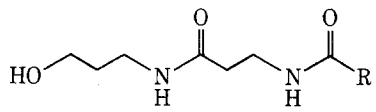

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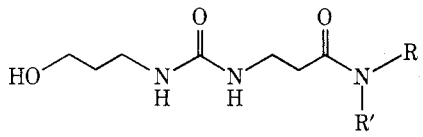

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phy of the diffusate on silica gel with a 7:2:1 mixture of 2-propanol–water–concentrated ammonia. Compound **9** was eluted between 3-aminopropanol and β-alanine and proved to be identical in all respects with synthetic **9** obtained by hydrolysis of **10** or by treatment of *N*-(3-hydroxypropyl)-β-phthalimidopropionamide [**11**, from β-alanine: (1) phthalic anhydride; (2) $ClCO_2Et$, Et_3N, 0°; (3) 3-aminopropanol], mp 166–167°, with hydrazine hydrate in EtOH (reflux) for 1 hr.[14]

The palytoxins are therefore substituted *N*-(3-hydroxypropyl)-*trans*-3-amidoacrylamides (**1**).

Acknowledgments. This work was supported by the U.S. Public Health Service. We are grateful to Lewis Cary and William Jankowski, Varian Associates, for determining the pmr and cmr spectra of Jamaican palytoxin.

Supplementary Material Available. The 300-MHz pmr spectrum of palytoxin from *Palythoa mammilosa* in 100% DMSO-d_6 will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.00 for photocopy or $2.50 for microfiche, referring to code number JOC-75-540.

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(7) The molecular weight of palytoxin from *P. toxica* was estimated to be 3300 and its molecular formula $C_{145}H_{264}N_4O_{78}$ from combustion and spectral (pmr and uv) data.[1]
(8) Carbon chemical shifts are reported in δ units (parts per million) relative to *p*-dioxane (δ 67.4 relative to Me_4Si) as an internal standard in D_2O.
(9) Only amide carbonyl absorption is observed in the infrared spectrum of palytoxin (see ref 1).
(10) Proton chemical shifts are reported in δ units (2 parts per million) relative to Me_4Si (δ 0) and the residual DMSO-d_5 peak (δ 2.52) as internal standards.
(11) P. F. Wiley, R. R. Herr, F. A. MacKellar, and A. D. Argoudelis, *J. Org. Chem.*, **30**, 2330 (1965).
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(13) Obtained from the Amicon Corp.
(14) All new compounds gave satisfactory elemental analyses.

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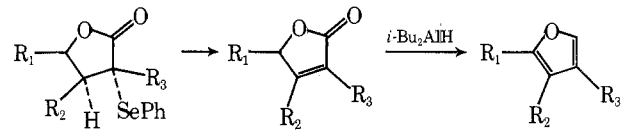
Organoselenium Chemistry. A General Furan Synthesis

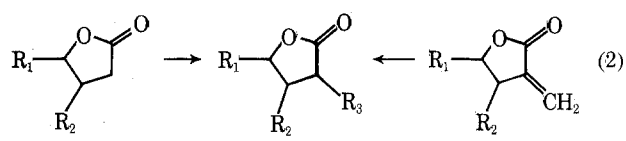
Summary: An efficient four-step synthesis of 2,4- and 2,3,4-substituted furans from γ-lactones *via* their corresponding butenolides is described.

Sir: The facile elimination of selenoxides derived from α-phenylselenenyl-γ-lactones with almost complete formation of endocyclic α,β-unsaturated butenolides suggested a general route to furans (eq 1).[1,2] We wish to report a gener-



I II III (1)

al method for the conversion of substituted γ-lactones into 2,4- and 2,3,4-substituted furans[3] *via* their corresponding butenolides (see Table I). The α-selenenylated γ-lactones of type I can be efficiently prepared by selenenylation of the corresponding α-substituted γ-lactones which are prepared by direct alkylation of lactone enolates[2,4] or by conjugate-addition of an organocopper reagent to an α-methylene-γ-lactone (eq 2).[5] The reaction sequence constitutes a



(2)

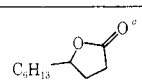
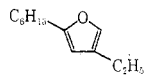
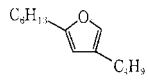
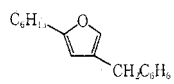
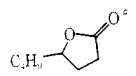
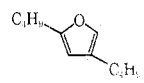
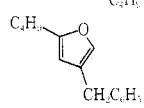
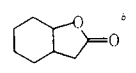
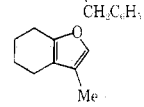
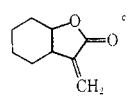
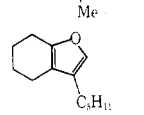
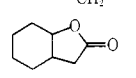
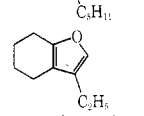
widely applicable method. As indicated in Table I, yields are generally high.

The method outlined above, however, is critically dependent upon only one of the two possible syn[6] modes of elimination predominating. α-Phenylselenenylated lactones have previously[2] been employed in the construction of fused α-methylene lactones with complete exclusion of the endocyclic double bond isomers.[7] We have observed, however, that selenoxides derived from I (R_3 = alkyl), in which there exists the possibility for two syn modes of elimination, result in >95% yield of the endocyclic olefin despite the statistical preference for exocyclic olefin formation. The high propensity for endocyclic olefin formation thus provides a useful $\Delta^{\alpha,\beta}$-butenolide synthesis as well as providing direct access to furans *via* reduction with diisobutylaluminum hydride[8] (see Table I).

A typical furan synthesis is illustrated below for the conversion of γ-decalactone[9] to 2-butyl-4-benzylfuran. The lithium enolate of γ-decalactone was prepared at −78° by slow addition (1 mmol/hr) of a solution of γ-decalactone (1 equiv, 1 *M* in THF) to a solution of lithium diisopropylamide (LDA) (1.05 equiv, 0.3 *M* in THF). After the mixture was stirred for 20 min, a solution of benzyl bromide (1.05 equiv, 1 *M* in THF) containing hexamethylphosphoramide (HMPA) (1.05 equiv) was added. The temperature was raised to *ca.* −40° and was maintained at that temperature for 3 hr. The reaction was quenched by the addition of 10% HCl and after usual work-up and chromatography on silica gel (hexanes/ether, 3:1) afforded α-benzyl-γ-decalactone (88%) [ir (film) 5.66 and 6.25 μ; nmr (CCl_4) δ 7.15 (s, 5 H), 4.18 (m, 1 H), 2.6–3.2 (m, 3 H)].

Selenenylation of α-benzyl-γ-decalactone was carried out by slowly adding (1 mmol/hr) a solution of the lactone (1.0 equiv, 1 *M* in THF) to a solution of LDA (1.1 equiv, 0.3 *M* in THF) cooled to −78°. After 20 min, the reaction mixture was treated with a solution of phenylselenenyl chlo-

Table I
Synthesis of 2,4- and 2,3,4-Substituted Furans

Example	Starting lactone	Yield[d] α-Alkylation	α-Phenylselenenylation	Elimination	Product	Yield[d] Reduction
1		72	70	80		88
2		60	80	98		75
3		88	72	85		99
4		70	72	99		84
5		98	83	85		99
6		90	88	95		66
7		99[e]	70	97		85
8		82	85	96		93

[a] See ref 9. [b] J. Klein, *J. Amer. Chem. Soc.*, 81, 3611(1959). [c] P. A. Grieco and N. Marinovic (unpublished results). [d] Yield represents pure compound isolated by chromatography; no attempt was made to optimize the yield. [e] Prepared by the addition of a solution of the α-methylene lactone (1.0 equiv, 0.25 *M* in THF) to a solution of lithium di-*n*-butylcopper (1.5 equiv, 0.15 *M* in THF) at −78°. After addition was complete, stirring was continued for 5.5 hr at −20°.[5]

ride[9] (1.1 equiv, 1 *M* in THF) containing HMPA (1.1 equiv). The temperature was maintained at −78° for 1 hr and −40° for 2 hr. Quenching with 10% HCl followed by usual work-up and purification on silica gel afforded a 72% yield of I ($R_1 = C_6H_{13}$, $R_2 = H$, $R_3 = CH_2C_6H_5$). To a solution of the above selenenylated lactone (1.0 equiv, 0.16 *M* in THF) at 0° containing a trace of acetic acid was added 30% hydrogen peroxide (*ca.* 6.0 equiv). After 30 min at 0°, the reaction was quenched by the addition of saturated $NaHCO_3$. Work-up afforded an 85% yield of butenolide II ($R_1 = C_6H_{13}$, $R_2 = H$, $R_3 = CH_2C_6H_5$) [ir (film) 5.71, 6.05, 6.24 μ; nmr (CCl_4) δ 7.18 (s, 5 H), 6.78 (m, 1 H), 4.75 (m, 1 H), 3.48 (t, J = 1 cps, 2 H)].

A solution of diisobutylaluminum hydride (DIBAL) (1.5 equiv, 0.5 *M* in THF) was added at −20° to a solution of the butenolide (1.0 equiv, 0.3 *M* in THF). After 3 hr at −20°, the reaction was quenched by the addition of 10% sulfuric acid and the reaction mixture was warmed to room temperature. Work-up afforded directly a 99% yield of III ($R_1 = C_6H_{13}$, $R_2 = H$, $R_3 = CH_2C_6H_5$) [nmr (CCl_4) δ 7.12 (s, 5 H), 6.90 (s, 1 H), 5.67 (s, 1 H), 3.60 (s, 2 H), 2.45 (t, 2 H)].

The high degree of endocyclic olefin formation during the elimination of the selenoxides derived from α-substituted α-selenenylated γ-lactones and the high degree of stereospecificity observed in the selenenylation of examples 6–8 associated with this approach to 3-substituted furans offers some advantages over existing methods.[3]

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References and Notes

(1) A report concerning the elimination of an α-phenylselenenylated γ-lactone with no alkyl group on the α carbon atom has been described by K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Amer. Chem. Soc.*, **95**, 6137 (1973). Also see H. J. Reich, I. L. Reich, and J. M. Renga, *ibid.*, **95**, 5813 (1973); D. L. J. Clive, *J. Chem. Soc., Chem. Commun.*, 695 (1973).
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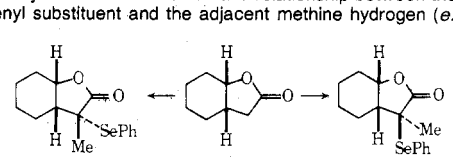
(7) This route to α-methylene lactones represents a special case in that the α-methyl and α-phenylselenenyl substituents were introduced stereospecifically so as to establish an anti relationship between the α-phenylselenenyl substituent and the adjacent methine hydrogen (*e.g.*, i → ii).



ii i iii

Likewise one can control the stereochemistry on the α carbon atom so as to establish a syn relationship between the α-selenenyl substituent and the adjacent methine hydrogen (*e.g.*, i → iii) (see ref 2).
(8) H. Minato and T. Nagasaki, *Chem. Ind. (London)*, 899 (1965).
(9) Commercially available from Aldrich.
(10) Fellow of the Alfred P. Sloan Foundation, 1974–1976.

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