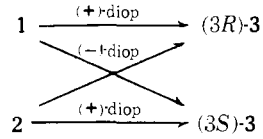
Chart I



It is noteworthy that the (−)-diop cobalt catalyzed isomerization of **1** and **2** exhibits a reaction stereochemistry opposite to that observed with the (+)-diop cobalt catalyst. The stereochemical correlation established is shown in Chart I. As the stereochemical integrity at C-3 remains intact upon acid hydrolysis, the present isomerization provides a practical route to optically active aldehydes, e.g., citronellal.

Unsubstituted allyl ethers (CH_2=$CHCH_2OR$) were isomerized into vinyl ethers by rhodium(I)[22] or ruthenium(II)[23] complexes. Isomerization of unsubstituted[24] or substituted[25] allyl alcohols to the corresponding aldehydes by rhodium(I) was also reported. The present cobalt catalyst lacks the activity for isomerization of allyl ethers and alcohols. Despite this limitation, the applicability to trisubstituted allylamine systems is considered to be quite significant, and the synthetic utility for chiral natural products is obvious. The scope and mechanism are under investigation.

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(13) *N,N*-Diethyl-3,7-dimethyl-1(*E*)-3-octadienylamine; identified by NMR spectrum, important signals at δ 0.87 (d, $-CHCH_3$, 6H), 1.0 (t, $-CH_2CH_3$, 6 H), 1.65 (s, $=CCH_3$, 3 H), 2.98 (q, $-NCH_2CH_3$, 4 H), 4.92 (d, $-CH=CHN-$, 1 H), 4.94 (t, $-CH_2CH=$, 1 H), and 5.91 (d, $=CHN$, 1 H, J_{H-H} 13.5 Hz).
(14) Technical grade, Nakarai Chemicals Ltd.
(15) Prepared by treating Ph_2PCl with *l*-menthol in pyridine; colorless liquid, bp 160 °C (0.01 Torr), $[\alpha]^{16}_D$ −56.5° (*c* 2.1, *n*-hexane).
(16) Prepared by reacting menthyl lithium with diphenylchlorophosphine; bp 139–142 °C (1.8×10^{-2} Torr), $[\alpha]^{24}_D$ −64.7° (*c* 3.4, *n*-hexane).
(17) The optical purity was assessed by comparing the $[\alpha]^{25}_D$ value (−64.7°, (*c* 3.4, *n*-hexane) of an authentic sample of *N*-[(3*R*),7-dimethyl-1(*E*),6-octadienyl]diethylamine.
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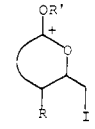
Stereoselective Epoxidation of Acyclic Olefinic Carboxylic Acids via Iodolactonization

Sir:

Many macrocyclic natural products pose a considerable synthetic challenge because of their stereochemical complexity. Our interest in the synthesis of these compounds has focussed initially on the stereoselective introduction of chiral centers in appropriate acyclic precursors. Recent work in this area has led to several novel and general methods for doing this; however, many of these approaches serve only to establish a specific relationship between the newly generated chiral centers and do not provide for relative asymmetric induction from preexisting ones.[1] In contrast, hydroxyl-directed epoxidation can be used to introduce two chiral centers with high 1,2- or 1,3-asymmetric induction in acyclic systems.[2] Iodolactonization has been used to functionalize double bonds in a regio- and stereoselective manner in a large number of cyclic cases,[3] but its potential for similar selectivity in acyclic systems has remained largely unexplored. Recently, Terashima and Jew reported an asymmetric synthesis of α-hydroxy acids in which the stereochemistry is established by a bromolactonization.[4] In this communication, we describe the development of iodolactonization as a means of epoxidizing acyclic olefinic acids with very high 1,2-asymmetric induction.

Under conditions involving kinetic control (I_2, aqueous $NaHCO_3$, and ether[5] or *N*-iodosuccinimide and $CHCl_3$), iodolactonization of several acyclic γ,δ- and δ,ϵ-unsaturated acids exhibits only moderate asymmetric induction.[6] Equilibration of a cyclic intermediate and therefore thermodynamic control over the stereochemistry can be achieved by reaction of the carboxylic acid with iodine in acetonitrile in the *absence* of base. Under these conditions, cis to trans equilibration occurs, via the protonated lactones **1a,** and affords the more stable

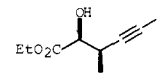


1a: R' = H
1b: R' = CH_3

trans isomers with very high stereoselectivity and in good yield. A high concentration of this protonated intermediate ($pK_a \approx -7$) is required, as shown by the fact that substitution of dimethylformamide ($pK_a \approx -1$) for acetonitrile ($pK_a \approx -10$) as solvent in the cyclization of **2b** leads to a kinetic mixture of **3b** and **4b** (3:4), even after a prolonged period.

As Table I indicates, this stereoselective iodolactonization procedure is general for a variety of γ,δ- and δ, ϵ-unsaturated acids. In the case of the disubstituted olefins **5a–c,** only γ-lactones are obtained, as would be expected from the greater stability of γ- over δ-lactones.[11] Understandably, little stereoselectivity is seen in the cyclization of 2-phenyl-4-pentenoic acid (**11**),[12] although the possibility that 1,3- or even 1,4-asymmetric induction may occur in the formation of appropriate six-membered lactones cannot be excluded.

The hydroxy acid derivatives **5** were prepared by conventional elaboration of the acetylenic ester **13,** which is formed in 69% yield from the reaction of ethyl *trans*-2,3-epoxybutanoate with 1-propynyldiethylalane. The δ,ϵ-unsaturated acids **8** were prepared from *meso*-2,4-dimethylglutaric anhydride[13]



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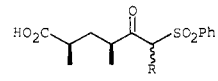

14a: R = H
14b: R = CH_3

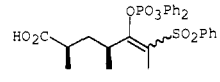

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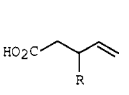
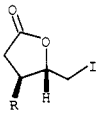
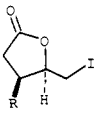
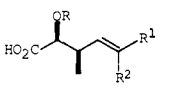
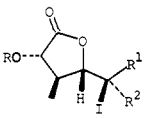
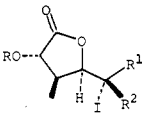
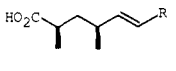
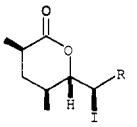
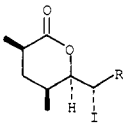
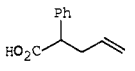
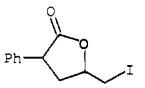
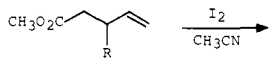
Table I. Stereoselectivity of Iodolactonization with Iodine in Acetonitrile[a]

Olefinic acid	Trans	Cis	Yield	Ratio, trans/cis[b]
				
2a: R = CH_3	3a	4a	84%	10:1
2b: R = Ph	3b	4b	98%	20:1
				
5a: R = Ac, R^1 = H, R^2 = CH_3	6a	7a	75%	20:1
5b: R = Ac, R^1 = CH_3, R^2 = H	6b	7b	77%	20:1
5c: R = R^1 = CH_3, R^2 = H	6c	7c	71%	20:1
				
8a: R = H	9a	10a	89%	20:1
8b: R = CH_3	9b	10b	52%	10:1
				
			98%	(3:2)[c]
11	12			

[a] Three equiv of I_2, CH_3CN, 0 °C, 2–12 h. [b] Ratios reported are lower limits, determined by ^{13}C NMR or VPC. [c] Stereochemistry unknown.

via the β-keto sulfones **14.** Borohydride reduction of **14a,** lactonization, and sodium amalgam reduction[14] afford the vinyl derivative **8a** in 66% overall yield from the anhydride. The *trans*-alkene **8b** was obtained by sodium in ammonia reduction of the enol phosphate **15.**[15]

Iodine in acetonitrile also causes cyclization of the methyl esters of these unsaturated acids, albeit at a very much slower rate.[7] The slow rate and high stereoselectivity observed (eq 1 and 2) are consistent with rate-determining dealkylation of an equilibrating mixture of cationic intermediates, **1b.** This



Eq. 1 R = CH_3 3a : 4a = 10:1 (80%)

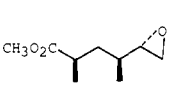
Eq. 2 R = Ph 3b : 4b > 10:1 (97%)

modification may prove useful in cases where a neutral reaction mixture must be maintained. Attempted application to the methyl ester **16a,** however, leads to the iodo ether **17.**[16,17] Iodoetherification competes with ester lactonization even when the oxygen is present as a methyl ether (**16b**), giving a 1:2 mixture of **17** and **6c.**

16a: R = H

16b: R = CH_3 17

Methanolysis of the iodolactones (methanol and Na_2CO_3, 25 °C) proceeds smoothly with concomitant loss of iodide and formation of the corresponding epoxides in quantitative yield. This overall epoxidation procedure complements the "phosphate extension" approach,[2c] which also takes advantage of the stereochemical control afforded by cyclic intermediates, and should prove useful in the synthesis of a variety of natural products. The use of epoxy ester **18** in a highly stereoselective synthesis of the insect sex attractant multistriatin[18] will be reported shortly. Moreover, the epoxide **19a** and its methyl



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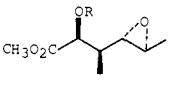

19a: R = H

19b: R = CH_3

ether **19b** are potential precursors to the ansa side chains of the rifamycins and streptovaricins which take advantage of the local plane of symmetry through C-23 of the rifamycins and the local C_2 axis through C-24 of streptovaricin D.[19]

Acknowledgments. This research was made possible by the generous support of the National Institutes of Health (Grant No. CA-16616), Chevron Research Co., Eli Lilly Co., and the National Science Foundation (through departmental Equipment Grant No. CHE 76-05512). We also thank Mr. Jerry L. Adams for performing the experiments involving acid **8b.**

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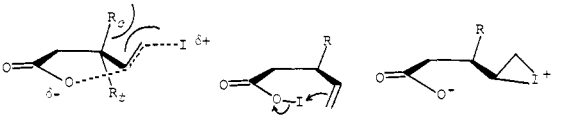
(6) Of particular interest are the cyclizations of the 3-methyl- and 3-phenyl-4-pentenoic acids **2a**[7] and **2b**,[8] because they afford predominantly the less stable cis isomers **4** (*N*-iodosuccinimide and $CHCl_3$, 25 °C; 1:3 **3a/4a** (82% yield); 1:4 **3b/4b** (87% yield)). Concerted[9] anti attack of electrophilic iodine and the carboxyl group on the double bond (as in i) would favor the trans lactones **3.** It appears likely, therefore, that the observed stereoselectivity



i ii iii

arises from preferential formation of iodonium ion iii, which leads to the cis lactone, as a result of intramolecular iodine transfer via an acyl hypoiodite (as in ii).[10] An interplay between the relative rates of iodonium ion formation, reversion to olefin, and cyclization to lactone clearly exists, however, because the other olefinic acids examined (see Table I) provide the trans lactones as the major kinetic products.

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Photochemistry of Carbanions. 1. Photoalkylation of Resonance-Stabilized Carbanions in Dimethyl Sulfoxide[1]

Sir:

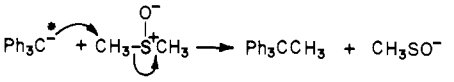
The photochemistry of carbanions has been a neglected topic in recent years, perhaps because of the complex mixtures encountered.[2] Our interest in this area was spurred by the conviction that use of low energy chromophores and visible light should minimize troublesome oxidation-reduction reactions. Recent developments have also made possible studies of solvent-separated highly delocalized carbanions in dimethyl sulfoxide.[3] Ultimately, we hoped to investigate the relation of pK_a of the conjugate acid to any photoproducts observed. Confirming our original expectation, the visible light irradiation of several resonance-stabilized carbanions in dimethyl sulfoxide produced clean and in most cases high yield conversion to products. Unexpected, however, was the identification of the major product in each case as the result of methylation at the formal carbanionic center.

The objects of our preliminary investigation were the conjugate bases of various indicators used in spectrophotometric pK_a determinations.[3,4] Thus, exposure of dimethyl sulfoxide solutions of triphenylmethyl anion to 0.1 M $FeCl_3$ filtered 450-W Hanovia light produced 1,1,1-triphenylethane as the major product (52%) along with ~5% of a minor product. Similarly, 9-phenylfluorenyl anion produced 9-methyl-9-phenylfluorene, 1,1,3,3-tetraphenyl-2-propenyl anion produced 1,1,3,3-tetraphenyl-1-butene, (4-diphenylyl)diphenylmethyl anion produced 1-(4-diphenylyl)-1,1-diphenylethane, and 9-methylfluorenyl anion produced 9,9-dimethylfluorene, although in low yield. These products along with yields and reaction times are listed in Table I.

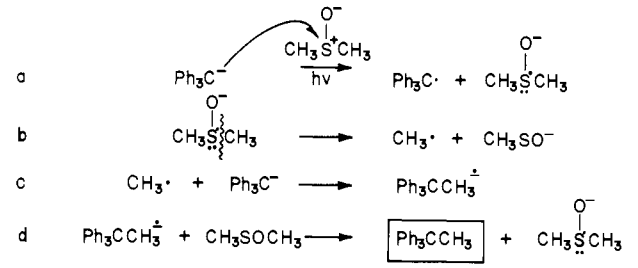
These results bear a gross resemblance to the ground-state methylation of hydrocarbons with sodium methylsulfinylmethide reported by Argabright.[5] However, photolysis of the carbanions in the presence of excess hydrocarbon failed to alter the product yields, conditions under which the presence of significant dimsyl anion concentration could be excluded.

Chart I

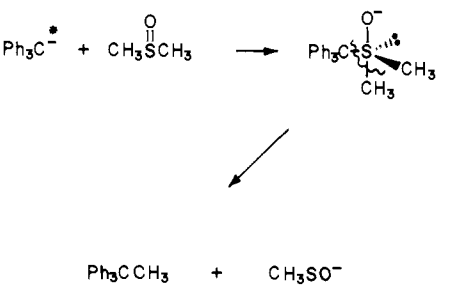
Mechanism I:



Mechanism II:



Mechanism III:



Ph_3CCH_3 + CH_3SO^-

Further, the use of appropriate solution filters excluded any possible light capture either by dimsyl anion or parent hydrocarbon.

Several mechanistic possibilities exist and are outlined in Chart I. Mechanism I involves direct nucleophilic attack on dimethyl sulfoxide. Mechanism II involves electron transfer to dimethyl sulfoxide followed by homolytic cleavage of the carbon–sulfur bond in the resulting radical anion to form methyl radical, which in turn recombines with triphenylmethyl radical or triphenylmethyl anion. This mechanism is equivalent to the $S_{RN}1$ mechanism of photostimulated aromatic substitution.[6] Mechanism III involves exciplex formation followed by decomposition via a double α scission from an oxysulfurane-like intermediate.[7]

Of the three mechanistic possibilities, mechanism I is least likely, involving as it does a nucleophilic process unknown in sulfoxides. Further, simple Hückel calculations show the excited state of triphenylmethyl anion to have near zero charge density at the central atom. Mechanism II has a great deal of precedent,[6] which is further supported by the tendency of dimethyl sulfoxide to produce methyl radicals upon dissociative electron capture[8] or oxidative addition of hydroxyl radical.[9] Furthermore, the electron-donating ability of triphenylmethyl anion is well established.[10] The long reaction times, however, suggest the nonintervention of a chain mechanism, and pho-

Table I. Results of Exploratory Photolysis of Carbanions[a]

Anion[b]	pK_a[c]	Product[d]	Reaction time, h	% yield[e]
Triphenylmethyl	31	1,1,1-Triphenylethane	3	52
Diphenylyldiphenylmethyl	29	1-(4-Diphenylyl)-1,1-diphenylethane	96	82
1,1,3,3-Tetraphenylpropenyl	26	1,1,3,3-Tetraphenyl-1-butene	12	80
9-Methylfluorenyl	22	9,9-Dimethylfluorene	48	1
9-Phenylfluorenyl	18	9-Methyl-9-phenylfluorene	18	66

[a] All data are for 10 mmol of anion in 200 mL of dimethyl sulfoxide. [b] Prepared according to the method of Bordwell et al.[3] [c] As determined by Bordwell et al.[3] [d] Determined by comparison with authentic material or independent synthesis. [e] Isolated yield by ether extraction. Actual yields were higher.

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