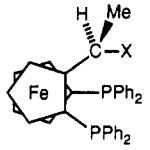
Table I. Aldol Reaction of TosMIC (2) and Aldehydes 3 Catalyzed by Chiral Silver Complexes[a] and Reduction of Oxazolines 4 with Lithium Aluminum Hydride To Produce α-Alkyl-β-(*N*-methylamino)ethanols 8

				4			8	
3	1	time,[b] h	ratio trans:cis (4)	yield,[c] %	% ee[d]	$[\alpha]^{20}_D$,[e] deg (% ee[f])	yield,[g] %	$[\alpha]^{20}_D$,[h] deg (configuration)
3a	**1a**	2	100:1	92	77 (4*R*,5*R*)[i]			
	1b	2	100:1	96	83 (4*R*,5*R*)[i]	+212 (86)	90	−35.6[k] (*R*)
3b	**1a**	2	100:1	96	74 (4*R*,5*R*)[j]			
	1b	2	60:1	95	77 (4*R*,5*R*)[j]	+239 (79)	82	−28.7 (*R*)
3c	**1a**	2	100:1	91	80 (4*R*,5*R*)[i]	+218 (77)	91	−15.8[l] (*R*)
	1b	2	100:1	97	73 (4*R*,5*R*)[i]			
3d	**1a**	1	100:1	94	73 (4*R*,5*R*)[j]			
	1b	1	100:1	94	77 (4*R*,5*R*)[j]	+200 (89)	89	−32.4 (*R*)
3e	**1a**	2	>20:1	94	83 (4*R*,5*R*)[i]	+300 (87)	71	−19.1[m] (*R*)
	1b	2	>20:1	93	75 (4*R*,5*R*)[i]			
3f	**1a**	2	100:1	94	86 (4*R*,5*R*)[j]	+341 (95)	68	−27.8 (*R*)
	1b	2	100:1	91	79 (4*R*,5*R*)[j]			
3g	**1a**	7	100:1	93	80 (4*R*,5*R*)[j]	+321 (86)	73	−37.7 (*R*)
	1b	7	100:1	97	85 (4*R*,5*R*)[j]			
3h	**1a**	9	30:1	96	85 (4*R*,5*R*)[j]	+296 (88)	70	−2.3 (*R*)
	1b	9	40:1	95	83 (4*R*,5*R*)[j]			

[a] The reaction was performed in CH_2Cl_2 at 25 °C; 2:3:catalyst = 1:1.5:0.01. [b] Reaction time for the aldol reaction. [c] Yield of product isolated by MPLC. [d] Enantiomeric excess as determined by HPLC analysis of the enantiomeric α-naphthylurea derivatives of amino alcohols 8. [e] *c* 1.0–1.1 (tetrahydrofuran). [f] Enantiomeric excess of the isolated product. [g] Yield obtained after bulb-to-bulb distillation. [h] *c* 1.0–1.5 (ethanol), unless otherwise noted. [i] Configuration determined by converting oxazoline 4 into α-alkyl-β-(*N*-methylamino)ethanol 8 of known absolute configuration. [j] Configuration assigned by similarity of optical rotations of 4 and 8. [k] The reported specific rotation is $[\alpha]^{20}_D$ −40.7° (*c* 1.3, ethanol). See: Ito, Y.; Amino, Y.; Nakatsuka, M.; Saegusa, T. *J. Am. Chem. Soc.* **1983**, *105*, 1586. [l] Specific rotation at 28 °C. The reported specific rotation for (*S*)-**5c** is $[\alpha]^{28}_D$ +23.48° (*c* 0.0921, ethanol). See: Brown, S. D.; Hodgkins, J. E.; Reinecke, M. G. *J. Org. Chem.* **1972**, *37*, 773. [m] Specific rotation at 25 °C. The reported specific rotation for (*S*)-**5e** is $[\alpha]^{25}_D$ +25.551° (*c* 10.794, ethanol). See: Koepke, S. R.; Kupper, R.; Michejda, C. J. *J. Org. Chem.* **1979**, *44*, 2718.

nitrogen atom, no oxazoline **4a** was produced after 3 h at 25 °C.



5: X = $NMeCH_2CH_2CH_2NMe_2$
6: X = $NMeCH_2CH_2OH$
7: X = NMe_2

The optically active oxazolines (**4a–h**) were converted to optically active α-alkyl-β-(*N*-methylamino)ethanols (**8a–h**) in good to excellent yield by reduction with $LiAlH_4$ in THF at room temperature.

The elucidation of the mechanistic differences between gold and silver catalysts in the asymmetric aldol reaction remains incomplete.

Supplementary Material Available: Melting points and ^1H NMR, ^{13}C NMR, and infrared spectra for *trans*-**4b–e,g,h** and **5f–h** and analytical data (or high-resolution mass spectra) for new compounds (2 pages). Ordering information is given on any current masthead page.

The Photochemistry of Pyran-4-ones: Intramolecular Trapping of the Zwitterionic Intermediate with Pendant Hydroxyl Groups

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Received September 10, 1990

Summary: Pyran-4-ones **5–11** bearing hydroxyalkyl side chains underwent efficient photocyclization to bicyclic oxyallyl zwitterions, and subsequent intramolecular nucleophilic trapping gave bicyclic cyclopentenone ethers **12–18** in good to excellent yield.

Pioneering studies by Barltrop[1] and Pavlik[2] have implicated bicyclic zwitterionic intermediates in the photorearrangement of pyran-4-ones to pyran-2-ones. The relative locations of substituents in starting materials vs products as well as the obvious analogy to the extensively studied cyclohexadienone series[3-5] support the intermediacy of a transient species such as **1** (eq 1). Even more compelling is the formation of adducts such as **2** when photolysis is carried out in hydroxylic solvents. Beyond the intrinsic mechanistic interest of this transformation, we were struck by its potential synthetic utility (i.e., formation of functionalized cyclopentenones of defined stereochemistry from planar heterocyclic precursors, and a possibly general entry into systems displaying enolonium-type reactivity).

(1) Barltrop, J. A.; Day, A. C.; Samuel, C. J. *J. Am. Chem. Soc.* **1979**, *101*, 7521.
(2) (a) Pavlik, J. W.; Kwong, J. *Ibid.* **1973**, *95*, 7914. (b) Pavlik, J. W.; Clennan, E. L. *Ibid.* **1973**, *95*, 1697. (c) Pavlik, J. W.; Pauliukonis, L. T. *Tetrahedron Lett.* **1976**, 1939.
(3) (a) Zimmerman, H. E.; Lynch, D. C. *J. Am. Chem. Soc.* **1985**, *107*, 7745 and references therein. (b) Zimmerman, H. E. *Adv. Photochem.* **1963**, *1*, 183.
(4) Schuster, D. I. *Acc. Chem. Res.* **1978**, *11*, 65.
(5) (a) Schultz, A. G. *Pure Appl. Chem.* **1988**, *60*, 981. (b) Schultz, A. G.; Plummer, M.; Taveras, A. G.; Kulling, R. K. *J. Am. Chem. Soc.* **1988**, *110*, 5547. (c) Schultz, A. G.; Macielag, M.; Plummer, M. *J. Org. Chem.* **1988**, *53*, 391.

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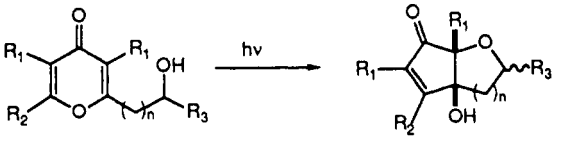
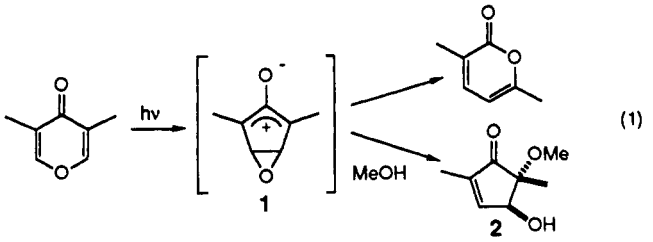
Table I. Photolysis of 2-(Hydroxyalkyl)pyran-4-ones[a]



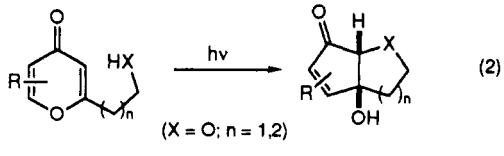
entry	substrate	R_1	R_2	R_3	n	solvent	product	yield (%)[b]	diastereomer ratio
1	5	Me	Me	H	1	MeOH	12	60[c]	-
2	5	Me	Me	H	1	TFE[d]	12	75	-
3	6	Me	Me	Me	1	MeOH	13	64[c]	1.9:1
4	6	Me	Me	Me	1	TFE[d]	13	84[e]	1.9:1[e]
5	7	Me	Me	Ph	1	MeOH	14	76[c]	1:1
6	7	Me	Me	Ph	1	TFE[d]	14	92	1:1
7	8	H	Me	Me	1	TFE[d]	15	75	1.6:1
8	9	Me	Me	H	2	TFE[d]	16	99	-
9	10	Me	Me	iPr	2	TFE[d]	17	61[e]	1.5:1[e]
10	11	H	H	H	2	TFE[d]	18	43	-

[a] Standard photolysis conditions: substrate was dissolved in either freshly distilled methanol or trifluoroethanol at a concentration of ca. 2.5 mM, dry N_2 was passed through the resulting solution for 15 min then the reaction mixture was photolyzed in a quartz vessel at ambient temperature until starting material was consumed (1–3 h) using a Hanovia photoreactor equipped with a 450-W medium-pressure Hg lamp. [b] Isolated yields after chromatography or recrystallization. [c] 14–16% of methanol adducts also isolated as a mixture of stereo- and/or regioisomers. [d] TFE = trifluoroethanol. [e] Diastereomer ratios and overall yields dependent upon photolysis time due to selective destruction of minor isomer.



(1)

To date, successful nucleophilic interception of the zwitterion has been limited to cases where the 4-pyrone substrate is photolyzed as a dilute solution in methanol or water, a requirement of the relative efficiency of bimolecular trapping vs unimolecular rearrangement. Thus, the use of a more synthetically versatile intermolecular trap is limited by its UV transparency and availability in sufficient quantity to serve as the solvent. We envisioned that attachment of the appropriate nucleophilic moiety to the photosubstrates via a short tether might obviate this rather serious practical limitation, while simultaneously allowing for the formation of a second, strategically valuble heterocyclic ring in the photoproduct (eq 2). We report here the initial results of our intramolecular trapping experiments with pendant hydroxylic moieties.



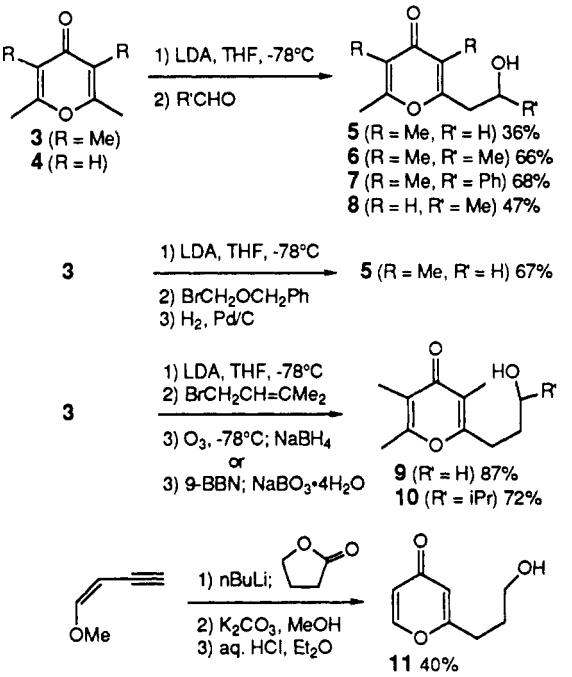
(2)

Substrates were generally prepared by deprotonation of the acidic methyl group at position 2 on intact pyrones 3[6a] or 4[6b] followed by either aldehyde condensation or alkylation/oxidation sequences (Scheme I). In the case of monosubstituted pyrone 11, a variation of the procedure of Crimmins and Bankaitis using 1-methoxy-1-buten-3-yne and butyrolactone proved to be most effective.[7]

Initial photolyses of 5–7 were carried out through quartz[8] in methanol solution both to allow a qualitative evaluation of the relative efficiency of intramolecular trapping vs the known solvent trapping reaction and to access products of the zwitterion pathway at a reasonable rate.[9] In the event, we observed efficient consumption of starting 4-pyrones and a marked preference in favor of the bicyclic intramolecular adducts in the range of 3.8:1 to 5:1 (Table I). In those cases which showed significant quantities of solvent trapping (entries 1, 3, and 5), changing the solvent from methanol to the much less nucleophilic trifluoroethanol completely suppressed the formation of intermolecular adducts. Subsequent runs (entries 7–10) were routinely carried out in trifluoroethanol.

It should be noted that ring closure to form 6-membered bicyclic ethers (entries 8–10) is at least as efficient as 5-ring

Scheme I



(6) (a) Letsinger, R. L.; Jamison, J. D. *J. Am. Chem. Soc.* **1961**, *83*, 193. (b) Available from the Aldrich Chemical Co.

(7) (a) Crimmins, M. T.; O'Mahony, R. *J. Org. Chem.* **1989**, *54*, 1157. (b) Crimmins, M. T.; Bankaitis, D. M. *Tetrahedron Lett.* **1983**, *24*, 4551.

(8) The measured λ_{max} values for 5–11 were 258–274 nm, with the more highly substituted pyrones 5–7 and 9–10 showing the expected bathochromic shift (av λ_{max} = 269 nm) vs lightly substituted substrates 8 and 11 (av λ_{max} = 259 nm). See the supplementary material for individual values.

(9) We and others[1,2] have observed a significant dependance upon solvent polarity for effective partitioning through the zwitterion pathway.

formation. Moreover, photolyses of substrates lacking alkyl substituents at positions 3 and 5 (entries 7 and 10) were observed to proceed nearly as well as the more highly substituted 4-pyrones. Previous studies had indicated the need for electron-releasing alkyl substituents for both efficient partitioning into the zwitterion manifold and effective nucleophilic capture relative to rearrangement to 2-pyrone.[10] The successful conversion of **8** and **11** into the typical bicyclic photoproducts implies a promising generality of this new reaction. Also of interest is the observation that for at least two substrates, extended photolysis time results in selective destruction of the minor diastereomer (entries 4 and 9).[11] Issues which remain to be addressed in future work include the mechanism and products of this decomposition pathway, the factors which influence diastereoselectivity of the initial closure of excited 4-pyrone to zwitterion, applicability to other tether lengths and other possible pendant nucleophiles.

(10) Electron-releasing substituents at positions 3 and 5 were presumed necessary to confer stability to the electron-deficient allyl cation portion of the zwitterion.[1]

(11) In most cases, the bicyclic cyclopentenone ether products are effectively inert to photolysis during the relatively short (1-3 h) time required for efficient conversion of starting material.

In summary, we have reported a significant new class of synthetic transformations based upon the efficient intramolecular trapping of a photogenerated oxyallyl zwitterion by a nearby hydroxyl moiety. The net conversion of planar heterocyclic 4-pyrone precursors to bicyclic cyclopentenone ethers represents a striking bond reorganization and increase in molecular complexity, providing possible access to a variety of cyclopentanoid targets. Further elaboration of this class of transformations is currently underway in our laboratories.

Acknowledgment. We thank Professor Michael Crimmins for helpful discussions. We also gratefully acknowledge partial support from the University of Utah Research Committee and the American Cancer Society Institutional Research Grant no. IN-178, as well as National Science Foundation Grants CHE-8100424 and CHE-8310031 for funds used for the purchase of departmental mass spectroscopy facilities.

Supplementary Material Available: Representative procedures for the preparation of substrates **7** and **9** and photolysis of **6**, along with physical data for compounds **5**-**18** (7 pages). Ordering information is given on any current masthead page.

Synthesis of the Lichen Metabolite (+)-Bourgeanic Acid and Conformational Analysis of Its Dilactone

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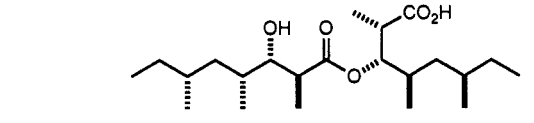
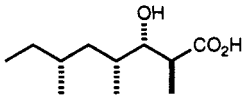
Summary: An enantiospecific synthesis of the depside (+)-bourgeanic acid via (-)-hemibourgeanic acid defines the latter as (2*S*,3*S*,4*R*,6*R*)-3-hydroxy-2,4,6-trimethyloctanoic acid and the former as its self-esterification product. Conformational analysis of the dilactone derived from bourgeanic acid shows that the eight-membered ring adopts a crown conformation with C_2 symmetry and all substituents in equatorial orientation.

The structure of (+)-bourgeanic acid (**1**), an aliphatic depside isolated from species of the lichen *Ramalina*,[1] was deduced by Bodo as the esterification product of two molecules of 3-hydroxy-2,4,6-trimethyloctanoic acid.[1,2] Saponification of **1** gave (-)-hemibourgeanic acid (**2**), the absolute configuration of which was proposed on the basis of an X-ray crystallographic analysis of its *p*-bromophenacyl ester.[3] An interesting property of **1**, noted by Bodo,[2] is the formation of an eight-membered dilactone **3** under mild dehydrating conditions.

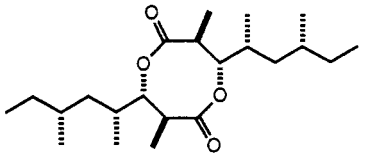
We now describe the first enantioselective synthesis of **1** and offer a rationale for its facile conversion to **3**. A signficant obstacle en route to **1** was self-esterification of the sterically hindered hemibourgeanic acid, for which a solution was devised through the β-lactone derivative of **2**.



1



2



3

Using methodology developed independently by Evans[4] and Sonnet,[5] the dilithio enolate of (2*S*)-1-propionyl-2-pyrrolidinemethanol (**4**) was alkylated with (2*R*)-1-iodo-2-methylbutane (**5**)[6] to give amide **6** (Scheme I). Hydrolysis of **6** afforded (2*R*,4*R*)-2,4-dimethylhexanoic acid (**7**), which was reduced to the corresponding hexanol **9** via methyl ester **8**. Oxidation of **9** under Swern conditions[8] led cleanly to aldehyde **10**, which was characterized as its

(1) Bodo, B.; Hebrard, B.; Molho, L.; Molho, D. *Tetrahedron Lett.* **1973**, 1631.

(2) Bodo, B.; *Bull. Mus. Natn. Hist. Nat., Paris*, 3ème sér. **1975**, *349*, 23.

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(4) Evans, D. A.; Takacs, J. M. *Tetrahedron Lett.* **1980**, *21*, 4233.

(5) Sonnet, P. E.; Heath, R. R. *J. Org. Chem.* **1980**, *45*, 3137.

(6) The iodide **5** was prepared from methyl (2*S*)-3-(benzyloxy)-2-methylpropionate[7] via (a) reduction ($LiAlH_4$, Et_2O, 98%); (b) bromination of the resulting alcohol (NBS, Ph_3P, CH_2Cl_2, 92%); (c) methylation ($Me_2Cu(CN)Li$, THF-Et_2O, -78 °C → -20 °C, 87%); (d) hydrogenolysis (H_2, 1 atm, 10% Pd-C, THF) followed by tosylation (*p*-TsCl, pyridine, 87%); and (e) displacement by iodide (NaI, acetone, reflux, 81%).

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