ican Chemical Society. Professor M. Jones, Jr., provided helpful discussion.

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[19] National Institutes of Health Postdoctoral Fellow, 1969–1970.

[20] American Chemical Society–Petroleum Research Fund Fellow, 1968–1969; Ph.D. Thesis, Princeton University, 1970.

[21] Presented at the IUPAC Conference on Cycloaddition, Munich, Germany, Sept 1970.

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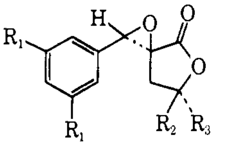
Darzens Condensation of α-Halolactones. Glycidic Lactones as Intermediates in Acetogenin Synthesis[1]

Sir:

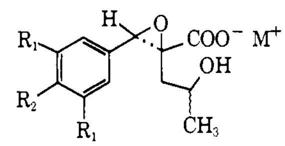
The development of methodology for synthesis of polyketide-derived natural systems has received much attention recently.[2] A major goal of these efforts remains the regulated elaboration of a ketide chain in open form and, toward this end, we have investigated procedures which would allow a homologation of the type $ArCHO \rightarrow ArCH_2COCH_2COCH_3$. We wish to report that condensation of an aromatic aldehyde with α-bromo-γ-valerolactone, and subsequent transformation of the resulting glycidic lactone, provides a convenient sequence for effecting this construction.[3]

The full scope of the method is presently under investigation but the following example is illustrative. Addition of an equimolar mixture of 3,5-dimethoxybenzaldehyde and α-bromo-γ-valerolactone (**1**, mixture of cis and trans) to a solution of potassium *tert*-butoxide in *tert*-butyl alcohol–tetrahydrofuran (3:1) (1 hr at 0°, 20 hr at 25°) gave epimeric lactones **2**[4] (mp 102–103°; ν_{max} 1780 cm^{-1}; nmr δ 1.33 (3 H, d, J = 6 Hz)) and **3** (mp 111–113.5°; ν_{max} 1780 cm^{-1}; nmr δ 1.46 (3 H, d, J = 6.5 Hz)) in 78% yield (ratio 3:1, respectively). Lactone **3** is converted to **2** through saponification–relactonization cycles and this observation, taken with the deshielded methyl group in **3**, provides the basis for stereochemical assignment. As has been previously noted in connection with the Darzens reaction of α-chloro esters,[5] condensation at the carbonyl group proceeds with high stereoselectivity. Saponification of the mixture of **2** and **3** with 3 M sodium hydroxide in ethanol–acetone afforded carboxylate **4** (84%) (mp 184–194° dec; ν_{max} 3400, 1600 (broad) cm^{-1}), which was irradiated (Hanovia 450-W lamp, Corex) in aqueous solution with provision for continuous removal of product by extraction into ether. After chromatography, hydroxy ketone **5** (62%) (ν_{max} 3600, 1710 cm^{-1}; nmr δ 1.14 (3 H, d, J = 6 Hz), 2.58 (2 H, d, J = 6 Hz), 3.1 (1 H, broad, exchanged with D_2O), 3.60 (2 H, s), 3.76 (6 H, s), 4.20 (1 H, m), and 6.36 (3 H, s)) was obtained[6] accompanied by the secondary photolysis product **6**.[7] Oxidation of **5** with Jones' reagent produced **7**,[8] characterized as the copper(II) chelate, mp 201–202°; **7** has recently been converted in four steps to the anthraquinonoid pigment endocrocin.[9]

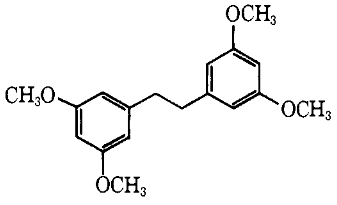
Alternatively, **5** was converted to the trans α,β-unsaturated ketone **8** (83%) (ν_{max} 1690 cm^{-1}; nmr δ 1.83 (3 H, d of d, J = 2, 6.5 Hz), 3.70 (2 H, s), 3.72 (6 H, s), 6.10 (1 H, d of d, J = 1.5, 16 Hz), 6.33 (3 H, s), and 6.85 (1 H, d of q, J = 6.5, 16 Hz)) *via* acetoxy ketone **9** followed by chromatography on alumina. Extension of this procedure to the synthesis of **10**, an intermediate of potential utility for construction of various, natural pyronoquinonoid systems,[10] and which has recently found use in the total synthesis of mitorubrin,[11] was realized by condensation of **1** with 3,5-dibenzoyloxy-4-methylbenzaldehyde[12] to give lactone **11** as a mixture of epimers. Saponification of **11** (0.3 M potassium hydroxide in ethanol–acetone) afforded the resorcinol **12** which, without purification, was photolyzed as described above to give **13**. Dehydration of the latter (acetic acid containing p-toluenesulfonic acid) furnished the trans α,β-unsaturated ketone **10**.[11]



2, $R_1 = OCH_3$; $R_2 = H$; $R_3 = CH_3$
3, $R_1 = OCH_3$; $R_2 = CH_3$; $R_3 = H$
15, $R_1 = R_2 = H$; $R_3 = CH_3$
16, $R_1 = R_3 = H$; $R_2 = CH_3$



4, $R_1 = OCH_3$; $R_2 = H$
12, $R_1 = OH$; $R_2 = CH_3$
14, $R_1 = R_2 = H$



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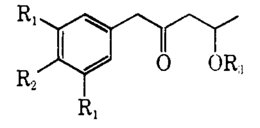

5, $R_1 = OCH_3$; $R_2 = R_3 = H$
9, $R_1 = OCH_3$; $R_2 = H$; $R_3 = Ac$
13, $R_1 = OH$; $R_2 = CH_3$; $R_3 = H$
18, $R_1 = R_2 = R_3 = H$

Photodecarboxylation of **14**, derived from the mixture of epimeric glycidic lactones **15** (mp 98–98.5°) and **16** (mp 150–151.5°), was excessively slow and, as an alternate route to the desired β-hydroxy ketone, **16** was

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[1] Presented in part at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968, Abstract P 170.

[2] T. Money, *Chem. Rev.*, 70, 553 (1970).

[3] M. S. Newman and B. J. Magerlein, *Org. React.*, 5, 413 (1949); M. Ballester, *Chem. Rev.*, 55, 283 (1955).

[4] Satisfactory elemental analyses were obtained for all new compounds.

[5] F. W. Bachelor and R. K. Bansal, *J. Org. Chem.*, 34, 3600 (1969).

[6] A mechanism has been proposed to account for formation of 5 [P. G. Sammes, *Quart. Rev., Chem. Soc.*, 24, 37 (1970)]. Our own (unpublished) and related observations [J. W. Chamberlin, *J. Org. Chem.*, 31, 1658 (1966)] support a process in which intramolecular energy transfer takes place from the initially excited aromatic nucleus to the carboxylate residue of 4 [for other examples, see C. Thiery, *Mol. Photochem.*, 2, 1 (1970), and references cited]. It has not been ascertained whether this transfer takes place from an electronically excited state, as implied by Sammes, or *via* a vibrationally excited ground state.

[7] B. K. Bullimore, J. F. W. McOmie, A. B. Turner, M. N. Galbraith, and W. B. Whalley, *J. Chem. Soc. C*, 1289 (1967).

[8] H. Mühlemann, *Pharm. Acta Helv.*, 26, 195 (1951).

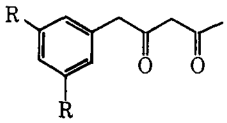
[9] W. Steglich and W. Reininger, *Chem. Commun.*, 178 (1970).

[10] W. B. Whalley, *Pure Appl. Chem.*, 7, 565 (1963).

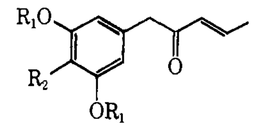
[11] R. Chong, P. W. Gray, R. R. King, and W. B. Whalley, *Chem. Commun.*, 101 (1970).

[12] Prepared from 3,5-dihydroxy-4-methylbenzoic acid [E. H. Charlesworth and R. Robinson, *J. Chem. Soc.*, 1531 (1934)] by (i) benzoylation (benzoyl chloride–pyridine), (ii) conversion to the acid chloride (thionyl chloride), and (iii) reduction with lithium aluminum tri-*tert*-butoxy hydride in diglyme at −78° [H. C. Brown and R. F. McFarlin, *J. Amer. Chem. Soc.*, 80, 5372 (1958)].

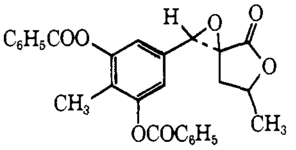
reduced with lithium aluminum hydride in ether and the resulting crude triol **17** was treated with lead tetraacetate in moist acetic acid to give **18** (45% based on **16**). Oxidation of **18** (Jones' reagent) provided diketone **19**, identified as the copper(II) chelate.[13]



7, R = OCH$_3$
19, R = H



8, R$_1$ = CH$_3$; R$_2$ = H
10, R$_1$ = H; R$_2$ = CH$_3$



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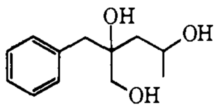

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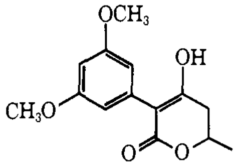
Functionality present within the system represented by **2** and **3** suggested the possibility of its rearrangement to a 5,6-dihydro-α-pyrone, an array found in a variety of acetogenins.[14] In fact, passage of boron trifluoride through a solution of **2** and **3** in benzene–dichloromethane (6:1) at 0° for 20 min initiated smooth conversion to dihydropyrone **20** (69%) (mp 150.5–153°; ν_{max} 3400, 2670, and 1700 cm^{-1}; nmr δ 1.42 (3 H, d, J = 6.5 Hz), 2.57 (2 H, d, J = 7.5 Hz), 3.74 (6 H, s), 4.58 (1 H, m), 5.8–6.5 (4 H, m, 1 H exchanged with D_2O)). Preferred migration of the carbonyl group to the benzylic cation is in accord with the recently noted rearrangement of glycidic esters to β-keto esters.[15] Treatment of **3** in dimethyl sulfoxide with 20% sulfuric acid at 80° for 3 hr, on the other hand, resulted in clean rearrangement to hydroxy acid **21** (33%; mp 131.5–132.5°; ν_{max} 3450, 1750, and 1600 cm^{-1}; nmr δ 1.30 (3 H, d, J = 6 Hz), 1.9 (2 H, m), 3.73 (6 H, s), 4.6 (1 H, m), 4.75 (1 H, s), 5.8 (1 H, broad, exchanged with D_2O), 5.98 (1 H, broad s, exchanged with D_2O), 6.38 (1 H, t, J = 2 Hz), 6.60 (2 H, d, J = 2 Hz)). Further applications of the foregoing and related transformations to synthesis of polyketide systems will be reported subsequently.



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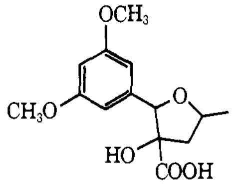

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(13) K. G. Hampton, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **29**, 3512 (1964).

(14) F. M. Dean, "Naturally Occurring Oxygen Ring Compounds," Butterworths, London, 1963, p 82.

(15) S. P. Singh and J. Kagan, *J. Amer. Chem. Soc.*, **91**, 6198 (1969).

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New Anionic Rearrangements. XII. 1,2-Anionic Rearrangement of Alkoxysilanes[1-3]

Sir:

Many organic ethers may be converted to isomeric alcohols in the presence of excess organolithium reagent by the classical Wittig rearrangement.[4,5] However, no analogous rearrangement has been described for alkoxysilanes. Instead, the reverse rearrangement in which a silylcarbinol rearranges to an alkoxysilane is a well-known reaction in organosilicon chemistry, due to studies by Brook and his students.[6] This "anti-Wittig" rearrangement takes place by an intramolecular anionic mechanism, *catalyzed* by a small amount of base.

$$R_3SiCR'_2OH \xrightarrow{\text{base}} HCR'_2OSiR_3$$

We now report the first example of a Wittig-type[7] rearrangement of an alkoxysilane to give the isomeric α-silylcarbinol. The rearrangement is expected to be quite general provided, as in the Wittig rearrangement, a proton on the carbon attached to oxygen in the alkoxysilane can be selectively metalated by an alkyllithium reagent.[8] Evidence indicates the silyl-Wittig and Brook rearrangements involve equilibration between deprotonated and neutral pairs of isomers, respectively.

Benzyloxytriethylsilane (**1**), bp 162° (20 Torr), n^{24}D 1.4867 [lit.[10] bp 262.6° (760 Torr), n^{20}D 1.4852], was prepared by condensation of benzyl alcohol and triethylchlorosilane in the presence of excess pyridine. The product was shown to be pure by gas chromatography, and the nmr spectrum confirmed structure **1**. When **1** was treated with a slight excess of *tert*-butyllithium in pentane at room temperature, and the mixture was subsequently neutralized with aqueous acid, the rearranged compound **2** was produced in high yield.

In a typical experiment, 26.8 mmol of *tert*-butyllithium was added to 5.0 g (22.4 mmol) of **1** in 50 ml of dry pentane at room temperature. A deep yellow-brown color, yellow in dilute solution, developed over the next 48 hr without any suspended solids appearing.

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(1) Previous paper in this series: R. West and H. F. Stewart, *J. Amer. Chem. Soc.*, **92**, 853 (1970).

(2) For a review of silyl anionic rearrangements see R. West, *Pure Appl. Chem.*, **19**, 291 (1969).

(3) Research sponsored by Air Force Office of Scientific Research (SRC)-O.A.R., USAF, Grant No. AF-AFOSR 69-1772 and 70-1904.

(4) G. Wittig and L. Löhmann, *Justus Liebigs Ann. Chem.*, **550**, 260 (1942).

(5) D. L. Dalrymple, T. L. Kruger, and W. N. White in "The Chemistry of the Ether Linkage," S. Patai, Ed., Interscience, New York, N. Y., 1967, p 617.

(6) A. G. Brook, *J. Amer. Chem. Soc.*, **80**, 1886 (1958); **81**, 981 (1959); A. G. Brook and B. Iachia, *ibid.*, **83**, 827 (1961); A. G. Brook, *Pure Appl. Chem.*, **13**, 215 (1966).

(7) The alkoxysilane → α-silylcarbinol rearrangement is formally analogous to the Wittig rearrangement, but whether or not it should be considered a true Wittig rearrangement is a matter of definition. The alkoxysilane rearrangement probably proceeds by an intramolecular mechanism involving a pentacoordinate silicon intermediate, whereas many Wittig rearrangements apparently proceed by cleavage–recombination reactions. See H. Schäfer, U. Schollköpf, and D. Walter, *Tetrahedron Lett.*, 2809 (1968); P. T. Lansbury, V. A. Pattison, J. D. Sidler, and J. B. Bieber, *J. Amer. Chem. Soc.*, **88**, 78 (1966).

(8) The reaction may however be limited by competing metalation at methyl groups attached to silicon. Thus benzyloxytrimethylsilane cannot be used as a substrate because metalation of the silylmethyl protons occurs.[9]

(9) H. F. Stewart, Ph.D. Thesis, University of Wisconsin, 1969, and G. A. Gornowicz and R. West, *J. Amer. Chem. Soc.*, **90**, 4478 (1968).

(10) B. N. Dolgov, N. P. Kharitonov, and M. G. Voronkov, *Zh. Obshch. Khim.*, **24**, 1178 (1954); *Chem. Abstr.*, **49**, 12275 (1955).