.4 ($ArCH_2$), 69.8 (CH_2O), 72.0 (CHN), 124.4 (CBr), 127.3 (CH_{Ar}), 127.6 (CH_{Ar}), 130.4 (CH_{Ar}), 132.7 (CH_{Ar}), 140.8 (C_q), and 166.6 (C═N); *m*/*z* (CI) 310 [100%, $(MH)^+$]. Calcd for $C_{15}H_{21}NO^{79}Br$ $(MH)^+$: 310.0807. Found: 310.0807.

(4*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-isopropyl-2-oxazoline [(*S*)-40]. White solid (71%); 2:1 mixture of diastereoisomers R_f (SiO_2, 2:1 hexanes:EtOAc) 0.38; ν_{max}/cm^{-1} 1664 (C═N); ^1H NMR δ (500 MHz, $CDCl_3$) 0.85 (3H, d, J = 6.8 Hz, CH_3, major isomer), 0.87 (3H, d, J = 6.8 Hz, CH_3, minor isomer), 0.93 (3H, d, J = 6.8 Hz, CH_3, major isomer), 0.96 (3H, d, J = 6.8 Hz, CH_3, minor isomer), 1.71−1.82 (1H, m, $CH(CH_3)_2$), 2.10−2.20 (1H, m, CH_AH_B), 2.33−2.43 (1H, m, CH_AH_B), 2.64−2.82 (2H, m, $ArCH_2$), 3.66 (1H, t, J = 7.8 Hz, PhCH, major isomer), 3.69 (1H, t, J = 8.1 Hz, PhCH, minor isomer), 3.88−3.95 (2H, m, CH_CH_DO, CHN), 4.01−4.21 (1H, m, CH_CH_D), 6.99−7.06 (1H, m, Ar), 7.15−7.27 (3H, m, Ar), 7.30−7.38 (4H, m, ArH), and 7.48−7.50 (1H, m, ArH); ^{13}C NMR δ 17.9 (CH_3, major isomer), 18.0 (CH_3, minor isomer), 18.7 (CH_3, major isomer), 18.8 (CH_3, minor isomer), 32.4 ($(CH_3)_2CH$, minor isomer), 32.5 ($(CH_3)_2CH$, major isomer), 33.5 (CH_2, minor isomer), 33.7 (CH_2, major isomer), 34.1 ($ArCH_2$, minor isomer), 34.2 ($ArCH_2$, major isomer), 45.1 (PhCH, major isomer), 45.2 (PhCH, minor isomer), 69.8 (CH_2O), 71.7 (CHN), 124.3 (CBr), 127.0 (CH_{Ar}, major isomer), 127.1 (CH_{Ar}, minor isomer), 127.3 (CH_{Ar}), 127.6 (CH_{Ar}), 127.8 (CH_{Ar}, major isomer), 128.0 (CH_{Ar}, minor isomer), 128.5 (CH_{Ar}), 130.3 (CH_{Ar}), 132.7 (CH_{Ar}), 139.6 (C_q, minor isomer), 139.9 (C_q, major isomer), 140.8 (C_q, minor isomer), 140.9 (C_q, major isomer), and 167.8 (C═N), *m*/*z* (ES) 386 [100%, (MH^+)]. Calcd for $C_{21}H_{25}NO^{79}Br$ (MH^+): 386.1120. Found: 386.1122.

(4*R*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-isopropyl-2-oxazoline [(*R*)-40]. Yield (68%): see data for (*S*)-**40**.

(4*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-*tert*-butyl-2-oxazoline [(*S*)-41]. White solid; mixture of diastereoisomers (72%); R_f (9:1 hexane:EtOAc) 0.2; ν_{max}/cm^{-1} 1669 (C═N); ^1H NMR δ 0.86 (9H, s, $C(CH_3)_3$, minor isomer), 0.90 (9H, s, $C(CH_3)_3$, major isomer), 2.06−2.21 (1H, m, CH_AH_B), 2.29−2.46 (1H, m, CH_AH_B), 2.61−2.86 (2H, m, $ArCH_2$), 3.62−3.75 (1H, m, PhCH), 3.81−3.89 (1H, m, CHN), 3.99−4.10 (1H, m, CH_CH_DO), 4.10−4.18 (1H, m, CH_CH_DO), 7.00−7.08 (1H, m, ArH), 7.16−7.41 (7H, m, ArH), and 7.49−7.51 (1H, m, BrCCH); ^{13}C NMR δ 25.8 (^tBu, minor isomer), 26.0 (^tBu, major isomer), 33.7 (CH_2, major isomer), 33.7 (CH_2, minor isomer), 34.2 (CH_2, major isomer), 34.4 (CH_2, minor isomer), 45.3 (PhCH, minor isomer), 45.4 (PhCH, major isomer), 68.6 (CH_2O, minor isomer), 68.6 (CH_2O, major isomer), 75.4 (CHN, minor isomer), 75.6 (CHN, major isomer), 124.4 (CBr), 127.0 (CH_{Ar}), 127.1 (CH_{Ar}), 127.4 (CH_{Ar}), 127.6 (CH_{Ar}), 127.9 (CH_{Ar}), 128.1 (CH_{Ar}), 128.5 (CH_{Ar}), 130.4 (CH_{Ar}), 132.8 (CH_{Ar}), 139.7 (C_q, major isomer), 140.0 (C_q, minor isomer), 141.0 (C_q, major isomer), 141.1 (C_q, minor isomer), 167.7 (C═N, minor isomer), and 167.8 (C═N, major isomer); *m*/*z* (ES) 400 [100%, $(MH^+]$. Anal. Calcd for $C_{22}H_{26}ONBr$: C, 66.0; H, 6.5; N, 3.5. Found: C, 65.8; H, 6.6; N, 3.3. Calcd for $C_{22}H_{27}NO^{79}Br$ $(MH)^+$: 400.1276. Found: 400.1279.

(4*R*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-*tert*-butyl-2-oxazoline [(*R*)-41]. Yield (80%): see data for (*S*)-**41**.

(4*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-phenyl-2-oxazoline [(*S*)-42]. White solid; mixture of diastereoisomers (40%); R_f (9:1 hexanes:EtOAc) 0.1; ν_{max}/cm^{-1} 1656 (C═N); ^1H NMR δ 2.16−2.30 (1H, m, CH_AH_B), 2.41−2.55 (1H, m, CH_AH_B), 2.68−2.89 (2H, m, $ArCH_2$), 3.73−3.79 (1H, m, PhCH), 4.03−4.11 (1H, m, CH_CH_DO), 4.53−4.63 (1H, m, CH_CH_DO), 4.53−4.63 (1H, m, CHN), 7.01−7.08 (1H, m, ArH), 7.18−7.45 (12H, m, ArH), and 7.49−7.52 (1H, m, BrCCH); *m*/*z* (CI) 420 [100%, (MH^+)]. Calcd for $C_{24}H_{23}NO^{79}Br$ $(MH)^+$: 420.0963. Found: 420.0957.

(4*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-benzyl-2-oxazoline [(*S*)-43]. White solid; 1:1 mixture of diastereoisomers (88%); R_f (9:1 hexanes:EtOAc) 0.25; ν_{max}/cm^{-1} 1645 (C═N); ^1H NMR δ 2.04−2.20 (1H, m, $PhCHCH_AH_B$), 2.28−2.46 (1H, m, $PhCHCH_AH_B$), 2.58−2.78 (3H, m, $ArCH_2$ and $PhCH_CH_D$), 3.07−3.15 (1H, m, $PhCH_CH_D$), 3.56−3.66 (1H, m, PhCH), 3.88−3.96 (1H, m, CH_EH_FO), 4.06−4.16 (1H, m CH_EH_FO), 4.34−4.46 (1H, m, CHN), 7.00−7.05 (1H, m, Ar), 7.14−7.36 (12H, m, Ph and Ar), and 7.48−7.51 (1H, m, Ar); ^{13}C NMR[32] δ 33.5 (CH_2, isomer A), 33.7 (CH_2, isomer B), 34.0 (CH_2, isomer A), 34.1 (CH_2, isomer B), 41.5 (CH_2), 44.9 (PhCH, isomer A), 45.0 (PhCH, isomer B), 66.9 (CHN, isomer A), 67.0 (CHN, isomer B), 71.5 (CH_2O), 124.4 (CBr), 126.4 (CH_{Ar}), 127.1 (CH_{Ar}), 127.2 (CH_{Ar}), 127.3 (CH_{Ar}), 127.6 (CH_{Ar}), 127.88 (CH_{Ar}), 127.9 (CH_{Ar}), 128.38 (CH_{Ar}), 128.42 (CH_{Ar}), 128.5 (CH_{Ar}), 129.2 (CH_{Ar}), 129.3 (CH_{Ar}), 130.4 (CH_{Ar}), 132. 7 (CH_{Ar}), 137.6 (C_q, isomer A), 137.7 (C_q, isomer B), 139.5 (C_q, isomer A), 139.6 (C_q, isomer B), 140.77 (C_q, isomer A), 140.8 (C_q, isomer B), 168.55 (C═N, isomer A), and 168.57 (C═N, isomer B); *m*/*z* (CI) 434 [100%, (MH^+)]. Calcd for $C_{25}H_{25}NO^{79}Br$ $(MH)^+$: 434.1120. Found: 434.1109.

(4*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-cyclohexylmethyl-2-oxazoline [(*S*)-44]. White solid; 3:2 mixture of diastereoisomers (49%); R_f (9:1 hexanes:EtOAc) 0.25; ν_{max}/cm^{-1} 1647 (C═N); ^1H NMR δ_H 0.83−1.01 (2H, m, C_6H_{11}), 1.08−1.32 (4H, m, C_6H_{11}-

(32) Assignment of isomer A or B is arbitrary.

CH_AH_B and C_6H_{11}), 1.34−1.48 (1H, m, C_6H_{11}), 1.58−1.75 (6H, m, $C_6H_{11}CH_AH_B$ and C_6H_{11}), 2.08−2.20 (1H, m, $PhCHCH_AH_B$), 2.30−2.44 (1H, m, $PhCHCH_AH_B$), 2.62−2.81 (2H, m, $ArCH_2$), 3.60−3.68 (1H, m, PhCH), 3.76−3.81 (1H, m, CH_CH_DO), 4.09−4.30 (1H, m, CHN and CH_CH_DO), 7.00−7.08 (1H, m, ArH), 7.16−7.38 (1H, m, ArH), and 7.48−7.51 (1H, m, HCCBr); ^{13}C NMR δ 26.2 (CH_2), 26.5 (CH_2), 33.4 (CH_2), 33.57 (CH_2, minor isomer), 33.61 (CH_2, major isomer), 33.8 (CH_2), 34.1 (CH_2, minor isomer), 34.2 (CH_2, major isomer), 34.7 (CH, minor isomer), 34.8 (CH, major isomer), 44.2 (CH_2, major isomer), 44.3 (CH_2, minor isomer), 45.1 (PhCH), 63.8 (CHN, minor isomer), 63.9 (CHN, major isomer), 73.0 (CH_2O, major isomer), 73.1 (CH_2O, minor isomer), 124.4 (CBr), 127.1 (CH_{Ar}, major isomer), 127.2 (CH_{Ar}, minor isomer), 127.4 (CH_{Ar}), 127.9 (CH_{Ar}), 128.6 (CH_{Ar}), 130.4 (CH_{Ar}), 132.8 (CH_{Ar}), 139.7 (C_q, minor isomer), 139.8 (C_q, major isomer), 140.9 (C_q, minor isomer), 141.0 (C_q, major isomer), and 167.7 (C═N); *m*/*z* (CI) 440 [100%, (MH^+)]. Calcd for $C_{25}H_{31}NO^{79}Br$ $(MH)^+$: 440.1589. Found: 440.1570.

(4*S*,5*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-methoxy-5-phenyl-2-oxazoline [(*S*,*S*)-45]. White solid; 3:2 mixture of diastereoisomers (55%); R_f (4:1 hexanes:EtOAc) 0.25; ν_{max}/cm^{-1} 1640 (C═N); ^{1}H NMR δ_H 2.15−2.39 (1H, m, $PhCHCH_AH_B$), 2.38−2.53 (1H, m, $PhCHCH_AH_B$), 2.70−2.88 ($ArCH_2$), 3.39 (3H, s, MeO, minor isomer), 3.41 (3H, s, MeO, major isomer), 3.46−3.54 (1H, m, CH_CH_DOMe), 3.65 (1H, dd, J = 9.6, 4.3 Hz, CH_CH_DOMe, major isomer), 3.66 (1H, dd, J = 9.7, 4.4 Hz, CH_CH_DOMe, minor isomer), 3.73 (1H, t, J = 7.7 Hz, $PhCHCH_AH_B$, minor isomer), 3.80 (1H, t, J = 7.8 Hz, $PhCHCH_AH_B$, major isomer), 4.08−4.17 (1H, m, CHN), 5.28 (1H, d, J = 6.6 Hz, PhCHO), 7.00−7.12 (3H, m, ArH), 7.17−7.38 (8H, m, ArH), 7.40−7.44 (2H, m, ArH), and 7.49−7.52 (1H, m, ArH); ^{13}C NMR δ 33.2 (CH_2, major isomer), 33.5 (CH_2, minor isomer), 34.1 (CH_2), 45.1 (PhCH, minor isomer), 45.3 (PhCH, major isomer), 59.2 (CHN), 74.26 (MeO, major isomer), 74.3 (CH_2O, major isomer), 74.39 (MeO, minor isomer), 74.42 (CH_2O, major isomer), 83.2 (PhCHO, minor isomer), 83.5 (PhCHO, major isomer), 124.4 (CBr), 125.2 (CH_{Ar}), 125.4 (CH_{Ar}), 127.3 (CH_{Ar}), 127.4 (CH_{Ar}), 127.7 (CH_{Ar}), 127.9 (CH_{Ar}), 127.96 (CH_{Ar}), 128.0 (CH_{Ar}), 128.1 (CH_{Ar}), 128.6 (CH_{Ar}), 130.5 (CH_{Ar}), 132.8 (CH_{Ar}), 139.4 (C_q, major isomer), 139.5 (C_q, minor isomer), 140.86 (C_q, major isomer), 140.88 ((C_q, minor isomer) and (C_q, major isomer)), 140.9 (C_q, minor isomer), 168.9 (C═N, major isomer), and 169.0 (C═N, minor isomer); *m*/*z* (CI) 464 [100%, (MH^+)]. Calcd for $C_{26}H_{27}NO_2{}^{79}Br$ $(MH)^+$: 464.1225. Found: 464.1219.

(4*S*)-{2-[3-(2-Bromophenyl)-1-phenylpropyl]-2-oxazolin-4-yl}-diphenylmethanol [(*S*)-46]. White solid; 2:1 mixture of diastereoisomers (41%); R_f (9:1 hexanes:EtOAc) 0.2; ν_{max}/cm^{-1} 1654 (C═N) and 3547 (OH); ^{1}H NMR δ 2.05−2.17 (1H, m, $PhCHCH_AH_B$), 2.24−2.40 (2H, m, OH and $PhCHCH_AH_B$), 2.61−2.78 (2H, m, $ArCH_2$), 3.73 (1H, t, J = 7.7 Hz, PhCH), 4.02−4.13 (2H, m, CH_2O), 5.28 (1H, t, J = 9.6 Hz, CHN, minor isomer), 5.32 (1H, t, J = 9.4 Hz, CHN, major isomer), 6.99−7.06 (1H, m, ArH), 7.09−7.40 (16H, m, ArH), 7.46−7.51 (1H, m, ArH), and 7.55−7.60 (2H. m, ArH); ^{13}C NMR δ 33.7 (CH_2, minor isomer), 33.8 (CH_2, major isomer), 34.2 (CH_2, minor isomer), 34.3 (CH_2, major isomer), 45.38 (PhCH, major isomer), 45.44 (PhCH, minor isomer), 69.1 (CH_2O, major isomer), 69.2 (CH_2O, minor isomer), 72.4 (CHN), 78.0 (Ph_2C, minor isomer), 78.2 (Ph_2C, major isomer), 124.3 (CBr, major isomer), 124.4 (CBr, minor isomer), 125.7 (CH_{Ar}), 126.7 (CH_{Ar}), 126.8 (CH_{Ar}), 127.0 (CH_{Ar}), 127.1 (CH_{Ar}), 127.3 (CH_{Ar}), 127.7 (CH_{Ar}), 128.0 (CH_{Ar}), 128.2 (CH_{Ar}), 128.6 (CH_{Ar}), 130.3 (CH_{Ar}), 130.4 (CH_{Ar}), 132.8 (CH_{Ar}), 139.4 (C_q, minor isomer), 139.7 (C_q, major isomer), 140.79 (C_q, major isomer), 140.84 (C_q, minor isomer), 144.0 (C_q, major isomer), 144.1 (C_q, minor isomer), 145.7 (C_q), 171.5 (C═N, minor isomer), and 171.6 (C_q, major isomer); *m*/*z* (CI) 526 [100%, (MH^+)]. Calcd for $C_{31}H_{29}NO_2{}^{79}Br$ $(MH)^+$: 526.1354. Found: 526.1372.

2-[3-(2-Bromophenyl)-1-phenylbutyl]-4,4-dimethyl-2-oxazoline (5). Clear oil (69%); R_f (SiO_2, 9:1 hexanes:EtOAc) 0.2; ν_{max}-(nujol)/cm^{-1} 1660 (C═N); ^{1}H NMR δ 1.26 (3H, s, CH_3), 1.27 (3H, s, CH_3), 1.46−1.74 (2H, m, $ArCH_2CH_2$), 1.84−1.96 (1H, m, $PhCHCH_AH_B$), 2.11−2.23 (1H, m, $PhCHCH_ACH_B$), 2.66−2.82 (2H, m, $ArCH_2$), 3.58 (1H, t, J = 7.8 Hz, PhCH), 3.86 (2H, s, CH_2O), 6.98−7.04 (1H, m, ArH), 7.12−7.36 (7H, m, ArH), and 7.48 (1H, d, J = 7.8 Hz, HCCBr); ^{13}C NMR δ 27.7 (CH_2), 28.2 (CH_3), 28.3 (CH_3), 33.5 (CH_2), 35.9 (CH_2), 45.2 (PhCH), 66.8 ((CH_3)$_2C$), 78.9 (CH_2O), 124.4 (CBr), 127.0 (CH_{Ar}), 127.3 (CH_{Ar}), 127.4 (CH_{Ar}), 127.7 (CH_{Ar}), 128.5 (CH_{Ar}), 130.2 (CH_{Ar}), 132.7 (CH_{Ar}), 140.0 (C_q), 141.4 (C_q), and 166.8 (C═N); *m*/*z* (ES) 386 [100%, (MH^+)]. Anal. Calcd for $C_{21}H_{24}ONBr$: C, 65.3; H, 6.3; N, 3.6. Found: C, 65.3; H, 6.8; N, 3.8. Calcd for $C_{21}H_{25}NO^{79}Br$ $(MH)^+$: 386.1120. Found: 386.1108.

2-[3-(2-Bromophenyl)-1-phenylpentyl]-4,4-dimethyl-2-oxazoline (6). Clear oil (60%); R_f (SiO_2, 9:1 hexanes:EtOAc) 0.2; ν_{max}-(nujol)/cm^{-1} 1661 (C═N); ^{1}H NMR δ 1.25 (3H, s, CH_3), 1.26 (3H, s, CH_3), 1.15−1.47 (2H, m, CH_2), 1.54−1.74 (2H, m, $ArCH_2CH_2$), 1.77−1.91 (1H, m, $PhCHCH_AH_B$), 2.03−2.17 (1H, m, $PhCHCH_ACH_B$), 2.68 (2H, t, J = 7.7 Hz, $ArCH_2$), 3.53 (1H, t, J = 7.8 Hz, PhCH), 3.85 (2H, s, CH_2O), 6.98−7.04 (1H, m, ArH), 7.11−7.33 (7H, m, ArH), and 7.49 (1H, dd, J = 8.0 and 1.0 Hz, HCCBr); ^{13}C NMR δ 27.1 (CH_2), 28.2 (CH_3), 28.3 (CH_3), 29.4 (CH_2), 33.6 (CH_2), 35.8 (CH_2), 45.3 (PhCH), 66.7 ((CH_3)$_2C$), 78.8 (CH_2O), 124.4 (CBr), 126.9 (CH_{Ar}), 127.2 (CH_{Ar}), 127.3 (CH_{Ar}), 127.7 (CH_{Ar}), 128.5 (CH_{Ar}), 130.2 (CH_{Ar}), 132.6 (CH_{Ar}), 140.2 (C_q), 141.7 (C_q), and 166.8 (C═N); *m*/*z* (ES) 400 [100%, (MH^+)]. Calcd for $C_{22}H_{27}NO^{79}Br$ $(MH)^+$: 400.1276. Found: 400.1292.

2-[3-(2-Bromophenyl)-1-phenylhexyl]-4,4-dimethyl-2-oxazoline (7). Clear oil (61%); R_f (SiO_2, 9:1 hexanes:EtOAc) 0.2; ν_{max}-(nujol)/cm^{-1} 1661 (C═N); ^{1}H NMR δ 1.27 (3H, s, CH_3), 1.28 (3H, s, CH_3), 1.20−1.45 (4H, m, 2 × CH_2), 1.53−1.63 (2H, m, $ArCH_2CH_2$), 1.75−1.87 (1H, m, $PhCHCH_AH_B$), 2.00−2.13 (1H, m, $PhCHCH_ACH_B$), 2.68 (2H, t, J = 7.7, $ArCH_2$), 3.52 (1H, t, J = 7.8 Hz, PhCH), 3.87 (2H, s, CH_2O), 6.99−7.05 (1H, m, ArH), 7.13−7.35 (7H, m, ArH), and 7.50 (1H, dd, J = 8.0 and 0.9 Hz, HCCBr); ^{13}C NMR δ 27.3 (CH_2), 28.2 (CH_3), 28.4 (CH_3), 29.0 (CH_2), 29.7 (CH_2), 33.7 (CH_2), 36.0 (CH_2), 45.4 (PhCH), 66.8 ((CH_3)$_2C$), 78.9 (CH_2O), 124.4 (CBr), 126.9 (CH_{Ar}), 127.2 (CH_{Ar}), 127.3 (CH_{Ar}), 127.7 (CH_{Ar}), 128.5 (CH_{Ar}), 130.2 (CH_{Ar}), 132.7 (CH_{Ar}), 140.3 (C_q), 141.9 (C_q), and 166.9 (C═N); *m*/*z* (ES) 414 [100%, (MH^+)]. Calcd for $C_{23}H_{29}NO^{79}Br$ $(MH)^+$: 414.1433. Found: 414.1439.

General Procedure for Reaction of 2-Haloarylalkyl-2-oxazolines with *tert*-BuOK/DMSO. Freshly sublimed potassium *tert*-butoxide (1.1 equiv) was dissolved in dry distilled DMSO (6 mL/mmol). The substrate oxazoline (1 equiv) in DMSO (6 mL/mmol) was then added and stirred for 5 min. Triethylamine (1 equiv) was added, and the resulting mixture was irradiated for 3−4 h. Water (6 mL/mmol) was added, and the aqueous phase was extracted with dichloromethane (3 × 12 mL/mmol). The combined organic extracts were washed (water (24 mL/mmol)), dried ($MgSO_4$), and concentrated to give the crude product.

Reaction of 2-[3-(2-Chlorophenyl)propyl]-4,4-dimethyl-2-oxazoline (4d). General procedure for *t*-BuOK with 3 h irradiation. After work up the ^{1}H−NMR spectrum showed the presence of only starting material.

Reaction of 2-[3-(2-Bromophenyl)-1-phenylpropyl]-4,4-dimethyl-2-oxazoline (4a) with *t*-BuOK. After the general procedure with 4 h irradiation, ^{1}H NMR and GCMS revealed the presence of a 1:2 mixture of the starting material **4a** and the dehalogenated product 2-[1,3-diphenylpropyl]-4,4-dimethyl-2-oxazoline **12** (n = 1, R = Ph); R_f (Al_2O_3, 19:1, hexane:EtAc) 0.3, ^{1}H NMR δ 1.25 (3H, s, CH_3), 1.26 (3H, s, CH_3) 2.09−2.18 (1H, m, CH_ACH_B), 2.37−2.44 (1H, m, CH_ACH_B), 2.59 (2H, t, J = 7.7 Hz, $ArCH_2$), 3.54 (1H, t, J = 7.7 Hz, PhCH), 3.81 (1H, s, CH_CH_DO), 3.82 (1H, s, CH_CH_DO), and 7.11−7.34 (10H, m, ArH); ^{13}C NMR δ 28.6 (CH_3), 28.8 (CH_3), 34.0, 35.9, 45.1, 67.3, 79.3, 126.3, 127.5, 128.3, 128.6, 128.8, 129.0, 129.1, 140.5, 141.9, and 167.1; *m*/*z* (EI) 293 (1%, M^+), 189 (100, $M-C_8H_8$), 91 (16).

General Procedure for Reaction of 2-Haloarylalkyl-2-oxazolines with MNH_2/NH_3^-. To a solution of ferric nitrate (0.03 equiv) in liquid ammonia (15 mL/mmol) at −78 °C in a quartz flask was added with caution either lithium or potassium metal (3 equiv). The resulting mixture was warmed to −33 °C and stirred until the blue color faded to a gray suspension (ca. 30 min). The substrate oxazoline (1 equiv) in dry THF (1 mL/mmol) was added dropwise over 5 min and stirred for a further 10 min. After allowing the mixture to warm to reflux (−33 °C), it was irradiated with UV for either 1 or 2 h, after which solid NH_4Cl was added with extreme caution! The liquid ammonia was allowed to evaporate while being slowly replaced by ether (20 mL/mmol). The ethereal solution was decanted, and the solids were washed with ether (2 × 50 mL/mmol). The combined portions were dried ($MgSO_4$) and concentrated.

Reaction of 2-[3-(2-Chlorophenyl)propyl]-4,4-dimethyl-2-oxazoline (4d) with MNH_2/NH_3. Following the general procedure above **4d** was reacted with $LiNH_2$ in liquid ammonia with irradiation for 2 h to yield after work up a 5:1 mixture of starting material **4d** and the reduced product **12**(n = 1, R = H).

Reaction of 2-[3-(2-Bromophenyl)-1-phenylpropyl]-4,4-dimethyl-2-oxazoline (4a) with MNH_2/NH_3. Precursor **4a** was added to a stirring solution of potassium amide in liquid ammonia as in the general procedure with 1 h irradiation. Dibromomethane as used as an internal NMR standard. The ^{1}H NMR revealed three separate species; these were starting material **4a** (51%), diphenylpropyl-2-oxazoline (31%) and the desired 4,4-dimethyl-2-(1′-phenylindan-1′-yl)-2-oxazoline **11** (n = 1, R = Ph) (16%); R_f (SiO_2, 9:1 hexanes:EtOAc) 0.35; ν_{max}(film)/cm^{-1} 1649 (C═N); ^{1}H NMR δ 1.24 (3H, s, CH_3), 1.40 (3H, s, CH_3), 2.30 (1H, ddd, J = 12.6, 7.7, 5.1 Hz, CH_AH$_B$), 2.82 (1H, ddd, J = 15.6, 7.7, 7.4 Hz, ArCH_CH$_D$), 3.00 (1H, ddd, J = 15.6, 7.9, 5.1 Hz, ArCH$_C$$H_D$), 3.18 (1H, ddd, J = 12.6, 7.9, 7.4 Hz, CH$_A$$H_B$), 3.90 (1H, AB doublet $J \approx$ 7.9 Hz, CH_EH$_F$O), 3.97 (1H, AB doublet $J \approx$ 7.9 Hz, CH$_E$$H_F$O), 7.06−7.11 (2H, m, ArH), 7.18−7.31 (6H, m, ArH), and 7.48−7.51 (1H, m, ArH); ^{13}C NMR δ 28.0 (CH_3), 28.3 (CH_3), 30.3 (CH_2), 41.3 (ArCH_2), 58.2 ((CH_3)$_2$*C*), 66.8 (Ph*C*), 79.4 (CH_2O), 124.7 (CH_{Ar}), 126.4 (CH_{Ar}), 126.5 (CH_{Ar}), 126.6 (CH_{Ar}), 126.7 (CH_{Ar}), 127.7 (CH_{Ar}), 128.3 (CH_{Ar}), 143.6 (C_q), 144.3 (C_q), 144.8 (C_q), and 167.6 (C═N); m/z (CI) 292 [100%, (MH)$^+$]. Calcd for $C_{20}H_{22}ON$ (MH)$^+$: 292.1701. Found: 292.1708. The reaction was repeated under identical conditions but at a dilution of one-tenth; the yields are shown in Table 1.

General Procedure for Reaction of 2-Haloarylalkyl-2-oxazolines with LDA in THF. To a solution of LDA (3 equiv) in either THF or 2:1 hexane:THF mixture (6 mL/mmol) at −78 °C under nitrogen was added a solution of the substrate (1 equiv) in the reaction solvent (3 mL/mmol). After stirring for 10 min the solution was allowed to warm to room temperature over 30 min, at which time more solvent was added (18 mL/mmol). In Method A the mixture was then stirred for between 0 and 48 h at between −30 °C and reflux. In Method B a quartz flask was used, and irradiation by a 400 W medium-pressure Hg arc placed ca. 15 cm from the flask was continued usually for 6 h. In both methods, after reaction, a saturated solution of ammonium chloride (10 mL/mmol) was added and the aqueous layer was extracted with three portions of ether (3 × 5 mL/mmol). The combined organic layers were washed with water (10 mL/mmol) and dried ($MgSO_4$) to give the crude product.

Reaction of 2-[3-(2-Bromophenylpropyl]-4,4-dimethyl-2-oxazoline (4d) with LDA. Using method B **4d** was reacted under UV radiation in quartz glassware for 4 h to yield after column chromatography starting material **4d** (29%), the desired 4,4-dimethyl-2-indan-1′-yl-2-oxazoline **11** (n = 1, R = H) (58%); R_f (SiO_2, 9:1 hexanes:EtOAc) 0.2; ν_{max}/cm^{-1} 1653 (C═N); ^{1}H NMR δ 1.28 (3H, s, CH_3), 1.30 (3H, s, CH_3), 2.29−2.47 (2H, m, CH_2), 2.87−2.98 (1H, m, ArCH_AH$_B$), 3.03−3.13 (1H, m, ArCH$_A$$H_B$), 3.93 (2H, s, CH_2O), 4.09, (1H, t, J = 7.9 Hz, CH), 7.08−7.27 (3H, m, ArH), and 7.30−7.34 (1H, m, ArH); ^{13}C NMR δ 28.2 (CH_3), 25.5 (CH_3), 29.2 (CH_2), 31.8 (ArCH_2), 44.4 (CH), 66.8 (*C*(CH_3)$_2$), 79.2 (CH_2O), 124.3 (CH_{Ar}), 124.6 (CH_{Ar}), 126.4 (CH_{Ar}), 127.3 (CH_{Ar}), 141.3 (C_q), 144.0 (C_q), and 167 (C═N); m/z (CI) 216 [100%, (MH)$^+$]. Calcd for $C_{20}H_{22}ON$ (MH)$^+$: 216.1388. Found: 216.1396. A mixture of styrene and 2-bromostyrene (**14**) (10%) with ^{1}H NMR spectra in agreement with the literature was also obtained. Yields for the same reaction carried out in Pyrex glassware with method A are shown in Table 1.

Reaction of 2-[3-(2-Bromophenyl)-1-phenylpropyl]-4,4-dimethyl-2-oxazoline (4a) with LDA. Precursor **4a** was reacted using method A for 48 h. Column chromatography, using 9:1 hexanes:EtOAc as elutant, afforded Indane **11** (n = 1, R = Ph) (75%), starting material **4a** (<1%), and the mixture of styrenes (2%). Yields for the same reaction in the dark and under irradiation for between 0 and 20 h with 1−3 equiv of LDA are detailed in Table 1.

Reaction of 2-[3-(2-Bromophenyl)-1-phenylbutyl]-4,4-dimethyl-2-oxazoline (5) with LDA. Method A yielded 55% of the desired 4,4-dimethyl-2-(1-phenyl-1,2,3,4-tetrahydronaphthalen-1-yl)-2-oxazoline **11** (n = 2, R = Ph); R_f (SiO_2, 9:1 hexanes:EtOAc) 0.25; ν_{max}(film)/cm^{-1} 1638 (C═N); ^{1}H NMR δ 1.28 (3H, s, CH_3), 1.38 (3H, s, CH_3), 1.54−1.69 (1H, m, CH_AH$_B$), 1.80−1.93 (1H, m, CH$_A$$H_B$), 2.03−2.12 (1H, m, C$H_CH_D$), 2.70−2.79 (1H, m, CH$_C$$H_D$), 2.83−2.89 (2H, m, Ar$CH_2$), 3.93 (1H, AB doublet J∼8.2, CH_EH$_F$O), 3.96 (1H, AB doublet J∼8.2, CH$_E$$H_F$O), 7.00−7.04 (2H, m, ArH), 7.07−7.27 (6H, m, ArH), and 7.31−7.34 (1H, m, ArH); ^{13}C NMR δ 19.2 (CH_2), 28.1 (CH_3), 28.3 (CH_3), 29.8 (CH_2), 37.8 (ArCH_2), 50.5 (Ph*C*), 66.8 ((CH_3)$_2$*C*), 79.1(CH_2O), 125.4 (CH_{Ar}), 126.3 (CH_{Ar}), 126.8 (CH_{Ar}), 127.8 (CH_{Ar}), 127.9 (CH_{Ar}), 129.2 (CH_{Ar}), 130.9 (CH_{Ar}), 137.3 (C_q), 137.9 (C_q), 146.6 (C_q), and 168.7 (C═N); m/z (CI) 306 [100%, (MH)$^+$]. Anal. Calcd for $C_{21}H_{23}NO$: C, 82.6; H, 7.6; N, 4.6. Found: C, 81.8; H, 8.0; N, 4.7. Calcd for $C_{21}H_{24}ON$ (MH)$^+$: 306.1858. Found: 306.1853. An X-ray structure for **11** (n = 2, R = Ph) confirmed the structure (see Supporting Information).

Reaction of oxazoline **5** using method B gave tetralin **11** (n = 2, R = Ph) in a 50% yield.

Reaction of 2-[3-(2-Bromophenyl)-1-phenylpentyl]-4,4-dimethyl-2-oxazoline (6) with LDA. Using Method A, several components were isolated by column chromatography.

2-(1-*n*-Butyl-1,5-diphenylpentyl)-4,4-dimethyl-2-oxazoline (13%): R_f (SiO_2, 4:1 hexanes:EtOAc) 0.4; ν_{max}(film)/cm^{-1} 1655 (C═N); ^{1}H NMR δ 0.81−0.88 (3H, m, CH_3), 0.93−1.34 (6H, m, 3 × CH_2), 1.27 (3H, s, (CH_3)$_2$C), 1.30 (3H, s (CH_3)$_2$C), 1.62 (2H, q, J = 7.6 Hz, CH_2), 1.89−2.15 (4H, m, 2 × CH_2), 2.49−2.65 (2H, m, CH_2), 3.73 (1H, d, J = 8.1 Hz, CH_AH$_B$O), 1H, d, J = 8.1 Hz, CH$_A$$H_B$O), and 7.10−7.34 (10H, m, 2 × Ph); ^{13}C NMR δ 14.0 (CH_3), 23.0 (CH_2), 23.1 (CH_2), 25.9 (CH_2), 28.2 ((CH_3)$_2$C), 31.5 (CH_2), 33.8 (CH_2), 34.0 (CH_2), 35.5 (CH_2), 47.2 (Ph*C*), 66.8 ((CH_3)$_2$*C*), 78.7 (CH_2O), 125.5 (CH_{Ar}), 126.2 (CH_{Ar}), 126.4 (CH_{Ar}), 128.1 (CH_{Ar}), 128.3 (CH_{Ar}), 142.4 (C_q), 143.8 (C_q), and 169.5 (C═O); m/z (ES) 378 [100%, (MH$^+$)]. Calcd for $C_{26}H_{36}NO$ (MH)$^+$: 378.2797. Found: 378.2811.

4,4-Dimethyl-2-(9-phenyl-6,7-dihydro-5*H*-benzocyclohepten-1-yl)-2-oxazoline (16): colorless needles (25%); ^{1}H NMR δ 0.72 (3H, s, CH_3), 1.07 (3H, m, CH_3), 1.22−1.32 (2H, m, CH_2), 2.01−2.20 (2H, m, CH_2), 2.56−2.69 (2H, m, CH_2), 3.23 (1H, d, J = 7.8 Hz, CH_AH$_B$O), 3.71 (1H, d, J = 7.8 Hz, CH$_A$$H_B$O), 6.54 (1H, t, J = 7.4 Hz, vinyl), 7.13−7.35 (6H, m, CH_{Ar}), 7.39 (1H, dd, J = 7.6 and 1.5 Hz), and 7.65 (1H, dd, J = 7.6 and 1.5 Hz); ^{13}C NMR δ 25.0 (CH_2), 27.7 (CH_3), 28.1 (CH_3), 32.4 (CH_2), 34.1 (CH_2), 66.6 (C_q), 79.0 (CH_2O), 126.5 (CH_{Ar}), 126.7 (CH_{Ar}), 127.2 (CH_{Ar}), 128.1 (CH_{Ar}), 128.4 (vinyl), 128.7 (CH_{Ar}), 131.1 (CH_{Ar}), 138.3 (C_q), 141.5 (C_q), 141.7 (C_q), 142.1 (C_q), and 163.4 (C═N); m/z 318 [100%, (MH)$^+$]. Calcd for $C_{22}H_{24}ON$ (MH)$^+$: 318.1858. Found: 318.1865. X-ray crystal diffraction data confirmed the structure (see Supporting Information).

4,4-Dimethyl-2-(4,5,6,7-tetrahydro-cyclohepta[jk]fluoren-7a-yl)-2-oxazoline (18): colorless needles (6%); ^{1}H NMR δ 1.24−1.30 (2H, m, CH_2), 1.26 (3H, m, CH_3), 1.27 (3H, m, CH_3), 1.95−2.18 (2H, m, CH_2), 2.25−2.42 (1H, m, CH_AH$_B$), 2.72−2.85 (2H,

m, CH_2), 2.94−3.01 (1H, m, CH_AH_B), 3.76 (1H, d, J∼8.1, CH_CH_DO), 3.81 (1H, d, $J \approx 8$ Hz, CH_CH_DO), 7.06 (1H, d, $J = 7.4$ Hz, CH_{Ar}), 7.30 (1H, d, $J = 7.4$ Hz, CH_{Ar}), 7.31 (1H, dd, $J = 7.4$ and 1.3 Hz, CH_{Ar}), 7.37 (1H, dt, $J = 7.4$ and 1.3 Hz, CH_{Ar}), 7.57−7.62 (2H, m (∼t), CH_{Ar}), and 7.69−7.71 (1H, m (∼d), CH_{Ar}); ^{13}C NMR unfortunately, there was insufficient material to obtain a clear spectrum; *m/z* (EI) 317 [100%, (M^+)], 274 (65), 203 (70), 100 (84). X-ray crystallographic data confirmed the structure (see Supporting Information).

4,4-Dimethyl-2-(9-phenyl-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-1-yl)-2-oxazoline (17): clear oil (19%); ^{1}H NMR δ 1.24 (3H, s, CH_3), 1.28 (3H, s, CH_3), 1.30−1.40 (1H, m, $C^6H_AH_B$), 1.68−1.89 (3H, m, $C^6H_AH_B$ and C^7H_2), 1.95−2.06 (1H, m, $C^8H_CH_D$), 2.47−2.66 (3H, m, $C^8H_CH_D$ and C^5H_2), 3.89 (1H, d, AB doublet, $J \approx 8.1$ Hz, CH_EH_FO), 3.94 (1H, d, AB doublet, $J \approx 8.1$ Hz, CH_EH_FO), 5.01 (1H, dd, $J = 5.9$ and 2.7, C^9H), 7.02 (2H, d, $J = 8$. Hz 1, $C^{10}H$), 7.10−7.31 (5H, m, C^3H, C^4H, $C^{11}H$ and $C^{12}H$), 7.44 (1H, dd, $J = 5.8$ and 3.4 Hz, C^2H); ^{13}C NMR δ 25.1 (C^7), 27.4 (C^6), 28.0 (CH_3), 28.1 (CH_3), 30.7 (C^8), 35.9 (C^5), 44.4 (C^9), 67.5 ($(CH_3)_2C$), 78.9 (CH_2O), 125.1 (C^{12}), 126.3 (C^3), 127.4 (C^{10}), 127.8 (C^2), 128.0 (C^{11}), 130.2 (C^1), 132.5 (C^4), 142.2 ($C^{9'}$ or $C^{9''}$), 142.3 ($C^{9'}$ or $C^{9''}$), 144.2 ($C^{4'}$), and 163.9 (C═N) (see Supporting Information for 2D NMR data); *m/z* (EI) 319 [100%, (M^+)], 291 (27), 290 (20), 247 (20), 228 (16), 219 (24), 202 (25), 189 (24). Calcd for $C_{22}H_{25}NO$: 319.1936. Found: 319.1933.

2-[1,5-Diphenylpentyl]-4,4-dimethyl-2-oxazoline (19) (7%): *m/z* (EI) 321 [20%, (M^+)], 202 (100), 188 (82), 91 (38). Yields were determined by a combination of ^{1}H NMR and GCMS analysis. Alkene **16** and fluorene **18** were obtained pure by crystallization from the fractions obtained from column chromatography. Reaction with method B gave the yields shown in Table 1.

Reaction of 2-[3-(2-Bromophenyl)-1-phenylhexyl]-4,4-dimethyl-2-oxazoline (7) with LDA. Reactions were carried out with both methods A and B. ^{1}H NMR spectroscopy revealed both reactions produced a multitude of products. Due to the small scale of these reactions (ca. 0.24 mmol), it was decided to combine the mixtures from both methods to enable column chromatography to be carried out with hope of identifying reaction products. The fractions (ca. 8) obtained from the column were mixtures of components which were analyzed by ^{1}H NMR spectroscopy and GCMS, which indicated the main products were analogous to those from **6**, i.e., compounds **20**−**23** (see Supporting Information).

Reaction of 2-[2-(2-Bromophenyl)-1-phenylethyl]-4,4-dimethyl-2-oxazoline (3) with LDA. Method A gave 2-phenanthren-9-yl-4,4-dimethyl-2-oxazoline (**35**) (88%); ^{1}H NMR δ 1.19 (3H, s, CH_3), 1.21 (3H, s, CH_3), 3.41 (2H, AB, CH_2O), 7.60 (4H, m, CH_{Ar}), 7.87 (1H, m, CH_{Ar}), 8.28 (1H, m, CH_{Ar}), 8.64 (2H, m, CH_{Ar}), and 9.02 (1H, m, CH_{Ar}); ^{13}C NMR δ 28.54 (CH_3), 30.94 (CH_3), 65.86 ($C(CH_3)_2$), 78.52 (CH_2O), 122.58 (CH_{Ar}), 122.76 (CH_{Ar}), 126.79 (CH_{Ar}), 126.91 (CH_{Ar}), 127.09 (CH_{Ar}), 127.23 (CH_{Ar}), 128.28 (CH_{Ar}), 128.81 (CH_{Ar}), and 129.60 (CH_{Ar}); *m/z* (GC-MS) 275. *m/z* (EI) 276 [99%, $(MH)^+$]. Calcd for $C_{19}H_{18}NO$ $(MH)^+$: 276.1388. Found: 276.1391.

Reaction of 3a with LDA and BuLi. To an LDA solution was added a solution of substrate **3a** (1 equiv, 500 mg) in dry THF (4.19 mL). After stirring for 10 min, the solution was warmed to rt over 30 min, at which time more dry THF (25 mL) was added along with *n*-BuLi (1 equiv, 0.6 mL). A sample was taken for EPR analysis, and the mixture was stirred for 48 h at rt. After 48 h, the reaction was quenched with a saturated solution of NH_4Cl (20 mL). The aqueous layer was extracted with ether (4 × 10 mL), the combined organic layers were dried (Na_2SO_4), and the solvent was evaporated. Chromatography (SiO_2, 8:2 hexanes:EtOAc) gave spirocompound **36** (0.37 g, 81%). The sample was hydrolyzed overnight in 2% HCl solution (50 mL). The reaction mixture was extracted with ether (50 mL), and the aqueous layer was treated with 10% sodium bicarbonate solution. The resulting mixture was extracted with DCM (3 × 50 mL). The combined organic layers were washed with brine and dried over (Na_2SO_4), and solvents were evaporated to give a yellow oil, which was purified by column chromatography (SiO_2 9:1 hexanes:EtOAc) to afford 2-butyl-2-phenyl-indan-1-one **37** (15%); ^{1}H NMR δ 0.84 (3H, t, $J = 7.4$ Hz, CH_3), 1.07−1.34 (2H, m, CH_2), 1.23−1.34 (2H, m, CH_2), 1.93−2.06 (1H, m, CH_AH_B), 2.08−2.20 (1H, m, CH_AH_B), 3.60 (1H, AB, CH_AH_B), 3.39 (1H, AB, CH_AH_B), 7.16−7.24 (1H, m, ArH), 7.24−7.33 (1H, m, ArH), 7.37−7.42 (1H, m, ArH), 7.34−7.45 (1H, m, ArH), 7.47−7.52 (1H, m, ArH), 7.58−7.65 (2H, m, ArH), and 7.75−7.80 (2H, m, ArH); ^{13}C NMR δ 13.9 (CH_3), 23.2 (CH_2), 26.9 (CH_2), 38.3 (CH_2), 41.0 (CH_2), 57.1 (C_q), 124.6 (CH_{Ar}), 126.1 (CH_{Ar}), 126.5 (CH_{Ar}), 126.6 (2 × CH_{Ar}), 127.6 (CH_{Ar}), 128.5 (2 × CH_{Ar}), 135.0 (CH_{Ar}), 136.4 (C_q), 142.5 (C_q), 152.8 (C_q), and 208.1 (C═O); *m/z* (GC-MS) 264; *m/z* (CI) 265 [99%, $(MH)^+$]. Calcd for $C_{19}H_{21}O$ $(MH)^+$: 265.1592. Found: 265.1594. EPR (9.5 GHz, with 100 kHz modulation, modulation amplitude 0.2 Gpp, power 1 mW) in THF solution at 320 K, complex multiplet at *g* 2.0034.

Reaction of (4*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-isopropyl-2-oxazoline (*S*)-40 with LDA. (*S*)-**40** was reacted according to method A. After column chromatography using 9:1 hexanes:EtOAc as eluant, diastereomeric indanes (*S,R*)-**47** and (*S,S*)-**47**(R^1 = *i*-Pr, R^2 = H) were obtained in a combined yield of 72%. The de was 42%, and (*S,S*)-**47** was found to be the major isomer after hydrolysis to the corresponding β-hydroxyamide and subsequent X-ray analysis.

(4*S*,1′*R*)-4-Isopropyl-2-(1′-phenylindan-1′-yl)-2-oxazoline (*S,R*)-47 (R^1 = *i*-Pr, R^2 = H). R_f (SiO_2, 9:1 hexanes:EtOAc) 0.2; $[\alpha]_D^{25}$ 96.8 ($c = 1.02$ in MeOH); ν_{max}/cm^{-1} 1655(C═N); ^{1}H NMR δ 0.94 (3H, d, $J = 6.7$ Hz, CH_3), 1.02 (3H, d, $J = 6.7$ Hz, CH_3), 1.90 (1H, sept, $J = 6.7$ Hz, CH), 2.26−2.34 (1H, m, $CH_AH_BCH_CH_D$), 2.79−2.89 (1H, m, $CH_AH_BCH_CH_D$), 2.97−3.07 (1H, m, $CH_AH_BCH_CH_D$), 3.19−3.28 (1H, m, $CH_AH_BCH_CH_D$), 3.87−4.04 (2H, m, CH_EH_F and CHN), 4.19−4.25 (1H, m, CH_EH_F), 7.09−7.38 (8H, m, ArH), and 7.46−7.49 (1H, m, ArH); ^{13}C NMR δ 17.9 (CH_3), 19.2 (CH_3), 30.5 (CH_2), 32.4 ($(CH_3)_2CH$), 41.2 ($ArCH_2$), 58.6 (Ph*C*), 70.1 (CH_2O), 71.8 (CHN), 124.6 (CH), 126.3 (CH), 126.6 (CH), 126.7 (CH), 126.8 (CH), 127.7 (CH), 128.2 (CH), 143.9 (C), 144.4 (C), 144.7 (C), and 168.8 (C═N); *m/z* (CI) 306 [100%, $(MH)^+$]. Calcd for $C_{21}H_{24}NO$ $(MH)^+$: 306.1858. Found: 306.1862.

(4*S*,1′*S*)-4-Isopropyl-2-(1′-phenylindan-1′-yl)-2-oxazoline (*S,S*)-47 (R^1 = *i*-Pr, R^2 = H). R_f (SiO_2, 9:1 hexanes:EtOAc) 0.15; $[\alpha]_D^{25}$ 106.9 ($c = 0.32$ in $CHCl_3$); ν_{max}/cm^{-1} 1654 (C═N); ^{1}H NMR δ 0.74 (3H, d, $J = 6.8$ Hz, CH_3), 0.85 (3H, d, $J = 6.8$ Hz, CH_3), 1.70 (1H, sept, $J = 6.8$ Hz, CH), 2.26−2.35 (1H, m, $CH_AH_BCH_CH_D$), 2.80−2.90 (1H, m, $CH_AH_BCH_CH_D$), 2.98−3.08 (1H, m, $CH_AH_BCH_CH_D$), 3.15−3.24 (1H, m, $CH_AH_BCH_CH_D$), 3.95−4.06 (2H, m, CH_EH_F and CHN), 4.19−4.26 (1H, m, CH_EH_F), 7.09−7.13 (1H, m, ArH), 7.17−7.30 (7H, m, ArH), and 7.41−7.48 (1H, m, ArH); ^{13}C NMR δ 17.6 (CH_3), 18.5 (CH3), 30.5 (CH_2), 32.6 ($CH(CH_3)2$, 41.3 (CH_2), 70.3 (CH_2O), 71.4 (CHN), 124.6 (CH_{Ar}), 126.3 (CH_{Ar}), 126.5 (CH_{Ar}), 126.6 (CH_{Ar}), 126.7 (CH_{Ar}), 127.7 (CH_{Ar}), 128.2 (CH_{Ar}), 144.0 (C_q), 144.2 (C_q), 144.6 (C_q), and 168.9 (C═N); *m/z* (CI) 306 [100%, $(MH)^+$]. Calcd for $C_{21}H_{24}NO$ $(MH)^+$: 306.1858. Found: 306.1865. Results for reactions under UV irradiation for 6 h and at lower temperatures in THF are shown in Table 3.

(1*S*,1′*S*)-1′-Phenylindan-1′-carboxylic Acid (2-Hydroxy-1-isopropylethyl)-amide (*S,S*)-48. (4*S*,1′*S*)-4-Isopropyl-2-(1′-phenylindan-1′-yl)-2-oxazoline (0.5 g, 1.6 mmol) in 2% hydrochloric acid solution (50 mL) was stirred at room temperature overnight. The reaction mixture was extracted with ether (50 mL), and the aqueous layer was treated with 10% sodium hydrogen carbonate solution. The resulting mixture was extracted with dichloromethane (3 × 50 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), and evaporated to give a yellow oil. The oil was left to stand until it had all crystallized and was then recrystallized from EtOAc/hexanes to give the amide (*S,S*)-**48** (0.5 g, 95%) as white needles; mp 115.5−117.0; $[\alpha]_D^{25}$ 8.9 ($c = 0.96$ in MeOH); ν_{max}/cm^{-1} 1638 (C═O), 3290 and 3357; ^{1}H NMR δ 0.65 (3H, d, $J = 6.9$ Hz, CH_3), 0.77 (3H, d, $J = 6.9$ Hz, CH_3), 1.66−1.82 (1H, m,

C*H*$(CH_3)_2$), 2.17 (1H, br s, OH), 2.36−2.45 (1H, m, C*H*$_A$H$_B$-CH$_C$H$_D$), 2.84−2.93 (1H, m, CH$_A$*H*$_B$CH$_C$H$_D$), 2.96−3.07 (1H, m, CH$_A$H$_B$C*H*$_C$H$_D$), 3.18−3.27 (1H, m, CH$_A$H$_B$CH$_C$*H*$_D$), 3.57−3.63 (1H, m, OC*H*$_E$H$_F$), 3.68−3.78 (2H, m, CHN and OCH$_E$*H*$_F$), 5.68 (1H, d, J = 7.4 Hz, NH), and 7.18−7.37 (9H, m, ArH); ^{13}C NMR δ 18.0, 19.5, 28.8, 30.8, 41.0, 57.9, 64.8, 66.0, 124.9 (CH$_{Ar}$), 125.4 (CH$_{Ar}$), 126.8 (CH$_{Ar}$), 127.1 (CH$_{Ar}$), 127.7 (CH$_{Ar}$), 128.1 (CH$_{Ar}$), 128.6 (CH$_{Ar}$), 143.2, 145.0, 145.1, and 175.4 (C═O); *m*/*z* (CI) 324 [100%, (MH)$^+$]. Anal. Calcd for $C_{21}H_{25}NO_2$: C, 78.0; H, 7.7; N, 4.3. Found: C, 78.2; H, 8.0; N, 4.4. Calcd for $C_{21}H_{26}NO_2$ (MH)$^+$: 324.1964. Found: 324.1964. X-ray diffraction data fully confirmed the structure (see Supporting Information) and indicated the stereochemistry was (*S*,*S*).

Reaction of (4*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-*tert*-butyl-2-oxazoline (*S*)-41 with LDA. After work up the ^{1}H NMR spectrum showed only diastereomeric indanes (*S*,*R*)- and (*S*,*S*)-**47** (R^1 = *t*-Bu, R^2 = H). Yields and selectivities were determined by both ^{1}H NMR (integration of ^{t}Bu signals) and GCMS (peak areas). An attempt was made to separate the two isomers from each other by use of column chromatography but gave an isomeric mixture of β-hydroxyamides as a result of hydrolysis.

(4S)-4-*tert*-Butyl-2-(1′-phenylindan-1′-yl)-2-oxazoline [(*S*,*S*)- and (*S*,*R*)-47 (R^1 = *t*-Bu, R^2 = H)]: ^{1}H NMR δ 0.63 (9H, s, $(CH_3)_3$, major isomer), 0.82 (9H, s, $(CH_3)_3$, minor isomer), 2.10−2.20 (1H, m, C*H*$_A$H$_B$CH$_C$H$_D$), 2.63−2.78 (1H, m, CH$_A$*H*$_B$CH$_C$H$_D$), 2.82−2.97 (1H, m, CH$_A$H$_B$C*H*$_C$H$_D$), 3.00−3.18 (1H, m, CH$_A$H$_B$-CH$_C$*H*$_D$), 3.69 (1H, dd, J = 10.4 and 8.2 Hz, CHN, minor isomer), 3.79 (1H, dd, J = 10.0 and 6.7 Hz, CHN, major isomer), 3.90−3.95 (1H, m, C*H*$_A$H$_B$O), 4.01−4.07 (1H, m, CH$_A$*H*$_B$O), 6.95−7.02 (2H, m, ArH), 7.02−7.16 (6H, m, ArH) and 7.28−7.37 (1H, m, ArH). Hydrolysis gave (1′*S*)-1-phenylindan-1-carboxylic acid (1′-hydroxymethyl-2′,2′-dimethyl-propyl)amide as a 3:2 mixture of isomers (80%), R_f (9:1 hexane:EtOAc) 0.1; ν_{max}(film)/cm^{-1} 1629 (C═N) and 3344 (NH and OH); ^{1}H NMR δ 0.68 (9H, s, $(CH_3)_3$, major isomer), 0.81 (9H, s, $(CH_3)_3$, minor isomer), 2.38−2.48 (1H, m, C*H*$_A$H$_B$CH$_C$H$_D$), 2.79−3.07 (2H, m, CH$_A$*H*$_B$CH$_C$H$_D$ and CH$_A$H-$_B$C*H*$_C$H$_D$), 3.18−3.30 (1H, m, CH$_A$H$_B$CH$_C$*H*$_D$), 3.35−3.49 (1H, m, CHN), 3.74−3.88 (2H, m, CH$_2$O), 5.67 (1H, d, J = 8.0 Hz, NH, minor isomer), 5.73 (1H, d, J = 8.0 Hz, NH, major isomer), and 7.16−7.37 (9H, m, ArH); ^{13}C NMR δ 26.6 ((*C*H$_3$)$_3$C, major isomer), 26.8 ((*C*H$_3$)$_3$C, minor isomer), 30.7 (CH$_2$, minor isomer), 30.8 (CH$_2$, major isomer), 33.0 ((CH$_3$)$_3$*C*, major isomer), 33.3 ((CH$_3$)$_3$*C*, minor isomer), 40.4 (CH$_2$, minor isomer), 41.2 (CH$_2$, major iomer), 60.5 (CHN, minor isomer), 60.6 (CHN, major isomer), 63.8 (CH$_2$O, minor isomer), 63.9 (CH$_2$O, major isomer), 65.9 (Ph*C*, minor isomer), 66.1 (Ph*C*, major isomer), 124.9 (CH$_{Ar}$), 125.38 (CH$_{Ar}$, minor isomer), 125.44 (CH$_{Ar}$, major isomer), 126.7 (CH$_{Ar}$, minor isomer), 126.8 (CH$_{Ar}$, major isomer), 127.1 (CH$_{Ar}$, major isomer), 127.2 (CH$_{Ar}$, minor isomer), 127.6 (CH$_{Ar}$), 127.9 (CH$_{Ar}$, minor isomer), 128.1 (CH$_{Ar}$, major isomer), 128.5 (CH$_{Ar}$, minor isomer), 128.6 (CH$_{Ar}$, major isomer), 142.9 (C$_q$, minor isomer), 143.0 (C$_q$, major isomer), 144.8 (C$_q$, major isomer), 144.9 (C$_q$, minor isomer), 145.0 (C$_q$, major isomer), 145.3 (C$_q$, minor isomer), 175.5 (C═O, major isomer), and 175.8 (C═O, minor isomer); *m*/*z* (ES+) 360 [100%, (MNa)$^+$]. Calcd for $C_{22}H_{27}NO_2Na$ (MNa)$^+$: 360.1939. Found: 360.1935.

Reactions of (*S*)- and (*R*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-*tert*-butyl-2-oxazoline (*S*)- and (*R*)-41 with LDA and (−)-Spartiene. Reactions were as described in the general procedures except that 3.5−10 equiv of (−)-spartiene (**50**) was added prior to addition of the oxazoline. The amount of THF added on reaching rt was adjusted such that the oxazoline concentration was equal to either 0.036 or 0.1 M. After a standard workup a small amount of product mixture was analyzed via GCMS to obtain the diastereomeric excess of the formed Indane (see Table 3).

Reaction of (4*S*)-2-[3-(2-Bromophenyl)-1-phenyl-propyl]-4-phenyl-2-oxazoline (*S*)-42 with LDA. Method A gave 4-phenyl-2-(1′-phenylindan-1′-yl)-oxazole (**49**) (60%); ^{1}H NMR δ 2.30−2.40 (1H, m, CH$_A$H$_B$), 2.78−2.88 (1H, m, CH$_A$H$_B$), 2.96−3.06 (1H, m, CH$_A$H$_B$), 3.15−3.24 (1H, m, CH$_A$H$_B$), and 6.98−7.70 (15H, m, vinyl and CH$_{Ar}$).

Reaction of (4*S*)-2-[3-(2-Bromophenyl)-1-phenylpropyl]-4-cyclohexylmethyl-2-oxazoline (*S*)-44. Methods A and B led to poor conversion but afforded impure 4-cyclohexylmethyl-2-(1′-phenylindan-1′-yl)-2-oxazoline (**47**) *m*/*z* (EI) 359 [100%, (M$^+$)], 193 (90), 115 (28). Analysis of the mixture by GC-MS gave the diastereomeric excesses, 16% (method A) and 16% (method B).

General Procedure for Reactions with LDA in the Presence of Iron(II) Chloride. To a solution of LDA (3 equiv) in either THF or 2:1 hexane:THF mixture (6 mL/mmol) at −78 °C under nitrogen was added a solution of the substrate in the reaction solvent (3 mL/mmol). After stirring for 10 min the solution was allowed to warm to room temperature over 30 min, after which time more solvent was added (18 mL/mmol) followed by addition of either 10 mol % or 1 equiv of anhydrous iron(II) chloride. The mixture was then stirred for 1 h, after which a saturated solution of ammonium chloride (10 mL/mmol) was added. The aqueous layer was extracted with three portions of ether (3 × 5 mL/mmol), and the combined organic layers were washed with water (10 mL/mmol) and dried ($MgSO_4$) to give the crude product.

Oxazoline **4a** was reacted in both THF and 2:1 THF:hexanes with addition of 0.1 or 1 equiv of $FeCl_2$. ^{1}H NMR analysis revealed the formation of 4,4-dimethyl-2-(1′-phenylindan-1′-yl)-2-oxazoline **11** (*n* = 1, R = Ph) (for data see above), 2-[1,3-diphenylpropyl]-4,4-dimethyl-2-oxazoline **12** (*n* = 1, R = Ph), and styrenes together with starting material. The product distributions are shown in Table 1.

Reaction of 2-Haloarylalkyl-2-oxazolines with NaH/DMSO. To NaH (60% dispersion in mineral oil) (32.4 mg, 0.81 mmol), under nitrogen, was added dry THF (1 mL) with stirring. NaH was allowed to settle, and THF was withdrawn using a syringe. This was repeated. Dry, distilled DMSO (4 mL) was then added slowly with stirring. After 10 min, oxazoline **4a** (1 mL, 0.27 M solution in dry DMSO) was added dropwise with stirring. Then with either heating and/or UV irradiation and/or $FeCl_2$ (1 equiv) the mixture was stirred for between 10 min and 4 h. Finely ground NH_4Cl (0.5 g) was added and stirred for 10 min. Water (5 mL) and ether (10 mL) were added, and the aqueous layer was extracted with ether (2 × 5 mL). The combined organic extracts were washed (water (5 mL)), dried ($MgSO_4$), and concentrated to give the crude reaction mixture. NMR spectroscopy showed the following products: 4,4-dimethyl-2-(1′-phenylindan-1′-yl)-2-oxazoline **11** (*n* = 1, R = Ph) and 2-[1,3-diphenylpropyl]-4,4-dimethyl-2-oxazoline **12** (yields in Table 1).

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Supporting Information Available: General experimental procedures; preparations of halophenylalkyl halides and chiral oxazolines; NMR and MS data for reaction of **7**; DFT Cartesian coordinates and total energies for radical anions **10**, **25e**, **25a**, and **27**; views of the SOMOs for **25e**, **25a**, and **27**; EPR spectra obtained from **4a**, **5**, and **6**; NMR spectra for precursor oxazoline derivatives, for **11**(*n* = 1, R = Ph) and **47**(R^1=*i*-Pr, R^2=H); 2D NMR spectra for **17**; X-ray diffraction data for **11**(*n* = 2, R = Ph), **(*S*,*S*)-48**, **16** and **18**. This material is available free of charge via the Internet at http://pubs.acs.org.

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