solution at room temperature is a general phenomenon. Its observation depends on the values of $k_0$ and $k_g$, specifically, low values of $k_0$ and high values of $k_g$. These conditions are evidently satisfied by $Cr(NN)_3^{3+}$ and further studies are underway to define the structural and solution medium parameters that regulate these rate constants.

## References and Notes


(1) Financial support of this work by the National Science Foundation (Grant No. CHE76-21050), the Natural Sciences and Engineering Research Council of Canada, and the North Atlantic Treaty Organization (Grant No. 658) is gratefully acknowledged.
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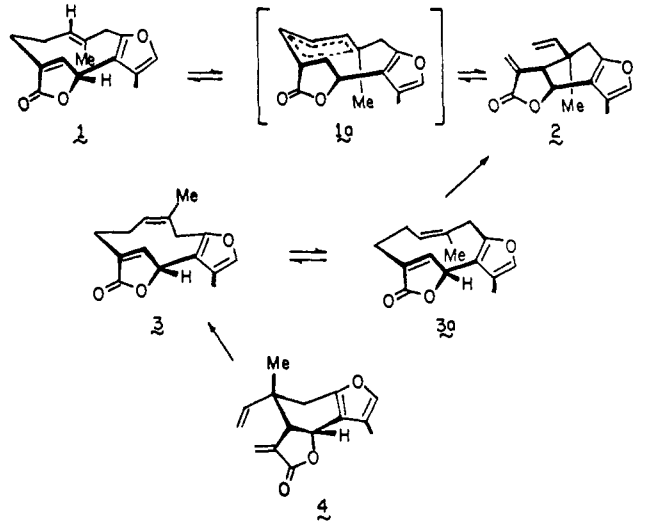
## Synthesis of (±)-Linderalactone, (±)-Isolinderalactone, and (±)-Neolinderalactone

*Sir:*

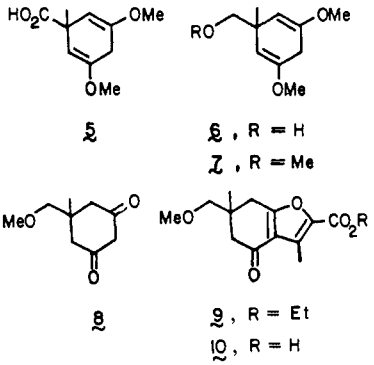
The germacrane furanosesquiterpenes, linderalactone (**1**), isolinderalactone (**2**),[1] and neolinderalactone (**3**)[2] were isolated by Takeda from the root of the shrub *Lindera strychnifolia* Vill. Their structures are based upon chemical degradation, and for linderalactone **1** an X-ray crystal structure is available.[3]



Linderalactone (**1**) has generated considerable interest because of its facile Cope rearrangement to isolinderalactone (**2**) (antipodal to the elemane sesquiterpenes); NOE studies have concluded that the stereochemical outcome of such rearrangements is dependent upon the conformation of the ten-membered ring.[4] Neolinderalactone exists at room temperature as a mixture of conformers **3** and **3a** in the ratio 4:1.[2b] Cope rearrangement of neolinderalactone gave isolinderalactone **2**, which therefore must proceed from the conformer **3a** rather than **3**.[4]

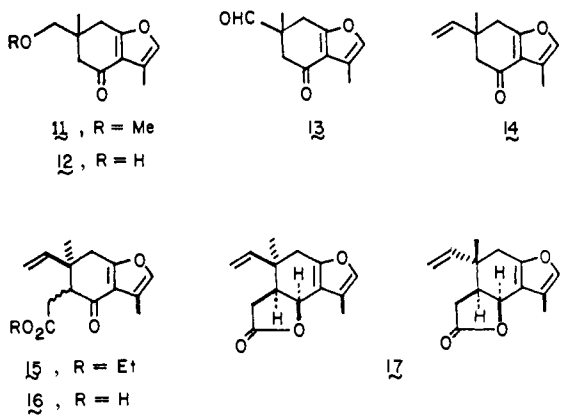
Here we report the total synthesis of **1, 2,** and **3** by an approach that, because of its strategy, does not need to rely upon any stereochemical or regiochemical controls.

Birch reduction of 3,5-dimethoxybenzoic acid and in situ alkylation with methyl iodide gave **5** (87%), which on treatment with lithium aluminium hydride gave the known alcohol **6**.[6]



After trying many protecting groups for the primary alcohol in **6**, and also attempting to avoid the use of protecting groups altogether, we converted **6** into the *O*-methyl ether **7** (NaH, MeI, THF), 95%.[7] Mild acid hydrolysis of **7** (4 N HCl, THF, 6 h at room temperature) gave the symmetrical β-diketone **8** (76%, mp 92–93 °C).[7] Condensation of **8** with ethyl 2-chloroacetoacetate in methanolic potassium hydroxide[8] gave the tetrasubstituted furan **9** (57%)[7] along with small amounts of the acid **10**. Because of the symmetry of **8** there are no regiochemical considerations in making **9**. The ester **9** was further hydrolyzed with methanolic potassium hydroxide to give pure **10**, mp 140–142 °C (85%). Decarboxylation of **10** proceeded best using the classical procedure Cu, pyridine, and diethylene glycol at 160–165 °C to give **11** (85%).[7] Demethylation of **11** using boron tribromide–dichloromethane −70 to +20 °C gave the alcohol **12** (96%),[7] which was oxidized directly to the aldehyde **13** using pyridinium chlorochromate (74%).[7] Methylenation of **13** using methylenetriphenylphosphorane in THF gave the vinyl derivative **14** (67% after bulb to bulb distillation).[7]

Introduction of the fused γ-lactone ring onto **14** poses no stereochemical problems since, as we will see, it does not matter if alkylation of **14** produces a mixture of epimers. Indeed it is



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desirable, since the stereochemical fates of subsequent reactions will lead inextricably to **1, 2,** and **3.**

Alkylation of **14** using lithium diisopropylamide in THF at −70 to −20 °C and quenching with ethyl bromoacetate gave **15** (82%)[7] as a mixture of epimers (~1:1 by NMR) at C-6.[9] Reduction of the C-7 carbonyl was achieved using sodium borohydride in 3 N NaOH–MeOH, and proceeded via the keto acid **16**,[7] to give the cis lactone **17** as a mixture of epimers at C-1 (60%). The epimeric lactones **17** appeared as a single compound on chromatography.

The mixture of epimeric lactones **17** was treated with lithium diisopropylamide in THF at −70 °C, followed by Eschenmoser's salt ($Me_2N^+CH_2I^-$),[10] and then warmed to 20 °C; workup with MeI followed by $Na_2CO_3$ gave the $\alpha$-methylene lactones isolinderalactone (**2**)[11] and *epi*-isolinderalactone (**4**). When the mixture of **2** and **4** was heated to 160 °C for a few minutes, **4** was irreversibly Cope rearranged into neolinderalactone (**3**), and **2** was reversibly Cope rearranged into linderalactone[11] (**1**). Prolonged heating at 260 °C slowly and irreversibly transformed neolinderalactone (**3**) into **2**[5] which again Cope rearranged to give linderalactone (**1**).[4] In this way the unnatural isomer **4** is in effect epimerized at the quaternary C-1 position through two Cope rearrangements, and consequently the synthesis leads to an equilibrium mixture of **1** and **2**.[2b,4]

In conclusion this first synthesis of the linderalactones **1, 2,** and **3** provides a unique opportunity to epimerize at a quaternary carbon atom using two Cope rearrangements, and thus avoid stereochemical considerations at C-1.

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(7) **7**: $\nu_{max}$ (thin film) 1695, 1664, 1205, 950, 905, 825 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.13 (3 H, s), 2.73 (2 H, br s), 3.10 (2 H, s), 3.33 (3 H, s), 3.55 (6 H, s) 4.50 (2 H, br s). **8**: $\nu_{max}$ ($CHCl_3$) 1705, 1610, 905 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.02 (3 H, S), 2.34 (2 H m), 2.54 (4 H, br s), 3.20 (5 H, s). **9**: $\nu_{max}$ (thin film) 2900, 1712, 1680, 1235, 1120, 1100 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.04 (3 H, s), 1.33 (3 H, t, $J$ = 7 Hz), 2.10–3.2 (4 H, m), 2.50 (3 H, s), 3.18 (2 H, s), 3.30 (3 H, s), 4.32 (2 H, q, $J$ = 7 Hz). **10**: $\nu_{max}$ ($CHCl_3$) 3200–2700, 1675 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.20 (3 H, s), 2.20–3.20 (4 H, m), 2.69 (3 H, s), 3.30 (2 H, s), 3.46 (3 H, s), 9.95 (1 H, br s). **11**: $\nu_{max}$ (thin film) 2910, 1674, 1420, 1100 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.20 (3 H, s), 2.30 (3 H, d, $J$ = 1.5 Hz), 2.49 (2 H, q, $J$ = 16 Hz), 2.88 (2 H, q, $J$ = 18 Hz), 3.31 (2 H, s), 3.43 (3 H, s), 7.18 (1 H, br s). **12**: $\nu_{max}$ (thin film) 3440, 1670, 1430, 1050 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.08 (3 H, s), 2.17 (3 H, d, $J$ = 1.5 Hz), 2.38 (1 H, br s, –OH), 2.40 (2 H, q, $J$ = 16 Hz), 2.79 (2 H, q, $J$ = 17 Hz), 3.47 (2 H, s), 7.08 (1 H, br s). **13**: $\nu_{max}$ ($CHCl_3$) 2720, 1738, 1680, 1440, 1075 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.25 (3 H, s), 2.12 (3 H, d, $J$ = 1.5 Hz), 2.58 (2 H, q, $J$ = 17 Hz), 2.95 (2 H, q, $J$ = 17 Hz), 7.03 (1 H, br s), 9.45 (1 H, s). **14**: $\nu_{max}$ (thin film) 3090, 2960, 1675, 1430, 1070, 920 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.15 (3 H, s), 2.12 (3 H, d, $J$ = 1.5 Hz), 2.41 (2 H, d) 2.78 (2 H, d), 4.90 (1 H, d, $J$ = 18 Hz), 4.70–6.0 (3 H, ABX, $J$ = 18, 10 Hz). **15**: $\nu_{max}$ (thin film) 3090, 1730, 1675 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 0.97 (3 H, s), 1.15 (3 H, s, epimers at C-1), 1.22 (3 H, t, $J$ = 7 Hz), 2.10 (3 H, d, $J$ = 1.5 Hz), 2.20–3.20 (5 H, m), 4.10 (2 H, q, $J$ = 7 Hz), 5.30–6.10 (3 H, m), 7.0 (1 H, br s). **16**: $\nu_{max}$ ($CHCl_3$) 3500–2600, 1710, 1670, 925 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.01 (3 H, s), 1.29 (3 H, s, epimers at C-1 (7:5)), 2.14 (3 H, d, $J$ = 1.5 Hz), 2.20–3.20 (5 H, m), 4.75–6.20 (3 H, m, two ABX systems), 7.10 (1 H, br s). **17**: $\nu_{max}$ ($CHCl_3$) 3090, 1770, 1638, 955 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 1.09 (3 H, br s), **1.99** (3 H, d, $J$ = 1.5 Hz), 2.1–3.0 (5 H, m), 4.85 (1 H, two triplets), 5.0–6.10 (3 H, two ABX systems), 7.0 (1 H, br s). **2** and **4**: $\nu_{max}$ ($CHCl_3$) 1759, 1635, 1265, 1144 cm$^{-1}$; NMR ($CDCl_3$) $\delta$ 0.98 (3 H, s assigned to **2**), 1.19 (3 H, s assigned to **4**), 2.02 (3 H, br s), 2.5–3.2 (3 H, m), 4.84 (1 H, m), 5.1–6.2 (4 H, m), 6.23 (1 H, dd, $J$ = 1.5 Hz), 7.03 (1 H, br s). All new compounds gave satisfactory microanalytical and/or accurate mass measurements.

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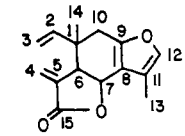

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(11) Linderalactone (**1**), isolinderalactone (**2**), and neolinderalactone (**3**) were readily (PLC) separated and identified. Comparison (TLC) of **1** and **2** was made with authentic samples kindly provided by Dr. Takeda. Spectra agreed with those reported,[1-3] and the Cope rearrangement[4] further demonstrated the identities of **1, 2,** and **3**.

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## Stereoelectronic Effects in the Reactions of Phosphate Diesters, Phosphoramidates, and Phosphonates. 3. Ab Initio Molecular Orbital Calculations of Transition States

*Sir:*

The hypothesis of stereoelectronic control in the reactions of tetracovalent carbon and phosphorus species and pentacovalent phosphoranes has recently received both experimental and theoretical support.[1-10] Deslongchamps[1] and co-workers have demonstrated selective cleavage of bonds which are antiperiplanar (app) to lone pairs on directly bonded oxygen and nitrogen atoms in tetrahedral carbon species. For phosphate ester hydrolysis Gorenstein et al.[8,9] have calculated reaction profiles and pentacovalent phosphorane transition-state energies which support a large stereoelectronic acceleration in the breaking of a P–O ester bond which is app to lone pairs on directly bonded oxygen atoms. In this communication we explore in further ab initio molecular orbital calculations the stereoelectronic effect on phosphorane transition states which do not have an app ester oxygen lone pair.

In an $S_N2(P)$ mechanism, the base-catalyzed hydrolysis of dimethyl phosphate, *O*-methyl-*N*-methyl phosphoramidate, and methyl ethylphosphonate (X = O, NH, or $CH_2$, respectively in eq 1) proceeds via transition states **1–3** shown in Figure 1.

$$CH_3O(CH_3X)PO_2^- + {}^-OH \rightarrow \underset{\textbf{1–3}}{CH_3O(CH_3X)PO_3H^{2-}} \rightarrow CH_3XPO_3H^- + CH_3O^- \quad (1)$$

Geometries for the two trigonal bipyramidal conformations t,g,−g and g,t,t shown were identical with the extensively optimized geometries for the dimethyl phosphoranes **1a** and **1b** previously calculated, except P–N, P–C, N–C, and C–C bond lengths of 1.740, 1.850, 1.40, and 1.48 Å, respectively, and a PNC bond angle of 115.3° were substituted where appropriate. In all cases a collinear $^-OH$ attack and $MeO^-$ leaving were assumed. The dimethyl phosphate reaction was shown to

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