

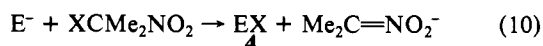
Table I. Yields of RCOCH(R')CMe<sub>2</sub>NO<sub>2</sub> (1), RCOC(R')=CMe<sub>2</sub> (2), [RCOCH(R')]<sub>2</sub> (3), and RCOCH(R')X (4) from the Reaction of RC(OLi)=CHR' and XMe<sub>2</sub>C=NO<sub>2</sub> in THF-Hexane (60:40)<sup>a</sup>

R, R'	X	conditions <sup>b</sup>	yield, %				(1 + 2)/3
			1 <sup>c</sup>	2 <sup>c</sup>	3 <sup>c</sup>	4 <sup>c</sup>	
<i>t</i> -Bu, H	Cl <sup>d</sup>	3 h	0, 0 <sup>e</sup>	72, 6 <sup>e</sup>	<5, 2 <sup>e</sup>	0, 0 <sup>e</sup>	>14
<i>t</i> -Bu, H	NO <sub>2</sub> <sup>d</sup>	3 h	0, 0 <sup>e</sup> , 0 <sup>f</sup>	20, 7 <sup>e</sup> , 25 <sup>f</sup>	30, 9 <sup>e</sup> , 27 <sup>f</sup>	15, 16 <sup>e</sup> , 13 <sup>f</sup>	0.7, 0.9 <sup>f</sup>
<i>t</i> -Bu, H	<i>p</i> -MePhSO <sub>2</sub> <sup>d</sup>	3 h	0	28	38	0	1.4
<i>t</i> -Bu, H	<i>p</i> -MePhSO <sub>2</sub> <sup>d</sup>	1.5 h, 13 vol % Me <sub>2</sub> SO	0, 0 <sup>f</sup>	45, 29 <sup>f</sup>	10, 6 <sup>f</sup>	0	4.5
<i>t</i> -Bu, H	<i>p</i> -MePhSO <sub>2</sub> <sup>d</sup>	1.5 h, 0 °C	25	10	48	0	0.8
Ph, H	Cl <sup>d</sup>	1 h, -20 °C, 13 vol % HMPA	0	97	0	0	∞
Ph, Me	Cl	1 h, 0-10 °C	70, 78 <sup>g</sup> , 66 <sup>h</sup>	0, 0 <sup>g</sup> , 0 <sup>h</sup>	23, 19 <sup>g</sup> , 22 <sup>h</sup>	0, 0 <sup>g</sup> , 0 <sup>h</sup>	3.0, 4.1 <sup>g</sup> , 3.0 <sup>h</sup>
Ph, Me	Cl	1 h	48, 0 <sup>e</sup>	0, 0 <sup>e</sup>	37, 0 <sup>e</sup>	0, 0 <sup>e</sup>	1.3
Ph, Me	Cl	1 h, 100% THF	50	0	28	0	1.8
Ph, Me	NO <sub>2</sub>	1 h	10	0	17	24	0.6
Ph, Me	<i>p</i> -MePhSO <sub>2</sub>	1 h	21, 26 <sup>g</sup> , 32 <sup>g,h</sup>	0, 0 <sup>g</sup> , 0 <sup>g,h</sup>	52, 47 <sup>g</sup> , 54 <sup>g,h</sup>	15, 5 <sup>g</sup> , 5 <sup>g,h</sup>	0.6, 0.4 <sup>g</sup> , 0.55 <sup>g,h</sup>
Ph, Me	Cl	1 h, 0 °C, 13 vol % HMPA	76, 52 <sup>f</sup> , 0 <sup>e</sup>	4, 11 <sup>f</sup> , 0 <sup>e</sup>	12, 14 <sup>f</sup> , 0 <sup>e</sup>	0, 0 <sup>f</sup> , 0 <sup>e</sup>	6.6, 4.0 <sup>f</sup>
Ph, Me	Cl	15 min, 0-10 °C, 13 vol % Me <sub>2</sub> SO	48	7	11	0	5.0
Ph, Me	Cl	1 h, 35 °C, 13 vol % Me <sub>2</sub> SO	28	21	13	0	3.8
Ph, Me	Cl	8 min, 30 °C, K <sup>+</sup> in Me <sub>2</sub> SO	0	7	31	0	0.2
Ph, Me	Cl	1 h, 5 °C, HMPA	0	5	31	0	0.2
Ph, Et	Cl	1 h, -10-0 °C, 13 vol % HMPA	73	0	13	0	5.6
Ph, <i>i</i> -Pr	Cl	1 h	4, 8 <sup>i</sup> , 0 <sup>e</sup>	0, 0 <sup>i</sup> , 0 <sup>e</sup>	66, 69 <sup>i</sup> , 0 <sup>e</sup>	0, 0 <sup>i</sup> , 0 <sup>e</sup>	0.06, 0.1 <sup>i</sup>
Ph, <i>i</i> -Pr	Cl	1 h, 0-10 °C, 13 vol % HMPA	35, 29 <sup>f</sup> , 25 <sup>h</sup>	0, 0 <sup>f</sup> , 0 <sup>h</sup>	42, 42 <sup>f</sup> , 37 <sup>h</sup>	1.5, 4 <sup>f</sup> , 7 <sup>h</sup>	0.8, 0.7 <sup>f</sup> , 0.7 <sup>h</sup>
Ph, <i>i</i> -Pr	Cl	1 h, 0 °C, 13 vol % Me <sub>2</sub> SO	24, 0 <sup>e</sup>	0, 0 <sup>e</sup>	32, 0 <sup>e</sup>	8.5, 29 <sup>e</sup>	0.8
Ph, <i>i</i> -Pr	Cl	1 h, 10 °C, 38 vol % Me <sub>2</sub> SO	16, 0 <sup>e</sup>	0, 0 <sup>e</sup>	23, 0 <sup>e</sup>	20, 44 <sup>e</sup>	0.7
Ph, <i>i</i> -Pr	Cl	1 h, 35 °C, K <sup>+</sup> in Me <sub>2</sub> SO	2, 0 <sup>e</sup>	0, 0 <sup>e</sup>	25, 0 <sup>e</sup>	18, 30 <sup>e</sup>	0.05
Ph, <i>i</i> -Pr	Cl	1 h, 5 °C, HMPA	0	0	0	44	-
Ph, Ph	Cl	3 h, 35 °C	<2, 0 <sup>e</sup>	0, 0 <sup>e</sup>	66, 0 <sup>e</sup>	0, 0 <sup>e</sup>	<0.02

<sup>a</sup> Satisfactory elemental analysis, <sup>1</sup>H NMR spectra and high resolution MS were obtained for all new compounds. The known dimers 3 isolated as the *meso*, *dl* mixtures, or as the pure isomers were demonstrated to be symmetrical dimers by <sup>1</sup>H NMR and my comparison with literature data. <sup>b</sup> Five millimoles of (*i*-Pr)<sub>2</sub>NH and 5 mL of THF were added to 5 mmol of *n*-BuLi in hexane (3.2 mL) at -40 °C. The solution was warmed to 0 °C, cooled to -20 °C, and the ketone added dropwise to give a solution ~0.5 M in E<sup>-</sup>. Additional reagents were added at 0 or 25 °C and the solutions irradiated with a 275-W sunlamp which in the absence of cooling maintained a reaction temperature of 35 °C. Unless otherwise indicated the molar ratio of E<sup>-</sup> to XMe<sub>2</sub>C=NO<sub>2</sub> was 1:1. <sup>c</sup> Based on <sup>1</sup>H NMR. For reactions with E<sup>-</sup>/XMe<sub>2</sub>C=NO<sub>2</sub> = 2, yields are based on the theoretical formation of 1 mol of product per mol of XMe<sub>2</sub>C=NO<sub>2</sub>. With E<sup>-</sup>/XMe<sub>2</sub>C=NO<sub>2</sub> ≤ 1, yields are based on the theoretical formation of 1 mol of 1, 2, or 4 and 0.5 mol of 3 per mol of E<sup>-</sup>. <sup>d</sup> Molar ratio E<sup>-</sup>/XMe<sub>2</sub>C=NO<sub>2</sub> = 2:1. <sup>e</sup> 0.05 M (*t*-Bu)<sub>2</sub>NO<sub>2</sub>, 25 °C, no irradiation. <sup>f</sup> 0.15 M Me<sub>2</sub>C=NO<sub>2</sub>Li. <sup>g</sup> Diluted 5-fold with THF. <sup>h</sup> Molar ratio E<sup>-</sup>/XMe<sub>2</sub>C=NO<sub>2</sub> = 1:2. <sup>i</sup> 0.5 M 12-crown-4-ether.

unimolecular and bimolecular reactions of XMe<sub>2</sub>C=NO<sub>2</sub><sup>-</sup>. However, the effect of X on the ratio 1/3 is easily explained if reactions (1) and (2) have merged and competition occurs as shown in Scheme I. Reaction of XMe<sub>2</sub>C=NO<sub>2</sub><sup>-</sup> with E<sup>-</sup> to form 1<sup>-</sup> or E<sup>-</sup> predicts that the ratio 1/3 should depend on the structure of X. However, the mechanism by which E<sup>-</sup> replaces X at a tetrasubstituted carbon atom is puzzling. Perhaps the formation of 1 and 3 involves a common intermediate distinct from free O<sub>2</sub>NCMe<sub>2</sub><sup>-</sup>. Electron transfer from E<sup>-</sup> to XMe<sub>2</sub>C=NO<sub>2</sub><sup>-</sup> would almost certainly be dissociative and the cage intermediate, [E<sup>-</sup> X<sup>-</sup> Me<sub>2</sub>C=NO<sub>2</sub>], is a possibility. Escape of E<sup>-</sup> from the cage would lead to 3 via reaction 7, while coupling of E<sup>-</sup> and Me<sub>2</sub>C=NO<sub>2</sub><sup>-</sup> in the cage would lead to 1<sup>-</sup>. It appears that as the ease of one-electron donation from the anion increases [e.g., from MeC(CO<sub>2</sub>Et)<sub>2</sub><sup>-</sup> to PhC(O<sup>-</sup>)=CHR'], the chain reaction involved shifts from one involving discrete step, (1)-(3), to a process in which reactions (1) and (2) are no longer distinct.

The competition between reactions 4 and 5 depends upon counterion and solvent (see Table I). For PhC(OLi)=CH-*i*-Pr the ratio 1/3 passes through a maximum as Me<sub>2</sub>SO or HMPA is added to the THF-hexane solvent. In 100% Me<sub>2</sub>SO or HMPA the ratio 1/3 is quite low for secondary enolate anions, perhaps reflecting that free monoenolate anions react with XMe<sub>2</sub>C=NO<sub>2</sub><sup>-</sup> or O<sub>2</sub>NCMe<sub>2</sub><sup>-</sup> to yield mainly E<sup>-</sup>. As Me<sub>2</sub>SO or HMPA is added to the THF-hexane solvent system, the E<sub>2</sub> elimination of HNO<sub>2</sub> from 1 becomes important, particularly at higher temperatures (Table I). With primary enolate anions it is difficult to prevent this reaction, and experiments with these anions were performed by using 2 equiv of E<sup>-</sup> to maximize the yield of 2. In solvents containing Me<sub>2</sub>SO or HMPA, chlorine atom or nitro group transfer occurs (reaction 10). Reaction 10 was observed in the



presence or absence of radical chain inhibitors, and from inhibited

experiments it is clear that 4 is not converted to 3 by an S<sub>N</sub>2 displacement.<sup>10</sup>

(10) The source of PhCOCH(Me)SO<sub>2</sub>PhMe-*p* mentioned in Table I is not clear, but it may involve the attack of E<sup>-</sup> on *p*-MePhSO<sub>2</sub><sup>-</sup>.

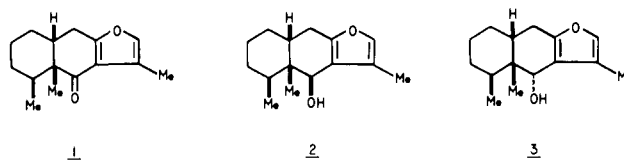
### Bis Heteroannulation. 3. Facile Syntheses of (±)-Ligularone and (±)-Petasalbine

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Ligularone (1) and petasalbine (2) are furanoeremophilanes isolated from the rhizomes of the *Ligularia* and *Petasites* genus of plants.<sup>1</sup> These same species produce at least 10 other com-

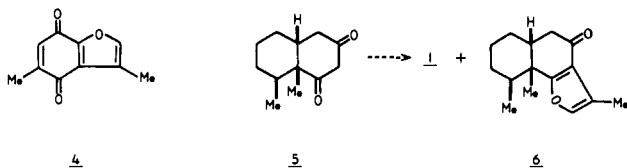


pounds having the basic skeleton of the furanoeremophilanes,<sup>1b</sup>

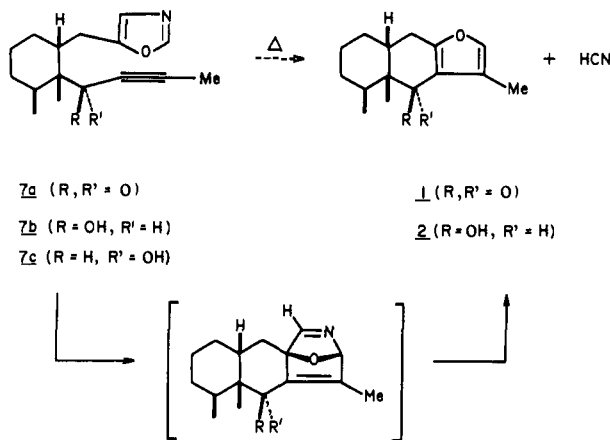
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and this observation has led to considerable interest in the development of synthetic routes to this class of sesquiterpenes.

The published work in this area has covered a variety of different approaches,<sup>2</sup> but frequently there is little control over regiochemical features throughout the course of the syntheses. Intermediate **5**, for example, gave ~10% of **1** along with 22% of isoligularone (**6**) in the final steps of the synthesis.<sup>2c</sup> Similar



difficulties were encountered in the elaboration of intermediate **4** via a Diels–Alder strategy.<sup>2a,b</sup> In view of these results we have developed an alternative route to the furanosesesquiterpenes which involves a process we have loosely termed as “bis heteroannulation”.<sup>4</sup> In this paper we describe a facile synthesis of intermediate **7a** and its high yield conversion to ligularone (**1**). Since **1** has previously been converted to petasalbine (**2**),<sup>3</sup> this work



also constitutes a formal total synthesis of **2**. In addition, however, we have further demonstrated that **7b** is readily converted to **2**. Although **7b** was not obtained in a highly stereoselective fashion, this latter conversion, in particular, further illustrates the extraordinary reactivity of the oxazoles in Diels–Alder reactions.<sup>5</sup>

The key intermediate for our synthesis of **7a** was the lactone derivative **11a**, and this material was readily derived via a Bayer–Villiger oxidation of perhydroindanone **9** (Scheme I). Selectivity in this reaction is presumably due to a relief of eclipsing interactions involving the substituents at C<sub>2</sub>, C<sub>3</sub> and C<sub>3a</sub> (cf. **10**): Migration in the desired sense (*path a*) would remove these interactions in the transition state leading to **11a**, while migration in the opposite sense (*path b*) would not. Once in hand, the desired conversion of **11a** to the acetylenic oxazole **7a** followed in a straightforward fashion as illustrated in Scheme II.<sup>8</sup> Thus, **11a**

was smoothly converted to the oxazole alcohol **12** through the use of a modified Schöllkopf reaction as previously described in our synthesis of evodone.<sup>4b,9</sup> This latter material was then cleanly oxidized<sup>10</sup> to the unstable aldehyde **13** which was directly condensed with lithiopropane to give a 55:45 mixture of the diastereomeric alcohols **7b** and **7c**. Oxidation of this mixture then gave a virtually quantitative yield of the single acetylenic ketone **7a**, and finally, **7a** gave a 92% yield of (±)-ligularone (**1**) upon refluxing in ethyl benzene (26 h).<sup>4</sup> The material thus obtained had identical NMR, IR, and UV spectral data as those reported for the naturally occurring substance,<sup>1c,11</sup> with further proof of the structure being provided by its conversion to epipetasalbine (**3**) following the published procedure.<sup>1c,3</sup>

In similar fashion acetylenic alcohol **7b** gave an 84% yield of (±)-petasalbine (**2**), whose <sup>1</sup>H NMR, <sup>13</sup>C NMR, and other spectral data were identical with those reported for the naturally occurring substance.<sup>1c,3,12</sup> Further proof of the structure was provided by conversion of synthetic **2** to both ligularone (**1**) and petasalbine acetate following the published procedures.<sup>1c</sup>

In many cases, we believe, the described procedures will represent the method of choice for the synthesis of furanosesesquiterpenes. Additional examples of this approach for the synthesis

(8) Physical and chemical properties for reported compounds. (a) **11a**: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.75 (d, 3 H, *J* = 7 Hz), 0.77 (s, 3 H), 1.19–1.75 (br m, 7 H), 1.83 (m, 1 H, collapsing to a triplet, *J* = 4 Hz, upon irradiation at 2.45), 2.45 (d, 2 H, *J* = 9 Hz, collapsing to a singlet upon irradiation at 1.83), 3.68 (d, 1 H, *J* = 11 Hz), 4.15 (d, 1 H, *J* = 11 Hz, collapsing to a singlet upon irradiation at 3.68); IR (CH<sub>2</sub>Cl<sub>2</sub>) 1740 cm<sup>-1</sup>; M<sup>+</sup> *m/e* 182; mp 31–32 °C for diastereomeric mixture. Anal. Calcd for C<sub>11</sub>H<sub>18</sub>O<sub>2</sub>: C, 72.49; H, 9.96. Found: C, 72.20; H, 9.75. (b) **12**: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.77 (d, 3 H, *J* = 7 Hz, collapsing to a singlet upon irradiation at 1.62), 0.94 (s, 3 H), 1.02–1.57 (br m, 6 H), 1.62 (m, 1 H, sharpens upon irradiation at 0.77), 1.88 (m, 1 H, sharpens upon irradiation at 2.60), 2.60 (dd, 1 H, *J* = 12, 15 Hz, collapsing to a doublet upon irradiation at either 1.88 or 2.86), 2.86 (dd, 1 H, *J* = 4, 15 Hz, collapsing to a doublet upon irradiation at either 1.88 or 2.60), 3.61 (m, 2 H, collapsing to two doublets, *J* = 11 Hz, upon addition of D<sub>2</sub>O), 6.76 (s, 1 H), 7.78 (s, 1 H); IR (CH<sub>2</sub>Cl<sub>2</sub>) 3635, 1510, 1480 cm<sup>-1</sup>; M<sup>+</sup> *m/e* 223; mp 74–75 °C. Anal. Calcd for C<sub>13</sub>H<sub>21</sub>NO<sub>2</sub>: C, 69.92; H, 9.48; N, 6.27. Found: C, 69.87; H, 9.63; N, 6.57. (c) **13**: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.85 (d, 3 H, *J* = 7 Hz, collapsing to a singlet upon irradiation at 2.06), 1.05 (s, 3 H), 1.08–1.64 (br m, 6 H), 1.91 (m, 1 H, sharpens upon irradiation at 2.74), 2.06 (m, 1 H, sharpens upon irradiation at 0.85), 2.74 (m, 2 H, collapsing to dd, *J* = 15 Hz, upon irradiation at 1.91), 6.78 (s, 1 H), 7.80 (s, 1 H), 9.61 (s, 1 H); IR (CH<sub>2</sub>Cl<sub>2</sub>) 2700, 1705, 1600, 1510 cm<sup>-1</sup>; M<sup>+</sup> *m/e* 221. (d) **7b**: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.78 (d, 3 H, *J* = 7 Hz, collapsing to a singlet upon irradiation at 1.91), 0.95 (s, 3 H), 1.01–1.73 (br m, 6 H), 1.75 (d, 3 H, *J* = 2.5 Hz, collapsing to a singlet upon irradiation at 4.38), 1.91 (m, 1 H, sharpens upon irradiation at 0.78), 1.98 (m, 1 H, sharpens upon irradiation at 3.17), 2.71 (dd, 1 H, *J* = 12, 15 Hz, collapsing to a doublet upon irradiation at either 1.98 or 3.17), 3.17 (dd, 1 H, *J* = 2, 15 Hz, collapsing to a doublet upon irradiation at either 1.98 or 2.71), 4.38 (br s, 1 H, sharpens upon irradiation at 1.75), 6.74 (s, 1 H), 7.77 (s, 1 H); IR (CH<sub>2</sub>Cl<sub>2</sub>) 3585, 2230, 1590, 1495 cm<sup>-1</sup>; M<sup>+</sup> *m/e* 261; mp 117–119 °C. Anal. Calcd for C<sub>16</sub>H<sub>23</sub>NO<sub>2</sub>: C, 73.53; H, 8.87; N, 5.36. Found: C, 73.28; H, 8.71; N, 5.10. (e) **7a**: <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 0.79 (d, 3 H, *J* = 7 Hz, collapsing to a singlet upon irradiation at 2.22), 1.02–1.60 (br m, 6 H), 1.21 (s, 3 H), 1.98 (s, 3 H), 2.06 (m, 1 H, sharpens upon irradiation at 2.79), 2.22 (m, 1 H, collapsing to dd, *J* = 4 Hz, upon irradiation at 0.79), 2.55 (dd, 1 H, *J* = 4, 15 Hz, collapsing to a doublet upon irradiation at either 2.06 or 2.79), 2.79 (dd, 1 H, *J* = 12, 15 Hz, collapsing to a doublet upon irradiation at either 2.06 or 2.55), 6.78 (s, 1 H), 7.78 (s, 1 H); IR (CH<sub>2</sub>Cl<sub>2</sub>) 2200, 1650, 1595, 1500 cm<sup>-1</sup>; M<sup>+</sup> *m/e* 259; bp 155 °C (0.002 mm). Anal. Calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>2</sub>: C, 74.10; H, 8.16; N, 5.40. Found: C, 73.99; H, 7.97; N, 5.20. (f) (±)-**1**: <sup>1</sup>H NMR, IR, and UV data identical with those reported;<sup>1c,11</sup> mp 70–71 °C (lit.<sup>2c</sup> mp 70.5–71 °C, synthetic; 64–65 °C, natural<sup>1c</sup>). (g) (±)-**3**: <sup>1</sup>H NMR and other spectral data identical with those reported;<sup>1c,3</sup> mp 69–70 °C (lit.<sup>1c</sup> mp 67–68 °C, naturally derived; synthetically derived (±)-**3** previously reported as an oil<sup>3</sup>). (h) (±)-**2**: <sup>1</sup>H NMR, <sup>13</sup>C NMR, and other spectral data identical with those reported for the naturally occurring substance;<sup>1c,3,12</sup> mp 73–74 °C (lit.<sup>1c</sup> mp 80–81 °C, natural; synthetically derived (±)-**2** previously reported as an oil<sup>3</sup>). (i) (±)-petasalbine acetate: <sup>1</sup>H NMR and other spectral data identical with those reported for the naturally derived substance;<sup>1c,11</sup> mp 33–34 °C (lit.<sup>1c</sup> mp 54–55 °C for the naturally derived substance).

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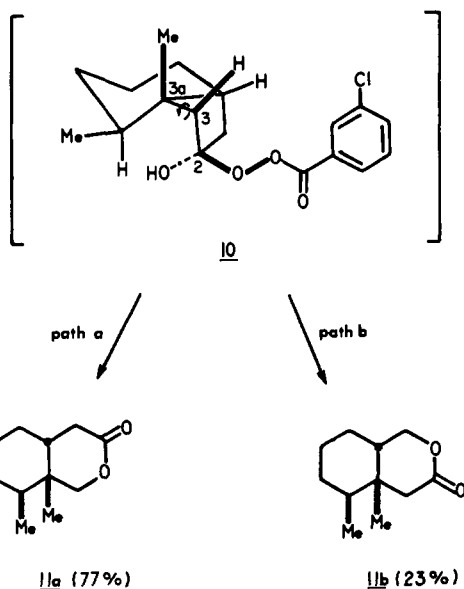
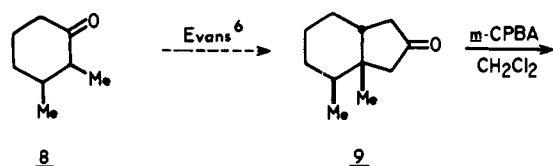
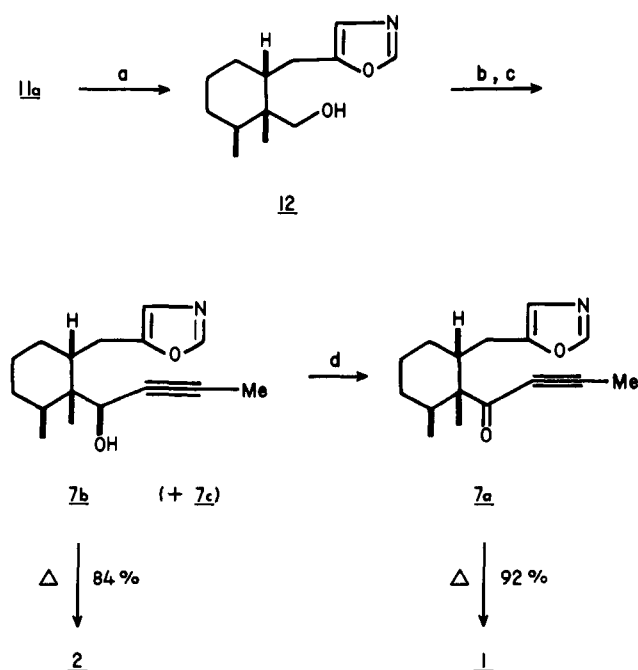
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(7) All yields refer to isolated and purified materials. All new compounds gave satisfactory elemental analyses and spectral data.<sup>8</sup> Yields have not been maximized.

Scheme I

Scheme II<sup>a</sup>

<sup>a</sup> (a)  $\text{LiCH}_2\text{NC}$ , THF, DMF, 51% yield. (b)  $\text{Me}_2\text{SO}$ ,  $(\text{COCl})_2$ , 99% yield. (c)  $\text{MeC}\equiv\text{Cl}$ , THF, 69% yield. (d)  $\text{Me}_2\text{SO}$ ,  $(\text{COCl})_2$ , 98% yield.

of highly oxygenated sesquiterpenes will be the subject of future communications.

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### High Enantioselectivity in Reductions with a Chiral Bis(NADH) Model Compound

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The stereospecificity in parallel with the remarkable rate enhancement under mild conditions which are available in enzyme reactions have attracted and prompted organic chemists interested in synthesis to simulate the enzymic stereospecificity apart from the rate acceleration.

In order to gain further insight into the detailed mechanism of the alcohol dehydrogenase catalyzed hydrogen transfer in vivo and also examine the potentiality of asymmetric reduction in nonenzymic synthesis, some simplified systems involving chiral 1,4-dihydronicotinamides as a coenzyme mimic have been devised, in which "biomimetic" asymmetric reductions have been developed with some measure of success.<sup>1</sup>

In the course of our studies on asymmetric reduction<sup>1f-j</sup> of activated carbonyls and carbon-carbon double bonds by the use of chiral 1,4-dihydronicotinamide (NAH) derivatives carrying polar groups in the chiral 3-carbamoyl moiety, we have found that one of the diastereotopic faces of dihydropyridine nucleus is specifically blocked in situ by the oxidized form NA through a charge-transfer interaction. This is further consolidated by the intermolecular chelation of intervening magnesium with the side chain hydroxyl groups of both nicotinamides, thus permitting an easier access of the substrate carbonyl to the unhindered face of dihydronicotinamide.<sup>1g</sup>

The exogenously orienting effect of the oxidized form which accumulated during the conversion was cogently supported by the stereochemical evidence<sup>1g</sup> and was in fact realized by the initial addition of the oxidized form NA as well as the external addition of either chiral or achiral aromatics capable of chelating and/or CT complexing.<sup>1f</sup>

On the basis of this rationale, it would be possible to effect the specific blockage of the dihydronicotinamide face more securely by means of an intramolecular device, eventually leading to much-improved asymmetric yields.

Thus designed and prepared are the novel chiral bis(NADH) model compounds whose intended  $C_2$  symmetry constrains the equivalent dihydropyridine nuclei to block the specific face of each other. In principle, this constitutes another advantage of the bis compounds over the corresponding mono derivatives ( $C_1$ ) in enantioselectivity.

In accord with the expectation, higher enantiomeric excess of the reduction products was obtained by the use of bis(NAH) 1, 2, and 3<sup>2</sup> involving L-prolinamide as the chirality-inducing center,

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