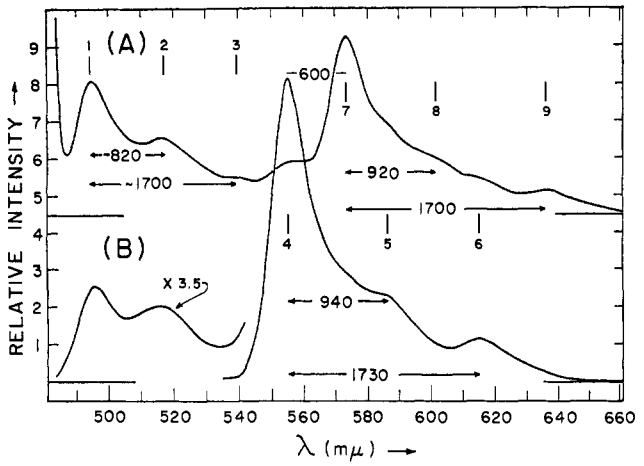

Figure 1. (A) The total luminescence spectrum of a microcrystalline suspension of camphorquinone in 3-methylpentane glass at 77°K. This spectrum is essentially identical with that of a solid film, a powdered solid, or a single crystal at 77°K. (B) The total luminescence spectrum of a glassy solution of camphorquinone in a mixed alcohol glass at 77°K. This spectrum is essentially identical with that of any of the solid samples listed above at 300°K. Vibrational analyses are indicated on the diagram.

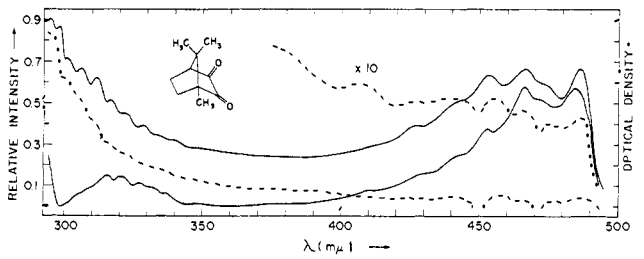

Figure 2. An uncorrected phosphorescence excitation spectrum (lower solid curve) and an absorption spectrum (upper solid curve) of a thin film of camphorquinone at 77°K. The emission wavelength monitored was 575 mμ. The thin film, which was of excellent optical quality, was grown by slow cooling of a melt between two quartz plates. This excitation spectrum, apart from some loss of resolution and some changes of relative excitation efficiency in the 380–410 and 320-mμ region, was identical with the same system at ~300°K where the emission wavelength monitored was 556 mμ; the relative excitation efficiency changes were not dissimilar to those found for a powdered sample under the same variations of temperature and of emission wavelength as shown in Figure 3. A phosphorescence spectrum corrected for all vagaries of lamp, optics, monochromator, and detection systems is also shown (dashed line). The two breaks in the corrected spectrum at ~450 and ~470 mμ are attributable to intense lamp emission lines; data at these two breaks are uncertain.

region by a factor of ~10. This observation accords with that of C T and may be similarly interpreted.[4] The excitation efficiency in the 380–410-mμ region, where TC inferred the presence of an $T_2 \leftarrow S_0$ excitation event may be supposed to corroborate the findings of TC. Thus, apart from the nonobservation of any significant $T_1 \leftarrow S_0$ excitation efficiency, our results substantiate, or may be supposed to substantiate, those of TC.

Some lower resolution excitation spectra are shown in Figure 3. Particular note should be paid to those for the powdered camphorquinone at 77 and 300°K. It is clear that these two phosphorescence excitation spectra are quite dissimilar, particularly with respect to the relative excitation efficiency in the 380–410-mμ region. The importance of this difference, *vis-a-vis* the $T_2 \leftarrow S_0$ excitation process, inferred by TC to lie in this energy

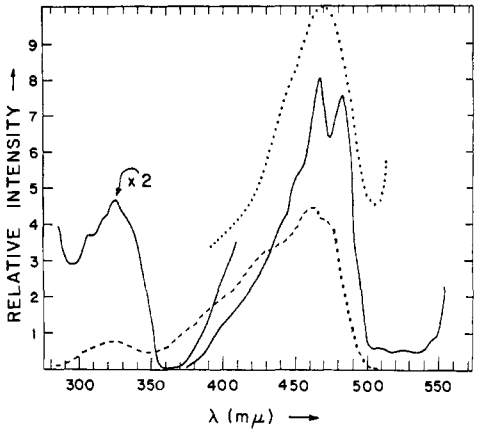

Figure 3. Excitation spectra (uncorrected) for camphorquinone luminescence: (·····) mixed-alcohol, glassy solution at 77°K; $\lambda_{emission}$ 556 mμ, (——) powdered solid at 77°K, $\lambda_{emission}$ 575 mμ; (-----) powdered solid at ~300°K, $\lambda_{emission}$ 556 mμ.

range, is unknown to us but the complexity of solid state processes do indicate that this inference should be viewed as provisional.

The TC results[4,8] were interpreted on the basis of a model which implied near-degeneracy of n+ and n– "nonbonding" oxygen orbitals. Since the photoelectron spectrum[9] indicates a separation of 1.7 eV between these orbitals, it is clear that the TC model of near n+/n– degeneracy is called into question. A revised model has been developed and has been applied to the interpretation of the absorption and emission spectroscopy of α-dicarbonyls[10] (including camphorquinone).

(8) E. Charney and L. Tsai, *J. Amer. Chem. Soc.*, 93, 7123 (1971).
(9) As obtained in these laboratories. See also J. R. Swenson and R. Hoffmann, *Helv. Chim. Acta*, 53, 2331 (1970).
(10) J. F. Arnett, G. Newkome, W. L. Mattice, and S. P. McGlynn, *J. Amer. Chem. Soc.*, 96, 4385 (1974).

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Oxazolines. XIV. An Asymmetric Synthesis of *R* and *S* Dialkylacetic Acids from a Single Chiral Oxazoline

Sir:

We recently reported[1] an asymmetric synthesis of 2-methylalkanoic acids starting from (4*S*,5*S*)-2-ethyl-4-methoxymethyl-5-phenyl-2-oxazoline (**2**, R = H, R′ = Me). The process involved metalation of the latter with lithium diisopropylamide (LDA) (−78°, THF) followed by introduction of an alkyl halide (−78°) producing the disubstituted oxazoline **2** (R = Me, R′ = alkyl). Acidic hydrolysis (3 *N* HCl, 95°) gave the (*S*)-(+)-carboxylic acids, **3**, in 60–67% optical yield. Two serious limitations, however, were noted for this scheme. (1) Although sequential alkylation of **1** with

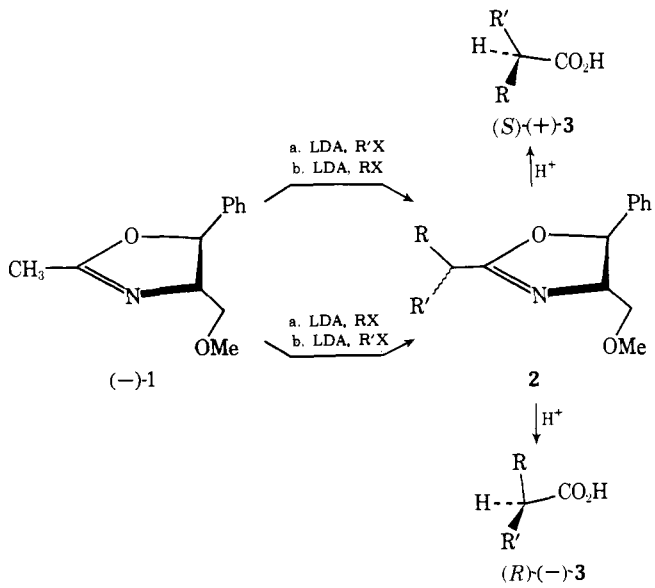
(1) A. I. Meyers, G. Knaus, and K. Kamata, *J. Amer. Chem. Soc.*, 96, 268 (1974). For additional work using chiral oxazolines in asymmetric syntheses see A. I. Meyers and M. E. Ford, *Tetrahedron Lett.*, 1431 (1974), and references cited therein; A. I. Meyers and K. Kamata, *J. Org. Chem.*, 39, 1603 (1974).

Table I. Sequential Alkylation of **1** by RX (−78°) followed by R′X (−78°) leading to (*S*)-(+) and (*R*)-(−) Acids

Entry	RX	R′X	Dialkylacetic acids **3**: $[\alpha]^{22}{}^{\circ}{}_{589}$[a]	% enantiomeric purity (EP)	Configuration[b]	% overall yield[c]
1	MeI	BuI	+12.4	66	*S*	65
2	BuI	MeI	+3.8	20	*S*	67
3	BuI	MeOTs	−9.0	48	*R*	63
4	BuI	Me_2SO_4	−9.7	52	*R*	65
5	BuI	$PhCH_2Cl$	+15.9[d]	70	*S*	66
6	$PhCH_2Cl$	BuI	−16.7[e,f]	73	*R*	67
7	*n*-PrI	MeOTs	−10.0	54	*R*	67
8	*n*-PrI	Me_2SO_4	−11.3	61	*R*	74
9	EtI	Me_2SO_4	−12.6	70	*R*	73
10	$PhCH_2Cl$	MeI	−0.21	~1	*R*	67
11	$PhCH_2Cl$	Me_2SO_4	−15.4	63[g]	*R*	58

[a] All rotations taken on a Perkin-Elmer 141 polarimeter in a 1-cm³ cell (10 cm) as neat samples except where indicated. [b] Based upon rotation and absolute configuration given by P. A. Levene and R. E. Marker, *J. Biol. Chem.*, **98**, 1 (1932). [c] Yields are based upon **1**. [d] *c* 9.14, benzene. [e] *c* 6.22, benzene. [f] M. B. Watson and G. W. Youngson, *J. Chem. Soc. C*, 258 (1968), report $[\alpha]^{20}D$ −22.8° (*c* 2, benzene). [g] A. W. Schrecker, *J. Org. Chem.*, **22**, 33 (1957), reports $[\alpha]^{22}D$ −24.6° (neat).

methyl iodide followed by *n*-butyl iodide gave (*S*)-**3** in 66% enantiomeric purity, the reverse order of alkyl introduction, which was expected to produce (*R*)-**3**,



(R′ takes priority over R)

gave, once again, (*S*)-**3** but in only 20% enantiomeric purity (Table I, entries 1 and 2). Similarly, introduction of benzyl chloride followed by methyl iodide gave nearly racemic acid (entry 10) whereas the reverse order of alkylation led to (*S*)-**3** in 70% enantiomeric purity.[1] (2) It appeared that one of the substituents on the chiral oxazoline **2** must always be a methyl group, thus limiting the synthesis to 2-methylalkanoic acids.

We now report that not only have we overcome these limitations but we have also observed pronounced temperature effects with regard to the stereochemical efficiency of the process. *It is now possible to prepare either R or S carboxylic acids*, **3**, *from the readily available oxazoline*, **1**, *by merely reversing the order of alkyl introduction.*[2] By simply utilizing methyl sulfate (or tosylate) in place of methyl iodide, the methyl group may be introduced with stereoselectivity comparable to the reverse addition sequence (Table I, entries 2–4). In fact, when the alkylations are performed at *ca.* −100°, both the (*S*)- and (*R*)-2-methylhexanoic acids are efficiently formed in 77 and 70% enantiomeric purities, respectively (Table II). Other examples where the methyl group is introduced after the larger group is in place are also given in Table I (entries 7–11). Furthermore, neither alkyl group need be methyl in order to obtain either enantiomer of the carboxylic acid. In entries 5 and 6 of Table I, it is seen that sequential alkylation of **1** with butyl iodide followed by benzyl chloride gives (*S*)-(+)-**3** (70% enantiomeric purity), whereas benzyl chloride followed by butyl iodide leads to (*R*)-(−)-**3** (73% enantiomeric purity).[3] It appears that it is possible to predict the absolute configuration of these dialkylacetic acids since introduction of the group with lower priority (Cahn–Prelog–Ingold sequencing), followed by introduction of the group with

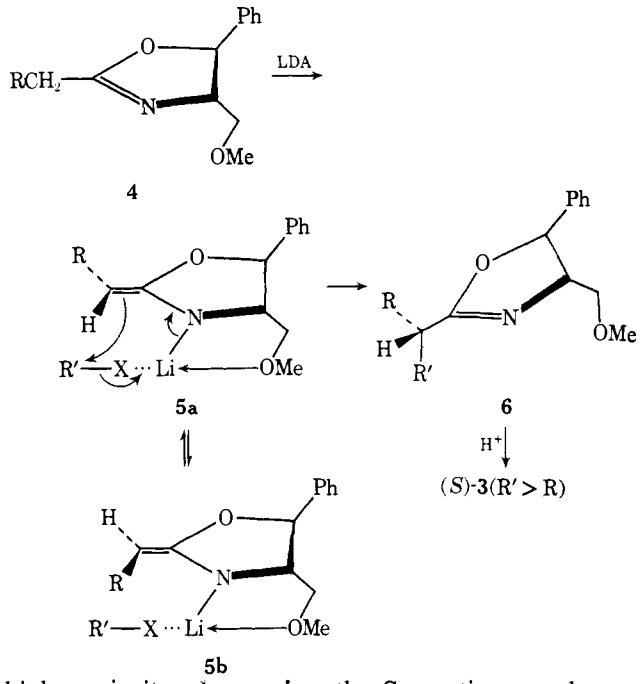
Table II. Asymmetric Synthesis of Acids, **3**, as a Function of Alkylation Temperature[a,b]

Oxazoline, **4**	R′X	Temp, °C	$[\alpha]^{22}{}^{\circ}{}_{589}$ (neat)	% enantiomeric purity (EP)	**3** Configuration
R = Me	*n*-BuI	−30	+5.1	27	*S*
	n-BuI	−45	+8.4	45	*S*
	n-BuI	−64	+10.0	54	*S*
	n-BuI	−78	+12.4	66	*S*
	n-BuI	−95	+14.5	78	*S*
	n-BuI	−105	+14.3	77	*S*
R = *n*-Bu	Me_2SO_4	−78	−9.7	52	*R*
	Me_2SO_4	−98	−13.1	70	*R*

[a] Reactions performed by treating **4** with 1.0 equiv of LDA in THF at −78° (0.5 hr) and then bringing the temperature of the solution to indicated values by use of appropriate cryostatic baths. The halide was added and reaction temperature maintained for 2–4 hr after which solutions were quenched in ice water. [b] Yields of acids, **3**, were all in the 68–82% range.

(2) Oxazoline (−)-**1** is prepared as previously described (ref 1) from commercially available (1*S*,2*S*)-(+)-1-phenyl-2-amino-1,3-propanediol (Strem Chemicals or Aldrich). The (1*R*,2*R*)-(−)-aminodiol utilized to prepare (+)-**1** is not commercially available (sample obtained from Dr. G. Moersch, Parke-Davis, Ann Arbor, Mich.).

(3) The use of tosylates or sulfates of higher alkyl groups (*i.e.*, BuOTs, Pr_2SO_4, etc.) were examined but found to alkylate poorly (10–20%) under the low temperatures required for stereoselective reactions.



higher priority, always gives the *S* enantiomer, whereas reversal of this order gives the *R* enantiomer.

Further studies to evaluate the nature of this process revealed that the asymmetric synthesis was independent of the temperature at which the proton was removed from **4**. Thus, lithio salts **5** (**a** and **b**) were generated at −22, −45, and −78° but were all alkylated at −78° to ultimately give (*S*)- or (*R*)-**3** in comparable enantiomeric purity. On the other hand, alkylation of **5** (**a** and **b**) at various temperatures gave significantly different optical yields of **3** (Table II). That lower temperatures increase stereoselectivity is no surprise since the $\Delta\Delta G^{\ddagger}$ for the competing transition state would be enlarged.[4]

The above results now allow a preliminary suggestion regarding the mechanism of this asymmetric synthesis. The proton removal from **4** gives rise to two isomeric lithiooxazolines **5** (**a** and **b**) which are probably interconvertible. Attack by the electrophile must be assumed to occur from the bottomside since it would be difficult to rationalize topside approach in view of the profound effect of methyl sulfate *vs.* methyl iodide. The rate of alkylation on **5a** must be faster than that in **5b** due to diminished steric interaction between the incoming *R* group and the *R* group already present. For methyl sulfate (or tosylate) a bulkier complex (**5a**) between the lithium cation and the oxygen atoms over that formed with methyl iodide results in widening the relative rates of attack on **5a** and **5b** causing greater stereoselectivity. If, as assumed, alkylation consistently occurs from the bottomside, this would lead to **6** which upon acidic cleavage provides the carboxylic acids **3**. All facts in hand to date are consistent with this mechanism and although further refinements are still necessary, it provides a useful working hypothesis to allow rational planning of future syntheses.[5]

Acknowledgment. Financial support from the National Institutes of Health, the National Science Foundation, and the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged. We wish to thank Professor Ronald Breslow for helpful discussions.

(4) J. D. Morrison and H. S. Mosher, "Asymmetric Organic Reactions," Prentice-Hall, Englewood Cliffs, N. J., 1971, p 40.

(5) All mono- and disubstituted oxazolines are new compounds and have been satisfactorily characterized by spectroscopic and elemental analytical methods.

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β-Oxido Carbenoids as Synthetic Intermediates. A Facile Ring Enlargement Reaction

Sir:

A number of important ring enlargement reactions have been devised within the last 10 years for the synthesis of macrocyclic derivatives.[1] These reactions assume an even greater importance with the increasing availability of certain medium- and large-ring compounds.[2]

The best current methods for a one-carbon ring enlargement involve (a) diazomethane reaction[3] or (b) the Tiffeneau–Demjanov rearrangement.[4] Both methods are of limited value in preparative work because of either the variety of products formed (for a) or the number of steps involved (for b).[5] We report herein a highly effective method for circumventing such difficulties based on the use of β-oxido carbenoids.[6]

Treatment of the dibromide **1** in tetrahydrofuran with 2 equiv of *n*-butyllithium in hexane at −78° for 30 min and 0° for 5 min led to 89% isolated yield of pure cyclotridecanone (**5**). Evidently the β-oxido carbenoid **2** was first formed and decomposed smoothly to the enolate **4**, probably *via* β-oxido carbene **3**[7] (Scheme I). Similarly, cyclohexanone, cycloheptanone, cyclooctanone, and cyclononanone were prepared from the corresponding dibromides in 92,[8,9] 70,[8,10] 80,[11] and 87%[11] yields, respectively.

Clearly, the principal side reaction in this case would be due to replacement of hydrogen by lithium[12] followed by decomposition to β-oxido monobromocarbene which would produce bromocyclotridecanone after hydrolysis.[6] It soon became apparent, however, that the major reaction pathway in the present case was

(1) For reviews see (a) C. D. Gutsche and D. Redmore, "Carbocyclic Ring Expansion Reactions," Academic Press, New York, N. Y., 1968; (b) P. R. Story and P. Busch, *Advan. Org. Chem.*, **8**, 67 (1972).

(2) G. Wilke, *Pure Appl. Chem.*, **17**, 179 (1968).

(3) (a) C. D. Gutsche, *Org. React.*, **8**, 364 (1954); (b) ref 1a, Chapter 4.

(4) P. A. S. Smith and D. R. Baer, *Org. React.*, **11**, 154 (1967); see, also, D. A. Evans, G. L. Carroll, and L. K. Truesdale, *J. Org. Chem.*, **39**, 914 (1974).

(5) For example, U. Schöllkopf and P. Böhme, *Angew. Chem., Int. Ed. Engl.*, **10**, 491 (1969).

(6) (a) H. Taguchi, H. Yamamoto, and H. Nozaki, *Tetrahedron Lett.*, 4661 (1972); (b) J. Villieras, C. Bacquet, and J. F. Normant, *J. Organometal. Chem.*, **40**, C1 (1972); (c) G. Köbrich and J. Grosser, *Tetrahedron Lett.*, 4117 (1972); (d) I. Kuwajima and Y. Fukuda, *Chem. Lett.*, 372 (1973); (e) G. Köbrich and J. Grosser, *Chem. Ber.*, **106**, 2626 (1973).

(7) Carbene induced ring enlargement: M. Fărcasiu, D. Fărcasiu, T. Conlin, M. Jones, Jr., and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **95**, 8207 (1973); A. D. Wolf and M. Jones, Jr., *ibid.*, **95**, 8209 (1973).

(8) Yields calculated from 2,4-DNP derivatives.

(9) 2,4-DNP: mp 157–158°, lit. mp 160° (Z. Rappoport, "Handbook of Tables for Organic Compound Identification," The Chemical Rubber Co., Cleveland, Ohio, 1964).

(10) 2,4-DNP: mp 143–144°, lit. mp 147° (ref 9).

(11) Identical in all respects with an authentic sample.

(12) G. Köbrich, *Angew. Chem., Int. Ed. Engl.*, **6**, 41 (1967); **11**, 473 (1972).