tion clearly exemplify the decreased mobility attending an inverse temperature transition. The loss of segmental motion demonstrated by the transition in Figure 2, on the basis of previous secondary structural studies,[4] is reasonably taken to be due to the addition of a hydrogen bond between the Val_1 NH and the Gly_4 C-O, which as noted above occurs concomitantly with the Val_1 γ-CH_3-Pro_2 δ-CH_2 hydrophobic side-chain association.[6]

The proposed biological role of the inverse temperature transition in the elastin system is in the mechanism of elastic fiber formation and the transition is fundamental to the molecular pathology of vascular and pulmonary tissues. In the vascular wall, varices occur at lower temperatures (at the surface of the extremities) where fiber formation is impaired; and the elastic fiber, because it is a hydrophobic construct, is a primary site of lipid deposition.[14] In lungs challenged by toxic atmospheres, a proline hydroxylating enzyme system is activated which hydroxylates the repeat peptides of elastin[15] and impairs the hydrophobic association required in fiber formation.[16] The histological result in lungs is fragmented and nonfunctional elastic fibers. The specific role of the polytetrapeptide within the precursor protein is thought to be one of raising the temperature of fiber formation. Wherein the other repeat peptides undergo temperature transitions below 37 °C, addition of the polytetrapeptide raises the temperature to the physiological range.

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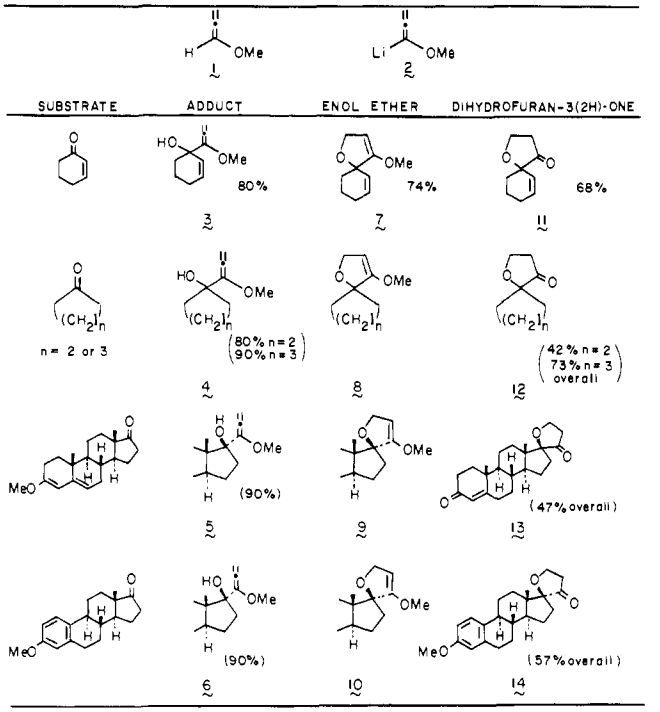
An Unusual New Allene Cyclization Reaction. Synthesis of Dihydrofuran-3(2*H*)-ones

Sir:

The readily available C_3 unit, methoxyallene[1] (**1**), has found a number of useful applications in organic synthesis over the past decade.[2] Our interest in β-acyl anion equivalents (homoenolates),[3] and the potential of **1** to serve in this capacity, decided us to examine some of the synthetic chemistry of **1**. Here are reported some unexpected and useful results from this investigation.

Deprotonation of methoxyallene in tetrahydrofuran at −78 °C using *n*-butyllithium gave the α-lithio-α-methoxyallene unit (**2**). Treatment of cyclohex-2-enone with **2** gave the 1,2 adduct **3** (see Table I). We were interested in either the alkoxide-accelerated [3,3]-sigmatropic shift[4] or the [1,3]-sigmatropic shift[5] of the adduct **3**. The terminal π orbitals of the allene are in the same plane as the cyclohexene π orbitals, and

Table I



[a] A typical experimental procedure is as follows. To a stirred solution of *n*-BuLi (27.7 mL, 1.6 M in hexane) in THF (20 mL) under N_2, at −78 °C, was added methoxyallene (3.0 g). The mixture was stirred for 0.5 h and 3-methoxyandrost-3,5-dien-17-one (4.29 g) in THF (5 mL) added. After stirring for 3 h at −78 °C, the mixture was worked up by quenching with saturated aqueous ammonium chloride solution, extraction (CH_2Cl_2), drying ($MgSO_4$), and evaporation which gave **5** (5.03 g, TLC, NMR, and IR show this material to be at least 95% pure). The adduct **5** (2.0 g) in dry *t*-BuOH (15 mL) was treated with KO-*t*-Bu (3.03 g) and dicyclohexyl-18-crown-6 (100 mg). The mixture was heated at reflux for 4 h. Workup by quenching in 6 N HCl (10 mL), extraction (CH_2Cl_2), drying ($MgSO_4$), evaporation, and chromatography of the residue over silica gel, eluting with ether–pentane (1:1), gave **13**, mp 167–168 °C (from MeOH–pentane) (0.86 g, 47%). [b] **3**: ν_{max}^{tf} 3440, 1954 cm^{-1}; τ 7.7–8.5 (6 H, m), 7.47 (1 H, s, D_2O, exchange), 6.58 (3 H, s), 4.53 (2 H, s), 4.28 (2 H, d). **4** (*n* = 2): ν_{max}^{tf} 3440, 1950 cm^{-1}; τ 8.22 (8 H, br s), 7.25 (1 H, s, D_2O, exchange), 6.58 (3 H, s), 4.53 (2 H, s). **4** (*n* = 3): ν_{max}^{tf} 3440 and 1950 cm^{-1}; τ 8.4 (10 H, br m), 7.25 (1 H, s, D_2O, exchange), 6.60 (3 H, s), 4.51 (2 H, s). **7**: ν_{max}^{tf} 1664 cm^{-1}; τ 7.9–8.4 (6 H, m), 6.5 (3 H, s), 5.58 (2 H, br s), 4.0–5.0 (3 H, m). **8** (*n* = 2): ν_{max}^{tf} 1668 cm^{-1}; τ 8.32 (8 H, s), 6.38 (3 H, s), 5.56 (3 H, s). **8** (*n* = 3): ν_{max}^{tf} 1665 cm^{-1}; τ 8.5 (10 H, m), 6.4 (3 H, s), 5.52 (3 H, s). **11**: bp 80 °C (0.75 mmHg); ν_{max}^{tf} 1750 and 1060 cm^{-1}; τ 8.48 (4 H, m), 8.06 (2 H, m), 7.58 (2 H, t, *J* = 8 Hz), 5.96 (2 H, t, *J* = 8 Hz), 4.73 (1 H, d, *J* = 11 Hz), 4.08 (1 H, m). **12** (*n* = 2): ν_{max}^{tf} 1750, 1060 cm^{-1}; τ 8.38 (8 H, s), 7.66 (2 H, t, *J* = 7 Hz), 6.06 (2 H, t, *J* = 7 Hz). **12** (*n* = 3): ν_{max}^{tf} 1750, 1060 cm^{-1}; τ 8.5 (10 H, m). 7.72 (2 H, t, *J* = 7 Hz), 6.08 (2 H, t, *J* = 7 Hz). **13**: mp 167–168 °C; ν_{max}^{Nujol} 1740, 1675, 1620, 1085, 1060, 885 cm^{-1}; τ 9.0 (3 H, s), 8.78 (3 H, s), 7.62 (4 H, m), 5.90 (2 H, t, *J* = 7 Hz), 4.28 (1 H, s), 8.0–8.8 (17 H, m); anal. C, H. **14**: mp 118–119 °C; ν_{max}^{Nujol} 1745, 1600, 1040 cm^{-1}; τ 9.1 (3 H, s), 8.9–8.0 (13 H, m), 7.57 (2 H, t, *J* = 7 Hz), 7.22 (2 H, m), 6.30 (3 H, s), 5.94 (2 H, t, *J* = 7 Hz), 3.48 (1 H, br s), 3.39 (1 H, d, *J* = 10 Hz), 2.92 (1 H, d, *J* = 10 Hz); anal. C, H.

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can participate in these modes of rearrangement. In the event when **3** was treated with potassium hydride in tetrahydrofuran at reflux, *no* reaction was apparent. Addition of dicyclohexyl-18-crown-6 to the above system caused a clean transformation of **3** into the enol ether **7:** ν_{max} 1664 cm^{-1}. Mild acid hydrolysis of **7** gave the spirodihydrofuran-3(2*H*)-one **11:** ν_{max} 1750 cm^{-1}; τ 8.48 (4 H, m), 8.06 (2 H, m), 7.58 (2 H, t, J = 8 Hz), 5.96 (2 H, t, J = 8 Hz), 4.73 (1 H, d, J = 11 Hz), 4.08 (1 H, m). It should be noted that we were unable to detect any products resulting from competitive [3,3]- or [1,3]-sigmatropic processes. It may well be that the [3.3]-sigmatropic process is precluded because the conformation of the cyclohexene ring does not allow good overlap of the orbitals required in the transition state leading to a [3.3] process.

Both cyclopentanone and cyclohexanone gave the adducts **4** (n = 2 and 3, respectively) when treated with **2**. Adduct **4** (n = 2) required 4 days in THF-KH-dicyclohexyl-18-crown-6 at reflux to accomplish the conversion into **8** (n = 2), while adduct **4** (n = 3) required only 12 h. The rate of the above reactions was considerably increased (to ~2 h) by conducting the cyclization in *t*-BuOH-*t*-BuOK-dicyclohexyl-18-crown-6 at reflux. Acid hydrolysis of **8** (n = 2 and 3) furnished the dihydrofuran-3(2*H*)-ones **12** (n = 2 and 3, respectively). A particularly interesting example of this new cyclization reaction is the conversion of 3-methoxyandrost-3,5-dien-17-one into the new class of 17-spiro steroid derivatives **13**,[6] in an overall yield of 47%. Estrone was converted through the same sequence into **14**, 57%.

In orbital terms a clear explanation is evident. The terminal π orbitals of the allene are orthogonal to the π orbitals of the enol ether portion of the allene system; consequently the developing negative charge at the central digonal carbon atom occurs in an orbital that is in the same plane as the methoxyl group, the required geometrical situation.[7]

Dihydrofuran-3(2*H*)-ones, while a comparatively simple functional array, are a somewhat rare class of compounds.[8] The muscarine alkaloids are virtually the only class of natural products that contain the dihydrofuran-3(2*H*)-one moiety.[9] The route described here offers the only method, at present, for converting a carbonyl group into a spiroannulated dihydrofuran-3(2*H*)-one. The examples on 17-keto steroids provide a unique functional array at 17 which has in itself further possibilities of elaboration.[10] From the point of view of carbohydrate synthesis, it is viable to view dihydrofuran-3(2*H*)-ones as deoxy sugars with the view to introducing functional groups at positions α and β to the carbonyl group.

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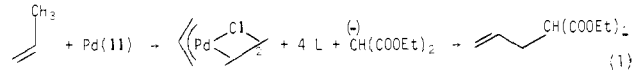
Palladium Catalyzed Allylic Alkylation of Olefins

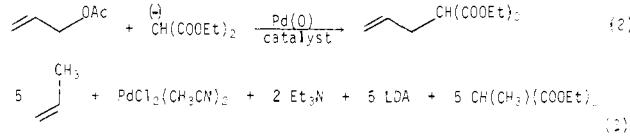
Sir:

Although allylic alkylation of π-allylpalladium halide complexes by stabilized carbanions in the presence of added ligands had been reported as early as 1965,[1] it has only been in the last few years that the process has been developed as a useful tool for organic synthesis.[2-15] The reaction can be carried out either stoichiometrically starting with an olefin and a Pd(II) complex (eq 1), or catalytically starting with allylic acetates and a Pd(0) complex (eq 2). In our studies of palla-



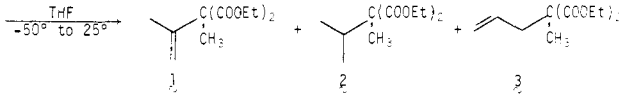
(1)

dium(II) assisted olefinic alkylations,[16] observations consistent with *direct catalytic allylic* alkylation of olefins were made and are summarized in eq 3. When olefin alkylation was car-



(2)

(3)



	1	2	3
5 h	90%	7%	0%
24 h	90%	7%	93%
42 h	90%	7%	180%

ried out using excess carbanion and excess amine, olefinic alkylation was complete and essentially quantitative after <4 h at 25 °C. On allowing the reaction mixture to stir for longer periods, *allylic* alkylation of the olefin was also observed. After 42 h there remained 97% olefinic alkylation products (**1, 2**) and 180% allylic alkylation product (**3**) (based on Pd), indicating that 2.8 mol of olefin reacted/mol of Pd. After 42 h, a considerable amount of metallic palladium was present, and no further reaction occurred. The same catalytic allylic alkylation of propene was observed using π-allylpalladium chloride as the palladium source. Thus treatment of 1 equiv of π-allylpalladium chloride with 10 equiv of triethylamine and then excess propene and $LiC(CH_3)(COOEt)_2$ (generated from

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