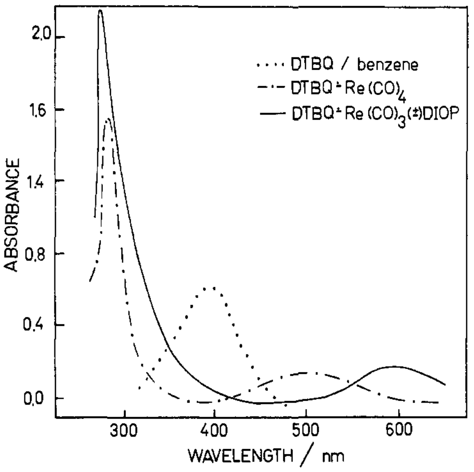

Figure 2. UV–visible absorption spectra of Q, $\mathrm{Q\dot{-}Re(CO)_4}$, and $\mathrm{Q\dot{-}Re(CO)_3}$–(±)-DIOP in benzene.

The assignment of the ESR parameters of the daughter radical $\mathrm{Q\dot{-}Re(CO)_3DIOP}$ is consistent with those reported for monosubstitution.[9] The g factor is 2.0010; $A_{\mathrm{Re}} = 37.4$ and $A_{\mathrm{P}} = 26.5$ G. Again, as expected, the two optically active daughter radicals, $\mathrm{Q\dot{-}Re(CO)_3}$–(+)-DIOP and $\mathrm{Q\dot{-}Re(CO)_3}$–(–)-DIOP, have the same ESR parameters as well as similar UV absorption spectra (Figure 2). In Figure 2 the visible band of the quinone ($\lambda_{\max} = 395$ nm) is shifted upon complexation to lower energy ($\lambda_{\max} = 505$ nm) which is shifted again ($\lambda_{\max} = 600$ nm) after ligand exchange with DIOP. These shifts are consistent with the explanation that the quinone π electrons are being delocalized onto the rhenium upon complexation and again onto the DIOP moiety upon exchange.

The measurement of the optical rotation for the optically active daughter radicals was carried out at 436 nm, since their absorption (Figure 2) in the 589-nm region (sodium line) would make it impossible to use the sodium line. The optical rotations as well as the specific rotation of the (±)-DIOP ligands were therefore also carried out at 436 nm and compared with those of the radicals (Table I). The results clearly establish the optical activity of the two daughter radicals. According to the Condon[15] formulation, the final result leading to the angle of rotation per unit length for dilute systems where the mean index of refraction is near unity is

$$\frac{\phi(k)}{l} = \frac{4\pi N\alpha k^2}{3mc}\sum_{n''}\frac{\mathrm{Im}(\langle g|\hat{R}|n''\rangle\langle n''|\hat{L}|g\rangle)}{k_{n''g}{}^2 - k^2} \tag{3}$$

Here, N is the number of molecules per unit volume, $\alpha = 1/137$, the fine structure constant, m, the electron mass, c, the velocity of light, and $k_{n''g}$ is related to the energy difference between an excited-state $|n''\rangle$ and the ground-state $|g\rangle$ by $E_{n''} - E_g = hck_{n''g}$. $\hat{R}$ and $\hat{L}$ are, respectively, the coordinate and orbital angular momentum operators for the molecule. It is expected that the energy difference between the excited and ground states for the radical systems is smaller than that of the DIOP ligand itself. The smaller specific rotation for the radical complexes would seem to suggest that the term $(\langle g|\hat{R}|n''\rangle\langle n''|\hat{L}|g\rangle)$ for the radical is also smaller than the corresponding term for the pure ligand. A further combined ESR, UV, OR, and ORD (optical rotary dispersion) study of stable optically active radicals should open up a new area for theoretical and physical examinations of the structure of these radical adducts. Currently, we have prepared some optically active quinones, such as *d*- or *l*-camphorquinone and used them as optically active spin traps for organometallic radicals. Some of these optically active quinone–organometallic radical adducts also exhibit interesting CIDEP (chemically induced dynamic electron polarization) phenomenon. A full account of further physical and chemical aspects of these unique optically active radical complexes will be published in the near future.

Acknowledgment. This research is supported by the National Sciences and Engineering Research Council of Canada and Queen's University. Delightful discussions with other members of our group, particularly Drs. Hutchinson and Depew and D. Weir, are cheerfully acknowledged.

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Total Synthesis of (±)-Pentalenolactone E Methyl Ester

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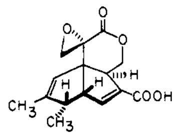
Following the discovery that various strains of *Streptomyces* produce pentalenolactone (**1**), an acidic lipophilic sesquiterpene possessing antibiotic properties,[1,2] have come a number of reports describing the isolation and characterization of several structurally related biosynthetic intermediates or shunt metabolites.[3,4] In contrast to **1**, however, these substances, e.g., pentalenolactone G (**2**), carry a *gem*-dimethyl moiety indicating that Wagner–Meerwein rearrangement has not yet been enzymatically implemented. During the course of recent biosynthetic experiments, Cane and Rossi treated the acidic fraction of an ether extract from *Streptomyces* UC5319 with diazomethane and obtained a new substance which they named pentalenolactone E methyl ester (**3**).[4a] Structural assignment to **3**, which is excreted (in acid form) into the fermentation broth during the early stages of growth prior to full production of **1**, was based on spectroscopic data. We now describe an expedient approach to this interesting tricyclic substance which confirms the original structural formulation.



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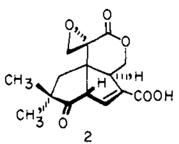

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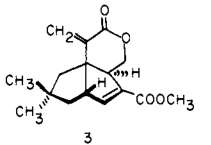

3

In a previous report[5] the basic principles of a new protocol for stereocontrolled lactone annulation was described. This scheme was used to transform the readily available keto ester **4** by controlled diisobutylaluminum hydride reduction and Claisen rearrangement to **5**. Following deketalization, chemospecific nucleophilic attack by methoxide ion at the aldehydo carbonyl can be achieved in methanol solution at room temperature. Intramolecular Michael addition of the alkoxide center within this intermediate to the proximal enone system delivers a single stereoisomer of **6**.

Our next concern was homologation of the carbonyl group in **6** to an α,β-unsaturated ester. During the course of initial experiments, it became clear that **6** was quite prone to retrograde (Grob) fragmentation in the presence of reasonably basic reagents

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(4) (a) Cane, D. E.; Rossi, T. *Tetrahedron Lett.* **1979**, 2973. (b) Cane, D. E.; Rossi, T.; Pachletko, J. P., in press.

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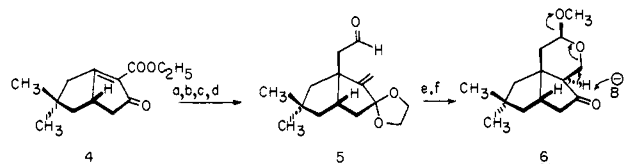
Chart I[a]

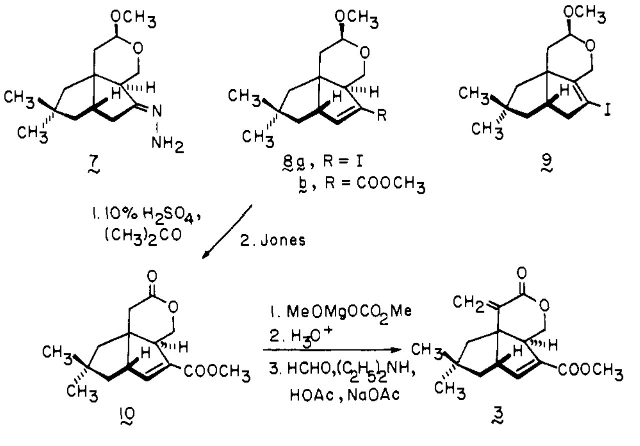


4 5 6

(a) HOCH$_2$CH$_2$OH, p-TsOH, C$_6$H$_6$. (b) (i-Bu)$_2$AlH, ether, −116 °C. (c) CH$_2$=CHOCH$_2$CH$_3$, Hg(OAc)$_2$. (d) decalin, 145–150 °C. (e) Py·HOTs, CH$_3$COCH$_3$, H$_2$O. (f) NaOCH$_3$ (catalytic), CH$_3$OH, 20 °C.

(see arrows). In view of the equatorial orientation of the methoxyl group, the resultant geometry is stereoelectronically appropriate for continuous overlap of the participating orbitals.[6] Furthermore, the adduct of **6** with trimethylsilyl cyanide is so disfavored in its equilibrium with the keto form that it proved not to be a serviceable intermediate. These complications were surmounted by heating **6** briefly with a solution of hydrazine hydrate in ethanol containing triethylamine. Oxidation of the resulting hydrazone (**7**, 95%) with iodine in the presence of trimethylamine (THF, 0°C)[8] provided in 74% yield a 2.2:1 mixture of the regioisomeric vinyl iodides **8a**[9] and **9**.[10] Although regiospecificity was not achieved in the formation of **8a**, extensive experimentation did reveal that trimethylamine reproducibly afforded the most favorable product ratio and that the relative distribution of vinyl iodides was more dependent upon the steric bulk of the base than its pK_a.[11] Chromatography on silica gel was successful in achieving separation of the positional isomers.

Reaction of **8a** with the nickel carbonyl–sodium methoxide reagent in methanol[12] gave rise in exceptionally high (93%) yield to methyl ester **8b** [IR (neat, cm^{-1}) 1720 and 1625; ^{1}H NMR (CDCl$_3$) δ 6.76 (br s, 1 H), 4.65 (t, J = 6.5 Hz, 1 H), 4.05 (B of ABX, J_{ab} = 12 Hz, J_{ax} = 7.5 Hz, 1 H), 3.70 (s, 3 H), 3.53–3.38 (m, 1 H) 3.33 (s, 3 H), 3.13–2.86 (m, 2 H), 1.9–1.1 (m, 6 H), and 1.03 (s, 6 H)] without any sign of double-bond equilibration or acetal destruction.



With the viability of our approach now on firm ground, attention turned to modification of the oxygen-containing ring. Unmasking of the lactone functionality was achieved uneventfully by sequential acidic hydrolysis in aqueous acetone solution and Jones oxidation (74% overall). Completion of the synthesis from **10**[13] was achieved in a straightforward manner. Because of the sterically encumbered nature of the methylene group α to the lactone carbonyl, tert-butoxybis(dimethylamino)methane[14] and its methoxy analogue proved ineffective in delivering the vinylogous amide. The need for more elevated temperatures was, however, conveniently and efficiently accommodated by methoxymagnesium carbonate[15] (large excess, 175 °C, 20 min). Subsequent treatment of the resulting lactonic acid with 37% formalin solution containing diethylamine, sodium acetate, and acetic acid[16] provided in 27% overall yield the target pentalenolactone E methyl ester, which was identical with the natural substance[17] by comparison of IR, ^{1}H NMR, and ^{13}C NMR spectra.

The concise, practical route reported here for the chemical synthesis of **3** can be expected to find application in other synthetic investigations, some of which we hope to report on in due course.

Acknowledgment. We are pleased to acknowledge the financial support of this research by the National Institutes of Health (GM-28468).

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[9] ^{1}H NMR (CDCl$_3$) δ 6.11 (s, 1 H), 4.56 (dd, J = 7 and 6 Hz, 1 H), 3.86–3.41 (m, 2 H), 3.35 (s, 3 H), 2.91–2.63 (m, 2 H), 1.80–1.13 (m, 6 H), 1.05 (s, 3 H), and 1.01 (s, 3 H).

[10] ^{1}H NMR (CDCl$_3$) δ 4.47 (dd, J = 8 and 3 Hz, 1 H), 4.35 (d, J = 12 Hz, 1 H), 3.98 ($^1/_2$ABX, J_{ab} = 12 Hz, J_{ax} = 2.5 Hz, 1 H), 3.45 (s, 3 H), 3.1–2.81 (m, 1 H), 2.66–2.33 (m, 2 H), 2.0–1.1 (m, 6 H), and 1.01 (s, 6 H).

[11] Some exemplary product ratios follow: (i-Pr)$_2$EtN, 1:0.75; Me$_2$NCH$_2$CH$_2$NMe$_2$, 2.22:1; Me$_2$N(C = NH)NMe$_2$, 1.6:1; 4-(dimethylamino)pyridine, 1.42:1; Et$_3$N, 1.38:1; pyridine, 1.38:1.

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[13] ^{1}H NMR (CDCl$_3$) δ 6.83 (br s, 1 H), 4.45 (d, J = 4 Hz, 2 H), 3.73 (s, 3 H), 3.30–2.96 (m, 2 H), 2.56 (s, 2 H), 2.05–1.18 (m, 4 H), 1.03 (s, 3 H), and 1.00 (s, 3 H).

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[16] Parker, W. L.; Johnson, F. *J. Org. Chem.* **1973**, *38*, 2489. For a later example of the use of this reagent, see ref 2b.

[17] We are grateful to Professor David Cane for kindly providing us with the authentic spectra of **3** as obtained from natural resources.

12-s-Cis—A Novel Conformation of Retinoids

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Vitamin A has been considered to exist in extended transoid conformation of the polyene chain with a 6-s-cis conformation andd slight loss of coplanarity between the 5,6 and 7,8 double bonds.[1] A similar conformation has been deduced for *trans*-[2–4] and 13-*cis*-retinal,[4,5] but the conformation of 11-*cis*-retinal was ambiguous past C-12. Thus, neither Becker and Grant[4] nor Rowan and Sykes[3] were able to conclude unequivocally whether the preferred conformation of the 12,13 single bond was s-trans, s-cis, out of the polyene plane, or freely rotating. In the course of our investigation of 12-(carbomethoxy)retinoic acid methyl ester isomers we had prepared the trans, 13-cis, 11-cis, and 11-cis,13-cis isomers (**1**–**4**). The latter diester **4** had been reported by Robeson and Cawley[6] who, on the basis of UV studies, had concluded that

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